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ORGANIC ANALYSIS:

A MANUAL

OF THE DESCRIPTIVE AND ANALYTICAL CHEMISTRY OF
CERTAIN CARBON COMPOUNDS IN COMMON USE.

FOR THE

QUALITATIVE AND QUANTITATIVE ANALYSIS OF ORGANIC MATERIALS;
COMMERCIAL AND PHARMACEUTICAL ASSAYS; THE ESTIMATION
OF IMPURITIES UNDER AUTHORIZED STANDARDS; FORENSIC
EXAMINATIONS FOR POISONS; AND ELEMENTARY
ORGANIC ANALYSIS.

BY

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"Outlines of Proximate Organic Analysis," "Qualitative Chemical
Analysis," etc.*

NEW YORK:
D. VAN NOSTRAND, Publisher,
23 MURRAY AND 27 WARREN STREET.
1887.

PREFACE.

The operator in chemical analysis requires for his direction a system of descriptive chemistry, to be as nearly complete as possible. In resorting to the hand-books of general chemistry for the record of physical and chemical constants the analyst is often disappointed. It belongs, therefore, to analytical chemistry to furnish chemical descriptions with special precision, and this is a service promoting independent chemical work. As a mere changeful body of directions, giving the latest expedients in methods, analytical chemistry cannot claim to have educational value. But as an operative introduction to the character and deportment of compounds, analysis becomes a logical mode of study, fruitful of important results.

For certain common carbon compounds it has been undertaken to furnish in this work, first, systematic chemical description, and thereupon the methods of analytical procedure, qualitative, quantitative, and for proofs of purity, all with liberal citations of the authorities for convenience of further reading. In the references an order is observed as follows: (1) name of the contributor, (2) year of the contribution, (3) volume and page, first of original and then of contemporary publications.

Respecting the assumed peculiarities of organic analysis, it more and more appears that the differences between inorganic and organic analysis have been greatly overstated, just as, at earlier periods, the distinction between inorganic and organic chemistry in general was overdrawn. With nearer acquaintance it is seen that the limits of error in determination of carbon compounds are by no means always wider than those in analysis of metallic bodies.

If the author of this work have done anything at all to rescue the analytical chemistry of carbon compounds from a disjointed position in chemical literature, he will have gained enough of recompense. He desires to make thankful acknowledgment of the encouraging favor which has been extended to his "Outlines of Proximate Organic Analysis" since its issue in 1874. While his own promise of further publication has waited long for fulfilment, works of distinct value have opportunely appeared in different parts of the same field, and the flow of good contributions has continued to increase everywhere. Organic analysis, as the determination of the unbroken compounds of carbon, no longer has an uncertain place in chemical learning.

ALBERT B. PRESCOTT.

UNIVERSITY OF MICHIGAN, ANN ARBOR,
October, 1887.

ORGANIC ANALYSIS.

ABSINTHIN. $C_{20}H_{28}O_4 . H_2O = 350$.—The neutral principle of the wormwood, Artemisia absinthium. Obtained by precipitating the hot-water extract of the leaves and tops by tannic acid, drying the precipitate with litharge, and extracting with alcohol. The absinthin may be purified by filtering the alcoholic solution through animal charcoal, evaporating, and redissolving in ether.

Absinthin solidifies from yellow drops to indistinct crystals, melting at 120° C., and decomposing at higher temperatures. It has an aromatic odor and a very bitter taste. It is almost insoluble in cold water, slightly soluble in hot water, freely soluble in alcohol or ether; soluble with a brown-red color in the **alkali hydrates.** The potassa solution, when acidified by hydrochloric acid, exhibits a yellow-green play of colors.—Concentrated **sulphuric acid** dissolves it with brown color changing to green-blue, and becoming dark blue on adding a very little water. Much water decolors it. If the alcoholic solution be treated with an equal volume of concentrated sulphuric acid a brown-red mixture results, and a violet color is obtained after adding a few drops of water.—**Froehde's reagent** gives a brown color changing to green and violet (Bach, 1874).—Absinthin precipitates **mercurous nitrate** dirty-yellow; **lead subacetate** brown-yellow; **barium acetate** brown.—*Boiling with dilute acids* decomposes absinthin without producing a glucose. Fehling's solution is not reduced by it; ammoniacal silver nitrate solution is reduced, with the formation of a mirror.

ACETIC ACID.—Essigsäure. Acide acétique. $C_2H_4O_2 = 60$. Methyl-carboxyl, $CH_3 . CO_2H$. Manufactured from alcohol or dilute alcoholic liquids by oxidation, or the acetous "fermentation," and from wood by destructive distillation yielding other products of value. It is produced in numerous chemical reactions.

Acetic acid is *identified* by its odor in the free state (*b*) and the more intense odor of its ethyl ester (*d*). The empyreuma of heated acetates is characteristic (*d*). It gives a distinctive color with ferric salts (*d*). It is *separated* by distillation, if necessary preceded by saponification (*e*). From butyrates, by the insolubility of the barium acetate in alcohol (Butyric acid, *e*). It is *estimated*, as free acid, by acidimetry (*f*), or gravimetric saturation; as alkali acetate, by the alkalimetry of the ignited residue (*f*). In *Acetate of Lime* by distillation and by special methods (p. 11). *Commercial Grades* and *Impurities*, p. 14. *Vinegar*, its standards of strength, impurities, and special tests, p. 15.

a.—Absolute acetic acid (Glacial Acetic acid, Eisessig) below about 15° C. is a crystalline solid, forming transparent tabular masses, melting at 16.7° C. to a colorless liquid. An acid of 87 per cent. melts below 0° C.; of 62 per cent. at −24° C. The absolute acid boils at 118° C. It has, at 15° C., the sp. gr. 1.0607 (water at 4° C.) (MENDELEJEFF).

b.—Acetic acid has a pure acidulous taste and a penetrating, vinegar-like odor. When concentrated it is an irritant to the skin or tongue, and should be diluted before tasting.

c.—Acetic acid is soluble in all proportions of water and alcohol; the absolute acid is soluble in all proportions of ether, and acts as a solvent for various essential oils, resins, camphors, phenols, and metallic salts. Diluted with water acetic acid gives an acid reaction with litmus. The metallic normal acetates are soluble in water; silver and mercurous acetates less freely than the others. Perfectly normal alkali acetates are neutral in reaction, as shown by phenol-phthalein or litmus, but potassium acetate is liable to be found alkaline, because slightly basic. Acetates in general lose acetic acid in hot solution, and in some instances by simple exposure, so that acetates exhale a perceptible acetous odor, and gradually become basic. Non-alkali acetates, in solution, become slightly turbid, by formation of carbonate, from carbon dioxide of the air.

d.—**Ferric chloride** or other ferric salt, added not in excess to solution of acetates, causes a red color by formation of ferric acetate. On boiling, a yellow-brown precipitate of basic acetate of iron is obtained, resolved finally into nearly pure ferric hydrate. The red liquid, before heating, is not decolored by adding mercuric chloride solution, nor taken up by shaking with ether, both these negative results giving distinction from Thiocyanic acid. The color is destroyed by adding sulphuric or hydrochloric acid—a distinction from Meconic acid.—By hot digestion with **sulphuric acid** and **alcohol**, ethyl acetate, or acetic ether, is formed, recognized by its penetrating, fragrant odor. This test is most efficient when the dry acetate, obtained from acidulous liquid by neutralizing with fixed alkali and evaporating, is treated with an equal quantity of alcohol and a double quantity of sulphuric acid, and heated or distilled. The odor of other ethyl esters is liable to be mistaken for this.—When dry acetates are strongly heated in a test-tube, carbon is separated and acetone, C_3H_6O, is evolved, capable of recognition by its odor.—By *distillation* of acetates with phosphoric or sulphuric acid, free acetic acid is obtained, with its characteristic odor.—Acetic acid is a stable compound, not oxidized by chromic acid nor by permanganates.

e.—Separations.—Aqueous solutions of acetates, if kept slightly alkaline with fixed alkali, can be concentrated without loss of acetic acid. The free acid distils very slowly, and its quantitative distillation requires thorough treatment. In distilling from acetates, phosphoric or sulphuric acid, or oxalic acid, is to be added, in some excess of the quantity needful to form normal salts with all the bases present. To obtain all the acetic acid it is necessary to distil to dryness, adding water and repeating several times, until the distillate ceases to be acid to litmus. When various organic matters are present, it is therefore usually better to displace with phosphoric acid, avoiding the action of sulphuric acid in distilling to dryness. Care is to be taken that the phosphoric acid is strictly free from volatile acids, and that salts of volatile acids other than acetic are not present. If hydrochloric acid or its salts are present, the addition of sufficient silver sulphate insures the retention of the chlorine. Further details respecting quantitative distillation are given under *f*.

To obtain the acetic acid of basic acetates insoluble in water, it is preferable to transpose them to alkali acetate by digesting with hot solution of sodium carbonate, filtering, and exhausting with hot water. The same operation may with advantage precede distillation in the case of lead acetate. Ethereal acetates, such as ethyl acetate, do not give up their acetic acid by displacing it with a non-volatile acid, but require first to be saponified by an alkali, when the alkali acetate is treated as before described. The saponification is effected by digesting with some excess of a solution of potassa in alcohol free from acetic acid, when all the alcohol may be removed by evaporation. Also, a volumetric estimation of the acetic acid of ethereal acetates may be readily and exactly made by saponifying with a known quantity of alcoholic potassa (see *f*).

f.—Quantitative.—In simple dilution with water, the specific gravity of acetic acid, if closely taken, is a practicable indication of percentage, according to tables of accepted authority, bearing in mind that acid of about 46 per cent. coincides in density with acid of 99 per cent. Even within the range to which it applies, the hydrometer is not exact enough, unless corrected in its reading by the analyst himself.—Saturation methods of estimation are to be preferred, especially that by *volumetric* solution of fixed alkali. Phenol-phthalein is the best indicator, but litmus will serve. Colored liquids may be diluted so as to show the phenol-phthalein indication. If 6.000 grams of the acid mixture be taken, each c.c. of normal solution of alkali indicates 1 per cent. of $C_2H_4O_2$, or real acid; each c c. of decinormal alkali, 0.1 per cent. With dilute acetic acid, 24.0 grams may be taken, when $\text{c.c.} \div 4 = \%$. But, owing to the vaporization of acetic acid, it is seldom advisable to take a stated weight for estimation. In a stoppered bottle, previously tared, pour 5 to 6 c.c. of the acid under estimation, stopper, take the weight, and titrate; grams taken : 6.000 :: c.c. of normal alkali : $x =$ per cent. real acid.

Gravimetric methods of saturation may be employed. 1.000 gram of *potassium bicarbonate* (or 0.530 gram dry sodium carbonate), taken in a tall beaker, may be neutralized with the acetic acid, the acid being added by weight from a small, light. lipped beaker, carrying a small glass rod with which to pour, adding at last drop by drop, and heating to expel the carbon dioxide. Then 60 ÷ grams of acid required = number per cent. of real acid present. Before testing the acetic acid, if much stronger than vinegar, it should be diluted, by weight, to from 2 to 15 times its own weight, so as not to be over 5 to 8% strength. Then 60 × the factor of dilution (2 to 15) ÷ number grams of the diluted acid required = per cent. of real acid present.—A gravimetric method with *barium carbonate* is as follows: A weighed quantity of the acetic acid (sufficient to contain 0.120 to 0.180 gram absolute acetic acid) is digested with excess of well-washed, precipitated barium carbonate, the precipitate is filtered and exhausted with hot water, the filtrate is precipitated by dilute sulphuric acid, with heating and washing as required in estimation of barium as sulphate, and the ignited barium sulphate weighed. ($BaSO_4 : 2C_2H_4O_2 :: 232.8 : 120 :: 1 : 0.5156.$) Grams of barium sulphate × 0.5156 = grams acetic acid absolute, in the quantity of acetic acid mixture under estimation. Free acids which form insoluble barium salts do not interfere. Oxalic acid will add by a trifling quantity to the result. Free acids which form soluble barium salts interfere altogether, but the addition of sufficient silver sulphate prevents interference of hydrochloric acid. Acetates and other salts of non-alkali metals precipitable by barium carbonate cannot be present.

The acetic acid of alkali and alkaline earth salts may be estimated *by ignition* of the dry salt, and titration of the resulting alkali carbonate, or alkaline earth, with volumetric acid. Each c.c. of normal solution of acid used indicates 0.06 gram of absolute acetic acid. Of course the acetate taken for estimation in this way must be of neutral reaction; or, if of alkaline reaction, its alkalinity (before ignition) must be estimated by titration, and the c.c. of acid so used must be deducted from the c.c. required in titrating the ignited residue from an equal quantity of the salt. This plan of estimation is not among the more trustworthy ones.

The acetic acid of *normal acetates of calcium*, *lead*, and other non-alkali metals, is sometimes estimated by methods of determination of the metal.

Valuation of "Acetate of Lime."—Acetate of Lime (Pyrolignate of Lime, Essigsäuren Kalk, Holzessigsäuren Kalk) is a product of the distillation of wood, used as a carrier of acetic acid toward concentration and purification. Its value lies in the amount of real acetic acid it contains. Three grades of it have been made—the "gray," "brown," and "black"—but the last-named grade is now seldom produced. Besides empyreumatic and carbonaceous matters, it is quite liable to contain butyrate, formate, and propionate;[1] also magnesium salts; and may contain chlorides. In the plan of wood distillation conducted at temperatures below charring,[2] *Acetate of Sodium* is usually manufactured instead of lime acetate, and no empyreumatic matter occurs.—In the valuation of acetate of lime, the methods mostly in use have been based on (1) *distillation of the acetic acid*, and (2) *the amount of soluble lime salts* present. A volumetric method (3) with evaporation of the acetic acid will also be given here.[3] The valuation should embrace an estimation of the moisture, and may present the proportion of magnesium acetate, if any be present. Samples are to be taken from every

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[1] Respecting the relation of these impurities to methods of estimation, LUCK, 1871: *Zeitsch. anal. Chem.*, **10**, 184.

[2] MABERY, 1883: *Am. Chem. Jour.*, **5**, 256.

[3] Respecting methods (1) and (2)—STILLWELL and GLADDING, 1882: *Jour. Amer. Chem. Soc.*, **4**, 94. SEELY, 1872: *Am. Chem.*, **2**, 324; **3**, 8. FRESENIUS, 1875: *Zeitsch. anal. Chem.*, **14**, 172; 1866: *Ibid.*, **5**, 315; 1874: *Ibid.*, **13**, 153. H. ENDEMANN, 1876: *Am. Chem.*, **6**, 294. A. A. BLAIR, 1885: *Am. Chem. Jour.*, **7**, 26.

fifth to tenth bag, fairly representing both large and small pieces, and inclosed in rubber bags or air-tight jars while sent and held for analysis. The moisture is always to be determined in a portion taken as soon as the sample is opened to the air. The sample is then pulverized and sifted in preparation for the analysis. Then a prepared portion taken parallel with that subjected to analysis is dried for estimation of its moisture, from which the percentage of acetic acid is at last corrected for moisture, whether for the figures on a dry basis, or on the air-dry basis of the primary samples (Stillwell and Gladding). Crystallized acetate of calcium contains water of crystallization and is efflorescent; the product "acetate of lime" may gain or lose water in the air, but in paper or wood packages it is likely to lose.

(1) *By distillation of the acetic acid.* The most trustworthy method. Of the prepared sample 5 grams are dissolved in 50 c.c. of water, at least 25 grams of glacial phosphoric acid are added, and the liquid distilled, repeatedly adding water, not permitting the liquid to be reduced to dryness, and persisting until the distillate ceases to have an acid reaction, or the retort to smell of acetic acid. According to Messrs. Stillwell and Gladding, if the retorted liquid be not reduced too low, not more than traces of hydrochloric acid can be carried over from chlorides, and the excess of phosphoric acid prevents production of insoluble calcium phosphate. All distillation of hydrochloric acid can be prevented by adding silver sulphate in the retort. Nitric acid must be tested for. Fresenius (1875) and Endemann (1876) describe apparatus by which steam is introduced into the retort, in a current of regulated force, for continuing the distillation. The total distillate is made to a desired definite volume, an aliquot part is measured out, phenol-phthalein added as an indicator, and titrated with standard solution of alkali (p. 10).

(2) *Methods depending on the quantity of soluble lime salts present.* Of these methods the one given by Fresenius (1874, where cited) is one of the best, and is adapted to the assay of pure grades, free from acid empyreuma and from magnesium salt. Of the sample 5 grams are treated with about 150 c.c. of water in a quarter-liter flask, 70 to 80 c.c. of normal solution of oxalic acid added, and the mixture diluted with water to the 250 c.c. mark. To compensate for the volume of the precipitate 2.1 c c. of water are added above the mark. After being shaken and standing for some time the precipitate is filtered out (through a dry filter). Of the filtrate 100 c.c. are titrated with normal

solution of alkali for acid as acetic acid. Then another portion of 100 c.c. is treated with calcium acetate to precipitate all the excess of oxalic acid. The calcium oxalate precipitate is filtered out, washed, dried, ignited, weighed as calcium carbonate, and the indicated quantity of oxalic acid calculated into its equivalent of acetic acid. The total acid as acetic acid in 100 c.c., *minus* the oxalic acid as acetic acid in 100 c.c., equals the true acetic acid in 100 c.c. of filtrate—that is, in $\frac{2}{5}$ of the sample assayed (or in 2 grams).

(3) A method proposed by GÖBEL[1] is given as follows: For the titrations a solution of soda, of which 1000 c.c. = 100 grams absolute acetic acid; a solution of phosphoric acid which titrates to phenol-phthalein of a strength equal to the soda solution; and a solution of hydrochloric acid which titrates to litmus of a strength equal to the soda solution. A weighed quantity of the acetate under assay is treated with some measured quantity taken as an excess of the standard phosphoric acid; the mixture evaporated to dryness; the residue treated with water and evaporated again, and until the odor of acetic acid is no longer obtained; the residue then treated with water and the mixture titrated for excess of phosphoric acid, with the standard soda, using phenol-phthalein, and noting the result in equivalent of acetic acid. Subtracting this figure from that for the acetic acid represented by the phosphoric acid first added, the difference is the figure for the acetic acid in the acetate taken—subject, however, to correction for free lime and lime carbonate in acetate of lime taken for assay. By titrating a weighed portion with the standard hydrochloric acid, adding an excess, expelling carbon dioxide, and bringing back to the neutral tint of litmus with standard soda, the acetic acid equivalent to the unsaturated earthy bases is found, and deducted for the correction.

A rapid method of assay, which has been much used, but is apt to give figures too high, is carried as follows: A weighed quantity of the acetate of lime is supersaturated with a known quantity of sodium carbonate in solution; the precipitate filtered out and washed; and the alkali of the total filtrate estimated as sodium carbonate by titration of an aliquot part. The loss of sodium carbonate due to the removal of acetic acid (and acid empyreuma) in the precipitation is calculated into acetic acid, and figured upon the quantity of acetate of lime taken.—BLAIR (1885, where cited) obviates the difficulty of the color of the

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[1] 1884: *Repert f. anal. Chem.*, **3**, 374; *Zeitsch. anal Chem.*, **23**, 264.

solution by filtering it through animal charcoal, and then obtains good results by this method.

g.—Commercial Grades and Common Impurities.—The strengths of acetic acid have been designated by a "No.," altogether different from vinegar numbers, but probably originating, under the British excise system, in the number of parts of four per cent. vinegar producible by dilution.[1] Thus No. 8 acid is that which diluted to eight parts will have about four per cent. strength. The two grades numbered on this system, in this country, are "No. 8" and "No. 12." Interpreted according to original intent, therefore, No. 8 should be of 32 per cent., and No. 12 of 48 per cent. strength. Dr. Squibb finds that the best qualities of No. 8 acid actually prove of near 30% strength, bearing label mark of s.g. 1.040; the poorer qualities of No. 8 are near 25% strength, and issued without a gravity mark. No. 12 acid is less common, and often runs from 38 to 40 per cent. of real acid.—The strengths of vinegar numbers refer, in the British custom, to the number of grains of dried sodium carbonate neutralized by one Imperial fluid-ounce. $\frac{1}{2}Na_2CO_3 : C_2H_4O_2 :: 53 : 60 :: 1 : 1.132$. The number × 1.132 = grains absolute acid per fluid-ounce (of grains 437.5 × s.g.) The number × 0.259 = grams absolute acid in 100 c.c. vinegar.—In this country vinegar numbers have been grains of sodium bicarbonate neutralized by one fluid-ounce, wine measure. $NaHCO_3 : C_2H_4O_2 :: 84 : 60 :: 1 : 0.7143$. The number × 0.7143 = grains absolute acid per fluid-ounce (of grains 455.7 × s.g.) The number × 0.1567 = grams absolute acid in 100 c.c. vinegar.

Much of the "Glacial Acetic Acid" of commerce is not over 75 per cent. of real acid (Squibb). It can easily be furnished of 99+ per cent., as required by U. S. Ph.

Of impurities in ordinary acetic acid, the more common are mineral acids, especially hydrochloric, empyreumatic bodies, and metallic salts. Empyreuma, and other foreign bodies having odor or taste, are recognized by these senses after neutralizing with potassa or soda. "When diluted with five volumes of distilled water, the color caused by the addition of a few drops of test-solution of permanganate of potassium should not be sensibly changed by standing five minutes at the ordinary temperature (absence of empyreumatic substances)."—*U. S. Ph.* According to Dr. Squibb,[2] when 1 c.c. of the acid, diluted with 5

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[1] Squibb, 1883 : *Ephemeris*, I, 258.

[2] 1883 : *Ephemeris*, I, 260.

c.c. distilled water, is treated with 3 drops of decinormal solution of permanganate, in comparison with the same addition to the distilled water, if the color does "not become fully brown" within ten minutes, it is "a very good acid indeed," but the glacial acid "should stand this modification of the permanganate test for more than an hour."

In vinegar the most common impurities are (1) free mineral acids, and (2) empyreumatic bodies (in "wood vinegar"). Besides, various made-up vinegars, and forms of diluted acetic acid, are substituted for or added to cider-vinegar.

The absence of *free mineral acid* is shown by an alkaline reaction of the ash. Let the residue be carefully ignited and the cold ash touched with wet litmus-paper. The residue can be ignited on the loop of platinum wire. All natural vinegars contain some alkali acetate, and in absence of mineral acids will give an alkaline reaction in the ash. If the vinegar be a mere diluted acetic acid, as a "white vinegar," a few drops of decinormal solution of fixed alkali are to be added before the evaporation, when a neutral reaction of the ash indicates free mineral acid.—To estimate the quantity of free mineral acid, take 50 grams of the vinegar, add of decinormal alkali from the burette enough to surely neutralize all free mineral acid, still leaving the reaction acidulous, evaporate, ignite with care against loss, and titrate back with decinormal acid. Then c.c. $\frac{N}{10}$ alkali — c.c. $\frac{N}{10}$ acid $\times 2 \times 0.0049 =$ per cent. of free mineral acid, as sulphuric acid. Using the factor 0.00364, the statement is obtained for hydrochloric acid, etc. Free sulphuric acid, in absence of chlorides, may be separated and determined as follows: 100 c.c. are evaporated on the water-bath nearly to dryness, treated with about 100 c.c. of alcohol, the mixture filtered, the alcohol evaporated off, and the residue diluted for the gravimetric estimation of the sulphuric acid in it, by precipitation with barium chloride. If chlorides be present in the vinegar, it is necessary to add silver sulphate before adding the alcohol, when both the free sulphuric and hydrochloric acids of the vinegar are estimated as sulphuric acid.

It must be remembered that sulphates and chlorides are liable to be present in legitimate vinegars, and the simple reactions with silver and barium, as prescribed for acetic acid, are not applicable in tests of vinegars in general. But, according to DAVENPORT,[1] "in a pure *cider vinegar*, nitrate of silver, nitrate

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[1] "Report of Inspector of Vinegar of the City of Boston," 1884, p. 4; of Inspector of Milk of the same, 1885, p. 10.

of barium, or oxalate of ammonium added after an excess of ammonia water, will neither of them give more than the slightest perceptible reaction." Also, "a drop of it in a loop of platinum wire, when ignited in a Bunsen lamp-flame, gives a pure potash flame without any yellow soda rays visible." "The addition of any practical amount of a commercial acetic acid to tone up the strength will give another color to the flame." Cider-vinegars yield a residue "always soft, viscid, mucilaginous, of apple flavor, somewhat acid and astringent to the taste." "If any corn glucose is present, the residue, when ignited in the platinum loop, will emit the characteristic odor of burning corn; and if the glucose was manufactured with the commercial sulphuric acid derived from copper-pyrites, it will, as the last spark glows through the carbonized mass, emit the familiar garlic odor of arsenic." *The percentage of solids in cider-vinegar*, by weight of residue, is generally required to be as much as 1.5 per cent. Dr. Davenport (1885) recommends that the legal limit be 2 per cent.

"When 20 grams of the vinegar are mixed with 0.5 c.c. of barium nitrate test-solution (1 to 19) and 1 c.c. decinormal silver nitrate solution, the filtrate from the mixture should give no reaction for chlorine or sulphuric acid. When two volumes are added to one volume of sulphuric acid and then one volume of ferrous sulphate solution poured over, no brown zone should appear between the layers. The evaporation-residue from 100 grams should not exceed 1.5 grams. The residue should not have a sharp taste, and its ash should have an alkaline reaction."—*Ph. Germ.*

The required strength of vinegars is given by U. S. Ph. of 1870 at 4.6%; Br. Ph., 5.41%; Ph. Germ., 6%; the "proof vinegar" of British Excise, 6%, or English "No. 24." In execution of the British law against adulterations of foods, the minimum limit of strength has been held at 3%. For "cider-vinegar," the limit recommended by Dr. Davenport, in the Boston City inspection, is 5 per cent. of real acetic acid; and the lowest limit there proposed, 4½ per cent.—In New York City the legal requirement, well enforced (1886), is 4½ per cent. of acetic acid as a minimum for all vinegars, and 2 per cent. of solids for cider-vinegars.

The following is the form of Inspector's Record and Analyst's Report, under the regulations of the city of Boston, 1886: "*Vinegar:* Date, ——; Time, ——; Proprietor's name, ——; No. —, —— Street; Sold by ——; Price paid, ——; Quantity, —— pint; Wholesaler's name, ——; Price paid ditto, ——;

District, ——; Cider, ——; White wine, ——; How marked. *Analysis:* Analysis No. ——; Acetic acid, ——; Residue, ——; Character of residue, ——; Chlorine, ——; Sulphates, ——; Calcium, ——; Color, ——; Free acid."

ACIDS OF THE FATTY SERIES, CnH_2nO_2. See FATS.

ACONITE ALKALOIDS.—*Natural alkaloids of plants of the genus Aconite* (Ranunculaceæ), *and artificial products of these alkaloids*—represented by *Aconitine*, $C_{33}H_{43}NO_{12} = 645$ (WRIGHT, 1877).

CONTENTS:—Chemical constitution; saponification changes; list of alkaloids with rational formulæ; dehydration changes; list of alkaloids with physiological effects; sources; yield. Analytical outline for crystallizable and for amorphous alkaloids of aconite: *a*, heat-reactions of each; *b*, taste and physiological effects; *c*, solubilities; *d*, qualitative tests, with limits; *e*, separation in general, from aconite root, from animal tissues; *f*, quantitative methods, gravimetric, volumetric, of produced benzoic acid; *g*, commercial grades and values.

Chemical constitution and character.—It has been established by Wright and his co-workers[1] that *the crystallizable alkaloids* of the aconite group are salts, or esters, of benzoic acid (or a derivative of this acid), and are readily *saponifiable by action of alkalies or strong acids*, to some extent even by water with heat. And the saponification results in the removal of either benzoic acid or a derivative of benzoic acid, and the formation of *amorphous alkaloids* in place of the crystallizable alkaloids saponified. The tendency of aconite alkaloids to become amorphous, with diminished physiological activity, is explained by saponification. Their liability to another and less obvious class of chemical changes, leaving them still crystallizable and with little loss of physiological activity, is shown by the proof that, *by action of strong acids, they suffer dehydration and form apo alkaloids.* That is to say, *alkalies*, with more or less readiness, and even hot digestion with water, cause saponification; and strong mineral *acids*, even concentrated organic acids in a degree, cause both saponification and dehydration to apo-compounds.[2] Various

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[1] C. R. A. WRIGHT, in part with A. P. LUFF, and with A. E. MENKE, 1877–1879: *Jour. Chem. Soc.*, 31, 143; 33, 151, 318; 35, 387, 399. *Phar. Jour. Trans.* [3] 8, 164–167. Further, MANDELIN, 1885: *Archiv d. Phar.* [3] 26, 97, 129, 161; *Phar. Jour. Trans.* [3] 15. JUERGENS, 1885: *Phar. Zeitsch. Russland.*

[2] It is a noteworthy correspondence that three active alkaloidal agencies of intense physiological power, in extensive medicinal use at present, Aconitine,

other transformations are brought about by agents not so commonly employed in processes of separation as are the alkalies and acids.

The following equations show *the changes of saponification*, by alkalies or acids, upon four of the crystallizable alkaloids of the aconites according to Wright:[1]

Crystallizable alkaloids. *Amorphous alkaloids.* *Benzoic acid.*

$$C_{33}H_{43}NO_{12}\text{ (aconitine)}+H_2O=C_{26}H_{39}NO_{11}\text{ (aconine)}+C_7H_6O_2$$

$$C_{31}H_{45}NO_{10}\text{(picraconitine)}+H_2O$$
$$=C_{24}H_{41}NO_9\text{(picraconine}+C_7H_6O_2$$

$$C_{66}H_{88}N_2O_{21}\text{(japaconitine)}+3H_2O$$
$$=2C_{26}H_{41}NO_{10}\text{(japaconine)}+2C_7H_6O_2$$

$$C_{36}H_{49}NO_{12}\text{(pseudaconitine)}+H_2O$$

Dimethylprotocatechuic acid.

$$=C_{27}H_{41}NO_9\text{(pseudaconine)}+C_9H_{10}O_4$$

The rational formulæ[2] of these alkaloids include the anhydride of benzoic acid, or of one of its derivatives, in the crystallizable members of the group; and include hydroxyl instead of the acid anhydride in the amorphous members of the group (Wright); as follows:

Aconitine, $C_{33}H_{43}NO_{12}=C_{26}H_{35}NO_7(OH)_3.O.(C_7H_5O)$
Aconine, $C_{26}H_{39}NO_{11}=C_{26}H_{35}NO_7(OH)_3.OH$
Japaconitine, $C_{66}H_{88}N_2O_{21}=2[C_{26}H_{39}NO_7O.O.(C_7H_5O)]O$
Japaconine, $C_{26}H_{41}NO_{10}=C_{26}H_{39}NO_7O.(OH)_2$
Pseudaconitine,[3] $C_{36}H_{49}NO_{12}=C_{27}H_{37}NO_5(OH)_3.O.(C_9H_9O_3)$
Pseudaconine, $C_{27}H_{41}NO_9=C_{27}H_{37}NO_5(OH)_3.OH.$

Atropine, and Cocaine, agree in being saponifiable alkaloids easily giving up either benzoic acid or some near derivative of benzoic acid. (Atropine: Kraut, 1865. Cocaine: Lossen, 1865. Aconitine: Wright, 1877.) Among other saponifiable alkaloids, yielding acids of the aromatic group, are piperine, and certain veratrum alkaloids.

[1] In saponification by alkali, the benzoic acid or its derivative is left in combination with the alkali, from which it is obtained by acidulation. In saponification by acid the amorphous alkaloid is obtained in salt of the acid.

[2] Wright (1879), in his last contribution upon the aconite alkaloids, strongly inferred the existence of *a* "*hypothetical parent-base*, $C_{33}H_{47}NO_{12}$" $=C_{26}H_{39}NO_7.(OH)_3.O.(C_7H_5O)$. Juergens (1885, where before quoted), by a modified process of extraction from the root, and thorough purification, obtained aconitine which, in elementary analysis, gave him numbers for $C_{33}H_{47}NO_{12}$. The alkaloid gave the intense numbing sensation upon the tongue, without a recognizable bitter taste.

[3] Mandelin (1885), by investigations (without elementary analysis), concluded that aconine and pseudaconine are the same, so that, in his view, aconitine and pseudaconitine differ only by their acidulous radicals as found by Wright.

The amorphous alkaloids are found in the plant, as well as obtained by alteration of the crystallizable alkaloids during separation from the plant.

The changes of dehydration to apo-alkaloids, by action of acids, is shown by the following comparisons of rational formulæ:

Aconitine, $C_{33}H_{43}NO_{12}=C_{26}H_{35}NO_7(OH)_3.O.(C_7H_5O)$
Apo-aconitine, $C_{33}H_{41}NO_{11}=C_{26}H_{35}NO_7(OH)O.O.(C_7H_5O)$

Aconine, $C_{26}H_{39}NO_{11}=C_{26}H_{35}NO_7(OH)_3.OH$
Apo-aconine, $C_{26}H_{37}NO_{10}=C_{26}H_{35}NO_7(OH)_2O$

Pseudaconitine, $C_{36}H_{49}NO_{12}=C_{27}H_{37}NO_5(OH)_3.O.(C_9H_9O_3)$
Apo-pseudaconitine, $C_{36}H_{47}NO_{11}$
$=C_{27}H_{37}NO_5(OH)O.O.(C_9H_9O_3)$

The natural alkaloid, japaconitine, has the constitution of a sesqui-apo-derivative.

Chief Sources of the Natural Aconite Alkaloids.

A. *Napellus*, root. "Aconite" of U. S. Ph. and Ph. Germ.	Aconitine. Aconine. Pseudaconitine } in small proportion, if at all. Pseudaconine } Picraconitine } (exceptionally present.)
A. *ferox*, root. "Indian Aconite." "Nepal Aconite." Bish, or Bikh. "Himalaya root."	Pseudaconitine. Pseudaconine. Aconitine } very little. Aconine }
Japanese aconite, root.	Japaconitine. Japaconine. Other alkaloids.
A. *lycoctonum*,[1] root.	Aconitine. Pseudaconitine. Amorph. alkaloids.
A. *anthora*, root.	Pseudaconitine. Amorph. alkaloids.
A. *paniculatum*, root.	Picraconitine.

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[1] A report of alkaloids from this plant, amorphous, and having an energetic effect like curare—DRAGENDORFF & SPOHN, 1884.

The chief Aconite Alkaloids: Synonyms, Crystallization, and Activity.

Name.	*Synonyms.*	*Formula.*	*Crystallization.*	*Physiolog. effect.*
Aconitine.	Cryst. aconitine. Napaconitine.	$C_{33}H_{43}NO_{12}$	Crystallizable, when free, as well as in salts.	Of typical aconite activity.
Pseudaconitine.	Napelline. Feraconitine. Acraconitine. English acon.	$C_{36}H_{49}NO_{12}$	Base and its salts crystallize with difficulty.	Approaches to or equals the activity of aconitine.
Japaconitine.	Cryst. alkaloid of Japanese root.	$C_{66}H_{88}N_2O_{21}$	Crystallizable both free and in salts.	Closely resembles aconitine in properties and effects.
Aconine.	Amorphous aconitine. A product of aconitine, by alkalies or acids.	$C_{26}H_{39}NO_{11}$	Amorphous, both free and in salts.	Of far lower activity than aconitine. Bitter.
Pseudaconine.	Amorphous aconitine. A product of pseudaconitine, by alkalies.	$C_{27}H_{41}NO_9$	Amorphous, free or combined.	Of far lower activity than aconitine. Bitter.
Japaconine.	Amorphous alkaloid of Jap. aconite. Product of japaconitine.	$C_{26}H_{41}NO_{10}$	Amorphous, free or combined.	Closely resembles aconine in properties and effects.
Picraconitine.	Inactive, bitter alkaloid of A. paniculatum and other species.	$C_{31}H_{45}NO_{10}$	Base cryst. with difficulty. Salts crystallize well.	Bitter. Not poisonous.
Picraconine.	Amorphous product of picraconitine.	$C_{24}H_{41}NO_9$	Amorphous.	Bitter. Not poisonous.
Apo-aconitine.	Product of aconitine, by action of acids.	$C_{33}H_{41}NO_{11}$	Crystallizable.	Of the same activity as aconitine.

Corresponding apo-derivatives, by action of acids on Pseudaconitine, Aconine, etc. (See p. 19.)

For medicinal uses the U. S. Ph. and Ph. Germ. admit only the tuberous root of A. Napellus; the Br. Ph., also U. S. Ph. of 1870, admit both "root" and leaf of A. Napellus; the Ph. Fran. authorizes the use of root and leaf of A. Napellus and A. ferox. It is understood that both Japanese aconite root[1] and root of A. ferox are largely used for the manufacture of medicinal alkaloid "aconitine." A. Sterkeanum contains poisonous alkaloids.

Yield of natural Aconite Alkaloids.—WRIGHT obtained, in 1876, from A. Napellus only 0.03 per cent. of pure aconitine, and only 0.07 per cent. of total alkaloids free from other matter. Again, from Japanese aconite roots 0.18 per cent. of mixed alkaloids. JUERGENS (1885) obtained, by a modified Duquesnel's process, of thoroughly purified aconitine (for elementary analysis) 0.02 per cent. By chemical assays (1883) LABORDE and DUQUESNEL found in A. Napellus root, of "crystalline alkaloids" from 0.05 to 0.40 per cent., averaging 0.15 per cent.; of "amorphous, insoluble substance" having an effect like aconitine in kind, "a few" tenths per cent.; and of "amorphous, soluble, bitter substance," about 1.5 per cent. ZINOFFSKI,[2] working by volumetric estimation with Mayer's solution (probably an inexact measure of total aconite alkaloids) in A. Napellus and other species, from the fresh leaf (calculated to basis of dry material) 0.73 to 1.38 per cent. total alkaloid; from the fresh stalks, 0.25 to 0.90 per cent.; and from the fresh flowers, 1.51, 1.65, and 5.52 (!) per cent. total alkaloids. HAGER (1863) reported finding in the best commercial root of A. Napellus from 0.64 to 1.25 per cent. [total alkaloids]. SQUIBB (1882) found the leaf of A. Napellus to have only about one-ninth of the physiological effect of the same quantity of the root. CULLAMORE (1884) found the action of A. ferox to be more intense in degree than that of an equal quantity of A. Napellus.

The "aconitine" of the market may contain any mixture of the aconite alkaloids—frequently aconitine, japaconitine, pseudaconitine, and the wholly amorphous alkaloids. Systematic physiological assay of four commercial grades of "aconitine," by Dr. SQUIBB in 1882, in comparison with good powdered aconite root, gave the following results: (1) Of unknown make had only the physiological potency of the root; (2) "Ordinary," 8 times the strength of the same weight of the root; (3) Pseudaconitine, 83 times the power of the root; (4) "Crystallized," 111 times the

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[1] Respecting Japanese and Chinese Aconites, see LANGGARD, also WASOVICZ, 1880: *Archiv d. Phar.*, **14**, 217, and **15**, 161; *Phar. Jour. Trans.*, [3] **10**, 149, 1020; *Proc. Am. Pharm.*, **29**, 170–182.

[2] Dragendorff's "Werthbestimmung," 1874, p. 13.

effect of the root. If we accept Wright's analyses, first above given, the total aconite alkaloids should have from 500 to 1400 times the potency of the same weight of root. Further, Dr. Squibb found that the article (4) was a nitrate containing not more than 80.7 per cent. of hydrated alkaloid. Aconitine was dropped in the last revision of the U. S. Ph. and in the last revision of the Ph. Germ. It is retained by Br. Ph. and Ph. Fran.

THE CRYSTALLIZABLE ACONITE ALKALOIDS are *identified* by their organoleptic effect (*b*), the agreement of their precipitations (*d*, p. 25) and solubilities (*c*), and by yielding benzoic acid or its derivative when saponified (p. 18, and under *f*). THE AMORPHOUS ALKALOIDS of the aconites are distinguished from the crystallizable ones by greater solubilities in water (*c*), greater reducing power (*d*), greater bitterness without lip-tingling effect (*b*), and by not yielding benzoic acid or its derivative when saponified (under *f*). Aside from sources and accompaniments, amorphous aconite alkaloids are, with difficulty, identified by a general agreement of precipitations (*d*), solubilities (*b*), and melting points (*d*). Aconite alkaloids are *separated from the aconite roots*, indeterminate matters, etc., by assay processes of extraction (*e*); from tissues, etc., in *analyses for poisons in the body* as directed, with procedure for identification (under *e*). The active alkaloids are separated by crystallization. The total alkaloids of aconite are *estimated* gravimetrically, or volumetrically (*f*). Separate estimation of the active alkaloids is proposed, by saponification and determination of the quantity of benzoic acid and veratric acid (*f*). For *practical estimation of active alkaloids alone*, by physiological assay, under *b*, p. 23. For *commercial grades and values*, *f*; *sources*, p. 19.

a.—*Aconitine* crystallizes anhydrous in rhombic or hexagonal tables, appearing in snow-white flakes; and its salts crystallize well. *Japaconitine* crystallizes well, both free and in its salts. *Pseudaconitine* and its salts do not crystallize without very careful treatment; from ether, or better a mixture of ether with petroleum benzin, it forms needles or sandy crystals, with 1 *aq.*, but unless the concentration be extremely slow only cauliflower-like efflorescence or a varnish layer will be obtained. The nitrate crystallizes when treated with care. *Picraconitine* crystallizes with difficulty as a base; its salts easily form good crystals. *Aconine*, *pseudaconine*, and *japaconine*, with their salts, are white, powdery solids, strictly uncrystallizable. The *apo-alkaloids* agree in crystallization with the aconite alkaloids from which they are formed—apo-aconitine being crystallizable, and apo-aconine amorphous. The Br. Ph. describes "aconitine" as "a white, usually amorphous solid"; the Ph. Fran. as "colorless rhombic tables." As found in the shops, "aconitine" (mixed alkaloid) is usually amorphous, often colored, sometimes in thin, partly effloresced plates, sometimes in large needles.

Aconitine melts at 184° C. (WRIGHT); *pseudaconitine* loses water of crystallization at 80° C., melts at 105° C., and decomposes at about 130° C.; *japaconitine* melts at 184° to 186° C.; *aconine* melts at 130° C.; *pseudaconine* at 100° C.; *picraconitine* does not melt on the water-bath; *apo-aconitine* melts at 185° C. These *alkaloids* all preserve a constant weight on the water-bath; when ignited they burn away slowly. As to sublimation, and microscopic identification of the sublimate, see HELWIG (1864)[1] and BLYTH (1878).[2]

b.—*Aconitine*, in solutions dilute enough to be safe for the trial, causes a tingling and characteristic numbness of the lip and tongue and pharynx, commencing after a delay of from a minute to a quarter of an hour, according to the extent of dilution. Dr. SQUIBB[3] found that 0.006 gram (0.1 grain) of good aconite root, in a solution of 3.7 c.c., or 1 fluid-drachm (of its soluble constituents), held in the anterior part of the mouth (previously rinsed) for sixty seconds, and then discharged, gave the tingling sensation (as a rule), commencing within 15 minutes and then continuing for a quarter or a half an hour. When the same volume of solution was made to contain the soluble part of 0.02 gram (0.3 grain) of the root, the tingling began in 5 to 10 minutes, increased for a time, and continued in all about 1.5 hours. If we accept the percentages of total alkaloid reported by Wright (0.07 to 0.18%), and grant the entire alkaloid to have the full activity of aconitine, then, on the foregoing data,[4] from 0.000004 to 0.00001 gram (0.00006 to 0.00015 grain) of this alkaloid in a fluid-drachm of solution held one minute in the mouth causes lip-tingling within a quarter of an hour.[5] But this de-

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[1] *Zeitsch. anal. Chem.*, 3, 52.

[2] *Jour. Chem. Soc.*, 33, 316.

[3] 1882: *Ephemeris*, 1, 125.

[4] It appears safe to assume that *the specific action* of the aconites is represented by their alkaloids. FLEMING found aconitic acid to have little effect upon rabbits when subcutaneously injected. TORSELLINI (1884) reported aconitic acid to have a paralyzing effect on the heart of a frog.

[5] "The physiological action of aconitine is excessively energetic, so much so as to render working with it a matter of considerable pain and difficulty, unless great care be taken in the manipulation, and more especially in avoiding the dust of the crystals of the base or its salts. A minute fragment, too small to be seen, if accidentally blown into the eye, sets up the most painful

gree of potency is not attained by commercial "aconitine."—Aconitine is commonly described as having a bitter taste, which, in proportion to its special activity, is not at all pronounced. Juergens (1885) found carefully-purified aconitine to have no recognizable bitterness. The bitterness of commercial "aconitine" is in inverse ratio to its purity, in freedom from amorphous aconite alkaloids.

The medicinal dose of absolute aconitine or pseudaconitine for a man is placed by Mandelin (1885) at 0.0001 gram ($\frac{1}{650}$ grain) in a single dose, and 0.0005 ($\frac{1}{130}$ grain) during 24 hours. Of Duquesnel's "aconitine" Sequin (1878) gave 0.0005 gram ($\frac{1}{130}$ grain) as a single full dose; and the same quantity of Hottet's "aconitine" was given as a single maximum dose by Gubler (1880). Of commercial crystallized "aconitine" of unknown strength, current authorities limit the first (or trial) dose at about 0.0002 gram ($\frac{1}{333}$ grain), but this is double the dose of absolute aconitine declared by Mandelin, as above.—The smallest *fatal dose* of absolute aconitine, or pseudaconitine, for a man is placed by Mandelin (1885) at 0.003 gram (near $\frac{1}{20}$ grain); for warm-blooded animals, 0.00005 to 0.000075 gram per kilogram of body-weight; for frogs, 0.0012 to 0.0024 gram per kilogram of body-weight. Blyth (1884) deduces that, of French aconitine or Morson's aconitine, by the mouth, the least fatal dose for a man is 0.002 gram ($\frac{1}{33}$ grain), equal to 0.000028 gram per kilogram of body-weight; for the cat 0.000075 to 0.00009 gram per kilogram of body-weight. With the frog (Dragendorff) 0.002 gram [aconite alkaloid] causes paralysis of the hind legs in a few minutes.

Dilatation of the pupil is not a constant effect of aconitine, but usually occurs in some stages of its action.

Pseudaconitine, indefinitely represented by the old "napelline," undoubtedly has nearly or quite the same physiological effect as aconitine. Cullamore (1884) found the action of Aconitum ferox root to be similar in kind to action of A. Napellus.

The wholly amorphous aconite alkaloids, aconine and pseudaconine, have but in a very low degree the specific activity of aconitine. Husemann (1884: *Phar. Zeitung*) found aconine to have a toxic effect on frogs and mice, an effect 300 to 400 times less than that of aconitine. Wright stated of aconine and of

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irritation and lachrymation, lasting for hours; whilst similar particles, if inhaled, produce great bronchial irritation, or profuse sneezing, and considerable catarrh or 'sore throat,' according to the part where they lodge."—C. R. A. Wright, *first report*.

pseudaconine that it is of *extremely bitter taste, but does not produce the slightest lip-tingling.*

The apo-alkaloids of aconite have the effect of the alkaloids from which they are derived. Apo-aconitine has the full physiological activity, and apo-aconine is an inactive bitter.

Picraconitine is very bitter, and quite destitute of the specific potency of aconitine.

Aconitine, and its allied bases, have a decided alkaline reaction, and neutralize acids perfectly, forming salts more stable than the free alkaloids. The nitrate is a favorite salt for crystallization.

c.—Aconitine is very little soluble in cold water (in 726 parts, JUERGENS, 1885), but dissolves in hot water, and in alcohol (24 parts of 90% alcohol), ether, benzene (sparingly when cold), freely soluble in chloroform, soluble in amylalcohol (DRAGENDORFF), does not dissolve in petroleum benzin or carbon disulphide. It requires 2806 parts of petroleum benzin for solution (JUERGENS). It is not dissolved from aqueous solutions of its salts by ether, or chloroform, or benzene.—*Pseudaconitine* is sparingly soluble in water, more freely soluble in alcohol and in ether than aconitine is (WRIGHT). *Japaconitine* is soluble in alcohol and in ether; *picraconitine* is very sparingly soluble in water. *Aconine* is freely soluble in water, alcohol, or chloroform, almost insoluble in ether, especially when free from alcohol (WRIGHT). *Pseudaconine* dissolves in water, or alcohol, or ether (WRIGHT). *Apo-aconitine* and *apo-aconine* dissolve in ether.

d.—The most delicate and distinctive test for the active alkaloids of the aconites is the physiological test for lip tingling, described on p. 23.

Aconite alkaloids—namely, aconitine and pseudaconitine—and their amorphous products, aconine and pseudaconine, are precipitated, from their nearly neutral solutions in hydrochloric acid, as follows (WRIGHT): by "bromine water, iodine dissolved in potassium iodide, tannin, gold chloride, mercuric iodide dissolved in potassium iodide, mercuric bromide in potassium bromide, and mercuric chloride. These precipitates dissolve on more or less largely diluting the fluids, the aconine precipitates being more soluble than the corresponding pseudaconine ones, which again, save in the case of tannin, are markedly more soluble than those of aconitine or pseudaconitine. Other things being equal, the mercuric chloride precipitates are more soluble than those formed with mercuric bromide, which are more soluble than those thrown down by mercuric iodide. Aconine is not precipitated by sodium carbonate or ammonia, save when the solution is evaporated almost to dryness, so that an oily liquid separates along with the solid sodium or ammonium salt ; pseudaconine behaves similarly, whilst aconitine and pseudaconitine are but sparingly soluble in excess of these reagents. Strong caustic potash precipitates all four bases, the aconitine and pseudaconine precipitates being only sparingly soluble in excess, the pseudaconine being much more readily soluble on diluting the fluid, and aconine being precipitated only in very concentrated solutions. Platinic chloride throws down precipitates only with strong solutions, especially with pseudaconine and aconine, the precipitates in all cases dissolving readily on dilution.—It is noticeable that *picraconitine* is scarcely distinguishable from aconitine in these reactions, excepting that with sodium carbonate and ammonia it is precipitated much less readily, the precipitate being formed only in concentrated solutions, and dissolving readily on dilution."

Further (WRIGHT), the amorphous alkaloids, aconine and pseudaconine, are distinguished from the crystallizable aconite alkaloids by greater reducing powers—reducing silver (slowly) from hot solution of silver nitrate or of ammoniacal silver nitrate ; and gold from the gold chloride precipitate, on standing. Aconine reduces Fehling's solution on boiling, a distinction from pseudaconine, which does not.—Both crystallizable and amorphous aconite alkaloids (like the ptomains) promptly reduce ferricyanide of potassium, as shown by a drop of ferric salt solution.

Limits.—The precipitation by iodine in potassium iodide is distinct (on a glass slide) in one grain of a solution of the alkaloid in 50,000 times its weight of water (WORMLEY). With the gold chloride, one grain of a solution of the alkaloid in 5,000 parts yields in a little time a quite fair precipitate ; diluted to 20,000 parts, after some time a just perceptible turbidity. With bromine in hydrobromic acid, one grain of a solution of one part of the alkaloid in 10,000 parts of water gives a quite fair precipitate (WORMLEY). The limit of the precipitation by potassium mercuric iodide (DRAGENDORFF) is about 0.0009 gram in 1 c.c. of acidified solution, acidulation diminishing the solubility of the precipitate. Phosphomolybdic acid gives a yellow precipitate, changing to blue on standing, and dissolving blue in ammonia—0.00007 gram alkaloid in 1 c.c. water acidulated with sulphuric acid giving a distinct precipitate after half an hour (DRAGENDORFF).[1]

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[1] A test for completely purified aconitine is given by JUERGENS (1885) as follows : The particle of solid alkaloid, or residue of its solution, on a glass

The color reactions by acids, Froehde's reagent, etc., are so widely varied by alterations and differences (impurities) of the aconite alkaloids that no dependence can be placed upon them, unless the results are interpreted by results of control tests made by the analyst upon strictly parallel aconite products.[1]

e.—Separations.—Aconite alkaloids are not vaporized, but are very slowly saponified, by concentration of their aqueous solutions on the water-bath. Such concentration should, if possible, be done in neutral solution, and action of alkalies is generally more destructive than action of acids. Dr. Squibb stated (1882) that the attenuated solutions of aconitine, and those of fluid extract of aconite, diminished in strength, shown by physiological action, after the second day; and in four days, the weather being warm, they became quite inert, the growth of cryptogams keeping pace with the loss of strength.—Aconite alkaloids can be shaken out or extracted from slightly alkaline (not from acidulous), cold, aqueous solutions, by ether, chloroform, etc., according to the solubilities in these respective liquids, given on p. 25. And from solution in these liquids acidulated water takes up the alkaloids

In separation from aconite root, the process of Duquesnel, modified by Wright and otherwise varied in details, well serves the purpose of an assay. The powdered root is percolated to exhaustion with alcohol (not acidulated) This is done much the best by the continuous operation of an extraction apparatus. The solution is concentrated, preferably by boiling under reduced pressure, to remove the alcohol, the liquid diluted with water to a limpid state, and just acidulated with tartaric acid. One part of tartaric acid to 100 parts of the root is the proportion of Duquesnel's process, in which the acid is added to begin

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slide, is treated with a drop of water acidulated with acetic acid, and a minute fragment of potassium iodide added, when presently rhombic tables appear under microscopic inspection. Obtained with 0.0000 5 gram.

[1] When aconite is dissolved in hot phosphoric acid previously fully concentrated on the water-bath, there appears, according to the purity of the alkaloid, a violet to brown color—at all events crystallized aconitine is but feebly colored by the phosphoric acid, and crystallized aconitine nitrate is not colored at all. The yellow color by sulphuric acid diminishes in the same way (Flückiger's "Pharm. Chem.," 1879). Concentrated aqueous phosphoric acid dissolves aconitine, giving on the water-bath a beautiful violet color, remaining for a day in the cold—a distinction from "pseudaconitine" (that is, "napelline," "Morson's aconitine," or "English aconitine"), which remains colorless (Heppe's "Die chemischen Reactionen," 1875, from Hubschmann, Hasselt, Herbst, Praag). "I found the color yellow at 80° C., reddish at 89° C., violet at 133° C."—Dragendorff in "Organische Gifte," 1872. Juergens (1885) obtained purified aconitine which gave no color reactions with phosphoric acid, sulphuric acid and sugar, or phosphomolybdic acid and ammonia.

with. The liquid is now filtered, by help of the filter-pump, and the resinous residue washed with a little water. The solution is now washed several times with ether, the total etherial washings being washed with a little water slightly acidulated with tartaric acid, returning the aqueous washing to the acidulous solution. Sodium carbonate is now added to a clearly alkaline reaction, and the liquid shaken out with ether to complete exhaustion. The etherial solution is concentrated in a flask as far as it may be without formation of residue, and then washed several times with water slightly acidulated with tartaric acid; seeing that the reaction is distinctly acid after shaking with the ether. The aqueous liquid is at once made barely alkaline by adding sodium carbonate (if deemed advisory, is washed once with light petroleum benzin), and then shaken out with ether, repeatedly, as before. The united etherial solution is concentrated, at last spontaneously, to crystallize; or when partly concentrated a little light petroleum benzin is added and the solution set at rest to concentrate and crystallize. In either case all resinous residues are thoroughly washed with ether by the filter-pump, and this etherial solution shaken out again with acidulated water, made alkaline, and shaken out with ether, concentrating this solution to crystallize as before. The crude crystallized and amorphous alkaloids may be purified by repeatedly dissolving them with ether, on the filter, by the filter pump, and "crystallizing" again, to obtain the total free alkaloids for weight.—Or the crude crystallized and amorphous alkaloids are treated with a strong solution of sodium nitrate at a gentle heat, and cooled for crystallization of the nitrates of the alkaloids. These may be further purified by treating their concentrated aqueous solution, made alkaline by sodium carbonate, with repeated portions of chloroform, to obtain all the alkaloid, and permitting the chloroformic solution to concentrate for crystallization of crystallizable alkaloids.—It is much better if a "liquid-extraction apparatus" be used throughout the process, instead of "shaking out" by many portions of the solvents. And it is much better to make the concentrations promptly, by partial vacuum, at temperature not above 60° C.

In separation from animal tissues, etc., in cases of possible poisoning, the same method, substantially, may be followed—extracting the neutral or neutralized mixture with alcohol, concentrating, then acidulating and filtering, as above directed. A mixture of chloroform and ether is preferred by some analysts, and chloroform alone by others, as a solvent for the extractions. If crystals are not readily obtained, the final purified portions may be obtained in concentrated neutral aqueous solutions for determinative tests. The physiological test should be first, and then drop tests are to be made upon a glass slide over white or black ground, under a magnifier. If the alkaloids of aconite be identified, a further effort should be made to obtain the crystals. The aconite alkaloids have been recovered from the liver and other organs, from the blood, and from the urine. Aconitine was detected by DRAGENDORFF in the stomach two months and nine days after death.[1]

f.—Quantitative.—Aconite alkaloids may be dried at 100° C. for *gravimetric* determination.—The gold salt of aconitine pure is best dried over sulphuric acid in the dark, when a constant weight at 100° C. may be rapidly assured, and the product weighed as $C_{33}H_{43}NO_{12}.HCl.AuCl_3$ (WRIGHT).—The gold precipitate of the probably mixed aconite alkaloids was found by DRAGENDORFF to have from 25 to 31 per cent. of gold, as separated by warming with sulphuric and oxalic acids.[2]

Volumetric estimation of (total) alkaloids of the aconites are made by Mayer's solution—with approximate results—as follows (DRAGENDORFF): The solution is made (by a previous approximate assay) to contain one part alkaloids to 150 or 200 parts of water, and slightly acidulated. The end of the reaction is found by filtering a drop or two, through a very small filter, upon a watch-glass, and adding a drop from the burette, when, if turbidity appears, the watch-glass and filter are drained and rinsed with a few drops of water into the alkaloidal solution, and another addition made from the burette. Each c.c. of the Mayer's solution indicates 0.0274 gram of the alkaloid (empirical), the amount to be increased by 0.00005 gram for each c.c. of the total liquid containing the precipitate. The results are near enough indications of the quantity of total alkaloids to be practically useful for commercial assays of aconites and their preparations—provided always that quantity of total alkaloids could serve a commercial purpose in absence of any index of the proportion of amorphous alkaloids.

A method of *estimation of the crystallizable and physiologically active alkaloids* was proposed by Mr. WRIGHT in 1877,[3] to be done by saponification, and estimation of the resulting benzoic

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[1] For the instructive account of analysis by Drs. DUPRÉ and STEVENSON, in the Lampson case, in London, in 1882, see *The Lancet*, March 18, 1882, p. 455; *Wharton and Stillé's* "Med. Juris.," vol. 2, 1884, Phila. ed., p. 634.

[2] "Gerichtl Chemie," 1872, p. 62.

[3] *Phar. Jour. Trans.*, [3] 8, 164–178.

acid, and dimethylprotocatechuic acid (see p. 18). Saponification is made complete by boiling alcoholic potash, or by water with digestion at 140°–150° C., in sealed tubes. Distilling with water separates the benzoic acid from the dimethylprotocatechuic acid. The weight of the benzoic acid is $\frac{1}{6}$ that of the aconitine. The weight of the dimethylprotocatechuic acid is $\frac{1}{4}$ that of the pseudaconitine.

g.—Commercial grades and values.—An elaborate pharmacological valuation of several brands of aconitine was made, using frogs, rabbits, dogs, and pigeons, by PLUGGE in 1882.[1] It was determined that Petit's "nitrate of aconitine" was eight times stronger than Merck's "nitrate of aconitine," and one hundred and seventy times stronger than Friedlander's; also, that "German aconitine" is variable. Of the samples examined by Plugge he found the following order of diminishing strength: "Nitrate of aconitine": (1) Petit's, (2) Morson's, (3) Hottet's, (4) Hopkins and Williams's "pseudaconitine," (5) Merck's "aconitine nitrate," (6) Schuchardt's "aconitine sulphate," (7) Friedlander's "nitrate of aconitine." These figures must not be taken as indicating the strength of all the alkaloids furnished under these respective brands. Dr. SQUIBB (p. 23) found the relative strength of four articles to be, in proportion: Duquesnel's "crystallized aconitine," 111; Merck's "aconitine from Himalaya root" (pseudaconitine), 83; Merck's "aconitine" (ordinary), 8; unknown "aconitine," 1; the powdered root of A. Napellus, 1.—The "Aconitine japonicum" of Merck claims to be japaconitine.

ACONITIC ACID. $H_3C_6H_3O_6 = 174$.—Found in *Aconitum Napellus* (monks-hood) and other species of Aconitum, in *Delphinium Consolida* (larkspur), in *Equisetum*, *Helleborus niger*, *Achillea Millefolium* (yarrow), *Adonis vernalis*, and other plants. It is a product of citric acid by heat, and occurs in various citric acid concentrated juices of commerce, in sugar-cane juice,[2] and in the scale from sorghum-sugar pans,[3] but it is not manufactured for use.—Crystallizes in white, warty masses, or very slowly in four-sided plates or hard needles. It darkens at 130° C., melts at 140° C., and boils at 160° C., when it gradu-

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[1] *Archiv d. Phar.*, [3] **20**; *Am. Jour. Phar.*, 54, 171. Also, on this question, HARNACK and MENNICKE, 1883.

[2] BEHR, 1877: *Deut. Chem. Ges. Ber.*, **10**, 351.

[3] H. B. PARSONS, 1882: *Am. Chem. Jour.*, 4, 39; *Jour. Chem. Soc.*, **42**, 766.

ally decomposes into Itaconic acid, $C_5H_6O_4$, and carbon dioxide. Citraconic anhydride and other pyrocitric acids occur at higher temperature. Aconitic acid is soluble in water, alcohol, and ether; its solutions have a strongly acid reaction, and a purely acid taste. It is tribasic and forms three classes of salts.—Free aconitic acid solution is precipitated by solutions of mercurous nitrate and lead acetate, and alkali aconitates are precipitated by lead nitrate, silver nitrate, and ferric chloride (red-brown). Calcium aconitate is only sparingly soluble in water. Phosphorus pentachloride, with heat, gives a cherry-red liquid, decolored by water. Nitric acid in boiling solution is deoxidized with evolution of brown vapors.

Aconitic acid is prepared from plants in which it exists as calcium salt, by evaporating the clear decoction to crystallize. The crystals of aconitate of calcium are dissolved by slight acidulation with nitric acid, and precipitated by acetate of lead, and the lead salt decomposed by hydrosulphuric acid. The residue of the filtrate is taken up by ether, and the acid remaining on evaporation of the ether is dissolved in water and crystallized in vacuum over sulphuric acid.[1] It is also separated from impurities by adding (to the dry mixture) five parts of absolute alcohol, then saturating the filtered solution with hydrochloric acid, and adding water, when aconitate of ethyl will rise as an oily layer, colorless and of aromatic odor. This ether may be transposed by potassium hydrate.

Aconitic acid may be best obtained, artificially, from citric acid.[2]

ACONITINE. See Aconite Alkaloids.

ÆSCULIN. $C_{15}H_{16}O_9 = 240$ (Schiff, 1870; Liebermann, 1880).—The bitter principle of the bark of the horse-chestnut (Æsculus hippocastanum). Not identical with gelsemic acid (Wormley, 1882). Obtained by precipitating a decoction of the bark with lead acetate, filtering, and, after removing the lead from the filtrate by hydric sulphide, concentrating to a syrup and allowing to crystallize. It may be purified by repeated crystallization from alcohol and finally from boiling water.

Crystallizes in snow-white, very small needles, arranged in

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[1] Buchner: *Pharm. Repert.*, **63**, 145. A method of separation from *Equisetum* was given by Baup in 1850: *Liebig's Annalen*, **77**, 293; *Jahr. d. Chem.*, 1850, 372.

[2] Pawolleck, 1876: with process, *Liebig's Annalen*, **178**, 150; *Jour. Chem. Soc.*, **29**, 375.

globular masses or in the form of fine powder. They have the composition $C_{15}H_{16}O_9\ 2H_2O$, and lose $1\frac{1}{2}H_2O$ at 110° C., and the rest of the water upon melting at 160°. It is odorless, slightly bitter, and reddens litmus. Soluble in 642 parts cold and $12\frac{1}{2}$ parts boiling water, in about 100 parts cold and 24 parts boiling alcohol; insoluble in absolute, slightly soluble in ordinary ether; soluble in dilute acids and alkalies. The aqueous solution (containing the merest trace of the glucoside) exhibits a distinct blue fluorescence, which is more marked if well-water is used, and is destroyed by addition of acids. The alkaline solutions are yellow, but exhibit a blue fluorescence. It is dissolved by **chlorine** water with red color which changes through brown-red to yellow. **Nitric acid** forms a yellow solution with it, which becomes red upon addition of excess of potassium hydrate. Boiling with dilute acids converts it into *æsculetin*, $C_9H_6O_4$,[1] and glucose. **Ferric chloride** colors its solutions green. It reduces alkaline **cupric** solution upon boiling. It is not precipitated by any of the metallic salts except **lead subacetate.** If a small portion of æsculin be treated with four drops of concentrated **sulphuric acid,** and to the slightly colored solution there be gradually added a solution of sodium hypochlorite, a bright violet coloration is obtained (RABY, 1885).

ALKALOIDS.—Nitrogenous carbon-compounds capable of neutralizing acids.

CONTENTS:—Basal character; solubilities in water, in the immiscible solvents, free and acidified; extraction by solvents; management of emulsions; filtering out; styles of "separators"; stoppers; siphon for separators; tests of completed extraction; the purity of the immiscible solvents; liquid-extraction apparatuses; forces affecting solubilities. Precipitation by alkalies; the scheme of Fresenius; the "general reagents" for the alkaloids, with the recovery of the alkaloid from each—(1) iodine, (2) Mayer's solution, volumetric uses, (3) phosphomolybdate, (4) bromine, (5) cadmium iodide, (6) bismuth, (7) tungsten compounds, etc., (8) tannin, (9) picric acid, (10) platinic and auric chlorides; color-reactions, with sulphuric acid alone and the several oxidizing agents, cane-sugar, etc.; Froehde's reagent; nitric acid; ferric chloride, etc. Microscopic methods; microsublimation, and "the subliming cell."

In their most obvious characteristics these compounds are mostly *divisible into two classes:* (1) Non-volatile Alkaloids, compounds of C, H, N, O; solids, melting and subliming usually with partial decomposition when heated. (2) Volatile Alkaloids, compounds of C, H, N; liquids of slight vaporization at ordinary temperatures and high boiling points. The natural alka-

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[1] On the constitution of æsculin and æsculetin, LIEBERMANN, 1880; WILL, 1883.

loids of the first class are far more numerous than those of the second class.

Both classes mostly include bodies of decided basic power; of an alkaline reaction restricted by sparing aqueous solubility; bases neutralizing acids in the production of their salts, which crystallize in characteristic forms of a good degree of permanence.

In water the free alkaloids have generally little solubility, but their sulphates, nitrates, hydrochlorides, and acetates mostly dissolve with abundance in this vehicle. In alcohol the free alkaloids dissolve in most cases with moderate abundance, and their common salts almost invariably dissolve largely.

In *the solvents immiscible with water*—ether, chloroform, benzene, petroleum benzin, amyl alcohol, etc.—the free alkaloids differ among each other as to their solubilities, which thus become important *means of separation.* The salts of the alkaloids are, with some important exceptions, insoluble in the solvents immiscible with water. Separations of alkaloids soluble in a liquid not miscible with water, from other substances soluble in the same menstruum, are, therefore, accomplished by first washing the acidulated aqueous solution to remove whatever non-alkaloidal matter is soluble in the applied menstruum, and then washing the alkaline aqueous liquid to take out the alkaloid itself.[1] Then, again, the non-aqueous (etherial) solution of the free alkaloid may be washed with acidulated water, when a salt of the alkaloid is formed and transferred to the aqueous liquid, as a step in separation.

The washing of the aqueous liquid with a solvent immiscible with water, sometimes designated as *the shaking out,* is commonly done by agitating in a cylindrical stoppered vessel (Fig. 1, p. 35), and leaving the mixture at rest for the immiscible sol-

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[1] This mode of using ether was proposed in 1856 by Otto, in modification of Stas's process for the recovery of alkaloidal poisons. The plan was adopted for chloroform by Rodgers and Girdwood in 1856; and for amyl alcohol by Uslar and Erdmann in 1861. In 1867 Dragendorff (*Phar. Zeitsch. f. Russland,* 6, Heft 10; *Zeitsch. anal. Chem.*, 7, 521; "Ermittelung von Giften," St. Petersburg, 1868, p. 242) presented a quite comprehensive scheme of separations by solvents immiscible with water, applied both in acidulated and in alkaline solutions. This scheme was translated by the author, in "Outlines of Proximate Organic Analysis" in 1875, and, more in detail, by S. Dana Hayes (*Am. Chemist,* 6, 378) in 1876. The plan of separation, first published in a pharmaceutical journal, and primarily for the uses of the toxicologist, has been extended by chemists everywhere, so that it is now the most common mode of separation of alkaloids for any purpose, in analysis or manufacture. Moreover, the way of "shaking out" by solvents immiscible with water is in frequent use for fats and acids and other bodies besides alkaloids.

vent to separate in a clear layer, which is then drawn off or decanted in some way. The solvent layer will be over the aqueous layer in the case of the ordinary solvents except chloroform, the layer of which will be under the watery liquid. A mixture of one volume of chloroform with three, or at the least two, volumes of ether is sometimes used as an immiscible solvent, lighter than water. Mixtures of alcohol (as a solvent) with ether, or chloroform, or amyl alcohol cannot be used in "shaking out," because the water removes the alcohol from the immiscible liquid. In fact, this liquid becomes water-washed by the operation, and there are advantages in taking a water-washed ether or chloroform to begin with, so that the disturbing presence of alcohol (and possibly of acids) may be avoided. It is to be borne in mind that ordinary stronger ether contains 4 or 5 per cent. of alcohol, and ordinary purified chloroform contains alcohol not exceeding 1 per cent.; also that both these liquids are liable to contain, and to acquire, free acids. It is even possible that, in shaking out with several portions of acidulous ether, the reaction of the aqueous liquid may be changed from alkaline to acid, and if this change be overlooked the separation may be reversed without the knowledge of the operator. The absence of free acid, therefore, is to be required of ether, chloroform, or amyl alcohol when one of these is used as a solvent upon an aqueous liquid. Washing with water, readily done by the analyst, serves to remove both alcohol and acids,[1] but the removal of acids is done sooner and with less waste by washing with alkaline water. What is said of "water-washed" solvents by no means applies to the commercial article known as "water-washed ether," which is of low grade, containing much alcohol, a slight extent of water-washing being substituted for other more efficient means in its purification.

Although the presence of alcohol somewhat lessens the separative power of the solvent, yet the addition of small quantities of alcohol is sometimes resorted to to promote the formation of a clear layer of the immiscible solvent, and (as a diluent) to resolve obstinate emulsions which now and then hinder the analyst. The various resources for preventing and destroying emulsions are named from time to time in the directions in this work. The resolution of an emulsion into the two clear layers of the immiscible liquids concerned is always promoted by some degree of miscibility between these liquids, just as a precipitate that has some slight degree of solubility, or that crystallizes, usually sub-

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[1] The use of water-washed solvents, as standard grades of constant composition, was proposed by the author in 1875 (*Pro. Am. Asso. Adv. Sci.*, **24**, i., 114).

sides the more readily to leave a clear liquid. Ether forms a layer sooner than chloroform, and benzene is liable to give more trouble in the formation of emulsions than either of the former. The operator will learn that in most cases it is better to avoid the production of an obstinate emulsion, not shaking violently enough to cause it, but, if necessary, obtaining the desired contact of the two liquids by a slow and prolonged reversing of the upper and lower ends of the separator. Precautions against emulsions, and devices for their resolution, are given with the various directions for separations of Atropine, Cocaine, Strychnine, and elsewhere in this work. Among such measures may be here enumerated: (1) the application of heat enough to cause a very slight or incipient boiling of the solvent, or of the water when amyl alcohol is the solvent; (2) the introduction of small portions of the clear solvent, with or without clear water, through a little tube, into the intermediary layer of emulsion; (3) the addition of a small portion of the fresh solvent, then gently agitated and set aside for separation of layers, this being done either with the whole liquid or with the emulsified portion of the liquid drawn off for the purpose; (4) the dilution of the solvent with alcohol; (5) gently jarring the separator; (6) filtrations.

The emulsified intermediary layer, drawn off by a siphon or pipette, or, if need be, the entire mixture, may be filtered, using a double paper filter (with four thicknesses all around), and wetting the filter with the heavier of the two constituent liquids. That is, with fresh chloroform, if this be solvent; with distilled water, if the solvent be other than chloroform. The first portion of the filtrate, or even the whole of it, may be returned through the filter, and the filter and lighter liquid remaining in it may be washed with successive small portions (or with a fine, continuous stream) of the heavier liquid.

As a "separator" the author prefers one with a cylindrical body and a short, conical base, the exit-tube being of small diameter and closed with a stopcock next to the body. The stoppered opening at the top of the separator should be of good width. Fig. 1 represents a convenient article, to be held by a "condenser clamp."


Fig. 1.

But instead of a "separator," a large test-tube, or test-glass with foot, may be used with convenience, if provided as follows: The top of this cylindrical tube is fitted just like that of a wash-bottle, with a stopper bearing a delivery-tube and blow-tube, as illustrated in Fig. 2. The delivery-tube is to be narrow, and play up and down in the stopper, to take off the liquid content, either the upper or lower layer, at any point. The blow-tube is so bent and long enough to enable the operator while blowing to see clearly the movement of the liquid at the inner end of the delivery-tube, when this is brought near the line. The division between layers may be carried to very near the outer end of the delivery-tube, when the remaining liquid is drawn back again. To rinse the delivery-tube the stopper is transferred to a tube containing a little of the clean solvent, which is shaken up and then blown out. To make an exact separation of the layers, a small quantity of the fresh chloroform or other solvent may be drawn in through the delivery-tube of the apparatus last above mentioned, next to the aqueous layer, without disturbing the layers, which are thus separated from each other. In other apparatus the introduction may be through a pipette.

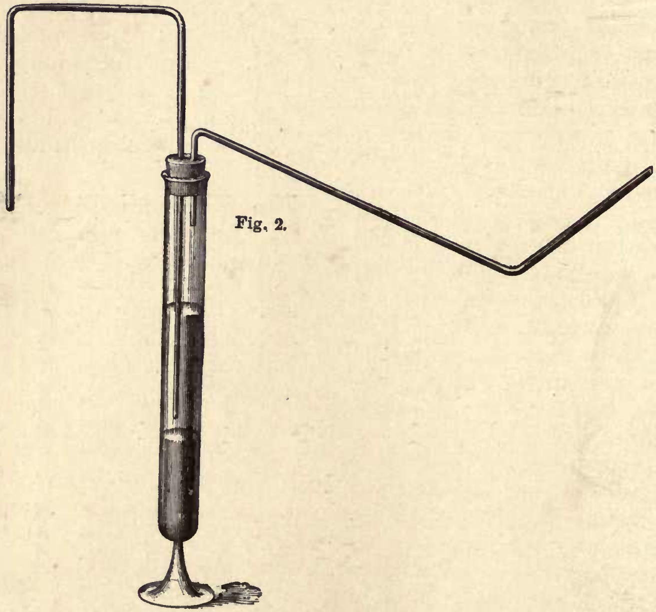

Fig. 2.

Rubber stoppers and tubes are acted on by ether and chloroform, and can only be used when the liquid does not come in contact with them, and then only for a short time, as they are soon injured and swollen by the vapor of these menstrua. Good, well-pressed corks serve for brief uses without special preparation; but to avoid waste of vapor in standing, and especially where the solvent is to be distilled, as described hereafter, the *corks should be rendered impervious,* after being fitted, by an application of chrome-gelatine. Four parts of gelatine are dissolved in 52 parts of boiling water, the solution filtered, and 1 part of ammonium dichromate added. This mixture is applied as a coating to the corks, and permanent cork connections may be completely sealed by covering the corks in place over upon the glass. After application the coating should stand two days in the light to harden.

It will occur to any analyst sometimes to make separations with immiscible solvents, as preliminary trials, or as small qualitative or quantitative tests of a tentative character, when a test-tube or vial is a sufficient container, and the one liquid may be drawn off from the other with a pipette. In using a mouth pipette, however, it is usually better to take out the aqueous layer, this being the less volatile liquid, and less liable to drip when the pipette, closed at the top, is being withdrawn. Also a simple siphon of narrow glass tubing bent in U-form may be filled with the solvent or with water, and used to draw off either layer from any container.

In any case, a separation by or from an immiscible solvent is of the nature of a washing, and complete removal of the dissolved body is not accomplished by a single division into the two liquid layers, or with a single portion of the solvent. Successive portions of the solvent must be applied, in repetition of the "shaking out." Especially is this true with ether, chloroform, and amyl alcohol, which dissolve in water to some extent. From two to five washings may be required. In any case of doubt and of importance, positive information must be gained by a test of the last "wash-liquid," as in ordinary quantitative analysis, and the washings repeated until the last liquid drawn off, or the residue therefrom, gives a negative result under some delicate test for the alkaloid operated upon. In all the cases where assay operations, by a single shaking out with (say) chloroform, have been verified by good authority as giving a correct result under a control analysis, it may be almost certainly set down that the correctness of the result lies in a happy balance of errors rather than in the clear truth. The loss of the alkaloid taken is just balanced by the gain of foreign matter which goes into the weight at the end. And if all the conditions of loss and of gain can be held constant, or nearly so, the method may give results of substantial correctness.

The purity of the immiscible solvents chosen for use must be assured. Let a good portion be evaporated to dryness in a weighed beaker, and the absence of fixed residue ascertained. The residue may well be taken up with acidulated water, and the solution subjected to test by some of the "general reagents for alkaloids," or by the chief qualitative test to be used in the contemplated analysis. If necessary, the solvents are to be purified by distillation.

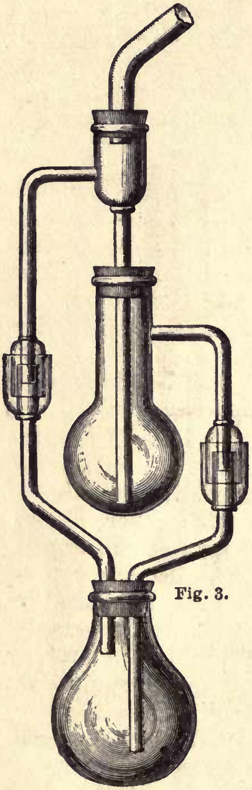

Fig. 3.

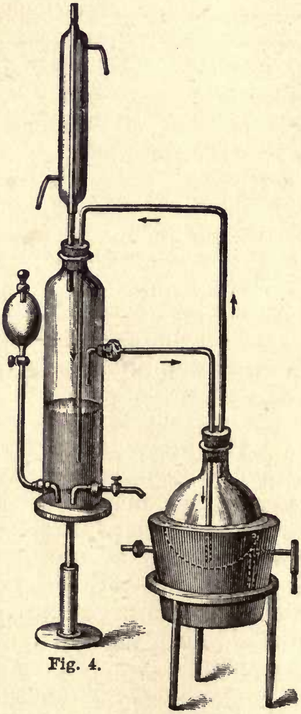

Fig. 4.

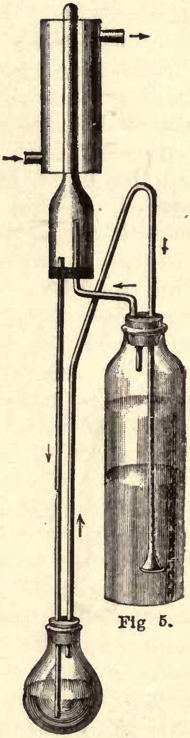

Fig 5.

To avoid the attenuation due to the use of repeated portions of solvent, as well as the expense of considerable quantities of the same, a plan of distillatory use of the solvent has been recently proposed, in the so-called "extraction-apparatus for liquids." This apparatus corresponds in principle to the extraction-apparatus of Tollens and others for the continuous percolation of solids, which have been for some years the favorite means of applying solvents to organic bodies, and is described under Plant Analysis. The immiscible solvent is distilled from its solution while it is being applied, in the apparatus of later device, to the aqueous liquid. The apparatus of SCHWARZ (1884)[1] is shown in Fig. 3. It is connected above with a returning condenser. The two connecting tubes serve, the one to carry vapor to the condenser, the other to conduct the overflow of condensed solvent back to the warmed reservoir—both these tubes having a mercury-joint provided for by an inclosing cup. NEUMANN'S apparatus[2] will be understood from Fig. 4. A. EILOART (1886)[3] describes a simple apparatus (Fig. 5) which can be set up by any chemist with glassware at hand, including a small condenser, the small glass tubing to be bent and fitted in stoppers, as shown in the figure. The tube delivering the solvent into the aqueous liquid may be made with a funnel-end, as figured, so that perforated platinum foil may be bound over the expanded orifice, and the solvent distributed in fine streams. This apparatus, in Fig. 5, applies the hot vaporous solvent to the liquid to be extracted, which is therefore maintained at near the temperature of boiling of the solvent. The same is true of the apparatus of Neumann and of Schwarz (Figs. 4, 3). For fats this heat of the aqueous mixture is needful, and for many substances, including some alkaloids, it may be desirable, but with some alkaloids it is not admissible. And Eiloart presents a modification of his apparatus in Fig. 6, whereby the solvent reaches the aqueous liquid from the condenser, and not directly from the distilling flask; so that, if the condenser be kept cold enough, there will be no heating of the aqueous liquid, the temperature of which may be regulated at will.

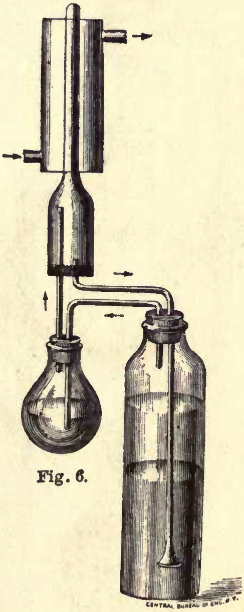

Fig. 6.

All the forms of liquid-extraction apparatus so far described in publications are devised for light volatile solvents, constituting the layer above the watery liquid. *For chloroform*, received in the layer below the aqueous one, the apparatus illustrated in

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[1] *Zeitsch. anal. Chem.*, **23**, 368.

[2] 1885: *Ber. d. chem. Ges.*, **18**, 3061.

[3] *Chem. News*, **53**, 281.

Fig. 7 may be used, with attention now and then, to transfer the chloroformic layer to the distilling flask. In doing this the valve leading to the condenser is closed, the lower valve is opened, and pressure then applied at the outer opening of the blow-tube until the chloroformic layer is siphoned over.

The degree of solubility in the immiscible solvents varies with forces of adhesion and cohesion not operative in dissolving from the dry mass. The solubility of an alkaloid, in agitating its acidulous watery solution with ether or benzene at the moment the liquid is made alkaline, may be more or less abundant than the solubility of the dry alkaloid in ether or benzene.[1] The moment of liberation of the alkaloid from its salt is certainly the most favorable time for its free solubility. Therefore many operators, in dissolving by agitation, add first the immiscible solvent and agitate, and then add the alkali for liberation of the alkaloid, when the agitation is continued. And it is to be borne in mind that the factors of solubility, reported for a certain solvent with great minuteness precisely as obtained by experiment at a given temperature, are liable to vary within liberal limits by influence of several conditions besides temperature.

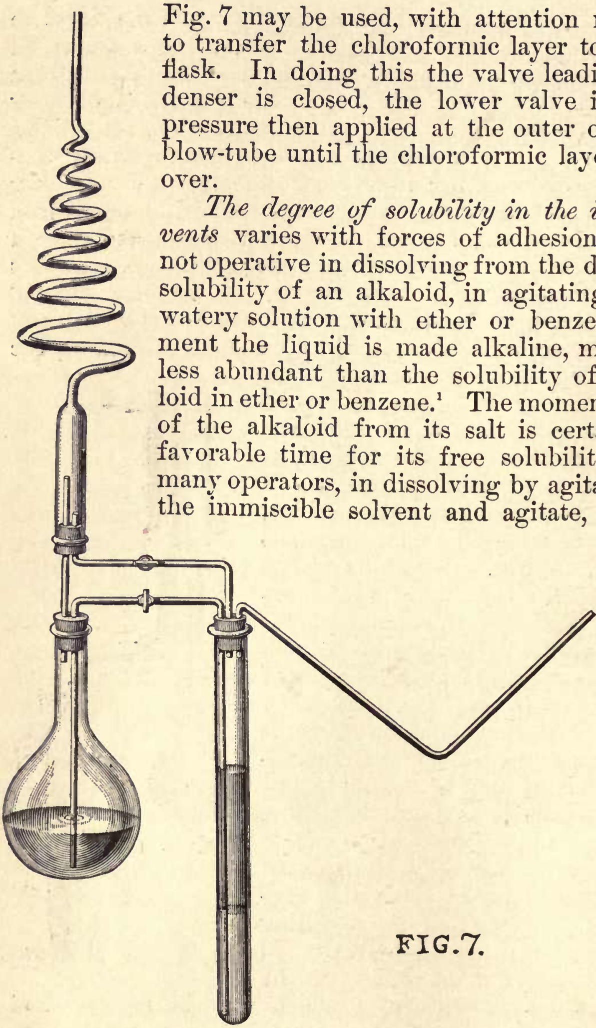

FIG.7.

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[1] "Comparative Determinations of the Solubilities of Alkaloids in Crystalline, Amorphous, and Nascent Conditions : Water-washed solvents being used." The author, 1875 : *Pro. Am. Asso. Adv. Sci.*, **24**, i. 111 ; *Am. Chem.*, **6**, 84 ; *Jour. Chem. Soc.*, **29**, 403.

A common plan for separation of alkaloids by reason of their diverse solubilities, brought into use at a very early period, requires no other menstruum than water, and consists in dissolving out the alkaloid as a salt, by use of acidulated water, and *precipitating the alkaloid free*, by adding an alkali to the clear aqueous solution. In operations of this sort alkaloids have relations like those of metallic bases other than the alkalies. Like the metallic bases, alkaloids are in some instances dissolved by free fixed alkalies, or an excess of this alkali precipitant, in other instances dissolved by an excess of ammonia, and in many cases not dissolved by excess of any alkali. An acidulous watery solution of cinchona bark, in the clear but colored filtrate, on adding solution of sodium hydroxide to excess, presents an abundant precipitate of the mixed impure cinchona alkaloids, colored by extracted matters. Precipitation by one of the alkalies or alkali earths has a place in various processes for preparation of alkaloids from vegetable sources, and a share among the means of qualitative and quantitative analysis. Thus in most of the methods of the morphiometric assay of opium, ammonia is added to the aqueous solution of morphine salt, when simple transposition occurs, as follows: $(C_{17}H_{19}NO_3)_2H_2SO_4+2NH_4OH=$ $2C_{17}H_{19}NO_3\ H_2O$(cryst. morphine)$+(NH_4)_2SO_4$. In one of the preferred methods the morphine is dissolved out of the opium by an excess of lime, the resulting lime-solution being treated with ammonium chloride, when a transposition occurs, precisely corresponding to that of a precipitate of aluminium hydroxide according to the equation: $K_2Al_2O_4+2NH_4Cl+4H_2O=$ $Al_2(OH)_6+2KCl+2NH_4OH$. And no more absolute separation of the chief alkaloid of opium than this crystalline precipitation (favored by the contact of immiscible solvents) has yet been established.

The action of certain of the alkalies, used in excess, to redissolve the precipitates they form in solutions of alkaloid salts, has been made available in analytical separations.

Fresenius's manual of qualitative analysis has long presented a scheme of separation, or of classification, of a few common alkaloids, as follows: Of Non-volatile Alkaloids, (1) those which are precipitated by potassa or soda from the solutions of their salts, and redissolve readily in an excess of the precipitant (morphine); (2) those which are precipitated by potassa or soda from the solutions of their salts, but do not redissolve to a perceptible extent in an excess of the precipitant, and are precipitated by sodium bicarbonate even from acid solutions (narcotine, quinine, cinchonine); (3) those which are precipitated by potassa from the solutions of their salts, and do not redissolve to a perceptible extent in an excess of the precipitant, but are not precipitated from (even somewhat concentrated) acid solutions by the bicarbonates of the fixed alkali metals (strychnine, brucine, veratrine, atropine). The solubility of quinine, and the far more difficult solution of the other cinchona alkaloids, in an excess of ammonia, is used in the valuable method of Kerner for separation of quinine from other cinchona alkaloids, and estimating the proportions or fixing the limits of the latter.

Finally, it remains to notice that, although the salts of the common mineral acids (sulphuric, hydrochloric, nitric) with the alkaloids, are soluble in water, there are certain double salts whereby nearly all alkaloids are precipitated, in somewhat complex compounds nearly insoluble in water. The precipitants are known as *The General Reagents for Alkaloids.* The most useful of these are (1) Iodine in solution of potassium Iodide, (2) Potassium Mercuric Iodide, (3) Phosphomolybdate, (4) Bromine in aqueous hydrobromic acid, (5) Potassium Cadmium Iodide, (6) Potassium Bismuth Iodide, (7) Tungsten compounds, phosphoantimonic acid, and ferric chloride with hydrochloric acid, (8) Tannic Acid, (9) Picric Acid.

In applying a precipitant to a solution of an alkaloid, when it is desired to avoid expenditure of the material under examination, a drop of the solution is to be treated with a drop of the reagent, on a glass slide placed over black paper. A hand-magnifier is serviceable.

(1) *Iodine in Potassium Iodide Solution* (Wagner, 1866).[1]—A decinormal solution of the free iodine: 12.66 grams of iodine in a liter of solution of iodide of potassium; or, 20 grams iodine and 50 grams potassium iodide per liter (Wormley). Applied, as it is, in acidified solution, it is in effect iodized hydriodic acid. Brown and flocculent precipitates; generally with very little solubility in water; formed more perfectly in acidulous solutions, and in those containing a little free sulphuric acid. Iodine tincture is a less useful form of the reagent. The precipitates are more or less soluble in alcohol. A very slight addition of the reagent is sufficient, and it is better not to use enough to give color to the solution. In a liquid liable to contain dissolved substances not alkaloids, the fact of precipitation is not strongly characteristic, while the absence of precipitation is conclusive for ordinary alkaloids.

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[1] *Zeitsch. anal. Chem.*, 4, 387.

On standing, the precipitates in most instances crystallize in somewhat characteristic forms, more perfectly from solutions in alcohol.

In composition (Hilger, 1869; Bauer, 1874) the precipitates are addition compounds, of different but related types. When quinine sulphate solution is treated with a little of the reagent, there is formation of $C_{20}H_{24}N_2O_2.HI.I$; with more of the reagent, quinine pentiodide, $C_{20}H_{24}N_2O_2.HI.I_4$, is formed; and in presence of excess of alcoholic iodine and sulphuric acid, various iodosulphates are formed, as stated more fully under Quinine, *d*, "Herapathite test." Atropine pentiodide, $C_{17}H_{23}NO_3.HI_5$, obtained by excess of the reagent, crystallizes from hot alcoholic solution, in fine blue-green, lustrous needles or plates. A corresponding tri-iodide is obtained by adding less of the iodine. Strychnine tri-iodide crystallizes from alcoholic solution in long, dark-brown prisms, of rhombic shapes, with bluish-metallic lustre. Thrown down as an amorphous precipitate it is red-brown. Berberine tri-iodide, $C_{20}H_{17}NO_4.HI_3$, crystallizes from hot alcohol in long, red-brown, diamond-lustrous needles. Piperine tri-iodide, $(C_{17}H_{19}NO_3)_2HI_3$ (Jörgensen, 1877), crystallizes from hot alcoholic solution in long, steel-blue needles of metallic lustre.

Recovery of the free alkaloid from the precipitates of hyperiodides may be accomplished as follows: The washed precipitate is dissolved in excess of aqueous sulphurous acid, and the solution evaporated on the water-bath, the sulphurous acid being kept in excess until the hydriodic acid is expelled, when the former is also driven off and the alkaloid remains as a sulphate.—The hyperiodide precipitates dissolve in solution of thiosulphate, and may be thereby separated from various foreign matters carried down by adding free iodine to organic extracts. If the thiosulphate solution be treated with the iodine solution in excess, the alkaloid is again precipitated.

(2) *Potassium Mercuric Iodide. Mayer's Solution.*[1]—The

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[1] F. L. Winckler, 1830. A. v. Planta-Reichenau, "Das Verhalten der wichtigsten Alkaloide gegen Reagentien" (S. 41), Heidelberg, 1846. Thomas B. Groves, "On some compounds of iodide and bromide of mercury with the alkaloids," 1859: *Jour. Chem. Soc.*, **11**, 97, 188; *Phar. Jour. Trans.*, **18**, 181; *Am. Jour. Phar.*, **36**, 535. Ferdinand F. Mayer, 1862–3: *Pro. Am. Pharm.*, 1862, 238; and *Chem. News*, **7**, 159; **8**, 177, 189; *Am. Jour. Phar.*, **35**, 20; *Zeitsch. anal. Chem.*, **2**, 225; *Jahr. Chem.*, 1863, 703. G. Dragendorff. "Werthbestimmung," 1874, p. 9 and elsewhere. A. B. Prescott, "Estimation of alkaloids by potassium mercuric iodide," 1880: *Am. Chem. Jour.*, **2**, 294; *Jour. Chem. Soc.*, **42**, 664; *Chem. News*, **45**, 114; *Ber. d. Chem. Ges.*, **14**, 1421.

solution proposed by Mayer is the one generally used for purposes qualitative or quantitative. It is a decinormal solution of $\frac{1}{2}(HgCl_2+6KI)$ = the hydrogen equivalent of Hg. Of dry, crystallized mercuric chloride, 13.525 grams; potassium iodide, 49.680 grams; separately dissolved in water, and the mixed solutions made up to one liter. The reactions of the solution appear to correspond with the formula $KIHgI_2.(KI)_3+2KCl$,[1] instead of $(KI)_2HgI_2+2KI+2KCl$. Dragendorff prefers to make quantities, above specified, to 2 liters instead of 1.

Mayer's solution is applied only in acidulous solutions, in testing for alkaloids; therefore ammonia does not interfere, as the precipitate of mercurammonium iodide is not formed in presence of free acids. The acidulation may be with sulphuric or hydrochloric acid, and may be strong without dissolving the precipitate. The solution tested must not be alcoholic, and must not contain acetic acid. Some organic matters other than alkaloids cause precipitates. With strychnine the precipitate is obtained in dilution of 1 to 150000; with quinine, in solutions of about the same dilution; while with morphine, or with atropine, solutions of 1 to 4000 do not give the precipitate. The precipitates are curdy or flocculent, and for the most part of a yellowish-white color.

Caffeine and theobromine are not precipitated by potassium mercuric iodide.

The composition of some of the alkaloid iodomercurates varies with conditions of concentration, excess of reagent, and acidity; while the precipitates of other alkaloids are nearly constant in composition. With strychnine the precipitate is not far from $C_{21}H_{22}N_2O_2HIHgI_2$[2]; with morphine the precipitate corresponds to a variable mixture of $(C_{17}H_{19}NO_3)_4(HI)_4(HgI_2)_3$ and $(C_{17}H_{19}NO_3)_4(HI)_6(HgI_2)_3$; with quinine the precipitation appears to be most nearly, though not closely, represented by $(C_{20}H_{24}N_2O_2)_2(HI)_3(HgI_2)_3$; and with atropine the gravimetric value of the precipitate does not correspond to its volumetric factor.

In volumetric use the "end-reaction" is denoted only by the

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[1] In the proportions for $(KI)_2HgI_2+2KCl$, the mercuric iodide remains dissolved only in concentrated or hot solution. The quantity of alkali iodide adopted by Mayer cannot be very much reduced and retain solubility at the decinormal dilution in the cold. A permanent solution with the help of bromide can be obtained as follows: $HgCl_2+4KI+KBr$: mercuric chloride, 13.525; potassium iodide, 33.12; potassium bromide. 5.94; water to 1000 by volume. This solution may be supposed to contain $(KI)_2HgI_2+KBr+2KCl$. (The author, 1880: *Am. Chem. Jour.*, **2**, 304.)

[2] The author, 1880: *Am. Chem. Jour.*, **2**, 296.

completed precipitation.[1] After the last addition from the burette the precipitate is either allowed to subside, or a little portion is filtered out and a drop of the reagent added from the burette to the clear solution. Some of the precipitates subside readily, strong acidulation usually favoring this result; with others much time is required, and titration in this way is generally slow. Filtration is the better way: using a minute filter, not over 5 millimeters or $\frac{1}{4}$ inch in radius, held in a loop of platinum wire or a coil of drawn-out glass tubing, over a glass slide placed upon black paper. A drop or two is taken, with the stirring-rod, from the mixture containing the precipitate, filtered through the wet filter, and treated over the black ground with a drop of the reagent from the burette, when the slightest turbidity can be seen. Before the end of the titration all the test-portions are drained and rinsed with a few drops of water passed through the filter into the mixture containing the precipitate.

In volumetric estimation the strength of the alkaloidal solution should usually be 1 of alkaloid to 200 of solution—a second estimation being made, if need be, for this graduation. The quantity of alkaloid precipitated by 1 c.c., under given conditions of concentration, etc., is stated with the directions for quantitative work on the several alkaloids described in this work. A quite full list of the volumetric factors for Mayer's solution was given by Mayer, and some of these have been subjected to control analyses by Dragendorff and others; but the presentation of such a list is here intentionally avoided. It must be understood that *the alkaloidal equivalent of one c.c. varies with the conditions*, especially with that of concentration. Unless the analyst has good authority for an alkaloid equivalent, given with specified conditions, he should standardize his Mayer's solution, with an alkaloid solution of known strength, for himself, holding degrees of concentration, acidulation, mass, and time the same for the titration of the solution of unknown strength that they are for the solution of known strength of alkaloid. The end of the reaction is the point when further addition of the reagent ceases to cause a precipitate. Before this point is reached, however, in some cases the addition of a drop of the solution of the alkaloid will cause a precipitate—the mixture having attained a composition of equilibrium (not very rare among chemical reactions) in which precipitation is caused by a drop of either the iodomercurate or the alkaloid solution. When the precautions here re-

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[1] Trials of various indicators for the end-reaction were reported by the author in *Am. Chem. Jour*, **2**, 304, where also attention is called to the error of Mayer's direction to titrate back with silver nitrate.

quired are observed, titration with Mayer's solution becomes a trustworthy means of estimation.

The alkaloids can be obtained from their iodomercurate precipitates by triturating the washed precipitate with stannous chloride solution and potassium hydroxide to strong alkaline reaction, and then exhausting with ether or chloroform or benzene as a solvent for the alkaloids. Strong alcohol can be used as a solvent if potassium carbonate be taken instead of potassium hydroxide.—Also, the mercury can be removed from the precipitates by dissolving in alcohol, adding acid if need be, treating with hydrogen sulphide gas, and filtering. The filtrate can be freed from iodine, if this be desired, after expelling the hydrogen sulphide, by adding some excess of silver nitrate solution, filtering, adding hydrochloric acid to the filtrate, and filtering again.

(3) *Phosphomolybdate.*[1]—A fixed alkali phosphomolybdate in strong nitric acid solution—in effect a solution of phosphomolybdic acid.

Applicable in acidulous solutions and in absence of ammonium salts and free ammonia, which also precipitate it.

It is prepared as follows: The yellow precipitate formed on mixing acid solutions of ammonium molybdate and sodium common phosphate—the ammonium phosphomolybdate—is well washed, suspended in water, and heated with sodium carbonate until completely dissolved. The solution is evaporated to dryness, and the residue gently ignited till all ammonia is expelled, sodium being substituted for ammonium. If blackening occurs, from reduction of molybdenum, the residue is moistened with nitric acid and heated again. It is then dissolved with water and nitric acid to strong acidulation; the solution being made ten parts to one of the residue. It must be kept from contact with vapor of ammonia, both during preparation and while preserved for use.

The precipitates of alkaloids, by adding this reagent to their acidified solutions, are amorphous, and of yellowish colors, sometimes orange-yellow, in other cases brown-yellow. In general they have very little solubility, and are obtained in very dilute solutions. Besides ammonia, other bodies not alkaloids are liable to give precipitates with this reagent. A negative result is trustworthy for the exclusion of more than traces of alkaloids in the solution tested. Most of the precipitates are soluble in ammonia, and those of alkaloids that are strong reducing agents mostly dis-

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[1] Sonnenschein, 1857: *Ann. Chem. Phar.*, **104**, 45. De Vrij: *Jour. de Pharm.*, **26**, 219. Struve, 1873: *Zeitsch. anal. Chem.*, **12**, 170.

solve with the blue color of reduced molybdic acid, or with some shade caused by admixture of blue. The ammoniacal solution is blue with aconitine, aniline, atropine, berberine, morphine, nicotine, and physostigmine. Alcohol and ether do not dissolve the precipitates, and acetic acid has but a slight solvent action.

The alkaloids can be recovered from the precipitates by adding potassium or sodium hydroxide solution, and shaking out with an immiscible solvent for the alkaloid, as ether, chloroform, benzene, or amyl alcohol. Adding potassium carbonate instead of hydroxide, strong alcohol can be added instead of an immiscible solvent.

A gravimetric value of the phosphomolybdate precipitate has been obtained for a few of the alkaloids, but it has not been ascertained what conditions are necessary to secure a constant composition.[1]

(4) *Bromine in aqueous hydrobromic acid.*—Wormley directs the use of aqueous hydrobromic acid saturated with bromine. Applicable to aqueous solutions of the salts of the alkaloids, neutral or slightly acidulous with a mineral acid, and in absence of acetic acid and of alcohol, which dissolve the precipitates. Besides alkaloids, the phenols and other bodies give precipitates with bromine. (See Phenol.) The limit of precipitation of the alkaloids is at dilution to from 5000 to 100000 parts—with morphine, 1 to 2500; with nicotine or conine, 1 to 10000; with aconitine, codeine, or brucine, 1 to 25000; with strychnine, narcotine, or veratrine, 1 to 100000 (Wormley). In general the precipitates are amorphous; with atropine, crystalline.

(5) *Potassium cadmium iodide* (Marmé, 1866).—Prepared by saturating a boiling concentrated solution of potassium iodide with cadmium iodide, and adding an equal volume of cold-saturated solution of potassium iodide. In diluted solution, precipitation is apt to occur.—This reagent precipitates the aqueous solutions of alkaloid salts, acidified by sulphuric acid, the precipitates being soluble in excess of the precipitant, or in alcohol. Amorphous at first, the precipitates become crystalline.—The alkaloids can be recovered from the precipitates as directed for those formed by potassium mercuric iodide.

(6) *Potassium bismuth iodide* (Dragendorff, 1866).—Prepared from bismuth iodide, in the way directed for the last-

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[1] It appears probable that a dilute solution of the phosphomolybdate, standardized by solution of an alkaloid of known strength, could be used to estimate the quantity of the same alkaloid under strictly parallel conditions. The end-reaction can be found as directed for Mayer's solution.

named reagent. Cannot be diluted. Applicable as a precipitant to aqueous solutions of alkaloid salts, strongly acidified with sulphuric acid.

(7) *Metatungstic acid*, *Phosphotungstic acid* (SCHEIBLER, 1860), *Silicotungstic acid* (GODEFFROY, 1876), and *Phospho-antimonic acid* (SCHULTZE, 1859), have been used as general precipitants for the alkaloids. GODEFFROY (1877) uses a solution of ferric chloride in hydrochloric acid as a precipitant for alkaloids.

(8) *Tannic acid* (BERZELIUS, HENRY, DUBLANC, HAGER), in solution with 8 parts of water and 1 part of alcohol, gives whitish, grayish-white, or yellowish precipitates with nearly all the alkaloids. In the larger number of instances these precipitates are easily soluble in acids, frequently dissolving in excess of the tannic acid; on the contrary, some of the alkaloids are precipitated by tannic acid only in strong acid solutions. Ammonia dissolves the tannates of the alkaloids.

Dilute acetic acid dissolves the precipitates of tannates of aconitine, brucine, caffeine, colchicine, morphine, physostigmine, and veratrine; acetic acid not dilute, the precipitate of quinine.—Cold dilute hydrochloric acid does not dissolve the precipitates of tannates of aconitine, berberine, brucine (dissolves sparingly), caffeine, cinchonine, colchicine (dissolves slightly), narcotine, papaverine, thebaine, solanine, strychnine (dissolves slightly), veratrine.—Cold dilute sulphuric acid does not dissolve the precipitates of tannates of aconitine, physostigmine, quinine, solanine, veratrine.—Precipitates are completely formed in solutions strongly acidulated with sulphuric acid, by aconitine, physostigmine, and veratrine, though none of these alkaloids gives a full precipitate in slightly acidulated solution.—Alkaloids are recovered from their tannates by mixing the moist precipitate with lead oxide or carbonate, drying the mixture, and extracting with an immiscible solvent or with alcohol.

(9) *Picric acid*, $HC_6H_2(NO_2)_3O$ (WORMLEY, 1869; HAGER, 1869).—Used in very dilute, saturated aqueous solution, or in a sparing addition of the alcoholic solution. Applied as a precipitant of alkaloids in their neutral solutions, or, better, in solutions acidulated with sulphuric acid. Many of the precipitates become crystalline, and give characteristic forms under the microscope; in general they have a yellow or yellowish-white color. With morphine the precipitate is formed, in drop-tests, in solution of 1 to 500; with aconitine, atropine, or veratrine, in solution of 1 to 5000; with brucine or narcotine, in a solution of

1 to 20000; with strychnine, 1 to 25000; with nicotine, in solution of 1 to 4000 (WORMLEY).—The alkaloids can be recovered from their picrate precipitates by adding an alkali solution and exhausting with a solvent immiscible with water, or by evaporating to dryness with a solution of potassium or sodium carbonate, and extracting with alcohol.—HAGER has used precipitation with picrate in some estimations of alkaloids. For cinchona alkaloids,[1] 10 grams of the powdered bark, covered with 130 c.c. water, with 20 drops of caustic potassa solution of s.g. 1.3, are digested at boiling temperature and stirred for a quarter of an hour. Of dilute sulphuric acid, s.g. 1.115, 15 grams are added, and the mixture boiled 15 to 20 minutes. When cold the whole is made up, by the addition of water, to 110 c.c. ("the volume of 110 grams of water"). The mixture is filtered, through a paper filter of 10.5 to 11 0 centimeters (8¼ inches) diameter, into a graduated jar, and the volume of the filtrate (about 60 c.c.) noted. To this filtrate (100 c.c. of which represents the 10 grams of bark) picric acid solution saturated in the cold is added, in quantity about 50 c.c., or enough to complete the precipitation (as ascertained by allowing a few drops to flow down the side of the vessel). After half an hour the precipitate is gathered on a weighed filter, washed, and dried between blotting-papers over the water-bath. The dried precipitate of picrates of cinchona alkaloids contains (according to Hager) two molecules of picric acid as anhydride, 440 parts, to one molecule of cinchona alkaloid, 308 to 324 parts, without water of crystallization. Or 8.24 parts of the precipitate indicate about 3.5 of mixed cinchona alkaloids. Then the noted number of c.c. of decoction taken: 100 :: the indicated quantity of mixed alkaloids in the precipitate : $x =$ quantity mixed alkaloids in the 10 grams of bark.

(10) *Platinic Chloride. Auric Chloride.*—Solutions of these salts, hardly to be classed as special reagents for alkaloids, yet give precipitates with the greater number of them. Platinic chloride is often required in establishing distinctions between alkaloids, as noted in this work under the qualitative reactions of the respective compounds. The same may be said of auric chloride. The melting points of the alkaloidal compounds of these metals serve as constants useful for identification, especially in distinguishing the derivatives of alkaloidal radicals. The composition of these metallic precipitates has in most cases been

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[1] 1869: *Phar. Centralh.*, p. 145; *Zeitsch. anal. Chem.*, 8, 477.

estimated from the percentages, respectively, of metallic platinum and metallic gold, left after ignition. These percentages were much depended upon in the earlier years of the chemistry of the alkaloids, and are given full and prominent statements in Gmelin's Hand-book of Chemistry.—The platinum precipitates are divisible into those which do and those which do not dissolve in hydrochloric acid—cinchonine and quinine, morphine, and strychnine being placed among those not readily soluble in this acid.—The platinum precipitates have a yellow or yellowish color. The gold precipitates of a number of the alkaloids blacken by reduction on standing.

Color-reactions of the Alkaloids.—In general it should be borne in mind that color-reactions are subject to variation (1) by impurities of the alkaloidal material, (2) by impurities of the reagent, and (3) by conditions of concentration, mass preponderance, temperature, and time. Also, that the best authority to guide the operator is the result of a control-test upon a known portion of the alkaloid in question, holding all conditions to be the same.

Concentrated Sulphuric Acid[1] dropped upon the dry alkaloid, on a white porcelain surface or on glass over a white ground, without heating, reacts as follows: *colorless* with atropine, caffeine, chelidonine, cinchonidine, cinchonine, codeine, hyoscine, hyoscyamine, morphine, nicotine, pilocarpine, quinidine, quinine, staphisagrine, strychnine, theobromine. Of these, on warming, a purplish to brown color is given by morphine. *Yellowish colors* are given by colchicine, gnoscopine, and jervine; *reddish colors* are given (either at once or after a short time) by apomorphine, brucine (pale rose), conine (pale), gelseminine, meconidine, narceine (to black), narcotine (yellow-red to violet and blue), nepaline, physostigmine, rhoeadine, sabadilline, sabatrine, solanine, taxine, thebaine, veratrine, and veratroidine; *bluish colors* are given by cryptopine, curarine (on standing), and papaverine; and *greenish colors* by beberine, berberine, emetine (brown to green), piperine, pseudomorphine, and rhoeadine.—Of *glucosides*, *reddish colors* (mostly bright) are given by amygdalin, colombin, cubebin, elaterin, hesperidin, phloridzin, populin, salicin, sarsaparillin, senagin, smilacin, syringin, tannic acids.

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[1] Traces of nitric acid, not infrequent as an impurity in "C. P. sulphuric acid," cause a great difference in the reaction with morphine and other alkaloids colored by nitric acid. See the composition of "Erdmann's reagent," given in the foot-note under Nitric Acid Color Tests. On the Reactions of Alkaloids with Sulphuric Acid, cold, warm, and hot—alone, with nitric acid, and with permanganate—see GUY, 1861–2: *Phar. Jour. Trans*, [2], **2**, 558, 662; **3**, 11, 112; *Zeitsch. anal. Chem.*, **1**, 90.

Froehde's Reagent—concentrated sulphuric acid containing molybdic acid.[1]—A solution of 0.001 gram of molybdic acid or alkali molybdate, in 1 c.c. of concentrated sulphuric acid (Dragendorff), freshly prepared by the aid of heat, and used when cold. Froehde took 0.005 gram of the molybdate to 1 c.c. of sulphuric acid, and Buckingham took as much as 1 part of molybdate to 15 of the sulphuric acid; but the more attenuated proportion of the molybdate (1 to 1840) gives the more distinctive reactions.—The reduction of molybdic acid to hydrated molybdic molybdate is attended with a bright blue color. This reduction occurs in concentrated sulphuric acid, by heat alone, at the temperature of incipient vaporization of the sulphuric acid. Numerous inorganic and organic reducing agents cause the reduction and give the color to molybdate. As a characterizing reaction it is applied mostly to alkaloids, when non-alkaloidal matter must be excluded, and the more dilute solution of molybdate is the more trustworthy.

Froehde's reagent gives *no color* with atropine, caffeine, cinchonidine, cinchonine, conine, delphinine, hyoscine, hyoscyamine, nicotine, strychnine, theobromine; *yellowish colors* with aconitine, colchicine, piperine; *reddish colors* with brucine, emetine (red changing to green), narceine (changing to blue), sabadilline (reddish-violet), solanine, thebaine (orange), veratrine (gradually, cherry-red); *bluish colors* with codeine (gradually, deep blue), morphine (violet to blue), narceine (yellow-brown to red and blue), staphysagrine (violet-brown); *greenish colors* with apomorphine (green to violet), beberine (brown-green), berberine (brown-green), emetine (red changing to green and turned blue by hydrochloric acid), quinine (pale), quinidine (pale).—*Of glucosides*, colocynthin gives slowly a cherry-red color; elaterin, yellow; phloridzin, slowly, blue; populin, violet; salicin, violet to cherry-red; syringin, blood-red to violet-red colors.

Nitric acid, of s.g. 1.40 to 1.42, applied in a drop to the dry alkaloid upon white porcelain, gives a color, frequently reddish, with numerous alkaloids. *No color* is obtained with atropine, caffeine, cinchonidine, cinchonine, conine, gelseminine, quinidine, quinine, strychnine, theobromine. *Yellowish colors* are obtained

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[1] Froehde, 1866: *Archiv der Phar.*, **126**, 54; *Zeitsch. anal. Chem.*, **5**, 214; *Pro. Am. Pharm.*, **15**, 241. Almén, 1868: *N. Jahr. f. Phar.*, **30**, 87; *Zeitsch. anal. Chem.*, **8**, 77. Kauzmann, 1869: *Zeitsch. anal. Chem.*, **8**, 105. Buckingham, 1873: *Jour. Chem. Soc.*, **27**, 715; *Am. Jour Phar.*, **45**, 179. Dragendorff, 1872: "Beitrage zur gericht. Chem. organ. Gifte." A. B. Prescott, 1876: "Froehde's Reagent as a Test for Morphine," *Am. Jour. Phar.*, **48**, 59; *Jahr der Pharm.*, 1876, 502. On various reactions of the blue oxide of molybdenum, see Maschke, 1873.

with aconitine (yellow to brown or red, variable), codeine (orange-yellow), morphine (yellow to red), narceine, narcotine, papaperine (orange), piperine (orange), rhoeadine, sabadilline (yellow), thebaine, veratrine. *Red colors* are obtained by aconitine (red-brown, variable), apomorphine, berberine (red-brown), brucine (blood-red), papaverine (orange-red), pseudomorphine (orange-red), physostigmine. A *blue* color is given by colchicine and by solanine (Dragendorff). – Some *glucosides* give bright colors; ligustrin and syringin, blue tints.

Sulphuric acid (concentrated), *followed by a minute addition of nitric acid* (s.g. 1.40–1.42), or of solid potassium nitrate.[1] *No color* is given by atropine, caffeine, cinchonidine, cinchonine, nicotine, pilocarpine, quinidine, quinine, staphysagrine, strychnine, theobromine. *Red colors* are given by brucine, curarine, narcotine (red-violet), nepaline, physostigmine, sabadilline, thebaine, veratrine (gradually, cherry-red). A *violet color* is given by morphine (under directions specified for that alkaloid). Codeine gives a succession of colors, as also does colchicine.

Sulphuric Acid and Cane Sugar.[2]—The substance to be tested, in the dry state, is mixed with 6 to 8 parts of cane-sugar, and a few milligrams of the mixture are placed upon a drop or two of concentrated sulphuric acid, over a white ground. The gradual browning of the sugar itself is disregarded, and will be covered by the bright colors of characteristic reactions. *No colors* are given by atropine, brucine, caffeine, cinchonidine, cinchonine, conine, nicotine, quinidine, quinine, strychnine, and theobromine. *Reddish colors* are given by codeine, curarine, gelseminine, morphine (purple-red, then blue-violet, dark blue-green, and lastly blackish-yellow—limit 0.0001 to 0.00001 gram), nepaline (gradually), sabadilline (reddish-violet). A *bluish* color by veratrine.—Various oils, and albuminoids, give bright colors with sulphuric acid and sugar.

Hydrochloric Acid, concentrated, gives colors with only a few alkaloids. *Reddish colors* are given by physostigmine, sabadilline, and veratrine.

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[1] Erdmann, 1861: *Ann. Pharm. Chem.*. **120**; *Zeitsch. anal. Chem.*, **1**, 224. Erdmann mixed six drops of nitric acid of s.g. 1.25 with 100 c.c. of water, and added ten drops of this mixture to 20 grams of sulphuric acid. Of this—"Erdmann's reagent"—8 to 20 drops were added to 1 or 2 milligrams of the solid to be tested, and the color noted after $\frac{1}{4}$ to $\frac{1}{2}$ hour.—Husemann, 1863: *Ann. Chem. Phar.*, **128**, 303—the well-known test for morphine. Dragendorff, 1868: "Ermittelung von Giften," p. 239.

[2] Schneider, 1872: *Ann. Phys. Chem. Pogg.*, **147**, 128; *Zeitsch. anal. Chem.*, **12**, 218. Respecting reactions with substances not alkaloids, Schultze, *Ann. Chem. Phar.*, **71**, 266.

Other Reagents for alkaloids as a class, or for groups of alkaloids.—Iodine in hydriodic acid, gold bromide, sodium gold thiosulphate, potassium gold iodide, lead tetra-chloride, and manganese perhydroxide in sulphuric acid, were reported upon by F. SELMI in 1877. Perchloric acid, FRAUDE, 1879–1880. Sodium arseniate with sulphuric acid, TATTERSALL, 1879. Cupric ammonium hydrate, NADLER, 1874. Ferric chloride and sulphuric acid, HOW, 1878. Fused antimonious chloride, SMITH, 1879. Nitroferricyanide of sodium, as a precipitant, HORSLEY, 1862.

The Microscopical Characteristics of alkaloids, in their various combinations, receive attention to some extent in all chemical literature upon these bodies, and in the description of the several alkaloids in this work. Among the special contributions are the following: HELWIG, 1865: "Das Microscop in Toxicologie." GODEFFROY and LEDERMANN, 1877: on cinchona alkaloids. WORMLEY, 1885: "Microchemistry of Poisons," 2d ed., Philadelphia. A. PERCY SMITH, 1886: identification of alkaloids by crystallization under the microscope, *Analyst*, **11**, 81.

On Microsublimation of Alkaloids: HELWIG, 1864: *Zeitsch. anal. Chem.*, **3**, 43; "Das Microscop in Toxicologie," 1865. GUY, 1867: *Phar. Jour. Trans.*, [2], **8**, 718; **9**, 10, 58, 106, 195, 370; "Forensic Medicine," London, 1875. STODDART, 1867. ELLWOOD, 1868. BLYTH, 1878: *Jour. Chem. Soc.*, **33**, 313. In this work, see under Caffeine.—*The Subliming Cell* of Dr. Guy, improved by Blyth, consists essentially of a ring of glass, about ¼ inch in thickness, or from ½ to ⅝ inch. This glass ring rests on an ordinary "cover-glass"—a thin disc used under this name in microscopy. Another cover-glass is placed upon the ring, which is of a diameter to fit the cover-glasses, and with them make a closed cell. The ring can be made of a section of glass tubing by grinding the edges. The cell, so constituted, was heated by Dr. Guy through a brass plate on which it rested. Dr. Blyth prefers to rest the cell upon liquid metal, using mercury for temperatures below about 100° C., and fusible metal for temperatures above this point. The liquid metal is contained in a porcelain capsule of about 3 inches diameter, supported on the ring of a retort-stand, and heated directly by the flame. A flask of suitable size, from which the bottom has been removed, is placed over the capsule, upon the ring of the retort-stand, and made to carry the thermometer, held in a perforated stopper and with its bulb immersed in the liquid metal by the side of the subliming cell.—A minute speck of the article tested is placed on the lower disc of the cell. Blyth's definition of a sublimate is this: "The most minute films, dots, or crystals, which can be observed by a quarter-inch power, and which are obtained by keeping the subliming cell at a definite temperature for sixty seconds."

ALOINS.—Varieties of a neutral crystalline principle obtained from the several kinds of aloes. As first described (T. & H. Smith, 1851), it was obtained from Barbadoes aloes, and was the body now named barbaloin. There have been described:

	Aloes.	*Yield.*[1]	Sommaruga and Egger, 1874.
Barbaloin	Barbadoes	20–25 per cent., at most, Tilden, 1872.	$C_{17}H_{20}O_7$
Nataloin	Natal	16–25 per cent., at most,	$C_{16}H_{18}O_7$
Socaloin	Socotrine Zanzibar	3 per cent. average, Plenge, 1885.	$C_{15}H_{16}O_7$

Tilden ascribes to barbaloin the formula $C_{34}H_{36}O_{14}.H_2O$, and to nataloin $C_{35}H_{28}O_{11}$; and Flückiger (1871) obtained for socaloin $C_{34}H_{38}O_{15}.5H_2O$.

Aloins are *identified* by their color-reactions with nitric and sulphuric acids, by which, also, and by production of chrysammic acid, they are distinguished from each other (*d*). Aloes is found in mixtures by treatment with acids, or by extraction with amyl alcohol and treatment with various reagents (*d*, p. 55). Chrysammic Acid, p. 56. As to physiological effects, with reference to valuations, *b*, p. 55.

a.—*Barbaloin*, crystallized from a concentrated aqueous solution of Barbadoes aloes, appears in tufts of small yellow prisms, losing 2.69 per cent. of water by drying at 100° C. or in vacuum. *Nataloin* exists in a crystalline state in Natal aloes, from which it is left on treating with an equal portion of alcohol at 48° C. or under, and when recrystallized forms thin, brittle, rectangular scales with some of their angles truncated. It loses no water at 100° C. *Socaloin* exists in Socotrine or Zanzibar aloes in prisms of good size; when recrystallized from methyl alcohol, tufted acicular prisms, which may be obtained 2 to 3 millimeters long. At 100° C. it loses about 12 per cent. of water.

b.—Aloins are without odor and have the taste of aloes. Their purgative power has been questioned, and while they have

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[1] Of 18 varieties of aloes, yields of from 2.2 to 31.3 per cent. were obtained: Dragendorff, 1874: "Werthbestimmung."

had some little medicinal use as therapeutic representatives of aloes, more in Great Britain than elsewhere, yet this use has not extended, although aloin is more agreeable for administration than the aloes from which it is extracted. DRAGENDORFF states (1874: "Werthbestimmung"), on experimental data, that (1) the resins of any variety of aloes, separated as insoluble in cold water, in doses of 0.35 gram (5 to 6 grains), prove inactive; (2) that perfectly pure aloins, in doses of 0.3 to 0.5 gram (5 to 7 grains), prove inactive with many persons; and (3) that the so-called aloes-bitter, soluble in cold water and containing either amorphous aloin or oxidized products, represents the activity of the drug; also (4) that the purgative power of an aloes is measured by the quantity of bromaloin precipitated from an aqueous solution of the drug, also by the quantity of precipitate by tannic acid. Dragendorff infers that aloin is converted into bodies having the purgative action of aloes. TILDEN (1876) found that all three aloins are decidedly uncertain and variable in their action, and seem to present no advantage over an equal dose of aloes, except perhaps that griping was rather less common under their use.

c.—The aloins are soluble in water, barbaloin the most freely of the three, socaloin in about 90 parts, and nataloin very sparingly. Alcohol dissolves all the aloins, socaloin requiring about 30 parts, and nataloin about 60 parts (230 parts absolute alcohol). In ether aloins are but slightly soluble, though socaloin dissolves in about 380 parts. Aloin "from the different varieties of aloes" is described in Br. Ph. (1885) as "sparingly soluble in cold water, more so in cold rectified spirit, freely soluble in the hot fluids. Insoluble in ether."

d.—**Nitric acid** (s.g. near 1.40 or 1.42), applied to the dry aloin on a porcelain slab, gives a bright red color with *barbaloin* or *nataloin*, not with socaloin. The crimson red of barbaloin fades quickly; the blood red of nataloin does not fade unless heated (HISTED, 1871; TILDEN, 1876). Boiling with nitric acid produces chrysammic acid, $C_{14}H_4(NO_2)_4O_2$ (tetranitrodioxyanthraquinone), of intense red color, from both barbaloin and nataloin, not from socaloin. Oxalic and picric acids, in addition, are obtained from *barbaloin* by action of boiling nitric acid (distinction from socaloin or nataloin). If *nataloin* be wet with concentrated **sulphuric acid**, and then touched by the vapor of strong **nitric acid** from a glass rod or by a minute fragment of potassium nitrate, a fine blue color is obtained (distinction from barbaloin or socaloin). Concentrated **sulphuric acid**, applied to the dry substance, and followed by a minute fragment of **potassium dichromate** (as in the fading purple test for strychnine), causes a green or greenish-purple color, changing to greenish-yellow.—**Alkalies** cause the decomposition of aloins. Solutions of aloes, too, lose their bitterness and their purgative power when made alkaline (G. McDonald, 1885).

Chrysammic Acid (see above) crystallizes in gold-glittering needles, or in yellow fern-leaves resembling picric acid. It detonates on heating. It is acidulous in reaction, and of intensely bitter taste. It is insoluble in cold water, easily soluble in alcohol and in ether. It forms colored salts with metallic lustre. Potassium chrysammate crystallizes with bright green lustre, or (from acid solutions) as bright crimson needles with a slight golden reflection.

Aloes. If a grain of aloes or dry mixture be dissolved in 16 drops of strong sulphuric acid, 4 drops of nitric acid (s.g. 1.42) added, and the mixture diluted with one ounce of water, a deep orange or crimson color will be obtained. On adding ammonia the color changes to a claret. All substances containing chrysammic acid behave nearly the same in this test, except that they turn pink on adding ammonia directly to their aqueous solutions, while the solutions of aloes do not (Cripps and Dymond, 1885).—If a fluid containing aloes be extracted with amyl alcohol, the residue left by evaporating this solvent will have a bitter taste, and when this residue is dissolved in water the solution will give precipitates with bromine in potassium bromide solution, basic lead acetate, mercurous nitrate, and tannic acid, and will reduce gold chloride and Fehling's solution. The dry residue will give a blood-red color with potassium cyanide and hydroxide (Dragendorff, Lenz, 1882).

AMYGDALIN. $C_{20}H_{27}NO_{11} = 457$ (Liebig and Wohler, 1837). $C_{12}H_{14}O_4.(OH)_7.C_7H_6.CN$ (Schiff, 1870).—A glucoside which occurs in the bitter almonds and in numerous other plants which yield hydrocyanic acid by natural fermentation. The bitter almonds, after removal of the oil by pressure, are digested twice with hot 95% alcohol, and allowed to stand for some time. The alcohol is decanted and concentrated to a syrup, from which the amygdalin is precipitated by ether. The precipitated amygdalin is washed with ether and recrystallized from boiling alcohol.

Amygdalin crystallizes from alcohol in colorless scales anhydrous or with $2H_2O$, from water in transparent prisms, becoming opaque in the air, and containing $3H_2O$. It becomes anhydrous at 110–120° C. It is odorless, of a slightly bitter taste and neutral reaction, and rotates the plane of polarization to the left. It is soluble in any proportion of hot and 12 parts cold water; in 11 parts boiling and 904 parts cold alcohol (s. g. 0.819); in 12 parts boiling and 148 parts cold alcohol (s. g. 0.939); insoluble in ether. Concentrated **sulphuric acid** dissolves it with violet-red color, which turns black on warming. The other mineral acids decompose it. In contact with *emulsin* and water (10 parts amygdalin, 1 part emulsin, and 100 parts water) it is changed into benzoic aldehyde (oil of bitter almonds), hydrocyanic acid, and glucose, as follows:

$$C_{20}H_{27}NO_{11}+2H_2O=C_7H_6O+HCN+C_{12}H_{24}O_{12}.$$

Through farther change of the hydrocyanic acid, formic acid also is formed. By boiling with dilute sulphuric acid the same reaction takes place, when formic acid is always formed. 17 parts of anhydrous amygdalin, or about 24 to 25 parts (theoretically, 19 parts) of the ordinary commercial amygdalin, yield, when fermented with emulsin, one part hydrocyanic acid and 8 parts bitter-almond oil. Boiling amygdalin with aqueous alkalies or baryta changes it to ammonia and *amygdalic acid* ($C_{20}H_{26}O_{12}$).

ANALYSIS, ELEMENTARY. See ELEMENTARY ANALYSIS.

ANALYSIS OF PLANTS. See PLANT ANALYSIS.

ANALYSIS, ORGANIC. See ORGANIC ANALYSIS.

ARBUTIN. $C_{12}H_{16}O_7 = 272$.—A glucoside found (about 3.5%) in the leaves of the bearberry (*Arctostaphylos Uva-ursi*) and in a number of other plants, especially in those belonging to the order Ericaceæ. It may be obtained by precipitating the decoction with lead subacetate, freeing the filtrate from lead by hydric sulphide, treating with animal charcoal, and crystallizing.

Crystallizes in bunches of silky needles which have the composition $(C_{12}H_{16}O_7)_2.H_2O$. They become anhydrous at 100° C. and melt at 170°, have a bitter taste and neutral reaction. Sparingly soluble in cold water, readily soluble in hot water and in alcohol; slightly soluble in ether. Boiled with dilute **sulphuric acid**, or subjected to the action of emulsin or another ferment contained in the bearberry, it is converted into *hydroquinone*, $C_6H_6O_2$, and glucose. Treated with manganese dioxide and sulphuric acid, it is oxidized to *quinone*, $C_6H_4O_2$, and formic acid. It does not reduce alkaline **cupric** solution, and is not precipitated by salts of the **metals.** Concentrated **sulphuric** acid dissolves it without color. **Nitric** acid turns it black, gradually dissolving it to a yellow solution. If an aqueous solution be rendered alkaline with ammonia and then **phosphomolybdic** acid added, it becomes blue [one part in 140,000 parts water gives a distinct color—JUNGMANN, 1871: *Am. Jour. Phar.*, **43**, 205].

ARICINE. See CINCHONA ALKALOIDS.

ASPARAGIN. $C_4H_8N_2O_3=132$.—Amido-succinamic Acid. Exists already formed in asparagus (*Asparagus officinalis*) and a great many other plants. It crystallizes from the cold-water extract of asparagus upon concentration to a thin syrup, and may be purified by treatment with animal charcoal and recrystallization from hot water.

The crystals are hard, brittle, transparent prisms of the trimetric system having the composition $C_4H_8N_2O_3 . H_2O$. They are odorless, have a slight, disagreeable taste, are permanent in the air, and become anhydrous at 100° C., above which temperature they are decomposed. Asparagin is soluble in 58 parts cold and 4.4 parts boiling water; in 500 parts cold and 40 parts boiling 60% alcohol; in 700 parts boiling 98% alcohol; insoluble in absolute alcohol, chloroform, ether, and benzene; easily soluble in acids and aqueous alkalies. It forms weak compounds with both acids and alkalies. In contact with the accompanying extractive substances, yeast or casein, etc., it is changed by fermentation into succinate of ammonium (sometimes with the intervening formation of aspartate of ammonium). When boiled with acids or alkalies it is resolved into *aspartic acid* ($C_4H_7NO_4$) or amido-succinic acid, and ammonia.

Respecting the *quantitative* estimation of asparagin, see the current reports of E. SCHULZE, 1881 to 1885.

ATROPINE. See MIDRIATIC ALKALOIDS.

BAKING POWDERS. See TARTARIC ACID.

BEBIRINE. *Biberine*, $C_{18}H_{21}NO_3$, dried at 100° C.—In Greenhart or Bibirin bark (British Guiana), H. RODIE, 1835; as "*Buxine*," in bark of Buxus sempivirens or Common Box, Faury, 1830, identified with bebirine by Walz in 1860 and Flückiger in 1869; as *Pelosin*, in Pareira Brava root (Chondrodendron tomentosum and Cissampelos Pareira), Wiggers, 1839, identified with bebirine by Flückiger in 1869.

a.—A white, amorphous powder, melting at about 145° C., and decomposing at a higher temperature. Its salts of common acids are uncrystallizable, pulverulent or resinous, and white or yellowish-white.

b.—The alkaloid and its common salts are odorless, with a strong and persistent bitter taste. Its effect is held to resemble that of quinine, and is given in about the same quantities.

c.—Very slightly soluble in water (6600 parts cold, 1500 boiling); soluble in 5 parts absolute alcohol and 13 parts of ether; soluble in chloroform, benzene, amyl alcohol, and carbon disulphide. Its solutions are strongly alkaline to test-papers. The sulphate, hydrochloride, and acetate are readily soluble in water; the solutions having a neutral reaction.

d.—The alkali hydrates and carbonates give precipitates, soluble in excess of the hydrates. Precipitates are caused by potassium mercuric iodide (white), potassium iodide, mercuric chloride, gold chloride (yellow-white), platinic chloride (pale yellow), and sodium phosphomolybdate (dissolved blue by ammonia, decolored by boiling), picric acid (yellow), sulphocyanate (reddish-white). *Nitric acid dilute and potassium nitrate give a white precipitate* (Flückiger); sodium phosphate, a white precipitate. The pure alkaloid does not reduce iodic acid.

e.—Bebirine has been prepared from the different plants in which it occurs, by extraction with acidulated water, and precipitation with soda or ammonia, with a precipitate by lead subacetate and extraction therefrom by dilute sulphuric acid (or by digesting the precipitate with magnesia and extracting with alcohol or ether). Purification by animal charcoal is sometimes used instead of, or after, the lead precipitation; the object in either operation being chiefly removal of resinous matter.

f.—The precipitated alkaloid loses 8.2 p. c. water (nearly $1\frac{1}{2}H_2O$) at 100° C.—Bebirine platinic chloride $(C_{18}H_{21}NO_3)_2(HCl)_2PtCl_4$ (Bödeker).—The Hydrochloride is $C_{18}H_{21}NO_3 . HCl$.—The Sulphate $(C_{18}H_{21}NO_3)_2H_2SO_4$ [Maclagen].

BENZOIC ACID. Benzoësäure. Acide Benzoïque. $C_7H_6O_2=122$ (monobasic). $C_6H_5 . CO_2H$. Carboxyl-benzene. Without isomers.—*Sources:*—Benzoic acid is found, uncombined, in the proportion of 10 to 19 per cent., in Benzoin, the balsamic resin of Styrax Benzoin, produced in Siam and Sumatra; also in smaller proportions in Balsam of Peru, in Balsam of

Tolu? (Bussy, 1876), in fruit of Vaccinium vitis-idæa (cowberry) (O. Löw, 1879), and in the Xanthorrhœa resins. It has been found in certain plums and other fruits. In combination with ethereal bases, forming essential oils, it is found in numerous balsams and resins, and in the oils of cinnamon, bergamot, origanum, and cananga (ylang-ylang). The fragrant oil slightly pervading the Benzoin is reported to be ethyl benzoate. The benzoates frequently accompany or substitute the compounds of cinnamic acid, and sometimes occur with coumarin. The suint of sheep's wool contains benzoates (Taylor, 1876). Benzoic acid is slowly formed by the atmospheric oxidation of oil of bitter almond (benzoic aldehyde), appears among the oxidation-products of cinnamic acid and various aromatic compounds, and results from certain decompositions of albuminoids. Schulze (1885) finds benzoic acid in the heavier (phenol-containing) coal-tar oils. Hippuric acid, in decomposing urine, may change to benzoic acid.

Benzoic acid is manufactured (1) from Benzoin, either, as "flowers of benzoin," by direct sublimation,[1] or in the wet way, as "crystallized benzoic acid," by dissolving with lime, precipitating from the calcium benzoate solution by adding hydrochloric acid, and recrystallizing from hot water to remove resin. (2) From the Hippuric acid of graminivorous animals, chiefly horses and cows, by concentrating the urine, acidulating with hydrochloric acid to obtain crystallized hippuric acid, and boiling the latter with crude hydrochloric acid, when benzoic acid and the by-product glycocoll are promptly formed:

$$CH_2.NH(CO.C_6H_5).CO_2H+H_2O \\ =C_6H_5CO_2H+CH_2.NH_2.CO_2H$$

(3) From the coal-tar product, Naphthalene, $C_{10}H_8$, which by treatment with nitric acid is converted into phthalic acid. $C_6H_4(CO_2H)_2$, when the latter, heated to about 350° C. with its equivalent of calcium hydrate, in absence of air, forms the lime salt of benzoic acid:

$$2C_6H_4(CO_2)_2Ca+Ca(OH)_2=(C_6H_5CO_2)_2Ca+2CaCO_3.$$

And (4) from Toluene, of the coal-tar distillates, $C_6H_5.CH_3$, known as toluol, by formation of trichloro-toluenes ($C_6H_5.CCl_3$), and conversion of the latter to benzoic acid. The pharmacopœias require the "natural benzoic acid." Of "artificial benzoic

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[1] Loewe, 1869, and Rump, 1878, maintain that part of the benzoic acid obtained is not ready formed in the benzoin, but requires to be separated from some combination, or union with another acid. The combination with cinnamic acid, $2C_7H_6O_2.C_9H_8O_2$, has been reported.

acid" the production from toluol is increasing, and little is made from phthalic acid. (See, further, under Impurities.)

Benzoic acid may be *identified* by its behavior in sublimation (*a*), toward solvents and precipitants (*c*), in reduction to bitter-almond oil, and in its reaction with ferric salts (*d*). From Cinnamic acid it is distinguished by not being oxidized to bitter-almond oil (*g*); from Salicylic acid by the color of the ferric salt. It may be *separated* (*e*) by distillation of the free acid (2) or from its salts (1); by solution in solvents not miscible with water (3); by precipitation as free acid from aqueous solution of its salts (4); by sublimation (5); from cinnamic acid (7); from milk (8) (p. 65). It can be *estimated* by acidimetry, and by weight of the free acid, or its lead salt (*f*). Directions for examination are given (*g*) as to impurities, accompaniments, and required quality for specific uses, and with regard to the sources of its production.

a.—Benzoic acid appears in pearly, lustrous, friable, and flexible plates or needles, or in flocculent masses of plate-like or needle-form structure, of hexagonal outline. From dilute alcohol six-sided prisms are obtained. The pure acid is colorless or white; that sublimed from benzoin is frequently yellowish to yellowish-brown, and this coloration is requisite in the description of the German pharmacopœia. The coloration deepens in long keeping. (See *g*.) The pure acid is permanent in the air. Specific gravity, 1.292, at mean temperature compared with water at 4° C. (Schrœder, 1880).—It melts at 121° C. (Carnelly, 1878), and (by same authority) boils at 249° C. (480.2° F.), subliming unchanged. But at 100° C., either dry or with steam, it vaporizes perceptibly, and its vapor irritates the throat and excites coughing. By direct heat, alone, as in a test-tube moved over a flame, it vaporizes without residue, the sublimate, if slowly deposited, crystallizing in needles. The vapors redden litmus paper. From benzoates heated with phosphoric acid, or bisulphate, the same vapors and sublimate may be obtained. Benzoic acid is carried over, to some extent, with vapor of alcohol, benzene, and other solvents of low boiling points. Boiled with strong alkalies in aqueous solution it suffers change.

b.—Benzoic acid has a sharp, acid taste, and when pure is without odor. The pharmacopœial acid, from benzoin, has an agreeable aromatic odor, slight in the acid by precipitation, strong in the acid by sublimation, sometimes resembling vanilla, and by authority of the Ph. Germ. somewhat empyreumatic.

That from toluol often has an almond odor; that from hippuric acid a urinous odor.—The medicinal dose of benzoic acid does not overgo 20 grains. Locally it sometimes causes mucous irritation.—In the human body benzoic acid is converted into hippuric acid, the reaction being the reverse of that given above (p. 60), and excreted in the urine. If large quantities of benzoic acid be administered, a portion may be carried into the urine without change.—Benzoic acid is an efficient antiseptic and antiferment, more powerful than salicylic acid. ARCHER (1878) used, for infusions, saccharine liquids, etc., about 4 grains to one pound, or near 0.06 per cent. ECCLES (1885) estimates about 0.04 per cent. to be sufficient for hypodermic medicated liquids.

c.—Benzoic acid dissolves in water as follows (BOURGOIN, 1879): at 15° C. (59° F.) in 408 parts; at 20° C. (68° F.) in 345 parts; in 17 parts of boiling water. In 500 parts water of ordinary temperature (*Flückiger's Phar. Chem.*) In 372 parts water (*Phar German.*) In 333 parts at 15° C.; 250 parts at 20° C. (*Hager's Commentar.*, 2d ed.) In 2½ to 3 parts of alcohol of ninety per cent.; in 2.2 parts absolute alcohol; in 1 part of boiling alcohol. In 2 to 3 parts of ether; 7 to 8 parts of chloroform; 8 parts of benzene. Freely in petroleum benzin, amyl alcohol, and dissolves in volatile oils and in fixed oils.

Benzoic acid has a decided acid reaction to test-papers, and causes effervescence in aqueous solutions of carbonates. Carbon dioxide decomposes alkali benzoate in alcoholic solution, causing a precipitate of alkali carbonate.—The metallic benzoates are normal salts of a good degree of stability. Ferric benzoate becomes in part basic in water, and mercurous benzoate in hot water forms mercury and mercuric benzoate. Both the normal and basic lead salts are obtained. The normal benzoates are either freely or moderately soluble in water; those of lead, silver, and mercury being sparingly soluble in hot water, but precipitated by adding solutions of alkali benzoate to the metallic salt solutions in the cold. Alcohol dissolves most benzoates sparingly or freely; it decomposes the benzoates of mercury. BENZOATE OF SODIUM crystallizes, with one *aq.*, in slightly efflorescent needles; from a drop of alcoholic solution, in microscopic star-form groups. The salt dissolves, with a neutral reaction, in about 2 parts cold water, and in 13 parts of 90% alcohol, not in ether or chloroform. Ammonium benzoate crystallizes anhydrous; it loses ammonia and acquires free acid when exposed to the air. Calcium benzoate crystallizes in feathery needles, with four molecules of water, efflorescent, and soluble in 20 parts of cold water.—Cinchonidine benzoate, normal, forms short prisms, anhydrous, soluble in 340 parts of water at 10° C.—Benzoates of methyl and ethyl are colorless, oily liquids, sinking in water, of pleasant and balsamic odors, boiling respectively at 199° and 212° C., not more than slightly soluble in water, freely soluble in alcohol.

d.—Aqueous solutions of benzoates, by addition of **hydrochloric acid** or sulphuric acid; give a voluminous, crystalline, white precipitate of benzoic acid, subject to its solubilities as stated above (*c*).—**Ferric chloride** solution, in a neutral benzoate solution, gives a flesh-colored, voluminous precipitate of basic ferric benzoate, formed more quickly if the reagent be slightly basic. The precipitate is not readily dissolved by acetic acid. Free benzoic acid, in excess of saturated solution, is slowly precipitated by the normal iron salt. If the solution tested be strongly alkaline in reaction, a misleading brown precipitate of ferric hydrate may occur. The ferric succinate precipitate is red-brown.—**Silver nitrate**, in neutral solution of a benzoate, forms a voluminous white precipitate of silver benzoate, soluble in hot water, then crystallizing on cooling, somewhat more soluble in alcohol, dissolved by acetic acid, also by ammonia, not obtained with free benzoic acid.—**Acetate of Lead**, in neutral solution of a benzoate, not too dilute, gives a white precipitate of lead benzoate, somewhat soluble in excess of the reagent, soluble in hot water, dissolved by acetate of ammonium, not by ammonia. Treatment with hydric sulphide resolves the precipitate into lead sulphide and free benzoic acid, the latter being separated by hot filtration or by help of alcohol. Also, if the lead benzoate be boiled with a requisite quantity of sodium sulphate, transposition of the metals is effected, and a filtrate of sodium benzoate may be obtained.—Barium chloride and calcium chloride give precipitates only in concentrated solutions of alkali benzoates, but the precipitation is promoted by free addition of alcohol.

Metallic magnesium, or aluminium, or sodium-amalgam, in solution of benzoic acid or benzoate, acidulated with only enough sulphuric acid to cause a moderate evolution of hydrogen, on standing from half an hour to several hours. effects the reduction to benzoic aldehyde ($C_6H_5.COH$), *bitter-almond oil*, recognized by its odor. This distinctive reduction is also obtained by passing the dry vapors of benzoic acid through faintly ignited zinc-dust.—Heated, with two or three parts of **lime** or with sodium or potassium hydrate, in a small distilling apparatus, a distillate of benzene is obtained: $C_6H_5CO_2H=C_6H_6+CO_2$.—With concentrated sulphuric acid, pure benzoic is not colored, but is dissolved. If glucose be present a blood-red color is obtained, as noted under Salicylic Acid, *d.*—Pure benzoic acid does not discolor the permanganate solution, nor reduce the potassium cupric (Fehling's) solution when heated, nor blacken ammonia-silver nitrate.

e.—Separation.—(1) Water cannot be evaporated from free benzoic acid without its serious waste, and it suffers a slight loss in evaporation of its solutions in alcohol, benzol, etc. For the concentration of its aqueous solution it is to be neutralized by adding just enough sodium carbonate. Ammonia is not retained in full combination. (2) Small quantities of free benzoic acid may be distilled over with water, and for this purpose benzoates may be decomposed by adding enough sulphuric acid. (3) Free benzoic acid may be obtained from any aqueous liquid by shaking with chloroform, or benzol, or ether, or carbon disulphide. The separation is by no means complete by one application of the solvent, and the more concentrated the aqueous solution the better. The chloroform or ether is caused to evaporate from the benzoic acid spontaneously or by a current of air from a bellows. Ether does not give as dry a residue as chloroform. If the chloroform or ether or benzol solution be shaken with repeated portions of very dilute aqueous alkali, the benzoic acid is brought back into watery solution of benzoate. Also, ether, chloroform, etc., may be used upon dry materials, in separations of benzoic acid. (4) Precipitation, in a concentrated aqueous solution, by hydrochloric acid, collecting the precipitate after standing and at the coolest practicable temperature, is a convenient method of separation. The mother-liquid, or filtrate, may be shaken with chloroform to recover the acid remaining in aqueous solution. Materials such as benzoin resin may be digested with some excess of lime or alkali, and the filtrate of aqueous benzoate precipitated with acid, as in the manufacture of natural benzoic acid in the wet way. (5) The finely divided material may be heated, dry, for sublimation. In preparing the sublimed medicinal acid, the vapors are made to rise from a wide dish, through a porous paper diaphragm, and are collected upon the inner surface of a cone of sized paper, the edges being fitted or pasted close. The temperature of the sand-bath, or iron plate, should be kept some time at about 145° C. (293° F.), and gradually raised at the close to 200° C. (392° F.), the operation requiring from one to four hours. A second sublimate may be obtained after pulverizing the fused material and taking a fresh diaphragm. The Ph. Fran. directs the addition of an equal weight of sand to the powdered benzoin. An analytic sublimation, for separation from fixed impurities may be conducted in a pair of clamped watch-glasses with ground edges well fitted, or closed with a narrow ring cut out of thin asbestos cloth. (6) Precipitation with lead acetate, as indicated under *d*, serves the demands of separation from substances not forming insoluble lead compounds. (7) From cinnamic acid by precipitation of the latter, in a cold neutralized solution, with manganous sulphate or chloride, avoiding any excess of this reagent. Manganous benzoate dissolves in about 20 parts of water; manganous cinnamate is but slightly soluble in water. Ether or chloroform solution separates free benzoic from hippuric acid. (8) From milk, MEISSL (1882) adds lime to alkaline reaction, evaporates to one-fourth, adds gypsum, and dries on the water-bath. The dry mass, powdered, is extracted with alcohol, after acidulation with sulphuric acid. The alcoholic solution is neutralized with baryta, concentrated, acidulated with sulphuric acid, and extracted with ether, from which the benzoic acid crystallizes almost pure.

f.—Quantitative.—Free benzoic acid, in absence of other acids, whether taken in distillates, or residues of separative solvents, or in original materials, can be quite closely estimated *volumetrically* with a standard solution of alkali (BÖCKMAN: "Untersuchungsmethoden," 1884), using litmus as the indicator. The weighed material for estimation is treated directly with an excess of the volumetric alkali measured from the burette, stirred to bring all the benzoic acid into solution as benzoate, when the liquid is titrated back with the proper volumetric acid. Each c.c. of normal solution of alkali (after deducting c.c. of normal solution of acid)=0.122 gram of benzoic acid. Taking 1.22 gram of the material, each c.c. of decinormal solution of alkali (after deducting for the acid used in titrating back)=1 per cent. of benzoic acid.

Benzoic acid may be weighed, directly, as $C_7H_6O_2$. For this purpose the best form is that of good crystals, either from a solution or by slow sublimation. The residue obtained by spontaneous evaporation, of chloroform, ether, or other separative solvent of free benzoic acid—also a clean precipitate—may be weighed. The acid is to be dried over sulphuric acid, any excess of liquid or adhering moisture being first taken up with blotting-paper.

Salts of benzoic acid are usually treated to obtain the free acid, as above described (*e*), but they may be precipitated, in a neutral solution, by lead acetate, as stated under *d*. The lead benzoate, $Pb(C_7H_5O_2)_2$, is washed with cold alcohol acidulated with one-half per cent. of acetic acid, and dried at 100° C. The weight multiplied by 0.5416 gives the quantity of benzoic acid.

g.—Impurities.—Chemically pure benzoic acid is precisely the same in all properties, whether manufactured from the balsamic benzoin or from urine, toluol, or naphthalene; but a chemically pure acid has not been manufactured, on a commercial scale, from any source. The chief uses of benzoic acid are (1) in medicine and (2) in the production of dyes. It is used, also, for the manufacture of food flavors and as an antiseptic. For medicinal purposes the pharmacopœias designate its source as follows:

Ph. Germ.—" From benzoin by sublimation . . . yellowish to yellowish-brown . . . with odor of benzoin, somewhat empyreumatic."

Br. Ph.—" From benzoin . . . by sublimation. Not chemically pure. Nearly colorless."

Ph. Fran.—" From benzoin " prepared by alternative directions (1) by sublimation, (2) by humid method.

U. S. Ph.—White scales or needles, " having a slight aromatic odor of benzoin."

There may be two reasons for requiring medicinal benzoic acid to be sublimed from "the gum": (1) the essential oil of benzoin obtained with the sublimed acid has a stimulant effect and an agreeable odor; (2) by outlawing the artificial product the injurious impurities frequently present in it may be avoided. The artificial acid, quoted as "German benzoic acid," has been for several years priced at from one-third to two-thirds the value of the natural acid, quoted as "English benzoic acid." Undoubtedly chemically pure benzoic acid will be made from hippuric acid or from toluol (Dymond, 1883; Jacobsen, 1881), and furnished at prices lower than those for the natural acid. But hitherto, in any production of the artificial acid for medicinal uses, with little encouragement for open statement, there has been more effort to counterfeit the chemical impurities of the natural sublimed acid than to avoid the chemical impurities of the artificial product. A chemically pure benzoic acid, from any source, is acceptable for the preparation of medicinal benzoates.

In sensible properties the acid recently sublimed from benzoin has a white or pearl color if sublimed slowly, at temperature of about 125°–140° C., with rejection of the last fraction of sublimate, even this, from some varieties of benzoin, being nearly colorless. But a sharp heat, of about 200° C., gives a yellowish sublimate, becoming yellowish-brown in its last portions, and in proportion to increase of color is the distinctness of empyreumatic odor obtained, in addition to the proper ethereal and vanilla-like odor of the benzoin obtained with colorless sublimates. The acid sublimed from Sumatra or Penang benzoin has only a faint odor, not vanilla-like. Any empyreumatic oil pervading the crystals darkens gradually by action of air, and colorless samples of sublimed benzoic acid are liable to acquire a yellowish tint on long keeping. Benzoic acid well prepared in the wet way (p. 60) is in water-white crystals, larger and not so much in flocculent masses as the "flowers of benzoin." It has but a slight ethereal odor of benzoin, without empyreuma. But if it has not been crystallized from the precipitate it will contain much resin of benzoin, with some color, and will not dissolve clear in hot water.—Artificial benzoic acid is frequently obtained in distinct prismatic crystals of considerable size. That from hippuric acid is apt to have a horse-stable odor; that from toluol, an odor of bitter-almond oil; and imitated "flowers of benzoin" may have ethereal or empyreumatic odors.

Cinnamic acid is occasionally present in all varieties of benzoin. In sublimation it requires a higher heat than benzoic acid, and its vapors are denser. Sublimed benzoic acid with empyreumatic odor and yellowish-brown color is likely to contain cinnamic acid, if it were present in the benzoin. Benzoic acid from benzoin by the wet way is by no means likely to be free from cinnamic acid, if this were present in the benzoin.

The impurities incidental to sources may be enumerated as follows: In natural benzoic acid by sublimation: Ethereal oil containing more or less styrol (cinnamene, C_8H_8), vanillin ($C_8H_8O_3$) if prepared from the true Siamese benzoin (Jannasch and Rump, 1878), and sometimes empyreumatic distillate. Also cinnamic acid.—In natural benzoic acid by the wet way: Cinnamic acid, resins, calcium chloride, ethereal oil.—In the product from hippuric acid: Ammonia or nitrogenous bodies readily yielding it, substances giving the odor of urine or of the perspiration of the horse, hydrocyanic acid (a product of hippuric acid by heat), and chlorides.—In toluol-benzoic acid: Chlorotoluenes, oil of bitter almond (benzoic aldehyde)—which is formed from dichloro-toluene, while benzoic acid results from trichlorotoluene—ammonium compounds, chlorides and sulphates.

Imitated natural benzoic acid is prepared by subliming from a mixture of (odorless) artificial benzoic acid, and either benzoin or the resinous residue after sublimation of the natural acid. Also, by addition of ethereal oils, etc.

Tests.—For cinnamic acid, by its oxidation, giving benzoic aldehyde, with odor of bitter-almond oil. One gram of the acid (itself free from almond odor) with half as much permanganate of potassium, rubbed in a mortar with a few drops of water (U. S. Ph.) A mixture of the acid with equal quantity of the permanganate and ten parts of water is warmed for a short time in a test-tube (Ph. Germ.) The test is delicate and sufficient, but the decoloration of a permanganate solution has no meaning in the quest for cinnamic acid.—*For the ethereal and empyreumatic oils* peculiar to natural benzoic acid by sublimation (chemical impurities in evidence of medicinal genuineness), their reactions as reducing agents upon permanganate, or upon silver in alkaline solution, are resorted to, as follows: Of the saturated water solution, when cold, 10 c.c. are treated with about 10 drops of solution of potassium permanganate (1 to 1000). With the true sublimed acid the color changes to red-brown and brown in from 1 to 2 minutes; with natural benzoic acid by precipitation and crystallization the color changes in 4 to 8 minutes; with various samples of artificial acid treated to imitate the natural sublimate, over 2 minutes (*Hager's Commentar*, 2d ed., 59).[1]—Boil 0.1 gram of the acid with 3 c.c. of water of ammonia; add about 5 drops of silver nitrate solution, and then drops of diluted hydrochloric acid until a permanent and decided turbidity is just reached (while there is still a very slight excess of ammonia). With true sublimed benzoic acid the slight precipitate is not white, but yellowish.—Concentrated sulphuric acid, with a smaller quantity of the benzoic acid, gives a yellowish color with the sublimed acid, becoming brown at 150° C.; while at this high temperature the chemically pure acid remains colorless, and traces of hippuric acid give a brown to black color.—*For ammonium or other nitrogenous compounds* accompanying an acid made from the urine, dissolve in a wide test-tube with a little alcohol and fixed alkali to strong alkaline reaction, heating to near boiling, and testing the vapor with moistened red litmus-paper and by the odor, for ammonia.—*For chlorides and sulphates*,

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[1] Hager severely criticises the Ph. Germ. direction to give 8 hours for this reaction. Upon this and other *tests of genuineness of natural benzoic acid*, see LENKEN, 1882; SCHAER, 1882; SCHNEIDER, 1882; SCHICKUM, 1882; SCHACHT, 1881; JACOBSEN, 1881; DYMOND, 1883.

test the saturated aqueous solution with silver nitrate solution, and barium chloride solution. *For chloro-toluenes*, slowly heat a portion under solid potassium or sodium hydrate (free from chloride) on platinum foil, dissolve the mass in water, filter if necessary, acidulate with nitric acid, and test with silver nitrate solution. Or apply the blow-pipe test for chlorine, with the copper bead, as directed by the U. S. Ph.—*For hippuric acid, and gross organic and inorganic adulterations*, heat a portion to vaporization and combustion, on platinum foil or clean porcelain. It should vaporize and burn, with only a residual stain: a coaly mass or incombustible residue indicating gross impurity.—Also, apply any of the solvents of benzoic acid, chloroform, ether, benzol, or carbon disulphide. Hippuric acid is but slightly soluble in ether or chloroform.—*For hydrocyanic acid*, distil a portion with a little water, and test the distillate for conversion into sulphocyanate. If a benzoate be tested, acidulate with sulphuric acid before distilling.

The medicinal benzoates (see *c*, p. 62) are especially liable to be found with the injurious impurities of artificial benzoic acid. They should be tested, as above indicated, for cyanides, chlorinated compounds, salts of hippuric acid, etc.

CINNAMIC ACID. Zimmtssäure. Cinnamylsäure. Acide Cinnamique. $C_9H_8O_2=148$ (monobasic). Phenyl-acrylic acid: $C_6H_5.CH.CH.CO_2H$.—*Sources:* As free acid or in combination with ethereal bases, in various balsams and with resins. Balsam of Peru contains often 10 per cent. of the acid free, and a larger quantity as cinnamate of benzyl (C_7H_7); tolu balsam, 10 or 12 per cent. of cinnamic acid, mostly free; storax, a variable quantity of the acid, mostly in combination; and some varieties of benzoin contain it. It is found in large crystals in old oil of cinnamon, formed by atmospheric oxidation of cinnamic aldehyde, ($C_6H_5.CH.CH.COH$) the cinnamon oil itself. The leaden packages in which oil of cinnamon is imported sometimes furnish a deposit of lead cinnamate with free cinnamic acid. It is producible from benzoic aldehyde. Further, see *g*.

Cinnamic acid is *characterized* by its crystalline form in a sublimate (*a*) and its precipitation as free acid (*c*). It is revealed, when only in traces, by its oxidation to benzaldehyde (*d*), a distinction from benzoic acid. Its metallic precipitates are not markedly characteristic, that with iron resembling benzoate (*d*). It is *separated* by methods used for benzoic acid, and from the latter with some difficulty (*e*). *Estimated* gravimetrically as free acid (*f*). Its natural combinations, and sources of production, are described in *g*.

a.—Cinnamic acid is a colorless solid, crystallizing (from vapor or solution) in monoclinic prisms or plates. Specific gravity (at mean temperature, water at 4° C. as 1.) 1.247 (Schrœder, 1879). It melts at 133° C. (271.4° F.) (Miller, 1877; Tiemann and Herzfeld, 1877). It boils at 300° to 304° C. (572°–579° F.) (E. Kopp, 1849), suffering partial decomposition unless heated gradually, the products containing cinnamene (C_8H_8), stilbene, carbon dioxide, etc. It vaporizes much below its boiling point.

b.—Without odor, and of an aromatic, slightly sharp taste. The vapors are pungent and excite coughing.—In doses of 5 to 6 grams (80 to 90 grains) it causes a just perceptible irritation of the throat. After its administration the urine contains cinnamic acid with hippuric acid, the latter probably preceded by oxidation to benzoic acid (Erdmann and Marchand, 1842).

c.—Very sparingly soluble in cold water, moderately soluble in boiling water, freely soluble in alcohol, soluble in ether. With litmus and other indicators it shows an acid reaction. The metallic cinnamates are monobasic, stable salts. Those of the alkali metals are soluble in water; of alkaline-earth metals more soluble in hot water; most others little soluble in water. Aqueous solutions of alkali cinnamates, on adding an acid, give a precipitate of cinnamic acid. By dry distillation they yield, among other products, benzaldehyde. Ethyl cinnamate boils at 266° C., is of specific gravity 1.3, nearly insoluble in water, soluble in alcohol and in ether. Methyl cinnamate has a specific gravity of 1.106, boils at 241° C., and is insoluble in water. Kraut and Merling (1881) mention a compound of cinnamic acid with hydrochloric acid.

d.—Oxidized with **permanganate of potassium,** or with dichromate of potassium and sulphuric acid, cinnamic acid yields benzaldehyde, or bitter-almond oil, recognized by its odor. The solid material may be treated with half as much solid permanganate, rubbing with a little water in a mortar. Or the solution may be charged with permanganate solution, and warmed. $C_6H_5.CH.CH.CO_2H+4O=C_6H_5.COH+2CO_2+H_2O$. The oxidation may continue to the conversion of the benzaldehyde into benzoic acid.—**Ferric salts** with solutions of cinnamates give a yellow precipitate of ferric cinnamate; **manganous** salts with excess of cinnamates, a white precipitate (none with benzoates); **lead** acetate, a precipitate of lead cinnamate; and **silver** nitrate, a stable white precipitate of normal silver cinnamate. The barium and calcium precipitates dissolve in hot water.

e.—Aqueous solutions of free cinnamic acid can be concentrated, and the residue can be dried on the water-bath, without loss of more than traces of the acid. Sublimation cannot be employed, under ordinary conditions, without waste by decomposition. Precipitation of cinnamic acid, in cold and not dilute solutions of cinnamates, by adding hydrochloric acid, serves well for separation. The free acid may be dissolved from aqueous or dry mixtures by repeated portions of ether.—Benzoic and salicylic acids are liable, if present, to appear in separates with cinnamic acid. Among solid sublimable acids may be further named succinic and gallic acids, but these are soluble in water. As to separation of cinnamic from benzoic acid, see the latter (*e*, 7, etc.)

f.—Cinnamic acid may be weighed, as $C_9H_8O_2$. For this purpose it may be prepared in crystals from alcohol or hot water, or in residue from ether, or in precipitate from cold concentrated solution.

g.—The appearance of cinnamic acid in analysis raises the question of its production, or liberation, by the operations of the analysis, from an ethereal salt of cinnamic acid, or from its aldehyde, or alcohol. Cinnamein, benzyl cinnamate, making a large part of Peru balsam and a small part of tolu balsam, is liquid at ordinary temperature, neutral in reaction, of sp. gr. 1.098 at 14° C., boiling with some decomposition at 340°–350° C., not soluble in water, soluble in alcohol, ether, or carbon disulphide. Styracin, cinnamyl cinnamate, is found in storax, crystallizing in needles or four-sided prisms, of sp. gr. 1.085 at 16° C., melting at 38° to 44° C., and distilling with steam at 180° C. without decomposition. It is insoluble in water, soluble in hot alcohol and in ether. Both cinnamein and styracin are easily saponified by digestion with fixed alkali or alkali carbonate, when the aqueous solution, by acidulation with hydrochloric acid, yields cinnamic acid. The styrone of storax and Peru balsam is cinnamic alcohol ($C_6H_5.CH.CH.COH_3$); and the cinnamene or styrol, of storax, is the related hydrocarbon, $C_6H_5.CH.CH_2$. The union of benzoic acid with cinnamic acid, $(C_7H_6O_2)_2C_9H_8O_2$, melts at 95° C.

BENZOYL-ECGONINE. See Coca Alkaloids.

BERBERINE. $C_{20}H_{17}NO_4=335$.—The yellow alkaloid of

Hydrastis canadensis, species of Berberis and Coptis, and other plants. As a hydrochloride, often commercially named *hydrastine.*[1]

Found as follows:

In Hydrastis canadensis, Ranunculaceæ, 1.3 to 1.8 per cent. (Lloyd).
" Coptis trifoliata, 4% (Perrins).
" " teeta (India), 8.5% (Perrins).
" Xanthoriza apifolia.
" Berberis vulgaris, Berberidaceæ, 12% (Perrins).
" " aquifolium.
" " aristata.
" Jeffersonia diphylla.
" Caulophylum thalictroides (Husemann's Pfl.)
" Jateorrhiza calumba (calumba root), Menispermaceæ.
" Minispermum canadense.
" Coscinium fenestratum (Ceylon calumba wood).
" Cœlocline polycarpa, Anonaceæ.
" Xanthoxylum clava Herculis, Rutaceæ.

In several of these sources berberine is accompanied with a colorless alkaloid. Its chemical relation to hydrastine is mentioned in the description of the latter.

Berberine responds to the general tests for alkaloids (*d*), among which it is at once *distinguished* by its color and by the crystalline precipitations of its hydrochloride and nitrate (*d*). These precipitations, as well as its abundant solubility as a free alkaloid in hot water, serve to *separate* it from other alkaloids. Its separation from its vegetable sources is outlined, with references, under *e*. It is *estimated* as free alkaloid or crystalline salt, gravimetrically; by Mayer's solution, volumetrically.

a.—In brown-red pencils, grouped in irregularly radiate clusters; also in branched, curved, and pointed prolongations; sometimes appearing orange-red to yellow. In amorphous and ob-

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[1] As first found in different plants, this alkaloid was named as follows:

In Geffraya inermis, bark,	by Huttenschmid,	in 1824, as *jamaicine.*
" Xanthoxylum clava H.,	by Chevallier and P.,	in 1826, as *xanthopicrite.*
" Hydrastis canadensis,	by Rafinesque,	in 1828, as *hydrastine.*
" Berberis vulgaris,	by Buchner and H.,	in 1830, as *berberine.*

"We . . . think it unfortunate that, since the name Hydrastis was accepted by botanists, it was not followed by chemists in the naming of its prominent constituent, the yellow alkaloid": J. U. and C. G. Lloyd, in "Drugs and Medicines of North America," 1884, p. 98.—An early paper on this alkaloid was that of J. D. Perrins, 1862: *Jour. Chem. Soc.*, 15, 339.

scurely crystalline forms it is yellow. At 120° C. it melts to a red-brown resinous mass. As crystallized from water, it loses 19.26% water at about 100° C. (Fleitmann), indicating about $5H_2O$ of crystal-water in air-dry crystals.—The hydrochloride, $C_{20}H_{17}NO_4HCl.2H_2O$, forms large, lustrous, golden-yellow crystals, in pencils, with ends both square and oblique, slightly grouped.—The *hydrobromide*, normal with $1\frac{1}{2}H_2O$, forms bright yellow, fine needles.—The *hydriodide*, normal, forms reddish-yellow needles.—The *nitrate* is a normal salt, in clear yellow needles.—Berberine *sulphate*, $(C_{20}H_{17}NO_4)_2H_2SO_4$, crystallizes in irregular oblong plates of garnet-red color, or in stellate spangles of lemon-yellow to orange-yellow color.—Berberine acid phosphate, $C_{20}H_{17}NO_4(H_3PO_4)_7$,[1] is a canary-yellow powder.

b.—Berberine and its salts are inodorous and of a bitter taste. It is given, medicinally, in doses of 2 to 5 grains; 60 grains having been taken without injury. Small animals are poisoned by it; 1 gram subcutaneously causing the death of dogs in 8 to 40 hours.

c.—The free alkaloid is soluble in about 500 parts of cold water, freely soluble in boiling water; sparingly soluble in cold, freely soluble in hot, alcohol; insoluble in ether or in petroleum benzin; slightly soluble in chloroform or in benzene.—Its solutions have a neutral reaction. In salts or from acidulated solutions it is imperfectly taken up by benzene, chloroform, or amyl alcohol, not by petroleum benzin.—It is permanent in the air and in solutions.—The solubilities of salts of berberine are indicated under *d.*

d.—The **caustic alkalies** color berberine brown, with formation of a resinous mass on boiling. On acidulating an aqueous solution of berberine with **hydrochloric or nitric acid** the salt of the alkaloid quickly crystallizes in bright-colored crystals, mostly golden yellow, thrown out of solution more perfectly by adding a considerable excess of the acid. The hydrochlorate is soluble in about 500 parts of water or 250 parts of alcohol (from data of Lloyd); the nitrate is very slightly soluble in dilute nitric acid (Perrins); the normal sulphate, in 10 parts of water or 293 parts of alcohol (Lloyd); the super acid phosphate, in 10 parts of water.

The *general reagents for alkaloids* give precipitates of berberine, mostly yellow—the phosphomolybdate turning blue on

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[1] Parsons and Wrampelmeier, 1877; Coblentz, 1884.

adding ammonia. The red-brown precipitate by iodine in potassium iodide solution, when crystallized from hot alcohol, appears in green, iridescent scales.—Concentrated **sulphuric acid** gives a brown to orange color; turning black to violet by adding **dichromate,** as in the fading-purple test for strychnine. **Froehde's reagent** gives a green to brown color. **Chlorine** water added to an aqueous acidulous solution of the hydrochloride gives a band of bright-red color at the point of contact, visible as a rose tint in a dilution to 250000 parts (KLUGE, 1875).—By distillation with milk of lime, or with lead dioxide, quinoline is obtained.

e.—Berberine is *separated* from Hydrastis canadensis (or other plant containing it), according to PERRINS (1862), by treating with boiling water to prepare a concentrated extract, extracting this with alcohol, adding a little water and distilling off the alcohol, then adding dilute nitric acid (Perrins) or hydrochloric acid in some excess, and leaving several days for the crystallization of the salt. To obtain the free berberine, add calcium hydrate or barium carbonate, extract with hot alcohol, and, after evaporating off the alcohol, crystallize from a hot watery solution, drying the crystals at a temperature not above 25° C. For the preparation of the various salts of berberine, as well as its recovery from the vegetable drugs containing it, see Lloyd's "Drugs of North America," **1**, 98.

From most alkaloids berberine is separated (1) by its greater solubility as free alkaloid in hot water; (2) by its much smaller solubility as hydrochloride in dilute hydrochloric acid. As to separations by the solvents immiscible with water, see (*c*), p. 73.

f.—*Quantitative.*—Berberine may be weighed as free alkaloid, anhydrous, by drying at 100°–110° C. The nitrate, normal, anhydrous, may be dried at 100° C. for weighing (PERRINS). The precipitate by potassium mercuric iodide, washed and dried at 100° C., contains very nearly 50 per cent. of anhydrous berberine (BEACH, and the author, 1876), corresponding nearly to the composition $(C_{20}H_{17}NO_4)_2(HI)_2HgI_2$ (48.55%). In the volumetric method by Mayer's solution Beach found the value of a c.c. of the solution to be 0.0425 gram of the anhydrous alkaloid. In results reported by the author in 1880[1] the washed iodomercurate was found to contain a mean of 52.10% of the alkaloid. Perrins weighed the washed and dried precipitate of platinic chloride $(C_{20}H_{17}NO_4)_2(HCl)_2PtCl_4$.

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[1] "Estimation of Alkaloids by Potassium Mercuric Iodide," *Am. Chem. Jour.*, **2**, 303.

BRUCINE. See STRYCHNOS ALKALOIDS.

BUTTER. See FATS and OILS.

BUTYRIC ACID. $C_4H_8O_2=88$ (monobasic). Normal butyric acid, or propyl-carboxyl, $CH_3CH_2CH_2.CO_2H$.[1]—The butyric acid of glycerides of milk fat, and of the butyrous fermentation, following the lactous fermentation, of sugar. Found among the fat acids of cod-liver oil.

Normal butyric acid is *characterized* by its odor when free and by the very different odor of its ethyl ester (*d*). It is *separated* by distillation, by solution in ether, and by the solubility of its calcium salt in alcohol (*e*). It is *estimated* by the acidimetry of the free acid (*f*). Further, see under Butter Fats, Index.

a.—Normal butyric acid is a colorless, limpid liquid, solidifying in tabular forms at —19° C., having a specific gravity of 0.958 at 14° C., boiling at 162.3° C., distilling completely by itself, better with water, and vaporizing at common temperature. Its oil-spot on paper is not permanent.

The butyrates are crystallizable, in tabular or needle-shaped forms, usually with fat-lustrous surfaces. When quickly heated they carbonize abundantly; when slowly heated they evolve rancid-smelling vapors and carbonize slightly.

b.—The odor of pure normal butyric acid somewhat resembles rancid butter, but is less disagreeable and more pungent, approaching to the acetous odor. The taste is acidulous and biting, and unless diluted it is somewhat caustic to the tongue and irritating to the skin. Its glyceride, conjugated with glycerides of non volatile fat acids, is a food constituent especially provided for the young in the order of nature. Ethyl butyrate has a fragrant odor of the pineapple, in which it is found.

c.—*Solubilities.*—Normal butyric acid is freely soluble in water, though but little soluble in aqueous solutions of sodium chloride and various other salts. It is freely soluble in alcohol and in ether. The solutions redden litmus, and decolor alkaline phenol-phthalein solution. The metallic butyrates, for the most part, save those of silver and lead, are soluble in water, and some

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[1] There are two butyric acids, as four-carbon members of the fatty acid series, CnH_2nO_2. The other one is Isobutyric acid $(CH_3)_2CH.CO_2H$. or dimethyl acetic acid. Isobutyric acid is found among the fat acids of castor oil.

of them dissolve in alcohol. Alkali butyrates are neutral to litmus. Ethyl butyrate is sparingly soluble in water, soluble in alcohol in all proportions.

d.—Normal butyric acid is identified by its pungent, rancid odor when free (*b*), and the pineapple odor of its ethyl ester, while its glyceride and its alkali salts are nearly odorless. Warming butyric acid or a metallic butyrate with a little **alcohol** and about twice as much undiluted **sulphuric acid,** the ethyl butyrate is readily formed, and odor obtained. If the butyric acid is free, in dilute solution, it should be neutralized with alkali and the solution concentrated for the test. Ethyl butyrate is stable, not readily saponified. Glyceride of butyric acid, butyrin, should be saponified by alcoholic potash before applying the test.—Calcium or barium chloride does not precipitate moderately dilute solutions of butyric acid or its salts. Silver nitrate gives a precipitate in moderately concentrated solutions. Lead acetate and subacetate, in moderately concentrated solutions, give precipitates which dissolve in alcohol or hot water, and melt on heating. Ferric chloride, in solutions of butyrates, gives a brownish-yellow precipitate, as formed in dilute solutions much resembling the benzoate, and not formed by free butyric acid except in concentrated solutions.

e.—Separation.—Normal butyric acid, in alkali salt solutions, can be concentrated on the water-bath without loss. By treating metallic butyrates with phosphoric acid or dilute sulphuric acid, and distilling persistently, all the butyric acid can be obtained.

Butyric acid is separated from acetic and other homologous acids by the greater solubility of barium butyrate in alcohol: The free acids are saturated with barium hydrate solution, the mixture concentrated enough to stiffen when cold, then treated with about ten parts of strong alcohol, set aside one or two hours, and filtered, washing with alcohol. The residue will contain the most of the acetate, while the butyrate will mainly be in the solution. Of absolute alcohol, 1000 parts dissolve 11.72 parts of barium butyrate, 0.28 parts of barium acetate, 0.05 parts barium formate, and 2.61 parts of barium propionate (Lucke, 1872).

Butyric acid may be recovered from aqueous mixtures, as a free acid, by saturating with sodium chloride or with calcium chloride, and shaking with ether. From the ethereal solution it is recovered, as alkali salt, by shaking with a slight excess of fixed alkali solution, or as free butyric acid, with only slight waste, by the spontaneous evaporation of the ether.

f.—Quantitative.—Butyric acid is estimated with ease, volumetrically, by standard solutions of alkali, fixing the neutral point either with litmus-papers or, more exactly, with phenolphthalein. Each c.c. of normal alkali saturates 0.088 gram, and each c.c. of decinormal alkali saturates 0.0088 gram, of absolute butyric acid. Of a mixture containing no other acid, if 4.4 grams be taken, c.c. of N alkali × 2 = per cent. of free butyric acid, or c.c. of $\frac{N}{10}$ alkali × 20 = per cent. of free butyric acid.

CAFFEINE. Theine. Guaranine. Coffein or Koffein. Cafeine (French). Methyl-theobromine. $C_8H_{10}N_4O_2=194.$[1] (Crystallizes with 1 *aq.;* also, anhydrous.)—A trimethyl xanthine: $C_5H(CH_3)_3N_4O_2$;[2] xanthine being producible from guanine, or uric acid.

In Tea	(prepared leaf of Camellia Thea),	2 to 3 per cent.
" Coffee	(dried seed of Coffea arabica),	1 per cent.
" Guarana	(crushed seed of Paulinia sorbilis),	4 per cent.
" Maté	(leaf of Ilex paraguayensis),	1½ per cent.
" Cola nut	(seed of Sterculia acuminata),	2 per cent.

These percentages are given to represent average yields.[3]

Caffeine is producible from theobromine and from xanthine (Strecker, Fischer)

Caffeine is *identified* by the murexoin test (*d*), and the form in which it crystallizes under the microscope (*a*). It shares its most distinctive tests with Theobromine, from which it differs greatly in solubilities. It is *distinguished from most other alkaloids* by non-precipitation with potassium mercuric iodide, by yielding cyanide when smelted with soda-lime (*d*), and by dissolving in water, and from acidulous mixture dissolving in chloroform, etc. (*c* and *e*). It is *separated* as stated under *e*, and *estimated* in tea, coffee, guarana, etc., by its weight, as obtained (1) by extracting with water and dissolving the residue in ether, (2) by extracting with water (and alcohol) and shaking out with chloroform, (3) by extracting with chloroform and dissolving the residue in water, (4) by sublimation (*f*). Tests for impurities, *g*.

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[1] Pfaff and Liebig, 1832: *Ann. Chem. Phar.*, **1**, 17.

[2] Strecker, 1861: *Ann Chem. Phar.*, **118**, 72, 151. E. Fischer, 1882: *Ann. Chem. Phar.*, **215**, 253–320; *Jour. Chem. Soc.*, 1883, Abs, 354. E. Schmidt, 1883.

[3] For tea and coffee and guarana, Dragendorff, 1874: "Werthbestimmung," 56. Squibb, 1884: *Ephemeris*, 606, 614, 616. For Paraguay tea, Byasson, 1878. For Cola nut, Heckel and Schlagdenhauffen, 1884: *Phar. Jour. Trans.*, *Am. Jour. Phar.* Also, Attfield, 1865. E. Schmidt (1883). And report of J. F. Geisler in article "TEAS" in this work.

a.—Caffeine appears in long, slender, flexible white crystals, of silky lustre, forming light, fleecy masses. The crystals have a specific gravity of 1.23 at 19° C. They are permanent in the air. On the spontaneous evaporation of a drop or two of an aqueous or chloroformic solution, dilute enough to crystallize slowly, on a glass slide, characteristic crystals are identified by a magnifying power of 100 to 300 diameters. The forms are chiefly acicular; finely pointed needles of some thickness at their overlapping basal ends making irregularly stellate groups, with a few separate needles. Among these, of later appearance and requiring the higher power above named, are the more characteristic forms, namely: six-sided crystals, dihexagonal pyramids and prisms, with a few rhombohedrons. From the chloroformic solution the stellate groups are found each with a single hexagonal crystal in its centre.

Anhydrous crystals are said to be obtained from ether or absolute alcohol. Dragendorff[1] directs to dry at 100° C. for a constant weight of anhydrous alkaloid; Commaile (1875) gives the same direction. Blyth (1878) states that at 79½° C. minute microscopic crystals in sublimate can be obtained, and a complete sublimation in long, silky crystals readily obtained near 120° C.; also that the high subliming points given by Pelouze and Mülder must have been given from faulty methods. When anhydrous, caffeine melts at 234° C. (Strecker, 1861), and the melted mass boils at 384° C. with partial decomposition, leaving no residuum.

b.—Caffeine is without odor and with a bitter taste. The maximum medicinal dose is about 3 grains: Br. Phar. dose 1 to 5 grains; Ph. Germ. maximum single dose 3 grains.[2]

c.—Caffeine is sparingly soluble in cold water; freely soluble in hot water and in chloroform; moderately soluble in alcohol and in benzene; slightly soluble in ether; nearly insoluble in petroleum benzin or carbon disulphide. Combination with acids scarcely hinders its solubility in chloroform or benzene. More particularly, *the hydrated crystals dissolve* in 68 parts of water at 15° to 17° C. (Commaile[3]); in 75 parts water at 15° C. (U. S. Ph.); in 80 parts cold water (Ph. Germ., Br. Ph.); in 9.5 parts of boiling water (U. S. Ph.); 10 parts boiling water (Hager's

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[1] "Werthbestimmung," 1874, p. 57.

[2] For physiological assays of tea, coffee, and guarana, in comparison with caffeine, Squibb, 1884: *Ephemeris*, **2**, 603, 610, 615, 617.

[3] 1875: *Compt. rend.*, **81**, 817; *Jour. Chem. Soc.*, 1876, i. 779.

Commentar); 2.01 parts water at 65° C. (Commaile). In alcohol of about 90 per cent., 35 parts at 15° C. (U. S. Ph.), 50 parts (Ph. Germ.), 40 parts at 15° to 17° (Commaile); in absolute alcohol it is less soluble, in 155 parts (Hager's Commentar). In ordinary ether it dissolves in 476 parts at 15° to 17° C. (Commaile), 600 parts (Hager). *The anhydrous alkaloid* dissolves in 75 parts water at 15° to 17° C (Commaile); in 165 parts absolute alcohol at 15° to 17° C. (Commaile); in 32 parts boiling absolute alcohol (Commaile); in 8 parts chloroform at 15° to 17° C., or 5¼ parts boiling chloroform (Commaile); in 2288 parts of anhydrous ether at 15° to 17° C. (Commaile); in 4000 parts of petroleum benzin at 15° to 17° C. (Commaile).

Caffeine is neutral to test-papers, notwithstanding its solubility in water. It is a very feeble base. Salts of caffeine are formed only by action of concentrated acids upon the alkaloid; they are all decomposed by water, alcohol, and ether, and those of volatile acids are decomposed by exposure to the air (E. Schmidt).[1] Many of the salts crystallize in needles, the hydrochloride, $C_8H_{10}N_4O_2.HCl$, in monoclinic forms. The caffeate crystallizes as $C_8H_{10}N_4O_2.C_8H_8O_4.2H_2O$. The sulphate has been obtained, from hot alcoholic solution, in crystals of the composition $C_8H_{10}N_4O_2.H_2SO_4$ (Schmidt). The citrate was reported by Lloyd (1881) as a possible definite salt, but so frail that it is decomposed by solvents which dissolve citric acid readily and caffeine sparingly: it is given by the Br. Ph. with the formula $C_8H_{10}N_4O_2.H_3C_6H_5O_7$ (implying that caffeine is here a tri-acid base). The double salts of caffeine are less instable (see *d*, platinum, etc.)

d.—Caffeine responds promptly to "*the murexid test*" as follows: A portion of solid material or a residue by evaporating a liquid to be tested, not over a grain or two at most, is taken in a white porcelain evaporating-dish, heated on the water-bath, then covered with from one to five drops of hydrochloric acid, when at once a minute fragment of **potassium chlorate** is added, the mixture evaporated to dryness and well dried on the water-bath. When cold the residue is slightly moistened with **ammonia** water applied by the point of a glass rod. In evidence of caffeine a purple color (that of *murexoin*) is obtained after the action of ammonia; a reddish-yellow to pinkish color before the action of ammonia. 0.00005 gram of caffeine, in a residue small enough to be covered by one drop of hydrochloric acid, yields decisive evidence by this test. Fuming nitric acid,

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[1] 1881: *Ber. d. chem. Ges.*, 14, 814; *Jour. Chem. Soc.*, 1881, Abs., 746.

or chlorine water, serves as the oxidizing agent, but less efficiently. The products of the oxidation include amalic acid and hydrocyanic acid.[1] By the action of ammonia the murexoin is formed. The amalic acid and murexoin are tetramethylated derivatives of the corresponding products obtained in the murexid test of uric acid, thus:

	By the oxidation (with other products).	*By the action of ammonia.*
Uric acid:	Alloxantin, $C_8H_4N_4O_7$.	Murexid, $NH_4.C_8H_4N_5O_6$.
Caffeine:	Amalic acid, $C_8(CH_3)_4N_4O_7$.	Murexoin, $NH_4.C_8(CH_3)_4N_5O_6$.

The murexoin purple from caffeine is decolored and *not* turned blue, by adding potassium hydrate solution, a distinction from the murexid purple from uric acid. The amalic acid stains the skin red (also a characteristic of alloxantin).

Tannic acid precipitates caffeine from aqueous solutions not very dilute, the precipitate being somewhat soluble in excess of the reagent.—**Phosphomolybdate** of sodium gives a yellowish precipitate, soluble in warm sodium acetate solution, from which free caffeine separates on cooling (Sonnenschein).—Platinum chloride and hydrochloric acid with concentrated solution of caffeine gives an orange-colored precipitate, dissolving when heated, crystallizing on cooling $(C_8H_{10}N_4O_2.HCl)_2.PtCl_4$, soluble in 20 parts of water (Stahlschmidt).—Potassium bismuth iodide gives a precipitate on standing, soluble in 3000 parts water (Thresh, 1880).—No precipitates are obtained with potassium mercuric iodide, or with iodine in potassium iodide solution (distinction of caffeine, theobromine, and colchicine from nearly all other alkaloids).—On heating caffeine with solid potassium hydrate, or boiling with strong solution of this reagent, methylamine is evolved and recognized by its strong, ammonia-like odor. Strongly heating a dry mixture of caffeine and soda-lime, ammonia is evolved, as with other alkaloids, while, in distinction from most other alkaloids, a part of the nitrogen is retained in cyanogen, as alkali cyanide, revealed by treating the mass with water and testing a filtered portion for cyanides.

e.—Separations.—Caffeine can be separated from the greater number of alkaloids by its greater solubility in water, and by its being dissolved from acidulous mixtures by chloroform, benzene, and (sparingly) by ether. From non-volatile matters it is separable by careful sublimation from a well-dried, finely powdered mass, at 100° to 150° C. (Blyth). Separations from tea, coffee, guarana, etc., are presented under *f.*

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[1] Rochleder, 1849: *Ann. Chem. Phar.*, 71, 1. Schwarzenbach, 1859.

f.—Quantitative.—The quantity of caffeine is determined gravimetrically by weighing the alkaloid. According to BLYTH (1878) dry caffeine begins to sublime at 79.5° C. (175° F.), but the same author states[1] that, so far as decided by his experiments, loss of the alkaloid does not occur at 100° C. until the material is quite dry, and there is no testimony to show that loss occurs from concentrating limpid aqueous solutions on the water-bath. At all events this has been done in many assay methods. And in nearly all methods except Blyth's it is directed to dry residues or crystals of caffeine at 100° C. for weight, an exposure to which the author just named demurs.

For estimation of the caffeine in tea, coffee, guarana, maté, or cola several processes are serviceable, as follows:[2] 1. DRAGENDORFF's process requires to exhaust 5 grams of the substance by maceration with boiling water, evaporating the filtrate with 2 grams magnesia and 5 grams of ground glass.[3] The pulverulent residue is transferred to a flask, macerated with 60 c.c. of ether for 24 hours, filtered, and the residue treated three or four times with the same quantity of ether. The ether is evaporated and the residue weighed. A smaller quantity of chloroform may be substituted, but does not give as pure alkaloid.

2. Dr. SQUIBB (1884) takes 10 grams of powdered *guarana* and 2 grams of calcined magnesia, boiling with 100 c.c. of water for five minutes, adding while hot 50 c.c. of strong alcohol, draining on a filter, and percolating the residue with a mixture of 60 c.c. of water and 40 c.c. of alcohol. Boil the residue again with 100 c.c. of this mixture of alcohol and water, and drain and percolate until exhausted, or until the total liquid amounts to 300 or 350 c.c. Evaporate this on a water-bath to about 20 c.c., and transfer to a separator, rinsing with a little water. Shake out with three or four portions each of 25 c.c. of chloroform. The chloroform solution is evaporated in a tared beaker for weight. The last chloroform washing may be evaporated in a separate

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[1] "Foods," 1882, p. 330.

[2] DRAGENDORFF, 1874, 1882: "Werthbestimmung," 57: "Plant Analysis," London, 1884, 62, 186. SQUIBB, 1884: *Ephemeris*, **2**, 606, 614, 616. BLYTH, 1877, 1882: *Analyst*, **2**, 39; "Foods," 330. COMMAILE, 1875: *Compt. rend.*, **81**, 817; *Jour. Chem. Soc.*, 1876, i 779.

[3] Those who depend upon the "extraction apparatus" for exhausting drugs in estimation may prefer to apply hot water to the drug by continuous percolation in this apparatus, heated by a sand-bath. Then the smaller quantity of solution can be evaporated in the receiver of the apparatus, after adding the magnesia and sand, by aid of a "filter-pump," at temperature not above 78° C.; and the final residue by evaporation of the ether, dried below 80° C. —A. B. P.

tared capsule for indication of the completion of the extraction. The caffeine is white and nearly pure. Further purification is done by dissolving in least sufficient quantity of hot water and letting the filtrate spontaneously evaporate to dryness.—*For tea* the directions are nearly the same, except that a coarse powder is taken, no alcohol is used, and the larger, more dilute portion of the percolate is concentrated by itself.—*For coffee* the method was the same as for tea (exhausting with water), except that when the percolate had been nearly evaporated 60 c.c. of alcohol were added, and the resulting precipitate filtered out and washed with a mixture of alcohol 3 and water 1, when the entire filtrate was evaporated to 20 c.c. This treatment is adopted to prevent the gelatinizing of the albuminous matter by the chloroform.

(3) **Commaile** directs to prepare 5 grams of the material with 1 gram of calcined magnesia in a firm paste, which is to stand 24 hours, and is then dried on the water bath [or in an air-bath below 80° C.] and powdered. It is then exhausted with boiling chloroform [applied in an extraction apparatus, from the receiver of which the chloroform is then distilled] and the residue dried [at a gentle heat]. 10 grams of powdered glass, previously washed with dilute hydrochloric acid, are then added, with hot water, which is then boiled, well shaken with the glass and poured on a wet filter. The residue is exhausted by washing with portions of hot water. The united filtrates are evaporated in a tared flask [exhausted by a pump, and dried at temperature not above 78° C.]

(4) **Blyth** proposes the sublimation of the caffeine from a paste of the aqueous extract mixed with magnesia, thinly spread on a thin iron plate, and covered with a tared glass funnel—the heat very gentle at first and very gradually raised to about 200° C., until a fresh funnel will receive no crystals by continuation of the heat for half an hour. But the author prefers to sublime in vacuum, obtained by a mercury pump, the paste being spread on a ground glass plate, fitted with a ground flanged funnel, when very gentle heat by a sand-bath is sufficient.

g.—Tests for Impurities.—Caffeine, gradually heated in a portion of about a grain in a test-tube over the flame, should completely sublime, leaving no residue, and yielding a sublimate, usually melted nearest the heat and crystalline beyond. Contact with cold concentrated sulphuric acid should not cause coloration, and on heating at 100° C. should darken but slowly. Contact with cold (colorless) nitric acid should not give immediate coloration. Caffeine should be colorless, should dissolve in 10 to 15 times its weight of boiling water, the solution remaining clear when diluted to 80 or 100 times its weight and cooled, and being neutral to test-papers. Respecting presence of theobromine, see under the latter.

CAFFETANNIN. See TANNINS.

CANTHARIDIN. $C_{10}H_{12}O_4=196$.—The highly poisonous, vesicating principle of the Spanish Fly (*Lytta vesicatoria*), which contains about 0.4%. It is also found in a great many other coleopterous insects. The powdered insects, after being moistened with acetic acid, are exhausted with chloroform or ether; the extract evaporated to dryness; the residue boiled with carbon disulphide (to remove fat), evaporated to dryness with a little caustic alkali, washed with chloroform, acidified, and agitated with chloroform, from which the cantharidin crystallizes on concentration. It may be purified by recrystallizing from alcoholic chloroform or from acetic ether.

Cantharidin crystallizes in colorless prisms of the dimetric system or in laminæ, which become soft at 210° C. and melt and sublime at 218° C. It sublimes, in part, at 180° C., but volatilizes at a much lower temperature together with the vapor of water, alcohol, etc. It is soluble in 5000 parts cold and 380 parts boiling **water** (more readily when just liberated by acids); in about 3500 parts cold and readily in hot **alcohol**; in 910 parts **ether**; 84 parts **chloroform**; 500 parts **benzene**; 1666 parts **carbon disulphide.** It is soluble in volatile and fat **oils**; very easily in aqueous **alkalies.** It is extracted from acid solutions by benzene, ether, chloroform, and amyl alcohol. Potassium hydrate solution extracts it completely from its solution in chloroform; and by this means it is easily purified. Cantharidin acts as a weak acid, forming salts which are (especially the combinations with the fixed alkalies) easily soluble in water, and which possess the vesicating property. Solvents do not extract the cantharidin from these solutions, but it is precipitated by acids. *Potassium cantharidate* is crystallizable, very readily soluble in **water,** soluble in 3300 parts cold and 110 parts boiling **alcohol,** insoluble in **ether** and **chloroform.** In not too dilute solutions, the potassium and sodium salts give precipitates with **barium** and **calcium chloride** (white), **copper sulphate** (green), **nickel sulphate** (green), **cobaltous sulphate** (red), **palladium chloride** (yellow, hair-shaped, afterwards crystalline), **lead acetate,** and **mercuric chloride.** Undiluted **sulphuric acid** dissolves cantharidin without decomposing it. Concentrated **sulphuric acid** and **potassium dichromate** decompose it with separation of green chromium oxide. 0.0001 gram cantharidin is sufficient to draw a blister.

For finding the *per cent.* of cantharidin in Spanish flies or preparations containing them, DRAGENDORFF washes about 25 grams of the powder with petroleum ether till all the fat is removed (counting 0.0108 gram cantharidin for every 100 c.c. of solvent used), stirs the residue with 5 grams magnesia or soda, and water, evaporates to dryness on the water-bath, powders, adds 25 c.c. chloroform, acidifies with dilute hydrochloric acid, and agitates with 30 c.c. ether, repeating this last operation four times with same quantity of ether. He washes the ether solution several times with water, evaporates to dryness, transfers the residue (with help of a little alcohol) to a small tared filter, washes with alcohol, then with 2 to 3 c.c. water, dries at 100° C., and weighs, adding 0.0077 gram for every 10 c.c. alcohol, and 0.0005 gram for every c.c. water used. According to this method he found 0.348% in a sample of powdered cantharides ["Werthbest.," 106].

CAPRIC, CAPROIC, AND CAPRYLIC ACIDS. See FATS AND OILS.

CARBOLIC ACID. See PHENOL.

CASTOR OIL. See FATS AND OILS.

CATECHU-TANNIN. See TANNINS.

CHELIDONINE. $C_{19}H_{17}N_3O_3=335$.—Found with sanguinarine in the herb, unripe seed-capsules, and root of the celandine (*Chelidonium majus*). The root contains the largest proportion.

Crystallizes in colorless, glittering tablets, with two molecules water, which are driven off at 100° C. It melts to a colorless oil at 130° C. and volatilizes with steam; is odorless and of a bitter, harsh taste; alkaline in reaction, forming colorless, crystallizable salts which possess an acid reaction. The sulphate and phosphate are readily soluble in water. Chelidonine is insoluble in water, and, when crystallized, soluble in ether and alcohol only after continued boiling; more soluble in chloroform. Fat and volatile oils dissolve it readily, benzene very slightly. Amylic alcohol extracts it most readily from solutions made alkaline.

The alkaline hydrates precipitate the alkaloid in white flakes (becoming crystalline) from solutions of its salts. It gives a precipitate with **platinic chloride**, not decomposed by water, containing 17.42—17.6% Pt. **Potassio-mercuric iodide** (MASING[1]) gives a precipitate $C_{19}H_{18}N_3O_3I.HgI_2$. One c.c. MAYER'S solution precipitates 0.01675 gram chelidonine (DRAGENDORFF[2]). **Iodine in alcohol** causes precipitation. Concentrated **sulphuric acid** dissolves it with bright colors, green at first, then brown, edged with red and violet, and, in presence of sugar, with rose-violet color, changing to cherry-red and blue-violet. **Froehde's reagent** gives a green color, changing to blue, brown, and black. Sulphuric acid and **potassium nitrate** give a green to blue color (KÜGELGEN, 1885).

The alkaloid is obtained from the root by precipitating the acidulated (H_2SO_4) water extract of the root with ammonia, dissolving out the sanguinarine by means of ether (the chelidonine is only *very slightly* soluble), then dissolving the residue in as little as possible acidulated (H_2SO_4) water, and adding twice the volume of concentrated hydrochloric acid, which precipitates the hydrochlorate (soluble in 325 parts water). This is decomposed by dilute ammonia, and, after purification by redissolving in acidulated water and repeating the above process as often as may be necessary, is crystallized from boiling alcohol (WITTSTEIN).

CITRIC ACID. $H_3C_6H_5O_7$=192. Citronensäure.—Found in the greater number of the most acidulous fruits; abundant in tomatoes, currants, gooseberries, raspberries, strawberries, blackberries, bilberries (GRAEGER, 1873), and tamarinds, and common in various parts of plants; occurring for the most part as free acid, but also as acid salts. Manufactured from lemons and from limes, both which contain about 5 per cent., or 10 per cent. of the juice (STODDARD, 1868), and from sour oranges of Florida and bergamot oranges of southern Europe, no interfering acids being present in these sources.[3] Cranberries contain over 2 per cent., with no other acid;[4] unripe gooseberries, 1 per cent.; and the red currant, about 1.3 per cent.[5] Used chiefly in

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[1] *Jour. Chem. Soc.*, 1877, i. 477.

[2] "Werthbestimmung," p. 102.

[3] Warington (*Jour. Chem. Soc.*, xxviii. 937) found in lemon-juice, lime-juice, and bergamot-juice formic and acetic acids, and some non-volatile acid giving soluble calcium salt.

[4] L. W. MOODY and the author: *Am. Jour. Phar.*, **50** (1878), 566.

[5] Hager's "Pharmaceutische Praxis," I., 52., with directions for manufacture. For lists of plants containing citric acid see Hager's "Untersuchungen," II. 109; Husemann's "Pflanzenstoffe," 555; Gmelin-Kraut's "Handbuch," v. 827. SILVESTRI, 1869: *Jour. de Phar. et de Chim.* [4], x. 305, reports 1 to 1½ per cent. citric acid in *Cyphomandra betacea*, Mexico and South America.

articles of food and medicine, but also to some extent to intensify certain colors and to remove mordants in dyeing.

Citric acid is *characterized* by its crystallization (*a*); by its reactions with calcium and lead salts, its barium salt in well-marked crystals, and a color reaction with ammonia (*d*), also by the limits of its reducing power (*d*). From Tartaric acid it is distinguished by its crystallization, its failure to give caramel odor when heated (Tartaric acid, *a*), and its weaker reducing power with chromate, etc. (*d*), and is well separated by not precipitating with potassium (Tartaric acid, *f*). From ordinary fruit acids it is approximately separated, by treatment of lime salts, in the scheme given under Malic acid, *e*. Other *separations* are noted at *e*, p. 88. *Estimation*, by volumetric alkali, and from weight of barium precipitate (*f*, p. 88); in fruit juices, by directions under Tartaric acid. Commercial forms and impurities are noted at *g*, p. 89.

a.—Citric acid *crystallizes*, from water solutions in the cold, as $C_6H_8O_7.H_2O=210$, and this is the hydration of the acid of commerce.[1] In very moist air the crystals deliquesce slightly; at temperatures from 28° to 50° C. they effloresce, and then at 100° C. become anhydrous; but exposed at once to heat of 100° C. the crystals melt. From boiling and saturated solution anhydrous crystals are obtained. The hydrated crystals are large, water-clear, right rhombic (trimetric) prisms.—At about 175° C. citric acid decomposes, giving off pungent vapors, containing Acetone, while Aconitic acid (soluble in ether) is formed in the residue and then decomposed ($C_6H_8O_7=C_6H_6O_6+H_2O$).

b.—Citric acid is soluble in its weight of water at common temperature, and in half its weight of boiling water; in about its own weight of ninety per cent. alcohol; insoluble in absolute ether or chloroform,[2] and but slightly soluble in pharmacopœial stronger ether or chloroform. Its water solution is inactive to the plane of polarized light. Standing in water solution it decomposes, and then gives misleading reactions of reduction.

c.—Citric acid, tribasic, forms normal salts, acid salts of one-third and two-thirds basal hydrogen, and basic double salts. The alkali metal salts are freely soluble in water; iron, zinc, and cop-

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[1] 8.57 per cent. of water. Warington (*Jour. Chem. Soc.*, xxviii. [1875], 927) found 8.72 per cent. as the mean of 17 representatives, with 8.46 per cent. and 9.35 per cent. as extreme ranges.

[2] Soluble in 44 parts ether, at 15° C.—BOURGOIN: *Zeitsch. an. Chemie*, 17 (1878), 502, from *Bull. Soc. Chim. Paris*, 29, 242.

per normal citrates moderately soluble; other non-alkali normal citrates mostly insoluble. Calcium citrate is somewhat soluble in cold, nearly insoluble in hot water. Citrate precipitates dissolve in citric and other acids by formation of soluble acid citrates; and dissolve in alkali hydrate solutions by forming basic double salts, such as the "soluble" citrate of iron and ammonium of pharmacy. Citric acid prevents the alkali precipitation of most heavy metals, the soluble double salts being formed. Indeed, numerous precipitations are prevented or hindered by presence of alkali citrates,[1] including most carbonates, phosphates (not ammonio magnesium), oxalates, sulphates, lead and barium chromates, ferric ferrocyanide, lead iodide and bromide, and arsenious sulphide. On the contrary, zinc and magnesium hydrates, lead sulphide, and most silver precipitates are not affected by citrates. Barium sulphate is precipitated in presence of citrates only on boiling. Equal basal proportions of citrate and of the precipitates most favor their solution, which seems to be due to the formation of double salts.—Alkali citrates are sparingly soluble in hot alcohol, less soluble in cold alcohol.

d.—**Solution of lime,** added to solution of citric acid to alkaline reaction or to citrates, causes no precipitate in the cold (distinction from Tartaric, Racemic, Oxalic acids); but on boiling a slight precipitate is formed (distinction from Malic acid). Solution of chloride of calcium does not precipitate solution of free citric acid even on boiling, nor citrates in the cold, but precipitates citrates (neutralized citric acid) when the mixture is boiled. The precipitate, $Ca_3(C_6H_5O_7)_2 . 2H_2O$, is insoluble in cold solution of potassa (which should be not very dilute and nearly free from carbonate), but soluble in solution of cupric chloride (two means of distinction from Tartaric acid); also soluble in cold solution of chloride of ammonium and readily soluble in acetic acid.—Solution of **lead acetate** precipitates from solutions of neutral citrates, and from even very dilute alcoholic solution of citric acid, the white citrate of lead, $Pb_3(C_6H_5O_7)_2 . \frac{1}{2}H_2O$, somewhat soluble in free citric acid, soluble in nitric acid, in solutions of all the alkaline citrates and of chloride and nitrate of ammonium, soluble in ammonia (formation of basic ammonium lead citrate). (Malate of lead is not soluble in malate of ammonium).—The precipitation with **barium** is given in *d.* But if now the solution, with excess of barium acetate (and a little free acetic acid—Fresenius), be heated about two hours on the water-bath, the

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[1] J. Spiller: *Jour. Chem. Soc.*, 10, 110; *Phar. Jour. Trans.*, [3] 17, 282; *Jahr. der Chemie*, 1857, 569.

barium citrate, as $Ba_3(C_6H_5O_7)_2 . 3\frac{1}{2}H_2O$, crystallizes in clinorhombic prisms (Kämmerer[1]).

A color-test for citric acid is made by heating with excess of ammonia-water—as 5 grams of the acid to 30 c.c. ammonia-water—in a sealed tube, at 120° C., for six hours.[2] On exposure to the air and light in an evaporating-dish the solution turns blue, slowly changing to green and becoming colorless. Usually small crystals form in the heated tube and afterward disappear. At 150° C. the solution turns green in the tube, but at 160° C. the reaction is not obtained. Tartaric, oxalic, and malic acids do not interfere. The least quantity of citric acid revealed by the test is 0.010 gram.

Nitrate of silver precipitates from neutral solutions of citrates white normal citrate of silver, not blackened by boiling (distinction from Tartrate).—Solution of **permanganate** of potassium is scarcely at all affected by free citric acid in the cold. With free alkali the solution turns green slowly in the cold. readily when boiled, without precipitation of brown binoxide of manganese till after a long time (distinction from Tartrate).—**Dichromate** of potassium solution is not reduced by citric acid (distinction from Malic, etc.)

e.—Citric acid is *separated* from acids making soluble lead salts, through precipitation with lead acetate and subsequent treatment with hydrogen sulphide. From tannins and gallic acid, as noted under Gallotannin. Insoluble citrates are converted to alkali citrates, as noted under gravimetric estimation, below.

f.—*The acidimetry* of citric acid, with *litmus* as an indicator, can be accurately done only by standardizing the alkali solution with weighed pure crystallized citric acid, using the same litmus-paper and holding the same conditions both in standardizing and in the estimation.[3] Warington states that the litmus color "changes in a perfectly gradual manner," that "the amount of alkali used is a little less than that required by theory to form trisodic citrate," and "the more delicate the litmus-paper the nearer does the experiment approach" a neutral reaction for the normal salt. But with *phenol-phthalein* as an indicator sharp results are obtained, the end reaction being exactly at formation

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[1] *Zeitsch. anal. Chemie,* 8, 298, with cuts of the crystals.

[2] Sabanin and Laskowsky: *Zeitsch. anal. Chemie,* 17 (1878), 73; *Jour. Chem. Soc.*, 1878, Abs., 342. The reaction was declared earlier in a Russian Dissertation by Sarandinaki, and in *Ber. d. chem. Ges.*, 5 (1872), 1100.

[3] Warington: *Jour. Chem. Soc.*, 28 (1875), 929, 927.

of $K_3C_6H_5O_7$, or the corresponding sodium salt.[1] In production of this normal salt each c.c. of a normal alkali solution represents 0.070 gram crystallized, or 0.064 of anhydrous acid.

For gravimetric estimation the precipitation most approved is that of **barium** citrate, to be weighed as sulphate.[2] It is most complete in solution of alcohol of 0.908 specific gravity. Previously the citric acid is obtained as alkali citrate; if free, by neutralization with soda; if combined with a non-alkali base, by warm digestion with an excess of sodium hydroxide or potassium hydroxide, filtering and washing—the filtrate being neutralized by acetic acid. In either case the carefully neutralized and not very dilute solution is treated with a slight excess of exactly neutral solution of acetate of barium, and a volume of 95 per cent. alcohol, equal to twice that of the whole mixture, is added. The precipitate is washed on the filter with 63 per cent. alcohol, and dried at a moderate heat. The citrate of barium contains a variable quantity of water, and is transformed into sulphate of barium by transferring to a porcelain capsule, burning the filter, and heating with sulphuric acid several times till the weight is constant. $3BaSO_4 : 2H_3C_6H_5O_7.H_2O :: 1 : 0.601$. Hager directs that barium or calcium citrate (washed with alcohol) be dried at 120° to 150° and weighed.

$$Ba_3(C_6H_5O_7)_2 : 2H_3C_6H_5O_7.H_2O :: 1 : 0.53232.$$

For estimation in Fruit Juices see Tartaric acid, *f* (Warington, Fleischer).

g.—In commerce the first form of citric acid is concentrated lemon-juice, lime-juice, and bergamot-juice, sometimes containing alcohol added for preservation, and liable to contain formic and acetic acids from decomposition. Crude calcium and magnesium citrates are made for transportation. In the citric acid manufacture normal calcium citrate is precipitated, and this is transposed with dilute sulphuric acid. Among *impurities* tartaric acid is the most frequent adulteration, being sometimes substituted altogether in some medicinal preparations, especially in dry "citrate of magnesia." Lead may be present from manufacture or storage, and calcium salt and traces of sulphuric acid may be left from manufacture.—The detection of Tartaric acid may be done by its potassium precipitation, applied as described under that acid at *d*, or by its reduction of dichromate in the way specified under Tartaric acid, *d*. Phosphoric acid is said to be

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[1] Thomson, 1883: *Chem. News*, 47, 135; *Jour. Chem. Soc.*, 44, 826.

[2] J. Creuse: *American Chemist*, I (1871), 424; *Zeitsch. anal. Chemie*, II (1872), 446.

sometimes present in the citric acid of commerce (BARFOED). It is most clearly detected after calcining the alkali salt.

CHAIRAMIDINE and **CHAIRAMINE, CHINOIDINE, CHINOLINE.** See CINCHONA ALKALOIDS.

CHRYSAMMIC ACID. See ALOINS.

CINCHAMIDINE. See CINCHONA ALKALOIDS.

CINCHONA ALKALOIDS.—Alkaloids of the bark of species of Cinchona and certain allied genera of the cinchoneæ. In the leaf and wood in very small quantities; most abundant in the bark of the root.

CONTENTS:—List of alkaloids, with description of those not used; the commercial alkaloids; the amorphous alkaloids and chinoidine; yield of the total and several alkaloids in different barks; chemical constitution; tabular comparison of characteristics; enumeration of means of analytical distinction; micro-chemical distinctions; separation and estimation of total alkaloids, (1) the plan of Prollius, (2) by extraction apparatus, (3) by amyl alcohol, Squibb's process, the Br. Ph. process, (4) by ethyl alcohol, the U. S. Ph. process; separation of the alkaloids from each other, enumeration of methods; quinine separation as sulphate in detail; separation by ether, Liebig's plan; by ammonia, Kerner's plan; cinchonidine separation, as tartrate, with subsequent removal of quinine; De Vrij's process; Muter's method; rotatory power of the alkaloids, in methods of estimation.—*Quinine*, analytical outline; (*a*) crystals and heat-reactions of the alkaloid and its salts; (*b*) taste and physiological effects; (*c*) solubilities of the alkaloid and its salts; (*d*) qualitative tests and their limits; (*e*) separations in general, from pills; (*f*) quantitative methods, gravimetric, volumetric, in herapathite; (*g*) tests for impurities; Kerner's quantitative method; the pharmacopœial tests of U. S., Germ., Fran.; ammonia test of salts other than sulphate, and of the free alkaloid and bisulphate; test of effloresced salts; Hesse's test; history of Liebig's test; Br. Ph. tests; water of crystallization of sulphate.—*Quinidine*, nomenclature, analytical outline; (*a*) crystals and heat-reactions; (*c*) solubilities; (*d*) qualitative tests; (*e*) separations; (*f*) quantitative work; (*g*) tests of purity.—*Cinchonidine*, analytical outline; (*a*) crystals and heat-reactions; (*b*) effects; (*c*) solubilities; (*d*) qualitative tests; (*e*) separation; (*f*) estimation; (*g*) tests of purity.—*Cinchonine*, analytical outline; (*a*) crystals and heat-reactions; (*c*) solubilities; (*d*) qualitative tests; (*e*) separations; (*f*) estimations; (*g*) tests of purity.—*Quinoline*, production; (*a*) forms and heat-reactions; (*b*) effects; (*c*) solubilities; (*d*) qualitative tests; tests for impurities.—*Kairines*, constitution and production, description and means of identification.—*Thalline*, constitution, description.—*Antipyrine*, constitution, description, tests, and impurities.

(*Crystallizable alkaloids in italic;* amorphous alkaloids in Roman.)

Quinine, $C_{20}H_{24}N_2O_2$. Pelletier and Caventou, 1820. See p. 125.

Quinidine, $C_{20}H_{24}N_2O_2$. Von Heijningen, 1849. (*Conchinine* of HESSE.) See p. 154.

Cinchonine, $C_{19}H_{22}N_2O$.[1] Pelletier and Caventou, 1820. See Index.

Cinchonidine, $C_{19}H_{22}N_2O$.[1] Henry and Delondre, 1833; Winckler, 1844; HESSE.

Diquinicine, $C_{40}H_{46}N_4O_3$. HESSE, 1878. Diconchinine. Apodiquinidine. The chief amorphous alkaloid existing in barks and found in chinoidine of commerce (p. 94). Fluoresces in sulphuric acid solution; gives the thalleioquin reaction; rotates to the right; forms only amorphous salts; and does not yield quinicine. Its relation to quinine or quinidine is shown by the equation: $2C_{20}H_{24}N_2O_2 - H_2O = C_{40}H_{46}N_4O_3$.

Dicinchonicine. HESSE, 1878. Dichonchonine. Apo-dicinchonine. Derived from cinchonidine and cinchonine; found in chinoidine of commerce; probably existing in amorphous condition in the bark; has not been completely isolated. ($C_{38}H_{42}N_4O$?) See Amorphous Alkaloids of Cinchona, p. 94.

[Quinicine, $C_{20}H_{24}N_2O_2$. PASTEUR, 1853; HOWARD, 1872; HESSE, 1878. Formed by melting sulphates or other salts of quinine or quinidine. Also by action of light. Not found in cinchona barks. Not fluorescent. Gives the thalleioquin reaction. Rotates feebly to the right. Amorphous, but can give rise to certain crystalline salts.]

[Cinchonicine, $C_{19}H_{22}N_2O$. PASTEUR, 1853; HOWARD, 1872; HESSE, 1878. Formed by melting sulphates or other salts of cinchonine or cinchonidine. Not contained in cinchona barks. Rotates to the right. Amorphous, but forms some crystalline salts.]

Hydroquinine, $C_{20}H_{26}N_2O_2$. HESSE, 1882. Fluoresces. Gives thalleioquin reaction. Rotates to the left.

Hydroquinidine, $C_{20}H_{26}N_2O_2$. HESSE, 1882; FORST and BÖHRINGER, 1882. Accompanies the quinidine of commerce. Also formed by action of permanganate on quinidine. Rotates to the left. Fluoresces. Gives the thalleioquin reaction.

Hydrocinchonidine, $C_{19}H_{24}N_2O$. HESSE, 1882. Found in commercial cinchonidine (when this is not in loose needles). Rotates to the left. Not fluorescent. The pure base melts below 100° C. Heated with acids it becomes amorphous.

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[1] SKRAUP, 1877; LAURENT, 1848. The formula $C_{20}H_{24}N_2O$, which has been long accepted, is from REGNAULT, and supported by Hlasiwetz, 1851. Skraup: *Chem. Centr.*, 1877, 629; *Liebig's Annalen*, **197**, 226.

In the bark of Remijia Purdieana and R. pedunculata (C. cuprea).[1]

Quinamine, $C_{19}H_{24}N_2O_2$. (Found in other barks, though most abundant in "cuprea" bark.) Dextrorotatory. HESSE, 1872, 1877; OUDEMANS, 1879. With sulphuric acid and a trace of nitric acid, colors orange to red.

Conquinamine, $C_{19}H_{24}N_2O_2$. *Quinidamine.* Accompanies quinamine. HESSE, OUDEMANS, 1881.

Quinamidine and Quinamicine, amorphous isomers of quinamine.

Homoquinine. In "cuprea bark." A compound of *Cupreine*, $C_{19}H_{22}N_2O_2$, and quinine, into which two alkaloids it splits and from which it may be synthesized. Levorotatory. PAUL and COWNLEY, 1881, 1885; Hesse, 1885.[2]

Cinchonamine, $C_{19}H_{24}N_2O$. ARNAUD, 1881, 1885; HESSE, 1885; SEE and ROCHEFONTAINE, 1885. Dextrorotatory. Colored reddish-yellow by sulphuric, yellow by nitric acid. With nitrates forms characteristic insoluble crystals; hence proposed as a test for nitrates (*Phar. Jour. Trans.*, [3], **15**, 772). Of a strong toxic effect.

Cusconine, $C_{23}H_{26}N_2O_4$. HESSE, 1877, in barks shipped from Cusco, in Peru. Difficult of crystallization. Rotates to the left. Accompanies Aricine.

Concusconine, $C_{23}H_{26}N_2O_4$. HESSE, 1883. Dextrorotatory. With sulphuric acid gives a green color. Free alkaloid is tasteless.

Chairamine, $C_{22}H_{26}N_2O_4$. HESSE, 1884. Dextrorotatory.

Conchairamine, $C_{22}H_{26}N_2O_4$. HESSE, 1884. Dextrorotatory.

Chairamidine, $C_{22}H_{26}N_2O_4$. HESSE, 1884. Amorphous. Dextrorotatory.

Conchairamidine, $C_{22}H_{26}N_2O_4$. HESSE, 1884. Levorotatory. Turns green with sulphuric acid.

In other barks.

Paytine, $C_{21}H_{24}N_2O$. In 1870, from a white Cinchona bark from Payta. Levorotatory. With chlorinated lime gives a dark red color. See, further, WULFSBERG, 1880.[3]

Aricine, $C_{23}H_{28}N_2O_4$. HESSE, 1879. PELLETIER and CORIOL, in 1829, in a bark from Arica. Found by HESSE, in 1882, in "cuprea" bark. Levorotatory. Not bitter, astringent taste (*Husemann's* "Pflanzenstoffe").

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[1] Hesse's summary: *Jour. Chem. Soc.*, 1885, Abs., 64.

[2] *Phar. Jour. Trans.*, [3], **15**, 221, 401. *Liebig's Annalen*, **230**, 55.

[3] *Phar. Jour. Trans.*, [3], **11**, 269.

Paricine, $C_{16}H_{18}N_2O$. Winckler, 1845. In bark from Para. Flückiger, 1870.

Cinchotine, $C_{19}H_{24}N_2O$. The *Hydrocinchonine* of Willm and Caventou. Accompanies cinchonine. Dextrorotatory. Skraup, 1879. Forst and Böhringer (1882) find it not an oxidation product, as they had before stated (1881).

Cinchamidine, $C_{20}H_{26}N_2O$. Accompanies cinchonidine. Levorotatory. Hesse, 1881.

The existence of Homocinchonidine (Hesse, 1877) is denied by Skraup (1880). Hesse's Hydroconquinine is believed by Forst and Böhringer to be identical with hydroquinidine. Hesse (1885) reports that the substance previously (1883) named by him as Concusconidine proves to be a mixture of alkaloids. Paytamine is an amorphous alkaloid accompanying Paytine.

Of artificial products, the purpose of this work requires description of only

Quinoline, C_9H_7N. Produced from cinchonine and other sources. See Index.

Kairines, $C_{10}H_{13}NO$. Derivatives of quinoline.

Thalline, $C_{10}H_{13}NO$. A methyl kairine.

The list of natural cinchona alkaloids above given is designed to include all those whose separate identity remains established, by the evidence published, up to 1886, but some omissions may have been made. The artificial derivatives, oxidation products, etc., are excluded from the list above, and have only a brief general history under Chemical Constitution of Cinchona Alkaloids. It will be observed that *the present chemistry of cinchona alkaloids* agrees with the chemistry following the work of Winckler in 1847 and Pasteur from 1853, *in the fundamental outlines* affecting the alkaloids in use, those most abundant in barks of the cinchona family as a whole. It is stated now, as it was over thirty years ago, that the two isomers *quinine and quinidine*, with the two isomers *cinchonine and cinchonidine*, constitute the greater part of the *crystallizable* alkaloids of the cinchonas. All the crystallizable alkaloids in use under pharmacopœial authority are carried under these four names. In elementary constituents, cinchonine and cinchonidine have each one atom of oxygen less in the molecule, and, according to recent determinations, have each CH_2 less in the molecule than quinine and cinchonine: $C_{22}H_{24}N_2O_2 — C_{19}H_{22}N_2O = CH_2 + O$.

To a limited extent other crystallizable alkaloids of cinchona are certainly carried into use under the names of the four principal alkaloids. It is specifically stated that hydroquinidine accompanies *commercial quinidine;* that hydrocinchonidine and cinchamidine are found with commercial *cinchonidine*, and that cinchotine sometimes contaminates *cinchonine.* Hydroquinine may go with manufactured *quinidine* or *quinine*, being found in the mother-liquors of the former. Quinamine, and probably conquinamine, are found in other barks besides "cuprea" bark, and may find their way into manufactured salts, where they should then be detected by reactions with sulphuric and nitric acids. Then the amorphous products quinicine and cinchonicine may be carried into crystalline forms of salts to some extent. And it is always understood that separations of cinchona alkaloids in manufacture are not absolute, so that the quinine salts of the market always contain, under certain limits, cinchonidine and cinchonine, perhaps quinidine, and under narrower limits may contain the amorphous alkaloids in general. The quinidine of commerce, according to Hesse, 1875, consists most often of cinchonidine with a little quinine.

Amorphous cinchona alkaloids.—The name *Chinoidine* (Quinoidine) was given by Sertürner, in 1828, to the amorphous alkaloidal substance left after separating quinine and cinchonine as then known, and which he believed to be a distinct alkaloid. Chinoidine was recognized as an easily fusible base, of strong alkalinity, forming uncrystallizable salts, and of full virtues as a febrifuge. Until about 1855 it was prepared, in connection with the crystallizable alkaloids, by uniform methods, from Calisaya barks of good strength, and therefore possessed a fairly constant character. About 1847 Winckler stated that chinoidine was in large part an amorphous transformation product of the crystallizable alkaloids of cinchona then known. During investigations commencing about 1853 Pasteur made it known that by fusing for some time a salt of one of the crystallizable alkaloids, or, in part, by hot digestion in acidulous solution, an amorphous modification is obtained, without change of elementary composition. The amorphous product of quinine and of quinidine he named *Quinicine;* and the amorphous product of cinchonine and of cinchonidine he named *Cinchonicine;* and it has been generally believed that these are the uncrystallizable alkaloids which exist already formed in the barks, as well as result from chemical treatment of the barks. All barks contain amorphous alkaloids; sometimes the larger portion of the alkaloids is amorphous. And the amorphous alkaloidal matter of cinchona has been in great part accounted for according to the nomenclature of Pasteur, almost down to the present time, so that we have had the familiar classification of the leading natural cinchona alkaloids, as follows:

$C_{20}H_{24}N_2O_2$: Quinine, Quinidine, [Quinicine].
$C_{20}H_{24}N_2O$: Cinchonine, Cinchonidine, [Cinchonicine].

Howard, in 1872, found quinicine and cinchonicine, made from quinine and cinchonine, to be capable of crystallizable combinations, while no salts crystallizable could be produced from natural amorphous alkaloids. And Hesse affirms (1878) that quinicine and cinchonicine, as isomers of quinine and cinchonine, are not present in the barks, are not formed to any great extent by ordinary methods of manufacture, and not found in chinoidine. They would be formed in the manufacturing treatment, the melting of chinoidine, only so far as the crystallizable alkaloids are subjected to this treatment, for it is stated by Hesse that the chief natural amorphous alkaloids, taken from the bark or from chinoidine, are not convertible into quinicine or cinchonicine, which are partly crystallizable. The most prominent natural amorphous alkaloids, those making up the larger part of the by-product chinoidine, according to Hesse, are (with a little liberty in translating Hesse's nomenclature) diquinicine and dicinchonicine, amorphous alkaloids having the constitution of anhydrides (apo-derivatives) respectively of quinine and cinchonine (see the equation under Diquinicine, p. 91). In this view the leading natural cinchona alkaloids are to be grouped as follows:

Crystallizable.	*Amorphous.*
$C_{20}H_{24}N_2O_2$: Quinine, Quinidine.	$C_{40}H_{46}N_4O_3$: Diquinicine.
$C_{19}H_{22}N_2O$: Cinchonine, Cinchonidine.	$C_{38}H_{42}N_4O$ (?) : Dicinchonicine.

By heating the chief crystallizable cinchona alkaloids with hydrochloric acid, at 140° to 150° C., in sealed tubes, for 6 to 10 hours, Hesse (1880)[1] obtained an apo-derivative from each. *Apoquinine* and *apoquinidine* each had the formula $C_{19}H_{22}N_2O_2$, the removal of CH_2 being effected by production of CH_3Cl, and both these new alkaloids were found to be amorphous in all their salts. They gave the thalleioquin reaction, were soluble in ether or alcohol, and showed fluorescence. Apocinchonine and apocinchonidine were each $C_{19}H_{22}N_2O$, isomeric with cinchonine, and each was crystallizable. But a *diapocinchonine*, $C_{38}H_{44}N_2O_2$, forming only amorphous salts, was obtained, readily soluble in alcohol, ether, or chloroform, and, Hesse states, distinct from the natural alkaloid dicinchonicine (p. 91), as well as from cinchonicine, formed by melting.

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[1] *Ber. deut. chem. Ges.*, **205**, 314; *Jour. Chem. Soc.*, 1881, Abs., 615; *Am. Jour. Phar.*, **53**, 105, 160.

The amorphous alkaloids difficult of separation have been less satisfactorily studied than the crystallizable ones, and it is strongly probable that diquinicine and dicinchonicine very imperfectly represent the amorphous alkaloids of the barks. Chinoidine usually contains quinidine in proportion larger than that of the other crystallizable alkaloids. Further than this it has as yet only been ascertained, that quinamidine and quinamicine are amorphous alkaloids found in some other barks besides those of Remijia; and that cusconine, chairamidine, and paytamine are amorphous accompaniments of the special crystallizable alkaloids of certain exceptional barks. Elementary analysis has been obtained of all these except paytamine.

Yield of Cinchona Alkaloids.

Of total alkaloids:[1]

In barks of different species and localities, from a maximum of about 15 per cent. to entire absence of alkaloids.
" Calisaya Ledgeriana, Java, 80 specimens, Moens, 1879, 12.50 to 1.09 per cent.
" Calisaya Javanica, De Vrij, 1879, 10.3 to 1.3 per cent.
" Cinchona officinalis, Broughton, 1872, 6.9 to 3.1 per cent.
" C. succirubra, Java, 1881, 9.8 to 3.2 per cent.
" China regia, 1855, 0.99 per cent. In China cuprea, 5.9 to 2 per cent.
" "Cinchona" of U. S. Ph., dried at 100° C., at least 3 per cent.
" "Red Cinchona Bark" of Br. Ph., between 5 and 6 per cent.
" "Cinchona Barks" of Ph. Germ., at least 3½ per cent.
" Cinchona barks, Ph. Fran., at least 2½ per cent. In Red barks, at least 3 per cent.

Of Quinine:

In Cinchona succirubra, Java, harvest of 1881, Moens, 2.5 to 0.4 per cent.
" C. Ledgeriana, Java, 1879, 11.6 to 0.8 per cent.
" C. officinalis, India, 1872, Broughton, 4.18 to 1.6 per cent.
" "Red Cinchona" and in "Yellow C.," dried at 100° C., U. S. Ph., at least 2 per cent.
" "Red Cinchona bark," Br. Ph., at least 3 per cent. quinine and cinchonidine.

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[1] For a report of the yield of individual and total alkaloids in 13 Bolivia Cinchona Barks, see Stoeder, 1878: *Archiv d. Phar.*, [3], **13**, 243; *Am. Jour. Phar.*, **51**, 22.

In Red Cinchona bark, Ph. Fran., at least 2 per cent. quinine as sulphate.

Of Cinchonidine:
In C. succirubra, Java, harvest of 1881, Moens, 5.2 to 1.3 per cent.
" C. Calisaya, 1873, Moens, 8 samples, 1.2 to 0.4 per cent.

Of Cinchonine:
In C. Calisaya, 1873, Moens, 8 samples, 1.1 to 0.1 per cent.
" China de Quito rubra, Reichardt, 0.39 per cent.
" China Huanuco, Reichardt, 2.24 per cent.

Of Quinidine:
In C. Calisaya, 1873, Moens, 8 samples, 0.9 to 0.86 per cent.
" China cuprea, in comparative abundance, Gehe & Co., 1884.

Constitution of Cinchona Alkaloids.—The derivation of cinchonine and quinine from Quinoline, C_9H_7N, inferred by Weidel in 1873, has acquired additional light every year, and promises to become clearly understood. The remarkable interest of the pyridine series and the derived quinoline series, in relation to natural alkaloids, is mentioned under Midriatic Alkaloids, with a statement of the central position of pyridine in the theoretical chemistry of natural alkaloids. Quinoline was obtained by Gerhardt in 1842 by distilling quinine with potash, and is so obtained from certain other alkaloids, cinchonine, strychnine, brucine. It is also found in considerable quantity in the heavier distillates (dead oil) from coal-tar. The hypothetical formulæ of pyridine and quinoline, as aromatic compounds analogous to benzene and naphthalene, with N in the place of one CH in the benzene ring and naphthalene double ring, was proposed about 1870. The midriatic base tropine is derived from pyridine. The synthesis of quinoline has been effected in several ways; that by Skraup in 1881, from aniline, nitrobenzene, and glycerine, is a practical working method, yielding quinoline identical with that distilled from cinchona alkaloids: $2C_6H_7N$ (aniline) $+ C_6H_5NO_2$ (nitrobenzene) $+ 3C_3H_8O_3$ (glycerine) $= 3C_9H_7N$ (quinoline) $+ 11H_2O$.

Since about 1880 there has been a most active interest in the field of pure chemistry lying between the quinoline series on the one side and the natural cinchona alkaloids on the other side. A vast amount of well-directed experimental work has been done, and great numbers of derivatives, both of the quinoline bodies and of cinchona alkaloids, have been produced and examined. It is an opinion sustained by men acquainted with the methods and difficulties of organic synthesis that quinine will be produced artificially. Meantime artificial quinoline derivatives, such as those brought before the world as Kairines, have been found to present physiological effects like those of quinine. As to the commercial production of quinoline itself, as a medicinal material, should its products come into general demand, it would perhaps continue to be made from cinchonine, unless manufacturers should exercise great care, in its production by Skraup's process, to avoid contamination with nitrobenzene (p. 97).

It is to be observed that both pyridine and quinoline bases have the characteristic of holding H_2, H_4, H_6 in addition combinations. The hydrogenized members of the quinoline series (hydroquinolines), with various substitutions, take character approaching that of the natural alkaloids. The gradually accumulating evidences, to which references are below given, render probable the following rational formulæ, with two quinoline nuclei in the alkaloid molecule:

Cinchonine: $C_9H_{10}N . C_9H_9N . (O . CH_3) = C_{19}H_{22}N_2O$.
Quinine: $C_9H_{10}N . C_9H_8N . (O . CH_3)_2 = C_{20}H_{24}N_2O_2$.

Both quinoline and pyridine tend to form tetra-hydrides; and tetrahydro-quinoline, $C_9H_7[H_4]N$, or $C_9H_{11}N$, is fruitful of derivatives having resemblances to natural alkaloids. In the hypothetical formulæ for cinchonine and quinine, the quinoline tetrahydride molecules drop an atom of hydrogen for union with each other, and another atom of hydrogen for each molecule of methoxide $(O . CH_3)$ taken. The systematic names, therefore, are respectively methoxy-tetrahydro-diquinoline and dimethoxy-tetrahydro-diquinoline.[1]

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[1] L. Hoffman and W. Königs, 1883: *Ber. deut. chem. Ges.*, 16, 727; *Jour. Chem. Soc.*, 1883, Abs., 1143. Königs, with Comstock and with Feer, 1885, 1884, with G. Körner, 1884. Königs. 1881: *Ber. deut. chem. Ges.*, 14, 1852; *Jour. Chem. Soc.*, 1882, Abs., 224: 1880: *Ber. deut. chem. Ges.*, 13, 911. Skraup, 1879: *Ber. deut. chem. Ges.*, 12, 1107: *Jour. Chem. Soc.*, 36, 810. Wichnegradsky (structure of cinchonine with both a quinoline and a pyridine nucleus), 1881: *Bull. Soc. Chim.*, [2], 34, 339; *Jour. Chem. Soc.*, Abs., 444. De Coninck, 1882–83. Knorr and Antrick (positions in the structure of quinoline), 1884: *Ber. deut. chem. Ges.*, 17, 2870, 2032; *Jour. Chem. Soc.*, 1885, Abs., 273; 1884, Abs., 1378. Claus and others. Diquinolines: Williams, 1881, *Chem. News*, 43, 145: Claus, 1881–82; Dewar, 1881; Tressider, 1884; Fischer (and Loo), 1884, 1885; Oestermayer, 1885. Krakau, 1885. Berend, Hartz, Kahn, Spady, Einhorn, 1885–86. Michael, 1885: *Am. Chem. Jour.*, 7, 182. "Ladenburg's Handwörterbuch der Chemie," i. 243–298, ii. 532–595 (63 pages on quinoline). Summaries of progress, 1882–85: *Am. Chem. Jour.*, 4, 64, 157; 5, 60, 72; 7, 200, (182).

COMPARATIVE CHARACTERISTICS OF THE CHIEF CINCHONA ALKALOIDS.[1]

<table>
<tr>
<td rowspan="4">$C_{20}H_{24}N_2O_2$ isomers.
——
Blue *fluorescence* in aqueous solutions with oxy-acids.
——
Give *the thalleioquin test.*
——
Crystallize as hydrates, efflorescent.</td>
<td colspan="2">*Levorotatory* to polarized light.
Sulphates soluble in about 1000 parts of *chloroform.*
Normal *tartrates* sparingly soluble in water.</td>
<td rowspan="4">$C_{19}H_{22}N_2O$ isomers.
——
Not fluorescent.
——
Do not give thalleioquin.
——
Crystallize anhydrous, not efflorescent.</td>
</tr>
<tr>
<td>**1. QUININE.**
Sulphate takes 740 parts *water* for solution.
Alkaloid soluble in 25 parts of *ether.*
Alkaloid soluble in some excess of *ammonia.*
Herapathite crystals but very slightly soluble.</td>
<td>**2. CINCHONIDINE.**
Sulphate soluble in 100 parts of *water.*
Alkaloid soluble in 188 parts of *ether.*
Alkaloid soluble in larger excess *ammonia.*
Tartrate less soluble than that of *quinine.*</td>
</tr>
<tr>
<td>**3. QUINIDINE.**
Hydriodide crystals take 1250 parts water for solution.
Alkaloid soluble in 30 parts *ether.*
Sulphate soluble in 100 parts of *water.*
Alkaloid soluble in larger excess *ammonia.*</td>
<td>**4. CINCHONINE.**
Alkaloid takes 370 parts *ether* for solution.
Alkaloid difficultly soluble in *ammonia.*
Sulphate soluble in 70 parts *water.*</td>
</tr>
<tr>
<td colspan="2">*Dextrorotatory* to polarized light.
Sulphates soluble in 20 to 60 parts of *chloroform.*
Normal *tartrates* more easily soluble in water.</td>
</tr>
</table>

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[1] Extended from Kerner (1880: *Archiv d. Phar.*, [3], **16**, 208–224). The solubilities of sulphates in chloroform, of alkaloids in ammonia, and the statements of number of parts of solvents, are here added. Respecting separation by solubilities, it must be understood that the solubility of an alkaloid in any solvent is affected by the presence of alkaloids less soluble in the solvent. This effect hinders separation by ether (Paul, 1877), and of the sulphates by chloroform (the author, 1878), not so much the separation of quinine sulphate by water (Hesse, 1886).

Cinchona Alkaloids, Distinctions *between* (for test-methods, conditions, etc., see under each alkaloid, *d*):

I. Of Quinine.

A.—*From Cinchonidine and Cinchonine:*

1. Fluorescence, in aqueous solutions of the sulphate and other oxy-salts.
2. The thalleioquin test—with bromine or chlorine followed by ammonia.
3. Sulphate crystallization.
4. Solution in ether.
5. Solution in ammonia.

   From cinchonine more perfectly than from cinchonidine.

6. Formation of herapathite, a crystalline iodosulphate.
7. Rotatory difference: from cinchonine, in direction; from cinchonidine, in degree.
8. Microchemical examinations (p. 101).

B.—*From Quinidine:*

1. Sulphate crystallization.
2. Non-precipitation by potassium iodide.
3. Non-solution of the sulphate in chloroform.
4. Formation of herapathite.
5. Rotatory difference, in direction.

II. Of Cinchonidine.

A.—*From Quinine* (I. A, 1, 2).

B.—*From Cinchonine:*

1. Tartrate precipitation.
2. Chloroformic solution of sulphate.
3. Rotatory difference, in direction.
4. Greater solubility in alcohol and in ether.

C.—*From Quinidine:*

1. Tartrate precipitation.
2. Non-precipitation by iodide.
3. Non-solution of sulphate in chloroform.
4. Rotatory difference, in direction.

III. Of Amorphous Alkaloids.

A.—*From the crystallizable alkaloids:*

1. By non-crystallization of the sulphate, and other salts, and the free alkaloid, under ordinary or microscopic observation.

B.—*From Cinchonine:*

1. By greater solubility in ether, or in dilute alcohol.

Microchemical distinctions between cinchona alkaloids.—Schrage (1874 and 1879), Godeffroy and Ledermann (1877), and Hesse (1878) have made contributions respecting distinctions drawn from the crystals formed under the microscope after adding **potassium sulphocyanate** solution.[1] Godeffroy and L. used *saturated solutions of sulphates* of the several alkaloids. Schrage used a solution of the alkaloidal salt in 100 parts of water, converting the sulphate of quinine into hydrochloride for the purpōse. But Hesse advises to use only saturated solutions of the alkaloid sulphates, prepared by dissolving in warm water and leaving in the cold till crystallization stops. Such a solution, by itself, should not exhibit crystals under the microscope. *The sulphocyanate* solution should be very concentrated, 1 part of the salt to 1 part of water. A drop of the alkaloid sulphate solution is placed on a glass slide, and a drop (Hesse), or a third to a fourth of drop (Schrage), of the reagent is placed on one side of the alkaloid solution, a cover-glass is put over, and the slide is placed, in level, under a power of about 110 diameters. With Schrage's proportions the crystal forms were completed in from a half-hour to several hours; with Hesse's proportions, in a few minutes to half an hour. In first contact with the reagent amorphous precipitation frequently occurs, followed by crystallization. The authors above cited differ from each other in certain important particulars. Thus, with quinine, Godeffroy and Ledermann assert that the sulphocyanate, so far as formed, is in amorphous globules as a final form, and that any stellate groups of crystals are those of unchanged quinine sulphate. Schrage, later, states that the amorphous globules are resolved into stellate clusters of crystals. And Hesse states that Godeffroy's appearances, with quinine, were due to presence of cinchonidine.

The analyst who would undertake the identification of impurities in cinchona alkaloids by the sulphocyanate reaction, or other test, in crystalline forms under the microscope, should govern his conclusions by the results of strictly parallel tests, made at the same time with alkaloids of known purity. The concentration of the alkaloidal salt solution and of the reagent, and the proportion of the one liquid to the other, must be held

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[1] Schrage, *Archiv d. Phar.*, [3], **5**, 504: **13**, 25; *Pro. Am. Pharm.*, **23**, 409; **27**, 488. Godeffroy and L., *Archiv d. Phar.*, [3], **11**, 515: *New Remedies*, **7**, 107 (April, 1878); *Am. Jour. Phar.*, **50**, 158; *Pro. Am. Pharm.*, **26**, 569. O. Hesse, *Archiv d. Phar.*, [3], **13**, 481; *Pro. Am. Pharm.*, **27**, 492. The publications above cited are illustrated with cuts. On the Identification of Alkaloids in general by Crystallization under the Microscope, a full report is made by A. Percy Smith, 1886: *Analyst*, **11**, 81 (illustrated).

without variation, and the disturbing influence of evaporation must be prevented by the cover-glass at once. It is not prudent to base conclusions upon a resemblance to forms figured by other operators. Even slight differences in the purity of the reagent or in the atmospheric temperature may cause differences in the form or the rate of crystallization.—The *quinidine* sulphocyanate crystals are more characteristic than those of the other alkaloids, and the reaction with potassium iodide is likewise a favorable one for microscopic recognition of quinidine.

SEPARATION AND ESTIMATION OF CINCHONA ALKALOIDS.—*Separation of the total Alkaloids from Cinchona Barks.*—Cinchona alkaloids exist in the barks in combination with the tannin —known as cinchotannic acid (DE VRIJ, 1878). Kinic (quinic) acid is also present in the bark, and, under action of certain solvents, unites with a part of the alkaloids. The cinchotannates of the alkaloids are almost insoluble, while the kinates are soluble, in cold water. Acidulated water readily dissolves the entire alkaloids.

In methods of analysis, with a few exceptions, the alkaloids are liberated by lime or other alkali, and dissolved from the powdered bark, in a free state, by alcohol, ether, or other solvent of the free alkaloids. But a removal of the alkaloids as hydrochlorides is sometimes resorted to. *The most favorable operations for removal of the alkaloids from the bark* may be classified as follows:

1. The powdered bark is macerated in a mixture of chloroform or ether, with alcohol and ammonia, and an aliquot part of the total liquid is taken (without washing) for the analysis (PROLLIUS, 1882; DE VRIJ, 1882; Ph. Germ.)

2. The powder mixed with lime is exhausted with ether in an extraction apparatus, Tollens's or other.

3. The powder mixed with lime is exhausted by digesting with a mixture of amyl alcohol and ether (SQUIBB, 1882), or amyl alcohol and benzene (Br. Phar., 1885).

4. The powder mixed with lime is exhausted by digesting and washing with alcohol (DE VRIJ, 1873; U. S. Ph., 1880, p. 78).

5. The acidulous decoction, in a part of the filtrate taken as a fraction of the total solution, is precipitated by picric acid, and the dried precipitate weighed (HAGER, 1869; given in this work under Alkaloids, p. 49).

The use of an extraction apparatus, best adapted to ether as a solvent, is a most rigidly exact and generally satisfactory way in this as in most solvent operations upon plants. But it loads the solution with more coloring and other extraneous matters, and takes longer, than the method placed first above. An aliquot part of the liquid, taken with due precautions, gives the operator quick and trustworthy results, and for ordinary uses this plan is here given the preference. Other operators prefer percolation or hot digestion, or both. The plans above enumerated have been carried out, in many cases *with separation of the alkaloids from each other, or of the quinine from the other alkaloids*, by different chemists, as follows:

1. *Methods on the Plan of Prollius.*[1]—*The directions of the German Pharmacopœia* of 1882 are in effect as follows: Pre-

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[1] PROLLIUS, 1881: *Arch. d. Phar.*, **209**, 85, 572; *Am. Jour. Phar.*, **54**, 59; *New Rem.*, **11**, 22. J. BIEL, 1882: *Phar. Zeitschr. Russland*, **21**, 250. DE VRIJ, 1882: *Jour. de Phar. et de Chim.*; *New Rem.*, **11**, 258; *Am. Jour. Phar.*, **54**, 59. KISSEL, 1882: *Arch. d. Phar.*, **220**, 120. Ph. Germ., **1882**, 63. FLÜCKIGER, 1883: *Phar. Zeit.*, vol. **28**; *New Rem.*, **12**, 274. A. PETTIT, 1884. Citations from above-named authorities: *Zeit. anal. Chem.*, **22**, 132; *Proc. Am. Pharm.*, **30**, 204; **31**, 133, 134.

Prollius proposed the ethereal solvent mixture (making it by weight of ether 88 per cent., of ammonia-water 4 per cent., of 92 to 96 per cent alcohol 8 per cent.) for assays of the ether-soluble alkaloids only, and directed a chloroform mixture for assays of the total cinchona alkaloids. But Biel, and Kissel, and De Vrij agree in the statement that Prollius's ethereal solvent removes *all* the alkaloids. Prollius, however, used only half as much of the solvent as is here directed, according to De Vrij. De Vrij emphasizes the required fineness of the powder. He would prefer a less aqueous solvent, made by saturating the alcohol with ammonia, and adding the ether. Biel says the time of maceration should be four hours, neither more nor less, while De Vrij found one hour enough as shown by control experiment. Kissel obtains the quantity of the pure alkaloids by subtracting from the quantity of crude alkaloid the weight of resins, wax, etc., left on a tared filter, in filtration of a solution of the crude alkaloidal residue in diluted sulphuric acid.—The chloroformic solvent of Prollius, above referred to, consisted of 76 per cent. alcohol, 20 per cent. chloroform, and 4 per cent. ammonia-water. The solution was wine-red, and to decolorize it a quantity of finely powdered calcium hydrate equal to the quantity of the bark is agitated with the decanted solution, which is then filtered, and this filtrate is weighed to obtain an aliquot part of the entire solvent taken. The weighed filtrate is evaporated, and the dried residue weighed as total alkaloid, not purified further.—In the use of the ethereal solvent Prollius decanted the clear solution (as in the directions above), and then supersaturated the ethereal solution with diluted sulphuric acid, when the alkaloidal salts were found in a dense aqueous layer. The ethereal layer was removed and washed, once with 2 c.c., then with 1 c.c. of water, the washings being added to the alkaloid solution. From the latter the alcohol is evaporated, when ammonia is added just to alkaline reaction, and the precipitate dried in a tared capsule and *weighed*.—The ethereal solution, if not distilled, should be evaporated in a flask or beaker of some depth to avoid creeping.—The purification of the crude alkaloids is a matter distinct from the removal from the bark, and may be varied at will of the operator. The separation by shaking out with chloroform (p. 33) will generally be preferred to precipitation by the Ph Germ.

pare *the solvent mixture* by taking together 85 parts by weight of ether (s.g. 0.724 to 0.728), 10 parts of alcohol (0.830 to 0.834), and 5 parts of ammonia-water (s.g. 0.960), making 100 parts by weight.—Treat 20 grams of the powdered cinchona with 200 grams of the solvent mixture, agitating thoroughly and repeatedly, macerate one day, and pour off 120 grams of the clear liquid.—Add 30 c.c. of decinormal[1] solution of hydrochloric acid, remove the ether and alcohol by distillation or evaporation, concentrating the volume to 30 c.c., and, if necessary, add more hydrochloric acid until the solution has an acid reaction. Then filter, and when cold add 3.5 c.c. of normal solution of potassa. After the alkaloids have separated add to the clear supernatent liquid enough potassa solution to complete the precipitation. Collect the whole precipitate upon a filter, and wash with small portions of water, successively poured on, until drops of the washings, when allowed to glide over the surface of a cold-saturated aqueous solution of quinine sulphate, no longer produce a cloudiness. After allowing the alkaloids to drain press them gently between bibulous papers, and dry them by exposure to the air until they can be perfectly removed to a glass capsule. Then dry them over sulphuric acid, and finally to a constant weight on the water-bath.—Of 200 grams total liquid, 120 grams were decanted, and 3 : 5 :: weight obtained : $x =$ weight of mixed alkaloids in the 20 grams of bark. Then $x \times 5 =$ per cent. of alkaloids in the bark.

Directions in detail for precautions against error, contributed by De Vrij and others for the method of Prollius, are presented as follows (observe last two foot-notes): The bark is to be very finely powdered. If of over 4% total alkaloids, take 10 grams, otherwise 20 grams for an assay. Place the weighed portion of the powdered bark in a glass-stoppered bottle previously tared, add of the ethereal solvent (above) 20 times the weight of the powder, take the exact total weight of bottle and contents, and agitate from time to time for four hours (BIEL. One hour, DE VRIJ. One day, Ph. Germ.) If any loss of weight is found, add of the solvent to restore it, and agitate and weigh again. Decant carefully so much of the solution as can be obtained perfectly clear (into a flask from which ether can be distilled), and by weighing the stoppered bottle find the exact weight of the decanted liquid. Distil (or evaporate) off the ether—avoiding

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[1] The Ph. Germ. directs to add 3 c.c. of normal solution of hydrochloric acid. Flückiger, finding the resulting volume of liquid too small for the filtration, advised the 30 c.c. of decinormal solution. Also advised the concentration to a definite volume of 30 c.c., not in the official directions.

its taking fire—then transfer the residual liquid to a small capsule tared with a short glass rod (rinsing with a little of the solvent), and evaporate and dry the residue on the water-bath. Weight of alkaloidal solution decanted from the bottle : weight of total solvent taken in the bottle :: weight of residue : $x =$ quantity of crude alkaloids in the amount of bark taken.—To obtain the pure alkaloids, the residue of the crude alkaloids is dissolved in diluted hydrochloric acid, the solution filtered and the filter washed, the filtrate made alkaline with sodium hydrate and repeatedly *shaken out with chloroform*, the chloroformic solution evaporated (or distilled) in a tared dish, and the residue dried at 100° C. and weighed. De Vrij found the pure alkaloids so obtained to be 16.5% less than the crude in the case of a red Java bark.

2. *Removal of the Alkaloids from the Bark by use of an Extraction Apparatus.*—For the use of an extraction apparatus upon cinchona bark, *with ether as a solvent*, the following excellent directions of Professor Flückiger are given:[1] Of a well-selected average specimen of the bark 20 grams are very finely powdered, moistened with ammonia-water, and, after standing for an hour, mixed with 80 grams of hot water; it is then allowed to cool, subsequently mixed with milk of lime (prepared by triturating 5 grams of dry caustic lime with 50 grams of water), and the mixture evaporated on a water-bath until it is uniformly converted into small, somewhat moist, crumb like particles. This is then transferred to a cylindrical glass tube about 2.5 centimeters (1 inch) wide and 16 centimeters (6.4 inches) long, the tube being fitted as the percolator of an extraction apparatus. The neck of this percolator is fitted with a rest of wire cloth, on which a disk of filtering-paper is held by a loose plug of cotton. The powder is packed quite compactly, and covered, at the top, with a plug of cotton which has been used to clean away the last traces of the bark. The percolator is put in place, under a condenser, in the extraction apparatus, into the receiver of which about 100 c.c. of ether is introduced, and the extraction is conducted, in the usual manner, over a water-bath for nearly a day, and until completed as shown by testing a little of the percolate. This may be tested, in the

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[1] "The Cinchona Barks," Power's translation, Phila., 1884, p. 69. *Other solvents* have been used on cinchona with an extraction apparatus. Chloroform is used in Carles's process (1873: *Zeitsch. anal. Chem.*, **9**, 497). Methylated Ether, and doubtless alcohol or Methylated Alcohol, can be well used in a form of extraction apparatus that would carry over the vapor with desirable rapidity.

ethereal solution, by about an equal volume of potassium mercuric iodide solution.[1]

When the extraction is completed, 36 c.c. of decinormal solution of hydrochloric acid (3.64 grams in 1 liter) are added to the ethereal solution in the receiver, when the ether is distilled off, and enough hydrochloric acid then added to give an acid reaction. When cold the liquid is filtered, the filter washed, and 40 c.c. of decinormal solution of soda (4 grams in 1 liter) are added. The precipitate is left at rest till the liquid above it is clear. Sodium hydrate solution (preferably of spec. grav. 1.3) is then added to complete the precipitation, the precipitate is collected on a filter, and gradually washed with a little cold water until a few drops of the washings, when allowed to flow on the surface of a cold-saturated neutral aqueous solution of quinine sulphate, cease to produce a turbidity. The drained precipitate contained on the filter is then gently pressed between bibulous paper, and dried by exposure to the air. It may afterward be readily removed from the paper without loss, and, after thorough drying upon a watch-glass over sulphuric acid, is finally dried at 100° C. and weighed. The weight of the precipitate, multiplied by 5, will give the total percentage of mixed alkaloids in the bark.

3. *The use of ethereal or benzolated mixture of Amyl Alcohol to dissolve the free cinchona alkaloids, which are then transferred to aqueous solution of the salts of these alkaloids.*—A.—*Squibb's Process:*[2] "Take of the powdered cinchona 5 grams; lime, well burnt, 1.25 grams; amyl alcohol, stronger ether, purified chloroform, normal solution of oxalic acid, normal solution of soda, and water, each a sufficient quantity—or double all the quantities throughout, as well as the size of the vessels, etc., if

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[1] The ethereal solution may be treated according to the following directions of **Flückiger**, or by any desired method for purifying the alkaloids from resins, etc.

[2] E. R. **Squibb**, 1882: *Ephemeris*, I, 106; **Br. Ph.**, 1885, 111.

Squibb digests first with amyl alcohol alone, then adds ether in larger volume "to facilitate percolation and evaporation." The Br. Ph. digests with a mixture of amyl alcohol with thrice its volume of benzene. Squibb takes the alkaloids out of the amylic liquid by aqueous oxalic acid; the Br. Ph., by aqueous hydrochloric acid. Squibb purifies the total free alkaloids by shaking out with chloroform in alkaline mixture. The Br. Ph. undertakes the separation of the quinine with cinchonidine by precipitation as tartrates, then precipitating the remainder of the alkaloids from the filtrate as free alkaloids, these separations serving also to purify. The method of Dr. Squibb, in his unrivalled explicitness of detail, provides with great care against inefficient treatment. The approximate separation with tartrate by the Br. Ph. corresponds very nearly to Squibb's approximate division into ether-soluble and ether-insoluble alkaloids, p. 117.

the barks be poor, or if it be desired to divide the errors of manipulation.

"Add to the lime contained in a 10 c.m. = 4-inch capsule 30 c.c. of hot water, and when the lime is slaked stir the mixture and add the powdered cinchona, stir very thoroughly, and digest in a warm place for a few hours or over night. Then dry the mixture at a low temperature on a water-bath, rub it to powder in the capsule, and transfer it to a flask of 100 c.c. capacity and add to it 25 c.c. of amyl alcohol. Cork the flask and digest in a water-bath at a boiling temperature and with vigorous shaking for four hours. Then cool and add 60 c.c. of stronger ether, of sp. gr. 0.728, and again shake vigorously and frequently during an hour or more. Filter off the liquid through a double filter of 10 c.m. = 4 inches diameter into a flask of 150 c.c. capacity, and transfer the residue to the filter. Rinse out the flask on to the filter with a mixture of 10 volumes of amyl alcohol and 40 of stronger ether, and then percolate the residue on the filter with 15 c.c. of the same mixture added drop by drop from a pipette to the edges of the filter and surface of the residue. Return the residue to the flask from whence it came, add 30 c.c. of the amyl alcohol and ether mixture, shake vigorously for five minutes or more, and return the whole to the filter. Again percolate the residue with 15 c.c. of the menstruum applied drop by drop from a pipette as before. Then put the filter and residue aside, that it may be afterward tested in regard to the degree of exhaustion.

"Boil off the ether from the filtrate in the flask by means of a water-bath, taking great care to avoid igniting the ether vapor, and also to avoid explosive boiling, by having a long wire in the flask. When boiled down as far as practicable in the flask transfer the remainder to a tared capsule of 10 c.m. = 4 inches diameter, and continue the evaporation on a water-bath until the contents are reduced to about 6 grams.[1] Transfer this to a flask of 100 c.c. capacity, rinsing the capsule into the flask with not more than 4 c.c. of amyl alcohol. Then add 6 c.c. of water and 4 c.c. of normal solution of oxalic acid, and shake vigorously and frequently during half an hour. Pour the mixture while intimately mixed on to a well-wetted double filter of 12 c.m. = $4\frac{3}{4}$ inches diameter, and filter off the watery solution from the amyl alcohol into a tared capsule of 10 c.m. = 4 inches

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[1] If only a very rough estimate of the total alkaloids be needed, this may be obtained by continuing the evaporation of the amyl alcohol solution to a constant weight, and subtracting from the result a half of 1 per cent. of the weight of bark taken (SQUIBB).

diameter. Wash the filter and contents with 5 c.c. of water applied drop by drop from a pipette to the edges of the filter and surface of the amyl alcohol. Then pour the amyl alcohol back into the flask over the edge of the filter and funnel, rinsing the last portion in with a few drops of water. Add 10 c.c. of water and 1 c.c. of normal solution of oxalic acid; again shake vigorously for a minute or two, and return the whole to the wetted filter and filter off the watery portion into the capsule with the first portion. Return the amyl alcohol again to the flask, and repeat the washing with the same quantities of water and normal oxalic acid solution. When this has drained through, wash the filter and contents with 5 c.c. of water applied drop by drop from a pipette. Evaporate the total filtrate in the capsule on a water-bath at a low temperature until it is reduced to about 15 grams, and return this to a flask of 100 c.c. capacity, rinsing the capsule into the flask with 5 c.c. of water. Add 20 c.c. of purified chloroform, and then 6.1 c.c. of normal solution of soda, and shake vigorously for five minutes or more. While still intimately mixed by the shaking pour the mixture upon a filter 12 c.m. = 4¾ inches diameter, well wetted with water. When the watery solution has passed through, leaving the chloroform on the filter, wash the filter and chloroform with 5 c.c. of water applied drop by drop. Then transfer the chloroform solution, by making a pin-hole in the point of the filter, to another filter of 10 c.m. = 4 inches diameter, well wetted with chloroform, and placed over a tared flask of 100 c.c. capacity. Wash the watery filter through into the chloroform-wet filter with 5 c.c. of the purified chloroform, and, when this has passed through into the flask, wash the chloroform-wet filter also with 5 c.c. of chloroform applied drop by drop to the edges of the filter. When the whole chloroform solution of alkaloids is collected in the flask, boil off the chloroform to dryness in a water-bath, when the alkaloids will be left in warty groups of radiating crystals adhering over the bottom and sides of the flask. Place the flask on its side in a drying-stove, and dry at 100° C. to a constant weight. The weight of the contents multiplied by 20 gives the percentage of the total alkaloids of the cinchona in an anhydrous condition, to within 0.1 or 0.2 of a per cent. if the process has been well managed."[1]

B.—*Br. Ph. Process.*—(1) *For Quinine and Cinchonidine:* "Mix 200 grains [or 12.5 grams] of the (red) cinchona bark, in

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[1] For an "Estimation of the Quinine," as represented by an ether-soluble division of the alkaloids, following the above method, by the same author, see p. 117.

No. 60 powder, with 60 grains [or 4 grams] of hydrate of calcium; slightly moisten the powder with ½ oz. [14 c.c.] of water; mix the whole intimately in a small porcelain dish or mortar; allow the mixture to stand for an hour or two, when it will present the characters of a moist, dark-brown powder, in which there should be no lumps or visible white particles. Transfer this powder to a six-ounce flask [one of about 170 c.c. capacity], add 3 fluid ounces [85 c c.] of benzolated amyl alcohol [amyl alcohol, 1 volume; benzene of sp. gr. about 0.850, 3 vols.], boil them together for about half an hour, decant and drain off the liquid on to a filter, leaving the powder in the flask; add more of the benzolated amyl alcohol to the powder, and boil and decant as before; repeat this operation a third time; then turn the contents of the flask on to the filter, and wash by percolation with the benzolated amyl alcohol until the bark is exhausted. If during the boiling a funnel be placed in the mouth of the flask, and another flask filled with cold water be placed in the funnel, this will form a convenient condenser which will prevent the loss of more than a small quantity of the boiling liquid. Introduce the collected filtrate, while still warm, into a stoppered glass separator; add to it 20 minims [1.1 c.c.] of diluted hydrochloric acid [of 10.58% real acid] mixed with 2 fluid-drachms [7 c.c.] of water; shake them well together, and when the acid liquid has separated this may be drawn off, and the process repeated with distilled water slightly acidulated with hydrochloric acid, until the whole of the alkaloids have been removed. The acid liquid thus obtained will contain the alkaloids as hydrochlorates, with excess of hydrochloric acid. It is to be carefully and exactly neutralized with ammonia while warm, and then concentrated to the bulk of 3 fluid-drachms [about 10 c.c.] If now about 15 grains [0.972 gram] of tartarated soda [potassium sodium normal tartrate], dissolved in twice its weight of water, be added to the neutral hydrochlorates, and the mixture stirred with a glass rod, insoluble tartrates of quinine and cinchonidine will separate completely in about an hour; and these collected on a filter, washed, and dried, will contain eight-tenths of their weight of the alkaloids, quinine and cinchonidine, which [in grains] divided by 2 [or in grams multiplied by 8] represents the percentage of those alkaloids. The other alkaloids will be left in the mother-liquor."—(2) *For total alkaloids:* "To the mother-liquor from the preceding process add solution of ammonia in slight excess. Collect, wash, and dry the precipitate, which will contain the other alkaloids. The weight of this precipitate [in grains] divided by 2 [or, in use of the metric quantities, its weight in grams multiplied by 8], and added to the percentage weight of the quinine and cinchonidine, gives the percentage of total alkaloids."

4. *The use of alcohol to dissolve the free cinchona alkaloids, then obtained by precipitation from aqueous solution.*[1]—The directions of the U. S. Ph. are as follows: "*For total alkaloids:* Cinchona, in No. 80 powder, and fully dried at 100° C., 20 grams; lime, 5 grams; diluted sulphuric acid, solution of soda, alcohol, distilled water, each a sufficient quantity. Make the lime into a milk with 50 c.c. of distilled water, thoroughly mix therewith the cinchona, and dry the mixture completely at a temperature not above 80° C. (176° F.) Digest the dried mixture with 200 c.c. of alcohol, in a flask, near the temperature of boiling, for an hour. When cool pour the mixture upon a filter of about six inches (15 centimeters) diameter. Rinse the flask and wash the filter with 200 c.c. of alcohol, used in several portions, letting the filter drain after use of each portion. To the filtered liquid add enough diluted sulphuric acid to render the liquid acid to test-paper. Let any resulting precipitate (sulphate of calcium) subside; then decant the liquid, in portions, upon a very small filter, and wash the residue and filter with small portions of alcohol. Distil or evaporate the filtrate to expel all the alcohol, cool, pass through a small filter, and wash the latter with distilled water slightly acidulated with diluted sulphuric acid, until the washings are no longer made turbid by solution of soda. [*Alternative directions, from this point, given below.*] To the filtered liquid, concentrated to the volume of about 50 c.c., when nearly cool, add enough solution of soda to render it strongly alkaline. Collect the precipitate on a wetted filter, let it drain, and wash it with small portions of distilled water (using as little

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[1] De Vrij, 1873: *Phar. Jour Trans.*, [3], 4, 241; *Proc. Am. Phar.*, **22**, 268. U. S. Ph., 1880, p. 78. A. B. Prescott in "Report on the Revision of the U. S. Ph.," New York, 1880, p. 26.

This is a direct and simple method, in common use and giving good results. The precipitation and washing is open to the objection, elsewhere noted, that quinine thereby suffers a little loss. This is avoided in *the alternative modification* by shaking out the total alkaloids with chloroform, given here from the "Report on Revision."

Gœbel (1884: *Proc. Am. Phar.*, **32**, 474) proposes, very properly, *the adaptation of the process to the plan of taking an aliquot part* of the alcoholic solution, as in Prollius's method, as follows: "Place 15 grams of cinchona—treated with milk of lime and perfectly dried—in a flask, add 150 c.c. of alcohol, weigh the whole, digest the loosely stoppered flask and contents for about two hours at 150° to 160° F., cool, replace the slight loss of weight by alcohol, filter, through a covered filter, 100 c.c. equivalent to 10 grams of the bark, and proceed with this extraction practically as directed by the Pharmacopœia."

as possible) until the washings give but a slight turbidity with test-solution of chloride of barium. Drain the filter by laying it upon blotting or filter papers until it is nearly dry.

"Detach the precipitate carefully from the filter and transfer it to a weighed capsule, wash the filter with distilled water acidulated with diluted sulphuric acid, make the filtrate alkaline by solution of soda, and, if a precipitate result, wash it on a very small filter, let it drain well, and transfer it to the capsule. Dry the contents of the latter at 100° C. (212° F.) to a constant weight, cool it in a desiccator, and weigh. The number of grams multiplied by *five* (5) equals the percentage of total alkaloids in the cinchona."

Alternative directions from point above noted: Concentrate the filtrate to the volume of 50 c.c. or less. Transfer, rinsing with a little water, to a glass separator of 100 to 150 c.c. capacity. Add solution of soda in decided excess, then at once add 30 to 40 c.c. of chloroform, stopper, agitate for a few minutes, set aside for an hour or two, and draw off the clear chloroform layer. In the same way extract with three smaller portions of the chloroform, using in all at least 120 to 130 c.c. of this solvent. The chloroform is then recovered by distillation or is slowly evaporated, the concentrated liquid is transferred, with chloroform rinsing, to a weighed dish, and the residue dried on the water-bath to a constant weight. The grams multiplied by 5 express the percentage of total alkaloids in the bark.[1]

SEPARATION OF CINCHONA ALKALOIDS FROM EACH OTHER.

I. SEPARATION OF QUININE.

A.—*From other cinchona alkaloids in general.*[2]

1. By crystallization of the sulphate in aqueous solution (p. 113).
2. " crystallization of herapathite (under Quinine, *f*, "Herapathite").
3. " solution in ether (p. 116).
4. " solution in ammonia (see under Quinine, *g*, "Kerner's Test").

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[1] "This I find," shaking out with 50 c.c. and then with three successive portions, each of 25 c.c. of chloroform, "will bring back invariably 5.99 out of 6.00 grams of pure mixed alkaloids, and is decidedly the most accurate method, given practice in the way of shaking, etc., so as to get the chloroform to settle quickly."—J. MUTER, 1880: *The Analyst*, London, 5, 223.

[2] There may be added, for trial, (5) separation by precipitation as Oxalate—Shimoyama, 1885: *Archiv d. Phar.*, [3], 23, 209.

B.—*From Cinchonidine.*

1. By recrystallizations of the sulphate (p. 113).
2. " solution in ammonia, in filtrate from saturated sulphate (p. 117).

C.—*From Quinidine.*

1. By non-precipitation with potassium iodide (see Quinidine, *f*).
2. " non-solution of the sulphate in chloroform.[1]
3. " precipitation as normal tartrate.

D.—*From Cinchonine.*

1. By non-solution of the sulphate in chloroform.[1]
2. " precipitation as neutral tartrate (compare "Separation of Cinchonidine," p. 118).

E.—*From Amorphous Alkaloids.*

1. By crystallization of the sulphate.

II. SEPARATION OF CINCHONIDINE.

A.—*From other cinchona alkaloids in general.*

1. After removal of Quinine, by precipitation with normal tartrate (p. 118).
2. By precipitation as tartrate, followed by removal from Quinine by I. A. 1, 2, 3, or 4.

B.—*From Cinchonine and Quinidine.*

1. By non-solution of the sulphate in chloroform.
2. " precipitation as neutral tartrate (p. 118).

C.—*From Quinine.*

1. By non-crystallization as sulphate, repeated (p. 113).
2. " solution in excess of ammonia after filtration of sulphate (p. 117).

D.—*From Amorphous Alkaloids.*

1. By crystallization as normal tartrate (p. 119).

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[1] Taken separately, quinine sulphate and cinchonidine sulphate each requires about 1000 parts of chloroform for solution, while quinidine sulphate dissolves in 20 parts, and cinchonine sulphate in 60 parts, of this solvent. Taken in mixtures of quinine or cinchonidine with quinidine or cinchonine, these differences of solubility are seriously diminished (the author with Mr. Thum, 1878: *Proc. Am. Pharm.*, **26**, 831).

III. Separation of Cinchonine.

A.—*From other cinchona alkaloids in general.*

1. By non-solution in ether (p. 116).
2. " more sparing solution in alcohol.

B.—*From Quinine.*

1. By not crystallizing as sulphate (see below).
2. " solution of the sulphate in chloroform (see note on p. 112).

C.—*From Cinchonidine.*

1. By solution of the sulphate in chloroform.
2. " non-precipitation as neutral tartrate (p. 119).

D.—*From Quinidine.*

1. By non-precipitation with potassium iodide (Quinidine, *e*).

E.—*From Amorphous Alkaloids.*

1. By dilute alcohol.
2. " ether.

Separation of Quinine (I. A, 1) *from other cinchona alkaloids in general, by crystallization of the sulphate in aqueous solution* —The solubilities of the sulphates of the four alkaloids in water at 15° C. (59° F.) is, respectively, quinine, 740 parts; quinidine and cinchonidine, each 100 parts; cinchonine, 70 parts. The comparative insolubility of quinine sulphate in cold water is the most trusty factor in Kerner's test for quinine, official in U. S. Ph., in Ph. Germ. since 1872, and in the Ph. Fran., 1884.[1] Sulphate insolubility also enters into the Br. Ph. test The insolubility of quinine sulphate is not materially affected by the presence of other cinchona alkaloidal sulphates,[2] which is, unfortunately, not true of the solubility of quinine in ether, or of the insolubility of quinine sulphate in chloroform.

To effect complete separations, however, several recrystallizations are necessary. Cinchonidine certainly opposes some resistance to separation from quinine. Hesse has recently reaffirmed[3] that quinine sulphate is fully freed from as much as 2 per cent. of cinchonidine sulphate by two crystallizations from boiling water.

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[1] Kerner, 1862: *Zeitsch. anal. Chem.*, **1**, 150; *Phar. Jour. Trans.*, [2], 4, 19; *Am. Jour. Phar.*, **34**, 417. 1880: *Archiv d. Phar.*, [3], **16**, 186; **17**, 438; *Jour. Chem. Soc.*, **40**, 63. Kerner rests the separation in good part upon the action of ammonia in the filtrate.

[2] The author and Mr. Thum, 1878: *Proc. Am. Pharm.*, **26**, 834. "Report on Revision U. S. Ph.," 1880, pp. 29, 116.

[3] Hesse, 1886: *Phar. Jour. Trans.*, [3], **16**, 818; (1885) [3], **15**, 869.

Davies (1885)[1] found numerous recrystallizations necessary to obtain a salt with constant rotatory power. Kerner (1880)[2] found that three to six crystallizations of commercial quinine sulphate suffice to give a perfectly pure salt, as shown by a constant behavior in his ammonia titration. Kerner (1880) further states that in crystallizing from *hot* watery solution a slightly basic salt is crystallized. In this case the cleaned crystals become slightly alkaline to test-paper, while the filtrate becomes acidulous to a corresponding degree.

To effect the utmost separation by one crystallization it is indispensable to hold the reaction of the initial solution exactly neutral, as a slight acidity increases the solubility of quinine sulphate. In separations for estimation, therefore, the reaction should be neutral. But in separation to prepare absolutely pure quinine salt, though at expense of partial loss, crystallization from acidulous solution is more efficient. De Vrij has advised to convert to the definite acid sulphate [by adding as much more sulphuric acid as the quantity required to convert the free alkaloids into neutral salts]; then crystallize the acid salt, recrystallizing as necessary; and finally form the normal salt by precipitating one-half as the hydrate, and dissolving the washed precipitate in solution of the remaining acid salt.

The following directions *for separation of quinine as sulphate* are in effect those of the U. S. Ph., 1880 (p. 79),[3] but with provision for better regulation of the use of acid and alkali, an increase of temperature in the digestion before crystallizing, and the drying to anhydrous instead of effloresced sulphate. The unchanged pharmacopœial text is enclosed in quotation-marks.

"To the total alkaloids from 20 grams of cinchona, previously weighed," or to a weighed quantity (0.5 to 5.0 grams) of any ordinary mixture of free cinchona alkaloids, taken in a weighed beaker of capacity of about 120 fluid parts for 1 part of alkaloids, add from a burette decinormal solution of sulphuric acid until the liquid is "just distinctly acid to litmus-paper" and retains this degree of acidity after 15 to 30 minutes' digestion on

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[1] Davies, 1885: *Phar. Jour. Trans.*, [3], **16**, 358. To same effect, Oudemans, *Jahr. Chem.*, 1876. It is surmised that a double sulphate of cinchonidine and quinine crystallizes, according to Koppeschaar (1885) with $6H_2O$. See, also, Yungfleisch, 1887: *Phar. Jour. Trans.* [3] **17**, 585.

[2] Kerner, 1880: *Archiv d. Phar.*, [3], **16**, 191. As to the ammonia test, see under Quinine, *g*, "Kerner's test." Kerner found that heating the solution *before* the crystallizing at 15° C. had little influence on the result.

[3] Given first in the author's contribution to "Report on Revision U. S. Ph.," 1880, p. 26. Data taken from the report of Prescott and Thum, 1878: *Proc. Am. Pharm.*, **26**, 834.

the water-bath.[1] Add now decinormal solution of soda from the burette until after stirring the reaction is "exactly neutral to the test-paper." Note the number of c.c. of acid and of alkali which have been added.[2] Add water "to make the whole weigh seventy times[3] the weight of the alkaloids." Heat to near boiling for five or ten minutes, "then cool to 15° C. (59° F.) and maintain at this temperature for half an hour. If crystals do not appear the total alkaloids do not contain quinine in quantity over *eight* per cent. of their weight (corresponding to *nine* per cent. of sulphate of quinine, crystallized). If crystals appear in the liquid pass the latter through a filter not larger than necessary, prepared by drying two filter-papers of two to three and a half inches (5 to 9 centimeters) diameter, trimming them to an equal weight, folding them separately, and placing one within the other so as to make a plain filter fourfold on each side. When the liquid has drained away wash the filter and contents with distilled water of a temperature of 15° C. (59° F.), added in small portions, until the entire filtered liquid weighs *ninety* times[4] the weight of the alkaloids taken. Dry the filter, without separating its folds," at 100° C.,[5] "to a constant weight, cool, and weigh the inner filter and contents, taking the outer filter for a counter-weight. To the weight of" anhydrous sulphate of quinine so obtained add 16.89 per cent. of its amount for water of crystallization.[6] "And add 0.12 per cent. of the weight[7] of

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[1] If the alkaloids be contaminated with resin and kinic acid, add enough more of the volumetric acid to surely dissolve all the alkaloids, avoiding excess of acid, and filter through a filter as small as possible, washing with the least quantity of hot water and a few drops of acid from the burette, until a drop or two of the washings cease to react for quinine when tested with a drop of Mayer's solution. To the filtrate add of decinormal solution of soda as many c.c. as have been added of the acid beyond the point of just perceptible acidity, bringing back the reaction to this point.

[2] Then (c.c. of decinormal acid — c.c. of alkali) × 0.03 [0.0324 to 0.0294] = nearly the quantity of total cinchona alkaloids present, in grams. But observe that if the alkaloids have been precipitated with soda, incomplete washing may have left behind sufficient alkali to affect the result.

[3] Or to make the whole measure of c.c. a number equal to 2.1 × (c.c. of decinormal acid — c.c. of alkali).

[4] Or until the liquid measures, in c c., 2.7 times (c.c. of decinormal acid — c.c. of alkali).

[5] The U. S. Ph. directs to dry at 60° C. (140° F.) to a constant weight as effloresced sulphate ($2H_2O$). Of this weight 11.5 per cent. is added to give the quantity of crystallized salt ($7H_2O$).

[6] To represent seven molecules, or 14.45 per cent. crystallization water. See under Quinine (*f*).

[7] That is, add 0.0012 of weight of crystals for each c.c. of total filtrate. This correction presumes that the saturated solution ($\frac{7}{9}$ of the filtrate) shall carry in solution 0.135 per cent. of crystallized salt (1 to 740), and that the washings ($\frac{2}{9}$ of the filtrate) shall hold 0.067 per cent. of cryst. salt, which is

the entire filtered liquid (for solubility of the crystals at 15° C.)" The sum equals the quantity of quinine as crystallized sulphate in the mixed alkaloids taken. If from 20 grams of the bark, multiply by 5 to convert to percentage. Of the crystallized sulphate ($7H_2O$), 74.31 per cent. is anhydrous quinine.

Separation of Quinine (I. A, 3) *from other cinchona alkaloids by ether.*—The ether solubilities of the alkaloids *taken separately* are for good ether very nearly as follows, at 15° C.: quinine in 25 parts of the ether, quinidine in 30 parts, cinchonidine in 188 parts, and cinchonine in 371 parts of ether. The amorphous alkaloids of cinchona have in general a very considerable solubility in ether. Quinidine occurs in so small quantities that its solubility is not regarded. But the different factors of solubility above stated are not available for separation, because, as every analyst experiences, they do not hold true in mixtures of the alkaloids. Thus in a mixture of quinine and cinchonidine, quinine is less soluble and cinchonidine is more soluble in ether than when these alkaloids are taken separately.[1] Nevertheless, separation by ether has been in use by quinologists more than any other separation. An analyst of bark learns by the manufacturer's results so to adjust the application of the ether that, for example, about as much of quinine will remain undissolved as there is of cinchonidine in solution. The use of ether in testing quinine for presence of cinchonine is credited to LIEBIG[2] in the test which bears his name. For use of ether in the assay of the mixed alkaloids for quinine, or for ether-soluble alkaloids, the author prefers the very practical directions of Dr. SQUIBB, who prefaces the following instructions[3] by the statement that "it

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half saturation. The degree of partial saturation of the washings (if held at 15° C.) is subject to the rate of application of the wash-water and its retention in the filter. Six experiments of the author with Mr. Thum (1878: *Proc. Am. Pharm.*, **26**, 834) gave a mean result equivalent to 0.00095 of crystallized sulphate for each c.c. of filtrate (stated as 0.00085 of effloresced sulphate for each c.c.) The exact average figures as 0.00081 of effloresced salt for each c.c. J. MUTER (1880: *Analyst.* **5**, 224) adds 0.000817 of crystallized sulphate for each c.c. of total filtrate, a filtrate which is about 80 per cent. saturated solution and 20 per cent. washings. Further evidence on the rate of this correction is desirable. The 0.12 per cent. correction may be too large. It is stated by CARLES (1872) that the solubility of the quinine sulphate is diminished by presence of ammonium sulphate; by SCHLICKUM (1885) that it is greatly diminished by presence of sodium sulphate. But these facts seem to afford no aid in separation of clean sulphate of quinine for weight, unless by a resort to washing with saturated solution of quinine sulphate and a correction proportional to the drying-loss.

[1] Experimental results are given by PAUL, 1877. KOPPESCHAAR (1885: *Zeits. anal. Chem.*, **24**, 362) infers that quinine and cinchonidine unite in a compound which is readily soluble in ether.

[2] A note on the history of the test is given under Quinine, *g*.

[3] 1882: *Ephemeris*, **1**, 111.

seems only practicable, in a general way, to reach near approximations by some method which is simple and easy of application":

"Into the flask containing the total alkaloids [from 5 grams bark, or 10 grams if poor in alkaloids], after these have been weighed, put first 5 grams of glass which has been ground up in a mortar to a mixture of coarse and fine powder, and then 5 c.c. of stronger ether (sp. gr. not above 0.725 at 15° C.) Cork the flask and shake it vigorously until by means of the glass all the alkaloids have been detached from the flask and ground up in the presence of the ether into fine particles. In this way the definite quantity of ether, which is large enough to dissolve all the quinine that could possibly be present, becomes entirely saturated with alkaloids in the proportion of their solubility, and the solution will necessarily embrace all the soluble ones as the quinine.—Next mark two test-tubes at the capacity of 10 c.c. each, and place a funnel and a filter of 7 centimeters (2.8 inches) diameter over one of them. Wet the filter well with ether, and then pour on to it the mixture of alkaloids, ether, and glass from the flask. Rinse the flask out two or three times on to the filter with fresh ether, and then wash the filter, and percolate the glass, with fresh ether, applied drop by drop from a pipette, until the liquid in the test-tube reaches the 10 c.c. mark. Then change the funnel to the other test-tube, and continue the washing and percolation with ether until the mark on the second test-tube is reached by the filtrate. Pour the contents of the two test-tubes into two small tared capsules, evaporate to a constant weight, and weigh them. The first capsule will contain what may be called the ether-soluble alkaloids. Subtract from the weight of these the weight of the residue in the second capsule, and the remainder will be the approximate weight of the quinine extracted from the 5 grams of bark." These weights multiplied by 20 will give the percentage of ether-soluble alkaloids and of quinine."—It is here understood that the terms "ether-soluble alkaloids" and "quinine" have a conventional meaning. And the conclusion is adopted that the quinine is all or nearly all obtained in the first 10 c.c. of filtrate, while of the less soluble alkaloids nearly equal quantities are obtained in the first and the second 10 c.c. of filtrates. Therefore the subtraction of the weight of the second residue from the weight of the first will give an approximation to the weight of the quinine.

Separation of Quinine (I. A, 4) *from other cinchona alkaloids by solution in excess of ammonia, after crystallization of the sulphate. An adaptation of Kerner's volumetric method.*

More fully studied for Cinchonidine than for quinidine or cinchonine.[1] *Application to a Precipitate or Residue of Quinine with small proportions of Cinchonidine* (I. B, 2).—The precipitate or residue is dried finally on the water-bath to a constant weight, and a weighed quantity, from 3 to 5 grams, of the dried alkaloids is taken. The alkaloids are treated with warm dilute sulphuric acid added with a little hot water to make the reaction just distinctly acidulous to litmus-paper, and retain this reaction after the alkaloids have been thoroughly saturated, when the mixture is exactly neutralized by adding dilute ammonia-water, and made up at temperature near 100° C. to a number of c.c. equal to 14.5 times the number of grams of dried alkaloid taken. The container is now placed in a bucket of water at about 15° C., along with a bottle of Standard Quinine Sulphate Solution (see Index) and a bottle of ammonia-water of sp. gr. 0.920, and the same temperature maintained for an hour or more, and adjusted at 15° C. near the close of this time. The two alkaloidal solutions are now filtered through dry filters, and the filtrates received in portions of 10 c.c. each, in test-tubes —the standard quinine filtrates on one side, and the filtrates from the alkaloids to be estimated on the other side. The filtrates are titrated, in repeated trials, by adding ammonia from a burette (registering $\frac{1}{20}$ c c.), until, on gently inclining or rotating the test-tube while it is closed by the finger, the precipitate at first formed is just redissolved.—Should the first 10 c.c. of filtrate under estimation require more than about 4.8 c.c. of the ammonia (0.920), after deducting the c.c. taken for 10 c.c. of the standard quinine, then a 10 c.c. filtrate under estimation should be diluted, by addition of the standard quinine filtrate, to 2, 3, or 4 times the 10 c.c. volume (20, 30, or 40 c.c.), and portions of 10 c.c. of this diluted filtrate tested. The results of these tests, after deducting the average c.c. of ammonia for 10 c.c. of standard quinine filtrate, are multiplied by 2, 3, or 4, to give the proper quantity of ammonia for 10 c.c. of the filtrate under estimation —Taking now the mean of the several titrations for 10 c.c. filtrate under estimation, after deducting the mean of titrations of standard quinine filtrate, each 0.32 c.c. = 0.1 per cent. cinchonidine in the mixed alkaloids estimated.

SEPARATION OF CINCHONIDINE (II. A, 1) *from other cinchona alkaloids in general, after removal of quinine, by precipitation*

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[1] KERNER, 1862. Improved in 1880: *Zeitsch. anal. Chem.*, **20**, 150; *Archiv d. Phar.*, [3], 16, 186–285; 17, 438–454; *Jour. Chem. Soc.*, **40**, 63. Discussion, in this work, under Quinine, *g.* "Kerner's Test."

with normal tartrate.—The quinine may be removed (1) by crystallization as a sulphate (p. 114), or (2) by solution in ether (p. 116). *For the purpose of an estimation, a deduction of the quantity of quinine* from the quantity of both quinine and cinchonidine is quite sufficient. To this end the following directions of MUTER,[1] here slightly varied, serve well:

The quinine is separated and estimated as crystalline sulphate (p. 114). A weighed portion of the mixed cinchona alkaloids is dissolved with hydrochloric acid enough to make the solution only slightly acid[2] to test-paper, and as concentrated as compatible with solution at 38° C. (or 100° F.)[3] The solution is made exactly neutral by adding sodium hydrate dilute solution, an excess of the precipitant, a saturated solution of tartrate of potassium and sodium (Rochelle salt) is added, and the mixture kept at 15° C. (59° F.) for an hour, stirring frequently with a glass rod. The precipitate is collected on a pair of filters as small as practicable and previously (dried and) counterbalanced with each other, and is washed with, say, 100 c.c. of water at 15° C., the filtrate and washings being received in a graduated measure. The precipitate is dried at 104° C. (or at 220° F.) and weighed, using the outer filter as a tare. For each c.c. of the total filtrate 0.00083 is added (MUTER) to the weight of the precipitate. The weight of anhydrous quinine sulphate is multiplied by 0.9151, or the weight of anhydrous quinine is multiplied by 1.231, to obtain the weight of anhydrous quinine tartrate, which is deducted from the weight of the precipitate. The remainder is the weight of anhydrous cinchonidine tartrate $(C_{19}H_{22}N_2O)_2C_4H_6O_6$, which, multiplied by 0.7967, gives the weight of cinchonidine. (For following separation of remaining alkaloids see p. 120).

Separation of Cinchonidine (II. A, 2) *by precipitation as tartrate, followed by removal from Quinine.* This plan differs from the preceding only in the order of the successive steps.—In precipitating first as tartrate, in case of Commercial Quinine Sulphate, DE VRIJ (1884) directs to take 5 grams of the salt, in 200 c.c. boiling water, and add 5 grams of Rochelle salt previously dissolved in very little boiling water. After 24 hours collect on a filter, wash with the smallest quantity of water, and dry in the

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[1] 1880: *Analyst*, 5, 224.

[2] Muter dissolves the mixed alkaloids in absolute alcohol, divides in two equal portions, taking one portion for quinine as a sulphate. The portion for cinchonidine is made just acid with hydrochloric acid, the alcohol evaporated off, and the residue dissolved in least quantity of water at 100° F.

[3] If the total alkaloids contain resins, kinic acid, etc., filter through a small filter, wash with as little dilution as possible, and if necessary concentrate.

air.—Kopp states that a double normal tartrate of quinine and cinchonidine crystallizes with 1 molecule of water.—Heilbig (1880), following De Vrij, *separates cinchona alkaloids in general*, by initial precipitation of tartrates, as follows: 2 grams of the mixed alkaloids are dissolved as acetates in 30 c.c. of water, and the solution mixed with 1 gram Rochelle salt and well stirred. The precipitate is washed with care to avoid its solution, and dissolved in 90 per cent. alcohol acidulated with 1.6 per cent. of sulphuric acid, and herapathite is formed (as directed under Quinine, *f*).—The filtrate is treated with potassium iodide for precipitation of quinidine. The filtrate from the latter is treated with soda, and the resulting precipitate, dried, is exhausted by absolute ether for removal of amorphous alkaloids, the remainder being cinchonine.

For separation of Cinchonidine, Quinidine, Cinchonine, and Amorphous Alkaloids from each other, after the estimation of Quinine, the directions of De Vrij are as follows: "Two grams of the pulverized mixed alkaloids are dissolved in weak hydrochloric acid to obtain a slightly alkaline solution measuring 70 c.c. By adding 1 gram of Rochelle salt to this solution," heating, cooling, stirring, and setting aside, as above indicated, "the tartrates of quinine and cinchonidine are separated; these are collected on a filter, washed with a little water, and dried on a water-bath. One part of these tartrates represents 0.80844 of quinine and cinchonidine: from the amount of these alkaloids thus found the amount of quinine already ascertained is subtracted, the remainder representing *the cinchonidine* present."—"In the filtrates from the tartrates, *quinidine*, if present, is precipitated by a concentrated solution of potassium iodide [compare under Quinidine, *d* and *f*]; one part of the dried hydriodide represents 0.86504 part of crystallized quinidine [0.7175 part of anhydrous quinidine]."—"The remaining solution is treated with caustic soda, and the precipitate (if any) washed with ether. The residue represents the amount of *cinchonine* (compare under Cinchonine, *f*)."—"Finally, by distilling the ether from the washings can be ascertained the amount of *amorphous alkaloid*, which often, in the case of analysis of Indian barks, contains traces of *quinamine*."

The directions of J. Muter,[1] for separation of *Quinidine, Cinchonine, and Amorphous Alkaloid*, taking the filtrate from Cinchonidine and Quinine tartrates (see p. 119), are as follows: "The filtrate from the tartrate is concentrated to its original

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[1] 1880: *Analyst*, 5, 224.

volume [that before the washing of the precipitate is probably intended], cooled, rendered just faintly acid by a drop of dilute acetic acid, and excess of saturated solution of potassium iodide is added with constant stirring. After an hour or so at 15° C. [compare under Quinidine, *f*] it is collected like the cinchonidine, and treated in every respect the same, and weighed, and the weight, having had 0.00077 added for each c c. of filtrate and washings, is multiplied by [0.7175], and result is *quinidine.*"—"The filtrate from the quinidine is made distinctly alkaline by sodium hydrate, and the precipitated cinchonine and amorphous alkaloid are filtered out in a similar manner, washed, dried, and weighed. The precipitate is then treated with alcohol of 40 per cent. to dissolve out the amorphous alkaloid, and again dried and weighed, and the difference is *amorphous alkaloid*, while the last weighing is cinchonine." But "the weight of the cinchonine and amorphous alkaloid together must have deducted from it 0.00052 for each c.c. of the filtrate from the quinidine hydriodide, and 0.00066 for each c.c. of the filtrate from the cinchonidine tartrate, and the balance is then the true weight, which, minus the amorphous alkaloid, gives the *cinchonine.*"

ROTATORY POWER OF CINCHONA ALKALOIDS.

The plane of polarized light is deviated to the left by quinine and cinchonidine, to the right by quinidine and cinchonine. Further, the *dextrorotatory* alkaloids include diquinicine, quinicine, cinchonicine, concusconine, conchairamine, chairamidine, and cinchotine; the *levorotatory* alkaloids include hydroquinine, hydroquinidine, hydrocinchonidine, homoquinine, cusconine, conchairamidine, paytine, aricine, and cinchamidine.—The degree of deviation, or specific rotatory power, varies between the free alkaloid and its salts,[1] and varies with different solvents, concentrations, and temperatures.

Quinine hydrate, in alcohol 97% vol., at 15° C., $[a]_{\mathrm{D}} = -(145.2^\circ - 0.657c$[2]$)$	Hesse,	1875.
Quinine hydrate in ether (0.7296), at 15° C., $[a]_{\mathrm{D}} = -(158.7^\circ - 1.911c)$	"	"
Quinine, anhyd., 5% sol. in chloroform, 15° C., $[a]_{\mathrm{D}} = -106.6^\circ$	"	"
Between 15° C. and 25° C., when $c = 3$, absolute rotatory power falls 1.56°	"	"

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[1] Further as to the influence of the acids, Oudemans, 1883; as to influence of solvents, the same author, 1873.

[2] c = concentration, or grams in 100 c.c. of solution.

Quinine sulphate, cryst., in alcohol 80% vol., (c=2), 15° C., $[a]\,\mathrm{D}=-162.95^\circ$	HESSE, 1875.
Quinine sulphate, cryst., in alcohol 60% vol., (c=2), 15° C., $[a]\,\mathrm{D}=-166.36^\circ$	" "
Quinine bisulphate, cryst., in water, (c=1 to 6), 15° C., $[a]\,\mathrm{D}=-(164.85^\circ-0.31c)$........	" "
Quinine sulphate, anhyd., in water, (c=4), 15° C., $[a]\,\mathrm{D}=-229.03^\circ$	" 1880.
Quinine sulphate, anhyd., in water, (c=1), 15° C., $[a]\,\mathrm{D}=-232.7^\circ$	DAVIES, 1885.
Quinine sulphate, anhyd., in water, (c=4). 15° C., $[a]\,\mathrm{D}=-233.75^\circ$........................	HESSE, 1886.
Quinine sulphate, anhyd., in water, 17° C., $[a]\,\mathrm{D}=-242\ 17^\circ$	OUDEMANS.
Quinine hydrochloride, in water, (c=1 to 3), 15° C., $[a]\,\mathrm{D}=-(165.5^\circ-2\ 425c)$.........	HESSE.
Cinchonidine, in alcohol of 97% vol., (c=1 to 5), 15° C., $[a]\,\mathrm{D}=-(107.48^\circ-0.297c)$.......	"
Cinchonidine sulphate, 6 *aq.*, in water, (c=1.06), 15° C., $[a]\,\mathrm{D}=-106.77^\circ$.................	"
Cinchonidine sulphate, anhyd., in 2.156% sol. in alcohol, $[a]\,\mathrm{D}=-153.95^\circ$...............	"

With 0.40 gram of the salt, with 3 c.c. normal solution hydrochloric acid, and water to make a volume of 20 c.c ("Concentration A" of Oudemans):

Quinine tartrate, cryst., $[a]\,\mathrm{D}=-215.8^\circ$......	OUDEMANS.
Anhyd.$=-220.07^\circ$..........	KOPPESCHAAR.
Cinchonidine tart., cryst., $[a]\,\mathrm{D}=-131.3^\circ$....	OUDEMANS.
Anhyd.$=-137.67^\circ$..................	KOPPESCHAAR.

Take 0.40 of *mixed tartrates of quinine and cinchonidine* (see under Separation of Cinchona Alkaloids by Tartrate, p. 119), dry at 125° to 130° C., dissolve as stated above for "Concentration A," observe rotatory power (a), then, to find $x=$ per cent. of quinine tartrate in the mixed tartrates:

$$220.07\,x+137.67\,(100-x)=100\,a.$$

And
$$x=\frac{100\,(a-137.67)}{220.07-137.67}.[1]$$

For the estimation of *cinchonidine in commercial quinine*

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[1] KOPPESCHAAR, 1885: *Zeitsch. anal. Chem.*, **24**, 362; *Jour. Chem. Soc.*, **49**, 182. OUDEMANS, 1875: *Arch. neerland. des Sci.*, **10**, 193; *Jahr. Chem.*, **1875**, 140. Further, 1877 and 1884.

sulphate Hesse[1] directs as follows: 2 grams of anhydrous commercial quinine sulphate, or an equivalent quantity of crystallized salts, are weighed in a flask of 25 c.c. capacity, mixed with 10 c.c. of normal solution of hydrochloric acid, the flask filled up to the graduation-mark with water, and, after the contents are thoroughly mixed by shaking, the solution is poured through a filter into the observation-tube, which is 220 millimeters long and is provided with a water-jacket for maintaining a constant temperature. From 12 to 20 observations are made with this solution, at 15° C., and the mean of the different readings is taken. Let $c =$ the observed deviation at the D line, and $y =$ the cinchonidine sulphate.[2] Then, if the observation-tube be 220 m.m., $y = (40.309 - c) \times 8.25$. For other lengths of the observation-tube let $C =$ the observed rotatory power, when $y = (229.03 - C) \times 1.452$.

Quinidine, deviation diminishes with elevation of temperature.

Quinidine hydrate, in alcohol of 97% vol., at 15° C., $[\alpha]_D = +(236.77° - 3.01c)$ .... Hesse.

Quinidine anhyd., in alcohol of 97% vol., at 15° C., $[\alpha]_D = +(269.57° - 3.428c)$ .... "

Quinidine hydrochloride, in alcohol of 97%, at 15° C., $[\alpha]_D = +(212° - 2.562c)$ .... "

Cinchonine, in alcohol, $c = 0.455$, $[\alpha]_D = +214.8°$
$c = 0.535$, $= 213.3°$
$c = 0.560$, $= 209.6°$ .... Oudemans.

Cinchonine sulphate, in water, $c = 0.855$, $[\alpha]_D = +170°$ .... Hesse.

Cinchonine sulphate, in 97% alcohol, $c = 0.374$, $[\alpha]_D = +193.29°$ .... "

Cinchonine hydrochloride, $[\alpha]_D = +(165° - 2.425c)$.. "

Quinicine, in 97% alcohol with chloroform, $[\alpha]_D = +(10.68° - 1.14c)$.

Cinchonicine, in chloroform, at 15° C., $[\alpha]_D = +46.5°$.

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[1] 1880: *Liebig's Annalen.* 205, 217; *Jour. Chem. Soc.*, 40, 315. Also, 1885: *Phar. Jour. Trans.*, [3]. 15, 869.

[2] If a be the angle of rotation of dry quinine sulphate, b the angle of anhydrous cinchonidine sulphate, and c the angle of the mixture, then if x be the quantity of quinine sulphate, and y the quantity of cinchonidine sulphate, the relative percentage of the last-named salt is expressed by the formula $y = \frac{a-c}{a-b}$. For a and b Hesse has found the numbers —40.309° and —26.598°; therefore $y = \frac{40.309 - c}{13.711}$, or, taking y as percentage, $y = (40.309 - c)\ 7.293$. On account of the common efflorescence of cinchonidine sulphate, Hesse modifies the formula to $y = (40.309 - c)\ 8.25$.

A single determination in a given solvent obviously cannot be used for estimation when more than two alkaloids of cinchona are present. But by use of different solvents, or different temperatures and concentrations, it has been proposed to undertake estimation in mixtures of three alkaloids. OUDEMANS has stated that optical estimation is practicable in the following-named mixtures: quinine and cinchonidine; quinine and quinidine; quinidine and cinchonidine; quinine and cinchonine; cinchonidine and cinchonine; quinine, quinidine, and cinchonidine; quinine, quinidine, and cinchonine; quinidine, cinchonidine. and cinchonine; quinine, cinchonidine, and cinchonine; and tartrate of quinine, and cinchonidine. KOPPESCHAAR[1] has advocated the superior efficiency of the optical way of estimating cinchona alkaloids, and DAVIES,[2] in report of the extended research already cited, expresses confidence in the optical estimation of cinchonidine in commercial quinine sulphate. HESSE, who engaged extensively in optical researches upon the cinchona alkaloids in 1875,[3] and published an optical method of valuation of quinine sulphate in 1880,[4] in 1886[5] admits a diminished confidence in the optical method for exact estimations, and says that "up to the present moment we are not in possession of any optical test by which we would be able to determine the amount of cinchonidine in commercial quinine sulphate and other quinine salts with any satisfactory degree of accuracy." And "while constant rotatory power in two successive recrystallizations of the same material [quinine sulphate] is satisfactory evidence of absence of cinchonidine in that particular material, it is not by any means the case that the rotatory power of similar materials of different origin is always the same." PAUL[6] has stated "that the results by the polariscope are much less trustworthy than those by other methods." KERNER[7] holds it to be manifestly impracticable to determine proportions of 1 and 1½ per cent. of cinchonidine sulphate, in mixtures of quinine sulphate, with even minute proportions of cinchonine and quinidine sulphates.

The influence of hydroquinine salt, in the optical valuation of quinine sulphate, is emphasized by HESSE in the communication

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[1] 1885: *Phar. Jour. Trans.*, [3], **15**, 809.
[2] 1885: *Phar. Jour. Trans.*, [3], **16**, 358.
[3] *Liebig's Annalen*, **176**, 203–233.
[4] *Liebig's Annalen*, **205**, 217–222.
[5] *Phar. Jour. Trans.*, [3], **16**, 818, March 27, 1886. Further, same journal, June 5, 1886.
[6] 1885: *Phar. Jour. Trans.*, [3], **16**, 361.
[7] 1880: *Archiv d. Phar.*, [3], **16**, 449.

last above cited from this author.[1] He places the rotatory power of the three alkaloids chiefly concerned in the estimation of commercial quinine sulphate as follows. The conditions of Oudemans (p. 122) are adopted:

For concentration A:	Quinine tartrate	(a) D =	216.6°
	Cinchonidine tartrate		134.6°
For concentration B:	Quinine tartrate		212.5°
	Hydroquinine tartrate		176.9°
	Cinchonidine tartrate		132.0°

Oudemans's own results were (see p. 122):

For concentration A:	Quinine tartrate	(a) D =	215.8°
	Cinchonidine tartrate		131.3°
For concentration B:	Quinine tartrate		211.5°
	Cinchonidine tartrate		129.6°

Quinine.—Chinin. $C_{20}H_{24}N_2O_2=324$. Crystals of full hydration, $C_{20}H_{24}N_2O_2.3H_2O=378$. Rational Formula, p. 98. Proportion in Cinchona Barks, p. 96. Accompanying Natural Alkaloids, p. 90. Methods of quantitative separation from Cinchona Bark, p. 102; from other Cinchona Alkaloids, p. 113. Means of Distinction from other Cinchona Alkaloids, schedule, p. 100. Microscopic identification, p. 101. Optical Rotation, p. 121. Crystallization and Heat-Reactions of the free alkaloid and its salts, p. 126. Solubilities of the alkaloid and of its salts, p. 128. Physiological effects, p. 127.

Quinine is *recognized* by the fluorescence of its sulphate solution (*d*), its bitterness (*b*), and the sparing solubility of its sulphate in water (*c*). It is *identified*, further, by the thalleioquin test, the agreement of various reactions, and the formation of herapathite (*d*). The *separation* of quinine from other cinchona alkaloids is indexed at p. 111; from the bark, given on pp. 102 to 111; from impurities of its commercial salts, and from various common alkaloids, also from Citrate of Iron, and from Coated Pills, page 134. Means of separation are noted under *e*. Quinine is *estimated*, as stated under *g*, by weight of the free alkaloid, by weight of the sulphate, by weight of the iodomercurate, by titration with Mayer's solution, and by weight of crystallized herapathite. The *impurities and deficiencies* of quinine

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[1] For a brief summary of the claims of De Vrij and Hesse see *Am. Jour. Phar.*, 1886, Aug., **58**, 389, editorial. Respecting optical estimations of quinine, treating the tartrates of the alkaloids, a paper is presented by D. Hooper, Ootacamund, India, 1886: *Phar. Jour. Trans.*, [3], **17**, 61.

salts (under *g*) are chiefly the other cinchona alkaloids, and varied quantities of water. The other cinchona alkaloids are subject to test by Kerner's method, qualitative or quantitative, and given for salts other than sulphate, the free alkaloid, the bisulphate, and for effloresced salts. Tests are given by Hesse's method, and by the directions of the pharmacopœias of the different nations. Concerning Liebig's test, and standards of water of crystallization, a full discussion is included under *g*.

a.—Free quinine usually appears in an amorphous or curdy or minutely crystalline white powder, or in crystals slightly effloresced. *The trihydrate* ($3H_2O$) forms needles, sometimes long and silky. Crystallizing under the microscope, four-sided prisms are obtained. The precipitate by alkalies from aqueous solution of quinine salts is at first amorphous and anhydrous, but gradually assumes crystallization as the trihydrate. From warm, dilute alcoholic solution anhydrous crystals have been obtained (Hesse, 1877). From ether, and most solvents other than water and alcohol, crystals are never obtained. A dihydrate ($2H_2O$) and a crystallizable monohydrate (H_2O) have been reported; also an amorphous hydrate with $9H_2O$. The precipitate by ammonia, dried in the air at ordinary temperature, and the residue from solution in ether dried in the same way or over sulphuric acid, retain one molecule of water (Fletcher, 1886). The trihydrate, nearly permanent in the air, loses all but about one molecule of the water slowly in the desiccator, quickly on the water-bath. All hydrates lose water gradually in warm temperatures, and on the water-bath quickly lose all but four or five per cent. (about one molecule) of the water, which is very slowly expelled (A. N. Palmer, 1876). At about 120° C. (248° F.) a constant weight of anhydrous alkaloid is promptly obtained. The trihydrate *melts* at 57° C. (134.6° F.); the anhydrous alkaloid melts, without loss, at 177° C. (350.6° F.) (Hesse, 1877), cooling to an opaque, crystalline mass permanent in the air. Strongly heated above the melting point, an amorphous, not crystalline sublimate is obtained.

Crystallization and heat-reactions of salts of quinine.[1]—*Quinine sulphate* forms fragile, filiform crystals on the monoclinic system, with $7H_2O$ (Kerner, 1880) or $8H_2O$ (Hesse, 1880). (See "Water of Crystallization," etc., under *g*.) The crystals are efflorescent. The hydration is reduced, slowly in ordinary air, promptly at 50° to 60° C., to $2H_2O$. The remaining water is expelled slowly at 100° C., or, by three hours' dry-

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[1] For chemical formulæ see "Solubilities," p. 129.

ing in a water-oven (H. B. Parsons, 1884), more quickly at 112° to 115° C. The anhydrous salt recovers the $2H_2O$ by exposure to the air. At or above 100° C. the salt soon begins to suffer alteration; at about 160° C. it exhibits a greenish phosphorescence, and above this temperature it melts, with conversion into quinicine sulphate, but without loss of weight. The salt is very slowly affected by the light. On ignition it burns very slowly, leaving no residue after complete combustion.—*Quinine bisulphate* forms orthorhombic four-sided prisms, or needles, sometimes nodular crystals ($7H_2O$), efflorescing in the air, more rapidly in warm air, to $1H_2O$, and becoming anhydrous at 100° C. It melts in a glass tube at 80° C. (Ph. Germ.) When anhydrous it melts at or below 100° C. "At 135° C. (275° F.) it is converted into bisulphate of quinicine" (U. S. Ph.), this conversion beginning at the melting point, also by exposure to sunlight, and being attended with a yellowish tinge. There is a doubly acid salt, crystallizable, with $7H_2O$, in prisms.—*Quinine hydrobromide* crystallizes in lustrous needles (H_2O), "permanent in the air but readily efflorescing at a gentle heat" (U. S. Ph.), and becomes anhydrous on the water-bath.—*Quinine hydriodide*, normal, is crystallizable in light yellow needles, instable, easily altered to a soft, resinous mass.—*Quinine nitrate* crystallizes with difficulty in very oblique prisms (H_2O), easily melted to an oily mass, and becoming anhydrous at 100° C.—*Quinine valerianate* crystallizes in pearly, triclinic crystals (H_2O), permanent in the air, melting at about 90° C., becoming anhydrous at 100° C., at which temperature it also begins to lose valerianic acid.—*Quinine normal tartrate*, H_2O, becomes anhydrous at 100° C.—*Quinine oxalate*, normal, crystallizes with $6H_2O$, in very fine needles.

b.—Quinine is odorless, and has a pure bitter taste of much intensity. The persistence and intensity of the bitter taste of quinine salts is in proportion to their solubility as brought in contact with the tongue. Of ordinary forms administered the tannate is the least and the free alkaloid next least bitter, the sulphate being less bitter than the bisulphate, hydrobromide, or hydrochloride.—Quinine is poisonous to the lower forms of animal life, in this effect being surpassed among vegetable poisons only by such as strychnine and morphine (Binz). For frogs the fatal dose is 0.05 to 0.1 gram ($\frac{3}{4}$ to $1\frac{1}{2}$ grain) internally, or about 0.0025 ($\frac{3}{8}$ grain) subcutaneously. For dogs about 0.12 gram per kilogram ($\frac{7}{8}$ grain per pound) of body-weight proves fatal (Bernatzik, 1867). Infusoria and bacteria are destroyed with somewhat concentrated solutions of quinine salts, quite variable strengths being required for different infusoria.—Quinine is antiseptic, hindering or stopping the alcoholic, lactous, butyrous, amygdalous, and salicylous fermentations (BINZ, "Husemann's Pflanzenstoffe," 1884), not the digestive action of pepsin.—Quinine is excreted *in the urine* to the extent of 70 to 96 per cent. of the amount taken. It appears in the urine as early, frequently, as one hour, and usually disappears as soon as forty-eight hours, after ingestion (KERNER, JURGENSEN, and FRAU). Quinine is found in the liver. In some small part, also, it suffers conversion in the system into *amorphous quinine* [diquinicine?], and an oxidation product, *Dihydroxyl-quinine* ($C_{20}H_{24}N_2O_4$) (KERNER), or, according to SKRAUP, *Chitenine* ($C_{19}H_{22}N_2O_4$). Kerner states that the physiological action of the oxidized product is much weaker than that of quinine. Chitenine is formed by action of permanganate on quinine, is insoluble in ether, fluoresces, and gives the thalleioquin reaction.

c.—Solubilities.—Quinine is sparingly soluble in water; quite freely soluble in alcohol, ether, chloroform, amyl alcohol; moderately soluble in water of ammonia, benzene, glycerine; and sparingly soluble in petroleum benzin. *The alkaloid trihydrate* is soluble in 1670 parts water at 15° C. (HESSE), in 1428 parts water at 20° C. (SESTINI, 1867), in 760 parts boiling water (REGNAULD, 1875), in 902 parts boiling water (SESTINI), in six parts of ordinary alcohol at 15° C., in $1\frac{1}{12}$ parts absolute alcohol (REGNAULD), in 2 parts boiling alcohol of 90%, in "about 25 parts of ether" (U. S. Ph.), in $22\frac{1}{2}$ parts of ether at 15° C. (REGNAULD), in "about 5 parts of chloroform" (U. S. Ph.) *The anhydrous alkaloid* is soluble in 1960 parts of water at 15° C. (HESSE), in about the same proportion of ether required for the hydrate (HESSE), in (near) 2 parts chloroform (PETTENKOFER, 1858), in 200 parts benzene at 15° C. or 30 parts boiling benzene (OUDEMANS, 1874).

Crystals, mostly needle-form, can be obtained from nearly all solutions. From benzene, crystals of $C_{20}H_{24}N_2O_2+C_6H_6$ are obtained (OUDEMANS). Solubility in ether is diminished by presence of other cinchona alkaloids (PAUL, 1877).

Quinine has a decided alkaline reaction, promptly shown upon test-papers in the aqueous solution. The normal salts of the stronger acids are neutral to litmus, the sulphate of manufacture not infrequently alkaline in the least perceptible degree.—Quinine salts of ordinary acids are soluble or moderately soluble in water and in alcohol, except the sulphate, which is only sparingly soluble in water. The proportion of water required for the free alkaloid at 100° C. is about that required for the sulphate at 15° C.

Solubilities of quinine salts. — *Quinine sulphate,* $(C_{20}H_{24}N_2O_2)_2H_2SO_4.7H_2O=872$, is soluble "in 740 parts of water and in 65 parts of alcohol at 15° C. (59° F.); in about 30 parts of boiling water, in about 3 parts of boiling alcohol, in small proportions of acidulated water, in 40 parts of glycerine, in 1000 parts of chloroform, and very slightly soluble in ether" (U. S. Ph.) Its solubility in water is decreased by presence of ammonium sulphate (Carles) or sodium sulphate (Schlickum, 1885); in chloroform is increased by presence of cinchonine or quinidine sulphate. From acidulous aqueous solution it is sparingly dissolved by amyl alcohol (Barfoed). In alcoholic solution it is precipitated by adding ether.—*Quinine bisulphate,* $C_{20}H_{24}N_2O_2H_2SO_4.7H_2O=548$, is soluble "in about 10 parts of water (with vivid blue fluorescence) and in 32 parts of alcohol, at 15° C. (59° F.); very soluble in boiling water and in boiling alcohol" (U. S. Ph.) It has a strongly acid reaction.—The doubly acid sulphate, $C_{20}H_{24}N_2O_2(H_2SO_4)_27H_2O$, is freely soluble in water and in alcohol.—*Quinine hydrobromide,* $C_{20}H_{24}N_2O_2HBr.H_2O=422.8$, is soluble "in about 16 parts of water and in 3 parts of alcohol, at 15° C. (59° F.); in 1 part of boiling water and less than 1 part of boiling alcohol; in 6 parts of ether, in 12 parts of chloroform, and moderately soluble in glycerine" (U. S. Ph.)—*Quinine hydrochloride* (muriate), $C_{22}H_{24}N_2O_2HCl.H_2O=378.4$, is soluble "in 34 parts of water, and in 3 parts of alcohol, at 15° C. (59° F.); in 1 part of boiling water and very soluble in boiling alcohol; when rendered anhydrous it is soluble in 1 part of chloroform" (U. S. Ph.) In 9 parts of chloroform (Hager's "Commentar").—Normal *quinine hydriodide,* instable, is more soluble than the sulphate.—*Quinine valerianate,* $C_{20}H_{24}N_2O_2C_5H_{10}O_2.H_2O=444$, is soluble in about 100 parts of water and in 5 parts of alcohol, at 15° C. (59° F.), . . . and slightly soluble in ether" (U. S. Ph.)—*Quinine tannate,*[1] amorphous, is but very little soluble in cold water (nearly tasteless), but is soluble in alcohol and slightly soluble in ether, and by long digestion with water is converted into soluble quinine gallate (Lintner).—*Quinine tartrate,* normal $(C_{20}H_{24}N_2O_2)_2C_4H_6O_6.H_2O$, is soluble in 910 parts of water at 10° C., much more soluble in hot water and in alcohol (Hesse, 1865).—*Quinine oxalate,* $(C_{20}H_{22}N_2O_2)_2$

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[1] Jobst, 1878. Flückiger's "Phar. Chemie," 425. Hager's "Phar. Praxis," iii. 291. Produced of very variable composition and properties. Ascribed formula, $C_{20}H_{24}N_2O_2(C_{14}H_{10}O_9)_3=25$ per cent. quinine. Jobst prepared it, 31 per cent. quinine; and found it in commerce from 7 per cent. to 22 per cent. quinine.

$H_2C_2O_4 . 6H_2O$, requires 898 parts of water at 10° C. for solution; 1446 parts at 18° C. (Shimoyama, 1885).

d.—Fluorescence.—In general, quinine salts with inorganic acids containing oxygen exhibit blue fluorescence in their aqueous solutions. The hydracids of chlorine, bromine, etc., the cyanogen hydracids, and thiosulphuric acid, in union with quinine, do not give fluorescence. By adding sulphuric acid the fluorescence is obtained with all the salts in aqueous solution. But the hydracids, if present, in proportion to their quantity diminish the reaction. Alcoholic solutions show little fluorescence; solutions in ether, chloroform, etc., none at all. The bisulphate fluoresces much more strongly than the normal sulphate, in solutions of equal strength, and the fluorescence of a neutral solution of the sulphate is much intensified by acidulating with sulphuric acid. —To obtain the full delicacy of the reaction, put the solution in a test-tube or beaker of such width that a depth of at least two inches is obtained. Place over a black ground, in a strong light falling horizontally from one direction, observing from above, comparing with a like column of distilled water, and, if necessary, shading the eye from the direct light and shading the liquid from the lateral light. Greater intensity is attained by throwing the light from a lens in a pencil upon the liquid.[1] So observed, 0.00005 gram quinine, in 5 c.c. acidulous solution, gives distinct fluorescence, and this (1 in 100000) is not the limit of dilution (Barfoed, 1881).—The fluorescence of quinine is shared by quinidine, and by diquinicine, hydroquinine, hydroquinidine; not by cinchonidine nor by quinicine.

Thalleioquin test.—Treated in a white porcelain dish with fresh **chlorine-water** or **bromine-water**, not in too great excess, or well diluted, and then with **ammonia** to just effect an alkaline reaction, a solution of quinine gives a green precipitate, thalleioquin, dissolving to a green solution by adding a further excess of ammonia. In more dilute solutions a precipitate is not obtained at all, but a green liquid. Bromine gives with dilute solutions a better result than chlorine (Zeller, 1880); an excessive action of either is to be avoided. According to Barfoed a fine reaction is given by 0.001 gram of quinine, in 5 c.c. of water acidulated with sulphuric acid, treated with 10 drops of very weak bromine-water or of fresh chlorine-water, and then with 2 drops of ammonia-water; but with 0.0005 gram, in 5 c.c., 2 drops

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[1] For more minute examination see Stokes, 1853; H. Morton, 1871; "Watts's Dict.," 3, 634; 8, 1193.

weak bromine-water and 1 drop ammonia-water, the limit is reached. Trimble (1877) has used the reaction for a colorometric method, and prepared a standard green solution by proportions of 0.01 quinine or quinine salt in 5 c.c. of fresh chlorine-water, adding 10 c.c. of ammonia-water and diluting to 100 c.c. —If the green ammoniacal solution be just neutralized with acid a blue tint is obtained, and, by acidulating, a violet to red color, returning to green again when ammonia is added in excess. If **ferricyanide** of potassium be added after the chlorine or bromine addition as above, and then ammonia barely enough for an alkaline reaction, a red color is obtained. **Frœhde's reagent,** with dry quinine, gives a slight green color (Dragendorff).—The thalleioquin test of quinine is shared by quinidine, diquinicine, and quinicine, also by hydroquinine and hydroquinidine, but not by cinchonidine nor cinchonine.

The alkali hydrates precipitate quinine from solutions of its salts, the precipitate becoming slowly crystalline (see *a*), and being quite readily soluble in excess of **ammonia,** and somewhat soluble in excess of ammonium carbonate, not of the fixed alkali hydrates, or only very slightly by potassa. Tartaric acid prevents the precipitation in solutions more dilute than about 1 to 300; and ammonium chloride increases the solubility of the precipitate.—In free ammonia the quinidine and cinchonidine precipitates are less soluble than that of quinine, and the cinchonine precipitate is but very slightly soluble.

The alkali **carbonates,** and, more slowly, the **bicarbonates,** precipitate quinine, insoluble or, with bicarbonates, but slightly soluble in excess.

Herapathite test.—Herapathite (Herapath, 1852) is one of the iodosulphates of quinine. Its formula (Jörgensen, 1876) is $(C_{20}H_{24}N_2O_2)_4(H_2SO_4)_3(HI)_2I_4.(H_2O)_n$. Dried at 100° C., it contains 55.055 per cent. anhydrous quinine. It crystallizes in plates, either rectangular or rhombic, of six or eight sides. By reflected light the crystals are very lustrous, or iridescent emerald-green; by transmitted light they are dichroic, in the direction of one axis nearly transparent, but when certain axes are superimposed they are nearly opaque. A play of dark and light shades is obtained with crystals of microscopic size floating in a drop of liquid under the cover-glass. The large crystals have the optical powers of tourmalines, but in greater intensity. Herapathite is at first nearly insoluble in cold water and soluble in 1000 parts hot water, but is decomposed by water with formation of quinine bisulphate and hydriodide. It dissolves in 50 parts boiling alcohol of 85% by weight; in 650 parts of cold alcohol of same strength. In 800 parts of 90% alcohol at 16° C. (Jörgensen). In 751 parts of 92% alcohol at 24.5° C. (76.1° F.) (De Vrij, 1875). It is always crystallized from alcohol, usually acidulated. The large crystals of herapathite can be mechanically separated from amorphous precipitate of other cinchona alkaloids.

De Vrij states (1882) that the best reagent for the qualitative recognition of crystallizable quinine, when in a mixture of cinchona alkaloids, is **the iodosulphate of chinoidine,** prepared as directed (under *f*) for quantitative uses. This is added to a solution of 1 part of cinchona alkaloids dissolved in 20 parts of 92–95% alcohol acidulated with 1.5% of sulphuric acid, this solution being then diluted with 50 parts of alcohol. The iodosulphate reagent is added (before heating) so long as a dark brown-red precipitate is formed, when, with slight excess of reagent, the liquid acquires a yellow color. The mixture is now heated to boiling, to dissolve the precipitate, then set aside for crystallization of the herapathite. Barfoed (1881) dissolves alkaloid supposed to contain 0.01 gram quinine in 20 drops, or 0.01 gram quinine sulphate in 10 drops, of a mixture of 25 drops of alcohol, 30 drops of acetic acid, and 1 drop of diluted sulphuric acid, heating to boiling. and then adding 2 drops of alcoholic solution of iodine (1 to 200) and setting aside. Crystallization may begin in 15 to 30 minutes.

Excess of iodine tends to produce *other iodosulphates of quinine.* Jörgensen (1876) describes three classes of these:

$$(C_{20}H_{24}N_2O_2)_4(H_2SO_4)_3(HI)_2I^n$$
$$(C_{20}H_{24}N_2O_2)_2(H_2SO_4)(HI)_2I^n$$
$$(C_{20}H_{24}N_2O_2)_3(H_2SO_4)(HI)_2I^n$$

Olive-gray, bronze, brown, blue, and black colors are found, as well as green shades; and needles, as well as plates. The results are governed mainly by the proportions of quinine, iodine, and sulphuric acid taken. *The other cinchona alkaloids* form iodosulphate precipitates, somewhat more soluble in alcohol, and less crystallizable, than quinine iodosulphate. Christensen (1881) states that cinchonidine, if present in at all large quantity, may be precipitated even by De Vrij's method with chinoidine. See also Cinchonine, *d.* Further citations from De Vrij are given under *f*, "*Quantitative*," p. 136.

General reagents for alkaloids.—**Potassium mercuric iodide,** or Mayer's solution, precipitates quinine in white flakes, appearing in acidulous solutions containing less than 1 part of the alkaloid in 100000 (*f*, p. 136).—**Phosphomolybdate** throws down quinine from acidulous solutions, the yellow-white, curdy precipitate being almost absolutely insoluble.[1]—**Iodine** in potassium iodide solution causes a reddish-brown precipitate. In solutions other than that of the sulphate the precipitate is at first soft or amorphous; in presence of sulphuric acid the precipitate approaches to the composition and appearance of herapathite. See Cinchonine, *d*.—**Platinic chloride,** in solutions not very dilute, a bright yellow precipitate, $C_{20}H_{24}N_2O_2(HCl)_2PtCl_4$, soluble in 1500 parts of cold water or in 2000 parts of boiling alcohol.—**Tannic acid,** a yellow-white amorphous precipitate (see p. 48), easily soluble in warm hydrochloric acid.—**Picric acid,** in saturated aqueous solution, a yellow amorphous precipitate, soluble in alcohol, from which it crystallizes.—Potassium **sulphocyanate,** in concentrated solutions, a white precipitate, more soluble than the sulphate (Hesse), used in microchemical examination, p. 101. —**Sulphates** give a precipitate in neutral solutions of hydrochloride and hydrobromide of quinine, if not diluted to the extent of the solubility of quinine sulphate.—Concentrated sulphuric acid causes no color; **Froehde's reagent** a greenish color.

Potassium iodide, in neutral solutions moderately dilute, does not precipitate quinine salts (separation from quinidine). A saturated solution of quinine sulphate is not affected. The slightest acidulation, such as may take place in the stomach, may result in the liberation of iodine and the formation of insoluble quinine iodides resembling herapathite.—**Normal tartrates,** as potassium sodium tartrate, precipitate moderately concentrated solutions of quinine salts, the normal tartrate of quinine being a little more soluble (*c*) than that of cinchonidine, and much less soluble than those of quinidine and cinchonine (to be observed in cinchonidine separation by tartrate).

e.—Separations.—All the cinchona alkaloids, in aqueous solutions of their salts, or other solutions of free alkaloid, are evaporated to dryness at 100°–125° C. without loss.—From substances insoluble in ether, chloroform, or amyl alcohol, quinine is separated by action of these solvents, none of which dissolves salts of quinine, except chloroform very slightly. Benzene in sufficient quantity dissolves quinine, as does aqueous ammonia. Methods of separation of quinine from Cinchona Bark are given, pp. 102 to 111; from other Cinchona Alkaloids, index at p. 111. From Morphine and from Strychnine quinine is pretty nearly separated by its solubility in ether, less fully separated by its solubility in ammonia. In the sulphates quinine is approximately

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[1] The author, 1877: *Am. Jour. Phar.*, 49, 483.

separated from Morphine and from Atropine by the differences of solubility in water. From Salicin it is well separated, as free alkaloid, by its insolubility in water.

From Citrate of Iron and Quinine.—The assay method of the U. S. Ph. is as follows: "The salt contains 12 per cent. of dry quinine. It may be assayed as follows: Dissolve 4 grams of the scales in 30 c.c. of water, in a capsule, with the aid of heat. Cool, and transfer the solution to a glass separator, rinsing the capsule; add an aqueous solution of 0.5 gram of tartaric acid, and then solution of soda in decided excess. Extract the alkaloid by agitating the mixture with four successive portions of chloroform, each of 15 c.c. Separate the chloroformic layers, mix them, evaporate them in a weighed capsule, on the water-bath, and dry the residue at a temperature of 100° C. (212° F.) It should weigh 0.48 gram."—The Br. Ph. process is as follows: "Fifty grains [or 4 grams] dissolved in a fluid-ounce [or 35 c.c.] of water and treated with a slight excess of ammonia gives a white precipitate, which, when dissolved out by successive treatments of the fluid with ether or chloroform, and the latter evaporated, and the residue dried until it ceases to lose weight, weighs eight grains [or 0.639 gram]."—Mr. J. C. Falk[1] advises to add 1 gram of tartaric acid in the U. S. Ph. process, as he found the 0.5 gram insufficient to keep the iron in perfect solution. The four portions of chloroform are often insufficient. The solvent should be applied till a portion ceases to give test for quinine. Analysts often find it difficult to recover the entire quantity added. The use of a continuous extraction-apparatus for liquids is desirable. Mr. Falk recovered 11.925 from the addition of 12. The recovered alkaloid is tested most readily by solubility in ether, more certainly by the application of the Ammonia Test to free alkaloid (p. 139).

Where the ammonia test is the official standard for quinine hydrate and its several salts, it is the just and indisputable standard for the alkaloid obtained from all preparations of quinine, such as pills, scales, elixirs, etc.

Of 34 samples of citrate of iron and quinine assayed by Dr. Davenport, State Analyst of Drugs in Massachusetts,[2] by the U. S. Ph. method, 85 per cent. fell below the pharmacopœial requirement, though the greater proportion were not in the pharmacopœial form of the preparation.

From Coated Pills of Quinine Salts.—The following method

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[1] 1884: *Am. Jour. Phar.*, 56, 316.

[2] "Fifth Annual Report State Board of Health," etc., Mass., 1884, p. 162.

contributed by Henry B. Parsons,[1] and verified by use in his constant practice, is confidently recommended: Take a sufficient number of pills to represent 20 or 40 grains of sulphate of quinine;[2] treat, in a very small Wedgewood mortar, with 5 c.c. cold water until the coating dissolves and a smooth and uniform paste is obtained; add 2 grams (31 grains) of freshly slaked lime in powder; mix thoroughly and dry the mixture slowly in the mortar by a steam or water bath. The dry mass is to be finely powdered and transferred[3] to a Tollens apparatus for continuous percolation,[4] and thoroughly extracted with stronger ether. Evaporate the ethereal solution in a weighed flask, dry for one hour at 125° C., and weigh as anhydrous quinine. Grams of anhydrous quinine $\times$ 20.7673 = grains of quinine sulphate ($7H_2O$).

f.—Quantitative. Gravimetric estimation as free alkaloid.—Quinine is frequently estimated by weighing the residue from a solution of the separated alkaloid in ether, chloroform, or amyl alcohol—a method without objection (see *e*, p. 134). The residue is preferably dried first at a very moderate heat or over sulphuric acid to avoid melting (*a*), and finally at about 120° C., and cooled in a desiccator. The objection to *precipitation* for weight is the loss by solubility in water. Sodium hydrate is without objection as a precipitant. In precipitating quinine sulphate acidulate solution with sodium hydrate, and washing on the filter until the washings gave no cloudiness with barium chloride, a loss of 11.6 per cent. of the quinine was sustained. The solubility in sodium sulphate solution is about the same as that in pure water. Dry quinine, washed on the filter, ordinarily loses about 0.0002 gram per c.c. of wash-water; but a watery filtrate fully saturated with quinine will contain about 0.0006

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[1] 1883: *New Rem.*, **12**, 67; *Proc. Am. Pharm.*, **31**, 270.

[2] The smaller number is sufficient if manipulations are made with care and the balance is sensitive to tenths-milligram.

[3] By use of a small steel spatula. The mortar then rinsed with a little of the ether.

[4] In absence of a Tollens apparatus good results may be obtained by a very careful operation on an aliquot part of the solution as follows: Transfer the dry mass to a small, flat-bottomed flask; measure in an exactly taken volume of stronger ether, [stopper, and weigh] and agitate the stoppered vessel, occasionally, while it stands for 12 hours or more. [Weigh again and add ether to restore the loss if any has occurred.] By use of a pipette measuring accurately [and agreeing with the measure by which the ether was taken], take off from the clear ethereal solution an aliquot part by volume of the ether taken, and evaporate as directed for the percolate.

Chloroform does not work as well as ether as a solvent.—With a faithful execution of the process the loss is not over ½ per cent.—In answer to the opinion of Masse (1885) that quinine suffers loss by action of lime at 100° C., see Passmore (1885).

gram per c.c. of the liquid (*c*).[1] The precipitate is preferably dried first at a gentle heat, and at last at about 120° C. (248° F.), as the last molecule of water is difficult to expel at 100° C. Heat to about 170° C. is borne without loss of alkaloid. The dried alkaloid must be cooled in a good desiccator, as it readily acquires water from the air.

Gravimetric determination *as crystallized sulphate, dried* at 100° C. (or 115° C.) to anhydrous sulphate, or at 60° C. to effloresced sulphate ($2H_2O$), is directed under Separation of Cinchona Alkaloids, p. 113.

Gravimetric determination *as quinine mercuric iodide* by precipitation of the acidulated solution of the sulphate, with Mayer's solution, gives fair results. The precipitate is washed, and dried at 100° C., when 2.900 grams indicate 1.000 gram of quinine (as dried at 100° C.)[2] The composition of the precipitate is perhaps liable to variation by action of solvents, but it is almost insoluble in water.—The precipitate *by phosphomolybdate*, in acidulated solution, may be washed, dried below 70° C., and weighed, when 1 gram of quinine is represented by about 3.665 grams of the precipitate,[3] the result being properly controlled by a parallel operation upon a known quantity of pure quinine.

Volumetric estimation by Mayer's Solution.—The precipitate, as stated under *d* (p. 132), has very little solubility, but its composition is probably varied by conditions of temperature, etc. According to Mayer, in dilution of 1 to 800, 1 c.c. of the reagent = 0.0108 gram of anhydrous quinine.[4] It is advisable to control the results by a parallel titration of a solution of quinine of known strength.

Estimation in herapathite (De Vrij, 1882). *Preparation of the Reagent, Iodosulphate of Chinoidine.*—Of commercial chinoidine 1 part is heated on the water-bath with two parts of benzene, whereby the chinoidine is partly dissolved. The clear, cold benzene solution is shaken with an excess of weak sulphuric acid, whereby a watery solution of acid sulphate of chinoidine is obtained. After ascertaining in a small part of this solution the amount of amorphous alkaloid contained in it, so that its whole

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[1] "Laboratory Notes," by the author, 1877: *Am. Jour. Phar.*, **49**, 481; *Jour. Chem. Soc.*, **32**, 933; *Jahr. Phar.*, 1877, 419.

[2] "Laboratory Notes," by the author, 1877 (where last cited).

[3] Last citation.

[4] Blyth, 1881: *The Analyst*, **6**, 161; *New Rem.*, **11**, 34; *Proc. Am. Phar.*, **30**, 410; *Jour. Chem. Soc.*, **40**, 1176. The factor $0.0108 = \frac{2}{3}$ of $\frac{1}{20000}$ of the molecular weight, and indicates the formula $(C_{20}H_{24}N_2O_2)_2(HI)^x, (HgI_2)_3$ for the precipitate, but this is not supported by the gravimetric results (A. B. Prescott, 1880: *Am. Chem. Jour.*, **2**, 294; *Chem. News*, **45**, 114).

quantity in the solution may be known, the clear solution is poured into a large capsule. For every two parts of amorphous alkaloid contained in the solution 1 part of iodine and 2 parts of iodide of potassium are dissolved in water. This solution is *slowly* added *with continuous stirring* to the liquid in the capsule, so that no part of it comes in contact with an *excess* of iodine. By this addition there is formed an orange-colored, flocculent precipitate of iodosulphate of chinoidine, which, either spontaneously or by a slight elevation of temperature, collapses into a dark brown-red colored resinous substance, whilst the supernatent liquor becomes clear and slightly yellow-colored. This liquor—which, if the direction is strictly followed, *must* still contain some amorphous alkaloid as a proof that no excess of iodine has been used—is poured off, and the resinous substance is washed by heating it on a water-bath with distilled water. After washing, the resinous substance is heated on a water-bath till all water has been evaporated. It is then soft and tenacious at the temperature of the water-bath, but becomes hard and brittle after cooling. One part of this substance is now heated with 6 parts of alcohol of 92 to 95 per cent. on a water-bath, and is thus dissolved, and the solution allowed to cool. In cooling, a part of the dissolved substance is separated. The clear dark brown-red colored solution is evaporated on a water-bath, and the residue dissolved in 5 parts of cold alcohol. This second solution leaves a small part of insoluble substance. The clear dark brown-red colored solution obtained by the separation of this insoluble matter, either by decantation or filtration, constitutes the reagent which, under the name of "iodosulphate of chinoidine," Dr. De Vrij uses both for qualitative and quantitative determination of the crystallizable quinine in barks.

The formation of herapathite, in the estimation, is directed by De Vrij as follows: Of the mixed alkaloids from a cinchona bark, 1 part (1 gram being sufficient) is dissolved in 20 parts of alcohol of 92 to 95 per cent., containing 1.5 per cent. of sulphuric acid (of which an excess above that for production of acid sulphates is avoided). The resulting alcoholic solution of the acid sulphates of the alkaloids is then diluted with 50 parts of pure alcohol. From the dilute solution so obtained the quinine is precipitated *at the ordinary temperature* by adding carefully, by means of a pipette, the above-mentioned solution of iodosulphate of chinoidine as long as a dark brown-red precipitate of iodosulphate of quinine (herapathite) is formed. As soon as all the quinine has been precipitated, and a slight excess of the reagent has been added, the liquor acquires an intense yellow color.[1] The beaker containing the liquor with the precipitate is now covered by a watch-glass, and heated till the liquid begins to boil and all the precipitate is dissolved. The beaker is then left to itself, and in cooling the herapathite is separated in the well-known beautiful crystals. After twelve hours' rest [finally at 16° C.] the beaker is weighed to ascertain the amount of liquid which is necessary in order to be able to apply later the necessary correction; for although the quinine-herapathite is very slightly soluble in cold alcohol, it is not insoluble (*d*, p. 131). It is ascertained with a small portion of the solution that enough reagent has been added, when the clear liquid is poured off, as far as possible, on a filter, leaving the majority of the crystals in the beaker, which is now weighed again to ascertain the amount of liquid, which is noted down. The crystals are now dissolved to recrystallize, for removal of traces of adhering cinchonidine iodosulphate, as follows: The crystals on the filter are washed into the beaker with a little of the alcohol, and all the crystals dissolved in just enough alcohol at the boiling point. After perfect cooling [and standing at 16° C.] the weight of the beaker is taken, the crystals carefully collected on a small filter, and the empty beaker weighed again. The difference in weight will indicate the amount of liquor, which is added to that of the first liquor. The sum of the weights of the liquor $\times$ 0.00125 = correction for solubility of the herapathite, provided the crystallization has been completed at 16° C.[2] The herapathite crystals on the filter are thoroughly washed with a saturated alcoholic solution of pure herapathite.[3] The washed crystals are drained, with tapping of the side of the funnel, the filter taken out and quickly pressed between blotting-papers, and as soon as air-dry the crystals are transferred from the filter to a fitted pair of watch-glasses, and dried on the water-bath (or at 100° C.) to a constant weight, avoiding the access of air. To the weight is added the correction for solubility, to obtain the total quinine iodosulphate, $(C_{20}H_{24}N_2O_2)_4(H_2SO_4)_3(HI)_2I_4$ (*d*,

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[1] If cinchonidine be present in large quantity, the author states that the due control of this slight excess of the reagent requires a great deal of practical experience, and must be studied on a solution of cinchonidine itself, taken in the proportions above directed.

[2] If another temperature has been employed, the solubility of the herapathite is to be determined by experiment at such temperature. In this the herapathite can be estimated by volumetric hyposulphite: 21.58 parts of iodine representing 100 parts of herapathite.

[3] A washing-bottle containing an excess of pure crystallized herapathite in 95 per cent. alcohol may be kept ready for application.

p. 132), of which one part contains 0.55055 part of anhydrous quinine.

g.—Tests for impurities and deficiencies.—The impurities or deficiencies of quinine salts to be generally regarded are, in order of importance, (1) other cinchona alkaloids in excess of a proper limit, and (2) an excess or deficiency of moisture or water of crystallization, causing variableness of strength. Quinine manufacture is mainly conducted by a small number of houses of well-known standing, and the product is carried in well-regulated commercial channels, so that it is but little exposed to the introduction of falsifications. The one cinchona alkaloid, not quinine, most difficult for the manufacturer to remove and for the analyst to estimate, and actually present in largest proportion in the product from barks in general, is cinchonidine. In the product of the "cuprea" barks, however, another alkaloid is introduced, which is cupreine, or the conjugated compound of cupreine with quinine known as homoquinine, and it becomes necessary to give general attention to the possible presence of this alkaloid.

The recognized tests for other cinchona alkaloids depend, in principal, upon (1) the removal of quinine as a crystallized sulphate (Kerner, 1862), (2) the separation of the free alkaloids by ether (Liebig's test), or (3) by excess of ammonia (Kerner, 1862), which is used also in all tests to liberate the alkaloids from their salts. Hesse's test (1879) depends upon principles (1) and (2), as also does Paul's (1877), while Kerner's test depends upon (1) and (3).

Kerner's test of Quinine Sulphate provides a uniform arbitrary measure, by certain fixed conditions, as follows: Quinine as a sulphate is macerated with water; the quantity of the water is 10 parts for 1 part of crystallized sulphate; at whatever temperature the maceration is commenced, it is invariably concluded at the temperature of 15° C., when the mixture is at once filtered; and of the filtrate 5 c.c. (for some purposes 10 c.c.) are treated with an accurately measured volume of ammonia-water of exactly known strength (s.g. 0.920 or 0.960) until a clear liquid is obtained, the ammonia-water being mixed at once with the filtrate by gently inclining or rotating the test-tube while this is closed with the finger.—With a small and not bibulous filter 1 gram of crystallized sulphate with 10 c.c. of water will easily yield the 5 c.c. of filtrate for one ammonia test. Directions often specify 2 grams of the crystals with 20 c c. of water; and for quantitative titrations it becomes proper to take 5 grams of the crystallized sulphate with the tenfold number of c.c. of water, to provide for several parallel ammonia tests;[1] but it will be observed that the required quantity of ammonia, the index of the test, is only placed in ratio to the 5 or 10 c.c. of the filtrate [where it acts not wholly independent of variations of atmospheric temperature], and has no ratio to the quantity of quinine sulphate taken. It will be further observed that the fixed proportion of water taken in maceration, 10 parts to 1 of the salt, controls the quantity and concentration of the alkaloids not quinine. The 10 parts of water at 15° C. would dissolve 0.1 part of cinchonidine, 10% of the quinine sulphate taken, and a smaller quantity of water would in most cases dissolve the entire quantity of alkaloids not quinine, but it is of importance that the solution of these alkaloids shall be made up to the same volume in every trial of the test. The quinine sulphate is in excess of saturation of this salt; indeed, one-fiftieth as much quinine salt would suffice to more than saturate the 10 parts of water.—In Kerner's method *the Quinine Sulphate is readily recovered in purified form*, almost without waste, and sometimes with gain, of value. Of the real quinine sulphate 99.86% remains on the filter as Recrystallized Sulphate of Quinine. It is dried by pressing gently between blotting-papers and setting aside in dry air, avoiding efflorescence. The quinine dissolved by the ammonia crystallizes on evaporation of the latter, and this separation has been adopted in purifying small quantities of quinine.

For 5 *c.c. of aqueous solution saturated at* 15° *C. the volumes of ammonia-water* of sp. gr. 0.92 (21.7% NH_3), and of sp. gr. 0.96 (10% NH_3), required to give a clear solution, are as follows (KERNER, 1880[2]):

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[1] HAGER arranges for special tests, in different portions of the filtrate, for single cinchona alkaloids, but of these special tests the only trusty one is that for quinidine, rarely present—a test made with 5 c.c. of the filtrate by adding 5 drops of a 1 to 20 solution of potassium iodide, stirring, and setting aside for crystallization of quinidine hydriodide.

[2] *Archiv d. Phar.*, [3], 17, 444. In these experiments with alkaloids other than quinine they were sometimes *added* (in known quantity of their sulphates) to the 5 c.c. of the filtrate from pure quinine sulphate, but in case of cinchonidine it was mixed with the crystallized pure quinine sulphate for one series of trials, and in certain of the tests there was maceration with water at 60° and at 80° C. before the crystallization at 15° C. These varied conditions made little difference with the results. But when the quinine and cinchonidine sulphates have been crystallized together, previous hot digestion increases the efficiency of the separation. See YUNGFLEISCH, 1887: *Phar. Jour. Trans.* [3] 17, 585; *Jour. de Pharm.* [5] 25, 5. The same is stated in general terms by PAUL 1877: *Phar. Jour. Trans.* [3] 7, 654. The author is indebted to E. A. RUDDIMAN for determinations of difference due to previous hot digestion, a report of which will soon be presented for publication.

	Ammonia of s.g. 0.960.	*Ammonia of s.g.* 0.920.[1]
With pure Quinine Sulphate.......	5.0 to 5.3 c.c.	3.0 to 3.3 c.c.
	Additional to above.	*Additional to above.*
For 0.001 gram Cinchonidine sulphate added....	0.40 c.c. to 0.44 c.c.	0.28 to 0.35 (*av.* 0.32) c.c.
For each per cent. of Cinchonidine sulphate........	2.0 c.c. to 2.2 c.c.	1.4 to 1.7 (*av.* 1.6) c.c.
For 0.001 gram Quinidine sulphate..........	1.16 c.c. to 1.34 c.c.	0.56 c.c. to 0.78 c.c.
For 1 per cent. Quinidine sulphate..	5.8 c.c. to 6.7 c.c.	2.8 c.c. to 3.9. c.c.
For 0.001 gram Cinchonine sulphate[2].........	0.62 c.c. to 0.80 c.c.	0.36 c.c. to 0.40 c.c.
For 1 per cent. Cinchonine sulphate..........	3.1 c.c. to 4.0 c.c.	1.8 c.c. to 2.0 c.c.

Kerner's test, in the pharmacopœial form, merely determines whether the article tested does or does not reach a certain recognized limit of impurity; but, as applied by the analyst, the ammonia-water should be added from the burette and the required number of c.c. should be noted, as an index of the degree of impurity, whether above or below the legal standard. The number of c.c. of ammonia-water (of pharmacopœial strength and under pharmacopœial conditions) is in itself a certain measure of value, already having a meaning to dealers and consumers, irrespective of interpretations in per cent. of cinchonidine or

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[1] Experiments by Mr. E. A. RUDDIMAN, made in an investigation now in progress in the University of Michigan, indicate that of ammonia water of s. g. 0.960 there are required only 1.5 times more than of the water of s. g. 0.920, though the latter is 2.2 times stronger than the former. Averages of ten titrations, for each degree between 15° and 25° C., agreed nearly with this ratio of 1.5 to 1.0.

[2] In respect to cinchonine (in presence of much quinine) these data are surprising. Taken separately, each in a cold-saturated sulphate solution (15° C.), Kerner in 1862 found the quantities of ammonia used to redissolve the alkaloid from 1 c.c. of the filtrate as follows: Of ammonia-water of s.g. 0.960, for quinine, 1.3 c.c.; for cinchonidine, 16 c.c.; for quinidine (*b* Quinidine). 15 c.c.; for cinchonine, over 300 c.c.—The experiments made by Mr. TEETER (Univ. Mich., 1880: *New Rem.*, **9**, 258) in defining the limits of the test of quinine sulphate only show that in the preponderating presence of quinine both quinidine and cinchonine require more ammonia than cinchonidine does.

other alkaloids. The ammonia measure, based upon fixed conditions of application, may be adopted over the world as a simple expression of comparative value. Against this preference for the ammonia measure it can hardly be urged that there is disagreement as to how many per cent. of cinchonidine are admitted under 7 c.c. or 6½ c.c. of ammonia. There may be disagreement as to the interpretation of any method of valuation.

Kerner's volumetric estimation of cinchonidine in commercial quinine sulphate is only an elaboration of his limit-test, so devised that the result is verified by a control analysis in each operation. It is as follows:[1]

Standard Quinine Sulphate (Normalchininsulphat) is prepared by recrystallizing the salt from hot solution, with such a slight addition of sulphuric acid as shall give a faint acid reaction, usually crystallizing from three to six times, and until two portions of a crop of crystals, macerated at about 15° C., the one in 10 parts of water and the other in 500 to 700 parts of water, in parallel conditions, on titration of 10 c.c. of filtrate with ammonia-water, require the same number of c.c. of ammonia for solution. Usually by the recrystallizations the salt becomes neutral in reaction.—The Standard Quinine Sulphate Solution is prepared freshly for use by rubbing the salt with about 100 times its weight of water in a mortar, rinsing into a glass-stoppered bottle,[2] and digesting along with the commercial quinine sulphate to be estimated, in the same conditions of temperature and time, as directed below.—Water of Ammonia of sp. gr. 0.920 of ordinary quality is all that is required as a reagent.—In the titration 5 grams of the sulphate of quinine to be tested are rubbed in a mortar with distilled water enough, so that when all is rinsed into a glass-stoppered bottle it shall just reach a mark of 50 c.c. volume. This bottle and the bottle containing the standard quinine sulphate solution are now set in the same vessel of cold water, at as near 15° C. as convenient, and left, with occasional careful shaking, for 12 to 18 hours. Or both bottles are warmed in the same vessel of water at near 100° C. for some time, shaking several times, and then set together in a vessel of cold water for an hour or more. The bottle containing the ammonia is placed in the same cold water, so that at the end of the

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[1] KERNER, 1862. Improved in 1880: *Archiv d. Phar.*, [3], 16, 186–285; 17, 438–454; *Jour. Chem. Soc.*, 40, 63; *New Rem.*, 10, 168.

[2] The standard quinine solution should be strictly neutral in reaction. If acidulous, it is to be brought back to the neutral point by adding to it, with agitation, just sufficient of quinine hydrate, freshly precipitated from the same solution and well washed.—A. B. P.

digestion it shall have the same temperature. The two quinine solutions are now filtered through two dry filters,[1] at the ordinary atmospheric temperature (which is preferably near that of the digestion), obtaining from the standard quinine solution the same volume of filtrate furnished by the other solution (40 c.c. or over). 10 c.c. of each of these solutions is taken, by a good pipette, in a test-tube for titration. The ammonia is added from a burette, which is better if it be long, and narrow enough to register in $\frac{1}{20}$ c.c. At first 5 c.c. of the ammonia are run in, the test-tube closed by the finger and given two or three circular motions to mix the liquid without shaking, and further smaller additions made, 0.3, 0.2, 0.1 c.c., and by drops, with the circular agitation after each addition, until the liquid becomes perfectly clear. Toward the last it is well to wait 5 to 10 seconds after each agitation before the next addition. The end reaction is complete clearing. Then at once the standard quinine solution is titrated in the same way, taking a fresh portion of ammonia in the burette. The 40 c.c. will suffice for *four* titrations of each quinine solution, from which the average can be taken.—Each 0.32 c.c. (or 0.3, round number, the extremes being 0.28 and 0.35 c.c.) of the excess of the ammonia required for the quinine under test (beyond that required for the standard quinine) indicates 0.001 gram of cinchonidine sulphate. This 0.001 gram of cinchonidine sulphate is estimated upon the commercial quinine salt represented by the (10 c.c.) portion of filtrate taken, or (having taken 10 c.c. of a 1 : 10 solution) each 0.32 c.c. of 0.920 ammonia (beyond that taken for the standard sulphate) indicates 0.1 per cent. of the cinchonidine impurity.

Should the percentage of cinchonidine be over 1.5, or at most 2.0, the results become inaccurate, owing to the gelatinizing of the precipitated alkaloid. In this case 10 c.c. of the filtrate under estimation may be diluted, by addition of standard quinine filtrate (of parallel digestion), to 20, 30, or 40 c.c., and portions of 10 c.c. of this diluted filtrate titrated. Then, after deducting the average c.c. of ammonia taken by 10 c.c. of standard quinine, the remaining c.c. are multiplied by 2, or 3, or 4, when each 0.32 c.c. = 0.1% cinchonidine, as before. The errors are stated not to exceed 0.05 per cent. of the commercial quinine salt.

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[1] The crystalline residues in the filters are to be saved, as *purified sulphate of quinine*, drying them by pressing the filters between blotting-papers, etc. It will be observed that the residue from filtration of the "standard quinine sulphate" solution is "standard quinine sulphate" prepared with an additional purification.

An approximate volumetric estimation is made in a short operation, according to Kerner (where last quoted), as follows: The quinine salt to be tested is macerated with ten times its weight of water at 15° C., 5 c.c. of the filtrate is taken in a test-glass of 10 c.c. capacity graduated in 0.1 c.c., 3 c.c. of water of ammonia of sp. gr. 0.920 are added and intermixed by gentle circular agitation of the test-glass while covered by the finger, and additions further made, at last by drops, until a clear liquid is attained, when the total volume is read and the volume of added ammonia is noted.—The required addition of only 3.0 to 3.3 c.c. of the ammonia-water would indicate absence of cinchonidine sulphate; use of 5 c.c. ammonia (0.920) indicates near 1 per cent. cinchonidine sulphate; and these data serve to show approximately the indication [1] (Kerner).

The U. S. Ph. (1880) *directions for Kerner's test* are as follows: "The residue of 1 gram of (crystallized) sulphate of quinine, dried to a constant weight at 100° C. for estimation of water, is agitated with 10 c.c. of distilled water, the mixture macerated at 15° C. (59° F.) for half an hour, then filtered through a small filter, 5 c.c. of the filtrate taken in a test-tube, and 7 c.c. of water of ammonia (sp. gr. 0.960) then added; on closing the test-tube with the finger, and gently turning it until the ammonia is fully intermixed, a clear liquid should be obtained. If the temperature of maceration has been 16° C. (60.8° F.), 7.5 c.c. of the water of ammonia may be added; if 17° C. (62.6° F.), 8 c.c.[2] may be added. In each instance a clear liquid indicates the absence of more than about 1 per cent. of cinchonidine [3] or quinidine, and of more than traces of cinchonine."

The Ph. Germ. (1882) *directions* are these: 2 grams of quinine sulphate are agitated with 20 c.c. of water at 15° C., and after half an hour filtered. To 5 c.c. in a test-tube ammonia [0.960] is added until the precipitated quinine is again dissolved. The required quantity of ammonia should not overgo 7 c.c.

The Ph. Fran. (1884) *directs* the 2 grams quinine sulphate

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[1] By a more minute calculation, if the ammonia-water hold its strength, each 0.32 c.c. added above about 3.3 c.c. indicates 0.2 per cent. of cinchonidine; so that 1 per cent. of cinchonidine is indicated by 4.9 c.c. (total addition), and 2 per cent. by 6.5 c.c. But exactness is not to be assumed without the help of the control analysis.—A. B. P.

Differences of 0.5° C., Kerner states, do not sensibly affect the result.

[2] These official allowances for temperature are more liberal than Kerner's results would justify.

[3] See the table from Kerner's figures, p. 141, according to which (at 15° C.) from 7.0 to 7.5 c.c. are required for 1 per cent. of cinchonidine sulphate.

in 20 c.c. of water to be digested hot for half an hour, then maintained at 15° C. by immersion in a bath of water of this temperature for half an hour with frequent agitation, and filtered. Of the filtrate, 5 c.c. are treated with 7 c.c. of ammonia-water of 0.960 sp. gr., when a precipitate after gentle intermixture, or a turbidity or crystalline deposit formed after 24 hours, indicates an unacceptable proportion of alkaloids other than quinine. Another portion of 5 c.c. is evaporated in a tared capsule to a weight constant at 100° C., when the weight of the residue should not exceed 0.015 gram.[1]

Temperature of the Filtrate in the reaction of the ammonia.—Hitherto the influence of temperature has been regarded only as affecting the solubility of the sulphate of quinine, and the concentration of this salt in the filtrate. The temperature of digestion has been regulated, while that of the filtrate and the ammonia-water has been left to vary with the warmth of the atmosphere. From experiments recently made by Mr. E. A. Ruddiman, in the laboratory in which the author is engaged, it appears that the temperature of the filtrate under addition of the ammonia is influential. With digestion and filtration at 15° C., the warmer the filtrate becomes, the less ammonia is required to redissolve the quinine. For each 1° C. increase of temperature in the titration, an average of 0.148 c.c. less of ammonia of sp. gr. 0.920 is required to redissolve the quinine. This average was drawn from over ten titrations for each degree between 14° C. and 26° C., the temperature of the filtrate being taken at the end of the titration, the filtration itself being always held with the digestion at 15° C. The extremes were 0.1 and 0.2 c.c., for 1° C. —In volumetric estimation by comparison with standard quinine sulphate, this influence of temperature of titration of the quinine will be the same in each of the parallel operations, and therefore will not vitiate the conclusion. But in the pharmacopœial tests, differences of titration temperature must affect the result, in part counteracting like differences of temperature in the digestion.—The effects of titration temperature upon the cinchonidine, cinchonine, and quinidine are questions under investigation.

In 1884 Mr. Henry B. Parsons[2] reported the application of the U. S. Ph. form of the test to 1033 samples of quinine sul-

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[1] The residue of pure quinine sulphate would be 0.00675, leaving 0.00825 to consist of other alkaloids or impurities—a quantity constituting about 1.6 per cent. of the commercial quinine sulphate tested.

[2] "The Practicability of Kerner's Test": *Proc. Am. Phar.*, **32**, 458.

phate, embracing 5 brands, of American, German, and Italian production, as follows:

Brand.	*No. samples.*	*Average c.c. Am.*	*Over 7 c.c. Am.*
No. 1. American.	16	9.5	16
" 2. "	217	5.7	1
" 3. German.	11	6.1	none
" 4. "	627	6.0	7
" 5. Italian.	162	6.8	35
Total,	1033	6.1 c.c. *av.*	59 (rejected).

Mr. Parsons states that "if the sample of quinine sulphate be dried before testing, as the U. S. Ph. directs, the amount of ammonia-water required to produce a clear solution is generally, but not always, about 0.5 c.c. greater than where the same sample is not dried before testing." Also, "the test is liable to mislead unless every detailed precaution is observed."—In 1884 B. F. Davenport, as State Analyst of Drugs in Massachusetts,[1] examined 28 samples, from seven makers, using the official form of Kerner's test, and found 28 per cent. of the samples to fall below the U. S. Ph. requirement.

The application of the Ammonia Test to Quinine Compounds other than the Sulphate requires their conversion into sulphate.[2]—This may be done, in an exact application of the test to *salts of quinine*[3] other than sulphates, very easily as follows: A weighed quantity, from 2 to 5 grams, of the salt is dissolved in about fifty times its weight or a sufficient quantity of water, the alkaloids completely precipitated with sodium hydrate solution, the precipitate washed until the washings give but little cloudiness with magnesium salt solution, and the washed precipitate rinsed through a perforation in the filter-point into a test-glass, graduated in ½ c.c. and measuring 20 to 50 c.c., filling to near the volume specified below. The mixture is heated for five minutes by immersing the test-glass in nearly boiling water,

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[1] "Fifth Ann. Report Mass. State Board of Health," etc., Boston, 1884, p. 161.

[2] In his first paper, in 1862, Kerner proposed to apply the ammonia test directly to salts not sulphate, directing the solution of the salt to be diluted to the limit of solubility of quinine sulphate (*Zeitsch. anal. Chem.*, 1, 161). The later report (1880) does not reach the application to other salts.

[3] To find, for any salt of quinine, the volume equal to 10 c.c. for each gram of crystallized normal sulphate producible from 1 gram of said salt: *Comb. no. of salt taken* (in equation to form. 1 mol. sulphate) : 872 : : 10 : x = c.c. desired.

and dilute sulphuric acid is added to maintain a slight acid reaction to litmus-paper during the digestion. The mixture is now exactly neutralized to litmus-paper by adding dilute ammonia-water, *the volume of the whole made up to a number of c.c. equal to*

11.5 times the number of grams of quinine hydrochloride taken,
10.3 " " " hydrobromide "
9.8 " " " valerianate "

when the mixture is placed for half an hour or longer in a bucket of water at 15° C. (59° F.), and filtered through a small filter. One or more portions of 5 c.c. are tested with ammonia-water, as in the pharmacopœial form of the test (see page 144), and the result judged for the salt taken, on the basis of quinine sulphate. Or, cooling parallel with "standard quinine sulphate" solution, for titration, as directed on p. 142, portions of 10 c.c. are titrated in comparison with "standard quinine," for percentage of cinchonidine, etc. The results will count, on the basis of the 5 c.c. or of the 10 c.c. of filtrate used, in per cent. of the salt of quinine taken. That is, each 0.32 c.c. of ammonia of sp. gr. 0.920 used for 10 c.c. of filtrate (beyond that used for the "standard quinine") indicates 0.001 gram, or 0.1 per cent., of cinchonidine hydrochloride in the commercial quinine hydrochloride taken, or of cinchonidine hydrobromide in commercial quinine hydrobromide taken, etc.

Under Hydrochlorate of Quinine the Br. Ph., 1885, states that "it may be converted into sulphate of quinine by dissolving it, together with an equal weight of sulphate of sodium, in ten times its weight of hot distilled water, and setting the mixture aside at 60° F. (15.5° C.) for half an hour. Such sulphate should respond to the characters and tests," etc., no further directions being given. The Ph. Fran., 1884, does not apply tests for cinchonidine to hydrochloride or hydrobromide of quinine. The Ph. Germ., 1882, directs to evaporate 2 grams of hydrochloride of quinine with 1 gram of sodium sulphate and 20 grams of water, to dryness, digest the residue with 12 grams of alcohol, evaporate the filtrate, and subject the resulting quinine sulphate to the test prescribed for this salt. The U. S. Ph., 1880, directs for quinine hydrochloride and hydrobromide alike that "1.5 gram be dissolved in 15 c.c. of hot distilled water, the solution stirred with 0.75 gram [for the hydrobromide, 0.60 gram] of crystallized sulphate of sodium in powder, the mixture maintained at 15° C. for half an hour, and then drained through a filter only large enough to contain it, until 5 c.c. of filtrate are obtained; upon treating this liquid as directed for the corresponding test under quinine (p. 144) the results there given should be obtained."—F. B. POWER[1] states that, following the U. S. Ph. directions, he obtained only from 2 c.c. of filtrate with the hydrobromide, and only about 1 c.c. of filtrate in testing the hydrochloride; and he proposes taking 30 c.c. of water instead of 15 c.c. for the 1.5 grams of hydrobromide or hydrochloride of quinine. C. N. LAKE[2] has avoided the difficulty in another way, adopted in a habitual use of the test upon these salts, namely: by repeatedly adding water and evaporating to dryness, with stirring, whereby the bulkiness of the precipitated mass becomes reduced, and the 5 c.c. of filtrate are obtained. The obvious remedy for deficiency of the filtrate (as remarked also by Mr. Lake) is to take larger quantities of the materials without altering their proportion to the water (see p. 139). Certainly the stated proportion of water is an influential factor in the test, not to be varied unless a correction be needful to preserve the conventional ratio[3] of 1 to 10 between the sulphate and the water. Such a correction, as seen on p. 147, would make a slight but appreciable difference with the hydrochloride, not an appreciable difference with the hydrobromide. Greater differences are probably due to the presence of sodium sulphate, and bromide or chloride, in the U. S. Ph. application of the test. At all events, the taking of twofold or threefold the quantities of the salts and the water directed by the U. S. Ph., in its specified proportions, does not constitute a departure from its authority for these tests.

In the ammonia test for purity of Quinine, free alkaloid, a weighed quantity, from 2 to 5 grams, either of the hydrate or of the anhydrous alkaloid obtained by drying to a constant weight at 100°–115° C., may be converted to normal sulphate by digesting with warm diluted sulphuric acid, as directed for the pre-

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[1] 1885: "Contributions Dept. Phar. Univ. Wis.," p. 11.

[2] 1885: "The Ph. Application of Kerner's Test to Quinine and its Salts": *Drug. Cir*, 29, 199 (Oct.)

[3] It is the concentration of the solution of alkaloids not quinine that is to be guarded against variation in the test—a test for the quantity of these alkaloids by measure of the concentration of the ammonia needful to dissolve them. The quinine sulphate concentration is securely constant, in solution sure to be saturated. The concentration of the solution of "other alkaloids" is not understood to be affected by the absorption of a good part of this solution by a bibulous mass of imperfectly crystallized salt. If the proportion of water were materially varied by entering into combination as crystallization-water, this variation would be a proper subject of correction. But in the two cases in hand more crystallization-water is liberated than is taken up, the difference being immaterial.

cipitated alkaloid on p. 146, making up to the conventional volume of the strictly neutral mixture and treating further, as there directed. Grams of quinine hydrate taken × 11.5 (or grams of anhydrous quinine × 13.4) = c.c. of conventional volume. Each 0.32 c.c. of ammonia-water of sp. gr. 0.920 used in titration of 10 c.c. of filtrate indicates 0.001 gram, or 0.1 per cent., of free cinchonidine in the commercial free quinine tested, etc. For 5 c.c. of filtrate not over 7 c.c. of ammonia-water of sp. gr. 0.960 should be required, to correspond to the pharmacopœial standard for quinine sulphate.

The U. S. Ph. test for Quinine (hydrate) converts the alkaloid into the sulphate by drying on the water-bath a wetted mixture of the quinine with half its weight of ammonium sulphate.[1]

In the ammonia test for purity of Quinine Bisulphate, it may be converted to the normal sulphate, without loading the solution with alkali sulphates, as follows: A weighed quantity, from 2 to 5 grams, of the bisulphate is dissolved, in a graduated test-glass, in about 12 times its weight of warm distilled water. The solution is carefully divided into two exactly equal portions by volume; from the one portion (taken in a small beaker) the alkaloid is fully precipitated by sodium hydrate solution, and the precipitate washed on a filter until the washings are made but slightly cloudy by barium chloride solution, when the drained precipitate is partly dried by blotting-paper and transferred from the filter to the other portion of the bisulphate solution, in the graduated test-glass (p. 146). The mixture is now heated (by immersing the test-glass in hot water), exactly neutralized to litmus-paper by adding dilute sulphuric acid or ammonia, and the volume made up to a number of c.c. equal to 8 times the number of grams of the bisulphate first taken, when the mixture is crystallized at 15° C. and further treated as directed on p. 144 or 142, taking 5 c.c. of the filtrate for the limit-test, or 10 c.c. for titration parallel with "standard quinine solution" to estimate cinchonidine. For 5 c.c. of the filtrate not over 7 c.c. of ammonia-water of sp. gr. 0.960 should be used, to correspond

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[1] Prof. Power (where cited on p. 148) found that with 1 gram quinine taken only 3 c.c. filtrate could be obtained. Mr. Lake (where cited, p. 148), taking the 1 gram quinine, obtained the required 5 c.c. of filtrate, in his practice as an analyst, by evaporating to dryness and adding water, which, he says, it was not necessary to do over three times. To take 2 to 5 grams of the alkaloid, with half its weight of ammonium salt, and the tenfold number of c.c. of water, involves no departure from the authority of the pharmacopœia for the requirement.

with the pharmacopœial standard for normal quinine sulphate. And for 10 c.c. of the filtrate each 0.32 c.c. of ammonia-water of sp. gr. 0.920 used (beyond that used for the "standard quinine") indicates 0.1 per cent. of cinchonidine bisulphate (cryst., $2H_2O$, HESSE) in the article under examination.

The U. S. Ph. directs that the dried salt be neutralized with ammonia, made up to 10 fluid parts for 1 part of crystals taken, then held at 15° C. and further treated as in the test of the normal sulphate. The same simple operation (drying the salt with the ammonia) is directed by the Ph. Germ. The presence of the ammonium sulphate resulting from the neutralizing with ammonia probably adds severity to the test; while the dilution to 10 fluid parts for 1 part of bisulphate amounts to 12.5 fluid parts for 1 part of normal sulphate formed, and certainly diminishes the severity of the test. The U. S. Ph. makes the operation upon 1 gram of the salt, and the Ph. Germ. upon 2 grams of the salt. POWER[1] has proposed to take 1 gram of the salt with 20 c.c. of water, because 10 c.c. of water fail to yield 5 c.c. of filtrate. Where the operator is unable to depart from the pharmacopœia, he should preserve the proportions of 1 to 10 for the grams of crystallized salt to the c.c. of the mixture digested at 15° C. If any departure be made in this proportion, it should be the adoption of the ratio of 1 to 8, when the salt is neutralized with ammonia or neutralized with its own alkaloid obtained from a divided portion of that taken.

The ammonia test of Effloresced Salts of Quinine.—The Sulphate and the Bisulphate are frequently effloresced when taken for the ammonia test, and the hydrate is apt to have less than $3H_2O$. The severity of the test is thereby increased, in proportion to the resulting increase of concentration of the alkaloids not quinine. All deviations of the concentration may be avoided by drying the salts to a constant composition, taking the anhydrous or the effloresced form by weight, and making up the volume for digestion at 15° C. according to the following data. Then 5 c.c. (or 10 c.c.) of the filtrate will in each instance have the same conventional limit of concentration for the sulphates of all the cinchona alkaloids:

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[1] Where cited on p. 148. The recommendation is to increase the proportion of water, when it is already 25 per cent. too large. The pharmacopœia does not take 1 gram of the dried salt, as Prof. Power's equation (p. 14, *loc. cit.*) represents, but "1 gram of the salt"—the words "previously dried at 100° C." qualifying "agitated with 8 c.c. of distilled water," and the procedure of drying being parallel to that more explicitly laid down for quininæ sulphas. LAKE (where cited on p. 148) has used the 1 gram with 10 c.c., and obtained the needful 5 c.c. of filtrate by evaporating to dryness, stirring, and adding water.

Taking 1 part by weight or "n" grams.	*Weight constant, C.*	*Molecules water.*	*Per ct. crystal. water.*	*Fluid parts (times "n" c.c.) of mixture.*
Crystallized quinine sulphate......	....	7	14.45	10.0
Effloresced “ “	See p. 126.	2	4.60	11.2
Anhydrous “ “	100°—115°	..	.....	11.7
Crystallized quinine bisulphate....	....	7	23.00	8.0[1]
Effloresced “ “	See p. 127.	1	4.09	10.0
Anhydrous “ “	100°	..	.....	10.3
Quinine hydrate.	See p. 126.	3	14.28	11.5
Anhydrous quinine................	100°—120°	..	.. ..	13.4

Hesse's test for Quinine Sulphate (see p. 116) differs in principle from Kerner's in using ether, instead of excess of ammonia, as a solvent of the quinine, and differs from *Liebig's test*[2] in

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[1] If the bisulphate be neutralized with its own alkaloid obtained from a divided portion of the salt weighed and taken, the ratio is the same.

[2] "*Liebig's Test.*"—The author is unable to cite published directions of Liebig for the test which has gone under his name for fully thirty years. The test, in a simple form, with far too large proportions of ether and ammonia, is very clearly given, in 1833, on the sole authorship of KINDT, as follows (*Berzelius's Jahresbericht*, **12** (1833), 218; from *Brande's Archiv*, **36**, 254): "Kindt hat folgende Methode zur Entdekkung der Gegenwart von Schwefelsaurem Cinchonin im Chininsalz angegeben. Man zerreibt 1 Gran vom Salze, schüttet es in ein Probirglas, und giesst 1 Drachme Aether darauf, womit man es umschüttelt; alsdann mischt man 1 Drachme Ammoniak zu und schüttelt wohl um. Wenn sich die Flüssigkeiten wieder scheiden, findet man die Scheidungslinie rein, wenn das salz frei von Cinchonin war, aber die geringste Menge Cinchonin im Salz setzsich deutlich erkennbar aus der Grenze zwischen beiden Flüssigkeiten ab." In 1842 CALVERT (*Jour. de Phar.; Ann. Chem. Phar.*, **48**, 242) undertakes to separate cinchonine by its insolubility in calcium chloride solution and in lime solution, and refers to the use of ammonia, but not to the use of ether, as a solvent of quinine. In 1843 R. HOWARD (*Phar. Jour. Trans.*, **2**, 645) says that cinchonine sulphate is not at all excluded from commercial quinine sulphate "by any test" which he has "happened to see recommended," and he gives a test by weight of crystals from a saturated sulphate solution. In 1852 SOUBEIRAN (*Jour. de Phar.*, 1852, Jan.; *Am. Jour. Phar.*, **24**, 166) cites Liebig's authority for the ether test, saying only "Liebig has suggested" the detection of cinchonine by treating 15 grains of the salt, with 2 ounces ammonia solution, and 2 ounces of ether, and so on, the proportions being nearly those given by Kindt in 1833, though the quantities are 15 times as large. From about this time (1852) the test is commonly mentioned in literature as Liebig's test; but in 1851 or 1852 ZIMMER (*Jahr. Chem.*, 1852, 745; *Chem. Gazette*, 1852, 449) gives the test, with the modern proportions of ether and of ammonia, without naming Liebig's authority. Also HENRI (1847) separates cinchonine by ether in a complex process, which is criticised by GUIBOURT in 1851–52, neither of these authors speaking of Liebig. In Gmelin's Chemistry (Cav. ed. **17**, 279) the method is entitled "The Quinine Test of Liebig," but among the references to as many as a dozen published authorities Liebig's name is not found. In this historical inquiry it may further be noted that when LIEBIG reported the elementary analyses of quinine and cinchonine, in 1831 (*Ann. Phys. Chem.*,

removing the excess of the quinine as a sulphate before separating by ether. The directions of Hesse are as follows:[1] A "quinometer" is provided, this being a test-tube 10–11 mm. (0.39 to 0.43 inch) wide, and 120 mm. (4.7 inches) long. The tube is marked at a capacity of 5 c.c., and again at a capacity of 6 c.c.; the entire capacity of the tube, which is fitted with a cork, being 10 or 12 c.c. Of the quinine sulphate to be tested, 0.5 gram is well shaken in a test-tube with 10 c.c. of hot water (50° to 60° C.), and set aside to cool for ten minutes, shaking with care to prevent the expulsion of the contents. The liquid is now passed through a filter of about 60 mm. (2.4 inches) diameter into the quinometer, up to the 5 c.c. mark; 1 c.c. of ether (sp. gr. 0.724 to 0.728) is added (up to the 6 c.c. mark), and then 5 drops of ammonia-water (sp. gr. 0.96), when the tube is corked and slowly shaken. Granular crystals appearing within 3 minutes after shaking indicate as much as 3 per cent. of cinchonidine; at 10 minutes after shaking, about 2 per cent. of cinchonidine. After standing 2 hours the appearance under a lens of granular crystals indicates cinchonidine; radiating needles, cinchonine or quinidine; no crystals, the absence of over 1 per cent. of cinchonidine, or 0.5 per cent. of quinidine, and of over 0.25 per cent. of cinchonine. Absence of crystals after 12 hours shows that less than 1 per cent. of cinchonidine is present. If now the cork be loosened, and the ether permitted slowly to evaporate, 0.5 per cent. of cinchonidine will leave a distinct crystalline residue. The final residue contains amorphous quinine.

The test of Sulphate of Quinine for Cinchonidine by the Br. Ph., 1885, on the principle of Hesse's test, is much more elaborate than the operation above detailed: "*Test for Cincho-*

Pogg., [3], **21**, 25), he specifies the purification of quinine by dissolving it, not in ether, but in ammonia (on the plan of Kerner's test), as follows: "Der breiartige weisse Niederschlag, welcher durch verdunstes Ammoniak aus der schwefelsauren Auflösung erhalten worden war, löste sich beim Erhitzen in der etwas freies Ammoniak enthaltenden Flüssigkeit vollkommen auf, und gab bei dem abkühlen ganz Ammoniak freie, sehr feine, glänzende, seidenartige Nadeln von Chinin."

Liebig's test was directed by *the U. S. Ph. of* 1860 *and of* 1870, in the following terms: "When 10 grains of the salt [Sulphate of Quinine] are agitated in a test-tube with 10 minims of officinal water of ammonia [0.960] and 60 grains of ether [0.750], and allowed to rest, the liquid separates into two transparent and colorless layers, without any white or crystalline matter at the surface of contact." It was generally stated that as much as 10 per cent. of quinidine sulphate would escape detection by this test. Undoubtedly larger percentages both of quinidine and cinchonidine are liable to fail of recognition with the test as commonly applied.

[1] O. Hesse, 1878: *Archiv d. Phar.*, [3]. **13**, 490; *Am. Jour. Phar.*, **51**, 135; *New Rem.*, 8, 139; *Jour. Chem. Soc.*, 36, 280; *Zeitsch. anal. Chem.*, **19**, 247.

nidine and Cinchonine.—Heat 100 grains (6.48 grams) of the sulphate of quinine in five or six ounces (142–170 c.c.) of boiling water, with three or four drops of diluted sulphuric acid. Set the solution aside until cold. Separate, by filtration, the purified sulphate of quinine which has crystallized out. To the filtrate, which should nearly fill a bottle or flask, add ether, shaking occasionally, until a distinct layer of ether remains undissolved. Add ammonia in very slight excess, and shake thoroughly, so that the quinine at first precipitated shall be redissolved. Set aside for some hours or during a night. Remove the supernatent clear ethereal fluid, which should occupy the neck of the vessel, by a pipette. Wash the residual aqueous fluid and any separated crystals of alkaloid with a very little more ether, once or twice. Collect the separated alkaloid on a tared filter, wash it with a little ether, dry at 212° F., and weigh. Four parts of such alkaloid correspond to five parts of crystallized sulphate of cinchonidine or of sulphate of cinchonine.

"*Test for Quinidine.*—Recrystallize 50 grains (3.240 grams) of the original sulphate of quinine as described in the previous paragraph. To the filtrate add solution of iodide of potassium, and a little spirit of wine [alcohol] to prevent the precipitation of amorphous hydriodides. Collect any separated hydriodide of quinidine, wash with a little water, dry and weigh. The weight represents about an equal weight of crystallized sulphate of quinidine.

"*Test for Cupreine* [see p. 92].—Shake the recrystallized sulphate of quinine, obtained in testing the original sulphate of quinine for cinchonidine and cinchonine, with one fluid-ounce (28.4 c.c.) of ether (sp. gr. 0.724–0.728) and a quarter of an ounce (7.1 c.c.) of solution of ammonia (of 10% strength), and to this ethereal solution, separated, add the ethereal fluid and washings also obtained in testing the original sulphate for the two alkaloids just mentioned. Shake this ethereal liquor with a quarter of a fluid-ounce (7.1 c.c.) of a ten per cent. solution of caustic soda, adding water if any solid matter separates. Remove the ethereal solution. Wash the aqueous solution with more ether, and remove the ethereal washings. Add diluted sulphuric acid to the aqueous fluid heated to boiling, until the soda is exactly neutralized. When cold collect any sulphate of cupreine that has crystallized out, on a tared filter, dry, and weigh.

"'Sulphate of Quinine' should not contain much more than five per cent. of sulphates of other cinchona alkaloids."

Water of Crystallization in Sulphate of Quinine.—Hesse[1]

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[1] 1880: *Ber. d. chem. Ges.*, 13, 1517–1520, and elsewhere.

has continued to maintain that perfect crystals of pure quinine sulphate have $8H_2O$ (16.18% of water). **Kerner**[1] affirms that no quinine sulphate is manufactured that contains over 14 to an extreme of 14.6% of crystallization-water; above this any contained water is free moisture. Also that it is not possible to dry the voluminous quinine sulphate of commerce without some degree of efflorescence. The Ph. Germ. (1882) (without formulæ) limits the loss by drying at 100° C. to 15%. The Ph. Fran. (1884) gives $7H_2O$ (=14.45%) in the formula, and limits the loss at 100° C. to 14.45%. The Br. Ph. (1885) gives $7\frac{1}{2}H_2O$ in the formula, and limits the loss at 100° C. to this molecular proportion, 14.3%. The U. S. Ph. (1880) gives $7H_2O$ in the formula, and limits the loss of weight at 100° C. to 16.18%. Mr. H. B. **Parsons**[2] reported the loss of water by drying three hours in a (boiling) water-oven, for 1015 samples, of American, German, and Italian makers, each sample representing 100 ounces, and taken from a can not previously opened. The average of loss of water, for all the samples, was 13.84%; for any single manufacturer the lowest average was 12.61%, and the highest average was 14.36%. The samples of one maker all approached closely to 12.53% ($6H_2O$). In the report the writer recommends, as others have done, the pharmacopœial adoption of effloresced quinine sulphate, the two-molecule salt, as a definite and stable form of the alkaloid.

Quinidine. The *Conchinine* of Hesse.[3] $C_{20}H_{24}N_2O_2=324$. In crystals with $2\frac{1}{2}H_2O=396$. Chinidine.—Rational Formula, p. 98; Proportion in Cinchona Barks, p. 97. Separation from the Bark, in total alkaloids, p. 102. Separation from Cinchona

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[1] 1880: *Archiv d. Phar.*, [3], 17, 453.

[2] 1884: *Proc. Am. Pharm.*, 32, 457.

[3] The name quinidine, in German "chinidine," was given to the alkaloid now universally known as cinchonidine, in 1833, by **Henry** and **Delondre**. *Quinidine* was itself discovered, in chinoidine, in 1849, by **Van Heijningen**, who then named it *b*-quinine; again, in commercial cinchonine, in 1851, by **Hlasiwetz**, who named it cinchotine. In 1853 **Pasteur**, believing that he identified Henry and Delondre's quinidine among cinchona alkaloids, and discovering another which in fact was Henry and Delondre's quinidine, he fixed to this the name cinchonidine, still retained. The name "quinidine" having thus been differently applied, **Hesse** (1874) proposes to drop it, and use the name "conchinine" for the isomer of quinine. Some of the German writers employ Hesse's nomenclature, but English-writing chemists translate the "conchinine" of Hesse into the English equivalent of German "chinidine," namely: *quinidine.* And this accords with the recommendation of the Quinological Congress at Amsterdam in 1877. Further see **Kerner**'s history of this nomenclature, 1880: *Archiv d. Phar.*, [3], 16 (reprints). The *b*-quinidine of Kerner in 1862 is the quinidine of the present time.

Alkaloids, index at p. 112. Distinction from other Cinchona Alkaloids, index at p. 100. Microscopic identification, p. 101. Rotatory Power, p. 123.

The free alkaloid has been hardly known in commerce, and its sulphate is less used than that of cinchonidine or cinchonine. The chinoidine obtained as a by-product from certain barks is rich in quinidine.

The *crystalline forms* and *heat reactions* of quinidine *and its salts* are given under *a*, the *solubilities* of the same under *c*, below. Quinidine is *identified* by its fluorescence in the sulphate and its response to the thalleioquin test (*d*), together with the free solubility of the sulphate in chloroform and its greater solubility in water. Also by precipitation as hydriodide (*d*). It is *separated*, by solution of the sulphate in chloroform, or precipitation with iodide, or otherwise (*e*); *estimated*, usually by weight of the hydriodide (*f*). Tests for *impurities* in quinidine sulphate are presented under *g*, p. 157.

a.—Quinidine crystallizes from alcohol, with $2\frac{1}{2}H_2O$, in large, lustrous, monoclinic prisms or needles, efflorescent in the air. From ether permanent rhombohedrons with $2H_2O$ are obtained; from boiling water permanent plates with $1\frac{1}{2}H_2O$ (HESSE). The whole of the water is removed at or below 120° C., and the dry alkaloid melts at 168° C. It begins to brown very slightly at 160° C. (BLYTH).—*Quinidine sulphate*, $(C_{20}H_{24}N_2O_2)_2H_2SO_4 . 2H_2O$, crystallizes in white, silky needles or in long, hard prisms, permanent in the air, giving up the water at 120° C.—*The bisulphate* crystallizes in asbestos-like prisms, with $4H_2O$.—*Quinidine hydrochloride* crystallizes in asbestos-like fibres, with H_2O.—*Quinidine oxalate*, normal, crystallizes with H_2O, in pearly plates or in prisms.

b.—In taste and physiological effects quinidine resembles quinine.

c.—Quinidine is soluble in 2000 parts of water at 15° C., in 750 parts of boiling water; in 26 parts alcohol of 80% at 20° C.; in 22 parts of ether of sp. gr. 0.729 at 20° C., or in 35 parts of the same at 10° C. (HESSE, 1868). In 80.9 parts ether of 0.72 sp. gr. at 19° C. (VAN DER BURG); in 76.4 parts of ether at 10° C. (DRAGENDORFF). In chloroform or amyl alcohol it is readily soluble; in petroleum ether difficultly soluble. Quinidine neutralizes acids in forming normal salts.

Quinidine sulphate of a neutral reaction is soluble "in 100 parts of water and in 8 parts of alcohol at 15° C.; in 7 parts of boiling water, and very soluble in boiling alcohol; also in acidulated water and in 20 parts of chloroform, but almost insoluble in ether" (U. S. Ph.) In 19.5 parts chloroform at 15° C., in 9 parts at 62° C. (HESSE, 1879).—*Quinidine hydrochloride* is soluble in 62.5 parts of water at 10° C., and freely soluble in hot water, in alcohol, and in chloroform; nearly insoluble in ether.—*Quinidine hydrobromide*, anhydrous (DE VRIJ, 1875), is soluble in 200 parts of water at 14° C.—*Quinidine oxalate*, $(C_{20}H_{22}N_2O_2)_2H_2C_2O_4 . H_2O$, dissolves in 150 parts of water at 15° C.

d.—In solutions of the sulphates, and especially in solutions acidulated with sulphuric acid, quinidine exhibits strong *blue fluorescence.* (See Quinine, *d.*) The chloroformic solution of the sulphate has a green fluorescence (HESSE, 1879).—Quinidine responds to *the thalleioquin test* (p. 130). Sulphuric acid gives no color; **Froehde's reagent,** a greenish color.—**Iodide of potassium** causes in neutral solutions of quinidine salts a crystalline precipitate of quinidine hydriodide, $C_{20}H_{24}N_2O_2HI$, soluble in 1250 parts of water at 15° C. (DE VRIJ). Immediate precipitation is obtained only in somewhat concentrated solution, and is incomplete. Full crystallization within the limit of solubility is obtained by warming the mixture and stirring it with a glass rod from time to time as it cools, then leaving some hours at a low temperature, stirring at intervals. The reagent should be neutral, and added in such proportion that the quantity of solid potassium iodide shall nearly equal the quantity of alkaloid in solution. The crystals slowly formed in dilute solutions are leaf-form. In acidulous mixtures of sufficient concentration bihydriodide of quinidine is formed, in golden crystals, soluble in 90 parts of water at 15° C. (DE VRIJ).—With the **alkalies** and alkali carbonates quinidine gives nearly the same reactions as quinine, the precipitate being very much less soluble in excess of ammonia. In presence of quinine the quinidine precipitate requires a good excess of ammonia to dissolve it, and the precipitate is apt to reappear, crystalline on standing.—With the **general reagents for alkaloids** quinidine reacts nearly the same as quinine, so far as the reactions have been examined.—The dextrorotatory power of quinidine is given on p. 123.

e.—*Separations* of quinidine are obtained chiefly (1) by its crystallization as hydriodide (*d*, *f*), and (2), except from cinchonine, by solution of the sulphate in chloroform (*c*). See Separation of Cinchona Alkaloids, p. 112, for an index of methods of separation. Also compare the special separations of Quinine (*f*), p. 141.

f.—Quantitative.—In estimating quinidine as hydriodide, crystallization is secured, as indicated under *d*, giving twenty-four hours for the crystals to form. The drained crystals, sparingly washed, are dried in a warm place, and weighed as $C_{20}H_{24}N_2O_2HI$, adding $\frac{1}{1250}$ of the weight of the crystallizing liquid and washings. The anhydrous quinidine constitutes 71.75 per cent. of the total hydriodide.

g.—Tests for impurities.—"The salt [sulphate] should not be more than very slightly colored by undiluted sulphuric acid (absence of [more than very slight proportions of] foreign organic matters). . . . If 0.5 gram each of sulphate of quinidine and of iodide of potassium (not alkaline to test-paper) be agitated with 10 c.c. of water at about 60° C. (140° F.), the mixture then macerated at 15° C. (59° F.) for half an hour, with frequent stirring, and filtered, the addition to the filtrate of a drop or two of water of ammonia should not cause more than a slight turbidity (absence of more than small proportions of conchonine, cinchonidine, or quinine)" (U. S. Ph., 1880). One part quinidine sulphate dissolved in 10 parts hot water is digested at 60° C. with 1 part potassium iodide, the mixture cooled, with agitation, and the filtrate tested with 1 or 2 drops of ammonia-water (Ph. Fran., 1884).

CINCHONIDINE.—The Quinidine of HENRY and DELONDRE (1833).[1] Isomeric with cinchonine, $C_{19}H_{22}N_2O = 294$.[2] Crystallizes anhydrous.—The free alkaloid is little known in commerce, but the sulphate since about 1876 has been used quite largely, and to a much greater extent than any other distinct cinchona alkaloid except quinine. Cinchonidine is the chief general impurity in quinine salts in use.

The Rational Formula is indicated at p. 98. Proportion in Cinchona Bark, p. 97. Separation from the Bark, in total alkaloids, pp. 102–111. Separation from other Cinchona Alkaloids, index of methods at p. 112. Distinction from other Cinchona Alkaloids, index of methods at p. 100. Microscopic identification, p. 101. Rotatory Power, p. 123.

The *crystalline forms and heat-reactions* of cinchonidine *and its salts* are given under *a*, and their *solubilities* under *c* (p. 158). Cinchonidine is characterized by *chemical reactions* stated under

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[1] Also of WINCKLER, 1844. See foot-note under Quinidine (p. 154). This alkaloid, isomeric with cinchonine or a mixture containing it, was named *cinchonidine* by PASTEUR in 1853, and by WITTSTEIN in 1856. At present all authorities agree in this name.

[2] SKRAUP, 1878. PASTEUR, $C_{20}H_{24}N_2O$, 1853. See foot-note under Cinchonine.

d (p. 159), the tartrate precipitate with concurring qualitative reactions being the chief dependence for *identification*. The alkaloid is *estimated* by weight of the tartrate or of the free alkaloid (*f*). The tests for *impurities* and the amount of water of crystallization of the sulphate are discussed under *g*, p. 160.

a.—Crystallization and heat reactions.—Cinchonidine crystallizes, anhydrous, in distinct, lustrous forms; from alcohol in short prisms; from dilute alcohol in fine, thin plates. It melts at 200°–201° C. (Hesse, Claus, 1881).—*Cinchonidine sulphate* crystallizes in white, silky, lustrous needles or in thin, quadratic prisms. "In colorless silky crystals, usually acicular" (Br. Ph., 1885). "Ordinarily from aqueous solution little concentrated, in brilliant needles, with $6H_2O$. From concentrated [hot] aqueous solution, in [hard] prisms, with $3H_2O$. And from alcohol in fine prisms, with $2H_2O$. The salt with $6H_2O$ is officinal" (Ph. Fran., 1884). The crystals containing $6H_2O$ effloresce to some extent in the air, losing either one or four of the $6H_2O$, as determined by the mode of production of the crystals (Ladenburg's "Handwörterbuch"). In moist air the anhydrous salt gains $2H_2O$. All water of crystallization is expelled on the water-bath. Cinchonidine sulphate with quinine sulphate crystallizes with $6H_2O$ (Koppeschaar, 1885).—*Cinchonidine hydrochloride*, with 1 molecule of H_2O, forms characteristic crystals, double pyramids, octahedrons (Hesse). From supersaturated solution silky, prismatic needles are sometimes obtained, with $2H_2O$. A bihydrochloride is also obtained, forming large, lustrous, monoclinic crystals with 1 molecule of water.—*Cinchonidine hydrobromide* crystallizes, with H_2O, in long, colorless needles (Ph. Fran.) The dihydrobromide, with $2H_2O$, crystallizes in very slightly yellowish prolonged prisms (Ph. Fran.)—*Cinchonidine tartrate*, normal, with $2H_2O$, is a white crystalline precipitate, becoming anhydrous at 100° C.—*Cinchonidine oxalate*, normal, crystallizes, with 2 or 6 H_2O, in prisms or a crystalline powder.

b.—Cinchonidine has a very bitter taste, and is administered in doses not far from those of quinine. In excess it is liable to prove poisonous, with action resembling that of picrotoxine (Sée and Bochefontaine, 1885). Death has resulted from taking 160 grains (Williams, 1884).

c.—Solubilities.—Cinchonidine is soluble in 1680 parts of water at 10° C., in 20 parts of 80% alcohol, in 76 parts of ether of sp. gr. 0.729, and easily soluble in chloroform (Hesse, 1865). In 16.3 parts of alcohol of 97% at 13° C., and in 188 parts ether of sp. gr. 0.72 at 15° C. (Hesse, 1880). Readily soluble in amyl alcohol. Slightly soluble in ammonia. In presence of quinine its solubility in ether is increased. The normal salts of cinchonidine, with ordinary acids, are neutral.

Cinchonidine sulphate, $(C_{19}H_{22}N_2O)_2H_2SO_4.6H_2O=794$ (see *a*), is soluble "in 100 parts of water and in 71 parts of alcohol at 15° C. (59° F.), in 4 parts of boiling water, in 12 parts of boiling alcohol, freely in acidulated water, and in 1000 parts of chloroform (the undissolved portions becoming gelatinous); very sparingly soluble in ether or benzene" (U. S. Ph.) In 300 parts boiling chloroform. Mixed with quinine sulphate it becomes somewhat soluble in ether (Paul, 1877). In presence of cinchonine or quinidine sulphate its solubility in chloroform is increased (Prescott and Thum, 1878). — *Cinchonidine hydrochloride*, $C_{19}H_{22}N_2O\ HCl.H_2O=348.4$ (see *a*), is soluble in 30 parts of water at 15° C., freely soluble in boiling water, in alcohol, and in chloroform, and soluble in 325 parts of ether at 10° C. (Carles, 1874). From the chloroformic solution, in long standing, there are formed prismatic crystals of an instable compound with chloroform (Hesse, 1875).—*Cinchonidine hydrobromide*, $C_{19}H_{22}N_2OH\,Br.H_2O=393$ (Br=80), is soluble in 40 parts of cold water, and freely soluble in hot water (Ph. Fran.)—*Cinchonidine tartrate*, $(C_{19}H_{22}N_2O)_2C_4H_6O_6.2H_2O$, is soluble in 1265 parts of water at 10° C., less soluble in solution of rochelle salt.—The normal *oxalate*, $(C_{19}H_{22}N_2O)_2H_2C_2O_4.6H_2O$, is soluble in 252 parts of water at 12° C. for 1 part of the anhydrous salt.

d.—Cinchonidine does not form fluorescent solutions nor give the thalleioquin reaction.—**Potassium sodium tartrate** and other normal tartrates precipitate cinchonidine, as normal tartrate (see above, *c*), crystallizing from hot solution in fine needles. An excess of the reagent renders the test the more delicate. A separation from cinchonine, and to some extent from quinidine, hardly at all from quinine.—Cinchonidine is precipitated from solutions of its salts by the **alkalies** and alkali carbonates, the precipitate appearing at first amorphous, slowly becoming crystalline, and being somewhat soluble in excess of ammonia (see Quinine, *g*, "Kerner's Test"). The **general reagents** for alkaloids give customary reactions with cinchonidine.—In the test for iodosulphate (see Quinine, *d*, Herapathite, p. 131) green crystals of golden lustre are obtained.—Respecting the microchemical test with sulphocyanate, see under Cinchona Alkaloids, p. 101; the levorotatory power, p. 122.

e.—*Separations* of cinchonidine are indexed under Cinchona

Alkaloids, Separation of, p. 112. Compare also with special methods for the separation of Quinine, p. 139.

f.—Cinchonidine can be *estimated*, *gravimetrically*, as anhydrous alkaloid by drying the precipitate obtained with sodium hydrate on the water-bath (*a*). More often it is estimated (according to directions given under Cinchona Alkaloids, Separation) by weight of the anhydrous tartrate $(C_{19}H_{22}N_2O)_2C_4H_6O_6 = 738$ (79.67% cinchonidine). The precipitate is dried on the water-bath.—As to optical estimation, see p. 124 under Cinchona Alkaloids.—For estimation in mixture with quinine, both as sulphates, by action of ammonia, see under Quinine, *g*, "Kerner's Test."

g.—*Tests for impurities.*—"If 0.5 gram of the salt [sulphate] be digested with 20 c.c. of cold distilled water, 0.5 gram of tartrate of potassium and sodium added, the mixture macerated, with frequent agitation, for one hour at 15° C. (59° F.), then filtered and a drop of water of ammonia added to the filtrate, not more than a slight turbidity should appear (absence of more than 0.5 per cent. of sulphate of cinchonine, or of more than 1.5 per cent. of sulphate of quinidine)" (U. S. Ph., 1880).[1] The test originated with HESSE (1875), who directed to digest 0.5 gram of the salt with 20 c.c. water at about 60° C., add 1.5 grams of the tartrate, and after an hour filter and test with ammonia. The Ph. Fran. (1884) directs digestion with boiling water, 40 parts, and an excess of the tartrate, then setting aside 24 hours before testing. The three parts of tartrate directed by Hesse give a little closer results than are obtained with addition of one part (*c*, p. 159). The test does not reveal quinine, tartrate of which takes 910 parts water at 10° C. to dissolve it, but shows either cinchonine or quinidine. To test for presence of quinidine, add to the filtrate from tartrate precipitation potassium iodide equal to quantity of cinchonidine salt taken, and stir from time to time, when quinidine will be revealed by precipitation, and the second filtrate can be tested, with a drop of ammonia-water, for cinchonine. Either quinine or quinidine will be revealed by fluorescence (Quinine, *d*).—The sulphate "should not be colored by addition of sulphuric acid (absence of foreign organic matters)" (U. S. Ph., 1880); should not suffer "more than a faint yellow coloration" (Br. Ph., 1885).

As to amount of *crystallization-water in cinchonidine sulphate*, see *a*. The loss by drying at 100° C. is limited by the

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[1] TEETER, *Univ. Mich.*, 1880: *New Rem.*, 9, 258.

U. S. Ph. and Br. Ph. to the amount of $3H_2O$, or 7.3 per cent.; by the Ph. Fran. to the proportion of $6H_2O$, 13.60 per cent. Five ordinary commercial samples, dried at 100° C. and cooled in a desiccator, gave a loss of from 6.36 per cent. to 7.04 per cent.[1]

Cinchonine. $C_{19}H_{22}N_2O=294$.[2] Crystallizes anhydrous.—See Cinchona Alkaloids, p. 97, for yield in cinchona barks, and p. 98 for chemical constitution.

Methods of Separation from the Bark, in the total alkaloids, are given pp. 102 to 111. From the other cinchona alkaloids the methods of separation are indexed at p. 113, the means of distinction are indexed at p. 100. Methods of microscopic inquiry, p. 101. Rotatory Power, p. 123. Crystallization and Heat-Reactions for the alkaloid and its salts, below. Solubilities of the alkaloid and its salts, p. 162. Physiological effects, p. 162.

Cinchonine is *identified* by the agreement of a number of alkaloidal reactions and solubilities, and, after separation, by negative results excluding other alkaloids (*d*); the reaction with ferricyanide, carefully obtained under the magnifier, is somewhat characteristic, as likewise is the iodine reaction. For separations, references are noted, in addition to those above, at *e*, p. 164. The alkaloid is *estimated* by its weight in the free state, anhydrous (*f*), and has been estimated by Mayer's solution (p. 164). Tests for *purity* are given (*g*) at p. 164.

a.—Crystallization and Heat-Reactions.—Cinchonine appears in white prisms or needles, anhydrous, in the monoclinic system, obtained by crystallization from alcohol. In watery solution of its salts ammonia gives a flocculent, crystalline precipitate; in solution of its salts in dilute alcohol needles are obtained by action of ammonia. It melts at 268.8° C. (Skraup, 1878). Quickly heated, at 248°–252° C.; slowly heated, at 236° C. (Hesse, 1880). Heated, not quite to the melting point, in a stream of hydrogen or ammonia, a sublimate is obtained, of undecomposed cinchonine, in prismatic needles, with products of partial decom-

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[1] Taking cinchonidine at $C_{19}H_{22}$ . . ., $6H_2O=13.60$ per cent. of the sulphate.
" " at $C_{20}H_{24}$ . . ., $6H_2O=13.13$ " "
" " at $C_{19}H_{22}$ . . ., $3H_2O=7.30$ " "
" " at $C_{20}H_{24}$ . . ., $3H_2O=7.03$ " "

[2] Skraup, 1878. Pasteur, 1853, $C_{20}H_{24}N_2O$. Skraup found it necessary to separate Cinchotine, $C_{19}H_{24}N_2O$ (p. 93), to obtain pure cinchonine for analysis. His figures support the new formula better than they do the old. Hesse accepts Skraup's formula; and it is taken as the basis of hypotheses of the constitution of cinchona alkaloids (p. 98). Pasteur's formula is retained in the Br. Ph. of 1885; Skraup's is adopted in the Ph. Fran. of 1884.

position (Hlasiwetz, 1851). In melting it turns brown and sublimes slowly.

Cinchonine sulphate, with $2H_2O$, crystallizes in short, hard, monoclinic prisms, transparent, of a vitreous lustre, permanent in the air, parting with all the crystallization-water at 100° C. Triturated at 100° C. it glows with greenish light. It melts at about 240° C.—*Cinchonine hydrochloride*, with $2H_2O$, forms four-sided rhombic prisms or fine, silky needles, permanent in the air, efflorescent in a desiccator, becoming anhydrous at 100° C., and melting at about 130° C.—*The hydrobromide* forms long, lustrous prismatic needles (Latour, 1870; Bullock, 1875).—*The hydriodide*, normal, crystallizes, with H_2O, from a hot-saturated solution, in hard, colorless, monoclinic prisms.—*The tartrate*, normal, with $2H_2O$, crystallizes from a hot solution in clusters of needles.—*Cinchonine oxalate*, normal, with $2H_2O$, appears in crystalline powder, or from dilute hot solution in large prisms, becoming anhydrous at 130° C.

b.—Free cinchonine is nearly tasteless at first, with an increasing bitter after-taste. The soluble salts of cinchonine are very bitter.—The dose of the sulphate is 1 to 10 grains (Br. Ph.)

c.—*Solubilities.*—"Almost insoluble in hot or cold water, soluble in 110 parts of alcohol at 15° C. (59° F.), in 28 parts of boiling alcohol, 371 parts of ether, 350 parts of chloroform, and readily soluble in diluted acids" (U. S. Ph.) In 3670 parts water at 20° C.; in 371 parts of ether of sp. gr. 0.73 at 20° C.; in 125.7 parts of alcohol of sp. gr. 0.852 at 20° C. (Hesse, 1862). In 356 parts of chloroform strictly alcohol-free, at 17° C., but more freely soluble in mixtures of chloroform and alcohol than in alcohol alone (Oudemans, 1873). In 40 parts of "chloroform" (Pettenkofer); in 35 parts of "chloroform" (Hager). Moderately soluble in amyl alcohol; sparingly soluble in hot benzene; scarcely at all soluble in cold benzene.[1] Nearly inso-

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[1] In 1875 the writer made determinations of solubilities of cinchonine in supersaturation with certain water-washed solvents, with the results which follow. The "nascent" state was that of liberation from sulphate solution by ammonia, while in contact with the hot solvent, all the solvents being applied at their boiling points:

Cinchonine.	*Ether.* At 15° C.: sp. gr. 0.7290.	*Chloroform.* sp. gr. 1.4953.	*Amyl alc.* sp. gr. 0.8316.	*Benzene.* sp. gr. 0.8766.
Crystallized.........	719	828	..	...
Amorphous..........	563	...	40	531
Nascent.............	526	178	22	376

From "Comparative Determinations of the Solubilities of Alkaloids in Crystalline, Amorphous, and Nascent Conditions: Water-washed Solvents being used."—A. A. A. S., 1875, **24**, i. 114; *Jour. Chem. Soc.*, **29**, 403; *Am. Chem.*, **6**, 84.

luble in petroleum benzin (Dragendorff). But slightly soluble in ammonia-water.—Cinchonine neutralizes the strong mineral acids, its sulphate having "a neutral or faintly alkaline reaction" (U. S. Ph.)

Cinchonine sulphate, $(C_{19}H_{22}N_2O)_2H_2SO_4.2H_2O$, is soluble "in about 70 parts of water and in 6 parts of alcohol at 15° C. (59° F.), in 14 parts of boiling water, 1.5 parts of boiling alcohol, 60 parts of chloroform, and easily soluble in diluted acids; insoluble in ether or benzene" (U. S. Ph.) In 65.5 parts water at 13° C. (Hesse).

Cinchonine hydrochloride, $C_{19}H_{22}N_2O\ HCl.2H_2O$, is soluble in 24 parts of water at 10° C.; in 1.3 parts of alcohol of sp. gr. 0.85 at 16° C.; in 273 parts of ether of sp. gr. 0.7305 at 15° C. (Hesse).—*The hydrobromide* dissolves in 18 parts of water at 21° C. (Bullock, 1875), and is freely soluble in alcohol.—*The hydriodide*, $C_{19}H_{22}N_2O\ HI.H_2O$, is freely soluble in water, in alcohol, and in chloroform, and somewhat soluble in ether.—*The normal tartrate*, $(C_{19}H_{22}N_2O)_2C_4H_6O_6.2H_2O$, is soluble in 33 parts of water at 16° C. (Hesse), the solution having a slightly alkaline reaction.—*The tannate* is very slightly soluble in water, and is not soluble in all proportions of cold hydrochloric acid.—Normal *oxalate*, $(C_{19}H_{22}N_2O)_2H_2C_2O_4.2H_2O$, dissolves in 104 parts of water at 10° C.

d.—In qualitative reactions cinchonine is characterized by negative results. It does not respond to the thalleioquin test; its solutions do not fluoresce; its hydriodide and its tartrate are freely soluble in water. Its periodides and iodosulphates are distinguished from those of quinine only by a careful observance of conditions. **Potassium ferrocyanide** solution not in excess, with slightly acidulated solutions of cinchonine salts, gives a yellowish-white precipitate of cinchonine ferrocyanide, at first amorphous, becoming crystalline on standing or while cooling, in radiate or fan-like clusters or rhombic plates, as seen under the microscope. The crystals are golden-yellow. The precipitate is soluble in excess of the reagent, more readily before crystallizing. The solution made by dissolving the amorphous precipitate in just enough excess of the reagent soon yields crystals again (a difference from the reaction with quinine, Barfoed). Quinine gives a precipitate more permanently soluble in excess of the reagent.—If a warm-saturated alcoholic solution of cinchonine be neutralized with hydrochloric or very slightly acidified with acetic acid, then to each c.c. about 10 drops of a one per cent. solution of **iodine** with potassium iodide be added, and water added to incipient precipitation, fine, lustrous red-brown to brown-yellow crystals of superiodide are gradually formed in the cooling of the liquid. The forms are four-sided rhombic plates. Under just these conditions, and in absence of sulphates, quinine gives a precipitate of tarry consistence (Barfoed, 1881). Treated as a sulphate, as directed under Quinine, *d*, for herapathite, cinchonine gives nearly black crystals, brown to brown-yellow when in thin layers under the microscope.

The general reagents for alkaloids precipitate cinchonine, in most cases quite perfectly. **Tannic acid** gives a precipitate not easily dissolved by hydrochloric acid. **The alkali hydrates** and carbonates give a quite complete precipitate of cinchonine (see *a*), not at all soluble in excess of sodium hydrate, and (in absence of other cinchona alkaloids) almost insoluble in excess of ammonia. (See under Quinine, *g*, "Kerner's Test"). In dilute solutions, and more favorably with excess of ammonia, the precipitate becomes crystalline on standing a short time, and is seen under the microscope in radiating tufts of needles.

e.—Separations of cinchonine are indexed under Cinchona Alkaloids, Separation of, p. 113. Compare also special modes of separation of Quinine, p. 139.

f.—Quantitative.—Cinchonine is estimated, gravimetrically, as free alkaloid, anhydrous. From aqueous solution of its salts it is precipitated by solution of sodium hydrate, washed with water, and dried at 100° C. It may be estimated by alkalimetry, with tenth or hundredth normal sulphuric acid solution. With Mayer's solution the equivalent of 1 c.c. was given by Mayer (1862) at 0.0102 gram, and the composition of the precipitate was indicated to be $C_{19}H_{22}N_2O\ HI\ HgI_2$ by Groves (1859), but further data are needful as to the value of the precipitation, and the action of the reagent is greatly affected by conditions.

g.—Tests for distinctions and impurities.—"A solution of the alkaloid in dilute sulphuric acid should not exhibit more than a faint blue fluorescence (absence of more than traces of quinine or quinidine). On precipitating the alkaloid from this solution by water of ammonia it is very sparingly dissolved by the latter (difference from and absence of quinine), and requires at least 300 parts of ether for solution (difference from quinine, quinidine, and cinchonidine)." If the sulphate "be macerated for half an hour, with frequent agitation, with 70 times its weight of chloroform at 15° C. (59° F.), it should wholly, or almost wholly, dissolve (any more than traces of sulphate of cinchonidine or sulphate of quinine remaining undissolved). It should not be colored by contact with sulphuric acid (absence of foreign organic matters)." "If 1 gram [of the sulphate] be dried at 100° C. until it ceases to lose weight, the residue, cooled in a desiccator, should weigh not less than 0.952[1] gram" (U. S. Ph., 1880). "Twenty-five grains of the salt should lose 1.26 grains of moisture when dried at 212° F. (100° C.), and should then almost wholly dissolve in four ounces by weight of chloroform" (Br. Ph., 1885).

QUINOLINE.—Chinoline. Leucoline. $C_9H_7N=129$.—The structure of naphthalene with N in the place of one CH (Körner, 1870). (See under Constitution of Cinchona Alkaloids, p. 97).

An artificial volatile alkaloid obtained as follows: (1) By distilling cinchonine or quinine, strychnine or brucine, with fixed alkali. In presence of copper oxide the quinoline is obtained nearly free from lepidine ($C_{10}H_9N$) and dispoline ($C_{11}H_{11}N$), next homologous members of the quinoline series ($C_nH_{2n-5}N$). (2) The later distillate of coal-tar, the "dead-oil," contains quinoline. For some years this product was held not identical but only isomeric with the quinoline from cinchonine, and it was named *leucoline*, C_9H_7N. In 1883 HOOGEWERFF and v. DORP obtained cinchonine-quinoline free from previous impurities, whereby its identity with the quinoline of coal-tar or bone-oil is believed to be established. The same investigators, however, find an isomer of quinoline in bone-oil. (3) From bone-oil. (4) By synthesis in several ways, best from nitrobenzene, with aniline, according to the equation on p. 97. As obtained from these several sources quinoline is itself one body.

But as manufactured, either for coloring matters or for medicinal purposes, quinoline is likely to retain some degree of impurities derived from its sources. Cincho-quinoline is accompanied by lepidine. Artificial quinoline is sometimes intermixed with nitrobenzene. Certainly for medicinal uses, at present, quinoline offered for sale should be presented with the name of its source.

a.—Quinoline is a colorless, mobile liquid, transparent when pure, very refractive, and turning brown by exposure in the air and light. Specific gravity, at 15° C., 1.084; at 20° C., compared with water at same temperature, 1.094 (SKRAUP, 1881). Boiling point, 231.5° C. (SPALTEHOLTZ) to 241.3° C. (KRETSCHY,

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[1] If cinchonine be $C_{19}H_{22}$ . . ., $2H_2O=4.99$ per cent. of the sulphate.
" $C_{20}H_{24}$ . . ., $2H_2O=4.80$ " "

1881). It evaporates slowly but completely, on exposure, so that the oil-spot it forms on paper disappears on standing. Crystallizes in a freezing mixture of carbon dioxide and ether.—The *hydrochloride* crystallizes in small white nodules; the *tartrate* in rhombic needles, forming under the microscope in columnar needles of good length; the salicylate appears in a reddish-gray powder.

b.—Quinoline has a pungent, aromatic taste, slightly resembling peppermint-oil in its after-taste, without bitterness. It has a slight aromatic odor like bitter-almond oil. It is administered in doses as high as 1 gram (15 grains) or 2 grams (30 grains) in twenty-four hours (DONATH, 1881). In overdoses, to animals, it promptly causes death by asphyxia.[1] It is strongly antiseptic and antizymotic. It coagulates albumen and myosin (BERENS). It prevents the lactic, not the alcoholic, fermentation (DONATH). It is not found in the urine after administration.

c.—Soluble in water, sparingly when cold, freely when hot. Soluble in all proportions in alcohol, ether, and carbon disulphide, and soluble in chloroform, benzene, amyl alcohol, carbon disulphide, and in fixed and volatile oils. *The salts* of quinoline are soluble in water. *The tartrate*, $(C_7H_9N)_3(C_4H_6O_6)_4$ (FRIESE, BERNTHSEN, 1881), is soluble in 80 parts of water at 16° C.; in 150 parts of 90% alcohol at 16° C.; in 350 parts of ether. It melts at about 125° C.

The hydrochloride, $C_9H_7N.HCl$ (OECHSNER, 1883), is soluble in water, alcohol, chloroform, ether, and benzene, in the last two solvents sparingly in the cold. Melts at 94° C., and volatilizes.

d.—Quinoline is indicated by its odor, obtained from its salts on addition of a fixed alkali. Alkali hydrates precipitate it, in solutions not dilute; the precipitate being soluble in excess of ammonia, and easily taken into solution by ether, chloroform, and other solvents of the base. Solutions of quinoline salts are precipitated by **the general reagents for alkaloids.** According to Donath, the limits of precipitation, in certain favorable proportions of reagents, were as follows: For iodine in iodide of potassium, 1 to 25000 parts; phosphomolybdate, 1 to 25000 parts; mercuric chloride, 1 to 5000 parts; potassium mercuric iodide, 1 to 3500 parts. The precipitate with phosphomolybdate, yellow-white, dissolves colorless in ammonia; with mercuric chloride, white. The precipitate by potassium mercuric iodide,

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[1] BERENS, 1885: *Ther. Gazette*, 9, 433.

on adding hydrochloric acid, crystallizes in amber-colored needles. No color is caused by sulphuric or nitric acid (Donath). By long heating with excess of sulphuric acid quinoline sulphonic acid is formed.

Tests for impurities.—In artificial quinoline by Skraup's process, nitrobenzene has been found as an impurity (C. Ekin, 1882). The salts should be completely soluble in water, the free base in water with sufficient acid. There should be no bitter taste (impurity from cinchonine). Alkali hydrates should not cause a colored precipitate. Cinchonine-quinoline, as prepared for use, and unless repeatedly distilled and recrystallized, contains lepidine (Hoogewerff and v. D); and therefore when treated with amyl iodide, and then with caustic alkali, gives a blue color, formation of a cyanine (Williams), $C_9H_7NC_5H_{11}.C_{10}H_9NC_5H_{11}I$.—Aqueous solution of pure quinoline salt [not alkaline] does not sensibly change the color of permanganate solution in the first eight or ten minutes (Hager).

Kairines.—Methyl or ethyl substitutions in oxy-quinoline-tetrahydride, $C_9H_{10}(OH)N$. The methyl compound is $C_9H_9(CH_3)(OH)N=C_{10}H_{13}NO$; the ethyl compound, $C_9H_9(C_2H_5)(OH)N=C_{11}H_{15}NO$. The name kairine is used for the hydrochloride. *Oxyhydro-methylquinoline* is termed Kairine M, and *oxyhydro-ethylquinoline* Kairine E or *Kairoline.* Derivatives of quinoline (E. Fischer, 1883) of medicinal interest. The free bases are not stable in the air.

a, *c.*—*The methyl base* crystallizes in rhombic forms; is sparingly soluble in water, soluble in alcohol, ether, and benzene, and acts as a strong base in forming salts. It boils at 114° C. *The hydrochloride*, $C_{10}H_{13}NO.HCl+H_2O$, forms lustrous, monoclinic crystals, generally found in a slightly colored crystalline powder, easily soluble in water. At 110° C. it loses its water of crystallization and turns violet. *The sulphate*, $(C_{10}H_{13}NO)_2H_2SO_4$, forms lustrous prisms.

The ethyl base crystallizes in scales or plates, melting at 76° C., slightly soluble in water, freely soluble in alcohol, ether, and benzene; hardly soluble in petroleum benzin. *The hydrochloride*, $C_{11}H_{15}NO.HCl$, forms white prisms, generally appearing in grayish-yellow crystalline powder, freely soluble in water, sparingly soluble in hydrochloric acid.

b.—The kairines have a bitter and saline, disagreeable *taste* and a penetrating *odor*. Ordinary doses are one-half to one gram

(7½ to 15 grains), and doses of 25 to 50 grains cause disturbance.[1] It is in part excreted unchanged in the urine (Mering, 1884). The ethyl compound differs from the methyl compound only in a somewhat longer duration of effect (Filehne).

d.—Kairines are indicated by the penetrating, characteristic odor of the free base, obtained in full from the salts on adding a fixed alkali, and by the bitter taste. In aqueous or alcoholic solution, treated with **oxidizing agents,** as dichromate and an acid, they give rosaniline colors, violet-blue to violet-red, in some reactions greenish tints being obtained. **Ferric chloride** gives a brown color in solutions, with gradual precipitation. Sodium **nitrite** in sulphuric acid solution gives orange to red colors. **Potassium ferrocyanide** gives an abundant precipitate; **phosphotungstic acid** a pale yellow precipitate. When the base is liberated, as in alkaline solutions, the kairines rapidly oxidize in the air, with deposition of brown, humus-like bodies.

Thalline. $C_{10}H_{13}NO$. Tetrahydroparaquinanisoil.—A derivative of paraquinanisoil.[2] One of the methyl kairines, isomeric with "kairine M."

Thalline appears in pale yellow crystals, melting at about 42° C., boiling at 282° C. without decomposition. Its salts are given in doses of 0.25 to 0.75 gram. It is sparingly soluble in cold, more freely in hot water, and soluble in alcohol, ether, and petroleum ether. It makes stable salts; but in all forms it is easy to suffer change, and the light affects it injuriously. The sulphate and tartrate are obtained in nearly white crystals or crystalline powder, melting at 100° C., with browning. The sulphate is freely soluble in water, nearly insoluble in ether, but is somewhat soluble in chloroform. Oxidizing agents produce an intense green color with thalline, hence its name. Ferric chloride is a favorable oxidizing agent for the purpose, giving a deep emerald-green color, not changed by acidulation with sulphuric acid, but changed by reducing agents.—In physiological effect thalline resembles the kairines.[3]

Antipyrine. $C_{11}H_{12}N_2O$.—A proposed commercial name for Dimethyl-oxy-quinizine, $C_9H_6(N.CH_3)(CH_3)(O)N$, the hypothetical base quinizine having the general formula $C_9H_9(NH)N$

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[1] On use of kairine as an antipyretic, Filehne, 1882–1883. American uses summarized in *Ther Gazette*, **9**, 122 (Feb., 1885).

[2] Vulpius, 1883: *Archiv d. Phar.*, [3], **22**, 840; *Jour. Chem. Soc.*, 1885, Abs., 398, 1022.

[3] Beyer, 1886: *Am. Jour. Phar.*, **58**, 196. Jaksch, 1884.

(L. Knorr, 1884[1]). Of interest for medicinal uses as an antipyretic.

a.—Antipyrine crystallizes in needles, melting at 113° C. In commerce it appears as a white, crystalline powder, sometimes slightly colored.

b.—Of a very mild bitter taste, not disagreeable, and a barely perceptible odor. Dose, 1 to 2 grams (15 to 30 grains).[2] Double that of quinine (Butler, 1885). 40 to 50 grains have caused serious effects. It appears in the urine in about two hours after its administration, and can be detected by applying the ferric chloride test to the entire urine (Caruso, 1885).

c.—Dimethyloxyquinizine is very freely soluble in water, alcohol, or chloroform; in about 50 parts of ether. The aqueous solution is neutral to test-papers. Antipyrine is a base of some strength, uniting with acids to form salts, from which it is set free by the alkali hydrates.

d.—**Ferric chloride** solution gives a decided red coloration, intense in solutions of 1 to 1000 parts; the color being changed to yellow by strong acidulation with sulphuric acid.[3] **Nitrous acid**, as obtained by adding a little potassium nitrite and acidulating with dilute sulphuric acid, gives a bluish-green color in dilute, a green crystalline precipitate in concentrated, solutions—characteristic of all the quinizines (Knorr). Two drops of fuming nitric acid, added to 2 c.c. of a 1 per cent. solution of antipyrine, cause a green color, and, after heating to boiling, another drop of the reagent gives a red color (Germ. Ph. Commission). **Tannic acid** gives a white precipitate in a 1 per cent. solution.

Tests for impurities—The solution in two parts of water should be neutral, and colorless or faintly yellowish, free from sharp taste, and not changed by solution of hydrosulphuric acid (Germ. Ph. Commission).

CINCHONICINE.—See Cinchona Alkaloids, pp. 91, 94.

CINCHONIDINE.—See Cinchona Alkaloids, pp. 157–161.

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[1] The quinizines are derived from quinoline by the introduction of (NH), with additional 2H, into the quinoline molecule. The (NH) is attached to the N in the ring, this N being united to carbon by only two bonds, instead of three as in quinoline. Knorr: *Ber. deut. chem. Ges.*, 17, 546, 2032; *Jour. Chem. Soc.*, 1884, Abs., 302, 1153, 1377; *Am. Druggist*, 13, 239, 193, 228 (1884).

[2] Respecting physiological and therapeutic effects, *Ther. Gazette*, 1885, 9, 344, 176, 517. Also Filehne, 1885: *Zeitsch. Klin. Med.*, 7; *Am. Druggist*, 13, 193.

[3] Pharmacopœia Commission of Germ. Apoth. Association.

CINCHONINE.—See Cinchona Alkaloids, pp. 161–165.

CINCHOTANNIN.—See Tannins.

CINCHOTINE.—See p. 93.

CINNAMIC ACID.—See p. 69.

COCA ALKALOIDS.—*Alkaloids of Erythroxylon Coca leaf.*

Cocaine, $C_{17}H_{21}NO_4$. The crystallizable natural alkaloid of fresh coca.

Ecgonine, $C_9H_{15}NO_3$, crystallizable. A product of cocaine by saponification, and liable, also, to be present in the leaf.

Benzoyl-Ecgonine, $C_{16}H_{19}NO_4$, crystallizable. A by-product of manufacture of cocaine from coca. (Present in the leaf?)

Anhydride of ecgonine, $C_9H_{13}NO_2$, crystallizable. Producible from ecgonine by moderately strong sulphuric acid with heat.

Hygrine, a liquid volatile alkaloid (Lossen, 1865) little known, reported to form crystallizable salts. The existence of this alkaloid is not established.

Amorphous alkaloids of coca. ("Cocainoidine, Cocaicine".) Said to be obtained in preparation of cocaine. Probably present in the leaf in some conditions of this article. Not studied.

Chemical constitution.—Cocaine, as an easily saponifiable body, prone to split, by hydration, into ecgonine, benzoic acid, and methyl alcohol, clearly has the immediate structure of methyl-benzoyl ecgonine: $C_9H_{13}(CH_3)(C_7H_5O)NO_3=C_{17}H_{21}NO_4$. The saponification of cocaine is accomplished by an acid which takes ecgonine into combination, or by an alkali which takes both benzoic acid and ecgonine into union, or even, it is probable, by digestion with water, whereby benzoyl and methyl slowly become hydroxides. But whenever the necessary conditions are fulfilled with any saponifying agent, the change is shown by the equation:

$$C_9H_{13}(CH_3)(C_7H_5O)NO_3+2H_2O$$
$$=C_9H_{15}NO_3+C_7H_5O.OH+CH_3.OH.$$

Ecgonine, by loss of CO_2, gives the constituents of a tropine. This change, effected by distilling the barium compound of ecgonine, shows a not distant chemical relationship between cocaine and the atropine group of alkaloids. And, like atropine, cocaine in decompositions is liable to form quite simple pyridine compounds, showing a direct relation to the pyridine series.

The saponifications of certain other well-known alkaloids, by digestion with alkali, or with acid, or with water, as stated in each instance, may be compared by the following equations. When the change is effected by acids the produced alkaloid is left in a salt; but when by an alkali, the produced acid is left in a salt. Ecgonine unites both with acid and with alkali.

$C_{17}H_{23}NO_3$ (atropine) $+ H_2O = C_8H_{15}NO$ (tropine) $+ C_9H_{10}O_3$ (tropic acid).

$C_{33}H_{43}NO_{12}$ (aconitine) $+ H_2O = C_{26}H_{39}NO_{11}$ (aconine) $+ C_7H_6O_2$ (benzoic acid).

$C_{17}H_{21}NO_4$ (cocaine) $+ 2H_2O = C_9H_{15}NO_3$ (ecgonine) $+ C_7H_6O_2 + CH_4O$ (meth. alc.)

$C_{22}H_{23}NO_7$ (narcotine) $+ H_2O = C_{12}H_{15}NO_3$ (hydrocotarnine) $+ C_{10}H_{10}O_5$ (meconine).

$C_{32}H_{49}NO_9$ (cevadine) $+ H_2O = C_{27}H_{43}NO_8$ (cevin) $+ C_5H_8O_2$ (methylcrotonic acid).

$C_{37}H_{53}NO_{11}$ (veratrine) $+ H_2O = C_{28}H_{45}NO_8$ (verin) $+ C_9H_{10}O_4$ (veratric acid).

$C_{17}H_{19}NO_3$ (piperine) $+ H_2O = C_5H_{11}N$ (piperidine) $+ C_{12}H_{10}O_4$ (piperic acid).

Except narcotine (and possibly piperine) the saponifiable alkaloids here given are the representative medicinal constituents of the plants wherein they are found: cevadine being the most active constituent of veratrum veride, as veratrine is of cevadilla. The acids formed in the saponifications are aromatic compounds easily reduced to benzoic acid, with the exception of methylcrotonic acid.

Yield of alkaloids from coca leaf.—By the process given following, Dr. Squibb obtains from well preserved lots of the dried leaves, shipped in bales, from 0.5 to 0.8 per cent. of alkaloid. Dr. Lyons obtained from the dried leaves, shipped in bales, 0.65 to 0.75, and even 0.80, per cent. of alkaloid. The alkaloidal product of these assays consists, when good leaves are taken, in the greater part of crystallizable alkaloid, though in some part of amorphous coca alkaloids. The crystallizable alkaloid is probably nearly all cocaine; at least both ecgonine and benzoyl-ecgonine must be pretty surely left behind in each method of assay, by the free solubility in water and the very slight solubility in ether of both of these alkaloids.

It is noteworthy that all the coca alkaloids, natural or produced, so far as reported, are readily soluble in water as free alkaloids, save only cocaine itself. Also that ecgonine and benzoyl-ecgonine are nearly insoluble in ether, which dissolves cocaine abundantly. *The solubilities* are further shown here:

	THE FREE ALKALOID.		THE HYDROCHLORIDE.	
	Water.	Ether.	Water.	Ether.
Crystallizable:				
Cocaine	Very slight.	Soluble.	Soluble.	Insoluble.
Ecgonine	Soluble.	Near insol.	Soluble.	
Benzoyl-ecgonine	Soluble.	Near insol.	Soluble.	
Amorphous:				
"Amorph. alkaloids."	Not freely.	Soluble.	Soluble.	Insoluble.
Hygrine	Soluble.	Soluble.	Soluble.	

AMORPHOUS COCAINE. Cocainoidine. Cocaicine.—The qualitative reactions and properties of the amorphous alkaloid obtained with cocaine in its preparation are designated by A. B. LYONS[1] as follows: The compounds are very difficult to crystallize. The precipitate produced in the hydrochlorate by alkalies did not crystallize at all (*compare below under Cocaine, d*), neither that by picric acid. In very dilute solutions (1 to 5000) gold chloride produced after some time minute prismatic crystals, wholly unlike in general appearance the fern-like forms from the crystallizable salt. Platinum chloride produced a few rosette-like aggregations.—On evaporation the amorphous alkaloid (probably not free from non-alkaloidal matter) invariably turned dark, and if the salt was evaporated quite to dryness it was found to be imperfectly soluble in water.

ECGONINE. $C_9H_{15}NO_3=185$ (LOSSEN, 1865). Crystallizes with $1H_2O$.—A pyridine derivative nearly related to the tropines. The alkaloidal body obtained by saponification of Cocaine. It crystallizes from absolute alcohol in monoclinic prisms. Melts at 198° C., with browning, and decomposes at higher temperatures. Has a slight bitter-sweet taste. It is freely soluble in water, soluble in alcohol, sparingly soluble in absolute alcohol, and insoluble in ether. In reaction it is neutral. It forms slightly crystallizable salts with hydrochloric and other acids,

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[1] 1885: *Am. Jour. Phar.*, 57, 475.

gummy compounds with alkalies, and a crystallizable salt with barium. The hydrochloride of ecgonine appears in a yellowish, crystalline mass, freely soluble in water and (Calmels and Gossin) in alcohol. Slightly soluble in alcohol (Lossen). Ecgonine platinochloride, $(C_9H_{15}NO_3.HCl)_2PtCl_4$, is soluble in water; less soluble in alcohol. The aurochloride is soluble in water and in alcohol. Barium salt of ecgonine (Calmels and Gossin, 1885) forms slender, prismatic crystals, freely soluble in water and in alcohol, slightly soluble in ether.—When the barium salt of ecgonine, as obtained, with barium benzoate, by saponifying cocaine with baryta, is distilled, an isotropine $(C_8H_{15}NO)$ is obtained (Calmels and G.) It will be observed that ecgonine, by loss of CO_2, presents the elements of a tropine.

Benzoyl-Ecgonine. $C_{16}H_{19}NO_4 = 289$. Crystallizes with $4H_2O$. Union of ecgonine with benzoic acid, the elements of H_2O being eliminated: $C_9H_{14}NO_3.C_7H_5O$. (W. Merck, 1885.[1] Z. H. Skraup, 1885.[2])—Found as a by-product of cocaine manufacture from coca leaves. Crystallizes in transparent flat prisms. When quickly heated melts [hydrated?] at 90° to 92° C., solidifies again and then melts [anhydrous?] at about 192° C. (Skraup). Melts, with browning, at 188.5° to 189° C. (Merck). Soluble freely in water, sparingly in alcohol, nearly insoluble in ether. It forms salts: the sulphate and acetate crystallize in prisms. The aurochloride, $C_{16}H_{19}NO_4.HCl.AuCl_3$, forms yellow scales, sparingly soluble in water, soluble in alcohol.—On heating benzoyl-ecgonine with methyl iodide and an equal volume of methyl alcohol, the synthesis of cocaine is obtained: $C_{16}H_{19}NO_4 + CH_3I = C_{17}H_{21}NO_4.HI$.

An anhydride of ecgonine. $C_9H_{13}NO_2$. (Calmels and Gossin, 1885.)—When ecgonine is heated with moderately strong sulphuric acid, an alkaloid is obtained which forms readily crystallizable salts both with acids and with alkalies, less soluble than corresponding ecgonine salts—the barium salt having the composition $BaO.(C_9H_{13}NO_2)_2$, and its hydrochloride forming stellate groups of prismatic needles. The platinochloride forms feathery groups of crystals, very soluble in water and in alcohol.

Hygrine. A volatile alkaloid found with cocaine in coca leaves (Lossen, 1865[3]). A thick, oily liquid of a pale yellowish

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[1] *Ber. d. chem. Ges.*, **18**, 1594; *Jour. Chem. Soc.*, Abs., 997.

[2] *Monatsch. Chem.*, 6, 556; *Jour. Chem. Soc.*, Abs., 1249. Also see Paul, 1885: *Phar. Jour. Trans.*, [3], **16**, 325.

[3] Wöhler and Lossen: *Ann. Chem. Phar.*, **121**, 374; **133**, 352. Lossen: "Dissertation."

color. Distils slowly with water; distils alone between 140° C. and 230° C. It has an odor resembling trimethylamine, and a burning taste. Had no poisonous effect on rabbits. It is soluble in water (not in all proportions); freely soluble in alcohol and in ether. It unites with acids, forming salts. The hydrochloride forms deliquescent crystals. It is precipitated by iodine in potassium iodide solution, mercuric chloride, silver nitrate, and stannous chloride.

COCAINE. $C_{17}H_{21}NO_4=303$ (Lossen, 1865). Chief alkaloid of the Erythroxylon coca leaf (Niemann, 1860).—For the *yield* from the leaf, and for *chemical constitution and relations* of the alkaloid, see above under Coca Alkaloids.

Cocaine is *identified* by its effect on the tongue or eye (*b*), and the agreement of its precipitations (*d*). It is distinguished from ecgonine or benzoyl-ecgonine by solubilities of the free alkaloid in water and in ether (*g*). Its *separations* are effected by use of ether, etc., and *from coca leaf* by several assay methods (*e*). *Estimation*, gravimetrically or volumetrically (*f*); also by obtaining limits of precipitations (*d*). Tests for *impurities* (*g*).

a.—Cocaine crystallizes in monoclinic prisms, obtained from concentrated alcoholic solution. It appears either in colorless, distinct crystals or in a white, crystalline or granular powder. The alkaloid imperfectly purified from the leaf, or that from injured leaves, is more or less dark colored, and contains amorphous coca alkaloid, partly liquid. Cocaine, free alkaloid, is often presented as an amorphous powder, cohering like magnesia (Squibb), and not quite white.—*The salts* are more crystallizable than the free alkaloid. The hydrochloride crystallizes with a general appearance like that of the free alkaloid; from concentrated alcoholic solution in short, rough prisms, among which rhombic plates may be found under the microscope; from dilute alcoholic solution long, brittle needles are obtainable; from aqueous solution, silky-lustrous needles. The hydrobromide crystallizes in colorless, radiating needles.—*The hydrochloride* is the chief form of the alkaloid in general use. It is furnished in different styles, including hydrated crystals of good size, minute anhydrous crystals, granules of obscurely crystalline powder, and amorphous powder.

Cocaine melts at 98° C. (Lossen). More strongly heated it vaporizes with decomposition of the greater portion. The hydrochloride parts with its water of crystallization (2 *aq.*) at or below 100° C.

b.—Cocaine has a bitter taste, and is without odor. Its decomposition products in mouldy coca leaves are said sometimes to present a tobacco-like odor.—Cocaine is distinguished by an intense local anæsthetic and blanching effect upon the mucous membrane, giving on the tongue a characteristic insensibility, a sudden cessation of feeling, lasting but a few minutes (Niemann, 1860). One drop of a four per cent. solution (about 0.04 grain) suffices to blanch the conjunctiva of the eye;[1] and by the same application to the tongue (previously rinsed clean) first the slight bitterness and then a decided numbness are perceived. These effects are evanescent, unless the application be repeated. The anæsthesia of an eye, for surgical operations, can be accomplished by the application of "5 drops of a 4 per cent. solution in two installations ten minutes apart" (E. R. Squibb, 1885).—Dilatation of the pupil of the eye is a general effect of cocaine, either applied to the eye or administered to the system. This effect is said not to be invariable; certainly the midriasis from cocaine is very far from reaching the intensity obtained by the atropine group of alkaloids. Nikolsky obtained with warm-blooded animals a constant widening of the pupil when under the action of cocaine. Dilatation was also observed with frogs.

The fatal dose of cocaine was found for dogs, by Danini (1873), 0.15 to 0.30 gram ($2\frac{1}{3}$ to $4\frac{2}{3}$ grains). In rabbits the hypodermic administration of 0.1 gram ($1\frac{1}{2}$ grain) per kilogram of body-weight caused death in a few hours, sometimes in a few minutes (v. Anrep, 1880). The hypodermic introduction of about $\frac{1}{20}$ grain caused dangerous symptoms in a girl of 12 years (*Ther. Gazette*, Feb., 1886, p. 88).

c.—Cocaine is very slightly soluble in water, soluble in alcohol, ether, chloroform, benzene, petroleum benzin, disulphide of carbon, and in fixed and volatile oils.—*The salts* of cocaine are soluble in water and in alcohol. *The hydrochloride* dissolves in less than its own weight of water; is freely soluble in alcohol, less readily in absolute alcohol and in chloroform, and is practically insoluble in ether, in petroleum benzin, and in fixed and volatile oils.—Cocaine solutions have a strongly alkaline reaction with litmus (not affecting phenol-phthalein), and form definite salts. The hydrochloride and hydrobromide are neutral in reaction. *Hydrochloride* crystals are permanent in the air; obtained

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[1] This specific use of cocaine was first announced by Dr. Carl Koller, of Vienna, at Heidelberg, in September, 1884 (*London Lancet*, 1884, p. 990). (v. Anrep, 1880; Schroff, 1862.) The extensive use of cocaine as a local anæsthetic rapidly followed the announcement of Dr. Koller.

in presence of water they have two molecules (9.6 per cent.) of water of crystallization, but anhydrous crystals can be obtained from alcohol. *Hydrobromide* crystals also contain two molecules (8.57 per cent.) of water of crystallization. Cocaine *citrate* is hygroscopic and does not easily crystallize. The *oleate* of cocaine readily crystallizes, and dissolves in oleic acid or in oils (LYONS). Aqueous solutions of cocaine salts after a few days suffer decomposition of the alkaloid, with vegetable cell growths, unless preserved by an antiseptic (SQUIBB, 1885). Neutral solution of the hydrochloride in freshly prepared distilled water, when secluded from the air in glass-stoppered bottles, keeps unchanged several months (POLENSKI, 1885).

d.—The local physiological test upon the tongue, and then upon the eye, for the (evanescent) effects above detailed, may be resorted to for identification. If the material tested be known only as alkaloidal matter, safety requires that the substance should be obtained in neutral solution of definite strength, the preliminary trials being made with such attenuations as would be harmless in case of the presence of aconitine or atropine, or other agent of most intense action. In the experiments of DR. SQUIBB (1887) a distinct impression, just short of numbness, was obtained by three out of four persons by holding one minute in the mouth $\frac{1}{100}$ grain (0.00063 gram) of cocaine in solution in one minim of water, the mouth having been previously rinsed. When the solution of alkaloid was dried on filter-paper, the limit of recognition was found to lie at $\frac{1}{4000}$ of a grain of the alkaloid, held in the mouth one minute (*Ephemeris*, 3, 918).

Mayer's solution gives a precipitate with cocaine hydrochloride. According to LYONS (1885)[1] the precipitate is visibly produced in one drop of a solution of the salt in 12500 parts of water. Precipitates in very dilute solutions are formed by **iodine** in potassium iodide solution, by **phosphomolybdate,** and by **tannin.** **Mercuric chloride** causes a precipitate in quite concentrated solutions, with a resulting red color like that of atropine (FLÜCKIGER, 1886). **Caustic alkalies,** including ammonia, added to moderately dilute solutions, cause a precipitation of the free alkaloid. The precipitate has a crystalline structure, either from the first or after standing a short time. Excess of ammonia does not dissolve the precipitate, but any considerable excess of fixed alkali will soon bring about saponification of the alkaloid, with partial solution. The **alkali carbonates** and bi-

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[1] *Am. Jour. Phar.*, 57, 473.

carbonates cause precipitation.—**Platinum chloride** and **Gold chloride** produce crystalline precipitates, the former reaction requiring moderate concentration.

Cocaine has a good degree of reducing power. **Ferricyanide paper,** prepared by wetting blotting-paper with a drop or two of a fresh mixture of equal volumes of potassium ferricyanide and ferric chloride solutions, on adding a drop or two of the alkaloid solution and shading from the light, gives reduction to the blue in the following ratio (CURTMAN, 1885[1]): With morphine in $\frac{1}{2}$ minute; cocaine, $1\frac{1}{2}$ minute; brucine, 6 m.; quinine, 7 m.; cinchonine, 10 m.; strychnine, veratrine, each 15 minutes. **Permanganate of potassium** is but slightly reduced at once, fully on standing or on boiling, and in concentrated cocaine solutions decinormal solution of permanganate produces a crystalline precipitate of cocaine permanganate, appearing under the microscope when fresh in beautiful violet-red crystals, rhombic nearly rectangular plates, frequently grouped in rosettes. (F. GIESEL, 1886; A. B. LYONS, 1886). A brown residue of manganic hydrate is soon formed (see *g*).

Saponification of cocaine was accomplished by LOSSEN (1865) with **hydrochloric acid** in hot digestion (100° C.), best in sealed tubes, continuing the digestion as long as the precipitation of benzoic acid is seen to increase. MACLAGEN (1885[2]) caused a saponification with **alcoholic potash,** or the cocaine "was dissolved in alcohol and strong solution of soda or potassa added," when "the odor of benzoic acid is quickly perceptible," soon disappearing. After a short time, if a little water be added, the alcohol driven off by a gentle heat, and the liquid acidulated, a precipitate of benzoic acid is obtained. Ammonia appeared to effect no saponification. CALMELS and GOSSIN (1885) effected the saponification by barium hydrate, in sealed tubes, at 120° C. The products are ECGONINE, Benzoic Acid, and Methyl Alcohol: $C_{17}H_{21}NO_4+2H_2O=C_9H_{15}NO_3+C_7H_6O_2+CH_4O$. By boiling in water, especially by long hot digestion, cocaine suffers saponification, and its solutions redden litmus (PAUL, 1886; FLÜCKIGER, 1886).

e.—Separations.—Cocaine is removed from aqueous solutions of its salts by adding ammonia to liberate the alkaloid, avoiding an excess, and shaking out with ether, chloroform, benzene, or petroleum benzin. From ethereal solutions the alkaloid is taken up by slightly acidulated water, upon agitation.

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[1] *Phar. Rundschau,* **3**, 252.

[2] *The American Druggist,* **14**, 23 (Feb., 1885).

From the coca leaves, the following process is used by LYONS:[1] Take 10 grams of No. 30 powdered coca leaves, or so much of this powder as will represent 10 grams of a sample of leaves carefully selected from toward the centre of the package. Place in a bottle of capacity of about 120 c.c., add 100 c.c. of a mixture of 95 volumes stronger ether and 5 volumes of a spirit of ammonia made by mixing 1 volume ammonia-water of sp. gr 0.9094 with 19 volumes absolute alcohol, stopper securely, and agitate well at intervals of half an hour for a day. Allow as nearly as possible 24 hours for the maceration: a perceptible loss of the alkaloid, doubtless due to the free alkali, results from macerating over 48 hours. Take out quickly 50 c.c. of the clear ethereal liquid into a separator. If there are floating particles, filter through a small filter, and wash with least sufficient quantity of ether. Add in the separator 5 c.c. of acidulous water containing $\frac{1}{60}$ by volume of sulphuric acid. Agitate well, allow the acid liquid to separate, draw the aqueous layer off into a bottle of the capacity of 30 c.c.; add again in the separator $2\frac{1}{2}$ c.c. of water slightly acidulated with sulphuric acid, shake out, leave to separate, and draw off; and repeat this washing once or twice more, receiving all the aqueous portions together. To the whole aqueous liquid, in the bottle, add 10 c.c. of ether, agitate, leave at rest, pour off the ethereal wash-liquid, add in the bottle 10 c.c. of fresh ether, then gradually add a slight excess of dry carbonate of sodium, with care to avoid loss by effervescence, cork securely, agitate well but not so violently as to cause emulsification, set at rest, and with a rubber-bulb pipette draw off the clear ethereal layer into a small tared beaker, to be now set in a warm place (about 45° C., 113° F.) While the ether is evaporating wash with a second and third portion of ether, and wash with ether until a drop of the aqueous fluid, acidulated, and treated with a minute drop of Mayer's solution, gives not more than a slight milkiness. The residue left by evaporation of the ether is inspected, and dried at 100° C. to a constant weight. The alkaloid obtained represents 5 grams of coca leaves. The percentage is obtained by dividing the milligrams of weight by 50.

The assay of coca leaves is conducted by Dr. E. R. SQUIBB[2] as follows: Of the coarsely powdered leaves 100 grams are moistened with 100 c.c. of water containing 5% of sulphuric acid, and packed moderately close in a cylindrical percolator. Using the same acid solvent, 500 c.c. of percolate are obtained, better by the help of a pump. The percolate is well mixed in a large

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[1] 1885: *Chicago Pharmacist*, Sept.

[2] *Ephemeris*, 3, 912 (Jan., 1887).

beaker with 50 c.c. of kerosene, when enough well-crystallized carbonate of sodium to saturate 500 c.c. of acid-water is gradually added, the requisite quantity having been previously determined by a trial upon 100 c.c. of the acidulated water.[1] During four or five hours of digestion the mixture is repeatedly stirred. The kerosene is drawn off by a separator or a small siphon. The extraction is continued with two additional portions each of 25 c.c. of kerosene. If a layer of emulsion appears it is drawn off separately, and stirred with asbestos, or sand, or dry filter-paper pulp, and the separated kerosene added to the larger portion. If the mixture have been shaken instead of stirred, the most of the kerosene will be found in emulsion.[2]

The kerosene solution of alkaloid (100 c.c.) is shaken vigorously, in a separator, with two portions of 10 c.c. of the acid-water, and one portion of 5 c.c. of the same. Now to the 25 c.c. of cocaine sulphate solution 10 c.c. of stronger ether are added, in a separator, and well shaken, then a moderate excess of sodium carbonate crystals is added. After the effervescence the mixture is shaken, the ether separated, and two more washings are made, each with 10 c.c. of the ether. The collected ether, perfectly free from aqueous solution, is evaporated in a weighed beaker of at least three times the capacity of the ether. The alkaloid will be in form of a light amber-colored varnish. As soon as the ether is wholly evaporated the beaker is cooled and weighed, and the tare subtracted. The highest yield obtained by Dr. Squibb has been 0.892%. On standing 24 to 48 hours the varnish-coat of alkaloid is converted into a white, crystalline crust, without change of weight.

TRUPHEME (1885) recommends an assay plan as follows: The coca leaves are exhausted with ether; after recovering the ether by distillation, the residual extract is treated with boiling water, mixed with magnesia, and dried. The dried mass is exhausted with amyl alcohol.

In all assay operations the continued action of hot acids, or hot fixed alkalies, or even of hot water, is to be avoided, as liable to cause saponification or other alterations.

f.—*Quantitative.*—Cocaine is estimated gravimetrically by

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[1] Excess of alkali is required, and sufficient excess is obtained by following the direction.

[2] Further assurance of the complete separation of the alkaloid is obtained by adding a little more sodium carbonate and shaking out with ether (25 c.c.), when the residue by evaporation of the ether may be tested on the tongue for cocaine.

drying at near 100° C., and weighing as anhydrous alkaloid (see *a*). Volumetrically, cocaine may be estimated with Mayer's solution, standardizing the reagent by a known solution of the alkaloid, and correcting the result by parallel titrations of the known solution and that under estimation, concentration being the same in each (p. 45).

g.—Tests for purity.—For the next revision of Ph Germ. the following requirements for cocaine hydrochloride are proposed:[1] A white, crystalline powder of faintly acid reaction, somewhat bitter taste, and causing a very characteristic insensibility of the tongue, intense but transient. . . . Concentrated sulphuric acid dissolves it with some foaming but without coloration, and no color is caused by solution in nitric or hydrochloric acid. The salt should dissolve in twice its weight of cold water; and when heated on platinum foil should leave no residue.—The Br. Ph. designates that the salt "dissolves without color in cold concentrated acids, but chars with *hot* sulphuric acid." Also, "the solution yields little or no cloudiness with chloride of barium or oxalate of ammonium." Some incidental impurities give yellow to red and rose-red colors with the cold sulphuric acid, which is said to be a severe but quite general test of purity.

Tests by solubilities (see table under Coca Alkaloids) of the free alkaloid. May be applied to cocaine salts by treating with dilute ammonia, avoiding much excess, draining, and washing with a very little water, when the precipitate may be dried at a gentle heat and used for the tests. The free cocaine should require not less than 1200 to 1800 times its weight of cold water to dissolve it (absence of any considerable proportions of ecgonine or benzoyl-ecgonine). Should also be completely soluble in ether. But for this test cocaine salts and any ammonium salt should be well removed.

According to the excellent investigation of DR. SQUIBB (1887, *Ephemeris*, 3, 906), the cocaine of commerce consists mainly of a larger portion of readily crystallizable salt with smaller varying proportions of difficultly crystallizable salt. The latter portion was found not to be inferior in physiological power. Further, *solubility in chloroform* was found a trusty indication of the proportion of the less crystallizable part, this requiring less chloroform to dissolve it. 0.4 gram of perfectly crystallizable hydrochloride takes 9 c.c. of chloroform of not less than 1.47 sp. gr. to dissolve it. The salt is precipitated from chloroformic solutions

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[1] The pharmacopœial commission of the Deutschen Apotheker-verein, 1885.

by adding ether.—The same investigator reports the "permanganate test of Giesel to be hypercritical and often fallacious."

CODAMINE.—See Opium Alkaloids.

CODEINE.—See Opium Alkaloids.

COLORING MATERIALS.—The scope of this work does not permit giving the descriptive chemistry[1] of the dye-stuffs and pigments in use at present. Several *systematic methods of analysis* of coloring matters, recently contributed by color chemists, are presented in the following pages. To these schemes for qualitative analysis some notes of description or of definition of color compounds are added, and references to convenient sources of descriptive literature are given. A list of published schemes of analysis of coloring matters is here offered, with the assurance that it is by no means a complete bibliography of methods of qualitative work upon colors.

The Chemical Determination of Commercial Coloring Materials. By treatment of the dye-stuffs alone, or of tissues colored by them.

For Blue coloring matters: vegetable blues, coal-tar blues, and prussian blue.—W. Stein, 1869: *Polyt. Centralbl.*, p. 1023; *Zeitsch. anal. Chem.*, 9, 128.

For Red coloring materials, mainly those of vegetable origin.—W. Stein, 1870. Given on pages 188 to 192 of this work, with addition of notes and references. A ready method.

For Violet colors, both those of vegetable origin and coal-tar derivatives.—W. Stein, 1870: *Polyt. Centralbl.*, p. 1504; *Zeitsch. anal. Chem.*, 10, 375.

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[1] The following references may be of some service to those in search of literature upon the descriptive chemistry of color substances:

Post's "Chemisch-Technische Analyse," Braunschweig, 1882. Pages 963 to 997: "Farbstoffe und zugehörige Industrieen." Natural organic colors: artificial colors, both mineral and organic.

Böckmann's "Chemisch-Technische Untersuchungs-Methoden," Berlin, 1884. Pages 245 to 336: "Theerfarben," von Dr. R. Nietzki. Pages 337 to 343: "Ultramarin," von Dr. E. Büchner.

Hager's "Pharm. Praxis," Ergänzungsband, 1883. Pages 951 to 987: "Pigmenta."

Slater's "Colors and Dye-Wares," London, 1879, pp. 217. Serviceable only for commercial definitions.

Crookes, 1882: "Dyeing and Tissue Printing," London.

"Bleaching, Dyeing, and Calico Printing." Published by J. and A. Churchill, London, 1883. With an account of Dye-Wares.

Koster, 1882: "The Hygiene of Coal-Tar Colors," Heidelberg. A full review in *Chem. News*, 48, 20.

Witz, Relation of Colors to Cellulose, 1884: *Ding. pol. Jour.*, 250, 271; *Jour. Soc. Chem. Ind.*, 3, 206.

For Greens and Yellows, from vegetable sources and from coal-tar.—W. Stein, 1870: *Polyt. Centralbl.*, p. 1055; *Zeitsch. anal. Chem.*, 10, 115.

For all the Colors, mainly those of coal-tar production.—Otto N. Witt, 1886. In the next following pages, with addition of brief definitions of commercial names. A quite elaborate scheme, presented by a chemist well known for important contributions on the chemistry of coal-tar dyes.

For Colors in general, mostly of vegetable origin.—F. Fol, 1874. Given in the following pages.

For the Coal-Tar Colors, as fixed upon Silk, Wool, and Cotton.—N. Bibanow, 1875: *Monit. scientif.*, [3], 4, 509; *Zeitsch. anal. Chem.*, 14, 106.

For Coal-Tar Colors and Vegetable Colors, as fixed upon fabrics.—J. Joffre, 1882: *Monit. scientif.*, [3], 12, 959; *Zeitsch. anal. Chem.*, 22, 610; *Chem. News*, 46, 217 (in full); *Jour. Soc. Chem. Ind.*, 1, 447 (in full).

For Coal-Tar Dye-Stuffs.—Böckmann's "Chemisch-Technische Untersuchungs-Methoden," 1884, pp. 328–333.

For the Principal Colors, taken as free dye-stuffs or in solutions.—Dragendorff, in "Gerichtl. Chem. Organ. Gifte," 1872. Given in this work in pages following. Presents a method of *separation by the immiscible solvents.*

For Colors in General, fixed upon dyed and printed fabrics.—Crookes's "Dyeing and Tissue Printing," 1882, p. 399.

For Coal-Tar Colors.—J. Spiller, 1880: *Chem. News*, 42, 191.

Witt's Plan of Qualitative Analysis of Commercial Coloring Matters,[1] chiefly Coal-Tar Dyes.

A.—*Red Coloring Matters.*

I. The color is insoluble in cold, and with difficulty soluble in hot water, but it is easily dissolved by alcohol.

1. The alcoholic solution is salmon-colored, without fluorescence. The solution in strong sulphuric acid is reddish-violet.—*Naphthalene-Carmine* (Karmin-naphte)

2. The alcoholic solution is reddish blue, and shows an intense orange-red fluorescence. Examined with the spectroscope, it shows a wide absorption-band, which completely extinguishes the yellow and green portions of the spectrum.[2] The solution in sulphuric acid is greenish-gray. On diluting, the solution first turns red, and then a reddish-violet precipitate is formed.—*Magdala-Red* (*Naphthalene-Red.* Rosenaphthalene).

3. Insoluble in cold water, slightly soluble in hot. The behavior of the alcoholic solution is precisely similar to magdala-red, only the absorption-band is more to the right, so that a portion of the yellow remains visible. The solution in sulphuric acid is colorless; on diluting, each drop of water as it enters the liquid causes a deep red color. By the further addition of water the whole liquid is colored a deep magenta-red. This reaction is different from that of magdala-red.—*Quinoline-Red.*

4. The alcoholic solution fluoresces in a similar manner, but the fluorescence is greener. The solution in concentrated sulphuric acid is lemon-colored to orange, and shows no striking change of color on the addition of water.—

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[1] Otto N. Witt, 1886: *The Analyst*, 11, 111 (translated by J. T. Leon). Not including anthracene products.

[2] A good pocket spectroscope, which, with ordinary adjustment, will show Fraunhofer's lines, is sufficient for the examinations in this scheme.

Eosins (*tetrabromfluoresceins*, $C_{20}H_8Br_4O_5$), soluble in alcohol (to be distinguished from each other by the difference in tint of dyed specimens).

5. The alcoholic solution is a dull bluish-red. The solution in strong sulphuric acid is green, on dilution becoming bluish-red.—*Rhodidine* (*Induline* of the naphthalene group).

II. The coloring matter is more or less soluble in cold water, easily soluble in boiling water.

a.—The solution is precipitated by soda.—Basal coloring matters.

1. The solution in water is bluish-red, changing on the addition of hydrochloric or sulphuric acid to a yellowish-brown. The red color is restored by the addition of sodium acetate. By boiling wool in a dilute ammoniacal solution which has only a slight red color, it is dyed a deep red. Zinc-dust permanently decolorizes the aqueous solution. The solid is either in the form of green crystals or has the appearance of a green metallic powder, which dissolves in sulphuric acid to a yellowish-brown solution.—*Magenta* (Fuchsin, *Rosaniline monacid salts*, p. 191).

2. The solution is bluish-red. Ammonia gives an orange-colored, flocculent precipitate, which dissolves in ether to a red solution with a red fluorescence. The solution in sulphuric acid is green; on diluting with water the color changes to blue or violet, and finally to red.—*Toluylene-Red* ($C_{15}H_{16}N_4$) (known in commerce as *neutral red*, generally very impure, and therefore not giving pure colors in the above reactions).

b.—The solution is not precipitated by soda. *Acid coloring matters, or basal colors of the Saffranin class of compounds* (*type* $C_{18}H_{14}N_4$).

1. On the addition of soda to the aqueous solution a change of color takes place, the solution becoming colored an intense blue. The solution in sulphuric acid is a brownish-yellow, becoming somewhat redder on dilution.—*Gallein* (*Pyrogallol-phthalein*, $C_{20}H_{10}O_7$).

2. By the addition of alcohol to the aqueous solution a distinct yellowish fluorescence is produced. The addition of acid produces no precipitate. Zinc-dust decolors the solution, but on contact with air the original color is immediately restored. The solution in sulphuric acid is green, and, on diluting, first becomes blue and finally red.—*Saffranin* and *Saffranisol* (to be distinguished from each other by the difference in tint of dyed specimens).

3. The aqueous solution is a pure red and shows a greenish-yellow fluorescence, which becomes more distinct the more it is diluted. The addition of acid gives an orange-yellow precipitate, which is soluble in ether. The ethereal solution is a pure yellow, without fluorescence. The solution in sulphuric acid is yellow.—*Eosin* (tetrabromfluorescein).

4. The aqueous solution is more of a bluish-red and shows no fluorescence. Acids give a straw-colored precipitate, soluble in ether to a liquid of the same color. Concentrated sulphuric acid gives a golden-yellow solution. Zinc-dust decolors the ammoniacal solution. If the colorless solution be dropped on blotting-paper, it acquires an intense bluish-red color by contact with the air.—*Eosin-Scarlet*, bromo-nitro-fluorescein, $C_{20}H_8Br_2(NO_2)_2O_5$.

5. The solution is bluish-red, without fluorescence. Acids give an orange-yellow precipitate soluble in ether. Strong sulphuric acid gives an orange-yellow solution. Zinc-dust and ammonia decolor the solution, and the color is not restored by contact with air.—*Phloxin*. *Bengal-Red*. (Eosins, to be distin-

guished from each other by the difference in tint. Bengal-red bears more to the blue.)

6. The hot-concentrated aqueous solution solidifies, on cooling, to a jelly. The addition of acids causes a brown, flocculent precipitate. On warming with zinc-dust and ammonia the solution first becomes a bright yellow and then colorless. Concentrated sulphuric acid dissolves it to a grass-green solution. On dilution the liquid first acquires a bluish tint, and then a dirty brown precipitate comes down.—*Biebrich-Scarlet* (Double Scarlet. From amido-azobenzene sulphonic acids with naphthols).

7. Barium chloride gives in an aqueous solution a flocculent red precipitate, which, on boiling, suddenly becomes crystalline and acquires a deep violet-black color. The solution is indigo-blue, turning violet and red on the addition of water.—*Crocein-Scarlet, 3B* (*Ber. d. chem. Ges.*, 15, 1352).

8. The aqueous solution is colored a bright blue on the addition of a minute quantity of acid. Cotton-wool boiled in an aqueous solution, either with or without the addition of soap, is dyed a fast red. The solution in sulphuric acid is slate-colored, and this tint does not change on diluting.—*Congo-Red.*

9. The hot aqueous solution solidifies on cooling, when there appears a separation of shining, bronze-colored crystals. The solution in strong sulphuric acid is violet, and diluting it with water causes a brown precipitate.—*Xylidine-ponceau* (Xylidine-red, from alpha-naphthol-sulphonic acid, D. P. 26012). [Richter's Organic Chemistry, Philadelphia, 1886, p. 453.]

10. The concentrated aqueous solution, mixed with magnesium sulphate, deposits, on cooling, long, shining crystals of the magnesium salt. The solution in sulphuric acid is violet. Wool is dyed by it a brilliant scarlet.—*Crocein-Scarlet, 7B Extra* (formed by the action of diazo-naphthionic acid on crocein-beta-naphthol-sulphonic acid).

11. The aqueous solution gives, with chloride of calcium or barium, an amorphous, flocculent precipitate. The solution in concentrated sulphuric acid is rose-red or carmine, and on diluting it a brownish-red precipitate comes down.—Coloring matters from beta-naphthol-disulphonic acid, to be distinguished from each other by the difference in tint of dyed samples: *Ponceau R, 2R, 3R. Anisol-Red, coccin.* (*D. R P.* 3229). [Richter's Organic Chemistry, Smith's edition, p. 469.]

12. Wool is dyed magenta-red. Chloride of calcium gives, in an aqueous solution, a crystalline precipitate. The solution in concentrated sulphuric acid is bluish-violet, becoming red on diluting.—*Acid Azo-Rubin* (*D. R. P.* 26012).

13. The color of the solution is a deep brownish-red. Wool is dyed the same color. The solution in sulphuric acid is blue; the addition of water gives a yellowish-brown precipitate. The hot-concentrated aqueous solution gives, on the addition of a drop of saturated soda solution, a precipitate of the sodium salt in the form of brown, pearly plates.—*Roccellin* (*Echtroth*). [Post's "Chem. Tech. Anal.," p. 983.]

14. Chlorides of calcium and of barium give a flocculent, amorphous precipitate. The solution in concentrated sulphuric acid is of an indigo-blue. —*Bordeaux-Blue* (*D. R. P.* 3229). [Diazonaphthalin-beta-naphtholdisulphonate.]

15. The aqueous solution has a fine bluish-red color, which is completely removed by caustic soda, and is again restored by acetic acid.—*Acid Magenta* [sodium rosaniline sulphonate].

B.—*Yellow and Orange Coloring Matters.*

I. The coloring matter is insoluble in cold water, and either totally or very nearly insoluble in hot water. On the other hand, it is soluble in alcohol.

1. The solution is lemon-colored. The color is either unaltered or slightly deepened by the addition of acids or alkalies.—*Chinophtalon.* [Chimaphilin.]

2. The color of the solution is golden yellow. It is unaffected by acids. It is turned a deep brownish-red by alkalies and by boracic acid.—*Curcumin dye* (Turmeric).

3. The color of the solution is golden-yellow. The addition of hydrochloric acid produces a red color. Amyl nitrite added to the hydrochloric acid solution produces no change of color on boiling, nor is nitrogen gas given off.—*Dimethylamido-azobenzol* (formerly used for coloring artificial wax from ozokerite).

4. Reactions similar to 3, except that amyl nitrite produces a change of color and a small quantity of nitrogen is given off.—*Amido-azobenzol*, $C_{12}H_9N_2.NH_2$.

II. The coloring matter is soluble in boiling water. Strong sulphuric acid dissolves it without any great change of color.

a.—Caustic soda produces no precipitate.

ACID COLORING MATTERS.

1. The solution is greenish yellow, having a very bitter taste. Alkalies color it a dark yellow. Unaffected by acids.—*Picric Acid* (*Trinitrophenic Acid*).

2. The solution is golden-yellow. Acids cause a white precipitate.—*Martius-Yellow* [*Naphthalene-Yellow*, $C_{10}H_5(NO_2)_2.ONa+H_2O$].

3. The solution is golden-yellow; not precipitated by acids. On the addition of chloride of potassium fine, needle-shaped crystals are precipitated.—*Acid Naphthol Yellow.*

4. The solution is brownish-yellow, and shows a magnificent green fluorescence, disappearing on the addition of hydrochloric acid, which also gives a precipitate.—*Fluorescein* (Uranin), *Benzyl Fluorescein* (Chrysolin). These two dyes can only be distinguished by a careful examination of the separated coloring acids. ["Watts's Dict.," viii. 1606. Richter's Chemistry, Organic, Smith's edition, p. 629.]

5. The solution is golden-yellow, and not precipitated by acids. It is not decolored either by zinc-dust and ammonia or by tin-salt and hydrochloric acid. —*Quinoline-Yellow.*

b.—Caustic Soda gives a precipitate.

BASIC DYES.

1. The precipitate with alkalies is yellow and is soluble in ether to a bright yellow solution, with a beautiful green fluorescence.—*Phosphine.* [Chrysaniline, $C_{19}H_{11}N(NH_2)_2$, with a little magenta.] (This delicate ether test can also be used to detect phosphine in mixtures, as, for example, with grenadine, maroon, etc.)

2. The precipitate with alkalies is milk-white; soluble in ether to a colorless solution with a greenish-blue fluorescence.—*Flavanilin*, $C_{16}H_{14}N_2$.

3. The precipitate with alkalies is milk-white. Ethereal solution colorless, without fluorescence. The yellow solution, when boiled with hydrochloric acid, gradually loses its color, and finally becomes colorless.—*Auramin.*

III. The coloring matter is soluble in water. The solution in concentrated sulphuric acid has a deep color.

AZO-COLORING MATTERS.

a.—Soda produces a precipitate.

1. The color to wool is yellow. The aqueous solution solidifies, on cooling, to a bluish-red jelly. The sulphuric acid solution is brownish-yellow.—*Chrysoidin* [diamido-azobenzene. **Böckmann**'s "Chem. Tech. Untersuch.," p. 308].

2. The color given to wool is orange-brown. The solution does not solidify on cooling. The solution in sulphuric acid is brown.—*Vesuvin* (*Bismarck-Brown*, Manchester-Brown, or Phenylene-Brown). [Triamido-azobenzene.]

b.—Soda does not produce a precipitate.

1. The solution in sulphuric acid is yellow, becoming salmon-colored on diluting. The aqueous solution is yellow.—*Tropœöline-Yellow.*[1]

2. The solution in sulphuric acid is yellow, changing to carmine-red on diluting. The aqueous solution is yellow, and the substance crystallizes out, on cooling, in glittering, golden scales. Dilute acids produce a reddish-violet precipitate.—*Methyl-Orange. Ethyl-Orange.*

3. The solution in sulphuric acid is violet, becoming on diluting reddish-violet, and at the same time forming a steel-gray precipitate. The aqueous solution is yellow, crystallizing out on cooling. Calcium and barium chlorides give a completely insoluble precipitate.—*Tropœölin OO. Diphenylamine-Yellow.* [$SO_3C_{12}H_9N_2.NHC_6H_5$.]

4. The solution in sulphuric acid is bluish-green, becoming violet on diluting, and forming a steel-blue precipitate. The aqueous solution is yellow; a crystalline precipitate separates from it on cooling. Barium chloride gives a yellow precipitate, which can be crystallized from a large quantity of water in shining plates.—*Jaune N* (*Yellow N*). [**Böckmann**, p. 310.]

5. The solution in sulphuric acid is yellowish-green, becoming violet on diluting, and forming a gray precipitate. The aqueous solution is yellow, depositing crystals on cooling. Calcium chloride gives an orange precipitate, which becomes red and crystalline on boiling.—*Luteolin.* [$C_{20}H_{10}O_8$. From protocatechuic acid.]

6. The solution in sulphuric acid is carmine, turning yellow on diluting. The aqueous solution is yellow, often cloudy, and becoming a deep red or violet on the addition of alcoholic soda.—*Citronin* (Indian-Yellow. Curcumin. Purrée). [Euxanthin, $C_{19}H_{16}O_{10}$.]

7. The sulphuric acid solution is a deep orange. On diluting no change of color takes place. The aqueous solution is orange; on adding calcium chloride fine crystals of the calcium salt separate out.—*Orange G* (*D. R. P.* No. 3229).

8. The sulphuric acid solution is a brown orange. No change of color occurs on diluting. The aqueous solution is yellow. A small addition of hydrochloric acid causes a crystalline precipitate; excess of hydrochloric acid causes a separation of the free acid in gray needles.—*Tropœölin O* (Chrysoin) [Resorcin-azo-benzene sulphonic acid].

9. The solution in sulphuric acid is carmine-red, becoming orange on diluting. The aqueous solution is a reddish-orange; chloride of calcium precipitates the fine red calcium salt, which crystallizes from a large proportion of boiling water in needles.—*Orange II.* (Mandarin). [Tropœölin OOO, No. II.]

10. The sulphuric acid solution is violet, becoming orange on diluting. The aqueous solution is orange-red, becoming carmine on the addition of caustic soda.—*Tropœölin OOO* [No. I.] (Orange 1).

Green Coloring Matters.

1. Soluble in water to an olive-brown solution. It easily dissolves in alkalies to a grass-green solution. Concentrated sulphuric acid dissolves it to

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[1] On Tropœölines in general see O. N. **Witt**, 1879: *Jour. Chem. Soc.*, 35, 179.

a dirty brown solution.—*Cörulein*, $C_{20}H_8O_6$. [Post's "Chem. Tech. Anal.," p. 991.]

2. Easily soluble in water, forming a bright green solution. Alkalies give it a rose-colored or gray precipitate. Strong acids color it yellow.—*Victoria-Green* [*Malachite-Green*. $C_{19}H_{13}N_2(CH_3)_4.OH$. E. and O. FISCHER, 1878–79: *Ber. d. chem. Ges.*, **11**, 2095; **12**, 796; *Jour. Chem. Soc.*, **36**, 236, 787].

3. Readily soluble in water, forming a fine blue-green solution. Acids color it yellow. Alkalies decolor the solution without producing any precipitate. A specimen of stuff dyed turns violet when heated above 100° C.—*Iodine and methyl-green.* [Hexamethyl rosaniline compounds. Böckmann's "Chem. Tech. Untersuch.," p. 298.]

4. Easily soluble in water to a correspondingly pale green solution. Acids first deepen the color, and then change it to yellow. Alkalies completely decolor the solution. Silk and wool can only be dyed in an acid-bath (distinction from methyl-green, which will dye in a neutral bath). Dyed samples can be heated with safety for a short time to 150° C.—*Helvetia-Green.* [Alkali-Green.] [Post's "Chem. Tech. Anal.," p. 987. Sodium sulphonate of malachite green.]

BLUE COLORING MATTERS.

1. Quite insoluble in water, soluble in alcohol to blue solutions of various shades. Hydrochloric acid at first causes no change, but on standing minute, sparkling green crystals are precipitated. Caustic soda produces a brownish-red coloration. Concentrated sulphuric acid dissolves it, forming a brown solution.—*Rosaniline-Blue.*[1] *Diphenylamine-Blue.*[2] (To be distinguished from each other by the difference in tint of dyed silk, especially with an artificial light.)

2. Insoluble in water. The alcoholic solution is colored red by the addition of hydrochloric acid. Unaltered by alkalies.—*Iodophenin.* [Derivative of Isatin, containing sulphur.]

3. Easily soluble in water. Hydrochloric acid gives a greenish precipitate. Caustic soda gives a violet-red precipitate. Zinc-dust reduces it, but the color is restored on contact with the air. It contains zinc.—*Methylene-Blue* [$C_{16}H_{19}N_3S$. Böckmann's "Untersuchungs-Methoden," p. 306]

4. Tolerably soluble in water. Acids color the solution yellowish-brown. Alkalies give a red-brown precipitate.—*Victoria-Blue.*

5. Readily soluble in water. The solution is almost completely decolored by acids. Wool abstracts the coloring matter from the alkaline solution, and becomes colored a deep blue after washing with water and treating with dilute acids.—*Alkali-Blue R*, and *6B.*[3] (Distinguished from each other by the difference in tint.)

6. Easily soluble in water. Wool can only be dyed in an acid-bath. The aqueous solution is not precipitated by alkalies. Zinc-dust decolors permanently. —*Water-Blue* (Wasserblau) *R*, *6B.*[4]

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[1] "*Aniline-Blue.*" "Insoluble Aniline-Blue." Spritblau. Triphenyl-rosaniline hydrochloride. Insoluble in water, sparingly soluble in alcohol, soluble in acetic acid or in aniline oil. The alkali sulphonates of triphenyl-rosaniline constitute "soluble blues," known as "alkali-blue" and "water blue," from the name of the solvent they require.

[2] Diphenylamine-Blue is inferred to be a triphenyl-para-rosaniline. It forms a sulphonic acid soluble with alkalies.

[3] "Alkali-Blue" is the *mono* sulphonic acid of triphenyl-rosaniline. It is not easily soluble in water alone, but on adding alkalies solution is readily obtained through formation of a sulphonate.

[4] "Water-Blue" consists of *poly* sulphonic acids of triphenyl-rosaniline, with $(SO_3H)_2$ to $(SO_3H)_4$ in the molecule. These sulphonic acids dissolve in water without the help of an alkali.

7. Easily soluble in water. Dyes only in an acid-bath. Zinc-dust and ammonia form a vat; that is, the color is restored on contact with air. The solution is permanently decolored by boiling with dilute nitric acid.—*Indigo carmine.* [Alkali salts of indigotin-disulphonic acid, as $C_{16}H_8N_2O_2(SO_3K)_2$]

8. Insoluble in water, soluble in alcohol. Alkalies color the alcoholic solution brownish-red to violet. Strong sulphuric acid dissolves it to a blue solution.—*Induline R*, 6*B*. [Azo-diphenyl Blue.] (The more soluble the dye the redder the color.)

9. Soluble in water. Acids give a blue precipitate. The solution is colored red to violet by alkalies. Zinc-dust and ammonia form a vat. Dilute nitric acid does not decolor the solution, even on heating.—*Indulines* soluble in water. (Distinguished from each other by difference in tints.) [Böckmann's "Untersuch.," p. 321.]

10. The commercial product is in the form of a gray paste. Soda solution gives a blue color on exposure to the air.—*Leukindophenol.*

11. The commercial substance is a gray paste, which dissolves in soda without any blue coloration. On adding glucose, and boiling, crystals of indigo-blue separate out.—*Ortho-nitrophenylpropiolic Acid.*

VIOLET COLORING MATTERS.

1. With difficulty soluble in water; soluble in alcohol. Sulphuric acid forms a cinnamon-colored solution.—*Regina-Purple* (*Diphenyl-rosaniline*).

2. Easily soluble in water. Alkalies give a precipitate. Hydrochloric acid colors the solution first green and then yellow.—*Methyl-Violet*, *R*, 6*B*. *Hofmann's Violet.* (Distinguished from each other by the difference in tint.) [Methyl-Violet is pentamethyl-rosaniline hydrochloride. It is the same as "Paris Violet." Hofmann's Violet is triethyl-rosaniline hydrochloride or hydriodide. For description see Böckmann's "Untersuch.," p. 296.]

3. Not readily soluble in water. Alkalies give a violet precipitate. Concentrated sulphuric acid dissolves it to a gray solution. On dilution the solution becomes successively grayish-green, sky-blue, bluish-violet, reddish-violet.—*Mauvein.* (*Perkin's Violet. Rosolane.*) [$C_{27}H_{24}N_4$. By oxidation of aniline oil with dichromate and sulphuric acid. Perkin, 1856.]

4. Soluble in water. Acids give a blue precipitate; alkalies a reddish-violet precipitate. With zinc-dust and an acid, as well as in an ammoniacal solution, it forms an excellent vat. The solution in strong sulphuric acid is emerald-green, becoming sky-blue on diluting.—*Laut's Violet* (*Thionin*).

5. Only soluble in boiling water. Hydrochloric acid colors the solution carmine-red. Sulphuric acid dissolves it to a blue solution, becoming red on diluting.—*Gallo-cyanin.*

6 Soluble in water to a reddish-violet solution. The addition of alcohol causes a red fluorescence. Strong sulphuric acid dissolves it to an emerald-green solution; on diluting the color changes to blue or violet.—*Amethyst, Fuchsia, Giroflée* (*Violet Saffranin Dyes*). [Saffranines are of the type $C_{18}H_{14}N_4$. For a brief description of the group see Richter's Chemistry, Organic, Smith's ed., p. 469; Böckmann's "Untersuch.," p. 302.]

Chemical Determination of Red Dye-Stuffs, according to Stein.[1]

With *fabrics*, a small portion, of about one-fourth inch square surface, is treated in a test-tube with a few c.c. of the reagents directed. The resulting color solutions are subjected to the tests.

I. The dye-stuff is warmed with ammonium sulphide. It turns more or less blue to greenish.—"*Aloes Dye*," a mixture of *Chrysammic and Aloetic acids* used upon wool and silk.

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[1] W. STEIN, 1870: *Polyt. Centralbl.*, p. 616; *Zeitsch. anal. Chem.*, **9**, 520.

II. The dye-stuff is boiled with aluminium sulphate [filtered, cooled, and filtered again, GOPPELSRÖDER, 1878].

A. The solution turns red with a golden-green reflex.—*Madder colors* (*Note* 1, following).

B. The solution turns red without any reflex. On diluting it with an equal volume of sodium sulphite solution, it is

(1) Bleached. *Aniline reds, Sandal, Brazil-wood, Corallin,* and *Safflower.* Add alcohol to 80 per cent. and boil. The solution
  (*a*) Colors decidedly (a) bluish-red—*Aniline-reds* (*Note* 2, p. 191).
    (b) yellowish-red—*Sandal* (*Note* 3, p. 191).
  (*b*) Does not color at all, or noticeably (Safflower, Brazil-wood, Corallin). Warmed with lime solution it assumes
    (a) no color—*Safflower* (Carthamus) (*Note* 4, p. 191),
    (b) a red color (Brazil-wood and Corallin). Warmed with dilute sulphuric acid it becomes
    (a) orange-red—*Brazil-wood* (*Fernambuc*),
    (b) yellow and discolored—*Corallin* (*Note* 5, p. 191).

(2) Not bleached (by the sulphite). *Archil, Lac dye, Kermes, Cochineal.* Add alcohol to 80 per cent. and boil. It becomes
  (*a*) decidedly red—*Archil* (*Orseille*) (*Note* 6, p. 192),
  (*b*) not red, or but slightly (Lac, Kermes, Cochineal). It is warmed by baryta solution. It takes
    (a) no color—*Lac Dye,*
    (b) colors (Kermes, Cochineal). It is warmed with lime solution; colors
      (aa) brown-red—*Kermes* (Coccus ilicis),
      (bb) violet—*Cochineal*[1] (Coccus cacti).

Note 1, upon Stein's scheme (above). The golden-green fluorescence, after hot treatment with aluminum sulphate, according to STEIN and others, is a distinction of natural madder-red from other reds, but is wholly due to the purpurin of the madder, and is not obtained with the alizarin. Since Stein's report artificial alizarin has gradually supplanted madder, and the latter is not now in extensive use. A brief description of alizarin and purpurin is here appended.

Alizarin. $C_{14}H_8O_4 = 240$. Di-hydroxy-anthraquinone. $C_6H_4 : C_2O_2 : C_6H_2(OH)_2$ [OH : OH=1 : 2]. "*Madder-Red.*" "*Alizarin-Red.*"—A product of anthracene, $C_{14}H_{10}$, of coal-tar, from which it is now chiefly obtained, by reactions of oxidation. Before 1869 it was wholly obtained from the root of the madder plant, *Rubia tinctorum* (*Krapp*, in the German). Natural and artificial alizarin are identical when each is perfectly purified. The natural alizarin comes from a glucoside of the plant, ruberithric acid, $C_{26}H_{28}O_{14}$. By boiling with dilute acids, also by a ferment in the madder root, two molecules of water are taken in, and a molecule of alizarin formed, with two of glucose.—In orange-colored or yellow prisms, or in a brown paste. Melting

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[1] Upon the distinction between cochineal, kermes, and lac, three colors alike in most reactions, see Stein's report, *Zeitsch. anal. Chem.*, 9, 522.

point, 282° C. (SCHUNCK). Insoluble in cold, slightly soluble in boiling water; soluble in alcohol, ether, methyl alcohol, benzene (more readily on warming), or carbon disulphide. Alkalies and alkali carbonates dissolve it in water, the solution being violet by transmitted, purple by reflected light. Concentrated sulphuric acid does not decompose it. From the alkaline solutions acids precipitate it in reddish flakes; and alum precipitates it with a red color. Alcoholic solution of alizarin, with acetate of copper or of iron, gives a purple precipitate; with barium hydrate solution, a blue precipitate.

Sublimation is a serviceable means of examining alizarin. Natural alizarin contains Purpurin, and artificial alizarin contains Anthraquinone, as impurities. Alizarin itself begins to sublime at 110° C.; the two purpurins at 160°–170° C. (SCHUNCK and ROEMER, 1880). The first sublimate from artificial alizarin, at temperatures below 140° C., will contain crystals of anthraquinone with the long orange crystals of alizarin (GOPPELSRÖDER, 1877–78). In natural alizarin—that is, when anthraquinone, hydroxyanthraquinone, and the anthraflavic acids are absent—continued sublimation at 140° C. removes the alizarin, which may thus be estimated by the loss.[1]

The name alizarine, in commerce, has been sometimes applied to an extract of madder flowers; and to Gerancin, a product of the action of strong sulphuric acid upon madder dye.

Alizarin-Blue. $C_{17}H_{19}NO_4$. Formed from Alizarin-Orange by heating with sulphuric acid and glycerin. A bluish-violet paste, of about 10% solid content. Soluble in alkalies with greenish-blue color, an excess of the alkali causing a precipitate. Colored red-brown by sulphuric or hydrochloric acid.

Alizarin-Orange. Nitro-Alizarin. $C_6H_4 : C_2O_2 : C_6H(NO_2)(OH)_2$ $[NO_2 : OH : OH = 1 : 2 : 3]$. In commerce as a yellow paste. Dissolves in sodium carbonate solution with yellow-red; in sodium hydrate solution with a red color; an excess of the caustic alkali precipitating the solution.

Purpurin. $C_{14}H_8O_5 = 256$. Tri-hydroxy-anthraquinone. $C_6H_4 : C_2O_2 : C_6H(OH)_3$ $[OH : OH : OH = 1 : 2 : 4]$. Can be produced from anthracene. The isomerides *Isopurpurin* or anthrapurpurin, and *Flavopurpurin* or "yellow alizarin," have a limited employment in dyeing. Purpurin crystallizes in orange-red needles, with one molecule of crystallization-water.

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[1] SCHUNCK and ROEMER, 1880: *Ber. d. chem. Ges.*, 13, 41; *Jour. Chem. Soc.*, 38, 424. The same, 1877: *Jour. Chem. Soc.*, 31, 665. Also, GOPPELSRÖDER, 1877: *Ding. polyt. Journ.*, 226, 30; *Zeitsch. anal. Chem.*, 17, 510.

It is more soluble than alizarin, either in boiling water, alcohol, or ether. The solution in alkali is red, in thin layers purple. A dilute alkaline solution soon bleaches in the air and light. With lime or baryta, in hot water, it forms a perfectly insoluble lake. Boiling alum solution takes up purpurin abundantly, forming a yellow-red solution of strong fluorescence, whereby madder-red is distinguished in the scheme of Stein (p. 188).

Note 2, upon the scheme of STEIN (p. 189). *Aniline-reds. Salts of Rosaniline*, $C_{20}H_{19}N_3 = 301$ (monobasic). The hydrochloride and acetate, as monacid salts, constitute "Magenta," "Fuchsin," and "Roseine." The nitrate is prepared as "Azaleine" and "Rubine." Rosanilines are triamido-toluyl-diphenyl methanes, the hydrated base having the structure $(C_6H_4.NH_2)_2(C_6H_3CH_3.NH_2)C.OH = C_{20}H_{21}N_3O$. The base forms monacid salts of red color, triacid salts of a yellow color, and diacid salts of little stability.—Commercial magenta or fuchsin appears in crystals of green metallic lustre. It is non-volatile, decomposing at about 220° C. It has a bitter taste. Rosaniline base is very slightly soluble in water, but melts in boiling water. The ordinary salts of rosaniline, the aniline-reds, are soluble in hot water and in alcohol, the solutions having a crimson-red color, and only impurities being left in insoluble residue. Addition of acids changes the color toward yellow, with formation of triacid rosaniline salts. Alkalies precipitate free rosaniline and destroy the color of the solution. Warmed with cupric chloride, aniline-reds show a blue color. They dye silk and wool a crimson-red, without a mordant.—*Rosaniline picrate* forms fine red needles nearly insoluble in water. The *tannate* is insoluble in water, but soluble in alcohol, methyl alcohol, or acetic acid. Tannic acid precipitates rosaniline from aqueous solutions of its ordinary salts.

Note 3. *Sandal-red* is turned brown by hot lime solution; but its red color is intensified and finally changed toward blue by hot diluted sulphuric, hydrochloric, or acetic acid.

Note 4. *Safflower-red* (African Saffron, False Saffron). The action of the lime solution is to decolor through a change to yellow. Ammonium sulphide decolors it, more readily by addition of ammonium hydrate. The red color is restored by acetic acid.

Note 5. *Corallin-red.* Peonin. Prepared from Aurin or Rosolic Acid. In violet powder or brown needles, soluble in water as a red solution having an alkaline reaction. With cupric chloride it is decolored to gray—a distinction from aniline-red, which is turned blue in this test.

Note 6. *Archil. Orseille.* Persio. The coloring matter derived from lichens of the genera Roccella and Leconora. Vegetable acids in these lichens are converted into *orcin*, or orcinol, $C_6H_3(CH_3)(OH)_2$ [1 : 3 : 5], a di-hydroxy-toluene. With ammonia this gives rise to *orcein*, or "lichen-red," $C_7H_7NO_3$, the chief constituent of archil dyes. Litmus and Cudbear also contain color derivatives of orcin, obtained from the lichens. Orcin is manufactured from toluene, as a source of orcein, for dyeing. Orcin is colorless when pure, but becomes reddish-brown by exposure to the air. Its crystals, with one molecule of water, melt at 58° C., and becoming anhydrous the mass distils at about 290° C. It is soluble in boiling water, alcohol, ether, or boiling benzene. It is capable of decomposing alkali carbonates with effervescence. Hypochlorites give, with even a trace of orcin, a transient, intense purple red color. Ammonia, with exposure to air, quickly converts orcin into orcein, with its deep purple-red color.—*Orcein* dissolves sparingly in water, to which it gives its red color, dissolves freely in alcohol, and freely in aqueous alkalies with violet-red tint. Acids precipitate it, in part, from the alkaline solution, and water precipitates it from the alcoholic solution. It is bleached by ammonium sulphide; also by zinc added to an ammoniacal solution previously acidulated.

Reactions of Coloring Materials, according to Fol.[1]

Blues.

Solution of citric acid or dilute hydrochloric acid is added.
  (*a*) Color changes to red or orange.—*Logwood-blue.*
  (*b*) Color does not change.
Solution of calcium chloride is added to a fresh portion of the dye-stuff.
  (*a*) Color remains unchanged.—*Prussian blue.*
  (*b*) Color changes.
Solution of caustic soda is added to a fresh portion.
  (*a*) The substance is decolorized.—*Aniline-blue.*
  (*b*) It remains unchanged.—*Indigo-blue.*

Yellows.

A portion is tested for *ferric oxide* by means of potassium ferrocyanide; another part is tested for *picric acid* by means of

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[1] F. Fol, 1874: *Ding. pol. Jour.*, **212**, 520.

potassium cyanide solution. The production of a blood-red color indicates picric acid.

If the colors do not appear, another portion is treated with a boiling solution of 1 part of soap in 200 parts of water.

(*a*) The color changes to brown, but becomes yellow again with an acid.—*Turmeric.*
(*b*) The color becomes very dark.—*Fustic.*
(*c*) The color remains unchanged.—*Weld. Persian berries. Quercitrin.*

Another portion is boiled with stannous chloride.

(*a*) The color remains unchanged.—*Quercitrin.*
(*b*) The color changes to orange.—*Persian berries.*

If *annatto* is the coloring matter present, the color changes to greenish-blue on boiling in concentrated sulphuric acid.

Reds.

The substance is treated with boiling soap solution.

(*a*) The color is entirely discharged.—*Saffron-carmine.*
(*b*) The color is slightly discharged.—*Aniline-red.*
(*c*) The color changes to yellowish-red or yellow.—*Brazil-wood* or *Cochineal.* A portion of the substance is treated with concentrated sulphuric acid.
  (1) A cherry-red color is produced.—*Brazil-wood.*
  (2) A yellowish-orange color is produced.—*Cochineal.*
(*d*) The color remains unchanged.—*Madder-red.* This color is not discharged by ammonium chloride, or by a mixture of equal parts of stannous chloride, hydrochloric acid, and water.

Greens.

May consist of blues and yellows in mixture, or of such substances as aniline-green.

The substance is heated on the water-bath with alcohol of 95 per cent.

(I.) The alcohol is colored yellow, while the substance becomes more and more blue.—*Indigo* or *Prussian blue* is present. The residue is washed and tested for these blues, as already directed. The alcoholic liquid is tested for yellows as above.

(II.) The alcohol is colored green, while the substance becomes less colored.—*Aniline green* or a mixture of *aniline-blue* with *yellow* is present.

A part of the substance is boiled with dilute hydrochloric acid.

(*a*) The liquid is colored blue or lilac.—*Aniline-green from methyl iodide* is present.
(*b*) The substance is decolored.—*Aniline-green from aldehyde.*
(*c*) The substance is colored blue, while the liquid becomes yellow.—*Aniline-blue mixed with yellow.*

Violets.

The substance is boiled in calcium chloride solution.
(*a*) It is unchanged.—*Alkanna-violet.*[1]
(*b*) It is colored nankeen-yellow.—*Madder-violet.*
(*c*) It is decolored.—*Cochineal-violet.*

Another portion is boiled in citric acid: the color is lightened. —*Aniline-violet.* To distinguish between the two aniline-violets, a third part is boiled in hydrochloric acid, which is diluted with three times its volume of water. After washing it appears blue-violet if ordinary aniline-violet is the color, while if Hofmann's violet is present the substance appears greenish, and after washing light lilac or bluish.

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[1] [*Alkanet.* The root of Anchusa tinctoria. A *red color*, termed alkanin, or anchusin. Used to color pomades and oils. Insoluble in cold water, soluble in alcohol, ether, benzene, petroleum benzin, carbon disulphide, fat oils, and essential oils, the resulting solutions having a red color. The fixed alkalies dissolve it with a *blue color*, sometimes used to color syrups. On neutralizing the blue alkaline solution, the alkanin is precipitated, red to brown. Ammonia reacts with production of *alkanna-green.* Alcoholic solution of alkanet with stannous chloride gives a crimson precipitate, with lead acetate a blue precipitate, with iron salts a violet precipitate, and with mercuric chloride a flesh-colored precipitate.]

SOLUBILITIES OF ANILINE DYES IN THE IMMISCIBLE SOLVENTS.[1]—TABLE I.

	Color of the Acid Solution.	FROM SOLUTION OR SUSPENSION IN WATER ACIDULATED WITH SULPHURIC ACID.				
		Petroleum benzin.	*Benzene.*	*Ether.*	*Chloroform.*	*Amyl Alcohol.*
Aniline-Blue, soluble.	Blue.	Extracts nothing.	Dissolves traces, colored on exposure.	Dissolves traces.	Traces.	Solution deep colored. Residue golden.
Aniline-Blue, insoluble.	Colorless; color, precip.	" "	" "	Deep colored solution. Golden residue.	Same as ether.	Same as ether.
Aniline-Brown (Havana-brown).	Dark brown.	Extracts only impurities.	Colored blue-yellow. Residue brown.	Dissolves very little.	" '	Dissolves freely.
Vesuvin-Brown.	Brown.	" "	Colored yellow. Residue brown.	Dissolves less than benzene.	" "	" "
Aniline-Orange.	Pale yellow; greenish flocks.	" "	Colored yellow. Res. brown-yellow.	Dissolves more than benzene.	Same as benzene.	" "
Aniline-Red.	Red.	Extracts nothing.	Extracts only impurities.	Traces dissolved colorless.	Same as ether.	Solution red. Residue iridescent.
Aniline-Violet, soluble.	Partly dissolved; violet.	" "	Dissolves only traces.	Traces dissolved.	Dissolves traces.	Solution violet. Residue iridescent
Aniline-Violet, insoluble.	Slight colored; mostly precip.	' "	Only impurities.	Colored lilac. Residue violet.	Slightly colored.	" "
Aniline-Yellow.	Pale yellow.	Colored yellow. Yellow crystals.	Colored yellow. Yellow crystals.	Dissolves more than benzin.	Same as ether.	Same as ether.
Corallin.	Dissolves little; yellow.	Only impurities.	Only impurities.	Dissolves easily. Residue orange.	Dissolves yellow to brown-red.	" "

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[1] From Dragendorff's "Gerichtl. Chemie Organ. Gifte," 1872.

TABLE II.

	Color of Ammoniacal solution.	FROM THE AMMONIACAL SOLUTION.				
		Petroleum benzin.	*Benzene.*	*Ether.*	*Chloroform.*	*Amyl Alcohol.*
Aniline-Blue, soluble.	Reddish.	Extracts nothing.	Extracts very little.	Extracts very little.	Dissolves very little.	Solution yellow. Residue blue.
Aniline-Blue, insoluble.	…………	Solution red-brown. Residue bluish.	Solution red-brown. Residue bluish.	Solution red-brown. Residue bluish.	Solution red-brown. Residue bluish.	Solution red-brown. Residue bluish.
Aniline-Brown (Havana-brown).	Light brown.	Solution green-fluorescent.	Same as benzin.	Dissolves less than benzene.	Dissolves less than benzene.	Solution dark brown, fluorescent.
Vesuvin-Brown.	" "	Solution yellow. Residue brown.	Solution orange. Residue brown.	Colored yellowish.	Colored yellowish.	Solution deep brown. Residue brown.
Aniline-Orange.	Brown.	Extracts nothing.	Dissolves traces.	Colored yellow.	Same as benzene.	Dissolves much less than from acid sol.
Aniline-Red.	Nearly colorless.	Dissolves traces.	Solution yellow and fluorescent.	Solution bluish. Residue red.	Same as ether.	Deep red solution. Residue blue-red.
Aniline-Violet, soluble.	" "	Dissolves nothing.	Dissolves nothing.	Dissolves traces.	Dissolves traces.	Solution violet. Residue violet.
Aniline-Violet, insoluble.	" "	Dissolves traces.	" "	Solution yellow.	Solution blue-violet.	Extracts less than from acid solution.
Aniline-Yellow.	Dark brown.	Solution first yellow, then colorless.	Dissolves traces.	Dissolves little. Solution yellow.	Dissolves traces.	Solution yellow. Residue yellow.
Corallin.	Bright purple.	Only impurities dissolved.	Only impurities dissolved.	Solution pale yellow.	Less than from acid solution.	Solution red.

REACTIONS OF DYES (DRAGENDORFF).[1]

	Concentrated Sulphuric Acid.	*Nitric Acid.*	*Ammonia.*	IN SULPHURIC ACID SOLUTION.			*Tannic Acid.*	HYDROCHLORIC ACID SOLUTION.	
				Iodine.	*Potas.-bis. iodide.*	*Potas. Mercur. iodide.*		*Platinic chloride.*	*Gold chloride.*
Alizarin.	Blood-red. Precip. by water.	Changes on boiling.	Dissolves purple-violet.	......	......	......	......	......	......
Aniline-Blue, soluble.	Blood-red to brown.	Dissolves blue.	Dissolve colorless.	Colors brown.	No precipitate.	No precipitate.	Not turbid.	Not turbid.	Not turbid.
Aniline-Blue, insoluble.	" "	" "	" "	Colors greenish.	" "	" "	" "	" "	" "
Aniline-Brown. (Havana-brown).	No change.	Dissolves brown.	Dissolves slightly.	Red solution.	Brown precipitate.	Red-brown precipitate.	Brown precipitate.	Brown precipitate.	Brown precipitate.
Vesuvin-Brown.	Dissolves brown.	Blood-red to brown.	Dissolves readily.	" "	" "	Brown precipitate.	" "	" "	" "
Aniline-Orange.	Dissolves brownish.	Dissolves pale yellow.	Dissolves reddish.	No precipitate.	No precipitate.	Turbidity.	Turbidity.	Not turbid.	Not turbid.
Aniline-Red.	Dissolves yellow.	Green, brown, diluting red.	Dissolves violet-red.	Colors greenish.	Little precipitate.	Violet precipitate.	Not turbid.	" "	Green precipitate.
Aniline-Violet, soluble.	Dissolves blood-red.	Dissolves deep blue.	Dissolves violet.	" "	No precipitate.	No precipitate.	" "	" "	Not turbid.
Aniline-Violet, insoluble.	Dissolves dark yellow.	Brown to green.	Violet, then colorless.	" "	Black precipitate.	Blue precipitate.	" "	Blue precipitate.	Black precipitate.
Aniline-Yellow.	Dissolves yellow.	Dissolves yellow.	Dissolves orange.	No precipitate.	No precipitate.	Turbidity.	Turbidity.	Not turbid.	Not turbid.
Chrysammic Acid.	Dissolves, with violet precip.	Dissolves green-yellow.	Dissolves red.	" "	" "	No precipitate.	Not turbid.	" "	" "
Corallin.	Dissolves yellow.	Dissolves yellow.	Dissolves purple.	" "	" "	" "	Turbidity.	" "	" "

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[1] *Loc. cit.*

CONCHAIRAMINE, CONCUSCONINE. See Cinchona Alkaloids, p. 92.

COTTON-SEED OIL. See Fats and Oils.

CREAM OF TARTAR. See Tartaric Acid.

CUPREINE. See pp. 92 and 153.

CRYPTOPINE. See Opium Alkaloids.

DYES. See Coloring Materials, p. 181.

ECGONINE. See p. 172.

ELEMENTARY ANALYSIS of Carbon Compounds.—*A qualitative analysis for the organic elements*, C, H, and N, is only made for the purpose of determining whether a carbon compound be present or not, or whether a given organic compound be nitrogenous or not. In the case of bodies not rapidly volatile, (1) *ignition in the open air*, either on platinum foil or in a glass tube open at both ends, will show carbonization in case a carbon compound be present. The fact of carbonization is shown first by the appearance of a black residue, and then by its gradually burning away. In the case of volatile bodies, or when for any reason the result of simply igniting the body by itself proves uncertain, a resort is had to (2) *ignition with copper oxide in a small combustion-tube*, with tests of the gas evolved. The dry substance is mixed with an excess of copper oxide (previously ignited and cooled), the mixture introduced into a small tube of hard glass, the tube being closed at one end and fitted at the other with a tubulated cork carrying a small glass tube bent at right angles. On applying heat, very gradually, to the combustion-tube, the resulting gas is passed into lime solution or baryta solution. If a precipitate be formed this is to be gathered in sufficient abundance, and its solubility in acetic acid with effervescence is tried, for the identification of carbon dioxide. Meantime it is observed whether there be condensation of liquid in the bent tube or not, and droplets so obtained may be tested, with anhydrous cupric sulphate, for water, as evidence of hydrogen. But this evidence is dependent upon the absence of moisture or hydrates in the contents of the combustion-tube. Unless the result of the simple test just mentioned be clearly conclusive, it is better to use the safeguards against moisture directed for Quantitative estimation of carbon and hydrogen. That is, the substance and the copper oxide are properly dried and secured from the moisture of the air, and the air in the filled combustion-tube is replaced by dried air, before the combustion. Then the combustion is conducted very slowly, and the small conducting tube is kept cold.—To be certain that carbon dioxide obtained by ignition does not come from carbonates—that is, from non-alkali carbonates or alkali bicarbonates—the material is first to be tested for carbonates. If these are present, enough of hydrochloric or sulphuric dilute acid is added, and the material dried again.

If it be found that a carbon compound be present, to find whether it be a nitrogenous compound or not, it is sufficient, in the greater number of cases, (3) to *heat the dry substance, well mixed with dry soda-lime*, when the nitrogen is given off in the form of ammonia. The heating must be to redness, and thorough drying of the material, as well as previous ignition of the soda-lime, render the operation much more convenient. An ordinary test-tube may be used for this combustion; but a section of combustion-tubing, of hard glass, with one end closed, serves better. The tube may be wrapped in a strip of copper gauze near the open end, and held by the forceps, while the heat of the flame is very gradually applied. The test for ammonia is made by moistened red litmus-paper, also by the odor, and the color given a drop of dilute solution of copper sulphate held on a loop of platinum wire. Bodies rich in nitrogen give the odor of singed hair when merely burned in the air. Heating with fixed alkalies does not cause the production of ammonia from the nitrogen of all organic bodies. Some bodies so treated yield vaporous alkaloidal compounds, mostly showing the alkaline reaction to litmus, but not exhibiting other characteristics of ammonia. Other bodies, as many of the nitro-compounds, when treated by combustion with fixed alkali, give no indication of the presence of nitrogen. For these it is necessary, and for all it is sufficient, to (4) *heat the substance with a fragment of metallic potassium* for some time (Spica, 1880), and then test the mass for cyanides. The fused mass is digested with hot water and a ferrous salt, acidulated, and a drop or two of ferric salt solution added. The blue color of ferric ferrocyanide gives evidence of nitrogen in the material taken. Also the test may be made for production of sulphocyanate by digesting the mass (after fusing with the potassium) with ammonium sulphide, and then acidulating.

A qualitative examination *for sulphur, phosphorus, sele-*

nium, and arsenic may be made by applying a strong oxidizing agent, and then testing for sulphuric, phosphoric, selenic, and arsenic acids. The material (free from the acids last named) is either digested with strong nitric acid (sp. gr. 1.42) or smelted with potassium nitrate, afterward treated with water, and the filtrate tested for the acids. For arsenic the material may be treated, as in the examination of animal tissues for arsenic, by drying, digesting with concentrated sulphuric acid and repeated small additions of nitric acid until the carbon compounds are oxidized, and the nitric acid then wholly expelled, afterward neutralizing with magnesia, and subjecting the filtrate to Marsh's test for the arsenical mirror. Arsenic will sometimes be found by igniting with sodium acetate, when cacodyl compounds are revealed by their odor. Phosphorus may usually be found by heating the carbonized material with powdered magnesium, intimately mixed, in the bulb of a reduction-tube, after which phosphorescence appears in the dark.

For chlorine, bromine, and iodine, as elements in an organic compound, it is necessary to effect such a decomposition as will bring the chlorine, etc., into union as chlorides, etc., or into the elementary form. Thus chloral, chloroform, and other similar compounds do not react with silver nitrate to form silver chloride, etc. The necessary liberation of the haloid elements is obtained in some cases by digesting with strong potassium hydrate solution, in other cases by igniting in mixture with an excess of lime (each of known purity), after which the aqueous filtrate may be acidified with dilute nitric acid, and treated with silver nitrate solution for precipitates. See further upon the *quantitative* determination of the halogens.

To remove organic substances, in preparation for a search for inorganic bodies in general, methods of ignition, use of oxidizing agents, application of solvents, and dialysis are described in the author's "Qualitative Chemical Analysis," third edition, paragraphs 773–778.

Finally, in qualitative analysis for the *elements* in a portion of organic matter, instead of the direct examination for these elements, above described, the analyst will most often determine at once what *organic compounds known in chemistry* he has in hand, recognizing their likeness by their sensible qualities, fixing their identity by well-tried qualitative reactions, resorting to approved means for their separation, and proving their purity by authorized tests for this purpose. A constant boiling point and prescribed melting and congealing points are sought. The qualitative determination of a known organic compound carries with it the evidence of the constituent elements of the compound. Just as qualitative tests for ortho-phosphoric acid, and for its purity, prove the presence of phosphorus and hydrogen and oxygen in combination as H_3PO_4; so qualitative tests for benzoic acid, and for its purity, suffice to show that only carbon and hydrogen and oxygen are present, and that these elements are united as $C_6H_5CO_2H$. The means of separating organic compounds, and purifying them, have much in common with like means for inorganic bodies. Solvents are applied, precipitations are made, crystallization is instituted, fractional distillation is performed, chemical reactions are applied; and these and other means, as given throughout this work, are persevered in until, in all qualities, *constants* are reached. But when in the course of research a new organic compound is obtained, and separated in purity, as shown by constant properties, it becomes necessary to find what elements it contains and in what proportion they stand. Qualitatively, in most cases it is evident from the origin and properties of the new body what elements it contains; so that the investigator may proceed at once to establish quantitatively, by the methods of organic combustion next to be described, in what proportions the elements are united, and then what molecular weight it has and under what chemical formula it is to find a place in science. Further upon the scope of qualitative and quantitative organic analysis, often termed "proximate organic analysis," and to what extent it depends upon elementary or "ultimate" organic analysis, see the article upon ORGANIC ANALYSIS in this work.

ELEMENTARY ORGANIC ANALYSIS, in the Quantitative Determination of the Elements of an Organic Compound—often termed "*Ultimate Organic Analysis*"—rests upon the principles already outlined for the Qualitative Determination of the Organic Elements. For the carbon and hydrogen a complete combustion is instituted in such a way that the combustion-products, carbon dioxide and water, are obtained as measures of these two fundamental elements. And this simple application of the chemistry of combustion has been the means of obtaining the quantitative composition of organic bodies, from the first establishment of chemical science to the present time.[1] For nitrogen, either an

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[1] LAVOISIER, 1781–1784: burning of the substance with a measured volume of oxygen, and measurement of the volume of carbon dioxide produced, for calculation of weight: *Mém. Acad. Sci.*, 1784–87. BERTHOLLET, 1810: *Mém. de l'Institut National*, II, 121. SAUSSURE, 1807–1814: *Ann. Chim. Phys.*, **62**, 225; **78**, 57; **89**, 273. GAY-LUSSAC and THENARD, 1810–1816: use of chlorate

ignition with fixed alkali is made to yield ammonia for determination, or, more often, combustion with its products carried over heated metallic copper is made to furnish free nitrogen for measurement. The oxygen is obtained by difference. Methods for direct estimation of the oxygen have been proposed from time to time, as briefly indicated in succeeding pages, but none of them has come into actual use.

The supply of oxygen for combustion is obtained as follows: (1) *From copper oxide.* This is either granular or in powder, coarse or fine. It is made by heating copper turnings or copper scale with nitric acid, finally to ignition, or by igniting copper nitrate prepared for the purpose. The granular form is obtained by incipient fusion. Both granulated and coarsely powdered copper oxide is to be of uniform size, by sifting, free from dusty oxide. For most uses in the combustion-tubes, the granular form moderately coarse, or that from the turnings, or the coarse powder is to be chosen, in preference to fine powder. That is, the column is to be sufficiently permeable by gases, so that it will not be necessary to have a channel over the oxide, in the tube. To intermix with the substance under analysis finely pulverized oxide is sometimes employed, or obtained by trituration of the granular form during the intermixing. Oxide of copper, when heated, must evolve no nitrous fumes nor carbon dioxide. It is hygroscopic to a considerable extent, and in combustion for carbon and hydrogen it must be absolutely dry. For nitrogen determinations it is desirable to have it dry. It may be ignited, in a hessian crucible, short of incipient fusion, and when still warm put up in a flask with a neck a very little wider than the combustion-tube, and closed by a perforated stopper bearing a drying-tube of chloride of calcium. Also, it may, with advantage, be dried by ignition in the combustion-tube, in a current of dried air. This may be done when the oxide is to be afterward removed from the tube to the flask in preparing the substance for combustion, and it may with still greater advantage be done when the substance is burned in a boat. In use copper oxide is reduced to cuprous oxide or to metallic copper. With

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as source of oxygen and introduction of copper oxide, also the determination of nitrogen: *Ann. Chim. Phys.*, **74**, 47; *Schweiger's Journal*, **16**, 16. DOBEREINER, 1816: *Schweiger's Journal*, **18**, 379. BERZELIUS, from 1814: the use of horizontal combustion-tubes of glass. LIEBIG, 1831: combustion with copper oxide, in detail nearly the same as "Liebig's method" sometimes employed at present: *Ann. Phys. Chem. Pogg.*, **21**, 1 (application to cinchona alkaloids). BRUNNER, 1838: oxygen gas supplied for combustion: *Ann. Phys. Chem. Pogg.*, **44**, 138. BUNSEN: intermixture with copper oxide in the combustion-tube.

the supply of oxygen gas at the close of combustion, the reduced copper is restored to oxide. Otherwise it may be restored by adding nitric acid, heating, and igniting.—(2) *From lead chromate.* This must contain nothing soluble in water, and yield no carbon dioxide when heated. It fuses at a red heat. It is prepared by melting in a hessian crucible and pouring out upon a stone slab, when it is pulverized moderately fine, sieved, and bottled for use. Or the melted chromate may be poured into water in a copper vessel, and the granulated mass collected, dried, and pulverized. It is not hygroscopic. In melting it adheres to the combustion-tube. In use it is reduced to the green chromic oxide with lead oxide. To use it a second time it is roasted, fused, and pulverized. After the second time it requires oxidation, by digesting the powder with nitric acid, drying, fusing again, and powdering.—Lead chromate is employed instead of copper oxide when sulphur, or selenium or tellurium, is present; also, when very difficultly oxidizable substances are in hand. Its greater efficiency as an oxidizing agent lies chiefly in its being fusible during the combustion.—MAYER (1855) introduced into the powdered lead chromate one-tenth its weight of potassium dichromate previously fused and pulverized. This mixture serves to expel from alkalies or alkaline earths, if these be present, the carbon dioxide they may have absorbed from the products of combustion.—(3) *A stream of oxygen gas is employed.* This is supplied most evenly and satisfactorily from a pair of gas-holders, the one filled with oxygen, and the other with atmospheric air, the stream from each being purified by passing through at least two U-tubes, one filled with pumice-stone and sulphuric acid, to dry the gas, and the other filled with fragments of potassium hydrate to remove carbon dioxide.—Also, without a gas-holder, a stream of oxygen is obtained by generating this element, in the further end of the combustion-tube itself, from lead dioxide, heated in an air-bath to 180°–200° C., or by heating mercuric oxide or potassium chlorate by the flame.—Oxygen is sometimes generated in the combustion-tube from chlorate of potassium placed in a platinum boat and subjected to heat.—In the preparation of oxygen for the gas-holder, chlorate of potassium, well mixed by trituration with one-thousandth of its weight of ferric oxide (FRESENIUS), is heated over the flame in a plain glass retort not over half filled. The heat is applied very gradually, and as soon as the salt begins to fuse the retort is gently shaken. When the air is expelled the connection is made with the gas-holder. If the proportion of ferric oxide be exactly adhered to, the evolution of gas will not be impetuous. 100 grams of the chlorate will yield about 27 liters of oxygen. Oxygen gas is tested for chlorine by passing it through silver nitrate solution, and for carbon dioxide by passing through lime solution. A splinter of wood which has been kindled and blown out should burst into a flame when introduced into a stream of oxygen gas.

The soda-lime used as the fixed alkali, for the conversion of organic nitrogen into ammonia in the combustion-tube,[1] is a mixture of two parts of calcium hydrate with one part of sodium hydrate. It is usually made by the evaporation of a solution of sodium hydrate with the proportional quantity of slaked lime. S. W. Johnson (1872[2]) recommends, as more convenient and even better, a mixture of equal parts of crystallized sodium carbonate and slaked lime, prepared by evaporating the mixture.[3] Soda-lime is obtained in granular form, more convenient for the greater part of its uses than the powdered form.—It should not evolve any trace of ammonia when heated with sugar; it should not be more than slightly moist; and (unless prepared upon Johnson's direction) should not effervesce very much upon the addition of acids. It is made ready for use by igniting in a hessian crucible at a gentle heat, and while warm it is put up in a well-corked bottle, or a bottle with a tubulated stopper carrying a drying tube containing both calcium chloride and a little granulated soda-lime.

Metallic copper is used, while heated, to reduce oxides of nitrogen in the combustion-tube, this being necessary, first, to prevent error in estimating carbon by the absorption of carbon dioxide; second, to avoid loss of nitrogen in estimating this element by its volume when free. Coils of copper gauze or foil, or spirals of copper wire, are heated to redness in the air long enough to oxidize the surface, and then heated in a stream of hydrogen to reduce the oxide formed. For the reduction the coils are introduced into a combustion-tube having a tubulated stopper at each end, and a current of hydrogen passed through

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[1] Varrentrapp and Will, 1841: *Ann. Chem. Phar.*, 39, 257.

[2] *Am. Chemist*, 3, 161; 1879: *Am. Chem. Jour.*, 1, 77.

[3] "Equal weights of sal-soda, in clean (washed) large crystals, and of good white and promptly-slaking quicklime, are separately so far pulverized as to pass holes of $\frac{1}{16}$ inch, then well mixed together, placed in an iron pot, which should not be more than half filled, and gently heated, at first without stirring. The lime soon begins to combine with the crystal water of the sodium carbonate, the whole mass heats strongly, swells up, and in a short time yields a fine powder, which may be stirred to effect intimate mixture and to dry off the excess of water, so far that the mass is not perceptibly moist, and yet short of the point at which it rises in dust on handling. When cold it is secured in well-closed bottles or fruit-jars, and is ready for use" (*where last above cited*).

until the air is expelled, when heat is applied as the stream of hydrogen continues. Coarsely granulated copper oxide, reduced by ignition in a current of hydrogen, is employed to some extent instead of the spiral coils, and is more efficient than they. All copper reduced by ignition in a stream of hydrogen is liable to contain traces of occluded hydrogen, from which error may arise unless precaution be taken.[1] At ordinary temperature it quickly absorbs moisture from the air.

Copper gauze and wire are also used in the combustion-tube in methods of combustion of non-nitrogenous bodies, requiring only to be cleaned by a momentary ignition in the clear flame before use.

Solution of Potassium Hydrate. To absorb carbon dioxide in potash bulbs, good potassium hydrate nearly free from carbonate is dissolved in an equal weight of water. Some chemists use a solution in 2 parts of water; others a solution in $\frac{2}{3}$ part of water. The solution dropped into diluted mineral acid should not effervesce. It should be strictly free from nitrite. It is sometimes used a second time. —Solid hydrate of potassium is also employed for absorption in elementary organic analysis, taken either in stick or in lump, the drier the better.

Chloride of Calcium. For absorption of the water resulting from combustion, *dried calcium chloride* strictly free from alka-

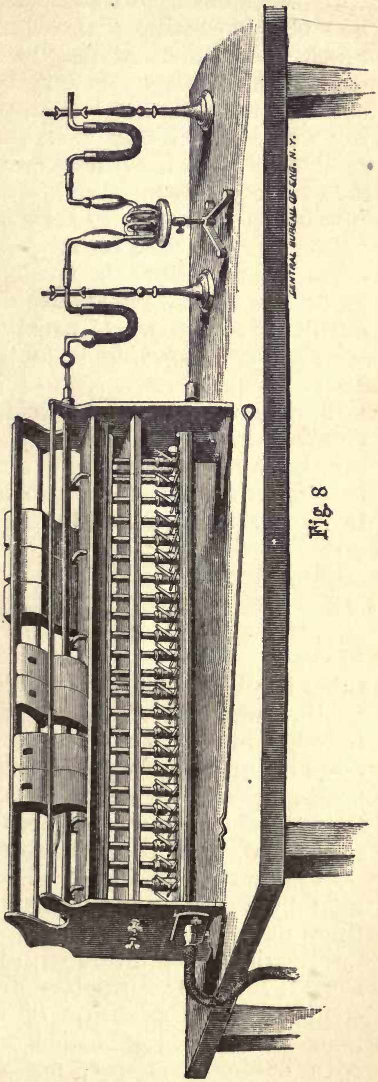

Fig 8

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[1] G. S. Johnson, 1876: *Jour. Chem. Soc.*, 29, 178.

line reaction is employed. In preparation the solution is stirred while evaporating, to granulate, and the residue dried at about 200° C. It consists of $CaCl_2.2H_2O$. The granulated form is much preferable. It may be tested, in concentrated solution, with litmus-papers. It may be prepared from crude fused calcium chloride by dissolving in lime solution, filtering, neutralizing with hydrochloric acid, evaporating to dryness, and heating as above directed. But to be well assured that the calcium chloride is free from uncombined bases, the operator should take the precaution to pass dried carbon dioxide through the filled chloride of calcium tube for an hour or two, and then a current of dried air to restore the normal weight of the tube.—For drying gases the crude, *fused calcium chloride*, in broken masses, is all that is required. It usually has an alkaline reaction.

Combustion-tubing is to be of hard potash-glass, mostly of 12 to 14 millimeters ($\frac{7}{16}$ to $\frac{1}{2}$ inch) inner diameter, and about 2 millimeters (not quite $\frac{1}{8}$ inch) thickness of glass. It is best obtained in lengths sufficient for two tubes—that is, in pieces mostly 5½ to 6½ feet long. For many purposes the combustion-tube is drawn out at one end, and preferably in bayonet form, as in Fig. 9. A section of tubing long enough for two combustion-tubes is readily so drawn and bent that when severed in the centre the two finished tubes are obtained. The edges are to be rounded in the flame. A combustion-tube is cleaned with a piece of muslin or paper attached to a stiff wire, and is dried by heating over a flame or on a water-oven, while from time to time the air is drawn out through a small tube carried in to the closed end, when it is well stoppered.

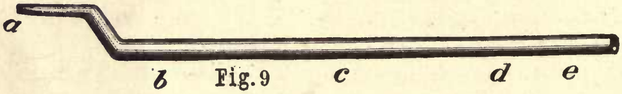

Fig. 9

Combustion-tubing of glass not sufficiently infusible may be used by wrapping it with copper gauze. Iron tubes are sometimes used, with special precautions, especially for nitrogen determinations by ignition with the soda-lime (CLOEZ, 1863; JOHNSON, 1879). A hard-glass tube may be used repeatedly for combustion in a stream of oxygen gas, and sometimes more than once for combustion with admixture of the substance with oxide of copper, not more than once for combustion with chromate of lead.

Chloride of Calcium Tubes, for the absorption of the water of combustion and for drying gases, are used of various patterns, including the one-bulb and two-bulb straight tube, and the U-tube with and without a bulb: Fig. 10, and in position in Figs. 8 and 16. The tubulated stoppers should be of rubber, or cork waxed over. An empty bulb in the horizontal part of the chloride of calcium tube has the advantage that it serves as a cup for a portion of the water which condenses in it, and the chloride of calcium the longer retains its power of absorption.—A tuft of cotton-wool is drawn into the tube, so as to rest firmly against and within the narrow part of the tube through which the current enters, when the fragments of calcium chloride are filled in, and at the other end a cover of cotton-wool or muslin is placed.—*Concentrated Sulphuric Acid* has been variously used, instead of calcium chloride, to absorb the water.[1]

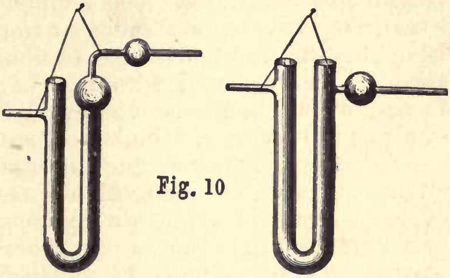
Fig. 10

Potash bulbs are of the two principal patterns, Geisler's, Fig. 11, which are to be preferred, and Liebig's, Fig. 12, which have long been used. When in use the larger bulb is placed next the combustion-tube. In being filled, the end which is nearest the combustion—the one into which the stream of gas is to enter—is inserted into the solution of potassa, and a sufficient amount of the liquid is drawn into the apparatus. The proper quantities of potash solution are shown in the figures.—Instead of a bulb apparatus for potash solution a large bulbed U-tube, filled with soda-lime, is sometimes used as an absorbent of the carbon dioxide of combustion.—*A potash tube*, either straight or

Fig. 11

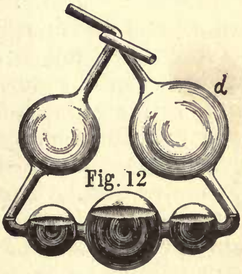

Fig. 12

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[1] Dibbits, 1876: *Zeitsch. anal. Chem.*, 15, 122; Morley, 1885: *Am. Jour. Sci.*, [3]. 30, 140; *Chem. News*, 54, 33.

U-form, filled with fragments of dry potassium hydrate or with granulated soda-lime, is used beyond the potash bulbs, and weighed with it. It guards against loss of water-vapor and of traces of carbon dioxide.

The Combustion-Furnace of ERLENMEYER is shown in Fig. 8, p. 205. It requires a good supply of gas. The combustion-furnace of GLASER, preferable for some combustions, is shown in Fig. 16. In the use of a gas combustion-furnace the supply of air must be regulated with that of gas to each burner. The furnace should be placed where it will be secure against currents of air or the access of acidulous or ammoniacal gases.

THE CONDITIONS OF SUCCESS in organic elementary analysis are attained by a watchful attention to details, with a faithful study of the sources of error, throughout the operation and in the preparation for it. The sources of error are so many that even an experienced operator, when commencing work with newly collected appliances, is quite liable to failure. When the work is well in hand, and operations upon material of known composition are made to succeed each other with almost invariable success, an important estimation may be undertaken with confidence in the result, but this is to be obtained as the mean of several nearly coinciding determinations.

ESTIMATION OF CARBON AND HYDROGEN IN BODIES NOT CONTAINING NITROGEN.—*Oxygen supplied by Copper Oxide. Analysis of Solids.—The substance to be analyzed*, obtained of exactly constant composition, in respect to hydration and freedom from all foreign matters, and (if pulverizable) in very fine powder, is introduced into a small weighing-tube—a light cylindrical container, with a caoutchouc or fine cork stopper, and of 3 to 6 c.c. capacity. For each elementary estimation from 0.3 to 0.4 gram is usually taken, and estimations may require repetition; therefore it is better to take from 2 to 4 grams of the sample at once in the weighing-tube, so that all the desired estimations can be made upon material of constant composition, without danger of loss or gain of moisture or other constituents. When it is desired closely to regulate the quantity of substance for each combustion, it is well to employ in addition a smaller weighing-tube to receive enough for one combustion, which is transferred from the larger weighing-tube. The management of liquids, soft solids, and very volatile matters is given hereafter (p. 213).

The charging of the combustion-tube, under whatever order of arrangements, is to be so effected that the entire contents of the tube—including the substance under analysis, the material supplying oxygen, oxygen gas, and atmospheric air—shall be strictly free from moisture before the combustion begins. To remove moisture and exclude it from the materials and the air entering into the combustion-tube, different orders of operation are adopted in different laboratories and directed by different authorities.

When the substance is not burned in a boat of platinum or porcelain, and when the oxygen is supplied by copper oxide, the work may be conducted as follows: The filled potash bulbs, dried with filter-paper at the ends and wiped clean, with the attached potash tube (if this be employed), are weighed, and both openings are afterward closed with sections of clean rubber tubing stopped with a bit of glass rod. The chloride of calcium tube is weighed, and its ends afterward closed. The weighing-tube, narrow and of considerable length, containing the substance for analysis, is weighed without opening it. There is provided granulated oxide of copper, which has been taken after ignition, and while warm, into a filling-flask,[1] as described on p. 202. The dry combustion-tube, with its drawn-out end sealed, is rinsed with some oxide of copper. About four inches (10 centimeters) of the body of the combustion-tube is filled with the oxide of copper, taken from the flask by the mouth of the tube. The substance is added, upon the layer of copper oxide, from the weighing-tube, which is introduced into the combustion-tube, avoiding the adhering of the substance to the inner surface. The weighing-tube is closed and put aside to weigh again. Another layer of oxide of copper equal to the first is taken into the combustion-tube, adding at first in such a way as to rinse the latter. With a stiff iron wire as long as the combustion-tube, bent in a single cork-screw turn at one end and in a ring at the other (Fig. 8), the substance is well mixed with the oxide of copper, leaving undisturbed about 4 centimeters (1½ inches) of the layer of oxide next to the bent end. Oxide of copper is added to fill to within about 6 centimeters (2½ inches) of the mouth. A porous plug of asbestos is added, leaving a good free space, to be kept clear of condensed water, between the asbestos and the tubulated caoutchouc stopper. If a cork stopper be used less space is required.

Another method of charging the tube, when copper oxide is the sole source of oxygen for combustion, provides for mixing

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[1] The copper oxide may be dried by ignition in the tube with advantage in this method as in others. The tube is filled with the oxide, then the open drawn-out end is connected with a set of drying-tubes, and dried air is either sent by a gasometer or drawn by an aspirator through the drying-tubes and the oxide of copper, while the latter is ignited.

the substance with some of the oxide of copper in a mortar of glass or unglazed porcelain. The warmed mortar is placed on a sheet of glazed paper on the table, and the oxide of copper is taken warm. Both the tube and the mortar are rinsed with some of the oxide of copper, and the rinsings put aside to be ignited again. After a layer of about an inch (2 centimeters) of the oxide of copper next to the bayonet-end of the tube, a mixture of the substance with oxide of copper is made by gentle trituration in the mortar, and added in such quantity with the mortar rinsings as will fill the tube to or a little beyond the middle of its body. The remainder of the tube is filled with the copper oxide to within about 2½ inches (or 6 centimeters) of the mouth, covering with a porous plug of recently ignited asbestos.

When the contents of the tube are in fine powder a channel for the easy passage of gases is made by tapping the tube upon the table as it lies in horizontal position. With granulated copper oxide, or that in coarse powder, a channel is usually to be avoided.

The removal of atmospheric moisture from the filled combustion-tube, when a gaseous supply of oxygen is not used, may be accomplished by attaching a drying-tube of chloride of calcium, and repeatedly pumping out the air, which is each time permitted to flow back through the drying-tube. A small exhausting-syringe may be used, or a filter-pump acting through a flask provided for the admission of air at will. But it is a more satisfactory way to pass a current of dried air, drawn by an aspirator or sent by a gasometer, through the tube from the drawn-out end, as directed further on to be done for another purpose after the combustion (p. 212). When the contents are dried the combustion-tube is kept closed by a caoutchouc stopper until connected with the weighed chloride of calcium tube and potash apparatus for the combustion.

Chromate of lead (p. 203) is used instead of oxide of copper for substances difficultly oxidizable, as well as when sulphur is present. In the charging of the tube it is used in the same manner as oxide of copper. Having a higher oxidizing power than copper oxide, a smaller quantity is required, and a narrower tube may be used. The contents of the tube should be dried the same as when oxide of copper is used.

Bichromate of Potassium, with *Oxide of Copper*, may be used as follows (Gintl, 1868): The combustion-tube is charged, first, with about 2½ inches (6 centimeters) length of granulated copper oxide; then with about 1¼ inches (3 centimeters) length of acid chromate of potassium which has been fused, pulverized, and kept dry; then the substance added from the weighing-tube, and again oxide of copper to make about 1¼ inches (3 centimeters). With the mixing wire (p. 205) the substance is well mixed, leaving undisturbed about half of the layer of copper oxide next the bayonet-end. The tube is filled with copper oxide; an asbestos support is placed, providing an open space next the tubulated stopper; and the contents of the tube are deprived of moisture, as before directed.

In making the combustion with oxide of copper, the combustion-tube is placed in the furnace with the end next the chloride of calcium tube projecting as far as the asbestos plug. A disc of copper foil may be employed as a shield over the tube to protect the stoppered end from too great heat. The tightness of the apparatus can be assured by expelling a little air, by heating the bulb of the potash apparatus nearest the combustion-tube until a few bubbles of air have escaped, when the liquid rises on the side heated and should then remain stationary. If the rubber connecting tubes are not snug they are bound with wire. The oxide of copper next the chloride of calcium tube is heated first, very gradually, to dull redness, and the heat is steadily carried toward the substance, not rapidly enough to cause a tumultuous escape of expanded air through the potash bulbs. At the end near the mouth the combustion-tube is maintained uniformly at a temperature high enough to prevent the condensation of water-vapor within, but not high enough to endanger melting the tubulated stopper if of caoutchouc, or charring it if of cork. The column of copper oxide, back to where the combustible substance begins to be intermixed, is held at dull red heat, not high enough to endanger blowing-out of the glass, while now the heat is carried very gradually back through the substance itself—so gradually that not more than one or two bubbles a second will pass the liquid in the potash bulbs. Certainly the bubbling should not at any time be too rapid to be counted. There should not be empyreumatic odor in the escaping air. When the air has been nearly all expelled, and the gas which passes out of the chloride of calcium tube consists mainly of carbon dioxide, the bubbles will pass through the last potash bulb only at considerable intervals, and these intervals will be longer if that portion of unmixed oxide of copper back of the substance be heated, as it may be in part and with caution, before the substance begins to burn. At the end of the operation all the contents of the tube are held at full heat. As the current of carbon dioxide ceases the liquid in the potash bulb next to the combustion-tube rises. Slight suction may now be applied to the potash tube.

At this time, or in anticipation of the time when the combustion with the copper oxide is completed, the heat is turned off under the rear end of the combustion-tube so that the drawn-out extremity is cooled, and this is then connected by a rubber tube with a set of tubes for thoroughly depriving air or oxygen of moisture and carbon dioxide. Such a set of tubes is described, together with the means of supplying oxygen and air, in the directions for combustion in a current of oxygen gas, following. The potash tube is connected with an aspirator, either the bell jar form shown in Fig. 16, or a bottle aspirator, serving not only as a pump but as means of regulating the flow of gases supplied, and of preventing recession of the current.

To remove now the carbon dioxide and water-vapor in the combustion-tube, and at the same time insure the absolute completion of the combustion, if oxygen gas has been provided, it is better to pass purified oxygen gas from the connection at the bayonet-end (Fig. 13) through the combustion-tube while it is heated. The connection is opened by breaking the point of the combustion-tube, in the rubber-tube, with a pair of pliers, and a sufficient stream of oxygen is passed. Now, as oxygen has a higher specific gravity than air, the former is to be removed from the absorption-tubes to be weighed, by washing it out with a stream of purified air. This is done by changing the connection from the oxygen gasometer to an air gasometer (the position of which is shown in Fig. 13), taking air through the same tubes for depriving it of carbon dioxide and moisture. Or, without a gasometer for air, the previous connection with the oxygen supply may be opened for the admission of air, purified as just stated, and drawn through by the aspirator, long enough to remove the oxygen. As soon as the stream of air is applied the heat may be diminished, turning it down very gradually to avoid the breaking of the combustion-tube.—*Without oxygen gas*, air

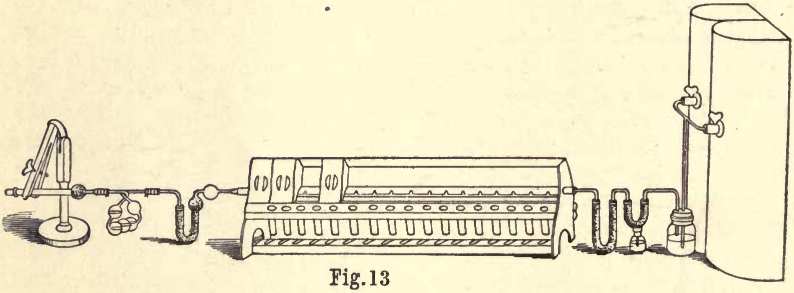

Fig. 13

dried and purified as above directed may be drawn through the combustion-tube while it is maintained at full heat, until the carbon dioxide is removed from the apparatus. *The combustion of a substance mixed with copper oxide and with a stream of oxygen* throughout the operation, as sometimes done, can be readily understood from the directions foregoing, together with those given in the following pages upon Combustion in a Platinum Boat with gaseous oxygen.—Again, some operators, with the benefit of experience, merely break the point of the combustion-tube in the open air, and draw through, by the aspirator or by the mouth, sufficient air to displace the gaseous content of the apparatus, as indicated by the bubbles no longer diminishing in size as they pass the potash bulbs.

The chloride of calcium tubes, and the potash bulbs with the potash tube, are at once closed with the caoutchouc caps, and are weighed without these additions.

With lead chromate the combustion is conducted so that the chromate between the substance and the mouth of the tube is not fused, but remains porous. The lead chromate intermixed with the substance is not fused at first, nor until the substance has all been heated; but it should be wholly fused at last, because it is a much more powerful oxidizing agent in the liquefied state.

The errors to be guarded against in combustion with oxide of copper or chromate of lead are those of too high figures for hydrogen and too low figures for carbon. With dry potash in the end tube, the use of an aspirator, and a stream of dry air to recover the carbon dioxide left in the apparatus at the close of the combustion, the loss of carbon may be avoided. To prevent an excess of hydrogen requires vigilance, its accomplishment lying mainly in the absolute removal of moisture before combustion.

It has been stated[1] that without the potash tube the carbon averages about 0.1% too low, while with the potash tube it averages near 0.05% too high; and that [without the substitution of dried air in the filled combustion-tube] the hydrogen averages 0.1 to 0.2% too high.

Liquids are weighed and introduced into the combustion-tube in glass bulbs. For volatile liquids these may be made by drawing out wide tubing, Fig. 14, the drawn-out portion being about 5 millimeters ($\frac{3}{16}$ inch) in external diameter, and in the wider portion about 3 centimeters ($1\frac{1}{4}$ inches) long. For either volatile or non-volatile liquids bulbs of the shape shown in Fig. 15

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[1] KEKULÉ's "Organische Chemie." 1867, i. 22.

may be employed. Bulbs are filled by passing through the flame to heat the air they contain, and then immersing the open end in the liquid, which presently rises to fill part of the tube. If the liquid be volatile, it may now be made to boil in the tube, when, the open end being inserted in the liquid, an additional quantity is obtained. If an open bulb be placed with its mouth under the surface of a liquid, and the whole put under an air-pump, on drawing out the air the liquid rises afterward in its place. Non-volatile and slightly volatile liquids are weighed and introduced into the combustion-tube in open bulbs; freely volatile liquids are weighed in sealed bulbs. In any case the weight of the empty bulb is taken before filling; and the capillary neck of the bulb is drained as fully as possible after filling. To seal the mouth it is held a moment in the flame, and when cool it is ready to be weighed.—The combustion of non-volatile liquids and soft solids is much better done with a stream of oxygen gas, in a platinum boat. The products of destructive distillation are burned almost as fast as formed, the substance itself being heated very gradually. On the other hand, when freely volatile bodies are burned in oxygen gas, care is required, owing to some liability of explosion in the combustion-tube. The use of oxygen gas to complete the combustion of the carbonaceous residues of volatile substances is, however, always desirable. And Warren[1] has presented a method of burning volatile bodies with oxygen gas, by means of a combustion-tube packed with asbestos, the heat being applied and the combustion effected only in the anterior end of the tube, while the substance is vaporized in the posterior end. A long combustion-tube is used, and the column of porous asbestos packing acts like the gauze of Davy's safety-lamp.—In filling the combustion-tube, when liquid or volatile bodies are to be burned with copper oxide, the coarsely granular oxide is taken, a layer of about two inches of the same is placed at the posterior end, the substance contained in two bulbs is introduced with some copper oxide between them, while the combustion-tube is upright, and the tube is filled up with copper oxide. If the bulbs have been sealed, a file-mark is made upon the neck, which is broken as the bulbs are dropped into the tube. Very volatile substances are sometimes introduced in small por-

Fig. 14

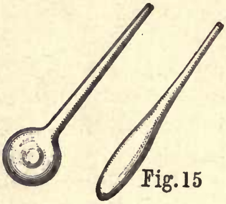

Fig. 15

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[1] 1864: *Chem. News. Zeitsch. anal. Chem.*, 3, 272.

tions, in several very thin bulbs, which, by holding a hot clay

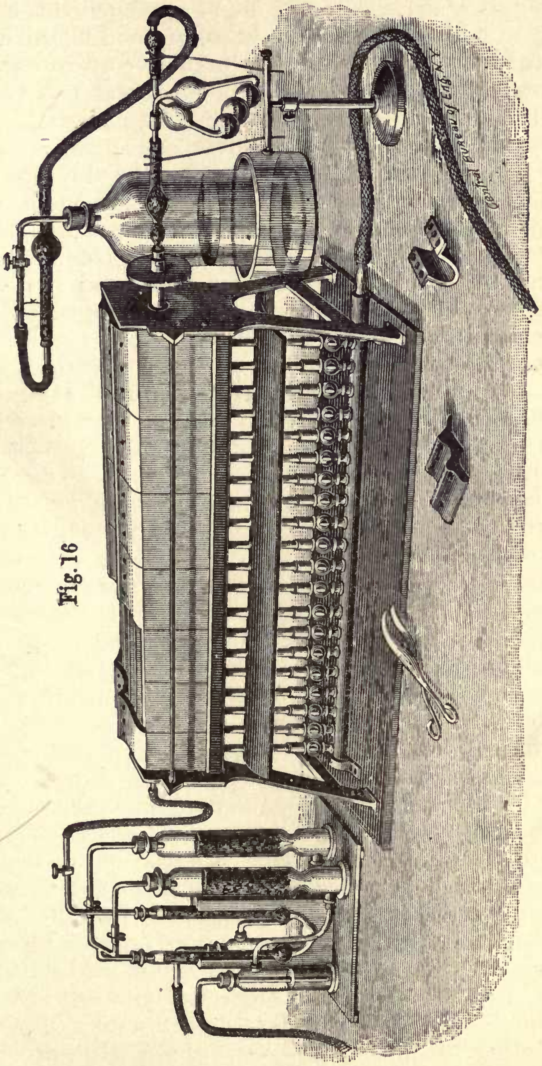
Fig. 16

shield near, are made to burst in the filled combustion-tube, either while only copper oxide in the front is heated, or before heating at all. Less volatile liquids, introduced in open tubes, may be intermixed with the oxide of copper by applying a single stroke of the exhausting syringe to the filled combustion-tube, causing the liquids to boil. Combustion-tubes of good length and width are required, with evenly coarse granular copper oxide filling the tube without a channel. Care is exercised to avoid explosions and the escape of unburned vapor. It is desirable to shield the combustion-tube under a firm cover of copper gauze.

Gaseous bodies are subjected to the special methods of Gas Analysis for elementary estimations. These methods depend mostly upon volume measures of the gases, with measures of the residues after their absorption, and the products of their combustion. Such a volume measure of the residue after absorption is made in the chief method of the analysis of solids for nitrogen, as described in the pages following. In the first elementary analysis of fixed bodies, by Lavoisier, the products of the combustion were measured in volume for the calculation of weight. Methods of organic analysis for carbon, founded on gas measurements, have been reported upon by Schulz (1866) and others. Gases may be subjected to the method employed for the relative determination of the carbon and nitrogen of fixed substances, by volume measurement after combustion, as devised by Liebig, Bunsen, Marchand, and others.

The combustion in a platinum boat, with gaseous oxygen and copper oxide, may be conducted, for a non-volatile substance, as follows: The furnace should have a secure, level, concave support for the combustion-tube. The furnace of Glaser (Fig. 16) has gutter-shaped iron supports, which may be placed together to form a continuous canal. The combustion-tube, of 12 or 14 millimeters (near ½ inch) internal diameter, and preferably 4 or 5 centimeters (1½ or 2 inches) longer than the furnace, is open at both ends, with fused edges and tubulated rubber stoppers. The platinum boat is of size to easily enter the tube. The oxide of copper, granulated, is taken cold. Copper gauze and wire are provided, the gauze in pieces about 2 centimeters (¾ inch) wide, rolled in plugs large enough to fit with easy friction in the combustion-tube, and cleaned by momentary ignition in a Bunsen flame. One of these plugs is pushed about 25 centimeters (10 inches) into the tube; from the other end the coarsely granular copper oxide is filled to within 6 to 8 centimeters (2 to 3 inches) of the opening, settling it by very slight tapping, following which is inserted another plug of the copper gauze of sufficient length, leaving a free space between it and the rubber stopper.[1]

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[1] A spiral of copper wire is used, forward of the plug, by some chem-

A shield of copper foil is put over this end (Fig. 16). A piece of copper gauze about 10 centimeters (or 4 inches) wide is rolled about a stiff copper wire of sufficient length, doubling a bit of the wire down firmly upon the first turn of gauze, and rolling the gauze to make a plug to fit the tube easily, when the free end of the wire is bent, forming a ring which will enter the tube, in which it is placed after igniting it for a moment.—*The gasometers* for oxygen and for air are filled, and connected with an *apparatus for removing moisture and carbon dioxide.* Each gasometer may be connected with a separate bottle of potassium hydrate solution, from which both connections may lead to a single deep U-tube filled with coarsely granular soda-lime, and then successively to three deep U-tubes filled with small lumps of dry fused calcium chloride. A U-tube containing pumice-stones wet with concentrated sulphuric acid may also be interposed at any point after the soda-lime. See Fig. 16. A mercury-valve (Fig. 17) is sometimes interposed between the combustion-tube and the purifying apparatus to prevent diffusion of products of combustion backward. A good chloride of calcium U-tube, with bulb on the horizontal part next the combustion, is filled; also the Geisler potash bulbs (Fig. 11) with the potash tube; and a bell-jar aspirator (Fig. 16) is provided, carrying a chloride of calcium tube.

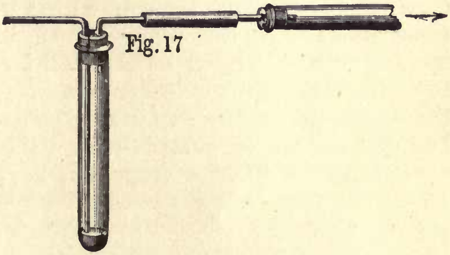

Fig. 17

The apparatus being put in place with the combustion-tube over the furnace, without the platinum boat, the tube is heated up throughout, and a slow current of the dry air is transmitted through the combustion-tube alone. Meanwhile the calcium chloride tube and the potash bulbs and tube are weighed without their caps, and then closed. When the column of copper oxide has been heated for ten or fifteen minutes the heat is turned down, the platinum boat is ignited and then cooled in a desiccator and weighed, and from 0.3 to 0.5 gram of the substance is trans-

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ists. All the metallic copper becomes coated with copper oxide during the heating in the stream of oxygen or air, and the copper oxide so formed makes an efficient oxidizing agent for the gaseous products of incomplete combustion. However this anterior end of the tube be filled, it is advisory to have a free space of 2 or 3 centimeters (an inch or more) next the caoutchouc stopper.

ferred to the boat. The weight may be taken in the boat, or, if the substance be affected in any way by exposure, the substance is added from a stoppered tube, weighed before and after it is taken (p. 208). The air-current is stopped; the chloride of calcium tube and the potash bulbs and tube are securely connected by caoutchouc tubes of clean inner surface, and the aspirator is connected in place. The stopper at the posterior end of the combustion-tube is taken out and the copper-gauze cylinder withdrawn, the platinum boat is inserted in its place near the short copper-gauze plug, the cylinder and posterior stopper replaced, and the connections made with the purifying apparatus and gasometers. The aspirator-valve is opened a little, a few burners nearest the chloride of calcium tube lighted and gradually turned up, and the heat increased to dull redness, not sufficient to distort the tube, and extended back to a safe distance from the gauze plug—governing the aspirator to take out the expanded air. The diminished gaseous tension within the apparatus tightens the connections. A difference of 12 to 15 centimeters (about 5 inches) in water level of the bell-jar aspirator is usually maintained. The gauze cylinder is now gently heated, and at about this point the stream of air may be exchanged for one of oxygen, running at first not faster than a bubble every two seconds. The space next the anterior stopper is kept dry without softening the rubber, and the heat is brought back to within 4 or 5 centimeters (1½ or 2 inches) of the platinum boat, when a gentle heat is turned up directly underneath the substance. The progress of the combustion is observed, and the heat so regulated by the changes in the substance and the bubbling in the potash bulbs as to obtain a gradual and even progress. When the substance is completely charred, and the bubbling through the potash solution abates, the heat under the boat is increased and the flow of oxygen quickened to about one bubble per second. The exchange of oxygen for air may be delayed till the substance is charred. When the carbonaceous matter in the boat has disappeared, the heat underneath it is lessened and the stream of oxygen quickened; soon after which the heat is partly turned down all along the tube, and the stream of oxygen exchanged for one of air. In a few minutes now the gasometer and aspirator may be shut off, and the potash bulbs and tube and the chloride of calcium tube at once detached, closed at their openings, wiped, and weighed (without their caps). The platinum boat may be weighed for estimation of ash. The combustion-tube is cooled very gradually, and is at once ready for another combustion, with the same copper oxide, free from moisture. The water in the bulb of the chloride of calcium tube is examined as to its purity, freedom from empyreuma, etc.

Liquid substances are weighed in bulbs or small tubes, as described on p. 213, placed upon the platinum boat, and subjected to combustion as above directed. *Volatile substances* are expelled from the bulbs containing them before the posterior portion of the copper oxide is heated, a hot clay shield being held over the boat for that purpose. The relations of these substances to elementary analysis have been stated further on p. 214.

ESTIMATION OF CARBON AND HYDROGEN IN NITROGENOUS COMPOUNDS.—The presence of nitrogen requires only such a change in the conditions of the combustion as shall prevent acidulous oxides of nitrogen being formed and carried into the potash bulbs to increase their weight. This is done by passing the products of combustion over metallic copper at red heat. The preparation of copper for this purpose is described on p. 204.

In combustion of nitrogenous compounds *with copper oxide*, as directed on pp. 208, 211, the combustion-tube is to be 12 to 15 centimeters (about 5 inches) longer than required for a non-nitrogenous body. A roll of copper foil about 12 centimeters (near 5 inches) long is prepared as directed on p. 217, heated in hydrogen gas (p. 204), and placed in a drying-oven at 100° C. The combustion-tube is filled in the ordinary way, leaving room for the gauze roll, which is introduced while warm from the drying-oven. Before the mixture of substance and copper oxide is heated in the tube the metallic copper is brought to a bright red heat, and so maintained during the combustion. If gaseous oxygen be supplied at the close of the operation, it is supplied sparingly, so as not to oxidize all the metallic copper until, near the close of the combustion, the nitrogen shall have been expelled, and only carbon remain to be burned.

In combustion of nitrogenous bodies, for carbon and hydrogen, *in a stream of oxygen gas*, the gauze copper roll of about 12 cm. length, as above described, is inserted in a space left for it in the anterior end of the combustion-tube (p. 216), chosen longer on this account. The copper oxide is first dried, in the heated tube, in a stream of dry air (p. 202); then the air is turned off, the roll of metallic copper warm from the drying-oven introduced into its place, the platinum boat with the substance inserted, the connections made, and the combustion commenced. The stream of air is not changed for one of oxygen until the continuance of the combustion demands it; and neither is used in such excess that the metallic copper becomes oxidized before the nitrogen has all passed out. To burn out the last traces of carbonaceous residue the stream of oxygen may be used freely. The roll of metallic copper is used but once.

ESTIMATION OF NITROGEN IN CARBON COMPOUNDS.—*Absolute determination by volume of the gas.* Of various serviceable methods for this estimation, the following are here presented:

Method of JOHNSON *and* JENKINS,[1] based in good part upon Dumas's Method.—The substance is burned in mixture with copper oxide, and, by help of oxygen generated from potassium chlorate, put in the rear of the combustion-tube, the gaseous products being all carried through a porous column of heated metallic copper of length sufficient not only to deoxidize nitrogen oxides but to absorb all the excess of oxygen. A short layer of heated copper oxide, front of the metallic copper, oxidizes any hydrogen held occluded by the metallic copper, also traces of carbon monoxide formed by the metal. The gases are received in a measuring-tube (azotometer), over potash solution, which they pass through, and which absorbs all carbon dioxide, nitrogen being left alone as a permanent gas, measured for quantity. Between the combustion-tube and the azotometer is introduced a mercurial air-pump, by which the combustion-tube is first fully exhausted of air before the combustion, and by which the gaseous products left in the tube after combustion are drawn out and delivered to the azotometer.[2] During the combustion the gases pass through the pump to the azotometer. After the initial exhaustion of the combustion-tube, carbon dioxide is generated in it by heating a short column of sodium bicarbonate placed in the very front of the tube, this carbon dioxide, like that formed in

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[1] S. W. JOHNSON and E. H. JENKINS, 1880: *Am. Chem. Jour.*, **2**, 27; *Zeitsch. anal. Chem.*, **21**, 274; *Chem. News*, **47**, 146. A valuable report on Prof. Johnson's method is given from continued experience in its use, in comparison with the Ruffle Method, by C. S. DABNEY, JR., and B. VON HERFF, 1885: *Am. Chem. Jour.*, **6**, 234. Also, valuable improvements in the pump, and a modification of the charging of the combustion-tube by T. S. GLADDING, 1882: *Am. Chem. Jour.*, **4**, 42 (illustrated). The "Official Methods of the Association of Agricultural Chemists for 1886–7" are given in *Bulletin No.* 12, *Department of Agriculture*, Washington, 1886, p. 52. Modifications of Dumas's Method are also given by G. S. JOHNSON, 1884: *Chem. News*, **50**, 191; *Jour. Chem. Soc.*, **48**, 189; and by ILINSKI (with ordinary laboratory apparatus), 1884: *Ber. d. chem. Ges.*, **17**, 1347; *Zeitsch. anal. Chem.*, **24**, 76.

[2] DABNEY (see last foot-note) says: "For getting the air, before combustion, and the nitrogen afterward, out of the tube, we have used carbon dioxide without a pump and have obtained excellent results. . . . Magnesite or manganese carbonate, put in the back end of the tube, are the best sources for this purpose. [See, following, SIMPSON's Method.] But more time is consumed in this way than with a *good*, fast-working, tight pump."

combustion, being taken up in the azotometer by the potash solution.

The copper oxide is directed to be made by heating copper scale with 10 per cent. of potassium chlorate and enough water to make a thin paste, stirring till dry, and igniting until the mass does not glow when stirred. The potassium chloride is to be washed out by decantation, and the copper oxide dried and moderately ignited. *Metallic copper* is used as fine copper gauze in rolls to fit the combustion-tube, or as granular oxide of copper reduced and cooled in a stream of hydrogen (p. 205). *Potassium chlorate* is prepared by fusing the commercial article in a porcelain dish and pulverizing when cold. *Sodium bicarbonate* is used, and must be free from organic matter. *Solution of potassa* is made by dissolving commercial potash in sticks in less than its weight of water, and permitting the excess to crystallize out when cold. The same solution may be used a number of times.—*The combustion-tube*, of best hard glass, should be about 28 inches (71 centimeters) long. The rear end is bent and sealed as in Fig. 20. It is best to protect the horizontal part with thin sheet copper or copper gauze, as directed further on.

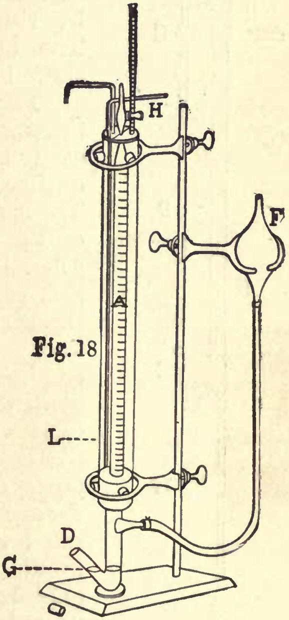

Fig. 18

The azotometer, Fig. 18, is a modification of SCHIFF's.[1] The gas is measured in an accurately calibrated burette, A, of 120 c.c. capacity, graduated to fifths c.c., and closed at the upper end by a glass stop-cock. The lower end is connected, by a perforated stopper about $1\frac{3}{4}$ inches (4.5 centimeters) long and $1\frac{1}{2}$ inches (3.8 centimeters) in diameter, with another tube, which has two arms, one, D, to receive the delivery-tube from the pump, the other to connect by a rubber tube with the bulb, F, of 200 c.c. capacity, for the supply of potash solution. The burette is enclosed in a water-jacket of about $1\frac{3}{4}$ inches (4.5 centimeters) external diameter. Its lower end is closed by the rubber stopper that connects the burette with the two-armed tube below. The upper end of the

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[1] 1868: *Zeitsch. anal. Chem.*, 7, 430. See also *ibid*, 1881: 20, 257.

jacket is closed by a thin rubber disk slit radially and having four perforations: one in the centre admitting the neck of the burette, and three others near the circumference. Through one of the latter a glass tube, L, bent as in the figure, reaches to the bottom of the jacket, another short tube passes through the disk (these tubes conveying water to and from the jacket), and the third hole supports the thermometer. The azotometer is held upright and firm on a stand by rings fitted with cork wedges around it. The bulb for the potash solution rests in a slotted sliding ring.

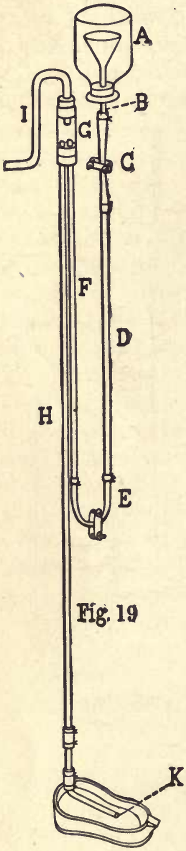

Fig. 19

The air-pump[2] used by Prof. Johnson is a Sprengel mercury-pump, modified so as to be easily constructed and durable. It is shown in outline, with some parts enlarged, in Fig. 19. Through a rubber stopper wired into the nozzle of the mercury reservoir, A, passes a glass tube, B, 4 inches (10.2 centimeters) long, and this connects by a stout rubber tube, C, with the straight tube, D, 3 feet (91.4 centimeters) long. The stout rubber tube, E, 6 inches (15.2 centimeters) long, connects D with a straight glass tube, F, of about the same length as D. G is a piece of combustion-tubing, 1½ inches (3.8 centimeters) long, closed below by a doubly perforated soft rubber stopper admitting the tubes F and H, and above by the singly perforated rubber stopper into which the tube I is fitted. The tube H has a length of 45 inches (114.3 centimeters). At the bottom it is connected by a fine black rubber tube (previously soaked in melted tallow) with a straight tube of 3 inches (about 7 centimeters), and this again in the same way with the tube K, of 7 inches (about 18 centimeters) length. The tubes H and K should have an internal diameter of 1.5 millimeters, F may be 2 millimeters, and D still larger. For H and F may be used slender Bohemian glass tubes of 4 millimeters external diameter. Their elasticity compensates for their slenderness. If heavy barometer tubes be used the stoppers and G must be of correspondingly larger dimensions. The joints at G must

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[2] A mercurial pump for nitrogen is also figured and described by DABNEY, 1885: *Am. Chem. Jour.*, **6**. 236.

be made with the greatest care. It is best to insert the lower stopper for half its length into G, and F and H should fit so snugly as to be inserted with effort when oiled. The tube I must be of stout glass, about a centimeter (0.4 inch) in diameter, and drawn at both ends to a gradual taper, the outer end bent to connect with the combustion-tube, the inner end when oiled turned into a perforation of about 0.5 centimeter (0.2 inch) in the upper stopper. The joints entering G are the only ones having to resist pressure into vacuum, and they must be made with the utmost care. If not secure without, they are to be trapped with glycerine. To do this pass F and H through a stopper of ½ inch (or 13 millimeters) greater diameter than G and placed below it, when, before inserting I, a jacket-tube 4 inches (10 centimeters) long is fitted upon this stopper, surrounding G. After I is inserted the trap is ready, to be filled with concentrated glycerine, which is preserved from dilution by adding a stopper to the outer tube, around I, split in halves for adjustment.—The two rubber tubes are both provided with efficient screw-clamps to govern the flow of mercury.—The tubes D, F, H, and I are secured by cork clamps and wires, or otherwise, to an upright plank, which is framed below into a heavy horizontal wooden foot on which rests the mercury-trough. The plank carries above a horizontal shelf for the support of the reservoir, A, the neck of which rests in a perforation in the shelf. At the fastenings of the tubes upon the upright support thick rubber tubes are interposed as elastic rests. The rubber tube joints should be wound with waxed silk. A glass funnel is used in A to prevent spattering of the mercury.

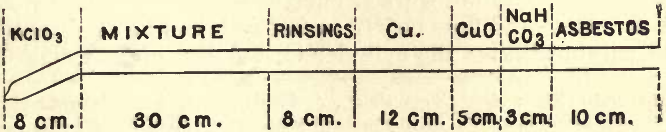

Fig. 20

The combustion-tube is charged as follows: Of the potassium chlorate from 3 to 4 grams, according to the amount of carbon to be burned, are placed in the tail of the tube, Fig. 20, followed by a plug of ignited asbestos just at the bend. Of the substance under analysis 0.6 to 0.8 gram, from the weighing-tube, is well mixed in a mortar (previously rinsed with the copper oxide) with dry (recently ignited) oxide of copper enough to fill 11 or 12 inches (28–30 centimeters) of the tube, and the mixture introduced through a funnel. The rinsings of the mortar with oxide of copper are added to fill about 3 inches (7.6 centimeters) of the tube, and a second asbestos plug placed. On this is placed the reduced copper for 4 or 5 inches (10 or 12 centimeters), then a third asbestos plug, then 2 inches (5 centimeters) of the copper oxide, and a fourth plug of asbestos, followed by 0.8 to 1.0 gram of the sodium bicarbonate.[1] The remaining space is loosely filled with asbestos to take the water of combustion and prevent it from flowing back upon the heated glass. The anterior part of the tube is wound with copper foil, leaving the rear of the metallic copper visible. The filled combustion-tube is placed in the furnace, on a level with the tube, I, of the pump (Fig. 19), and carefully connected with the latter by a close-fitting rubber stopper moistened with glycerine.—*The azotometer is prepared and tested as follows:* The bottom is filled with mercury to about the level indicated by the dotted line G (Fig. 18). The arm D is securely closed by a rubber stopper. The stop-cock H is greased, the plug inserted, and the cock left open. The potash solution is poured into F until A is nearly full, and some solution remains in the bulb F, which is now raised carefully in one hand, while the other hand is upon the stop-cock H. When the solution has risen in A very nearly to the glass cock, the latter is closed, avoiding contact of the alkali with the ground glass bearings, when the bulb is replaced in the ring and lowered as far as may be. If the level of the solution in the azotometer does not fall in 10 or 15 minutes, it is tight.—*The pump is set in operation* by putting its delivery-tube K in a trough of mercury, supplying the reservoir, A, with at least 500 c.c. of mercury, and cautiously opening the clamps C and E. If the mercury does not start at once, repeatedly pinch the rubber at E. It should flow nearly as fast as it can be discharged at K, and without filling the cylinder G. A complete exhaustion

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[1] GLADDING (1882: *Am. Chem. Jour.*, 4, 45) dispenses with chlorate of potash, and puts about 0.6 gram bicarbonate of soda in the tail of the tube (1). The space 2 is filled with about two inches of ignited asbestos. The substance at 3 is mixed with copper oxide, as fine as sea-sand, without dust. At space 4 is another 0.6 gram of the bicarbonate; then is placed a layer of copper shot, and again a layer of coarsely granulated copper oxide (6). The analysis is begun by drawing the potash solution nearly to the top of the azotometer, then turning up lamps under 6, and at the same time starting the pump. When a perfect vacuum has been obtained and the copper oxide (6) is red hot, the lamp just beyond 1 is turned up, and a gentle heat, just sufficient to drive off the carbon dioxide from it and not to heat space 3, is applied. When the tube is full of carbon dioxide this lamp is turned off and the tube again exhausted. By this process of washing out the tube several tenths of a c.c. of additional gas are obtained and almost the last traces of air removed. On running the heat back the bicarbonate at 4 gives off carbon dioxide, and refills the tube before the combustion of the substance at 3 begins.

of the combustion-tube can generally be obtained in 5 to 10 minutes' working of the pump. If the mercury becomes expended before the desired exhaustion is obtained, the clamp C is closed and the mercury returned to A. Complete exhaustion is denoted by a clanking or rattling sound of the falling mercury, and a half a minute after this is heard the clamp C may be closed. If the mercury column in H remains stationary for some minutes, the connections are tight. The mercury trough is closed and the tube K placed in a capsule.—Before *connecting the azotometer*, heat is applied to the part of the combustion-tube containing the bicarbonate of sodium. Water-vapor and carbon dioxide are evolved, filling the vacuum in the pump and displacing the mercury in the tube H. The azotometer is placed at hand, its bulb F is taken from the ring and supported in a box near the level of the tube D, the stopper of which is now removed without greatly changing the level of the mercury (G). The tube D is filled half full or more with water. As soon as the mercury has fully escaped from the pump-tube K, this is inserted in the azotometer-tube D. A few bubbles are allowed to escape through the water, and then the tube K is passed down so that the gas escaping from the pump enters the azotometer. It will facilitate the delivery of the gas if the extremity of the pump-tube just touches the inside of the azotometer-tube, as near as possible to the surface of the mercury. The carbon dioxide is absorbed in passing through the caustic potash solution, and no permanent gas should be obtained. In spite of all precautions very minute bubbles of permanent gas will occasionally ascend, but, as will be seen on observing the amount of potash solution so displaced, the error thereby occasioned is extremely small.

In the combustion the anterior cupric oxide is first heated to full redness, and then the metallic copper. Then the combustion of the substance is steadily carried on, so that the flow of gas into the azotometer is about one bubble a second, or a little faster. When the horizontal part of the tube has all been heated, and the evolution of gas has nearly ceased, the potassium chlorate is heated so as to boil vigorously with generation of oxygen. Any remaining carbon of the substance now burns rapidly, and the reduced copper oxide is promptly reoxidized. When the layer of metallic copper in the anterior part of the tube begins to be oxidized, the generation of oxygen is stopped and the heat lowered all along the tube, keeping the metallic copper still at faint red heat. After a few minutes now the pump is started, slowly at first, having some vessel under the azotometer-tube D to receive the mercury. A few minutes' pumping suffices to clear the tube, full exhaustion being indicated as stated on p. 225.[1]

The azotometer is now removed from the pump, the azotometer-tube D is closed by its rubber stopper, the bulb (F) is raised in its ring to such a height that the potash solution in it is nearly on a level with that in the burette, the filling-tube L is connected with water-supply, a thermometer is inserted in the top of the water jacket, and the water allowed to run until the temperature and the volume of the gas are constant. The level of the solution in the bulb is now accurately adjusted to that in the burette, and the temperature and the volume of the gas are read, as also the height of the barometer.—When 50 per cent. potash solution is used no correction for tension of aqueous vapor is used by Prof. Johnson, following the authority of Schiff.[2]

The volume read off is *reduced to volume at* 0° C. by dividing by 1 + (degrees temperature C. observed × 0.003665). That is, $\frac{\text{c.c of observed volume}}{1 + (\text{observed temp. C.}^\circ \times 0.003665)} = \text{c.c. volume at } 0^\circ \text{C.}$

The volume at observed barometric pressure is *reduced to volume at* 760 *millimeters barometric pressure* by the (inverse) proportion, 760 : mm. of observed pressure :: c.c. observed vol. : $x =$ c.c. at 760 mm.

At 0° C., and 760 mm. bar., 1000 c.c. of (dry) nitrogen weigh 1.25616 grams.

The corrections, therefore, may be stated: $\frac{\text{mm. bar.} \times 0.0012562}{(1 + 0.00367\ T)\ 760} =$ gram weight of 1 c.c. at T temperature. The value of this fraction is given in a table for T 0° to 30°, by J. T. Brown: *Jour. Chem. Soc.*, [2], 3, 211; *Watts's Dict. Chem.*, vi. 147.

Correction for temperature, pressure, and water-vapor tension is made by the formula:

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[1] See Gladding, under p. 224.

[2] Hugo Schiff, 1868: *Zeitsch. anal. Chem.*, 7, 432. This author found in several determinations that air dried by passing through a 50 per cent. potash solution, at 24° C., still contained only 108 to 113 milligrams water in 19 liters. This would give to nitrogen a reading about 0.007 of its volume too high. His determinations of nitrogen, by his procedure in the absolute method, were uniformly a little too low, thus: 12.9 instead of 13.2; 31.4 instead of 31.8; 9.0 to 9.1 instead of 9.1; 3.8 to 3.9 instead of 3.9. The deficiency he ascribed to retention of traces of nitrogen oxides. And the author advises to neglect the correction for aqueous vapor, in compensation for the margin of loss.

$$P = 0.0012562 \times V \times \frac{1}{(1 + 0.00367\ T^\circ)} \frac{B-f}{.\ 760}$$

Wherein P = the grams weight of the nitrogen measured.
V = c.c. of observed volume.
T° = temperature of the azotometer-jacket in degrees C.
B = millimeters of barometric reading.
f = tension of water-vapor, at T°, found in millimeters.

Of the tables convenient for consultation, to shorten calculations for nitrogen, are those of Battle and Dancy, for use in Analysis of Commercial Fertilizers, 1885: North Carolina Experiment Station, Raleigh, N. C. Also, for general uses, Kohlman und Frerichs, "Rechentafeln," 1882: Leipzig.

The correction for water-vapor tension is purposely neglected by some chemists, on the ground (already mentioned) that strong potash solution leaves the gas nearly dry.[1] On the other hand, the results by Johnson's procedure in absolute method for nitrogen are more apt to be over than under the true quantity (see the citation from Dabney, under Ruffle's Method). When the correction is required it is made as follows: Consult a table of Tension of aqueous vapor at various temperatures (this tension being irrespective of pressure), and find the tension, in height of mercury, for the observed temperature. Subtract this tension from the barometer reading in the operation in hand, as in the formula above.

Method of Maxwell Simpson (1855).—Combustion by a mixture of copper oxide with mercury oxide, the tube having been cleaned of air by a current of carbon dioxide liberated by heating a carbonate. The excess of oxygen is taken up by a good quantity of heated metallic copper in the combustion-tube; the carbon dioxide by potash solution in a receiver; and the nitrogen is measured over mercury for the calculation of its weight. The mercuric oxide is to be prepared by precipitation with fixed alkali, washing with water and then with dilute phosphoric acid, and drying at 100° C.—The combustion-tube, about 80 centimeters (31.5 inches) long, is closed in a rounded end by fusion.

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[1] Owing to the fact that the strength of the potash solution varies, and the water-vapor tension is therefore uncertain, Galterman (1885) collects the nitrogen over potash solution in a non-calibrated tube, thence transferring it to a measuring-tube over distilled water. The full tension of the water-vapor is deducted.

A mixture of 12 grams of manganese carbonate or of magnesite, previously dried at 100° C., with 2 grams of the mercuric oxide, is introduced into the tube. A plug of recently ignited asbestos is inserted, pushing it down to within 3 centimeters (about 1 inch) of the mixture, and next is added 1 gram of the mercuric oxide. Of the substance under analysis about 0.6 gram is taken, from a weighing-tube, for intermixture in a mortar with 45 times its weight of a prepared mixture of 4 parts of finely powdered and recently ignited copper oxide, with 5 parts of the dried mercuric oxide. The whole is transferred to the combustion-tube, the mortar is rinsed with some more of the mixed oxides, and the rinsings added. A second plug of ignited asbestos is pushed down to within about 30 centimeters (near 12 inches) of the first, leaving the mixture of oxides loose; a layer of 6 to 9 centimeters ($2\frac{1}{2}$–$3\frac{1}{2}$ inches) of the copper oxide is added and a third plug of asbestos placed; and lastly a layer of as much as 20 centimeters (near 8 inches) of metallic copper, prepared by reducing granular copper oxide in a stream of hydrogen at low temperature (or in a stream of carbon monoxide). The combustion-tube is now drawn out and turned down, and connected by a section of rubber tubing with a delivery-tube adapted to reach beneath the surface of mercury in the trough. The combustion-tube is tapped on the table to form a channel for the escape of the gases, and placed in the furnace.—A receiver is provided, as shown, with the trough of mercury, in Fig. 21. The receiver has about 200 c.c. capacity; the glass stop-cock should enable it to hold mercury when filled with it and set up in place; a delivery-tube is firmly connected with its neck, and it is tubulated on the side near its base. This tubule carries an upright filling-tube, with contraction near the tubule. It is filled with mercury, placed in the trough with the tubule under the mercury, and about 20 c.c. of strong solution of potassium hydroxide passed into it. A measuring-tube for the nitrogen gas is represented in Fig. 22. But instead of both the receiver and measuring-tube here described, the azotometer figured on p. 221 may be used.

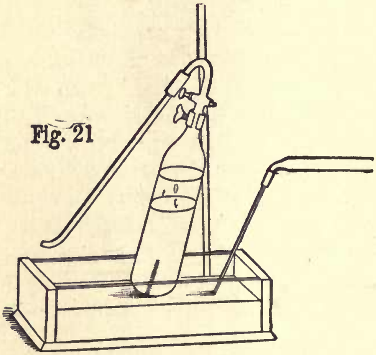
Fig. 21

About half of the carbonate in the posterior end of the combustion tube is heated, so that the air is driven out by a current of carbon dioxide; and at the same time a part of the tube occupied by the metallic copper and the copper oxide is heated. The escaping gas is tested for air, from time to time, by receiving a few bubbles in an inverted test-tube containing solution of potash; and when the bubbles are completely taken up by the solution, and the anterior part of the tube is well heated, the delivery-tube from the combustion is inserted in the lateral tubule of the receiver. The substance in mixture with the oxides is now gradually heated, beginning next the clear copper oxide, until the whole tube, except that occupied by carbonate in the rear, has been at full heat, and no further delivery of gas is observed. Next, the remainder of the carbonate is heated, so as to sweep out the nitrogen remaining in the tube. The delivery-tube is now withdrawn from the receiver, which is left for an hour for the absorption of the last traces of carbon dioxide.

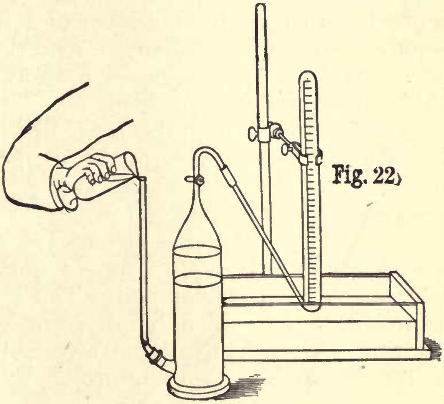
Fig. 22.

The nitrogen gas is transferred to the measuring-tube, Fig. 22. The stopper inserted into the lateral tubule of the receiver is moistened with mercuric chloride solution to prevent its carrying in air. A drop of water is placed in the measuring-tube before it is filled with mercury and inverted in the cistern. The stop-cock in the neck of the receiver is carefully governed to obtain a very gradual delivery of the gas, and is closed each time that the mercury is poured into the filling-tube, below the contraction in which the mercury is not permitted to fall in the beginning of the transfer. Close the stop-cock as soon as it is reached by the potash solution, leaving the nitrogen in the delivery-tube to compensate for the air it contained to begin with.

For calculation of weight from volume, with corrections for temperature and pressure, see p. 226.

A VERY SIMPLE METHOD FOR ABSOLUTE DETERMINATION OF NITROGEN, when carefully conducted, will give good results.

An operation as follows, with copper oxide as the sole supply of oxygen, with Schiff's azotometer, and without a pump, will give true results, though requiring more time than the method of Johnson or that of Simpson.—The copper oxide is dried by ignition in a current of dry air in a combustion-tube with bayonet-end. In a combustion-tube of good length, closed (with round end) at the rear, a layer of manganese or magnesium carbonate is placed first, as stated on p. 228, then a plug of asbestos, then a short layer of copper oxide, then the substance mixed with copper oxide, mixing in a mortar or in the tube. About two-thirds of the tube should remain for the layers of copper oxide and metallic copper. The latter may be a roll of ignited copper gauze or a layer of reduced granular oxide, and should be 5 to 8 inches long. Anterior to this may be, as proposed by Professor Johnson, a short layer of copper oxide to oxidize any occluded hydrogen.

In the combustion the air is first expelled by liberating carbon dioxide from a part of the carbonate in the rear; the anterior layers of metallic copper and copper oxide are kept at full red heat; the substance is burned very slowly, and much time is taken in oxidizing the last of the carbonaceous residue; and finally the tube is swept out by ignition of the remaining carbonate in the posterior end. The gases from the tube are received directly into a Schiff's azotometer, over strong potash solution. In measuring the nitrogen, the room and apparatus being of uniform temperature, a thermometric reading is obtained.

ESTIMATION OF ORGANIC NITROGEN BY ITS CONVERSION INTO *Ammonia. The Soda-Lime process of Varentrapp and Will.*—The nitrogen of nitrates is not included in this estimation. The substance is heated in a combustion-tube in mixture with soda-lime, the products being carried through a layer of red-hot soda-lime of at least half the length of the tube, and received in a solution of acid. The ammonia remaining in the tube after the combustion is swept out by burning a short layer of oxalic acid in the rear, also by aspiration. If the substance be rich in nitrogen it is diluted with cane-sugar. The gaseous ammonia from the combustion-tube is received in a known volume of a standard solution of oxalic or sulphuric acid, which is afterward titrated (PÉLIGOT's modification); or is received in hydrochloric acid for gravimetric estimation with platinic chloride.—Using Péligot's modification, Prof. S. W. JOHNSON found[1] that, with various

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[1] 1879: *Am. Chem. Jour.*, 1, 75; 1872: *Am. Chemist*, 3, 161.

substances, under a series of determinations, "the soda-lime process is, to say the least, equal in accuracy with the absolute determination," by volume of free nitrogen. At bright red heat, with soda-lime, ammonia is not decomposed.

A combustion-tube of 14 to 30 inches (35 to 75 centimeters) length, and near ½ inch (10 to 12 millimeters) width, is sealed round at one end (Fig. 23). The Erlenmeyer's *gas-furnace* is the most convenient. The best *bulbed U-tube* is that shown in the figure. *The acid* is of about normal strength, titrated with an alkali solution of about half-normal, the latter being exactly valued with a standard acid solution prepared with care. Prof. S. W. Johnson uses standardized hydrochloric acid and standard solution of ammonia, and titrates with cochineal tincture as an indicator. The same indicator should be used in all titrations; and if the acid solution become colored from the combustion, litmus tincture is not applicable. Litmus-papers, blue and red, serve very well. *The soda-lime*, preferably granulated, otherwise coarsely powdered, is heated to remove all moisture, which is strictly excluded until the article is used. It may be used warm if the substance is stable enough to suffer no change therefrom. *Oxalic acid* should be heated on the water-bath to remove all water of crystallization. *Asbestos*, recently ignited, is required.

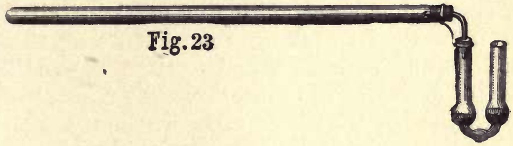
Fig. 23

In the charging of the combustion-tube a layer of about 1¼ inches (3 centimeters) of the dried oxalic acid is introduced into the rear of the tube, followed by about the same length of soda-lime. The substance under analysis is added from the weighing-tube, in quantity about 0.5 gram, to some of the soda-lime in a mortar (previously rinsed with the soda-lime), and a mixture made which, with the rinsings of the mortar, will fill the tube to a point from two-fifths to one-half its length from the closed end. Or the mixture of the substance with the soda-lime is made in the tube by means of a stirring-wire (Fig. 8), so as to form a layer of near the length just stated. In either case, if the substance be very rich in nitrogen, about an equal quantity of dried cane-sugar may be taken with it in the mixture. The remainder of the tube is filled with the soda-lime to within about 2 inches (5 centimeters) of the rubber stopper, placing a loosely porous plug of the asbestos, nearly an inch (or 2 centimeters) in length, as a secure guard against the carrying forward of alkaline dust or spray, and leaving a free space next the stopper. A shield may be put over the end of the tube (Fig. 16). The U-tube is filled and connected as shown in Fig. 23. The more that moisture has been excluded from the soda-lime, the easier will be the combustion. But the use of warm soda-lime in intermixture with the substance must not be adopted without assurance that no traces of ammonia are generated in such mixture. If the soda-lime be well granulated, or even coarsely powdered, with fine particles sifted out, it is better not to triturate in making the mixture of the substance, and to do without a channel formed by tapping the horizontal tube on the table, favoring the more intimate contact of empyreumatic gases with the hot soda lime. But if there are layers of fine powder in the tube, a channel must be provided.

In the combustion the layer of unmixed soda-lime is first heated, beginning at the anterior end, and increasing and extending the heat at such a moderate rate that the air-bubbles shall not pass out faster than about two to each second. The heat at the anterior end is so graduated as to prevent condensation of water-vapor in the tube, and not to soften the rubber stopper. When the mixture of substance is reached the layer of clear soda-lime must be at full red heat, and so preserved while the flames are advanced backward more gradually than before, delivering only about one bubble every second. The carbonized substance is at last burned out with a full red heat. and when the delivery of gas has nearly or quite ceased the oxalic acid is very gradually heated, so that the carbon dioxide shall not be tumultuously evolved. The carbon dioxide is generated only long enough to sweep out the combustion-tube, when the U-tube may be detached. The acid liquid should be as little colored and empyreumatic as possible. The anterior end of the combustion-tube, in the space in front of the asbestos plug, should not change moistened red litmus-paper.

In titrating the acid for the amount of ammonia it has received, the volumetric alkali is added from the burette directly to the U-tube until the neutral point is very nearly obtained, with litmus-papers or other indicator, not phenol-phthalein. The acid is now transferred to a beaker, with very little rinsing-water, and the titration completed. The value of the alkali solution is found by a volumetric acid of absolute standard. $17 : 14 ::$ quantity of ammonia $: x =$ quantity of nitrogen.

Combustion-tubes with the posterior end drawn out are sometimes used, and the residual ammonia obtained by aspiration, or by sending through a current of carbon dioxide.

The gravimetric determination of the ammonia, as ammonium platinic chloride, is done by the ordinary method, as found in works on inorganic analysis, washing the precipitate with alcohol or ether-alcohol, and igniting in a weighed crucible. 194.4 parts of Pt represent 14 parts of N.

Combustion with soda-lime in an iron tube may be done with good results,[1] as the writer has verified. The tube should be about a third longer, and a little wider, than a glass tube for the same combustion. Special precaution is necessary to avoid burning or melting the stoppers.

Combustion with soda-lime, sulphur, and thiosulphate. RUFFLE'S METHOD, 1881. Reduction by a powerful deoxidizer in presence of a strong alkali. Obtains the nitrogen of organic, ammoniacal, and nitric combinations. Carried out in the same way as the Varentrapp-Will method in Péligot's modification. The method has been well sustained. DABNEY (1885, already cited) found this method, in application to *fertilizers* containing small amounts of nitrogen, to give results as close as those by Johnson's process for free nitrogen, the latter method giving often a little too high, the former a little too low figures for the nitrogen. Greater precautions are required for bodies rich in nitrogen. Details are presented in the Official Methods of the Association of Agricultural Chemists for 1886–7, Bulletin No. 12, Department of Agriculture, Washington, 1886.

RELATIVE DETERMINATION OF THE NITROGEN AND CARBON.—Applicable when the proportional quantity of nitrogen is not small, or not less than N to 4 C = 14 of nitrogen to 48 of carbon. The substance is burned, with copper oxide, and the products passed over hot metallic copper, in a combustion-tube, so as to deliver in a graduated tube the nitrogen and the carbon dioxide. After taking the volume measure of the gases the carbon dioxide is taken up by alkali and measurement taken again. Methods of Liebig, Bunsen, and Gottlieb are employed.

THE DETERMINATION OF CARBON, HYDROGEN, AND NITROGEN, in one operation, is described by C. G. WHEELER, 1866: *Am. Jour. Sci.*, [2], **41**, 33. Also by W. HEMPEL, 1878: *Zeitsch. anal. Chem.*, **17**, 409; *Jour. Chem. Soc.*, **36**, 278. Recently by P. JANNISCH and V. MEYER, 1886: *Ber. d. chem. Gesel.*, **19**, 949 (preliminary notice).

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[1] See also JOHNSON, 1879: *Am. Chem. Jour.*, **1**, 82.

The direct estimation of oxygen has been reported upon as follows: Baumhauer, 1866; Maumenè, 1862; Mitscherlich, 1867, 1868; Ladenburg, 1865; Cretier, 1874.

Estimation of Nitrogen by Combustion in the moist way.—The well-known process published by Prof. Wanklyn in 1877 depends on the conversion of the nitrogen of organic compounds into ammonia by the action of permanganate in a very dilute solution of alkaline reaction, the ammonia already contained in the substance being previously distilled off. Its value, in water analysis, is relative rather than absolute, and depends upon its applicability to nitrogenous organic compounds in an extremely dilute solution, so that the changes likely to occur in a concentration of the water are avoided. For the analysis of pure nitrogenous compounds various plans of moist combustion have been proposed of late years. Of these the following method has received general commendation from chemists who have reported trials of it—a method in which oxidation by adding dry permanganate to a concentrated acid solution is preceded by the alterative action of hot sulphuric acid of full strength:

Moist Method of Kjeldahl.[1]—For bodies moderately rich in nitrogen 0.250 gram is taken; for bodies with only about 1.5% of nitrogen 0.7 gram is taken. The substance is placed in a boiling-flask of about 100 c.c. capacity, with a long and narrow neck, and of glass capable of resisting the strongest acids. The flask is placed upon asbestos cloth or copper gauze over a lamp supplying a strong heat, 10 c.c. of pure sulphuric acid of full strength is added, and digestion instituted (under a hood) at a temperature only a little below the boiling point of the sulphuric acid. Sulphurous acid vapors escape. To prevent loss by spirting, the flask is somewhat inclined during the effervescence. After the liquid comes to rest the digestion is continued (still near the boiling point, as shown by occasional bumping) until the liquid becomes gradually of light color, and finally entirely clear. To

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[1] J. Kjeldahl, Carlsberg Laboratory of Copenhagen, 1883: *Zeitsch. anal. Chem.*, 22, 366; *Chem. News*, 48, 101; *Am. Chem. Jour.*, 5. 456. Fresenius, 1884: *Zeitsch. anal. Chem.*, 23, 553. Czeczetka, 1886: *Monatsch Chem* , 6, 63; *Jour. Chem. Soc.*, 48, 688. Wilfarth, 1885: *Chem. Cent.*, 1885, 17; *Jour. Chem. Soc.*, 48, 837. Bosshard, 1886: *Zeitsch. anal. Chem.*, 24, 199; *Jour. Chem. Soc.*, 48, 837. C. Arnold, 1886: *Archiv d. Pharm.*, [3], 23, 177; *Jour. Chem. Soc.*, 48, 688. Details are defined in the "Official Methods of the Association of Agricultural Chemists," Department of Agriculture, Bulletin No. 12, Washington, 1886. The use of phenolsulphonic acid is introduced into the process by Jodlbauer, 1886: *Chem. Cent.*, p. 433; *Jour. Chem. Soc.*, 49, 834.

hasten this result a little fuming sulphuric acid or phosphoric anhydride is added. With these additions a digestion of about two hours is usually sufficient. But at 100° to 150° C. the formation of ammonia is imperfect and the object not attained. The lamp is now removed, and, while the liquid is hot, finely pulverized potassium permanganate is carefully added, either in very small portions or in a very fine stream, which may be carried through a delivery-tube. The reaction is violent, even accompanied by small flames, and it is made as gradually as it can be without interrupting it. When the oxidation is complete a green color appears, and the addition of the permanganate is discontinued. The liquid may now be warmed for a few minutes, but not on any account strongly heated. The liquid is cooled, and diluted with water, when the green color changes to brown.

When again cool the liquid is introduced into a distillatory apparatus, the generating flask holding about $\frac{3}{4}$ liter, and connected with an upward-sloping top-piece to prevent liquid being carried over by spirting, and through the condenser into a receiver containing an accurately measured quantity of acid of known strength. About 40 c.c. of solution of sodium hydrate of sp. gr. 1.30 are quickly introduced into the distilling flask. [A Welter's safety tube may be provided for this purpose.] And to prevent bumping a little metallic zinc is introduced, the hydrogen from which secures an even action.

The completed distillate is titrated for the ammonia it has received (as in the estimation of Varentrapp and Will).

Kjeldahl found his method inapplicable to certain alkaloids, cyanides, volatile acids, and nitrogen oxides. It reduces nitrates in presence of organic matter to ammonia, but incompletely (compare WARINGTON, 1885: *Chem. News*, **52**, 162).

Upon the Determination of Total Nitrogen, organic, ammoniacal, and nitrous, see BULLETIN No. 12, Chemical Division, DEPARTMENT OF AGRICULTURE, Washington, 1886, pp. 34, 52. Also, GERMAN MANURE MANUFACTURERS' ASSOCIATION, 1884: H. H. B. Shepherd, translator. Also, HOUZEAU, 1885. RUFFLE's method to this effect is referred to on p. 233.

BODIES CONTAINING SULPHUR, *in estimation of carbon and hydrogen*, are subjected to combustion with lead chromate instead of copper oxide, and the front of the column of lead chromate is not heated to full redness.—WHEN CHLORINE, BROMINE, or IODINE is present, in combustion to estimate carbon and hydrogen, a coil of silver wire is placed in the front of the combustion-tube to retain the halogens, which otherwise may interfere with the result. Chlorine forms cuprous chloride, which will condense in the calcium chloride tube. Copper holds chlorine but imperfectly, and the same is true of lead.

THE ESTIMATION OF SULPHUR, in organic analysis of compounds not volatile, may be done by fusing with potassium hydrate and nitrate, in a silver dish, until the mass will be white on cooling. The mass is dissolved in water, acidified by nitric acid, and the quantity of sulphuric acid determined by precipitation with barium chloride in the manner required in quantitative work. *Volatile* compounds can be oxidized with a mixture of sodium carbonate and potassium nitrate in a combustion-tube. Potassium dichromate is also employed as an oxidizing agent in the same way.

CHLORINE, BROMINE, and IODINE are estimated by igniting the substance with an excess of pure quicklime, in a narrow combustion-tube. The tube is filled with the lime mixed with the substance, followed by a short column of lime alone, and a channel made by tapping the tube on the table. After the ignition the contents of the tube, when cold, are carefully transferred to a flask containing water, and treated with dilute nitric acid, rinsing the tube with the water and then with the acid. The solution is filtered, the residue and filter washed, and the halogens precipitated by silver nitrate solution. With iodine it is better to exhaust first with water, and add silver nitrate solution to the filtrate, then treat the residue with dilute nitric acid and add the acidulous filtrate to the one containing the silver. By this means the liberation of iodine by action of nitric acid is avoided. The silver precipitate is treated as in ordinary quantitative work for the halogens.

ESTIMATION OF SULPHUR OR OF HALOGENS is effected by the method of CARIUS[1] From 0.15 to 0.40 gram of the substance is treated with a calculated quantity of nitric acid sufficient to furnish 4 times the required amount of available oxygen, or of acid of sp. gr. from 20 to 60 times the weight of the substance. The digestion is done in a closed tube, sealed, at 120° to 140° C., for some hours. For estimation of chlorine, silver nitrate is added with the nitric acid before digesting. Details may be found in the original papers and in manuals of quantitative analysis.

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[1] 1860–65: *Ann. Chem. Phar.*, **116**, 11; **136**, 129; *Zeitsch. anal. Chem.*, **1**. 217, 240; **4**, 451; **10**, 103.

DEDUCTION OF CHEMICAL FORMULÆ.—In the first place, *the molecular weight* of the substance is to be ascertained, if possible.

(1) If the compound be sufficiently vaporizable its Vapor Density[1] is to be determined and accepted as evidence of the molecular weight. With the weight of air as the unit of gravities, vapor density $\times$ 28.86 $=$ molecular weight. With hydrogen as the unit, vapor density $\times 2 =$ molecular weight.

(2) If the substance have a definite capacity of combining, as a base or an acid, its combining number can be determined by its proportions in formation of salts. If an acid, it is needful to ascertain whether it be monobasic, bibasic, or tribasic in its capacities of combination. Certain classes of bases are subject to the corresponding question, whether monacid or not, but the natural nitrogenous bases are mostly monacid.

(3) If the substance be found to hold a definite relation to other substances, as shown by its formation, its decomposition, or by chemical resemblance to members of homologous series, its molecular weight may be inferred from such relations.

If now m be the molecular weight of a compound;
p, the percentage of a constituent element;
x, the combining number of this element;
a, its atomic weight, and
y, the number of its atoms in the molecule,
$100 : p :: m : x.$ And $x \div a = y.$

Whether the molecular weight be obtainable or not, an empirical statement of atomic numbers can be derived at once from the centesimal figures of the analysis by dividing the percentage number of each element by its atomic weight. The provisional formula so obtained is reduced, by common divisors, to lower terms, and to such terms as best accord with its probable molecular weight, in its apparent classification among compounds of known molecular formulæ.

Allowances must be made for the real limits of error in analysis, and consideration must be had to the liability of weigh-

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[1] For ordinary purposes the most ready and satisfactory method of obtaining Vapor Density is that of VICTOR and CARL MEYER, 1878: *Ber. d. chem. Ges.*, 10, 2253; *Zeitsch. anal. Chem.*, 19, 214; "Watts's Dict. Chem," 8, 2094. See also reports by V. MEYER, 1876–7: *Ber. d. chem. Ges.*, 9, 1216; 10, 2067; 11, 1867; *Zeitsch. anal. Chem.*, 18, 294; 17, 373. HOFMANN's Method was given in 1868: *Ber. d. chem. Ges.*, 1, 198; *Zeitsch. anal. Chem.*, 8, 83. BUNSEN's Method, 1867: *Ann. Chem. Phar.*, 141, 273; *Zeitsch. anal. Chem.*, 6, 1. Method of TROOST and DEVILLE, 1860: *Ann. Chim. Phys.*, [3], 58, 257. A good summary of the literature of vapor-density determination is given in "Roscoe and Schorlemmer's Chemistry," vol. 3, part 1, p. 84 and after. Also see "Beilstein's Organische Chemie," 2d ed., p. 17.

able impurities, including moisture, in the article taken for combustion. Probable limits of error are represented in general by a comparison of published results of analyses by authorities of credit, and, more definitely, by the experience of the analyst himself with substances of known composition.

Even in empirical formulæ the well-known law of conjugate atomic numbers of carbon compounds should be respected, namely, the numbers of the atoms of uneven valence (the perissads, H and N) should together make an even number. Thus in the molecule of morphine, with N_1 we have H_{19}; in the molecule of quinine, with N_2 we have H_{24}. That is, in ordinary non-nitrogenous organic molecules, those containing C, H, and O, or those containing C and H, there is always an even number of atoms of hydrogen. But in nitrogenous molecules (of C, H, N, O, or C, H, N) the atomic number of hydrogen is even *only* when nitrogen presents an even atomic number. The law applies to haloid elements and to phosphorus, when these elements of uneven valence are present.

The low atomic weight of hydrogen gives low centesimal differences for one atom of this element, so that its atomic number is taken as the number which, under the rule, lies nearest the atomic number calculated from centesimals.

The establishment of *a rational formula* for a compound is a work of investigation, both synthetic and analytic, as obtained by reactions of formation and of decomposition. It requires studies of all chemical relations, led on by analogies from every point of view. An understanding of the chemical structure of the molecule is gained step by step in the investigation. A derived chemical formula can be made "rational" only to the extent that the chemical forces of the constituent elements have been revealed in their proportional power. In the study of isomerides, for the "position" of atoms in molecules, the atomic position is to be defined as a mode of statement of the chemical functions of the elements. At the same time it may be said that the evidence gained for relative "position" of atoms in a molecule is of the same character as the evidence upon which we predicate the existence of the molecule as a whole.

FATS AND OILS.[1]—Glycerides, and bodies related thereto

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[1] A good general summary of the chemistry and technology of the neutral fats is presented in the article "Chemical and Analytical Examination of Fixed Oils," A. H. ALLEN, 1883: *Jour. Soc. Chem. Indus.*, 2, 49.—A compact technical summary of the analytical chemistry of fats is presented in BENEDIKT'S "Analyse der Fette und Wachsarten," Berlin, 1886, pp. 296.

either by physical properties and uses or by production, are treated in the following pages under the heads here given:

Fatty Series, $C_nH_{2n}O_2$: *Stearic Acid; Palmitic Acid;* Myristic, Lauric, Capric, Caprylic, Caproic acids.

Fatty Series, $C_nH_{2n-2}O_2$: *Oleic Acid.*

Ricinoleic Acid; Linoleic Acid; Hypogaic and Physetoleic acids.

Fat Acids and Fats, Quantitative Determination of: (1) Hehner's number; (2) Reichert's number; (3) Köttstorfer's number, or capacity of saturation; Tables of Hehner's and Köttstorfer's numbers; (4) Iodine number of Hübl; (5) Mean Molecular Weight; (6) Specific Gravities; (7) Melting and Congealing points; (8) Calculation of Acid and Neutral Fats.

Distinctions of Fat Oils by Solubility in Glacial Acetic Acid; Table.

Separation of Mineral Oils from Fats: descriptive list; method by saponification; extraction after saponification, in solution, in dry mass, with Soxlet's apparatus, estimation by Köttstorfer's numbers; examination of the liquid and solid non-saponifiable bodies.

Separation of Fat Acids from Fats.

Separation of Resins from Fat Acids.

Rosin Oils.

Drying and Non-Drying Oils.

Linseed Oil; Olive Oil; Cotton-seed Oil; Castor Oil; Lard; Tallow; Oleomargarin.

Butter: bibliography; constituents; estimation of constituents, of artificial color, or rancidity (acidity); detection of foreign fats by solvents; Scheffer's method; odor test; soap viscosity; microscopical examinations; butter fat, properties: butter substitutes; methods of chemical estimation of butter fat—Hehner's, Reichert's, Köttstorfer's; interpretation of Hehner's number, of Reichert's, of Köttstorfer's; specific gravity as a means of distinguishing from substitutes; iodine number of Hübl; scope of butter analysis and forms of certificates, in Massachusetts, in New York, in Pennsylvania, at Agricultural Department at Washington; what is a sufficient chemical analysis of butter.

C_2H_{2n+2}

FATTY SERIES OF ACIDS, $C_nH_{2n}O_2$.—The following-named members of the $C_nH_{2n}O_2$ series are described in this work, and will be found under their respective names. Formic, Acetic, and Valeric Acids are not constituents of Fats. The others are described in the next following pages. For Butyric Acid see p. 75.

Volatile.

Formic Acid..........	CH_2O_2	or	$H.CO_2H$
Acetic Acid...........	$C_2H_4O_2$	"	$CH_3.CO_2H$
Butyric Acid—normal..	$C_4H_8O_2$	"	$CH_3CH_2CH_2.CO_2H$
Valeric Acid—isovaleric.	$C_5H_{10}O_2$	"	$(CH_3)_2CH\,CH_2.CO_2H$
Caproic Acid—isobutyl-acetic...............	$C_6H_{12}O_2$	"	$(CH_3)_2CH(CH_2)_2.CO_2H$
Caprylic Acid—normal.	$C_8H_{16}O_2$	"	$CH_3(CH_2)_6.CO_2H$
Capric Acid...........	$C_{10}H_{20}O_2$	"	$CH_3(CH_2)_8.CO_2H$?
Lauric Acid...........	$C_{12}H_{24}O_2$		

Non-Volatile.

Myristic Acid..................	$C_{14}H_{28}O_2$
Palmitic Acid..................	$C_{16}H_{32}O_2$
Stearic Acid	$C_{18}H_{36}O_2$

Stearic Acid.—$C_{18}H_{36}O_2=284$ (monobasic). Found as a normal glyceride in common vegetable and animal fats, in which it is the ordinary constituent of highest melting point.

a.—Crystallizable from alcohol in white, lustrous tables, or needles; or congealing from a melted portion in crystalline, translucent masses of considerable hardness. It melts at 69.2° C. At about 360° C. it begins to boil with decomposition of a considerable part. Under reduced pressure, at 100 millimeters, it boils at 291° C. With superheated steam it distils with but little decomposition. Its specific gravity as a solid at 11° C. is that of water at the same temperature, but at higher temperatures it floats upon water, and the melted acid just above 69.2° C. has the specific gravity of 0.8454.

The melting point can be found, quickly, by immersing the bulb of the thermometer for a moment in the melted stearic acid (free from water), then suspending the coated bulb in the middle of a beaker of water, to which heat is applied, and noting the temperature at which the fatty coat melts from the bulb. To purify stearic acid from salts, preparatory to this test, it may be repeatedly dissolved in alcohol, filtered, and evaporated to dryness. (Further, see Determination of the Melting and Congealing Points of Fatty Bodies, Index.)

The normal glyceride, stearin, or "tristearin," $C_3H_5(C_{18}H_{35}O_2)_3$, is crystallizable, and, when pure, of pearly-white lustre. It melts, according to modification due to previous heating, at a temperature from 55° C. to 71.6° C. Stearin crystallized from ether melts at 71.6° C., and then congeals to a crystalline mass at 70° C.; but heated only 4° C. above the melting point, it does not then congeal until reduced to the temperature of about 52° C., when it appears as a wax-like mass and will melt again at 55° C. A sample of stearin (not entirely pure), melting at 65.5° C., at this temperature had the specific gravity 0.9245 (Benedikt[1]).

The metallic stearates are fusible bodies, in some instances crystallizable, more often amorphous, and of plaster-like or soap-like consistence.

b.—Stearic acid and stearins are odorless and tasteless.

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[1] "Analyse der Fette," Berlin, 1886.

c.—Stearic acid is insoluble in water. It is soluble in about 40 parts of absolute alcohol at ordinary temperatures, moderately soluble in 90% alcohol when hot, very sparingly when cold. On cooling the hot alcoholic solution abundant crystals are obtained. It is readily soluble in ether. The solutions redden litmus-paper, and decolor the alkaline phenol-phthalein. At 23° C. it dissolves in 4.5 parts of benzene or in 3.3 parts of carbon disulphide.

Stearin, the neutral glyceride, is insoluble in water, somewhat soluble in boiling alcohol, from which it crystallizes out almost wholly when cold. It dissolves in about 200 parts of ether—a solubility more sparing than that of the softer neutral fats—and dissolves in chloroform, benzene, petroleum benzin, and carbon disulphide.—The alkali stearates are somewhat difficultly and imperfectly soluble in water. They dissolve in hot water, with slight turbidity, the solution gelatinizing when cold. On agitating the gelatinized mass with much water in the cold, a turbid mixture is obtained, with formation of difficultly soluble acid stearate along with free alkali. In hot alcohol the alkali stearates are easily soluble, the greater part congealing in the cold, so that only a dilute solution is permanently obtained. The non-alkali metallic stearates are insoluble in water, and for the most part insoluble in alcohol or ether. In some instances, however, they yield free stearic acid to the action of ether. In general they are gradually decomposed by action of water, yielding hydrate of the metal and free stearic acid.

d.—The aqueous solutions of alkali stearates, dilute and turbid, on addition of solution of **barium** or **calcium chloride,** or other non-alkali salt, show an abundant precipitate of metallic stearate. An alcoholic solution of stearic acid, with a solution of barium or calcium acetate to which a little alcohol has been added, gives a precipitate of stearate of the metal. The barium precipitate is gelatinous and bulky; the magnesium precipitate, crystalline and pulverulent. To the action of water these precipitates yield hydrates of barium, etc., while free fat remains behind. The precipitates are to some extent dissolved by boiling alcohol, and on cooling the solution crystalline precipitates are obtained.—Solutions of alkali stearates are precipitated by addition of dilute acids, the resulting stearic acid appearing in a milky subdivision with curdy clumps. By heating the mixture a clear, oily layer slowly rises, and on cooling solidifies to a crust. Or the precipitate while cold may be filtered out, washed with hot water, drained dry, and dissolved from the filter with hot alcohol or with cold ether. On evaporation the stearic acid is obtained, crystalline or congealed, as preferred. Also the crude precipitate of stearic acid may be dissolved by shaking out with several portions of ether.

e.—Separation.—Stearic acid is obtained from its glyceride, stearin, by first saponifying with potash, and then decomposing the soap with acid. The saponification is done by boiling gently with alcoholic solution of potassa until a clear solution is obtained. Ten parts of the fat are treated with 8 to 10 parts of 70 to 85% alcohol, and 4 to 6 parts solid potassa. The most of the alcohol is evaporated off, and the cold liquid treated with dilute acid for liberation of the stearic acid, as directed above (*d*). From non-alkali stearates, acidulating with an acid that does not precipitate the metal, and shaking out with ether, is usually the most expeditious method of separating the stearic acid.

From oleic acid stearic acid (with other solid fat acids) is separated *by insolubility of lead stearate in ether*, as follows. The free fat acids are to be perfectly saponified with potassa or soda; the neutral solution of the alkali soap, with some alcohol, is precipitated with lead acetate, and the precipitate washed, dried, and exhausted with ether in repeated portions, when the lead salts of the solid fat acids will be left undissolved, and the lead oleate can be obtained by evaporating the ethereal solution. The details may be governed as follows (KREMEL[1]). Of the free fat acids 2 to 3 grams are exactly weighed into a flask of 100 to 150 c.c. capacity, treated with about an equal quantity of dry caustic potash and 10 c.c. of alcohol of 95 per cent. strength, on the water-bath, to complete saponification. The mass is diluted with a little water, neutralized with acetic acid, using phenol-phthalein as an indicator, the alcohol evaporated off on the water-bath, the residue dissolved in 80 c.c. hot water, and the liquid precipitated with lead acetate solution. When cold the free precipitate is poured upon a filter of 10 cm. (near 4 inches) diameter, and the whole precipitate is washed several times with hot water. The precipitate adhering to the flask is melted on the water-bath, cooled, drained, and dried at a gentle heat, as is also the precipitate in the filter. The contents of the flask are now treated with ether, poured through the same filter, in repeated portions, until the whole precipitate is exhausted of ether-soluble substance. On vaporizing the ether in the filter the lead stearate can be detached, and added to that in the

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[1] Consult also MUTER: *Analyst*, 2. 73.

flask, where the whole is treated with diluted hydrochloric acid, and exhausted with ether. The filtered ethereal solution is evaporated in a tared beaker and the residue weighed as stearic acid (including all solid fat acids). For the oleic acid (the total of liquid fat acids) the ethereal solution of lead salt is evaporated to dryness, and the residue treated with diluted hydrochloric acid and then with ether, as directed for the solid fat acids.

Stearic acid (with palmitic acid) is separated from oleic acid *by the solvent action of a mixture of alcohol and glacial acetic acid* (DAVID, 1878[1]). In the proportion of 300 c.c. of alcohol of 95 per cent. strength with 220 c.c. of glacial acetic acid, at 15° C., the oleic acid is just soluble, while the solid fat acids are insoluble. A greater proportion of the acetic acid precipitates oleic acid from its alcoholic solution ; a smaller proportion permits the solution of stearic and palmitic acids. A weighed portion of one or two grams of the fat acids under examination, in a flask provided with a tight stopper, is treated with the solvent mixture. in twenty-four hours' digestion at about 15° C., with occasional shaking. The mixture is then filtered, washed first with the solvent mixture, then with cold water, gathered into a weighed dish, melted, drained of water, dried in a desiccator or at 100° C., and weighed as stearic acid.

f.—Quantitative.—Free stearic acid, in absence of other acids, or a total of fat acids to be estimated as stearic acid, may be determined in quantity *by acidimetry*, using phenol-phthalein or litmus as an indicator, and taking the fat acid in alcoholic solution. Each c.c. of normal solution of alkali represents 0.284 gram of stearic acid. Taking 2.84 gram of the material under estimation, each c.c. of decinormal solution of alkali equals 1 per cent. of free stearic acid.

Free stearic acid, as obtained by precipitating an alkali stearate in aqueous solution with a diluted acid, washing with water, melting to separate water, and drying, may be weighed as $C_{18}H_{36}O_2$. Also the residue of its ethereal solution may be melted, brought to a constant weight, and weighed in the same way.

From Oleic acid stearic acid is separated as directed under *e*, p. 242; in mixture with Palmitic acid stearic acid is estimated by methods given under Fat Acids, Quantitative Determinations of, (5) and (7), p. 250.

g.—Stearic acid is the "stearin" of the candle industry.

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[1] *Ding. pol. Jour.*, 231, 64; *Zeitsch anal. Chem.*, 18, 622 ; Benedikt's "Analyse der Fette" (1886), p. 81; *Am. Jour. Phar.*, 55, 356.

For determinations of commercial value see under reference last given, especially methods (4) to (8).

Palmitic Acid.—$C_{16}H_{32}O_2 = 256$ (monobasic). Margaric Acid.[1] Found as a normal glyceride in ordinary vegetable and animal fats.

a.—As free acid, crystallizable from alcoholic solution in fine needles, sometimes grouped in sheaves, or congealing from a melted mass in partly crystalline forms of pearly lustre. Melts at 62° C., at which temperature the liquid has the sp. gr. 0.8527. At about 350° C. it distils with partial decomposition. It leaves a permanent oil stain on paper. Under the reduced pressure of 100 millimeters it distils at 268.5° C.—The glyceride, Palmitin, $C_3H_5(C_{16}H_{31}O_2)_3$, is crystallizable, in pearly lustrous forms. It melts at temperatures from 50.5° to 66.5° C., according to its previous exposure to heat. Strongly heated it carbonizes abundantly.

b.—Palmitic acid, as well as palmitin, is odorless and of a bland, oily taste.

c.—Palmitic acid is insoluble in water, and but sparingly and slowly soluble in cold alcohol, requiring 10.7 parts of absolute alcohol for solution, but hot alcohol dissolves it more freely, yielding crystals as the solution cools. It dissolves freely in ether. The alcoholic solution has an acid reaction.

The normal glyceride, palmitin, is but slightly soluble in cold alcohol, moderately soluble in hot alcohol, and soluble in ether, chloroform, benzene, petroleum benzin, and in carbon disulphide.

Alkali palmitates (soaps of palmitin) are soluble in water, with tendency to turbidity from slight decomposition, increased by dilution; more permanently soluble in alcohol, scarcely at all soluble in ether.—Non-alkali metallic palmitates are insoluble in water or ether. Lead palmitate is insoluble in alcohol. Barium and calcium palmitates are slightly soluble in alcohol.

d.—In qualitative reactions palmitic acid does not sensibly differ from stearic acid. Its distinction from stearic acid requires quantitative work.

e.—Separations of palmitic acid are made with stearic acid, or, if this be absent, by the same methods given for stearic acid separation (Stearic Acid, *e*).

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[1] This synonym is used by some French chemists.

f.—Quantitative determinations of palmitic acid alone are done by the methods given for Stearic acid. When in mixture with stearic acid, methods of indirect determination are resorted to, as given under Fatty Acids, Quantitative Estimation of, (5) and (7).

g.—Palmitic acid enters into the stearic acid known in commerce and in candle manufacture as "Stearin," and into "Oleomargarin." See under these heads (Index).

Myristic Acid, $C_{14}H_{28}O_2$.—The fourteen-carbon member of the $C_nH_{2n}O_2$ series of fat acids. Closely resembles Lauric acid. A solid, melting at 53.8° C., at which temperature the liquid has sp. gr. 0.8622. It is insoluble in water, sparingly soluble in cold alcohol and in ether.

Lauric Acid.—The $C_{12}H_{24}O_2$ acid obtained from fats is a solid, fusible at 48.6° C., and of sp. gr. 0.883 at 20° C. It crystallizes from alcohol in needles. It does not vaporize, alone and under ordinary pressure, without being mostly decomposed, but distils with steam. In large quantities of boiling water sensible traces are dissolved.

Capric Acid, $C_{10}H_{20}O_2$.—The capric acid obtained from fats is solid at ordinary temperatures, forming small tabular crystals, melting at 31.3° to 31.4° C., boiling at 268°–270° C., and of sp. gr. 0.93 at 37° C. It is soluble in about 1000 parts of water; its calcium salt, very slightly soluble in water.

Caprylic Acid, $C_8H_{16}O_2$.—The caprylic acid obtained from fats congeals at 12° C. to a crystalline mass, melting at 16.5° C. Boils at 236°–237° C. At 20° C. has sp. gr. 0.914. Of a sweet taste. Soluble in 400 parts of water. The calcium salt dissolves in 200 parts of water.

Caproic Acid, $C_6H_{12}O_2$. *Isobutyl-acetic acid.* Found as a glyceride in fats.—Congeals at − 18° C., boils at 199.7° C., is scarcely at all soluble in water. At 20° C., sp. gr. 0.925. Of a sweetish taste. The calcium salt dissolves in 37 parts of water.

Fatty Series of Acids, $C_nH_{2n-2}O_2$. Oleic acid series. The following members of this and other immediately related series are found in fats:

Oleic Acid....... $C_{18}H_{34}O_2 = C_{17}H_{33}.CO_2H$.
Hypogaic Acid, Physetoleic Acid } $C_{16}H_{30}O_2 = C_{15}H_{29}.CO_2H$.

SERIES $C_nH_{2n-2}O_3$:
Ricinoleic Acid... $C_{18}H_{34}O_3$.

SERIES $C_nH_{2n-4}O_2$:
Linoleic Acid.... $C_{16}H_{28}O_2 = C_{15}H_{27}.CO_2H$.

OLEIC ACID, $C_{18}H_{34}O_2 = 282$.—The members of the fatty series $C_nH_{2n-2}O_2$ contain two atoms of hydrogen less than corresponding members of the fatty series $C_nH_{2n}O_2$, and by action of reducing agents the former are in general convertible into the latter. The normal glyceride of oleic acid, olein, $C_3H_5(C_{18}H_{33}O_2)_3 = 884$, is found in greater or smaller proportion in most vegetable and animal fats, and in non-drying oils.

a.—Pure oleic acid is a colorless oil, congealing at 4° C., melting at 14° C., at which temperature the liquid has sp. gr. 0.898. Under ordinary pressure it does not distil alone undecomposed, but is carried over with superheated steam at about 250° C.—The triglyceride, olein, is a liquid which congeals at low atmospheric temperatures, and in vacuum distils slowly without decomposition.

b.—Oleic acid is a bland, tasteless, when pure nearly or quite odorless liquid, indifferent in physiological action.

c.—Oleic acid is insoluble in water, soluble in alcohol not very dilute, and separated from the solid fat acids by its greater solubility in a mixture of acetic acid and alcohol. It is soluble in chloroform, benzol, petroleum benzin, and in the fixed oils.—The triglyceride, olein, is somewhat soluble in absolute alcohol, in fact much more so than are stearin and palmitin, but is insoluble in dilute alcohol.—Pure oleic acid is neutral to litmus-paper, but it gives the acid reaction with phenol-phthalein, decoloring the alkaline mixture of this indicator at formation of normal alkali oleates.—By exposure to air for a short time oleic acid suffers such changes as impart to it an acid reaction, and it soon becomes rancid and of a yellowish color.—The alkali oleates are soluble in water, the solution becoming somewhat turbid by decomposition when diluted with water, though bearing dilution better than stearate or palmitate. The oleates of non-alkali metals are insoluble in water, but more or less freely soluble in alcohol, and in some instances (including the lead salt) soluble in ether. The silver oleate is not soluble in ether.—The alkali oleates are precipitated from their aqueous solutions by sodium chloride, and to some extent by excess of alkalies. Sodium oleate is soluble in 10 parts of water at 12° C., in 20.6 parts of alcohol of 0.821 applied at 13° C., or in 100 parts of boiling ether. From absolute alcohol it is crystallizable. Potassium oleate, in ordinary moist condition, is soft or gelatinous, and is much more soluble in water or alcohol or ether than is the sodium salt. Barium oleate is insoluble in water, and but very slightly soluble in alcohol. Magnesium-alkali oleate possesses a capacity of slight and transient foaming in aqueous solution, perhaps due to a tardy precipitation, and distinguishing it from calcium oleate in the soap test of hard waters.

d.—Oleic acid is characterized by its consistence as a liquid non-volatile fatty body, and by the action of oxidizing agents upon it. **Nitric acid** with metallic copper, fuming nitric acid, mercury nitrates, or other form of nitrous acid, in digestion with oleic acid, produces its isomer elaidic acid, as in digestion with olein it forms elaidin, glyceride of elaidic acid. Elaidic acid is a solid, and its formation is indicated first by a soft waxy, and finally by a resinous consistence. Elaidic acid dissolves in alcohol, from which it crystallizes in tabular forms, melting at 45° C. —**Bromine** acts readily, and iodine or chlorine quite easily, on oleic acid, producing dibrom-stearic acid, an addition product of oleic acid, $C_{17}H_{33}Br_2.CO_2H$, on the type of the $C_nH_{2n}O_2$ series. To 7 parts of the oleic acid 4 parts of bromine are added, drop by drop, stirring after each addition. The product is yellowish, of an oily consistence. To form the di-iod-stearic acid, molecular proportions of the oleic acid and of the iodine are taken, each being dissolved in alcohol, when the iodine solution is gradually added, this being the reaction of Hübl's estimation, giving the iodine number.

e.—*Separations.*—In manufacture oleic acid is separated from the solid fat acids by filtration under pressure at low temperatures above the congealing point of the oleic acid.

For methods of separation from the solid fat acids by solvents, etc., see Stearic acid, *e*. Directions for separation (production) from olein by saponification are essentially those given under Hehner's method.

f.—*Quantitative.*—Oleic acid is estimated volumetrically by standard solution of potassa or soda, using phenol-phthalein as an indicator. Each c.c. of normal solution of alkali represents

0 282 gram of oleic acid. Taking 2.82 grams of material, each c.c. of decinormal solution of alkali counts 1 per cent. of oleic acid. Taking 14.1 gram of material, c.c. of normal solution of alkali × 2 = per cent. oleic acid. Gravimetric estimation of free oleic acid is effected by adding to the free acid, in a layer over an aqueous liquid, a weighed portion of recently fused beeswax or paraffin, heating to melt the solid, and when cold detaching the oily mass, drying in a tared capsule, and weighing, when the weight of the wax is subtracted. Also free oleic acid, dissolved in ether, may be freed from the latter by evaporation in a tared beaker or flask, avoiding oxidation by exposure to the air, and the weight of the oleic acid may be obtained.

g.—The U. S. Ph. gives the following specifications for oleic acid: "At 14° C. (57° F.) it becomes semi-solid, and remains so until cooled to 4° C. (39° F.), at which temperature it becomes a whitish mass of crystals. At a gentle heat the acid is completely saponified by carbonate of potassium. If the resulting soap be dissolved in water and exactly neutralized with acetic acid, the liquid will form a white precipitate with test solution of acetate of lead. This precipitate, after being twice washed with boiling water [drained and dried], should be almost entirely soluble in ether (absence of more than traces of palmitic and stearic acids). Equal volumes of the acid and alcohol, heated to 25° C. (77° F.), should give a clear solution, without separating oily drops upon the surface (fixed oils)."—The specifications of the Br. Ph. are as follows: "A straw-colored liquid, nearly odorless and tasteless, and with not more than a very faint acid reaction. Unduly exposed to air it becomes brown and decidedly acid. Specific gravity 0.860 to 0.899. At 40° to 41° F. (4.5° to 5.0° C.) it becomes semi-solid, melting again at 56° to 60° F. (13.3° to 15.5° C.) It should be completely saponified when warmed with carbonate of potassium, and an aqueous solution of this salt neutralized by acetic acid and treated with acetate of lead should yield a precipitate which, after washing with boiling water, is almost entirely soluble in ether."

RICINOLEIC ACID, $C_{18}H_{34}O_3 = 298$.—The fat acid constituting, in its normal glyceride, the principal part of castor oil. In composition an oxy-oleic acid of the proportions $C_nH_{2n-2}O_3$.

a.—A thick oil, of sp. gr. 0.940 at 15° C., congealing at −6° to −10° C., and does not vaporize undecomposed. The lead salt melts at 100° C.

b.—The glyceride, as obtained in castor oil, is odorless, with a mild taste and slightly acrid after-taste, and exerting a cathartic effect.

c.—Ricinoleic acid is insoluble in water; soluble in all proportions in alcohol and in ether. The lead salt is soluble in ether. Castor oil is soluble, at 15° C., in 2 parts of 90% alcohol or 4 parts of 84% alcohol. It is but slightly soluble in petroleum benzin, paraffin oil, or kerosene, though it takes up about its own volume of petroleum benzin.

d.—Ricinoleic acid is but very slightly oxidized by exposure to air. Treated with bromine it takes two atoms of bromine in the molecule of the acid, forming $C_{18}H_{34}Br_2O_3$, corresponding to the reaction of oleic acid. In the elaidin reaction, by action of nitric acid, ricinelaidic acid is formed, isomeric with ricinoleic acid, and fusible at 50° C.

LINOLEIC ACID, $C_{16}H_{28}O_2=252$.—The only well-known member of the series of fat acids $C_nH_{2n-4}O_2$. In the normal glyceride forms the principal portion of linseed oil, representative of the drying oils. In oxidation, or "drying," it forms addition products, such as $C_{16}H_{28}Br_4O_2$, corresponding in composition to $C_nH_{2n}O_2$. Therefore in reaction with oxidizing agents it has twice the saturating power per molecule possessed by oleic acid.

a.—Linoleic acid is a permanent liquid of a pale yellow color and sp. gr. 0.9206 at 14° C. The glyceride, as obtained in linseed oil, congeals at −16° C. (GUSSEROW), −27° C. (ARCHBUTT and ALLEN), and melts at 16° to 20° C. (GLÄSSNER).

b.—Linseed oil has a characteristic odor and taste.

c.—Insoluble in water, readily soluble in alcohol and in ether. Of a feeble acid reaction, and capable of neutralizing alkalies to phenol-phthalein and other indicators.

The barium and calcium salts dissolve in hot alcohol. Ether dissolves the linoleates of lead, zinc, copper, and calcium.

d.—Linoleic acid is easily oxidized by exposure to the air. In thin layers in a few days it forms a solid, resin-like body known as Oxylinoleic acid, and afterward takes on the character of a neutral body, insoluble in ether, and sometimes termed Linoxyn.

HYPOGAIC ACID, $C_{16}H_{30}O_2$.—A white solid, crystallizing in needles, melting at 33° C., not readily vaporizing in ordinary conditions without decomposition. By exposure to air soon becomes rancid, acquiring a brown color, and giving origin to volatile acids. In the elaidin test it is changed to its isomer gaidic acid, fusible at 39° C.

PHYSETOLEIC ACID, isomeric with Hypogaic acid, $C_{16}H_{30}O_2$, melts at 30° C., and is not affected by the elaidin test.

FAT ACIDS, QUANTITATIVE DETERMINATIONS OF.—Besides the methods of volumetric and gravimetric estimation of separate fat acids, or of total fat acids in terms of stearic acid, by equivalence of saturation, *certain special determinations* have been made, upon stated authorities, as indices of composition, related to ascertained limits, representing values for given uses.

(1) The number of parts of *insoluble fat acids* obtainable from 100 parts of clear neutral fat (HEHNER's number).

(2) The number of c.c. of decinormal alkali solution saturated by the *volatile fat acids* distilled from 2.5 grams of the fat (REICHERT's number).

(3) The number of milligrams (thousandths) of potassium hydrate saturated by saponifying 1 gram (one part) of the fat (KÖTTSTORFER's number). The saponification number.

The methods above named have been devised to distinguish butter from its substitutes.

(4) The percentage of iodine which the oleins of the fat will take into combination by a defined procedure (HÜBL's iodine number).

(5) The molecular weight, as obtained by acidimetry. (The quantity saturated by 1000 c.c. normal solution of alkali.) For mixtures of palmitic and stearic acids.

(6) The specific gravity, as a limited indication.

(7) The melting and congealing points.

(8) Calculation of constituent Fat Acids and Neutral Fats.

(1) *Estimation of the insoluble fat acids:* HEHNER's Method.[1] —To obtain the butter fat from butter melt a portion on the water-bath, leave the liquid to settle while melted, decant the clear liquid only upon a dried filter in a hot funnel, and take the filtrate. It must be perfectly clear and not lose weight on

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[1] O. HEHNER, 1877: *Zeitsch. anal. Chem.*, 16, 145. HEHNER and ANGELL, 1877: "Butter, its Analysis and Adulterations." London, second edition. MUTER, 1876: *Analyst*, 1, 7. DUPRÉ, 1876: *Phar. Jour. Trans.*, [3], 7, 131. JONES, 1877: *Analyst*, 2, 20. FLEISCHMANN and VIETH. 1878: *Zeitsch. anal. Chem.*, 17, 287. Manipulation at the Depart. of Agriculture, Washington, REPORT DEPT. AGR., 1884, Prof. WILEY, Chemist, p. 60. Further, see citations under Butter Fat.

the water-bath. Keep in a light beaker, and take out for an analysis from 3 to 4 grams of the clear fat into an evaporating-dish of about 5 inches (13 centimeters) diameter, using a glass rod to be left in the evaporating-dish, and weighing the beaker before and after the removal to obtain the exact weight of fat taken. Add 50 c.c. of alcohol of about 85%, and 1 to 2 grams of pure (alcoholic) potassium hydrate, and warm and stir the mixture until a clear solution is obtained. After five minutes' further warm digestion add a few drops of distilled water, and if a turbidity is caused continue the digestion until the addition of water produces no turbidity. If this satisfactory saponification is not attained the failure is probably due to a too great dilution of the potash with alcohol, and the operation is to be commenced anew. If the alcohol be too strong, saponification is prevented. The clear saponified solution is now evaporated over the water-bath to a syrupy consistence, and the residue dissolved in 100 to 150 c.c. of water. To the clear liquid add diluted sulphuric or hydrochloric acid to a strongly acid reaction. The creamy separate of the insoluble fat acids rises for the most part to the surface. Heat of a bath of water below boiling is now applied to melt the precipitate, and continued for half an hour and until the layer of fat acids above is perfectly clear and the aqueous liquid below is nearly clear. Meantime a filter of 4 to 5 inches (10 to 13 centimeters) diameter, of the closest filter-paper (Swedish), is dried in the water-box. The filter should be close enough to transmit hot water only by drops. A small beaker is weighed, also a filter weighing-tube and this tube with the filter, to give the weight of the latter.

The weighed filter is placed in a funnel wetted and half-filled with water. The watery liquid and melted fat are then poured from the dish upon the filter, which is not to be at any time more than two-thirds filled; the dish and rod are rinsed with boiling water, and washing with boiling water is to be continued until the washings cease to redden litmus-paper, about ¾ liter (700 to 1000 c.c.) of filtrate being usually obtained.[1] (The rinsing of the dish seldom leaves behind more than a milligram of fat, but this is saved by taking it up with a little ether and the solution added to the fat acids in the beaker afterward.) The

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[1] Fleischmann and Vieth (1878) advise care to avoid imperfect solution of lauric acid (abounding in cocoanut oil), washing until 5 c.c. of the filtrate ceases to change the color of one drop of litmus tincture added thereto. E. Waller and his associates (1886: Report N. Y. State Dairy Commissioner) wash with six or seven instalments of hot water (about 100 c.c. each), rinsing off between each with about 25 c.c. of cold water.

drained funnel is set well down in a beaker of cold water, and when the fat acids have hardened the filter is detached, drained, and placed in the weighed beaker.[1] This is heated on the water-bath to a (nearly) constant weight. Weigh after about two hours' drying, and after a half-hour's further drying weigh again. If any drops of water collect below the fat add a drop or two of alcohol. In this drying there may be slight increase by oxidation of oleic acid, and slight decrease by vaporization of fat acids. If the filter have been close enough no fat globules will have passed, and none will be revealed by microscopic examination of the filtrate.

The weight of the beaker and contents, minus the weights or tares of the beaker and·the filter, leaves the weight of the fat acids, which is to be divided by the weight of purified fat taken, to obtain the proportion ($\times 100 = \%$) of insoluble fat acids.

If 87.5 be accepted as the full per cent. of insoluble fat acids in butter, and 95.5 as the per cent. of insoluble fat acids in "meat fats," then $95 5 - 87.5 = 8$, and 8 : found percentage minus 87.5 :: 100 : $x =$ per cent. of "meat fats" present in the clear fat examined. For the calculation of percentage in entire butter see under Butter, Interpretation of Results.

Dalican modifies Hehner's process by taking 10 grams of the clear butter fat in a flask of 250 to 300 c.c. capacity, and adding 80 c.c. of 85% alcohol, and 6 grams of sodium hydrate dissolved in 6 to 8 c.c. water, when by 30 to 40 minutes of warming and stirring the saponification is ended. The alcohol is evaporated off, 150 c.c. of water added, and 25 c.c. of hydrochloric acid diluted with four parts of water are added in small portions at a time, rotating the flask after each addition. The mixture is now heated over the water-bath for 25 to 30 minutes, until the fat layer separates with perfect clearness and white points are no longer seen. The flask is set aside for 30 minutes, and then cooled with water. After two hours the fat layer is broken with a glass rod, the water poured on a wetted filter, about 250 c.c. of boiling water added in two portions to the flask, shaking after adding the first portion. The flask is then set aside 40 minutes, cooled by immersion in water, and the water decanted on the filter as before. This washing by decantation, as above, is repeated until the decanted liquid ceases to redden litmus-paper on 20 minutes' contact, 8 or 10 washings being necessary.

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[1] "The insoluble acids are brought into a tared dish, any in the filter or flask being dissolved in ether, dried at 100° C. with stirring with absolute alcohol to remove water, and weighed." H. W. Wiley, Chemist Dept. Agriculture, Washington, Report of 1884.

The insoluble fat acids are finally gathered in a tared porcelain capsule or evaporating-dish, the flask being washed with hot water, and all washings passed through the filter. The filter must be kept wet, and the slight portion of fat acids upon it can easily be detached. The drying is done at 100° to 110° C., at first for an hour, and a second weight is taken in 15 or 20 minutes. For results with vegetable and animal fats see tables following; also Butter Fat.

(2) Reichert's *method*[1] embraces the estimation of the volatile fat acids, separated by distillation. "Reichert's number" is the number of c c. of decinormal solution of alkali taken to neutralize the distilled fat acids from 2.5 grams of fat. Sometimes, however, results are specified for 5 grams or for 10 grams of the fat.

Of the clear filtered fat 2.5 grams are taken in an Erlenmeyer's flask of about 150 c.c. capacity, with 1 gram potassium hydrate and 20 c.c. of 80% alcohol, and the whole digested on the water-bath, with shaking by circular motion until saponification is complete and no more pasty masses remain. Now 50 c.c. of water are added, then 20 c.c. of diluted (1 to 10) sulphuric acid, and the mixture distilled. To avoid bumping a slight stream of air may be introduced. The distillate is received in a 50 c.c. flask, into which is set a funnel carrying a wetted filter, receiving the distillate, so that any insoluble fat acid otherwise possible in the distillate may be rejected. The first 10 or 20 c.c. of distillate are returned to the flask; then 50 c.c. are distilled. The volume of the distilled liquid should always bear the same proportion to that of the distillate. This distillate is charged with a few drops of phenol-phthalein solution, and titrated with the decinormal solution of alkali, until the color of the alkali reaction becomes constant. The required number of c.c. (2.5 grams of fat having been taken) is Reichert's number.

Meissl's modification of Reichert's process[2] undertakes a more complete distillation of the volatile fat acids, and the use of weaker alcohol in saponification to avoid etherizing the acids, as follows: 5 grams of the clear filtered fat are treated in a flask of 200 c.c. capacity with 2 grams of solid potash and 50 c.c. of 70% alcohol (free from acidity or aldehyde), over the water-bath,

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[1] E. Reichert, 1879: *Zeitsch. anal. Chem.*, 18, 68; *Jour. Chem. Soc.*, 36, 406. Allen, 1885: *Analyst*, 10, 103. R. W. Moore, 1885: *Jour. Am. Chem. Soc.*, 7, 188; *Analyst*, 10, 224; *Am. Chem. Jour.*, 6, 417: *Chem. News.* 50, 268; *Jour. Chem. Soc.*, 48, 300, 1014. E. Reichardt, 1884: *Zeitsch. anal. Chem.*, 23, 565; *Jour. Chem. Soc.*, 46, 1219.

[2] E. Meissl, 1880: *Bied. Cent.*, 1880, 471; *Jour. Chem. Soc.*, 38, 828.

with stirring, until saponified perfectly. The alcohol is evaporated, and the thick soap is dissolved in 100 c.c. of water, precipitated with 4 c.c. of diluted (1 to 10) sulphuric acid, and, after the addition of a few pieces of pumice-stone, distilled with use of a Liebig's condenser. Of distillate 110 c.c. are received in a flask marked at this capacity, this quantity being obtained in about an hour. The distillate is filtered into a flask marked at 100 c.c., and this volume of the filtrate is titrated, after addition of phenol-phthalein or litmus, with decinormal solution of alkali. The number of c.c. required is increased by its one-tenth, and for Reichert's number (on 2.5 of fat) the result of this operation is divided by two. To exclude all interferences a control analysis without fat may be conducted parallel with the assay.

The Reichert's numbers of fats are given under Butter Fat.

(3) *Köttstorfer's method.*[1] Determination of the number of milligrams of potassium hydroxide necessary to saponify 1 gram of the fat—the "Verseifungszahl," or saponification number. The operation requires (1) solution of hydrochloric acid, and (2) alcoholic solution of potassa, both of about half-normal strength. Also (3) a decinormal solution of alkali, exactly standardized. The potassa solution is made of caustic potassa purified by alcohol, dissolved in the least sufficient proportion of water and diluted to standard with alcohol free from fusel oil. It may be prepared by filtration through animal charcoal. If the alcohol be pure a solution of the designated strength will not become darker than yellowish.

Of the purified fat 1 to 2 grams are digested in a covered beaker or flask of about 70 c.c. capacity, with just 25 c.c. of the alcoholic potassa solution, on the water-bath, at near boiling of the liquid, stirring with a glass rod, to perfect saponification. It is believed to be necessary to take precautions against the escape of ethyl butyrate.

One c.c. of phenol-phthalein solution is added, and the liquid titrated with the standard hydrochloric acid to the neutral point. Another 25 c.c. of the potash solution alone is titrated with the hydrochloric acid solution, and the latter titrated with the decinormal alkali. The number of c.c. of the standard alkali taken for the 1 gram of fat, minus the hydrochloric acid in the titration, converted, according to the comparisons made, into milli-

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[1] J. Köttstorfer, 1879: *Zeitsch. anal. Chem.*, 18, 199, 431; *Jour. Chem. Soc.*, 36, 983, 1069; *Analyst*, 4, 106. Moore, 1885: *Jour. Amer. Chem. Soc.*, 7, 188; *Analyst*, 10, 224; *Chem. News*, 50, 268; *Am. Chem. Jour.*, 6, 417; *Jour. Chem. Soc.*, 48, 300, 1014.

grams of potassium hydroxide, gives the saponification number sought.

The details are carried out upon fats of butter and its substitutes by Prof. Wiley (1884) as follows: The dried and filtered butter-fat is weighed in a small beaker with a 2 c.c. pipette. Five stout half-pint beer-bottles of clear glass, with rubber stoppers secured by a spring, are provided. Three portions, of 2 c.c. each, of the fat melted at about 35° C. are introduced severally into three of the bottles, weighing the beaker and pipette after each addition, and noting the exact weight of fat taken in each of the three bottles. Of the alcoholic potash solution just 25 c.c. is now run into each of the five bottles. The bottles are stoppered and placed on the same steam or water-bath, and shaken every five minutes until the fat is saponified. Then the bottles are cooled, opened, and 1 c.c. phenolphthalein solution added to each. Each of the five portions is now titrated with the half-normal hydrochloric acid to the neutral point. The two blanks give an average for the strength of the alcoholic potash, and the three portions of fats give an average for the amount of potash neutralized in saponification.—That is, the mean number of c.c. of hydrochloric acid for one of the two blank portions, *minus* the mean of c.c. of the same acid calculated for 1 gram of fat in one of the three fat-portions, *equals* the no. c.c. of the hydrochloric acid neutralized by the total fat acids in 1 gram of the fat. This last no. of c.c. of hydrochloric acid is to be titrated with the exactly standardized decinormal alkali, and the required no. of c.c. of the latter is multiplied by 5.6 to obtain the milligrams KOH for the fat acids of 1 gram of fat.

Köttstorfer's Number, the milligrams of KOH to saponify 1 gram of fat, is to be distinguished from the "*Saturation-Equivalent*" of fats. The latter term is defined as the number of milligrams of fat saponifiable by 1 c.c. of normal alkali solution. For the triglycerides it is the third of their molecular weight; or it is the hydrogen-equivalent number of the fat. 56000 ÷ Köttstorfer's number = "saturation-equivalent"; and 56000 ÷ "saturation-equivalent" = Köttstorfer's number.

Perkins[1] combines the methods of Hehner, Reichert, and Köttstorfer, as follows: Of the clear fat 1 to 2 grams is saponified; an excess of a cold-saturated solution of oxalic acid is added, and the fat acids separated in the cold, and then washed on the filter with hot water. The filtrate is made up to 200 c.c., and distilled

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[1] F. P. Perkins, 1878: *Analyst*, 3, 241; *Zeitsch. anal. Chem.*, 19, 237.

to give 100 c.c. of distillate (according to Reichert), this being titrated with alkali and the result stated in milligrams of potassium hydroxide to saturate the volatile acids from 1 gram of purified fat. The insoluble fat acids, as washed, are dissolved in 100 c.c. of hot alcohol, and this solution, or an aliquot part of it, titrated with decinormal alkali, calculating the result into milligrams of potassium hydroxide for the insoluble fat acids of 1 gram of fat. The former number plus the latter number gives the milligrams of potassium hydroxide to saturate all the fat acids of the 1 gram of purified fat.

Percentages of Insoluble Fat Acids. Hehner's Numbers.

Olein	95.75	Theoretical quantity.
Palmitin	95.28	“ “
Stearin	95.73	“ “
Butyrin	87.41	“ “
Oleomargarin	95.56	Hehner's determinations.
Cotton-seed oil	95.75	(Bensemann).
	94.29	(E. Waller, 1886).
Cotton stearin	95.5	(Muter).
Lard	96.15	(West-Knights).
Olive oil	95.43	“
	95.09	(E. Waller).
Peanut oil	95.00	“
Palm oil	95.6	(Hehner).
Sesamé oil	95.48	(E. Waller).
Theobroma oil	94.59	(Bensemann).
Seal oil	90.68	(E. Waller).
Rape oil	95.10	(Bensemann).
Cocoanut oil	86.43	(Moore).
	80.78	(E. Waller).
Butter fat, lowest	86.6	(Hehner and Angell).
“ highest	88.5	“ “
“ common maximum	87.5	“ “

Butter fat, lowest of nine		88.50	Wiley, Washington, 1884.
“ highest “		89.89	
From 26 genuine American butters.	lowest.	86.40	E. Waller, New York, 1886.
	highest	90.24	
From 25 butters, Pennsylvania	lowest.	86.7	C. B. Cochran, 1886.
	highest	87.7	

Saponification Coefficients: Köttstorfer's Numbers (*p.* 254).
(Milligrams of KOH neutralized in saponifying 1 gram of Fat.)

Stearin		188.8	By calculation.
Olein		190.0	“
Palmitin		208.0	“
Butyrin		557.3	“
Beef Tallow		196.5	Köttstorfer.
“ “ commercial		196.8	“
Mutton Tallow		197.0	“
Lard		195.7	“
Olive oil		191.8	“
Rape “		178.7	“
Butter Fat	mean	227.0	“
	lowest	221.5	“
	highest	233.0	“
Fat of Rancid Butter—about 1.5 lower than when fresh.			“
Cocoanut oil		250.3	(Moore, 1884).
“ “ washed		246.2	“
“ “ 49.3%, Oleomargarin 50.7%		220.0	“
Cocoanut oil 70.2%, Oleomargarin 29.8%		234.9	“

Almond oil, sweet	194.7–196.1	(Valenta, 1883).
Apricot oil	192.9	“
Bitter Almond, fixed oil	194.5	“
Castor oil	181.0	“
	176–178	(Allen, 1884).
Cotton-seed oil	195	(Valenta).
Lard oil	191–196	(Allen).
Linseed oil	189–195	“
	195.2	(Moore).
Olive oil	191.7	(Valenta).
	191–196	(Allen).
	185.2	(Moore).
Peanut oil	191.3	(Valenta).
	196.6	(Moore).
Sesamé oil	190.0	(Valenta).
Sperm oil	130.0–134.4	(Allen).
Theobroma oil	199.8	(Moore).
Train oil	190–191	(Allen).

Messrs. Waller and Martin (1886: Report of the Dairy

Commissioner of the State of New York) obtained, from 25 genuine American butters, Köttstorfer's numbers from 220.6 to 230.1 (extremes); a rancid butter, 223.0; the same deodorized, 219.45; and from the insoluble fat acids of a butter, 214.25. From oleomargarin 188.65; another, 191.6. From mutton suet, 203.25; beef suet, 199.2; lard, 195.85. From cotton seed oil, 162.0 to 193.05; average of five, 183.47.

(4) *Determination of Fat Acids by their capacity of combination with iodine.*—The fat acids, whether free or in their glycerides, form combinations with iodine, bromine, or chlorine. One molecule of oleic acid or ricinoleic acid takes two atoms of iodine; one molecule of linoleic acid, four atoms of iodine; addition products being formed.

The directions of HÜBL[1] for finding the percentage of iodine taken into combination (the iodine number) are as follows, commencing with preparation of the needful reagents: (1) *Iodine solution.* Of iodine 25 grams are dissolved in 500 c.c. of alcohol (free from fusel oil); of mercuric chloride 30 grams are dissolved in 500 c.c. of the alcohol, and this solution filtered if necessary; when the two solutions are united, and, after 6 to 12 hours' standing, titrated with the standardized thiosulphate solution, and the standard noted.—(2) *Thiosulphate solution.* A solution of about 24 grams of sodium thiosulphate in the liter is made, and its iodine value accurately determined with a weighed quantity of freshly sublimed iodine. About 0.2 gram of resublimed iodine is placed in a small glass tube closed at one end and provided with a similar tube enough larger to serve as a cover, both tubes being previously dried and weighed. The iodine is heated in the inner tube, on a sand-bath, until it melts, then covered with the outer tube, cooled in a desiccator, and weighed. The cover is now removed and both tubes are placed in a stoppered flask containing 1 gram of potassium iodide (neutral and free from iodine) dissolved in 10 c.c. of water. When the iodine has dissolved, the solution of thiosulphate of sodium is added from a burette until the iodine color is reduced to a faint yellow, a little starch solution is added, and the titration completed to the extinction of the blue color. The iodine value of the thiosulphate solution is now written.—(3) *Chloroform.* The purity of chloroform is assured for this assay by digesting 10 c.c. of it with 10 c.c. of the iodine solution at ordinary temperature for two or three hours' and titrating to the extinction of the iodine with the thiosul-

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[1] 1884: *Ding. pol. Jour.*, 253, 281; *Jour. Chem. Soc.*, 46, 1435; *Am. Chem. Jour.*, 6, 285.

phate solution, the stated quantity of which should be consumed. —(4) *Potassium iodide solution.* One part of pure iodide of potassium in 10 parts of water. It should be neutral in reaction, and should not contain any free iodine.

For the assay, 0.2 to 0.3 gram of a drying oil, or 0.3 to 0.4 gram of a non-drying oil, or 0.8 to 1.0 gram of a solid fat, is taken in a close-stoppered flask of about 200 c.c., and 10 c.c. of the chloroform are added for solution. Of the iodine solution 20 c.c. are added in exact measure, and, if the mixture does not become clear after shaking, a little more chloroform is added. The quantity of iodine should be sufficient to leave a dark brown color after one and a half or two hours' standing, the time to be taken for the reaction. In titrating the remaining excess of the iodine, 10 to 15 c.c. of the potassium iodide solution and, after shaking, 150 c.c. of water are added, when the thiosulphate solution is added, with shaking, until the color of both the aqueous layer and the chloroform layer is reduced to a pale yellow, when starch solution is introduced and the extinction of the iodine completed. For close results the iodine and thiosulphate solutions should be standardized just before or after the assay. The number of parts of iodine taken by 100 parts of the fat is known as its iodine number. Using a sufficient excess of iodine in the reaction, quite constant results are promised.

Iodine Numbers.

Oleic acid, $C_{18}H_{34}O_2$	90.07 89.8 to 90.5	By calculation. By experiment.
Ricinoleic acid, $C_{18}H_{34}O_3$...	85.24	By calculation.
Linoleic acid, $C_{16}H_{28}O_2$.....	201.59	" "

Linseed oil..............	158	(Hübl).	155.2	(Moore).[1]
Hempseed oil............	143	"		
Walnut oil..............	143	"		
Poppy oil...............	136	"	134	"
Cotton-seed oil..........	106	"	108.7	"
Sesamé oil..............	106	"	102.7	"
Rape and Rubsen oils....	100	"	103.6	"
Olive oil................	82.8	"	83.0	"
Olive-seed oil...........	81.8	"		
Castor oil...............	84.4	"		
Almond oil (sweet).......	98.4	"	98.1	"
Mustard oil (fixed).......			96.0	"

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[1] R. W. Moore, 1885: *Am. Chem. Jour.*, 6, 416.

Bone oil	68.0	(Hübl).		
Cod-liver oil	123 to 141	(Kremel).		
Lard	59.0	(Hübl).	61.9	(Moore).
Oleomargarin	55.3	"	50.0	"
Palm oil	55.5	"	50.3	"
Tallow	40.0	"		
Wool fat	36.0	"		
Cacao butter (theobroma oil)	34.0	"		
Mace oil (nutmeg butter)	31.0	"		
Butter fat	31.0	"	32.8 to 38.0	"
" " very old			19.5	"
Cocoanut oil	8.9	"	8.9	"
Japan wax	4.2	"		
Fat acids of bone oil	57.4	(Morawski and Demski).		
Fat acids of tallow of beef	25.9 to 32.8	" "		
Fat acids of cocoanut oil	8.4 to 8.8	" "		
Fat acids of linseed oil	155.2 to 155.9	" "		
Fat acids of olive oil	86.1	" "		
Fat acids of cotton seed oil	110.9 to 111.4	" "		
Fat acids of castor oil	86.6 to 88.3	" "		
Mineral oils (petroleum, shale)	Seldom above 14	Valenta (1884).		
Rosin oils	43 to 48	"		

Messrs. Waller and Martin (1886: Report of N. Y. State Dairy Commissioner) found Hübl's numbers as follows:

Ayrshire butter	34.7
Jersey " sweet cream	36.7
" " sour cream	30.5
Native "	30.5
Devon " sour cream	37.0
Rancid "	40.5
Oleomargarin	50.9 to 54.9
Cotton-seed oil	108.4
Linseed oil (average of 2)	165.4
Cocoanut oil (average of 2)	7.8
Commercial Stearin	1.7

(5) *Estimation of Stearic and Palmitic Acids separately in mixtures of the two, by the mean molecular weight of the mixture.*—The molecular weights of stearic and oleic acids, 284 and 282, do not differ from each other enough to give any value to this method applied to mixtures of these two acids. It is applicable to tallows from which the olein has been removed by pressure.—About 50 grams are treated for the separation of the fat acids, by digesting with 40 c.c. potassium hydrate solution of sp. gr. 1.4, and 40 c.c. of alcohol. After boiling to full saponification, one liter of water is added and the liquid boiled about three-fourths of an hour to remove the alcohol, diluted sulphuric acid is added to complete precipitation, the precipitate is well washed with water, melted until clear of water, drained and dried. An accurately weighed portion of about 5 grams of the clean fat acids is dissolved in alcohol, and titrated, by adding normal or other standard solution of alkali in some excess, using phenol-phthalein as an indicator, and bringing back the neutral point by a corresponding solution of acid, when the number (n) of c.c. of normal solution of alkali for saturation of 1 gram of the fat acids is found. Then $1000 \div n =$ mean molecular weight. Now let x be the desired per cent. of the one fat acid, and b its molecular weight; y the desired per cent. of the other acid, and c its molecular weight—while a is the mean molecular weight as found from titration. Then $x = 100 \dfrac{a - c}{b - c}$, and $y = 100 - x$. With stearic and palmitic acids $x = 100 \dfrac{a - 256}{28}$.

(6) *Determination of Specific Gravity of the Fats.*—The determination of the liquid fats is made at customary standard temperatures, as of other liquids, by weight in a specific-gravity bottle, or a Sprengel's tube, or by a hydrometer. The specific gravity of the waxes and very hard fats is usually taken in the solid state, at customary temperatures, and so stated. In case of many fats, however, the density of the solid state is measurably dependent upon the conditions of solidification. And the specific gravity of the softer solid fats is more often taken in the liquid state, at some stated temperature well above the melting point—by Stoddart at 100° C., by Muter at 37.8° C. (100° F.)—and usually taking water at the same temperature as the standard.

In adjusting the temperature of a specific-gravity bottle or a Sprengel's tube, immersion in water is employed. The water is warmed in a beaker, or other convenient vessel, in which the gravity bottle or tube is securely suspended, the filling up of the exact volume of the liquid fat being adjusted at the noted temperature. Then the operation is repeated with water instead of fat, to obtain the divisor representing the unit of density.—The Westphal balance is conveniently employed, the counterpoise being suspended and weighed in the oil, contained in a vessel surrounded by water in a larger vessel to which heat is applied.

To take the specific gravity of a melted fat by the hydrometer, a small hydrometer is most convenient, and the oil is contained in a corresponding small cylinder which can easily be immersed in a hot water-bath. A constant water-bath of constant temperature is convenient for habitual use in this operation.

Methods by dropping into liquids of known and adjusted density have been proposed by chemists. Hager (1880) drops melted fat into alcohol, keeping the drops separate, then transfers them to mixtures of alcohol, water, and glycerine, until an equilibrium is found. A list of densities of fats and resins, so determined, is published.[1] A similar method was proposed for butter fat, using methylated spirit, by Cassamajor (1881), and further described under Butter. The counterpart principle, of employing specific-gravity beads of graded density, has been developed by Mr. Wigner (1876[2]), especially for melted fats.

Blyth recommends taking the specific gravity of butter fat, clarified and filtered, as a solid at 15° C., by weight in suspension in water, with a weighted tube, on the general plan of solids lighter than water.[3]

The ratio of expansion of butter fat, lard, etc., on increase of temperature, has been reported on by Wigner (1879[4]).

Specific Gravities of Fat Oils classified by Benedikt, taking figures of Allen (1884), and others, at 15° C.:

A. Sp. gr. under 0.883..	1. Liquid waxes from marine animals:		
		Sperm oil..........	0.875–0.883
	2. Oils of unknown composition:		
		Shark oil..........	0.865–0.867
		African fish-oil.....	0.867

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[1] *Zeitsch. anal. Chem.*, 19, 239; *Jour. Chem. Soc.*, 38, 70; *Phar. Jour. Trans.*, [3], 10, 287.

[2] *Analyst*, 1, 145.

[3] 1880: *Analyst*, 5, 76.

[4] *Analyst*, 4, 183.

B. 0.883 to 0.912	Oil from cranial cavities: Liquid waxes with glycerides	0.908
C. 0.912 to 0.920	1. Non-drying oils:	
	Almond oil.........	0.917–0.920
	Peanut oil.........	0.916–0.920
	Olive oil...........	0.914–0.917
	Mustard oil.........	0.914–0.920
	2. Oils of marine animals.	none.
	3. Oils of land animals:	
	Lard oil............	0.915
	Tallow oil..........	0.916
	Neat-foot oil.......	0.914–0.916
	Bone oil............	0.914–0.916
D. 0.920 to 0.937......	1. Vegetable oils:	
	(*a*) Feebly drying, sp. gr. less than 0.930:	
	Cotton-seed oil...	0.922–0.930
	Sesamé oil.......	0.923–0.924
	Sunflower oil.....	0.924–0.926
	(*b*) Strongly drying oils:	
	Hempseed oil....	0.925–0.931
	Linseed oil	0.930–0.935
	Poppy oil.......	0.924–0.937
	Walnut oil.......	0.925–0.926
	2. Oils of marine animals:	
	Cod-liver oil.......	0.923–0.930
	3. Oils of land animals..	none.
E. Sp. gr. above 0.937..	1. Vegetable oils. Of cathartic effect:	
	Croton oil.........	0.942–0.943
	Castor oil..........	0.960
	(Boiled linseed oil.)	
	2. Oils of land animals..	none.

SPECIFIC GRAVITIES OF FAT OILS at 15° C. (MUNICIPAL LABORATORY OF PARIS, 1884):

Almond oil...........	0.917	Olive oil.............	0.9163
Peanut oil	0.917	" " common.....	0.9163

Colza oil	0.9154	Sesamé oil	0.9226
Cotton-seed oil (white)	0.9254	Norwegian whale oil	0.9257
" " " (brown)	0.930	South Sea " "	0.927
Beechnut oil	0.922	American " "	0.925
Linseed oil	0.9325	Cod-liver oil (pale)	0.928
Cameline oil	0.9252	" " " (brown)	0.9254
Walnut oil	0.926	Neat-foot oil	0.9142
Poppy oil	0 925	Sheep-foot oil	0.9187
Tallow oil	0.9029.		

To compare the specific gravity of one oil with that of another oil (Donny, 1864): Color the one oil with alkanet or other tinctorial matter, and, while both oils are at same temperature, let fall a few drops of the colored oil into a portion of the other in a test-tube.

Specific Gravities of Solid Fats at 15° C. (Dieterich, 1882):

Wax, white	0.973	Common Resin, American	1.108
" yellow	0.963–0.964	Common Resin, French	1.104–1.105
" Japan	0.975	Theobroma oil	0.980–0.981
Ceresin, white	0.918	Paraffin, medium	0.913–0.914
" half white	0.920	Tallow, beef	0.952–0.953
" yellow	0.922	" sheep	0.961
Ozokerite, crude	0.952		
Spermaceti	0.960		
"Stearin"	0.971–0.972.		

Specific Gravities of Solid Fats at 15° C. Hager (1879):

Butter Fat, clarified	0.938–0.940
" several months old	0.936–0.937
Artificial butter	0.925–0.930
Lard, fresh	0.931–0.932
Tallow, beef	0.925–0.929
" sheep	0.937–0.940
Cocoanut oil, fresh	0.950–0.952
" very old	0.945–0.946
Stearic acid, melted	0.946
" " crystallized	0.967–0.969
Beeswax, yellow	0.959–0.962
Ceresin, yellow	0.925–0.928
" white	0.923–0.924
" very pure white	0.905–0.908
Common resin	1.100

SPECIFIC GRAVITIES OF SOLID FATS. *At* 100° *C., compared with water at* 15° *C.* BENEDIKT (1886), from ALLEN (1884) and KÖNIGS (1883):

A. Fats not containing glycerides of lower fat acids:

1. Vegetable:	Theobroma oil	0.857
	Palm oil	0.857
	Japan wax	0.873
2. Animal:	Lard	0.861
	Tallow (beef or mutton)	0.860
	Horse fat	0 861
	Oleomargarin	0.859

B. Fats containing glycerides of lower (volatile) fat acids:

1. Vegetable:	Cocoanut oil	0.863
	Palm-kernel oil	0.866
2. Animal:	Butter fat	0.865–0.868

(7) *Determination of the Melting and Congealing Points of Fats.*—A simple method of finding *the melting point* is that of the inspection of the fat, taken congealed on the bulb of a thermometer, in a beaker of water to which heat is applied, as described under Stearic acid, *a.*

Sometimes a few drops of the melted fat are taken up in a glass tube of 1 to 3 millimeters internal diameter, bound against the bulb of a thermometer, congealed, and immersed in a beaker of water or other liquid to which heat is gradually applied. The capillarity of the tube influences the movement of the fat, so that the melting point obtained in this way is somewhat higher than that obtained by observation of the fat taken as a coating of the thermometer bulb. Some observers have wider tubes—taking a "funnel-tube" of about 2 centimeters diameter in the upper portion and 7 millimeters diameter in the lower portion—a few drops of the melted fat being taken and congealed on the side of the wider part, just above the narrowing of the tube. Some authors designate the "beginning of the melting point" as the temperature at which the fat begins to flow down the side of the tube, and "end of the melting point" as that at which it becomes wholly liquid.

The sinking point of HEHNER and ANGELL is the temperature at which a glass bulb of 3.4 sp. gr. and 1 c.c. in volume will sink in the melted fat. The bulb is blown from a piece of glass tubing of ¼ inch diameter, and is drawn off pear-shaped with a very tapering end. The bulb should displace as nearly as possible 1 c.c. of water, and should be so weighted by the introduction of mercury as to weigh 3.4 grams. Differences of 0.005 to 0.01 weight have little effect on the results. The following directions for taking "the sinking point" of butter will indicate the method of application to any fat. Of the butter 20 to 30 grams are melted in a beaker over the water-bath, then poured into a test-tube ¾ inch wide and 6 inches long, filling to within two inches of the top. The tube is kept warm until the fat is clarified by the settling of the water, curd, and salt, when the fat is solidified at 15° C. by immersing the tube in water of this temperature. (The cone of depression on the top of the fat serves to indicate its relative fusing point. Pure butter fat shows only a slight depression, while admixtures with fats of high melting points show a considerable hollow cone.) The tube is now placed in about one liter of cold water, in a beaker, the test-tube being secured so that the top of the fat is about 1½ inches below the surface of the water. Heat is now applied to the beaker by a sand-bath or by asbestos felt, over a lamp. The surface of the fat is made level, and the weighted bulb placed thereon. The water is stirred from time to time. A thermometer is placed in the water, with the bulb near the surface of the fat, and the temperature read off just as the globular part of the bulb has sunk beneath the fat.

Hehner and Angell found the average sinking point of the fat of 24 genuine butters to be 35.5° C. (96° F.), with extremes of 34.3° to 36.3° C. (93.7°–97.3° F.) Of the fatty acids of butter fat, 40.5° to 42.1° C. Of beef tallow, average, 50.6° C. (48.3° to 53.0° C.); of mutton tallow, 50.9° C. average (50.1° to 51.6° C.); of lard, 41.1° to 45.3° C.; of stearin, 62.8° C.; of cacao butter, 34.9° C.; of palm oil, 39.2° C. To calculate the mean sinking point of a mixture of two fats of known composition, having their respective sinking points (S_1 and S_2), and percentages in the mixture (F_1 and F_2):

$$\frac{(F_1 \times S_1) + (F_2 \times S_2)}{F_1 + F_2} = \text{sinking point of the mixture.}$$

Results of admixture are compared with calculated averages, as follows:

66.7%	butter and	33.3%	tallow,	43.1° C.	found,	42.08° C.	calculated.
73.0	"	27.0	"	42.3	"	40.2	"
10.0	"	90.0	"	48.8	"	49.6	"
85.0	"	15.0	"	38.1	"	38.1	"

Hassall uses a light bulb, weighing 0.18 gram, and of the volume of about 0.5 c c., sunken in the solidified fat in a test-tube ⅓ inch wide and 4 inches high. "*The rising point*" is taken at the temperature when the bulb rises, during the gradual application of heat, by the softening of the fat. Hassall also records "the *point of clearance*," when the fat becomes clear, this point being usually 1° or 2° C. above the rising point.

The congealing point is more often inconstant than the melting point. It is sometimes taken as the point of commencing turbidity in a mass of melted fat, and sometimes as the point of formation of a coherent solid. DALICAN made determination of the congealing point by use of a test-glass 10 or 12 centimeters (4 or 5 inches) long and 1.5 or 2 centimeters (0.4 or 0.5 inch) wide. The tube is two-thirds filled with the fat, warmed, and the fat stirred with a glass rod, to liquefy the contents. A thermometer, graduated in fifths, is suspended in the fat, loosely adjusted by a perforated cork at the mouth of the tube, the bulb resting in the centre of the fat. When crystallization commences on the edge the mass is stirred with the bulb of the thermometer, by which the temperature is caused to fall a little, after which it soon rises to near the point before noted, and when it stands constant for two minutes the temperature is taken as the congealing point. Some fats, in congealing, show a rise of temperature after the solidification has fairly set in, and the maximum of this rise is sometimes taken as the congealing point (see the table at p. 271).

MELTING AND CONGEALING POINTS *of mixtures of Stearic and Palmitic acids* (HEINTZ):

Stearic acid.	*Palmitic acid.*	*Melting point.*	*Congealing point.*
100%	0%	69.2° C.	—.–° C.
90	10	67.2	62.5
80	20	65.3	60.3
70	30	62.9	59.3
60	40	60.3	56.5
50	50	56.6	55
40	60	56.3	54.5
32.5	67.5	55.2	54
30	70	55.1	54
20	80	57.5	53.8
10	90	60.1	54.5
0	100	62.0	

Congealing Point *of mixtures of Solid fat acids* ("Stearic acid") *and Liquid fat acid* ("Oleic acid") *as obtained from Tallow* (Dalican, 1880):

Congealing point. °C.	*"Stearic acid" in* 100 *parts of Tallow.*	*"Oleic acid" in* 100 *parts of Tallow.*
35°	25.20 parts.	69.80 parts.
35.5	26 40	68.60
36	27.30	67.70
36.5	28.75	66.25
37	29.80	65.20
37.5	30.60	64.40
38	31.25	63.75
38.5	32.15	62.85
39	33.45	61.55
39.5	34.20	60.80
40	35.15	59.85
40.5	36.10	58.90
41	38.00	57.00
41.5	38.95	56.05
42	39.90	55.10
42.5	42.75	52.27
43	43.70	51.30
43.5	44.65	50.35
44	47.50	47.50
44.5	49.40	45.60
45	51.30	43.70
45.5	52.25	42.75
46	53.20	41.80
46.5	55.10	39.90
47	57.95	37.05
47.5	58.90	36.10
48	61.75	33.25
48.5	66.50	28.50
49	71.25	23.75
49.5	72.20	22.80
50	75.05	19.95
50.5	77.10	17.90
51	79.50	15.50
51.5	81.90	13.10
52	84.00	11.00
52.5	88.30	6.70
53	92.10	2.90

MELTING AND CONGEALING POINTS *of the Acids of Solid Fats* (HÜBL).

Fat acids of	*Melting.*	*Congealing.*
Oleomargarin	42.0° C.	39.8° C.
Palm oil	47.8	42.7
Tallow	45.0	43.0
Wool fat	41.8	40.0
Cacao butter	52.0	51.0
Mace oil (nutmeg oil)	42.5	40.0
Butter fat	38.0	35.8
Cocoanut oil	24.6	20.4

MELTING AND CONGEALING POINTS *of the Fat Acids of Oils* (BACH).

Fat acids of	*Melting.*	*Congealing.*
Olive oil	26.5–28.5° C.	Not under 22° C.
Cotton-seed oil	38.0	35.0
Sesamé oil	35.0	32.5
Peanut oil	33.0	31.0
Sunflower-seed oil	23.0	17.0
Rape oil	20.7	15.0
Castor oil	13.0	2.0

CONGEALING POINT *of mixtures of certain proportions of commercial Stearic acid of stated melting points, as obtained from Tallow* (SCHEPPER and GEITEL, 1882).

Congealing point of the tallow-fat acids.	*The tallow-fat acids containing in per cent. of "Stearic acid" of congealing point of*			
	48° C.	50° C.	52° C.	54.8° C.
10° C.	3.2	2.7	2.3	2.1
15°	7.5	6.6	5.7	4.8
20°	13.0	11.4	9.7	8.2
25°	19.2	17.0	14.8	12.6
30°	27.9	23.2	21.4	18.3
35°	39.5	34.5	30.2	25.8
36°	42.5	36.9	32.5	27.6
37°	46.0	40.0	34.9	29.6
38°	49.5	42.6	37.5	32.0
39°	53.2	45 8	40.3	34.3
40°	57.8	49.6	43.5	37.0
41°	62.2	53.5	47.0	40.0
42°	66.6	57.6	50.5	42.9
43°	71.8	62.0	54.0	46.0
44°	77.0	66.2	58.4	49.8
45°	81.8	71.0	62.6	53.0
46°	87.5	75.8	67.0	56.8
47°	93.3	80.9	71.5	60.8
48°	100.0	87.2	76.6	65.0
49°	....	93.0	81.7	69.5
50°	....	100.0	87.0	74.5
51°	....	....	93.5	79.8
52°	....	....	100.0	84.8
53°	....	....	....	90.1
54°	....	....	....	95.3
54.8°	....	....	....	100.0

CONGEALING POINTS *of Oils* (MUNICIPAL LABORATORY OF PARIS).

Olive oil............	+ 2° C.	Beechnut oil......	−17.5° C.
Cod-liver oil........	0	Cameline oil......	−18
Rape oil............	− 3.75	Poppy oil........	−18
Colza oil...........	− 6.25	Linseed oil.......	−27.5
Peanut oil...........	− 7	Hempseed oil.....	−27.5
Almond oil.........	−10		

Melting and Congealing Points *of Solid Fats*, Wimmel (1868).

	Melting point.	*In congealing become turbid at*	*In congealing, temp. rises to*
Tallow, beef, fresh....	43° C.	33° C.	36–37° C.
“ “ old......	42.5	34	38
“ sheep, fresh...	47	36	40–41
“ “ old....	50.5	39.5	44–45
Lard................	41.5–42	30	32
Butter fat, fresh......	31–31.5	19–20	19.5–20.5
Firkin butter........	32.5	24	25.5
Japan wax..........	52.5–54.5	40.5–41	45.5–46
Cacao butter.........	33.5–34	20 5	27–29.5
Cocoanut oil.........	24.5	20–20.5	22–23
Palm oil, fresh, soft..	30	21	21.5
“ “ hard.	36	24	35
“ old........	42	38	39.5
Mace oil (nutmeg oil).	43.5–44	33	41.5–42
Beeswax, yellow......	62–62.5	congeal just below the melting point without development of warmth.	
Spermaceti...........	44–44.5		
Other Authorities:			
Cholesterin..........	145–146		
Isocholesterin.......	137–138		
Ceresin (ozokerite)....	58–84		
Cetyl alcohol........	50		
Ceryl alcohol........	79		
Myricyl alcohol......	85		

Stearin Percentage in Oleomargarin, according to Congealing Points.[1]

Congealing at °C.	*Per cent. of Stearic ac. of 48° C.*[2]	*Congealing at °C.*	*Per cent. of Stearic ac. of 48° C.*	*Congealing at °C.*	*Per cent. of Stearic ac. of 48° C.*
5.4°	..	20°	12.1	35°	39.5
6	0.3	21	13.2	36	43.0
7	0.8	22	14.5	37	46.9
8	1.2	23	15.7	38	50.5
9	1.7	24	17.0	39	54.5
10	2.5	25	18.5	40	58.9
11	3.2	26	20.0	41	63 6
12	3.8	27	21.7	42	68.5
13	4.7	28	23.3	43	73.5
14	5.6	29	25.2	44	78.9
15	6.6	30	27.2	45	83.5
16	7.7	31	29.2	46	89.0
17	8.8	32	31.5	47	94.1
18	9.8	33	33.8	48	100.0
19	11.1	34	36.6		

Rüdorff (1872).

	Melting point.	*Congealing point.*	*In congealing, temperature rises to*
Yellow wax....	63.4	61.5, 62.6, 62.3	
White wax....	61.8	61.6	
Paraffin...	49.6	49.6	
"	52.5, 54.0	53.0	
"	53.0	52.9	
"	52.7, 53.2	52.7	
Spermaceti......	43.5	43.4	
"	44.1, 44.3	44.2	
Stearic acid, commercial	55.3	55.2	
	56.2, 56.6	55.8	
	56.0, 56.4	55.7	
Japan wax.....	50.4, 51.0	....	50.8
Cacao butter...	33.5	....	27.3
Mace oil (nutmeg).......	70, 80	....	41.7, 41.8
Tallow, sheep..	46.5, 47.4	32, 36	a few degrees.
" " ..	43.5, 45.0	27, 35	

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[1] Benedikt's "Analyse der Fette," p. 131.

[2] Congealing point.

(8) *Calculation of the constituent Fat Acids and Neutral Fats, and the value for production of Fat Acids and Glycerin.*

Let n equal the number of c.c. of standard solution required to saturate the free fat acids of 1 gram of the material, taken up in alcoholic solution, using phenol-phthalein as an indicator, and titrating with alkali at once. Let m be the number of c.c. of the standard alkali of the value of 1 c.c. of normal alkali. In normal solution, $m = 1$; in decinormal solution, $m = 10$, etc. Let c be the number of c.c. of $\frac{1}{m}$ normal alkali taken to saturate both the free and combined acids in 1 gram of fat, as directed under Determination of Mean Molecular Weight (p. 261). Let a be the mean molecular weight of the fat, found from c, as directed on p. 261. Then *per cent. of free fat acids* $= \frac{n\,a}{10 \times m}$. *Per cent. of neutral fat* $= 100 -$ per cent. of free fat acids.

(9) *Distinction of Fat Oils by Solubility in Glacial Acetic Acid* (Valenta,[1] 1884).—When the oil, and glacial acetic acid of sp. gr. 1.05662, in equal volumes, are mixed in a test-tube, and if solution does not occur at ordinary temperatures, the mixture warmed, it will be found that—

1. At ordinary temperatures (15°–20° C.) Castor oil and Olive oil are perfectly dissolved.

2. At temperatures from 23° C. to the boiling of the acid, solution is obtained with Palm oil, Mace oil, Cocoanut oil, Palm-kernel oil, Olive oil, Theobroma oil, Sesamé oil, Almond oil, Cotton-seed oil, Peanut oil, Beef Tallow, American Bone oil, Cod-liver oil, Press Tallow. See table below.

3. Imperfectly dissolved at boiling of the acetic acid—Rape oils.

For distinctions between members of the 2d class the mixture is heated in the test-tube until solution is effected, when a thermometer is introduced, and, *as the mixture cools, the temperature of commencing turbidity* is noted:

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[1] *Ding. pol. Jour.*, **252**, 296; *Zeitsch. anal. Chem.*, **24**, 295; *Jour. Chem. Soc.*, **48**, 93; **46**, 1078.

Name of the Fat.	*Sp. Gr. of the fat.*	*Turbid at*	*Remarks.*
Palm oil	....	23° C.	Fresh fat.
Mace oil	....	27	
Cocoanut oil	....	40	
Palm-kernel oil	....	48	Old rancid fat.
Olive oil, green	0.9173	85	Second pressed, probably containing olive-kernel oil.
Theobroma oil	....	105	
Sesamé oil	0.9213	107	
Almond oil	0.9186	110	From sweet almonds.
Cotton-seed oil	0.9228	110	
Olive oil, yellow	0.9149	111	Oil first pressed.
Peanut oil	0.9193	112	
Apricot oil	0.9191	114	
Beef Tallow	....	95	Very fine hard tallow.
Bone Fat (American)	....	90–95	
Cod-liver oil	....	101	
Press Tallow	....	114	Melt. 55.8° C. Hard, fine.

Solubilities of Oils in Glacial Acetic Acid, Barnes (1876).—1 volume of glacial acetic acid dissolves of fixed oil of almonds, 7 vols.; olive oil, 8 vols.; cod-liver oil, 7 vols.; linseed oil, 7 vols.; turpentine oil, ½ vol.; copaiba oil, $\frac{1}{20}$ vol.; lemon oil, 2 vols.; juniper oil, 1 vol.; all proportions of castor oil and croton oil.

SEPARATION OF MINERAL OILS AND OTHER NON SAPONIFIABLE BODIES FROM THE FAT OILS OR GLYCERIDES.[1]—The determination, in qualitative or quantitative result, of mixtures of the FAT OILS or glycerides with *mineral oils* (petroleum and shale oils), *tar oils* (neutral coal oils), *paraffins*, *rosin oils*, *resins*, and *waxes*. Excluding the few instances in which a volatile hydrocarbon or

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[1] E. Geissler, H. Hager, 1880: Summary in *Zeitsch. anal. Chem.*, **19**, 114. Lux, 1885: *Zeitsch. anal. Chem.*, **24**, 357. A. H. Allen, 1881: *Chem. News*, **44**, 161; **43**, 267. Benedikt: "Analyse der Fette," 1886, pp. 102–126: "Nachweis und quantitative Bestimmung solcher fremder Beimengungen, welche in der Fettsubstanz gelöst oder mit ihr zusammengeschmolzen sind."

mineral oil can be separated from fixed oils *by distillation*, either with or without steam, the analysis requires first *the saponification* of the saponifiable substances. Of the bodies named above with the mineral oils, only the resins are fully saponifiable, besides which only the waxes saponify at all. The waxes give the acids to alkalies in production of soap-like compounds, while the base, unlike glycerin, remains undissolved after the saponification.

When the fat is readily saponifiable, and especially when the non-saponifiable substance is not much soluble in aqueous soap solution, simple saponification, with dilution of the mixture, serves for the separation, more satisfactorily with large quantities: 50 grams material in a 300 c.c. flask, with 50 c.c. alcohol and 40 grams caustic soda (which will dissolve clear in alcohol), digested with stirring at about 90° C. until dissolved, then boiled for 40 minutes, 150 c.c. water added (while boiling), boiled 50 minutes longer, and poured into a cylindrical separator. When the non-saponifiable oil has risen to a clear layer, this is poured off into a tared dish, the surfaces of the separator and the liquid washed with a few portions of ether, the ether evaporated, and the weight taken.

But in general the mineral oils and resin oil dissolve in soap solution to an extent preventing full recovery by the above-given method. The solubility is diminished by largely diluting the soap solution, but this is quite impracticable because it decomposes the soap itself, giving a mixture turbid with free fat acids. Therefore it is necessary to employ a solvent not miscible with aqueous solutions—as ether or petroleum benzin—by which the paraffin oil or like unsaponified matter may be "extracted" from the solution. This may be done by "shaking out" in the ordinary way. Ether is almost always the best solvent, giving least difficulty in emulsification, though often troublesome in this respect. To avoid permanent emulsification the agitation may be done by gently elevating alternate ends of the separator. The details are given by Allen and Thompson (1881) in effect as follows:

Of the material 5 grams are taken, digested with 25 c.c. of an alcoholic soda solution (80 grams caustic soda per liter) until saponification is complete and the alcohol evaporated, treated with 50 c.c. of hot water to dissolve the soap, and the liquid introduced into a separator of about 200 c.c. capacity. 20 or 30 c.c. of water are added, and when cold the liquid is shaken with 30 to 50 c.c. of ether. Separation can be promoted by addition of a little alcohol. From three to four successive portions of ether are usually required. The residue obtained in a tared beaker or flask by evaporation of the ethereal solution is weighed.

With use of petroleum benzin upon a dried saponified mass of the material under examination, the authors last quoted proceed as follows: 10 grams of the material, in an evaporating-dish of five inches diameter, are digested with 50 c.c. of an eight-per-cent. alcoholic solution of caustic soda, stirring and gently boiling, adding 15 c.c. of methyl alcohol, and boiling again. About 5 grams of sodium carbonate are now stirred in, and then 50 to 70 grams of ignited clean sand, the mixture dried for 20 minutes on the water-bath, transferred to an extraction apparatus, exhausted with petroleum benzin (wholly volatile at 80° C.), and the residue, after evaporation of this solvent, weighed as non-saponifiable matters. Ignited, these should leave only a trace of ash. In presence of much mineral oil or resin oil a portion of soap is taken up by the benzin, and the extraction of the solution by ether is more trustworthy.

Extraction of the dried soap with benzin is carried out by Donath (1873), in analysis of stearin candles for paraffin, as follows: 6 grams are saponified by digestion with alcoholic potash, the alcohol evaporated, the residue dissolved in water, and the solution precipitated with calcium or barium chloride. If much paraffin be probably present, some sodium carbonate is added, to give earthy carbonate to the precipitate. The precipitate holds the paraffin completely, and is washed on the filter with hot water, drained and dried at 100° C., and exhausted with petroleum benzin in an extraction apparatus. The error does not overgo 0.3% of the paraffin.

Benedikt (1886) recommends the use of *a liquid extraction apparatus* in treating the aqueous soap solution with ether or petroleum benzin. See under "Extraction Apparatus—For Liquids," p. 38.

Estimation of non-saponifiable admixture may be made by calculation of the Köttstorfer's number (factor of saponification) (p. 254) of the mixture (a_1) compared with that of the pure saponifiable fat, as known (a). Then the per cent. of non-saponifiable matter $(\mathrm{N}) = 100 - \frac{100\,a_1}{a}$.

Small percentages of fat in mixture with hydrocarbons may be estimated by a quantitative determination of the glycerin resulting from saponification, using the permanganate-oxidation method. (See Glycerin, *f*).

Examination of the non-saponifiable matters.—Of these the ordinary articles are as follows: Liquid—petroleum oils, shale oils, tar oils, resin oils; Solid—paraffin, ceresin, solid fat alcohols, cholesterin, isocholesterin.—Of *the liquids*, the Mineral Oils from petroleum and from shale are distilled over at 250°–300° C., and of sp. gr. 0.855 to 0.900; vaselin oil at 250°–350° C., and of sp. gr. 0.900 to 0.930.—The Tar Oils distilled from coal-tar as "dead oils," from 240° C. to 350° C.,[1] purified by soda-lye, are used as lubricating oils, and have sp. gr. above 1, indeed above 1.010. As to Rosin Oils, see page 280. Of *the solids*, Paraffins are white, odorless, of sp. gr. 0.869 to 0.943, distil without change, are graded by congealing points 38° to 82° C., and dissolve in alcohol. Ceresin or Ozokerite is not distilled, is purified by sulphuric acid, and agrees in general with paraffin in specific gravities and congealing points.

In the elaidin test the mineral oils remain nearly or quite unchanged.—Iodine numbers (p. 258) distinguish mineral oils from rosin oils.—Glacial acetic acid, 100 grams, at 50° C., dissolves 2.6 to 6.5 grams of various mineral oils; about 17 grams rosin oils. In determining these solubilities 2 c.c. of the oil to be tested may be treated in a stoppered test-tube with 10 c.c. glacial acetic acid, warming in a water-bath at 50° C. and agitating, filtering through a filter just moistened with the glacial acid, and determining the quantity of acetic acid in a weighed portion of filtrate by titrating with standard alkali.—Acetone is used for separation of mineral oils from rosin oils, as specified under Rosin Oils.—For the solid non-saponifiable matters the melting points are observed (see Melting and Congealing Points of Solid Fats, p. 271). Treated with an equal weight of anhydrous glacial acetic acid, boiling some time with a return-condenser, the fat alcohols (cetyl alcohol, etc.) dissolve completely, cholesterin crystallizes on cooling, and paraffins or ceresins swim undissolved while hot and congeal on cooling.

Non saponifiable matters (hydrocarbons or other bodies) in the Fats and Waxes. (ALLEN and THOMPSON, 1881.)—By saponification and extraction with petroleum benzin there were found of unsaponifiable matter—in Lard, 0.23%; Cotton-seed oil, 1.64%; Olive oil, 0.75%; Rape oil, 1.00%; Cod-liver oil, 1.32%; Japan wax, 1.14%; Spermaceti, 40.64%; Beeswax, 52.38%; Rosin oil, 98.72%; Mineral oils, 99.90%.

ESTIMATION OF FREE FATTY ACIDS IN FATS.[2]—The plan of

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[1] A summary of the fractions of coal-tar distillation is given under Phenol.

[2] GEISSLER, 1878: *Ding. pol. Jour.*, 227, 92; *Zeitsch. anal. Chem.*, 17, 393; *Jour. Chem. Soc.*, 34, 534. BURSTYN, 1872. HAGER, 1877. WIEDERHOLD,

Geissler, an ethereal solution of the oil being titrated with standard alcoholic alkali, to the neutral reaction of phenol-phthalein, is generally applicable, and capable of variation to meet technical demands. As a solvent for the fats and oils, ether or alcohol-ether may be employed, or (GROGER) 5 to 10 parts of hot alcohol may be used. The solvent must be free from acidity. Ether is neutralized for this purpose by adding to a portion a drop or two of phenol-phthalein solution, and then drops of alcoholic alkali, until the color of the indicator begins to appear after shaking. For one part of the oil, weighed for estimation, 2 or 3 parts of ether are usually sufficient. The alcoholic alkali solution may be made with good alcoholic potassa, and alcohol free from fusel oil (if need be, filtered through animal charcoal), and in most cases should be very dilute, approximately 20th normal, or weaker. After titrating the ethereal solution of the weighed quantity of the oil, with the alcoholic alkali, just the required quantity of this is again taken and titrated with standard acid. Generally decinormal acid may be used, or a solution of acid in which 1 c.c. corresponds to 0.001 gram of the fat acid under estimation. It is better to express the results in percentages of fatty acids in the fats examined, provided a representative acid can be taken—as *n* per cent. of free acid *as oleic acid*. BURSTYN's numbers, or degrees of acidity in fats, are the c.c. of normal alkali solution neutralized by 100 c.c. of fat; or (KÖTTSTORFER) 100 grams of the fat.

ARCHBUTT distils a mixture of the oil with purified methyl alcohol, repeating once, and titrates the distillate.

Separation of Common Resin from Fats and Soaps.—A satisfactory method, trustworthy for either Quantitative or Qualitative purposes, is that of GLADDING,[1] dependent on ether-solubility of the silver salt, and corresponding to the separation of oleic acid by ether-solubility of its lead salt. Fatty salts of silver are insoluble, resin salt of silver soluble in ether.—The free fat acids are to be obtained, with the rosin, neutral fats being first saponified, soaps being treated with acid, and the total free fatty acids washed with water and dried if need be. For *quantitative* separation the directions are as follows:

About 0.5 of the fat acids is accurately weighed into a small flask, and 20 c.c. of 95 per cent. alcohol added for solution. A

1877. KÖTTSTORFER, rancid butters, 1879: *Zeitsch. anal. Chem.*, **18**, 436. GROGER, 1882: *Ding. pol. Jour.*, **244**, 307. ARCHBUTT: *Repert. f. anal. Chem.*, **4**, 330.

[1] 1882: *Am. Chem. Jour.*, **3**, 416; *Jour. Chem. Soc.*, **42**, 663; *Chem. News*, **45**, 169; *Zeitsch. anal. Chem.*, **21**, 585.

drop of phenol-phthalein is added, then a saturated alcohol solution of caustic potash is added by drops until the color of an alkaline reaction is obtained after agitation, when one or two drops of the alcoholic potash are added in excess. The liquid is now held at the temperature of boiling alcohol for ten minutes, while the flask is loosely corked. When cold the contents of the flask are transferred to a 100 c.c. graduated cylinder, rinsing with concentrated ether, and diluting with this solvent just to the 100 c.c. mark. The cylinder is well corked and shaken for a moment, and about 1 gram of pure silver nitrate, neutral in reaction, rubbed to an impalpable powder, is added to the solution, and the whole shaken vigorously for 10 or 15 minutes until the precipitate will settle clear. The volume is restored, if need be, to 100 c.c. by adding ether and shaking, and of the supernatent liquid 50 to 70 c.c., as an aliquot part (m c.c.) of the whole 100 c.c., is siphoned off by means of a slender siphon (previously filled with ether) into a second stoppered 100 c.c. cylinder, passing the liquid through a small filter if not perfectly clear. The siphon and filter are rinsed with a little ether into the second cylinder. To make certain that the silver precipitation is complete, a little pulverized silver nitrate is shaken up with the clear liquid. Now a mixture of 7 c.c. of hydrochloric acid (sp. gr. about 1.12) and 14 c.c. of water are added, and the whole shaken vigorously until the silver is wholly converted to chloride. When the precipitate has settled perfectly, the volume (n c.c.) of the ethereal liquid is read, and an aliquot part (o c.c.) of this ethereal solution is siphoned off into a tared beaker, rinsing the siphon into the beaker with a little ether, and the ether evaporated gently, to obtain the weight of the residue. The residue is the resin, representing, through both the aliquot divisions, the entire resin in the fat taken. A small but nearly constant proportion of oleic acid is taken up as silver salt by the ether, and left with the resin in the final residue; therefore a correction is made as follows: for every 10 c.c. of the ethereal solution of silver salt siphoned off, 0.00235 gram is deducted Then having w as the number of grams of residue obtained in the analysis, and a as the number of grams of fat taken for analysis, to find x the per cent. of resin in the fat acids, the calculation is as follows:

$$x = \frac{10000\, n w}{a m o} - \frac{2.35}{a}.$$

For *qualitative* purposes the same operation, performed in good, strong stoppered cylinders or test-glasses, without weighing or measuring portions, will give trustworthy results. The final residue is to be examined, when cold, as to brittleness, solubilities, etc., for identification of resin of turpentine or common rosin.

Rosin Oils. Resin Oils. Harzöle.[1]—Of complex and variable composition, consisting of polymeric terpenes and other hydrocarbons, and oxidized bodies. It is obtained as a product of the destructive distillation of common resin (resin of turpentine).

Rosin oils are known by specific gravity and distillation (*a*), by sensible properties (*b*), and by reactions (*d*). *Separated*, in most cases, best by saponification and ether-solution (*e*). Found with other oils (*g*).

a.—A liquid of a brownish-yellow color, and a violet to blue fluorescence. Sp. gr. 0.96 to 0.99. When distilled a portion passes over below 250° C., considerable below 300° C., and almost all below 360° C. (Rémont). The lightest fractional distillates, when obtained, boil at 103° to 106° C., and from light resin oil distillates boiling at 80° C. have been obtained. Strong dextro-rotatory powers are possessed by some rosin oils; others are inactive, still others levo-rotatory.

b.—Rosin oil has a characteristic taste, and an odor of common rosin, the odor of refined rosin oil obtained only after heating.

c.—Insoluble in water, slightly soluble in alcohol, soluble in all proportions in ether, chloroform, carbon disulphide, petroleum benzin, acetone, petroleum lubricating oils, essential oils, and glyceride oils.

d.—Not saponifiable (see *e*).—Shaken with dry **stannous chloride**, or better, stannous bromide (Allen, 1884), a violet color is slowly obtained.—Nitric acid, chlorine, bromine act as oxidizing agents, with uncertain force, sometimes with violence. With sulphuric acid, blackening occurs. The vapor burns with a smoky flame.

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[1] History and description: Rémont, 1880–81: *Bull. Soc. Chim.*, [2], 33, 461, 525; *Jour. Chem. Soc.*, 38, 683; 40, 202. Schaedler: "Die Technologie der Fette und Oele der Fossillien, sowie der Harzöle und Schmeirmittel," 1885–86, Kapitel xvi.—Composition: Tilden, 1880: *Ber. d. chem. Ges.*, 13, 1604; *Jour. Chem. Soc.*, 40, 101. Kelbe and Worth, 1882: *Ber. d. chem. Ges.*, 15, 308. Renard, 1882: *Bull. Soc. Chim.*, [2], 36, 215: *Jour. Chem. Soc*, 42, 64.—Analysis: Demski and Morawski, 1885: *Ding. pol. Jour.*, 258, 82; *Analyst*, 10, 231.

e.—Separation of rosin oils from fixed oils by distillation is slow and imperfect, but may yield a distillate of rosin oil sufficient for identification by odor and other properties.—Separation from glycerides by saponification of the latter is more satisfactory, but, as with mineral oils, the result is not well attained by simple aqueous dilution of the soap solution. Rosin oils are somewhat soluble in strong solutions of soap, and dilution of the solution separates fat acid from the soap. Saponifying with alkali in alcoholic solution, expelling the alcohol, and diluting with water short of turbidity of the soap solution alone, the liquid is shaken out with portions of ether, the ether evaporated from the ethereal separate, and the residue tested by odor when hot, by taste, by stannous chloride, and by gravity, for rosin oil.

Separation from Mineral Oils by acetone as a solvent is done as follows (Demski and Morawski, where cited). Rosin oils dissolve in all proportions of acetone. 50 c.c. of the sample of oil are shaken up several times with 25 c.c. of acetone in a 100 c.c. graduated cylinder, and then left at rest for some time. If the liquid separates into two layers, 10 c.c. of the upper are drawn off, and the amount of oil in it determined after evaporation of the acetone. The density of this residue is judged by adding water to a few drops of it, and then alcohol until the oil just begins to sink. Finally it is required to determine the amount of rosin oil which it is necessary to add to the sample of oil under examination to enable it to dissolve in half its volume of acetone. As soon as perfect solution is effected the liquid gives a fairly permanent froth when shaken. With American mineral oils 35% of rosin oil is at once detected by its solubility in acetone; with Caucasian and Wallachian oils 50% is at once detected.

g.—Rosin oils are used legitimately for lubricating purposes. As adulterants they have a wide distribution, in lubricating oils, in linseed oil, olive oil, and even in castor oil and the essential oils.—Rosin Grease is a saponaceous paste made by mixing slaked lime with rosin oil.

Drying and Non-drying Oils, Distinctions between.—(1) *Elaidin Test.* The action of fuming nitric acid, or of nitric acid with metallic copper or metallic mercury, or the action of a concentrated solution of mercuric nitrate, in warm digestion, noting the result each quarter of an hour, and later each hour. Non-drying oils are converted into a solid mass, termed elaidin, a glyceride of elaidic acid (p. 247), which is isomeric with oleic acid. The reaction, therefore, is not an oxidation, though effected by an oxidizing agent.

(2) *Warming effect of Sulphuric Acid* (MAUMENÉ, 1881; ALLEN, 1881[1]). The sulphuric acid should be anhydrous. It may be prepared by heating to 320° C., and cooling to the temperature of the oil. Of the concentrated acid 10 c.c. are taken in a beaker, and 50 grams of the oil are added, when the mixture is slowly stirred with the thermometer bulb until, after rising, the thermometer begins to fall, when the degree is noted, the initial temperature of the oil and acid is subtracted, and the elevation of temperature obtained.

	ELEVATION OF TEMPERATURE.	
	Maumené.	*Paris City Laboratory.*
Non-drying:		
Olive oil	42° C.	51–55.5° C.
Peanut oil	....	62
Cotton-seed oil	....	69.5
Sweet-almond oil	53.5	....
Beechnut oil	65	....
Castor oil	47	....
Sheep-foot oil	....	51.5
Olein (oleic acid) of saponification	....	47.5
Drying:		
Poppy	70.5	73
Hemp	98	....
Walnut	101	....
Linseed	133	114.5
Train oils:		
Cod-liver oil	103	....
" " brown	....	89.5
Sperm oil	....	63.5–73

(3) *Iodine numbers.* The fat acids of the drying oils have a

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[1] A. H. ALLEN, *Analyst*, 6, 102.

greater capacity for iodine combination than the non-drying oils. See pp. 258, 259.

(4) *Oxygen-absorption.* The greater the "drying" capacity of an oil, the more oxygen it absorbs on a given exposure to air. Precipitated metallic lead is added to favor oxidation and enable a measure of the oxidation to be made (LIVACHE, 1883 [1]). The lead is prepared by precipitating lead acetate solution with zinc, at once washing the precipitate with a little water, then with alcohol, then with ether, and drying in a vacuum. In a large tared watch-glass one gram of the lead is taken, and from 0.6 to 0.7 gram of the oil is dropped slowly upon the lead, and the weight of all taken, giving the weight of oil. The test is set aside, at medium temperature, in a place free from vapors or dust, and the weight taken after 18 hours, to 4 or 5 days, or longer.

	INCREASE OF WEIGHT.		OF THE FAT ACIDS.
	After 2 *days.*	*After* 7 *days.*	*After* 8 *days.*
Linseed oil	14.3%	...	11%
Walnut oil	7.9	...	6
Poppy oil	6.8	...	3.7
Cotton-seed oil	5.9	...	0.8
Beechnut oil	4.3	...	2.6
Colza oil	0.0	2.9%	2.6
Rape oil	0.0	2.9	0.9
Olive oil	0.0	1.7	0.7

Oxygen-absorption has been studied by W. Fox,[2] who determines the oxygen absorbed by direct estimation. About 1 gram of the oil is sealed in a tube of 100 c.c. capacity, or 5 or 6 drops of the oil (weighed) are placed in a well-ground, stoppered flask of 200 c.c. capacity; the whole heated in an oil-bath at 104.5° C. (220° F.) for about four hours; the tube or flask opened under water, the remaining gas measured in a eudiometer, also the remaining oxygen estimated by pyrogallol and potash, using the precautions and corrections of gas analysis, for estimation of the quantity of oxygen gas taken up by the weighed quantity of oil.—The author finds that avidity for oxy-

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[1] *Compt. rend.*, **97**, 1311; *Jour. Chem Soc.*, **46**, 532.
[2] 1883: *Analyst*, **8**, 116; *New Rem.*, **12**, 367.

gen is influenced largely by presence of fat acids formed by standing open to the air, and that the differences thus due to age and exposure are removed by heating the oil to 204° C. (400° F.)—The author holds the value of lubricating oils to be largely dependent on their non-absorption of oxygen. Also, he claims that his method gives the surest detection of cotton-seed oil in admixture with olive oil. He gives the following results in *c.c. of oxygen absorbed:* Linseed oils—Baltic Sea, 191; Black Sea, 186; Calcutta, 126; Bombay, 130; American, 156. Cotton-seed oil, refined, 24.6; rape-seed oil, brown, 20; rape-seed oil, colza, 17.6. Olive oil, highest, 8.7; lowest, 8.2.

LINSEED OIL.[1]—Leinöl. Huile de lin. Flachsöl. Chiefly the triglyceride of Linoleic Acid (p. 249), $C_3H_5(C_{16}H_{27}O_2)_3=794$.—A fixed oil expressed from flaxseed, the seed of Linum usitatissimum, of which it should form as much as 25 per cent.

See Drying and Non-drying Oils, under Fats, p. 281.

a.—A yellowish or yellow oily liquid, of the sp. gr. about 0.936 (U. S. Ph.), at 15° C. 0.9347 (SCHÜBLER), 0.9325 (SOUCHÈRE), 0.930–0.935 (ALLEN). Specific gravity of the total fat acids, at 100° C., 0.8599 (ARCHBUTT and ALLEN). Congeals at −16° C. after a few days (GUSSEROW); −27° C. (CHATEAU). Melts at —16° to —20° (GLÄSSNER). The total fat acids congeal at 13.3° C. (HÜBL); melt at 17.0° (HÜBL). *Boiled Linseed Oil* has sp. gr. 0.940–0.941.

b.—Linseed oil has a slight peculiar odor and a bland taste.

c.—Insoluble in water; soluble in 5 parts absolute alcohol, in 1.5 parts ether.

d.—Linseed oil, treated with nitrous acid, does not yield elaidin. Mixed with concentrated sulphuric acid, as directed under Drying and Non-drying Oils, Distinctions between, p. 282, very high numbers are obtained. Treated with iodine, large absorption capacity is found (pp. 258 and 259). For oxygen-absorption see Drying Oils, etc., p. 283.

e, f.—For Separation and Valuation of Linseed oil, see Drying Oils, p. 281, and Linoleic Acid, p. 249.

g.—Linseed oil is adulterated with cotton-seed oil, mineral

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[1] Schaedler: "Technologie der Fette und Oele," 1883, p. 494. Benedikt, "Analyse der Fette," 1886, p. 215.

oils, rosin oil, niger-seed oil, rape-seed oil, hemp-seed oil, and fish oils. Mustard, rape, and hemp seeds are gathered with flax-seed. Specific gravity of mineral oils is lighter than of linseed oil, usually from 0.880 to 0.905; while resin oil is heavier, 0.96 to 0.99. Non-drying oils are indicated by the elaidin test, by not generating the full quota of heat with sulphuric acid, by not absorbing the proper amount of oxygen, and by lower iodine numbers, according to directions given under Drying Oils, p. 281. Presence of hydrocarbon or mineral oils is shown by their non-saponification, sometimes revealed by fluorescence, and sometimes by distillation, as specified under Separation of Mineral Oils from Fat Oils, p. 274. Examination for Rosin Oil is directed under the latter, p. 281.

Boiled Linseed Oil is prepared by exposure to a high temperature, by which it undergoes oxidation and acquires increased readiness for oxidation. Dryers are added, also, in the "boiling," to promote oxidation by the atmosphere. Manganese and lead oxide, used as dryers, leave traces of these metals in the oil, so that they may be detected in the ash.

Boiled linseed oil is frequently adulterated with a very little rosin and with rosin oil.

Olive Oil.—The fixed oil expressed from the fruit of Olea europœa. Olivenöl, Baumöl. "Sweet oil." Among the best are Provence oil and Florence oil. Lucca and Gallipoli oils are good brands. Sicily oil is seldom of best quality. Olive oil is adulterated and substituted by cotton-seed oil, rape oil, poppy oil, sesamé oil, peanut oil.

a.—A pale yellow, or light greenish-yellow, oily liquid, of sp. gr. 0.915 to 0.918 (U. S. Ph. and Ph. Germ.) At 15° C., best 0.9178; Gallipoli, 0.9196 (Clark); 0.914 to 0.917 (Allen). At 18° C., yellow-green 0.9144, dark 0.9199 (Stilurell). Specific gravity of the fat acids, at 100° C., 0.8429–0.8444 (Archbutt).—Congealing point, turbid at 2° C., solid at −6° C. Of the fat acids, congealing point 21.2° C., melting point 26° C. (Hübl); congealing point not under 22° C., melting point 26.5 to 28.5° C. (Bach).

b.—Of a nutty, oleaginous, and faintly acrid taste, and nearly without odor.

c.—Sparingly soluble in alcohol, readily soluble in ether.

g.—*Tests for purity.*—"If 1 part of olive oil be agitated in a test-tube with 2 parts of a cold mixture prepared from equal volumes of strong sulphuric acid and of nitric acid of sp. gr. 1.185, and the mixture be set aside for half an hour, the supernatent, oily layer should not have a darker tint than yellowish (a dark color indicating the presence of other fixed oils). If 12 parts of the oil be shaken frequently during two hours with 1 part of a freshly-prepared solution of 6 grams of mercury in 7.5 grams of nitric acid (sp. gr. 1.40), a perfectly solid mass of a pale straw color should result; and if 1 gram of the oil be shaken for a few seconds with 1 gram of a cold mixture of sulphuric acid (sp. gr. 1.830) and nitric acid (sp. gr. 1.250), and 1 gram of disulphide of carbon, no green or red layer should separate on standing. If 5 drops of the oil are let fall upon a thin layer of sulphuric acid in a flat-bottomed capsule, no brown-red or dark zone should be developed within three minutes at the line of contact of the two liquids (absence of appreciable quantities of other fixed oils of similar properties)."—U. S. Ph.

"At about 10° C. it begins to grow turbid by crystallization, at 0° C. acquires a salve-like thickness. When 5 grams of the oil are shaken with 15 drops of nitric acid of sp. gr. 1.38, neither the acid nor masses swimming upon it should take a red color. Fifteen parts of olive oil which have been strongly shaken with a mixture of 2 parts water and 3 parts of fuming nitric acid should form a whitish mass, not red nor brown, separating in 1 or 2 hours in a solid mass, while the liquid is scarcely colored." —Ph. Germ.

"Pale yellow or greenish-yellow, with a very faint, agreeable odor, and a bland, oleaginous taste; congeals partially at about 36° F. (2.2° C.)"—Br. Ph.

Specific gravity of mixtures of Olive oil with stated percentages of other oils, at 15° *C.* (SOUCHÈRE, 1881, using Lefèbre's Oleometer):

Name of the oil.	*Sp. gr. of the oil admixed.*	10 *per ct.*	20 *per ct.*	30 *per ct.*	40 *per ct.*	50 *per ct.*
Olive.......	0.9153	....	....	....	....	
Colza.......	0.9142	0.91519	0.91508	0.91497	0.91486	0.91475
Sesamé.....	0.9225	0.91602	0.91674	0.91741	0.91818	0.91890
Cotton-seed..	0.9230	0.91607	0.91684	0.91761	0.91838	0.91915
Walnut.....	0.9170	0.91547	0.91564	0.91581	0.91598	0.91615

Congealing and Melting points of Fat Acids of Olive oil with stated percentages of fat acids of other oils (BACH,[1] 1883):

Fat acids from	*Congealing at*	*Melting at*
Pure olive oil................	Above 22° C.	26.5–28.5° C.
Olive oil with 20% cotton-seed oil........................	28°	31.5°
Olive oil with 20% sunflower-seed oil..................	18	24
Olive oil with 33⅓% rape-seed oil........................	16.5	23.5
Cotton-seed oil, alone........	35.0	38.0
Castor oil, alone.............	2.0	13.0

TURKEY-RED OIL.—A thoroughly non-drying oil suitable for technical use in dyeing cotton turkey-red. Grades of olive oil have generally been used. Partly unripe olives, macerated in boiling water before being pressed, yield an oil rich in extractive matter and favorable for this use. In the elaidin test a solid and firm elaidin, of white color, should be obtained.

OLIVE-KERNEL OIL.—From the kernel or nut of the olive, by pressure, or extraction with carbon disulphide. Distinguished from olive oil by its dark greenish-brown color and a quite free solubility in alcohol or glacial acetic acid.

COTTON-SEED OIL.[2]—Baumwollensamenöl or Baumwollenol. Huile de Coton. Oleum gossypii seminis.—A fixed oil expressed from the seed of species of Gossypium. The crude oil contains as much as 15 pounds of color substance per ton (LONGMORE). The color substance, termed gossypin, is soluble in alkalies, and from alkaline solution precipitated by acids. Treatment with soda lye of five or six per cent. at 60° F. is adopted in purification of the oil, only a small part of which saponifies. The soapy mixture containing the color, when digested with strong soda lye and then neutralized with sulphuric acid, yields a precipitate of the gossypin.

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[1] *Chemiker-Zeitung,* 7, 356; *Zeitsch. anal. Chem.,* **23**, 259; *Am. Jour. Phar.,* 55, 354.

[2] Production, Uses, and Properties, C S. Munroe, 1885: *Am. Chem. Review,* 5, 26. Purification, J. Longmore, 1886: *Jour. Soc. Chem. Industry.*

a.—The crude oil is a thick, brownish, turbid liquid, which deposits a slimy residue. The clarified oil is clear orange yellow; better purified grades light yellow. Fully refined cotton-seed oil is of a very pale straw color.—Sp. gr., at 15° C., 0.922–0.930 (Allen); 0.9228 (Valenta); at 17° C., 0.923 (Scheibe); at 18° C., crude oil 0.9224, refined oil 0.9230, white oil 0.9288 (Stilurell). Sp. gr. of the fat acids at 100° C., 0.849 (Archbutt).—Congeals to deposit stearin at 12° C.; solidifies fully at 0° to −1° C. The fat acids congeal at 30.5° C. (Hübl), at 35.0° C. (Bach), at 35.5° C. (Valenta); melt at 35.2° C. (Allen); begin to melt at 39°–40° C., melt wholly at 42°–43° C. (Benseman).

b.—The well-refined oil has only a slight earthy odor, and a bland, perceptibly nutty taste.

c.—Solubility in glacial acetic acid, according to Valenta, is stated at p. 273, and furnishes a distinction from olive oil.

d.—Stirred with **potassium hydrate solution,** crude cotton-seed oil colors blue in the upper layer, becoming violet on exposure to the air. The same colors are developed on saponifying with alcoholic potassa, but are hardly made perceptible with the most fully refined oil.—When a drop of **sulphuric acid** is added to a larger quantity of unrefined oil, bright red to brown coloration is produced. The test is better made with near equal quantities of oil and sulphuric acid of sp. gr. 1.76, gently warming the mixture after observing the first effect. The refined oil responds very slightly to this test.—In the *elaidin test* cotton-seed oil gives elaidin, with reddish-yellow to brownish-yellow colors, these tints being obtained also with nitric acid of sp. gr. 1.42 added in equal volume.—Silver nitrate in ether-alcoholic solution is gradually reduced, with dark colors, but this is in a degree common to seed oils and olive oil. Bechi (1885) uses a 1% solution of silver nitrate in strong alcohol, adding 5 c.c. of this solution to a mixture of 25 c.c. alcohol and 5 c.c. of the oil, and warming to 84° C., when olive oil, he states, does not color if cotton-seed oil be absent.—Cotton-seed oil contains about 1.64% of non-saponifiable matter (Allen and Thompson, Rödiger). By full saponification and extraction of the dry soap with petroleum benzin (p. 275) a distinction from olive oil is obtained.

Cotton-seed oil is a very feebly drying oil. For its identification, and distinction from olive oil, by this property, tests are made by oxygen-absorption (p. 283), warming effect of sulphuric acid (p. 282), and the iodine numbers (p. 258). Its separate fat acids, in the oxygen-absorption test, unlike the entire oil, rank with wholly non-drying oils.

The high melting and congealing points of the fat acids of cotton-seed oil distinguish it from most other similar oils (*a*, and pp. 265, 269).

Distinctions between cotton-seed oil and olive oil are further given under the head of the latter, p. 285. The saponification numbers of olive oil and cotton-seed oil are too near each other to furnish a means of distinction.

Cotton-seed Stearin.—Baumwollenstearin. Vegetable Margarin. Vegetable Stearin.—The residue of cold-pressed cotton-seed oil. A sample examined by Muter had sp. gr. 0.9115–0.912 at 37.7° C. (100° F.), and gave 95.5% insoluble fat acids, perfectly soluble in hot absolute alcohol as well as in ether. The melting point was 32.2° C., the melted liquid having a yellow color and odor of cotton-seed oil. It congealed again at about 1° C. A sample examined by Mayer melted at 39° C.

Castor Oil.—Oleum Ricini. Ricinusöl. Huile de ricin, de castor.—A fixed oil expressed from the seed of the Ricinus communis. See Ricinoleic Acid, of which it is in chief part the glyceride, p. 248. Ricinolein is $C_3H_5(C_{18}H_{33}O_3)_3 = 931$.

a.—"An almost colorless, transparent, viscid liquid; of sp. gr. 0.950–0.970."—U. S. Ph. Sp. gr. at 15° C., 0.9613–0.9736 (Valenta); at 18° C., 0.9667 (Stilurell); at 23° C., 0.964 (Dieterich). Congeals at —10° to —18° C. Fat acids congeal at 3° C.; melt at 13° C. (Hübl). "When cooled it becomes thicker, generally depositing white granules, and at about —18° C. (0.4° F.) it congeals to a yellowish mass."—U. S. Ph.

b.—"Of a bland, afterwards slightly acrid and generally offensive taste, and a faint, mild odor."—U. S. Ph.

c.—"Soluble in an equal weight of alcohol [0.820 at 15 6° C.] and in all proportions of absolute alcohol or glacial acetic acid."—U. S. Ph. At 15° C. in 2 parts 90%, and in 4 parts 84% alcohol. Not soluble in petroleum benzin, kerosene, or paraffin oil, but dissolves about one and a half volumes of kerosene or paraffin oil. The solubility in alcohol is much varied by temperature.

d.—Castor oil is to a very slight extent a drying oil. Exposure to air causes it to become perceptibly thicker. In the heating effect of sulphuric acid (p. 282), and in the iodine number of the oil or its acid (p. 258), castor oil stands not far from olive oil. It gives the elaidin reaction. Its saponification number is comparatively low (p. 257).

g.—Impurities and substitutions.—The solubilities in alcohol and in glacial acetic acid, quoted under *c* from the U. S. Ph., furnish a generally satisfactory means of revealing impurities. The absorption of a little petroleum benzin has been used by Hager for detection of adulterations as follows: One volume of the oil is agitated in a test-tube with 2 volumes of the benzin, and set aside. The lower layer should be increased to from 1.6 to 1.75 of the original volume of the castor oil. In case of adulteration the lower layer will be proportionally deficient.

Under direction of the New York State Board of Health, in 1881, Prof. G. C. Caldwell[1] examined 16 samples, of which 9 were considered adulterated, 1 with sesamé oil, 4 with cotton-seed oil, 2 with peanut oil, and 2 with cotton-seed oil or peanut oil or both. While giving a caution against dependence upon single tests (not thoroughly subjected to control analyses), Prof. Caldwell advises the legal adoption of test limits.

LARD.—Adeps. Schweinschmalz. Graisse de porc.—"The prepared internal fat of the abdomen of Sus scrofa, purified by washing with water, melting, and straining."

a.—A soft, white, unctuous solid, of sp. gr. about 0.938 (U. S. Ph.) at 15° C.; at 100° C. (water at 15° = 1) 0.861 (KÖNIGS). Melts at or near 35° C. (U. S. Ph.), 42°–48° C. (KÖNIGS). At 26° C. melted lard begins to congeal, and during congelation the temperature rises to 30° C. (SCHAEDLER). The *fat acids* melt at 35° C., and congeal again at 34° C. (MAYER).—When rancid, lard acquires a yellowish color.

b.—Lard when fresh and good has a faint odor free from rancidity, a bland taste, and a neutral reaction. In the air it soon becomes rancid and of an acid reaction.

c.—It is entirely soluble in ether, petroleum benzin, and disulphide of carbon.

d, *e*, *f*.—The saponification number of Köttstorfer, for lard, is 195.8; 195.3–196.6 (VALENTA). The iodine number of Hübl, 59.0. The per cent. of insoluble fat acids (Hehner's number), 96.15 (WEST-KNIGHTS); of non-saponifiable matter, 0.23 (ALLEN and THOMPSON). The per cent. of olein is given by BRACONNOT

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[1] *Analyst*, 7, 97; from *Sanitary Engineer*.

at 62; by calculation from the iodine number, 68.4. The melting and congealing points of the fatty acids are named under *a*. See Fat Acids, Quantitative Determination of, (1) to (9), pp. 250, 274.

g.—Impurities.—Of these the most common is dilution with water, either with or without lime, alum, or other adjuvant, forming "watered lard"; and those next most probable in this country are "cotton stearin" (p. 289), and mixtures of tallow or tallow stearin with cotton-seed oil. Cocoanut oil has also been used.

"Distilled water, boiled with lard, should not acquire an alkaline reaction (absence of alkalies), nor should a portion be colored blue by iodine (absence of starch). A portion of the water, when filtered, acidulated with nitric acid, and treated with test solution of nitrate of silver, should not yield a white precipitate soluble in ammonia (absence of common salt). When heated for several hours on the water-bath, under frequent stirring, lard should not diminish sensibly in weight (absence of water)."—U. S. Ph.

"Hot alcohol shaken with the lard, and when cold diluted with an equal part of water, should not affect litmus-papers. When 2 parts of the lard are boiled with 2 parts of (15%) potash solution and 1 part of alcohol, until the mixture becomes clear, and evaporated over the water-bath, the residual soap should dissolve in 15 parts of warm water on the addition of 10 parts of alcohol."—Ph. Germ

Dr. Muter, in 1882,[1] made report to the Public Analysts of a sample of lard adulterated with "cotton stearin," of density of 0.912 as a liquid at 37.8° C. (100° F.), yielding 95.5% fat acids all insoluble, and requiring some time to solidify at 4.4° C. (40° F.) The high density was the obvious indication that it was not lard alone. The sample represented a grade appearing on the market.—Alleged adulteration of "prime steam lard" with cotton-seed oil products, in Chicago in 1883, was made the occasion of a protracted trial before the Board of Trade of the City of Chicago.[2]

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[1] *Analyst*, 7, 93.

[2] The evidence of a good number of American chemists in this case, with proceedings and findings, was published by the Board of Trade: "McGeoch, Everingham & Co. *vs.* Fowler Brothers," pp. 280, 1883, Chicago. Samples of known admixture of lard with tallow, lard with cotton-seed oil, and of pure lard were submitted to four chemists and to one microscopist for analysis. The reports were not in accord with each other, and to a great extent failed of their object. A method of separation by use of alcohol-ether as a solvent was

Respecting Microscopical Examination of lard and other fats, Dr. J. H. LONG has contributed a valuable summary,[1] with original micro-photographs.

LARD OIL.—Schmalzöl. Specköl.—By pressure of lard at about 0° C., the residue being the Solar Stearin or Lard Stearin of the candle industry. Sp. gr. of lard oil, 0.915 (ALLEN). Saponification number, 191–196 (MOORE).

TALLOW OIL. Talgöl.—By pressure of tallow at low temperatures, much lower than are employed for oleomargarin.

OLEOMARGARIN.—This term has been primarily applied to a product of purified fresh tallow with rejection of a good part of its stearin. The invention of Hippolyte Mège, of Paris, France, prescribed that fresh suet should be immersed in a brine of common salt and sodium sulphite or other addition, then crushed between rollers and washed, and digested at 103° F. (39.4° C.) with sheep's stomachs and calcium biphosphate (U. S. patent, 1873), at animal temperature with infusion of a pig's stomach in acidulated water (Br. patent, 1869; Bavarian patent), with fresh sheep's stomachs and a very little carbonate of potash in other specifications. By specifications at the 103° F. or at the animal temperature, but practically at 112° F. *or* the necessary temperature, the digested tallow (freed from the cells) melts, and is decanted. It is now allowed to cool to some adjusted temperature (86° to 98° F.), and kept at rest to "crystallize" out "stearin in the form of teats." The decanted liquid is further (or instead of the operation of "crystallization") cooled to solidify, and then subjected to pressure, either in a press or in a centrifugal extractor. The liquid product was oleomargarin.[2]

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much employed, as were also the color tests of Chateau. One witness only states the use of Köttstorfer's method, and no mention was made of determinations by iodine numbers, or by the congealing and melting points of the fatty acids after removal of oleic acid. Separation of oleic acid by action of ether on the lead salts was cited by several of the witnesses. Prof. Remsen stated that, in his opinion, "the limits of variation in the composition of lard" had not been ascertained so as to enable a chemist to determine the question of its adulteration.

[1] "Some Points in the Micro-Chemistry of Fats." JOHN H. LONG, Sc.D. Chicago Academy of Sciences, 1885.

[2] Patents were issued in 1871 in the United States to H. Bradley and to W. K. Peyrous to make the grosser animal fats equal to the best lard, for cooking purposes. In 1873, besides the U. S. issue of the Mège patent, a patent was issued to E. Q. Parafe for the manufacture of an article designated as "oleomargarin." Further see F. BONDEL, 1874: "Extract from report of MÈGE-

The transformation of this into "artificial butter" was undertaken by Mège through churning with milk, or cows' udders, or other treatment.[1] In this country manufacturers of oleomargarin have been practically free from any restrictions of patents, and have conducted the details according to methods governed by the discretion of each producer. Indeed, everywhere the general essentials consist most often in melting at 60° to 65° C. (140° to 149° F.), decanting to clarify, "crystallizing" at 35° C. (95° F.), and pressing at this temperature for "prime margarin" or oleomargarin, the solid residue being known as "prime press-tallow," and used mainly for candles.

At the present time lard is extensively treated for a product corresponding to oleomargarin, and used in butter substitutes. In these, also, cotton-seed oil, or fractions of it, sesamé oil, and cocoanut oil have been employed in some quarters.

Oleomargarin proper, from tallow, has given the following numbers: Sp. gr. at 15° C., 0.924–0.930 (Hager); at 100° C., 0.859 (Königs). For percentages of stearin in oleomargarin, corresponding to degrees of congealing point of the total fat acids, see table at p. 272. Iodine number, 55.3 (Hübl), 50.0 (Moore). Hehner's number (per cent. insoluble fat acids), 95.56. Saponification number of Köttstorfer, 195 to 197.4. Reichert's number, 0.4 to 0.6 (Cornwall).

Butter.[2]—The immediate constituents are four: water, curd or casein, salt, and fats. Of these the following percentages occur: *Water:* proper maximum of good butter, 12% (Hehner, Wiley). Of 19 samples reported by the Agricultural Dept. the lowest percentage of water was 7.34; the highest, 14.31; next highest, 14.06%. Of 49 samples reported by the Board of Health

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Mouriez to the Board of Health of the Department of the Seine on the Product named 'Artificial Butter,'" *Amer. Chemist*, New York, 4, 370. Mège-Mouriez, 1872: *Moniteur Scientifique*, [3], 2, No. 369; *Amer. Chem.*, 3, 231. H. A. Mott, 1876: "Manufacture of Artificial Butter," *Amer. Chem.*, 7, 233. *Agriculture of Pennsylvania Reports*, 1885: pp. 219–265. "Second Annual Report of the New York State Dairy Commissioner," 1886, pp. 190, 312.

[1] Further on this subject see Tidy and Wigner, 1883: *Analyst*, 8, 113.

[2] Hehner and Angell, 1877: "Butter, its Analysis and Adulterations." A. W. Blyth, 1882: "Foods," etc., pp. 283–305. Fox and Wanklyn, 1884: "Anal. of Butter," *Analyst*, 9, 73. Bell, method by sp. gr., 1876: *Phar. Jour.*, [3], 7, 85. Eastcourt, sp. gr., 1876: *Chem. News*, 34, 254. Cassamajor, sp. gr.. 1881: *Jour. Am. Chem. Soc.*, 3, 81. Hager, odor test of the burning fat, 1880: *Zeitsch. anal. Chem.*, 19, 238. Wiley, 1883–85: Reports of Department of Agriculture at Washington. Also, New York State Dairy Commissioner's Report for 1886. See citations under Butter Fat, p. 298; under the several processes of estimation of fats, pp. 256, 257, 260, 269. Scheffer, 1886: *Pharm. Rundschau*, 4, 248.

of Mass., 1885, the maximum was 12.16 per cent. *Curd:* from 0.5 to 1.2% (WILEY); averaging 2.2% (HEHNER and ANGELL). *Salt:* average, 2.5% (HEHNER). Of 22 analyses of WILEY, from 1.9 to 4.4%. "Should never exceed 8%" (H. and A.) *Fats:* the remainder, in the 30 analyses of Hehner and A., highest, 90.2%; lowest, 76.4%.—A more minute account of constituents is undertaken by KÖNIG,[1] for average of 123 samples: fat, 83.27%; water, 14.49; casein, 0.71; milk sugar, 0.58; salts, 0.95; of the dry substance, the fat being 97.34%. The fats contain traces of color matter, lecithin, and cholesterin, besides the glycerides.

Water. The estimation of the water is accomplished by drying a weighed quantity of 3 or 4 grams in the air-bath at a temperature not above 110° C., using a tared porcelain or platinum evaporating-dish of about 40 c.c. capacity. Traces of free volatile acid may be present, and will be driven off. The dish is shaken from time to time. When a nearly constant weight is reached the difference of weight is taken. Absolute alcohol may be added to favor the removal of the last portions. Other operators add a weighed quantity of pure dried sand.

Fat. The residue in the dish is melted, and treated with portions of about 10 c.c. of ether (or petroleum benzin), decanting the clear ethereal solution, filtered if necessary, into a weighed beaker. The filter should be dried and weighed in a filter-tube or pair of watch-glasses. The treatment is continued until a portion of the ethereal solution, evaporated on a glass slide, ceases to leave an oily residue. On evaporation or distillation of the ether or benzin the weight of the fat is obtained, or this may be afterward calculated from the difference between the weight of the butter and the sum of the weights of the water and the curd with the salt. According to WILEY, the best method of separating the curd is to dry the butter in a dish (without sand) with a small stirring-rod, at 105° C., adding a little absolute alcohol. The dried residue when cold (and after weighing for water-loss) is treated with ether or petroleum benzin, and filtered and washed through a Gooch crucible, using an ether-wash-bottle. The crucible is dried at 105° C. The weight of residue, diminished by the amount of salt determined as sodium chloride by volumetric estimation, equals the weight of curd.—The fat may also be separated by keeping the butter melted for some time in a tube until it rises in a perfectly clear liquid. In a graduated tube the volume of fat may be taken for its approximate estimation.

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[1] "Die menschlichen Nahrungs- und Genussmittel," 1883, ii. 279.

Curd and Salt. The residue insoluble in ether is dried and weighed, adding the increased weight of the filter after drying it with its contents and weighing in the filter-tube, the sum representing the curd plus the salt. The residue is now burned, with the filter, in the dish, to a white ash, weighed as the salt. If for any reason it be desirable, the "salt" may be examined and its sodium chloride estimated volumetrically. Also the casein may be estimated directly, with exclusion of milk sugar, by washing the residue insoluble in ether with water acidulated with acetic acid, drying, and weighing. Wiley estimates the casein by moist combustion with alkaline permanganate, nesslerizing the distillate, and calculating from the nitrogen.

Separation of artificial coloring matters of butter fats and oils (MARTIN, 1885).—To 5 grams of the dry butter fat, or any dry fat, add 25 c.c. of carbon disulphide, and shake gently until the solution is complete. Now add 25 c.c. of water, made slightly alkaline with caustic soda or potash, and shake again gently. The alkaline water will dissolve out the coloring matter. This can be separated out and determined qualitatively by the spectroscope or other means, and quantitatively by making up a standard solution of annato, or whatever the color may be, and applying the colorometric method. If the color is slight a quantity larger than 5 grams should be taken.—Alcohol may be applied to melted butter to extract artificial color. Besides annato, curcuma and saffron are employed (MUNICIPAL LABORATORY OF PARIS); also carrot extract and marigold. Carrot extract, in carbon disulphide solution, is not dissolved out by alcohol on shaking with the latter, until a drop of ferric chloride dilute solution is added, when, after shaking and standing, the alcohol extracts the carrot color completely, and if no other color be present the carbon disulphide solution becomes colorless (R. W. MOORE).

An account of colors proposed or asserted to have been added to butters is given in the report of the N. Y. State Dairy Commissioner for 1886.

The natural color of grass-fed butter, to which the name "lactochrome" has been applied, is bleached by exposure to air and sunlight, and disappears upon about eight hours' exposure to direct sunlight in a layer of 0.5 centimeters thickness (SOXHLET).

Rancidity of Butters.—KÖTTSTORFER[1] estimates the free acid of butters as a measure of their rancidity, using the method of simple titration by alcoholic potash in an ether solution of the fat, as adopted for fats in general by GEISSLER, with details given

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[1] 1879: *Zeitsch. anal. Chem.*, 18, 436; *Jour. Chem. Soc.*, 36, 1069.

on p. 277. Three to ten grams of clear butter fat, prepared by melting and filtering (as directed under Butter Fat, p. 299), are weighed into a flask of about 50 c.c. capacity, treated with ether (freed from acidity as directed on p. 278) enough to dissolve it, phenol-phthalein added, the acid of the mixture titrated with the alcoholic potash, and the value of the latter taken by titration with decinormal acid, just as directed on p. 278. The *degree of acidity* is equal to the number of c.c. of normal solution of alkali required to neutralize the acid in 100 grams of fat. Also, c.c. normal solution × 0.088 = grams butyric acid. And, taking 100 grams of fat, c.c. normal solution × 0.088 = per cent. of free fat acids, estimated as butyric acid. The percentage in the butter fat × .85 (or the found proportion of fat in the butter) = percentage of the butter.

The author reports the acidity of the fats of 24 butters. Of these 19 did not overgo 8 degrees acidity of the fat, and the average acidity of the 19 was 4°. Of the five above 8° one reached 41.6°. The author gives the opinion that for good butter the fat should not exceed 8 degrees of acidity (0.704% butyric acid). The average of good butters, 4° acidity, corresponds to 0.372 per cent. of butyric acid in the fat, or about 0.32 per cent. in the entire butter.

Detection of Foreign Fats by their relation to Solvents.—Tests of *butter fat* by solvents have been proposed as follows: Hoorn (1872) used *petroleum benzin* of sp. gr. 0.69 at 15° C. and boiling at 80°–110° C. Filsinger (1880) applied a mixture of 4 vols. *ether* of sp. gr. 0.725 with 1 vol. *alcohol* of sp. gr. 0.805, at 18°–19° C., for 12 hours.

W. G. Crook (1880) employs, as a "first test" of butter fat, *carbolic acid* (1 lb. Calvert's No. 2 with 2 f. oz. water). Of the purified fat 10 grains (0.648 gram) are treated in a (graduated) test-tube with 30 minims (1.5 c.c.) of the carbolic acid, at about 66° C. (150° F.), with agitation. After some time pure butter forms a perfect solution. Fat of tallow (beef or mutton) or lard separates in a defined layer, as does olive oil. The percentages of volume of the mixture, taken by the lower (heavier) layer, are given for each of these fats, from 44 to 50 per cent.[1] On cooling, more or less precipitate occurs in the upper layer. So small a proportion of lard as five per cent. did not appear in a lower layer, but after 24 hours gave a crystalline turbidity unlike that of butter fat.

A method of distinction between true butter fat and the meat

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[1] *Analyst*, 4. 111; *Zeitsch. anal. Chem.* (with notes by Lenz), 19, 369.

fats by *solubility in a mixture of amyl alcohol and ether* is proposed by E. SCHEFFER.[1] Of rectified amyl alcohol 40 volumes are mixed with 60 volumes of ether of sp. gr. 0.725. One gram of the clear butter fat is treated, in a test-tube of 12 c.c. capacity, with 3 c.c. of the solvent mixture. After tightly corking the tube is digested, with shaking, in a water-bath gradually raised from 18° to 28° C. If the butter fat is pure a clear solution is obtained. If the solution be incomplete more of the solvent is added from a burette. For 1 gram of unmixed lard 16 c.c. of solvent is required; for 1 gram of tallow, 50 c.c.; for one gram of pure stearin, 550 c.c. of the solvent. A mixture of 10% lard fat with butter fat took 3.9 c.c.; 20% lard fat, 4.8 c.c.; 40% lard fat, 6.5 c.c.; 90% lard fat, 14.4 c.c. The theory of the test is simply that there is more tristearin in meat fats than in butter fat, although not all the stearic acid of the latter is held in tristearin.

Cohesion figures[2] are obtained in "BLYTH's Pattern Process" (1880), fully detailed by the author in his work on "Foods" (1882), giving distinctions between butter fat and various other fats.

Viscosity of Butter Soaps.—The recent report of S. M. BABCOCK[3] shows that oleomargarin soaps are far more viscous in solution than butter soaps. From the differences given, in tabular comparison, it appears probable that when this method of examination shall have been perfected, it will serve to distinguish true butters from mixtures of foreign fats, even when the percentage of adulteration is as low as five. The author states that "there is little doubt that by making the solution more alkaline the addition of one per cent. of adulteration to any given sample of butter would be shown." In the determinations the New Viscometer[4] of the author was used. It is of further interest that the insoluble fat acids of butter were found to give soaps much less viscous than those of corresponding mixtures of stearic and palmitic acids from meat fats, from which the investigator was forced to conclude that "it is probable that the acids of butter are isomers of those from other fats."

Microscopical Detection of Foreign Fats in Butter.—This

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[1] 1886: *Pharm. Rundschau*, 4, 248. Favorable review by H. W. WILEY, 1887: *Science*, 9, 114.

[2] TOMLINSON, 1861-62. CRANE, 1875.

[3] Report of the Chemist to the New York Agricultural Experiment Station, Geneva, N. Y., distributed Jan. 30, 1887.

[4] S. M. BABCOCK, 1886: *Chemical Section of Am. Asso. Advance. Sci.*, Buffalo Meeting.

subject has been recently reported upon quite fully by Dr. THOMAS TAYLOR.[1] Reports upon Taylor's microscopical method have been made by Prof. H. A. WEBER[2] and by Prof. H. W. WILEY.[3] The last-named two observers do not find that mixtures of butter with tallow and lard products can be distinguished from pure butter by the process of Dr. Taylor.

A brief summary of microscopical methods is given under "Optical Methods" in the Report of the N. Y. State Dairy Commissioner for 1886, p. 271. A useful monograph, with cuts from original micro-photographs, was published by Dr. Long in 1885,[4] recounting the examination of butter and other fats.

MYLIUS (1879[5]) has also reported on the microscopical examination of butter.

An odor-test by the burning of butter in a wick has been proposed by HAGER (1880). A wick is placed in the melted butter, lighted and burned for two or three minutes, and extinguished. Oleomargarin gives the odor of a tallow candle. Of this test Messrs. WALLER and MARTIN (1886) say: "All fats when heated to decomposition yield vapors of acrolein which smell the same in all cases. That part of the fat volatilized which has suffered only partial decomposition is what is observed, and is at best a very uncertain quantity. Add to this source of error the fact that old samples of butter have naturally a decided tallowy taste and smell, and it will be seen that the odor in any case is a very uncertain test."

BUTTER FAT.[6]—Glycerides of palmitic (stearic) and oleic

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[1] "Butter and Fats. To distinguish one fat from another by means of the Microscope." By Thomas Taylor, M.D., Microscopist to the Department of Agriculture, Washington, D. C. *Proceedings of the American Society of Microscopists.*—Also various papers, beginning in the *Quarterly Microscopical Journal*, New York, 1876. A paper in *Proceedings Am. Assoc. Adv. Sci.*, 1885.

[2] Chemist Ohio Agricultural Experiment Station. *Bulletin* No. 13, 1886, March 1.

[3] Chemist Depart. Agriculture at Washington, 1886.

[4] "Some Points on the Micro-Chemistry of Fats. JOHN H. LONG. 1885. Chicago Academy of Sciences."

[5] *Ber. d. chem. Ges.*, **12**. 270.

[6] See citations under "Butter," p. 293. Further, R. W. MOORE, "Notes on Köttstorfer's Method," etc., 1884: *Chem. News*, **50**, 268; "Notes on the Hübl Method," 1885: *Am. Chem. Jour.*, **6**, 416. On Reichert's and other methods. 1885: *Jour. Am. Chem. Soc.*, **7**, 188; *Analyst*, **10**, 224. HANSSEN and SCHMITT, 1884: *Bied. Cent.*, 1884, 707; *Jour. Chem. Soc.*, **48**, 197. A. H. ALLEN, "On Reichert's Method," 1885: *Analyst*, **10**, 103. KÖTTSTORFER on Reichert's and other methods compared with his own, 1879: *Zeitsch. anal. Chem.*, **18**, 435. REICHARDT, 1884: *Archiv d. Phar.*, **222**, 99; *Zeitsch. anal. Chem.*, **23**, 565; *Jour. Chem. Soc.*, **46**, 1219.

acids, and conjugated glycerides of these acids with volatile fat acids, ($C_nH_{2n}O_2$), chiefly butyric acid.[1]

Preparation from butter, for analysis. The butter is preserved in the melted state, on the water-bath, with slight shaking or stirring at intervals, until the fat rises in a layer nearly clear. A dry filter is prepared in a hot funnel, in a warm place, and the nearly clear fat poured on it. The filtrate must be perfectly clear, and not lose weight on the water-bath.—For determination of specific gravity the butter is melted at 50° to 60° C., in no case reaching 70° C., and at least 50 c.c. of filtrate obtained.

Specific gravity, at 15° C., 0.926 (CASSAMAJOR), 0.9275 (A. W. BLYTH), 0.936–0.940 (HAGER); at 37.8° C. (100° F.) (water at same$=$1), 0.911–0.913 (BELL); at 100° C. (water at 15° C.$=$1), 0.865–0.868 (KÖNIGS); at 100° C. (water at 100° C. $=$ 1), 0.901–0.904 (WOLKENHAAR); at 40° C. (water at same $=$ 1), 0.912 (WILEY).

Melting Point. Not well defined. *Of butter*, softens at 20.5° to 31.1° C., and melts at 24.4° to 37.2° C. (PARKES and BROWN); by the rising of a light glass bulb, mean 33.7°, by clearing of the liquid, mean 35.5° C. (HASSALL); by the sinking of a weighted bulb, average of 24 samples, 35.5° C. (HEHNER and ANGELL); by rising in capillary tubes immersed in water, 31° to 36° C. (HEISCH); by the running of a solidified drop of butter, next a thermometer-bulb, on a surface of mercury, 27° to 29° C. (REDWOOD). *Of butter fat*, 33°–36° C. (WILEY). *Of the fat acids*, 38.0° C. (HÜBL). *Of insoluble fat acids*, 39° to 43° C. (WILEY, 1884).

Congealing Point. Of butter fat, 23° to 30° C. (WILEY). *Of the fat acids*, 35.8° C. (HÜBL), 37.5° to 38° C. (MUNICIPAL LABORATORY OF PARIS). *Of the insoluble fat acids*, 34.5° to 38° C. (WILEY).

Per cent. of insoluble fat acids, 87.5 (HEHNER). Milligrams of KOH to saponify 1 gram of fat (KÖTTSTORFER), 227. Number of c.c. of $\frac{N}{10}$ potash solution to neutralize the distilled fat acids

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[1] The simple glyceride tributyrin does not appear to be present in butters. Conjugated glycerides, such as $C_3H_5(C_{16}H_{31}O_2)_2(C_4H_7O_2)$, are inferred to be the sources of the butyric acid of saponification. Mr. HEHNER, however, presents another view: "Both the dipalmitate-monobutyrate and the dioleate-monobutyrate would yield less insoluble acids than are found in practice, the former 80.2 and the latter 84.6 per cent. But a mixture of compound ethers such as would be obtained by substituting in the *tri*palmitate or *tri*oleate of glyceryl one atom of the acid radical by the radical of butyric acid would very approximately yield such proportions of insoluble and soluble fat acids as are actually found." It is to be observed that the question is complicated by the presence of volatile fat acids of larger molecular weights than butyric acid. At all events, the volatile fat acids obtained from 100 parts of butter fat average about 6 parts.

from 2.5 gram of fat (Reichert), 14.0; not less than 13.0 (Meissl). Iodine number of Hübl, 26.0 to 35.1; fat from very old butter, 19.5 (Moore).

Butter Substitutes.—Oleomargarin is described at p. 292, with some description of treatment adopted to give it a sensible resemblance to butter. At present prepared lard fat (p. 290) is used as much or more than prepared tallow fat. Frequently a vegetable oil is used with either lard fat or oleomargarin proper (tallow fat). The vegetable oil most used is cotton-seed oil (p. 287); after which are to be named sesamé oil and cocoanut oil. Of these substitutes—two animal fats and three vegetable fats—only cocoanut oil approaches in composition to butter fat. It must be remembered that the fats and combinations of fats presented as substitutes for butter are subject to constant change. The Report of the Dairy Commissioner of the State of New York for 1886 says "the only materials used, according to the statements of the manufacturers, are oleomargarin ('oleo-oil'), lard, cotton-seed oil, sesamé oil, and annatto." The term "butterine" has been more commonly applied to the mixture of deodorized lard and butter prepared by churning with milk. "Suine" is a term applied to a grade of butterine with very large proportions of lard. The work last mentioned describes, besides the oils just named, those of peanut (ground-nut), ben, mustard, colza, rape, cameline, cocoanut, cocoa, palm, cacao, and bone.

Principal Chemical Methods of Estimation of Butter-Fat.

(1) Parts Insoluble Fat Acids in 100 parts Fat. Hehner's number, pp. 250, 256.

(2) C.c. $\frac{N}{10}$ alkali for Volatile Fat Acids in 2.5 grams Fat. Reichert's number, p. 253. By Meissl's method, p. 253.

(3) Milligrams KOH to saponify 1 gram of the Fat. Köttstorfer's number, pp. 254, 257. Perkins's combination plan, p. 255.

As a single estimation, that denoted by Reichert's number (probably with Meissl's manipulation) is here unhesitatingly recommended in preference to any other. But Hehner's number is of nearly an equal value, and next is ranked the number of Köttstorfer, the latter being of the three the most easily obtained.—Respecting (4) indications by specific gravity, see p. 261. (5) Hübl's iodine numbers, p. 258. (6) The melting and congealing points of butter substitutes may or may not differ from that of true butter fat. Respecting the obtaining and applying of data of melting and congealing points, "the sinking point," and "the point of clearance," see p. 265. (7) The percentage of casein, estimated by moist combustion for nitrogen (WILEY) (p. 295), may serve as an aid in establishing a conclusion, though it is to be remembered that a small percentage of poor butter may introduce as large a proportion of nitrogen as would be found in certain samples of the best butter.

Interpretation of results.—(1) *Hehner's number.*—Hehner gives as extremes for true butter fats 86.6 and 88.5 per cent. of insoluble fat acids. If "lower than 88 per cent., the butter must be declared genuine"; if "higher than 88.5 per cent., we conclude that adulteration has taken place"; while, "in case sophistication is proved beyond a doubt, we base the calculation upon a lower figure, namely, 87.5." Taking, then, 87.5 as the percentage of insoluble fat acids in true butter, and taking 95.5 as the percentage of the same in fats used as adulterants (p. 256), we have 8 as the difference of Hehner's number due to the substitution of foreign fat for butter. If now

$$\left.\begin{array}{ll} a = \text{parts of insoluble fat acids} \ldots\ldots \\ A = \text{" foreign fat} \ldots\ldots \\ B = \text{" butter fat} \ldots\ldots \\ C = \text{" entire butter equal to the butter fat} \end{array}\right\} \text{In 100 parts of the fat analyzed.}$$

D = " true butter in 100 parts of the entire butter analyzed,

$$8 : a - 87.5 :: 100 : A. \quad \text{Or, } A = 12.5\,(a - 87.5).$$

$$B = 100 - A.$$

85[1] $: 100 :: B : C.$ Or, $C = 1.1765\,B.$

$$A + C : 100 :: C : D. \quad \text{Or, } D = \frac{100\,C}{A + C}.$$

Of course the factors 87.5, 95.5, and 85 are subject to chemical estimations of the per cent. of insoluble fat acids in butter fat and in adulterating fats, and the per cent. of butter fat in true butter. The per cent. of insoluble fat acids is itself the best statement of results by Hehner's method, and it should be given, for information of those who can understand it, while the calculated per cent. of true butter is given only when required, and may be accompanied with a statement of the conditions on which it is based. The conversion of the percentage of butter fat into that of entire butter is more properly made by use of the actual percentage of total fat found in the butter as sold, instead of the general average figure, 85, above assumed. But even with the use of this factor from the butter in question, there remains the

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[1] See p. 294.

uncertainty as to how much of the water in the sample was introduced as a part of the true-butter fraction, and how much was introduced as a part of the oleomargarin fraction, or was due to manipulation of the mixture. Therefore the opinion is here given that the simple figure known as Hehner's number is the best expression of results by Hehner's method. (See the following corresponding discussion of interpretation of Köttstorfer's number, p. 304). A table of Hehner's numbers of the principal fats concerned in butter adulteration is given on p. 256. Of 29 true butters reported upon by the Department of Agriculture at Washington,[1] five gave between 88.5 and 89.0 per cent. of insoluble fat acids, three Alderneys gave from 89.0 to 89.26 per cent., and one, an Alderney, gave 89.89 per cent. The Food Analyst of the Pennsylvania Board of Agriculture, Prof. C. B. Cochran, found the extremes of fixed fat acids from fat of 25 genuine butters to be 86.7 to 87.7 per cent.[2]

Rancid Butters give nearly the same percentages as fresh butters (Fleischmann and Vieth), the slight differences being in the direction of an increase.

(2) *Interpretation of results by Reichert's Estimation.*[3]—The c.c. of decinormal alkali to neutralize the volatile acids of 2.5 grams of fat. Each c.c. decinormal alkali indicates 0.0088 gram of butyric acid; and 0.0088 gram butyric acid in 2.5 grams of fat is equal to 0.00352 gram butyric acid in 1 gram of fat, or 0.352 in 100 grams of fat. Then, Reichert's number × 0.352 = per cent. of volatile acids (as butyric acid) in the fat; and per cent. butyric acid ÷ 0.352 = Reichert's number.

Reichert found true butters to give numbers from 13.55 to 14.45, average 14.0, and declared any butter giving less than 12.0 c.c. must be adulterated. Dr. G. C. Caldwell reported to New York State Board of Health estimations of 27 samples of butter yielding Reichert's numbers from 12. 7 to 15.5. Messrs. Waller and Martin (Report New York State Dairy Commissioner, 1886) obtain, from 26 American butters, on first 50 c.c. of distillate, numbers of Reichert's method from 12.2 to 16.3 as extremes. They also carried eight additional distillates, in extension of Meissl's plan, by which they compute that only from 75 to 85 per cent. of the total volatile acid comes over in the first 50 c.c.

Prof. C. B. Cochran, West Chester, Pa., Food Inspector of

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[1] 1884: p. 63, Report of the Chemist, H. W. Wiley.

[2] Unpublished report communicated to the author.

[3] Directions for estimation and bibliography, p. 253.

the Pennsylvania Board of Agriculture,[1] has found the extreme minimum of the Reichert's numbers of known genuine butters to be 12.5 (c.c. of tenth-normal sol. for 2½ grams fat); and this chemist holds that Reichert's number 11.5 is the proper minimum limit to govern an analyst in condemning butters inspected by law. He has finally come to rely almost exclusively upon the Reichert's numbers.

In Reichert's own analyses lard gave 0.30; raw tallow, 0.25; rape oil, 0.25; oleomargarin butter, 0.95. Cocoanut oil gave 3.70.

Reichert proposes this formula for calculation of per cent. of true butter fat in an admixture of fats: (Reichert's number — 0.30) × 7.30 = percentage of true butter fat. The probable error = ± 0.24 × (Reichert's number — 0.30).

Meissl, using his modification (p. 253), places the minimum limit of the Reichert number at 13. R. W. Moore (1885[2]) reports the following tabulated comparisons of chemical data for the distinction of butter from its substitutes, with discussion of the various methods, and recommends Reichert's method, especially when cocoanut oil is in question. Hübl's number gives the percentage of iodine taken (p. 258):

	Numbers of			
	HEHNER.	KÖTTSTORFER.	HÜBL.	REICHERT.
Butter, samples.........	86.01	227.0	19.5	13.25
	86.49	224.0	38.0	13.1
Oleomargarin, samples...	95.56	197.4	50.0	0.6
	...	195.0	50.0	0.4
Butter, 50%............ Oleomargarin, 27.5%..... Cocoanut oil, 22.5%......	89.50	227.5	35.4	8.7

The specific gravity of the cocoanut oil used was 0.9167 at 37.7° C., "which is sufficiently high to bring the mixtures above the sp. gr. of 0.911, which is that of butter." Waller and Martin (1886) found cocoanut oil to give a Reichert's number of from 2.7 to 3.7.

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[1] Unpublished communication to the author.

[2] *Jour. Am. Chem. Soc.*, 7, 188; *Analyst*, 10, 224.

Meissl (1879) found that soft butters yield higher proportions of volatile acids than hard butters. Butter oil gives higher numbers in Reichert's method than entire butter.

Rancidity reduces the quantity of the volatile acids of butter.

The quantity of *volatile fat acids by Reichert's method* is by no means identical with the quantity of *soluble fat acids*, though the latter should include the former. It will be observed that insoluble fat acids are filtered out of the distillate, if obtained in it, in Reichert's operation. A good number of the analysts of butter practise the estimation of its soluble fat acids by titration of the filtrate and washings from the insoluble fat acids. Without doubt these results have value. Along with Hehner's method they are easily obtained in a combination process. Dividing per cent. butyric acid by 0.352, the quotient may be compared with Reichert's number. It is believed, however, that Reichert's estimation of volatile acids has greater constancy than an estimation of the soluble fat acids, and therefore the combination plan of Perkins (p. 255) is given in this work instead of processes including estimation of soluble acids, without distillation.

The per cent. of soluble fat acids in butter averages at least 5.5, and, according to most authorities, should not fall below 5. Messrs. Waller and Martin (1886) obtained from 26 American butters (genuine) the extremes of from 4.49 to 7.25% volatile acids, as butyric acid, six or seven washings with hot water being taken for the total filtrate titrated (p. 251). It may be remarked that the percentage of total volatile fat acids, from the same butters, show less variation, the extremes standing 5.52 and 6.87, as butyric acid, these being obtained by prolonged distillation (beyond the 50 c.c. distillate of Reichert).

(3) *Interpretation of Köttstorfer's number*, the milligrams of KOH neutralized in saponifying 1 gram of fat: a measure of the saturating power of the total fat acids. Directions for the estimation, p. 254; Table of numbers for Fats and Oils, p. 257. Bibliography, pp. 254, 298.

In Köttstorfer's conclusion (1879) a number not lower than 221.5 indicates unadulterated butter, this being the lowest limit of true butter. The highest limit he placed at 233, and the average 227. For oleomargarin the number 195.5 was taken as the average, and for lard the same. If a number (n) be lower than 221.5, the percentage of oleomargarin (x) is found by the formula, $x = (227 - n)\ 3.17$.

That is, if the limit number be overpassed by any butter in question, its amount of adulteration is judged by comparison with the average number of true butter—a plan corresponding to that followed under Hehner's method. Then we have as data for calculating the percentage (x) of adulterating fat, from Köttstorfer's number (n) for any mixture of fats:

$$227 - 195.5 = 31.5) : (227 - n) :: 100 : x$$

And

$$\frac{100\,(227 - n)}{227 - 195.5} = 3.17\,(227 - n).$$

The average number of any adulterating fat in question is to be substituted for 195.5; and the number 227 is to be held subject to correction as the average number for true butter. The difference 31.5 may be varied by ± 5.75 in cases of extreme composition of true butter fat, causing ± 18% difference in the interpretation.

Rancid butters gave Köttstorfer a number, for the fat, 1.5 lower than fresh butter.

Mr. Wigner, in 1879, stated that "any butter fat which requires near 22.6% KOH for saponification [number 226], as determined by the titration process, may be safely passed as genuine; but any lower result should be checked by a further analysis."

(4) *Specific Gravity as a means of distinguishing the Fat of Butter from that of its Substitutes.*[1]—Specific-gravity list, p. 299.—Taken by Mr. Bell as a liquid at 100° F. (water at same = 1), using a specific-gravity bottle. By Mr. Cassamajor, as a solid, at 15° C., floated in alcohol of known density. By Mr. Wigner, as a liquid, at temperatures adjusted (water at 60° F. = 1) by the suspension of specific-gravity bulbs, using data furnished. By Mr. Estcourt, as a liquid, at near the boiling point of water, by use of the Westphal balance.

According to Mr. Bell, butter fat (not rancid) rarely falls below 0.910 (at 100° F., water at same), the usual range being 0.911 –0.913, and the fat of rancid butter sometimes falling in density to 0.908. The fats of tallow and lard, 0.902.8 to 0.904.6.

Cassamajor found that true butter fat, congealing in the alcohol from melted drops, was held in equilibrium at 15° C. by alcohol of specific gravity 0.926 [15.6° C.] or 53.7 per cent. [volume]. Oleomargarin, treated in the same way, was held in equilibrium at 15° C. by alcohol of sp. gr 0.915, or of 59.2 per

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[1] J. Bell, 1876: *Phar. Jour. Trans.*, [3], 7, 85. Wigner, 1876: *Analyst*, 1, 145. Cassamajor, 1881: *Jour. Am. Chem. Soc.*, 3, 83; *Chem. News*, 44, 309; *Jour. Chem. Soc.*, 42, 341. Hehner and Angell, 1877: "Butter," pp. 76–86. Benedikt, 1886: "Analyse der Fette," p. 263.

cent. strength [by vol.] Quoting, also, the experiments of LEUNE and HARBURET,[1] Mr. Cassamajor proposed to estimate proportions of oleomargarin, in mixture with butter fat, by a scale of graded strengths of alcohol between 53.7% and 59.2, calculatingon the basis of 5.5 alcoholic percentage for total difference between the two fatty bodies.

Cocoanut oil has sp. gr. 0.9167 at 37.7° C. (100° F.), about 0.0037 above the highest density of butter fat, so that mixtures of oleomargarin and cocoanut oil could easily give the specific gravity of butter fat. Rancid butter fat approaches in specific gravity to the oleomargarin fats.[2]

Specific Gravities of Fats and Oils are given in Tables pp. 262, 265.

C. B. COCHRAN[3] has used a glass bulb displacing 1 c.c. and of sp. gr. 3.4, for the "sinking point" temperature, and has compared the data so obtained with figures of sp. gr. at 100° F. (water at same = 1), with results, for spurious butters, as follows:

Specific gravity, 905.97 to 911.89.
Sinking point, 92.5° F. to 99° F.

The Iodine Numbers of HÜBL, of frequent application in the analysis of Fats in general, have a very limited application in the analysis of butter, so far as shown for any adulterations hitherto made. Directions for the estimation, p. 258; tables, p. 259.

Scope of Chemical Analyses of Butter and forms of Certificates, as required of Public Analysts.[4]

The following form of report is used (in 1886) as a tag-record by the Inspector of Foods of the *city of Boston*, Mass., under the regulations of the city and the laws of the State: "BUTTER: Date, ——; Time, —— A.M. —— P.M. *If a store:* Proprietor's name, ——; No. —; Street, ——; sold by ——; price paid, ——; quantity, —— lb.; wholesaler's name, ——; price paid ditto, ——; District. ——. *If a wagon:* Proprietor's name, ——; name on wagon, ——; driver in charge, ——; locality, ——. Butter, ——. Oleomargarin, ——.

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[1] 1881: Municipal Laboratory of Paris: *Moniteur Scientifique.*

[2] Further on the effects of Rancidity, JONES, 1879: *Analyst*, 4, 39.

[3] Food Inspector, Penn. Board of Agriculture, in unpublished communication made (1886) to the author.

[4] DEPARTMENT OF AGRICULTURE AT WASHINGTON, *Reports* for 1884, p. 55. *Mass. State Board of Health*, etc., *Reports* for 1884, pp. 97, 118; 1885, p. 132.

Butterine, ——. Imitation butter, ——. Whether marked properly, ——. Remarks: ——. Collector, ——. ANALYSIS: Analysis No. ——. Inspection page, ——. Melting point, ——. Fat, ——. Curds, ——. Ash, ——. Water, ——. Insoluble Acids, ——. Soluble Acids, ——. ——."

The report of the State Board of Health, etc., of the *State of Massachusetts* for 1885 gives a list of samples of butter reported upon, with items: "Inspector's number, price per pound, per cent. insoluble fatty acids, remarks." "The highest limit of insoluble fatty acids in genuine butter fat—90 per cent.—has been taken as the dividing line between the genuine and the artificial product."[1]

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[1] *The Laws of Massachusetts in relation to the Sale and Inspection of Butter, Oleomargarin, Cheese, etc.*

[Sections 17, 18, 19, 20, and 21 of Chap. 56 of the Public Statutes, as amended by Chap. 310 of the Acts of 1884, and Chap. 352, Acts of 1885]

SECTION 17. Whoever, by himself or his agents, sells, exposes for sale, or has in his possession with intent to sell, any article, substance, or compound made in imitation or semblance of butter or as a substitute for butter, and not made exclusively and wholly of milk or cream, or containing any fats, oils, or grease not produced from milk or cream, shall have the words "Imitation Butter," or, if such substitute is the compound known as "Oleomargarin," then the word "Oleomargarin," or, if it is known as "Butterine," then the word "Butterine." stamped, labelled, or marked, in printed letters of plain, uncondensed Gothic type not less than one-half inch in length, so that said words cannot be easily defaced, upon the top and side of every tub, firkin, box, or package containing any of said article, substance, or compound. And in cases of retail sales of any of said article, substance, or compound not in the original packages, the seller shall, by himself or his agents, attach to each package so sold, and shall deliver therewith to the purchaser, a label or wrapper bearing in a conspicuous place upon the outside of the package the words "Imitation Butter," "Oleomargarin," or "Butterine," as the article may be, in printed letters of plain, uncondensed Gothic type not less than one-half inch in length.

SEC. 18. Whoever, by himself or his agents, sells, exposes for sale, or has in his possession with intent to sell, any article, substance, or compound made in imitation or semblance of cheese or as a substitute for cheese, and not made exclusively and wholly of milk or cream, or containing any fats, oils, or grease not produced from milk or cream, shall have the words "Imitation Cheese" stamped, labelled, or marked, in printed letters of plain, uncondensed Gothic type not less than one inch in length, so that said words cannot be easily defaced, upon the side of every cheese-cloth or band around the same, and upon the top and side of every tub, firkin, box, or package containing any of said article, substance, or compound. And in cases of retail sales of any of said article, substance, or compound not in the original packages, the seller shall, by himself or his agents, attach to each package so sold. and shall deliver therewith to the purchaser, a label or wrapper bearing in a conspicuous place upon the outside of the package the words "Imitation Cheese," in printed letters of plain, uncondensed Gothic type not less than one inch in length.

SEC. 19. Whoever sells, exposes for sale, or has in his possession with in-

Under the action of the Dairy Commissioner of *New York State* some of the analysts of butter (in 1886) report upon printed blanks as follows for butters found to be spurious: "Certificate of Analysis of a —— sample of —— 'Butter'; marked ——; received from ——, per ——, on ——. This sample contains: Animal [vegetable] and Butter [or total] Fat, ——; Curd, ——; Salt (ash), ——; Water at 100° C., ——. Analysis of the Fat present in the sample: Soluble fatty acids (by distillation) (on a dry basis), ——; Insoluble fatty acids, ——; Specific Gravity of the dry fat, at 100° F. Titer, —— [Reichert's number]. (This sample is composed —— of foreign fat, and is not produced from unadulterated milk, or cream from the same. It contains coloring matter, whereby it is made to resemble butter, the product of the dairy, and is made in imitation and semblance of butter produced from unadulterated milk, or cream from the same.)"

The Food Analyst of the Board of Agriculture of Penn., Prof. Cochran, cites the following results of official analyses of butters:

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tent to sell, any article, substance, or compound made in imitation or semblance of butter or cheese, or as a substitute for butter or cheese, except as provided in the two preceding sections, and whoever defaces, erases, cancels, or removes any mark, stamp, brand, label, or wrapper provided for in said sections, or changes the contents of or in any manner shall falsely label, stamp, or mark any box, tub, article, or package marked, stamped, or labelled as aforesaid, with intent to deceive as to the contents of said box, tub, article, or package, shall for every such offence forfeit to the city or town where the offence was committed one hundred dollars, and for a second and each subsequent offence two hundred dollars.

Sec. 20. Inspectors of milk shall institute complaints for violations of the provisions of the three preceding sections when they have reasonable cause to believe that such provisions have been violated, and on the information of any person who lays before them satisfactory evidence by which to sustain such complaint. Said inspectors may enter all places where butter or cheese is stored or kept for sale, and said inspectors shall also take specimens of suspected butter or cheese and cause them to be analyzed or otherwise satisfactorily tested, the result of which analysis or test they shall record and preserve as evidence; and a certificate of such result, sworn to by the analyzer, shall be admitted in evidence in all prosecutions under this and three preceding sections. The expense of such analysis or test, not exceeding twenty dollars in any one case, may be included in the costs of such prosecutions. Whoever hinders, obstructs, or in any way interferes with any inspector, or any agent of an inspector, in the performance of his duty, shall be punished by a fine of fifty dollars for the first offence, and of one hundred dollars for each subsequent offence.

Sec. 21. For the purposes of the four preceding sections, the terms "butter" and "cheese" shall mean the products which are usually known by these names, and are manufactured exclusively from milk or cream, with salt and rennet, and with or without coloring matter.

	Reichert's number.	Hehner's number.	"Butter" reported to be
No. 1	3.1 c.c.	88.9%	Not genuine.
2	4.2	93.45	" "
3	3.0	92.9	" "
4	14.0	....	Genuine.
5	12.6	....	"
6	1.6	....	Not genuine.
7	14.15	....	Genuine.
8	13.0	....	"
9	14.15	....	"
10	1.5	....	Not genuine.
11	0.75	....	" "
12	1.0	....	" "
13	11.7	....	Passed.
14	0.7	....	Not genuine.
15	0.85	....	" "
16	1.6	....	" "
17	1.0	....	" "
18	2.4	....	" "
19	12.1	....	Passed.
20	5.2	....	Not genuine.
21	12.8	....	Passed.
22	0.6	....	Not genuine.
23	13.7	....	Genuine.
24	3.0	....	Not genuine.
25	12.5	....	Passed.
26	12.2	....	"
27	16.3	....	"
28[1]	13.3	....	"
29	15.2	....	"
30	15.5	...	"

The Agricultural Department at Washington for 1884, Prof. Wiley, Chemist, reports tabulated analyses, with statements of "No., name, made at, made by, bought at, price, color [to the eye], water, casein, salt. fat, melting point, solidifying point, saturation equivalent (56000 ÷ Köttstorfer's number), soluble

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[1] No. 28: Fats, 78 per cent.; water, 17.38 per cent.; curd, 2.4 per cent.; ash, 2.21 per cent.

acid (in per cent. as butyric, obtained by titration of filtrate from insoluble fat acids), insoluble acid, melting point insoluble acid, solidifying point insoluble acid, saturation equivalent of insoluble acid" (56000 ÷ Köttstorfer's number for the insoluble acids).

What is a sufficient chemical analysis of butter?—A single faithful estimation, whether of (1) the insoluble fat acids, (2) the soluble acids distilled, or (3) the saponification number, as these estimations are detailed in pp. 250 to 255, may give such a result that no further evidence is needed to prove the butter to be not a genuine one. And the result of an estimation by any one of these established methods may be in itself sufficient to prove that a certain sample does not consist mainly or largely of oleomargarin. Besides, oleomargarin, lard products, and cotton-seed oil, or any mixture of these three, may be distinguished with certainty from pure butter fat by any one of the methods just named (Hehner's, Reichert's, or Köttstorfer's). Further, any mixture of oleomargarin, or lard product, or cotton-seed oil, or combination of these foreign fats, with a smaller proportion of butter fat of average or nearly average composition, must be clearly revealed not a pure butter fat by the result of a true estimation according to Hehner, or Reichert, or Köttstorfer. Adulteration with the foreign fats above named, when in proportions not less than half, and when with butter fat of about average composition, can invariably be declared as adulterations by analysis under one of the three methods here referred to. And what is here stated as true of oleomargarin or prepared tallow fat, and lard fat, and the fat of cotton-seed oil is known to be true of numerous vegetable fats, some of which have been used in butter substitutes, and is true of known fats with a very few exceptions.

When a question of small proportions of foreign fats in mixture with large proportions of average butter fat is presented, it is to be understood that there is a limit to the diminution which foreign fat may undergo and still remain capable of detection by one of the estimations above enumerated, or by any mode of analysis. Just what percentage of foreign fat marks such limit it is difficult to state. Granting that the butter fat of the mixture be of average composition, the limit must lie in such low percentages of foreign fat as would be of improbable occurrence in adulteration for commercial ends. But when the possibility of admixture with butter fat of exceptional composition is introduced into the question, the limit of quantity of foreign fat capable of detection by chemical estimation rises to a place among percentages which are quite possible among the devices of adulteration. If the article be rancid a somewhat abnormal composition of butter fat may have been acquired.

A rule has prevailed, in the interpretation of results under several methods of analysis, that only when the result stands outside of the *extremes* obtained among the results of varying samples of genuine butter fat shall a butter be declared (qualitatively) adulterated. But when so declared adulterated a (quantitative) statement of the proportion of the adulteration may be based upon the deviation from the *average* of results of genuine butter fat. This rule has been discussed at p. 302. Its bearing may be illustrated by an application under Hehner's method, as follows: If the insoluble fat acids be found at 88.0% of the clear fat the article is declared not adulterated. If found at 88.5% the article is not declared adulterated (on this evidence alone). If found at 88.6% insoluble fat acids, an adulteration of 13¾% of foreign fat in the total fat is reported under the rule. At the same time, if the extreme limit of 88.5% insoluble acids in exceptional butter fat be taken as the datum of calculation for the quantitative report on 88.6%, as was taken for the qualitative verdict on 88.5%—that is, giving the article on trial the benefit of possibilities in both the cases alike—from 88.6% of insoluble fat acids only 1.43% of foreign fat in the total fat would be declared. And a logically guarded report could state that, from the evidence of 88.6% of insoluble fat acids, it appears that an adulteration of foreign fat has been made, in quantity from about 1.5 to about 23 per cent., and probably near 13 per cent.

In order to reach a secure conclusion respecting the fact of adulteration in cases of admixture of foreign fats with large proportions of butter fat, and in order to give the percentage of foreign fat within limits brought as near each other as possible, more than one of the estimations (Hehner's, Reichert's, Köttstorfer's) should be made. The three estimations, with determination of the specific gravity of the fat as a fourth, furnish together a body of evidence more trustworthy in cases of difficulty as to the fact of adulteration, and more exact respecting percentages, than can be drawn from any smaller number of determinations. Still other determinations, as those of melting and congealing points, and the quantity of casein, sometimes give additional advantage. In case of doubt every means of investigation should be used. And all important estimations should be obtained in triplicate or duplicate results.

FORMIC ACID.—Ameisensäure. $CH_2O_2 = 46$. Hydrogen-carboxyl, $H.CO_2H$, the first member of the fatty acid series, $C_nH_{2n+1}CO_2H$.—Obtained by distilling the bodies of ants with water. A constituent of the exudate carried with the stings of insects and of stinging nettles. A product of numerous organic reactions, including a rapid action of alkalies upon chloral, and a feebler action of alkalies upon chloroform, also the action of potassium upon carbon dioxide and water, or of hot potassium hydrate solution upon carbon monoxide. Prepared by distillation from oxalic acid and glycerin. A common result of destructive distillation.

Formic acid, when free and not dilute, is *recognized* by its odor and irritating effect on the skin (*b*). Tests of *identification* are obtained in the color with ferric salt, the precipitates with lead acetates and alcohol, the reduction of silver or mercury, and the generation of carbon monoxide with sulphuric acid (*d*). *Separations* are made by distilling formate with phosphoric acid, and by the insolubility of lead or calcium formate in alcohol (*e*). *Estimations* are conducted acidimetrically, by weight of lead formate, and by weight of mercury reduced (*f*). Certain *impurities* are liberated by holding calcium formate in alcohol (*g*).

a.—Formic acid is a colorless liquid, of specific gravity of 1.221 at 20° C., boiling at 100° C., the 77.5 per cent. acid at 107.1° C., and crystallizing, when pure, below 0° C. Metallic formates heated to decomposition do not form a carbonaceous residue.

b.—The odor of formic acid is pungent, in proportion to the concentration of its aqueous solution, the vapor from the strong acid having a slightly suffocating effect reminding of sulphurous acid. The taste is purely acidulous. The effect is irritating, the strong acid causing burning and itching of the skin, a biting sensation of the tongue, and a tingling of the nostrils.

c.—Formic acid is miscible in all proportions with water and with alcohol. The metallic formates are generally soluble in water and but little soluble in alcohol. The normal metallic formates mostly exhibit a neutral reaction with litmus-paper; the normal lead formate being neutral, and the basic lead formate alkaline in reaction. The formates crystallize readily.

d.—**Ferric chloride,** in a neutral solution of alkali formate, forms ferric formate, of red color, and precipitated on boiling, a reaction closely resembling that of acetic acid.—Normal **lead**

acetate precipitates concentrated solution of an alkali formate, the normal formate of lead being soluble in 65 parts of cold water. By adding to the mixture twice its volume of alcohol the precipitation is much increased. If basic lead acetate solution be saturated with alcohol it serves to precipitate formic acid, free or combined, quite completely, as the basic formate of lead is very little soluble in alcohol of moderate strength. The precipitate of lead formate dissolves freely in hot water, and on cooling the solution needle-form crystals of lead formate are obtained, more perfectly after several hours.—**Silver nitrate** solution gives a white, crystalline precipitate of silver formate, only in quite concentrated solutions. On standing or warming the precipitate blackens by reduction to metallic silver. In more dilute solutions the metallic silver is the first form of the precipitate, and best obtained in neutral or feebly acidulous solution, free ammonia being avoided. Reduction by vapor of formic acid is to be adopted if non-volatile reducing agents are liable to be present, and is accomplished by slightly acidulating the mixture with sulphuric acid and immersing the test-tube for some time in boiling water, while a disk of filter-paper previously wetted or crossed with solution of silver nitrate is bound over the mouth of the tube.—**Mercurous nitrate** gives a precipitate of mercurous formate, soluble in 500 parts of water. Reduction to metallic mercury is obtained on standing twenty-four hours, more readily on warming.

Concentrated **sulphuric acid**, at a gentle heat, resolves formic acid into carbon monoxide and water ($CH_2O_2 = H_2O + CO$). The formic acid or its salt is warmed with about three times its volume of the sulphuric acid. With a considerable quantity the resulting gas may be burned at the mouth of the test-tube, with a blue flame. No carbon dioxide is obtained, carbonates being absent—a difference from oxalic acid. Heated with strong alkali, in the air, formate is changed to oxalate.—*Ethyl formate* is developed by distilling a dry formate with about an equal quantity of alcohol and a double quantity of sulphuric acid, undiluted. The ester has a characteristic fragrance, said to resemble that of peach-kernel—not sharply distinguished from esters of homologous acids as obtained in qualitative tests.

e.—Separations.—Free formic acid may be separated *from water and other non-acidulous volatile bodies* by neutralizing with fixed alkali and evaporating to dryness on the water-bath. From the residue, or any portion of formate, by adding phosphoric acid and distilling at 100° C. or a little above. If sulphuric acid be used instead of phosphoric it must be well diluted, and the dilution maintained by adding water from time to time, long distillation being now required.—*From acetic acid* free formic acid may be separated by digesting with enough lead oxide to cause a permanently alkaline reaction, evaporating to dryness, and exhausting the residue with alcohol. The filtrate will contain the acetic acid as lead basic salt, and the residue will contain the formic acid in combination, from which it can be recovered by distilling from phosphoric acid or by thorough treatment with hydric sulphide gas and following filtration. Instead of lead oxide, calcium carbonate or magnesium oxide may be employed, recovering the formic acid by distilling from phosphoric acid.

f.—Quantitative.—Free formic acid may be estimated volumetrically by titrating with alkali, using litmus or phenol-phthalein as an indicator.—The lead formate obtained by precipitation with lead normal acetate and alcohol, as directed under *d*, may be washed with alcohol, dried, and weighed as normal lead formate.—In a mixture of formic and acetic acids the formic acid is capable of estimation by its reduction of mercury. The mixture is digested some time with an excess of yellow mercuric oxide, the washed residue treated with dilute hydrochloric acid to remove the remaining oxide, and the metallic mercury gathered, washed, and weighed. $HgO + CH_4O = Hg + CO_2 + H_2O$. $Hg : CH_4O :: 199.7 : 46 :: 1 : 0.2303$.

g.—Impurities of acetic, hydrochloric, nitric, or other acids forming calcium salts soluble in alcohol may be found by digesting the acid mixture with excess of calcium carbonate, evaporating to dryness, and treating with alcohol, when the filtrate will contain the calcium salts of the acids mentioned.

FUSEL OIL.—Fuselöl. Huile de pommes de terre (potato oil).—The sum of the heavy alcohols obtained as a by-product in the manufacture of ethyl alcohol in its ordinary forms. A portion of higher-boiling distillate received after distillation of commercial alcohol or distilled spirits. A variable body of amyl alcohols with smaller proportions of adjacent alcohols of the $C_nH_{2n\ 2}O$ series, as products accompanying ethyl alcohol in the common alcoholic fermentation. Obtained in the fermentation of potatoes, indian corn, marc of grapes, and in smaller quantities by the fermentation of other materials used as sources of sugar. Fusel oils from their several sources differ from each other in composition, but amyl alcohols form by far the larger part of all of them. Acids of the $C_nH_{2n}O_2$ series are found in fusel oils, where they are formed by oxidation of the alcohols. Ethereal salts occur by action of fusel oil acids upon fusel oil alcohols and upon ethyl alcohol, as a result of "ageing."

The alcohols of fermentation, found in fusel oils, are chiefly as follows:

Per cent. by vol.	–	*Boiling, C.*	*Spec. grav.*
27.5[1]	Inactive amyl alcohol, isobutyl carbinol............$(CH_3)_2.CH.CH_2.CH_2OH$.	131.4°	0.812
13.0 6.0[1]	Active amyl alcohol, secondary-butyl carbinol... ....$CH_3.C_2H_5.CH.CH_2OH$...	128°	0.808[2]
5.0[1]	Iso-butyl alcohol, propyl carbinol....................$(CH_3)_2.CH.CH_2OH$.......	108.4°	0.802
6.5[1](?)	Normal butyl alcohol ...... $CH_3.CH_2.CH_2.CH_2OH$..	116°	0.810
Traces.	Tertiary butyl alcohol.......$(CH_3)_3.COH$.............	84°	0.779
3.0[1]	Normal propyl alcohol ......$CH_3.CH_2.CH_2OH$...	97.4°	0.807
15[1] (?)	Secondary propyl alcohol....$CH_3.CH(CH_3)OH$........	82.8°	0.788
[3]	A primary hexyl alcohol.....$C_6H_{13}OH$...	150°	....

The identification of several of the alcohols given above is not well established. The isomerides of different fusel oils are not the same. Rabuteau (*loc. cit.*) obtained 17 per cent. of products boiling above 132° C., and including some amyl alcohols. ORDONNEAU (1886: *Rep. anal. Chem.*) obtained from *wine brandy* twenty-five years old the following: normal propyl alcohol, 0.040%; normal butyl alcohol, 0.218%; normal [!] amyl alcohol, 0.084%; normal hexyl alcohol, 0.0006%; normal heptyl alcohol, 0.0015%; propionic, butyric, and caprilic ethers, 0.004%; œnanthic ether, about 0.004%; acetic ether, 0.035%; ethylaldehyde, 0.003%; acetal, 0.035%; amine bases, 0.004%. The same author states that alcohol from maize, beets, or potatoes contains isobutyl instead of normal butyl alcohol, and contains amyl and propyl alcohols, and pyridine, probably collidine. Wine yeast (elliptic) produces normal butyl alcohol; beer yeast (globular) no butyl alcohol. Except the uncertain report of secondary propyl alcohol, above quoted, and the traces of tertiary butyl alcohol, the alcohols found in fusel oil are primary, and therefore capable of forming acids without breaking up.[4]

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[1] RABUTEAU, 1878: *Compt. rend.*, **87**, 501; *Jour. Chem. Soc.*, **36**, 36.

[2] LE BEL, 1873: *Ber. d. chem. Ges.*, **6**, 1362.

[3] FAGET: *Liebig's Annalen*, **88**, 325—normal hexyl alcohol.

[4] Of pentyl alcohols, $C_5H_{11}OH$, eight are possible, and seven are known: three primary alcohols, three secondary alcohols, and one tertiary alcohol. There are four butyl alcohols, C_4H_9OH, two primary and two secondary, all

The fusel oil acids are not found in quantities sufficient for their satisfactory separation. Of ethereal salts, ethyl salts have been mainly found, instead of amyl salts, in fusel oils. Ethyl alcohol is retained in various quantities, limited by present English excise law to be below 15 per cent. of commercial fusel oils.

a.—Fusel oils are received by distillations beginning at 105° to 125° C., and ending at 132° to 137° C. Between 105° and 120° C. the most of the iso-butyl alcohol is obtained; between 128° and 132° C. the amyl alcohols are mostly distilled.

b.—*In physiological effects* the fusel oils have a stifling, harsh, spirituous *odor*, quite characteristic and subject to differences which reveal to the expert the source of the fusel oil. Even a slight inhalation excites coughing. Objectionable proportions of fusel oil in alcoholic liquors are recognized by first evaporating off the ethyl alcohol and obtaining the odor of the warmed residue. For the U. S. Ph. test of "alcohol" it is prescribed that "if mixed with its own volume of water and one-fifth its volume of glycerin, a piece of blotting-paper on being wet with the mixture, after the vapor of alcohol has wholly disappeared, should give no irritating or foreign odor (fusel oil)." "A little [rectified spirit] rubbed on the back of the hand leaves no unpleasant smell after the spirit has evaporated" (Br. Ph.)

In their effects on the system the alcohols of the $C_nH_{2n+2}O$ series have an intensity which increases with the molecular weight. Rabuteau (1870), mainly from experiments with frogs, estimated the intensities of effect of ethyl, butyl, and amyl alcohols to be, respectively, as 1, 5, and 15. Dr. B. W. Richardson[1] states that the action of amyl alcohol is that of butyl alcohol intensified. In the third stage of the action there are pronounced tremors of regular recurrence, reduction of temperature, and profound coma. Recovery requires sometimes two or three days. In recovery the restoration of the temperature is delayed longest. After death from amyl alcohol the blood is excessively venous.

c.—*Solubilities.*—The amyl alcohols of fusel oil are said to dissolve in about 40 parts of cold water. According to Bal-

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known. The two possible propyl alcohols, C_3H_7OH, are included in the list above. Of the seventeen hexyl alcohols, isomerides of $C_6H_{13}OH$, eight are known at present, four being primary.—It is evident, upon a very simple acquaintance with chemical law, that there can be but one ethyl alcohol, in whatever mixture it be found. Differences in the physiological effects of various alcoholic beverages are not due to any difference in the ethyl alcohol contained therein.

[1] 1875: Cantor Lectures, London.

BIANO (1876[1]) the inactive amyl alcohol of fusel oil is soluble in about 50 parts of water at 14° C., and less soluble in water at 50° C. Iso-butyl alcohol is soluble in 10 parts of water at 15° C. One part of inactive amyl alcohol takes up about 0.08 parts of water; one part of iso-butyl alcohol, about 0.15 parts of water. Fusel oil is freely soluble in ether, chloroform, and the other immiscible solvents of general use. Of the *amylsulphates of barium*, that formed from inactive amyl alcohol is two and a half times less soluble in water than is that from active amyl alcohol—a difference made available for separation of these isomers.

d.—In the qualitative identification of fusel oil the odor, and the effect of inhalation, are the means in most common use. In testing fusel oil in liquors or commercial alcohol the ethyl alcohol is made to evaporate before obtaining the odor. The Br. Ph. and U. S. Ph. directions for examination by odor are given under *b:* Separation by an immiscible solvent, as described under *e*, may be adopted preparatory to any qualitative examination. In ordinary analyses of alcoholic liquors or commercial alcohols, the ethyl alcohol has to be separated by careful distillation for the estimation of "strength," and the residue of such distillation, while warm, is to be examined for odor.

Concentrated sulphuric acid, on contact with fusel oils, enters into formation of amylsulphuric acids, $HC_5H_{11}SO_4$, presenting a red color.[2] According to VITALI (*loc. cit.*), when the sulphuric acid is added to a smaller quantity of fusel oil the color is red, growing brown-red on standing and on heating. Equal volumes of the amyl alcohols and the sulphuric acid give a dark and dull red color; but with an excess of the fusel oil different tints are obtained, cherry-red, violet, azure-blue, and green, in the order of the increasing excess of fusel oil. When to a drop or two of sulphuric acid, on a white porcelain surface, an equal volume of the fusel oil is first added, and then additional portions of the latter, cherry-red and violet tints are obtained, and at the proportions of five or six volumes of the fusel oil the azure-blue color is reached. The addition of ether to the colored mixture increases the brilliancy of the tints.

The test may be applied to the residue left after evaporation of a chloroformic or ethereal solution, obtained by shaking out

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[1] *Ber. d. chem. Ges.*, 9. 1437.

[2] PELLETAN, 1825: *Ann. Chim. Phys.*, [2], 30, 221. Amylsulphuric acid of iso-butyl carbinol (inactive amyl alcohol), CAHOURS, 1839: *Ann. Chem. Phar.*, 30, 291. As a color test for fusel oil, further, VITALI, 1884: *Archiv der Phar.*, [3], 21, 964; *Zeitsch. anal. Chem.*, 23, 426; *Analyst*, 9, 196.

as stated under *e*, and as so applied the test is trustworthy for negative results showing the absence of material proportions of fusel oil. But inasmuch as numerous non-volatile bodies give colors with sulphuric acid, an indication of the presence of fusel oil should be verified, in this test, by applying it to a fractional distillate from the liquor or commercial alcohol under examination—a distillate obtained between about 120° and 134° C.

For the qualitative use of MARQUARDT's plan of separating amyl alcohols directions are given below under *f*. This method is very delicate. The odor of the valeric acid is highly distinctive.—The reaction of JORISSEN, obtained by mixing with a little colorless aniline oil and a few drops of sulphuric acid, for a fine red color, depends on the presence of furfurol (aldehyde between furfuryl alcohol and pyromucic acid) present in fusel oils.[1] —SEVALLE (1881) determines the presence of fusel oil by turbidity of its alcoholic mixture when heated.—TRAUBE[2] tests brandy, after dilution to about 20 per cent. of strength, by the height to which the liquid rises in a capillary tube, as compared with a pure spirit of the same strength.—The etherification of amyl alcohols, to form esters of acetic acid, has been included among methods for recognition. The liquid is warmed or distilled with alkali acetate and sulphuric acid. The odor of amyl acetate is that of pears. This odor, however, is quite liable to be covered by that of acetic acid or ethyl acetate, so that caution should be observed in interpretation of the result.

e.—The separation of fusel oil by distillation gives practically conclusive results, but is certainly not without waste. *Separation by immiscible solvents* is generally employed. BETELLI[3] adds to a certain quantity of the commercial alcohol six or seven times its volume of water, and shakes with chloroform enough to make after subsiding a very small layer, which is drawn off and evaporated for test of the residue. With only 5 or 6 c.c. of the alcohol, and 15 to 20 drops of the chloroform, 0.05 per cent. of fusel oil was detected, the final test being that of etherification to amyl acetate ("pear oil") by digesting the residue with alkali acetate and sulphuric acid. Before applying the immiscible solvent it is proper to reduce the concentration of the ethyl

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[1] FÖRESTER, 1882: *Ber. d. chem. Ges.*, 15, 230.

[2] 1886: *Ber. d. chem. Ges.*, 19, 892; *Jour. Chem. Soc.*, 50, 743. Follows a report on relation between capillarity and molecular weight, and on specific capillarity, 1885: *Jour. prakt. Chem.*, [2], 31, 177, 514; *Jour. Chem. Soc.*, 48, 866, 1033.

[3] 1875: *Ber. d. chem. Ges.*, 8, 72; *Zeitsch. anal. Chem.*, 14, 197.

alcohol, either by distilling it off or by adding water. See the directions given below under *f*.

f.—Quantitative.—For the estimation of fusel oil the method of Marquardt[1] is here given: The fusel oil is separated from a diluted alcoholic liquid by shaking out with chloroform; the amyl alcohol is oxidized to valeric acid; the acid is taken up by barium carbonate, and the barium salt is estimated, to represent the quantity of amyl alcohol oxidized. Of the alcoholic liquid under examination 150 grams are to be diluted with an equal volume of water, and agitated with 50 c.c. of chloroform (of ascertained purity) for about a quarter of an hour. The aqueous layer is separated and again extracted with 50 c.c. of chloroform for the same length of time. The operation is repeated the third time. The united portions of chloroform are treated, in a strong flask, with a solution of 5 grams dichromate in 30 grams of water, and 2 grams of sulphuric acid, digesting for about six hours with frequent agitation while the flask is well corked. The contents of the flask are then distilled until about 20 c.c. remain, when this residue is diluted by addition of about 80 c.c. of water, and again distilled until only about 5 c.c. remain. The entire distillate is then digested with heat for half an hour with barium carbonate, an erect condenser being employed to return the distillate to the flask. The chloroform is then separated by distillation, and the aqueous residue concentrated to a volume of 5 c.c. The excess of barium carbonate is filtered out, and the filtrate with the washings evaporated in a weighed dish on a water-bath to dryness. The residue is weighed, and afterwards dissolved in water and a few drops of nitric acid, and made up with water to 100 c.c., of which 50 c.c. are taken to estimate the barium, and 50 c.c. to estimate the chlorine (derived from the chloroform by action of the dichromate). The quantity of barium combined with the chlorine is calculated, and deducted from the total barium in the 50 c.c. From the remaining quantity of barium the quantity of valeric acid is calculated, and from this the quantity of amyl alcohol. Then $BaSO_4 : 2C_5H_{12}O :: 232.8 : 176 :: 1 : 0.7560$. And the weight of barium sulphate $\times\ 0.756 =$ the weight of amyl alcohol.

For exact results the chloroform used is to be purified by subjecting it to the operation as described—treatment with solution of dichromate and sulphuric acid, distillation, digestion of

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[1] L. Marquardt, 1882: *Ber. d. chem. Ges.*, 15, 1370, 1661; *Analyst*, 8, 106; *Jour. Soc. Chem. Ind.*, 1, 331, 377; *Jour. Chem. Soc.*, 42, 1235, 1327. A favorable report upon Marquardt's method is given by G. Lunge, V. Meyer, and E. Schulze, 1884: *Chem. Cent.*, p. 854; *Jour. Chem. Soc.*, 48, 708.

the distillate with barium carbonate, and redistillation. To purify ordinary chloroform it is necessary to repeat the process several times.

In the *qualitative* use of the test 30 to 40 grams of the spirit are diluted with water so as to contain 12 to 15 per cent. of alcohol, and the liquid shaken up with 15 c.c. of pure chloroform. The chloroform solution is washed with about an equal volume of water, and, after the latter has separated, is evaporated to dryness. To the residue are added a little water, one or two drops of sulphuric acid, and permanganate of potassium enough to give a red color after 24 hours.

The estimation of fusel oil by measurement of the increase of volume of the chloroform layer, after shaking out, making comparison with a standard spirit, has been undertaken by B. Röse, and advanced by Messrs. Stutzer and Reitmair,[1] but the method is not well sustained.[2]

The quantities of fusel oils present in alcoholic liquors have not been generally obtained upon trustworthy data. In certain whiskeys there were obtained, in the analyses of Dr. Dupré, from 0.18 to 0 24 parts of amyl alcohol to 100 parts of ethyl alcohol. N. P. Hamberg[3] has given figures for the fusel oil in beer as follows: 1.14 gram of fusel oil in 100 liters of the beer, or about 0.00114 per cent.

GALLIC ACID.—$C_7H_6O_5 = C_6H_2(CO_2H)(OH)_3 = 170$. A trihydroxy-benzoic acid [$CO_2H : OH : OH : OH = 1 : 3 : 4 : 5$]. Gallussäure.—Found in nutgalls, sumach, tea, and, accompanying tannins, in a large number of plants. Gallic anhydride, as digallic acid, occurs in gallotannic acid, and gallic acid is a natural fermentation product of certain glucoside-tannins. It is in use in medicine, as a reducing agent in photography, and in hair dyes. It is not a tanning agent. Gallotannic acid, in the human body, is soon converted into gallic acid. The gallic acid of commerce is wholly manufactured from the tannin of galls.

Gallic acid, as a separate solid, is *identified* by its sensible properties and decomposition products (*a*); in solution, by its

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[1] Summary by Uffelmann, 1886: *Ding. pol. Jour.*, **261**, 439; *Jour. Chem. Soc.*, **50**, 1079. B. Röse, 1885: *Archiv d. Phar.*, [3], **23**, 62.

[2] Lunge, Meyer, and Schulze, 1884: *Jour. Chem. Soc.*, **48**, 709.

[3] 1885: *Trans. Royal Acad. Stockholm; Schmidt's Jahrbucher der Medicin*, **201**, 27.

reactions with iron salts, lime, and antimony, and its reducing power (*d*). It is distinguished from tannins by non-precipitation of gelatin, alkaloids, and antimony in presence of ammonium chloride. *Separations* from tannins, various acids, and from metals are indicated in *e*, methods of estimation in *f*, and tests for purity in *g*.

a, b.—Gallic acid crystallizes, as $C_7H_6O_5.H_2O = 188$ (9.5% crystal water), in gray-white silky needles, or triclinic prisms, odorless, of an astringent and slightly acidulous taste, and acid reaction. The crystals are permanent, but lose all their water at 100° C. If the dry acid be gradually heated, in a glass tube, at 210° to 215° C. (410°–419° F.), a white or yellowish white sublimate of pyrogallol appears, in droplets, crystallizing on cooling: $C_7H_6O_5 = C_6H_6O_3 + CO_2$. A dark residue remains. Heated quickly, in a porcelain capsule, at about 250° C. (482° F.), metagallic acid, $C_6H_4O_2$, is formed, in a black lustrous residue, soluble in strong alkali solution, with dark-brown color. Heated very gradually, with concentrated sulphuric acid, in a test-tube, to about 150° C. (302° F.), the mass turns wine-red to carmine-red. If now cooled and poured into water, the latter will be colored yellow-brown, and a red-brown precipitate of rufigallol (rufigallic acid) partly crystalline (in rhombohedrons) will appear. If the precipitate be washed and dried, then treated with very strong potassium hydroxide solution, a blue color changing to violet is obtained. Traces of rufigallol may be taken up with acetic ether. Baryta water also gives a blue color with rufigallol. If gallic acid be warmed with potassium hydroxide, tannomelanic acid, of a black color, is produced. All alkaline solutions of gallic acid soon darken in the air.

c.—Gallic acid is soluble in 100 parts of cold or 3 parts of boiling water, the hot-saturated solution giving abundant crystals on cooling. It is freely soluble in alcohol, soluble in 39 parts of absolute ether, freely soluble in acetic ether, scarcely at all soluble in chloroform, benzene, or benzin. Gallic acid, by structure monobasic, is stated to form three classes of metallic salts by the displacing of one, two, and three atoms of its hydrogen, only the alkali salts being soluble in water. Aqueous solutions of the acid soon decompose, with deposition of humus-like products.

d.—**Solution of lime,** added to an alkaline reaction, causes a white turbidity, changing to blue, later to green. **Acetate of lead** gives an abundant white precipitate, not especially characteristic. **Ferric salts,** and, more perfectly, the ferroso-ferric solutions, with free gallic acid, give a deep blue or blue-black precipitate, decolored by boiling (with reduction of ferric to ferrous salt), and decolored by sufficient acetic acid or by excess of alkalies. **Tartrate of antimony and potassium** causes a precipitate, which, in distinction from gallotannin, is prevented or dissolved by ammonium chloride. Precipitates are not obtained with gelatin, or albumen, or starch, or with the alkaloids (all distinctions from gallotannin).

Lead acetate with free gallic acid gives a bulky white precipitate, which by warming condenses to a heavy powder, easily washed. The fresh precipitate, with sodium or potassium hydroxide, turns red.

As a reducing agent gallic acid is in general only a very little less forcible than tannin. Permanganate is promptly decolored by gallic acid. Fehling's solution is turned from blue to yellow-brown at once, but the cuprous precipitate is very slowly obtained after heating for some minutes. Silver nitrate is slowly reduced, after warming, sometimes in part as a mirror. Molybdate of sodium or ammonium reacts as with gallotannin. Ferric salts are partly reduced by boiling with gallic acid.

e.—Gallic acid may be *separated* from tannin by full precipitation of the latter with cinchonine sulphate and filtration. By precipitation with some excess of gelatin, filtering (concentrating the filtrate if need be), adding alcohol enough to throw down all the gelatin, and filtering again. Also by digestion with rasped hide. From the fruit acids, with tannin, if it be present, by calcium acetate, acetic acid and alcohol, or by acetic ether solution. From all acids not precipitated with lead acetate by this reagent, as above, separating the lead from the precipitate by treatment with hydrosulphuric acid and filtration. Recent lead hydrate removes all but a trace of free gallic acid. From its iron salts it is obtained by treatment with oxalic acid to fully change the color, and extraction of the mixture with acetic ether.

f.—*Quantitative.*—The estimation of gallic acid, in solution free from other oxidizing agents, may be accurately done by titration with permanganate, in presence of indigo solution, as in Löwenthal's method for tannin (see under Tannin).[1] The gallic acid consumes more permanganate than an equal weight of tannin does, and more than does the quantity of tannin from which it could be obtained.[2] The permanganate solution may be standardized by freshly dissolved weighed gallic acid of given purity.

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[1] Löwenthal, 1877: *Zeitsch. an. Chem.*, 16, 39.

[2] Procter, *Chem. News*, 36, 60.

Tannin, if present, must be first removed as in Löwenthal's method.—Gallic acid may be estimated, in absence of tannin, by the increase of weight of zinc oxide. A weighed quantity of the oxide, freshly ignited, is digested with the solution of free gallic acid, filtered out, washed, dried at 110°–120° C., and its increase of weight taken as gallic acid.—A method, after Fleck, by precipitation as copper salt, giving approximate results in presence of tannin, is conducted as follows: The prepared solution is fully precipitated with a filtered solution of cupric acetate; the precipitate washed and then exhausted with cold solution of carbonate of ammonium. The last solution, containing all the gallate of copper with a very little tannate, is evaporated to dryness, the residue moistened with nitric acid, ignited, and weighed as oxide of copper. This weight multiplied by 0.9 gives the quantity of gallic acid, the full ratio being 0.9126, but allowance is made for solution of a little tannate by the carbonate of ammonium. The ratio between oxide of copper and tannic acid is 1.304.

g.—"An aqueous solution of gallic acid should not precipitate alkaloids, gelatin, albumen, gelatinized starch, or solution of tartrate of antimony and potassium with chloride of ammonium (distinction from tannic acid)" (U. S. Ph.)

GALLOTANNIN. See TANNINS.

GLYCERIN. Glycerol. $C_3H_8O_3 = 92$. $(C_3H_5)'''(OH)_3$.—Propenyl, $C_3H_5 = CH_2.CH.CH_2$, is a residue of propane, the third member of the marsh-gas series. Glycerin is produced, along with candle-manufacture and the production of the fat acids ("stearin" and "olein"), by saponification of the fats, with water as superheated steam, or with lime, or with sulphuric acid. It occurs also among the products of the alcoholic fermentation of sugar.

Glycerin taken alone is *recognized* by its sensible properties (*a*); in dilute forms or in certain admixtures it is revealed by the bead-test with borax, its power of neutralizing boracic acid, and the odor of its vapors when strongly heated (*d*). *As a reducing agent* it affects permanganate promptly in alkaline mixture, scarcely at all in neutral or acid liquids, and does not alter Fehling's solution. It is *separated* from substances more volatile than water by their distillation, and from non-volatile substances by its own distillation at a heat a little above that of the water-bath; from matters insoluble in alcohol, by use of this solvent, best by use of lime and alcohol (*e*). It is *estimated* gravimetrically by careful evaporation with alcohol-ether; volumetrically by the permanganate reaction, forming oxalic acid (*f*). *Tests* and *authorized standards of purity* (*g*, p. 328).

a.—Glycerin is a colorless, clear, syrupy liquid, capable of crystallization in low winter temperatures, taking forms of the rhombic system, or congealing in white, crystalline masses, nearly or quite anhydrous, the melting point being 22° C. Specific gravity at 15° C., taking water at same temperature as standard, 1.26468 (MENDELEJEFF), 1.2653 (GERLACH); at 15° C., taking water at 0° C., 1.26358; at 17.5° C., 1.262 (STROHMER). Glycerin is very hygroscopic, and at ordinary temperatures it vaporizes in only the slightest degree, but at 100° C. it vaporizes or distils to a sensible extent. At this temperature and 760 millimeters barometric pressure it has a vapor tension of 64 millimeters. At 290° it boils with partial decomposition, evolving vapor of acrolein, C_3H_4O. With superheated steam at 180° to 200° C. it distils completely. Evaporated in an open dish at 150° to 200° C., when perfectly pure, it leaves no residue behind. Heated in a capsule, at 92° C. vapor rises almost imperceptibly, at 100° C. quite perceptibly, at 130° C. abundantly, without irritating products to a sensible extent at last-named temperature (TRIMBLE, 1885).

b.—Glycerin has a pure sweet taste of much intensity, without odor. Undiluted it has a heating effect when applied to the surface.

c.—Exposed to the air glycerin absorbs water, finally to the extent of about 50 per cent., and is soluble in all proportions of water and of alcohol. In mixture with water the volume is reduced and the temperature raised, the greatest liberation of heat being obtained with 58 parts of glycerin to 42 parts of water, in which proportions the contraction of volume is about 1.1 per cent., and the elevation of temperature about 5° C. In ether, glycerin is slightly soluble, 1 part of glycerin of sp. gr. 1.23 requiring 500 parts of ordinary ether for solution. It is soluble in a mixture of 3 parts of alcohol and 1 part of ether; also in a mixture of 2 volumes of absolute alcohol and 1 volume of common ether. Not soluble in chloroform, benzene, or fixed oils. Soluble in a mixture of equal weights of chloroform and alcohol. Glycerin when pure is neutral to all indicators. Glycerin dissolves the alkaline earths to a considerable extent, with chemical combination. If the solutions be charged with carbon dioxide the earths are mainly precipitated. With lead it forms the glyceride, $C_3H_6PbO_3$, crystallizable in fine white needles. Sodium glyceride, $C_3H_7NaO_3$, is a white, hygroscopic powder, resolved by water into glycerin and sodium hydroxide.

d.—"If a fused bead of **borax** on a loop of platinum wire be moistened with glycerin previously made slightly alkaline with diluted solution of soda, and after a few minutes held in a colorless flame, the latter is tinted deep green."—Glycerin abstracts boric acid from borax, so as to affect the reaction to litmus. If a **borax** solution be colored (blue) with litmus, and a solution containing glycerin, neutral in reaction, be also colored with blue litmus, on mixing the solutions a red color will be obtained. Warming restores the blue color, but the red reappears when the liquid is cool again.—If a portion of glycerin be heated to boiling in a dry test-tube, the characteristic acrid *vapors of acrolein* will be obtained. If in aqueous mixture, the glycerin must be concentrated for the test, which is also rendered more delicate by the addition of a little dry phosphoric acid or potassium bisulphate. Glycerin alone is not carbonized by heating with either of these agents.—If 2 drops of glycerin (free from bodies carbonized by sulphuric acid) be mixed with 2 drops each of melted **phenol** and **sulphuric acid,** and heated somewhat over 120° C. to the production of a resinous mass, and when cold ammonia be added, a fine carmine-red color will be obtained.

Permanganate solution, acidulated with sulphuric acid, is but very slowly decolored by glycerin, and even by boiling heat the oxidation of the glycerin is difficult. But in alkaline solution of the permanganate decoloration by glycerin is prompt, the reaction being as follows (Benedikt and Zsigmondy): $C_3H_8O_3 + 2K_2Mn_2O_8 = K_2C_2O_4 + K_2CO_3 + 4MnO_2 + 4H_2O$. Fehling's solution is but very slightly reduced by glycerin. A quite concentrated solution of pure glycerin, boiled 10 minutes with Fehling's solution, and then set aside for 24 to 48 hours, yields some precipitate of the cuprous hydroxide. But dilution of the glycerin with ten volumes of water prevents the reaction.

e.—Separations.—Glycerin in watery mixture is not concentrated by evaporation without loss, neither is any part of it obtained anhydrous by continued evaporation. From 100° to 130° C. glycerin alone distils unchanged (Trimble, 1885). From solution in alcohol it can be recovered almost without loss in the residue left by gentle evaporation with additions of a little absolute alcohol from time to time.—Glycerin may be separated *from fluid extracts of vegetable drugs, also from wines, or from sugars and gums*, as follows: Slaked lime is added, the liquid is treated with a little alcohol and evaporated to dryness at a very gentle heat, adding small portions of alcohol in completing the evaporation, and then exhausted with several portions of alcohol of about ninety per cent. strength by weight. The clear alcoholic solution is evaporated, with the alcoholic filter-washings if filtration has been required, and the residue will be approximately pure glycerin. In the case of certain extracts, and as a precaution in separating from unknown matters, it is desirable to take up the glycerin residue with a mixture of two volumes of absolute alcohol and one volume of stronger ether, filtering if need be, and evaporating again. With quantitative precautions in completing the extractions, and washing filters, then evaporating in weighed beakers, the operation will serve as a good practical estimation, though of course absolute glycerin is not obtained for weight. Instead of the ether-alcohol, a mixture of equal weights of chloroform and alcohol does well in some cases as a solvent for purification, but the former is generally the best. The lime is an essential aid in holding sugars, gums, and many extractive matters, from solution in the ninety-per-cent. alcohol.[1] *From soaps* glycerin is obtained by acidulating with dilute sulphuric acid for removal of the fat acids, addition of barium carbonate for removal of excess of sulphuric acid, when alcohol is added, alkali sulphates filtered out, and evaporation conducted with the addition of alcohol and filtration.

f.—Quantitative.—Estimation of glycerin of fats. About 30 grams of the dried and filtered clear fat, with 15 grams potassium hydroxide or 21 grams sodium hydroxide dissolved in the least sufficient amount of water, and 50 c.c. alcohol, are digested

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[1] The use of the lime with the alcohol was reported upon, for estimation of the glycerin of wines, by E. REICHARDT, 1875: *Archiv d. Phar.*, [3], 7, 408: *Zeitsch. anal. Chem.* (1878), 17, 109. An elaborate examination of this method of separating glycerin from wines was made by NEUBAUER and BORGMAN, 1878: *Zeitsch. anal. Chem.*, 17, 445. These authors found a considerable impurity in the glycerin extracted from wines by Reichardt's directions, but they were able to recover very nearly the quantity of glycerin added to wines. Control analyses by Reichardt's method, in separation from cane sugar, grape sugar, and medicinal fluid extracts, were made by the author and another (A. B. Prescott and O. H. Koehnle) in 1878: *New. Rem.*, New York, 7, 354. From mixture with sucrose 99.8 per cent. of the glycerin taken was recovered: from mixture with glucose 99.7 per cent. was recovered: in both cases the glycerin being obtained free from sugar. From fluid extracts of cinchona and of gentian, to which sugars had been added, there were separated 97.6, 98.6, and 95.4 per cent. of the glycerin added. The ether-alcohol mixture mentioned in the text separated pure glycerin from sucrose, but not from glucose, some of which was taken up with the glycerin. The same was found to be true of the chloroform-alcohol mixture referred to in the text.

over the water-bath to perfect saponification. The alcohol is evaporated off, the soap dissolved in water, diluted sulphuric acid is added, and the mixture warmed, until the separation of the surface-layer of fat acids is complete. When cold the fat crust is removed, the aqueous liquid filtered, and the fat acids washed on the filter; or the fat acids are filtered out as in Hehner's method (p. 250). The excess of sulphuric acid in the filtrate is taken up with barium carbonate, the filtrate evaporated, with additions of alcohol, to a thin syrupy consistence, then treated with a mixture of 3 parts of 95% alcohol and 1 part of ether and filtered, washing the filter with the same mixed solvent. This filtrate is evaporated in a platinum dish, at 100° C., until two weighings do not differ over 3 to 5 milligrams, or dried in a desiccator to a constant weight. The residue is then ignited, and the weight of the ash deducted.

The glycerin of strictly neutral fats can be calculated from Köttstorfer's number—the milligrams of potassium hydroxide to saponify 1 gram of fat. Taking these milligrams as thousandths of a gram, $3KOH : C_3H_8O_3 :: 168 : 92$.

Estimation by oxidation with permanganate (Benedikt and Zsigmondy.[1]) The reaction is stated under *d*, and the resulting oxalic acid is the measure obtained. The fat is saponified with potash and methyl alcohol, the alcohol evaporated off, the residue dissolved by hot water, the soap decomposed by diluted hydrochloric acid, and the fat acids melted and set aside until fully clear. Some hard paraffin is added to the fat acids, the mixture cooled and filtered, and the residue washed. The filtrate is neutralized with potassa, and is now ready for the reaction.—First add 10 grams potassium hydroxide,[2] and then add, at ordinary temperature, of a permanganate solution of about 5% strength sufficient to render the liquid no longer green but blue or black in color. The mixture is heated to boiling, with precipitation of manganese dioxide, and then enough sulphurous acid is added to make the red liquid colorless, and the mixture filtered through a wet filter large enough to contain at least half at once, and the residue well washed with boiling water. If the last washings be turbid with manganese dioxide, a little acetic acid is added. The liquid is now heated to boiling, and fully precipitated by calcium acetate or chloride. The oxalate of calcium precipitated is esti-

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[1] 1885: *Analyst*, 10. 205, from *Chem. Zeit.* An investigation of this and other methods, now being made by A. J. Baumhardt and the author, will be communicated at an early date.

[2] Fox and Wanklyn (1886: *Chem. News*, 53, 15) take a quantity of material containing not over 0.25 gram of glycerin, and add 5 grams of KOH.

mated at the discretion of the operator. But inasmuch as the precipitate is liable to contain, as impurities, calcium silicate and calcium sulphate, it is better to estimate the oxalate volumetrically with permanganate, or, after ignition, by titration with half normal hydrochloric acid, using dimethylanilin orange as an indicator. The hydrochloric acid may be standardized by anhydrous sodium carbonate. 106 parts of Na_2CO_3, or 72.8 parts of HCl, indicate 90 parts of $H_2C_2O_4$, or 92 parts of glycerin.—In this operation methyl alcohol is used because ethyl alcohol, if employed, is not wholly expelled, and suffers oxidation by permanganate in alkaline liquid with formation of oxalic acid. Soluble fat acids do not interfere. The method is applicable to any ordinary neutral mixture of glycerin.—Benedikt and Zsigmondy obtained the following percentages of glycerin: From olive oil, 10.15–10.38; linseed oil, 9.45–9.97; tallow, 9.94–9.98–10.21; butter, 11.59; Japan wax, 10.3–11.2; beeswax, 0.

g.—Tests of purity.—The U. S. Ph. prescribes as follows: "Glycerin should be neutral to litmus-paper. Upon warming a portion of 5 or 6 grams with half its weight of diluted sulphuric acid, no butyric or other acidulous odor should be obtained. A portion of 2 or 3 grams, gently warmed with an equal volume of sulphuric acid in a test-tube, should not become dark-colored. A portion of about 2 grams, heated in a small open porcelain or platinum capsule, upon a sand bath, until it boils, and then ignited, should burn and vaporize so as to leave not more than a dark stain (absence of sugars and dextrin, which leave a porous coal). A portion heated to about 85° C. (185° F.) with test solution of potassio-cupric tartrate should not give a decided yellowish-brown precipitate, and the same result should be obtained if, before applying this test, another portion be boiled with a little diluted hydrochloric acid for half an hour (absence of sugars). After full combustion no residue should be left (metallic salts). Diluted with ten times its volume of distilled water, portions should give no precipitates or colors when treated with test solutions of nitrate of silver, chloride of barium, sulphide of ammonium, or oxalate of ammonium (acrylic, hydrochloric, sulphuric, and oxalic acids, iron and calcium salts)."

"Shaken with an equal volume of sulphuric acid, no coloration, or only a very slight straw coloration, should result. When gently heated with diluted sulphuric acid, no rancid odor is produced. Sp. gr. about 1.25" (Br. Ph.)

"Sp. gr. 1.225 to 1.235. Heated in an open dish to boiling, and then ignited, it should burn without residue. It should not reduce ammoniacal solution of silver nitrate, at ordinary temperature, within half an hour. Warmed with an equal volume of sodium hydrate solution (15%), it should not be colored, nor should ammonia be developed; and gently warmed with diluted sulphuric acid, no disagreeable rancid odor should be given" (Ph. Germ.)

Sp. gr. 1.242. Undergoes complete combustion, leaving no residue (Ph. Fran.) Impurities: lead salt, lime, lime sulphate, sodium chloride, oxalic acid, butyric acid. Adulterations: excess of water, dextrin, glucose syrup, honey (Ph. Fran.)

The sulphuric acid test is doubtless severe enough if the directions of the U. S. Ph. be followed with omission of the gentle warming, as sufficient elevation of temperature results from the admixture. *The silver nitrate test* is much influenced by the conditions of time and light. If treatment with test solution of silver nitrate for half an hour, in the dark, be adopted, the test is certainly not too severe. *The combustion test* is efficient for the exclusion of carbohydrates.

Messrs. Patch, Warder, and Goebel have each lately reported upon the quality of glycerin sold in the United States.[1]

GUARANINE. See CAFFEINE, p. 77.

HOMATROPINE. See MIDRIATIC ALKALOIDS.

HOMOQUININE. See CINCHONA ALKALOIDS, p. 92.

HYDRASTINE. $C_{22}H_{23}NO_6 = 397$ (MAHLA, 1863).—The colorless alkaloid of Hydrastis Canadensis, or "golden seal" root, in which it accompanies the yellow alkaloid berberine. Hydrastine is also a commercial name for medicinal preparations of the yellow alkaloid berberine, from Hydrastis.[2] Perrins obtained

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[1] *Proc. Am. Pharm.* for 1885: 33, pp. 481, 484, 485.

[2] The colorless alkaloid of Hydrastis was announced as a crystallizable alkaloidal body, in 1851, by DURAND, of Philadelphia, who proposed the name "hydrastine," but was left in doubt because unable to obtain crystallizable salts. The name "hydrastine" had been given to the yellow alkaloid of golden seal by RAFINESQUE in his "Medical Flora of the United States," vol. i., 1828. In Europe the yellow alkaloid had been found in other plants and named "jamaicine" by HUTTENSCHMID in 1824, "xanthopicrite" by CHEVALLIER and PELLETAN in 1826, and "berberine" by BUCHNER and HERBERGER in 1830, with a better description by FLEITMAN in 1847. The yellow alkaloid was found in Hydrastis by DURAND in 1851, and identified with the yellow alkaloid of Berberis and other plants by MAHLA as late as 1862, and by PERRINS, 1863. Prof. LLOYD states (1884) that "there is little indication that the term hydrastine," as applied to the yellow alkaloid of Hydrastis, "will be sup-

1½ per cent. from the dried root. Lloyd states the yield in manufacture to be ¼ to ¾ per cent.

Hydrastine is *characterized* by its crystalline form when free, and the amorphous condition of its salts (*a*), with the reactions it gives as an alkaloid (*d*). It is *prepared* from golden seal as directed (*e*), and *estimated* gravimetrically (*f*).

a.—Hydrastine forms four-sided prisms, orthorhombic, lustrous when perfect, usually broken and opaque white. The crystals melt at 135° C. (MAHLA), at 132° C. (POWER), and in strong heat decompose with odor of phenol.—The *salts of hydrastine* refuse to crystallize. The hydrochloride is anhydrous, $C_{22}H_{23}NO_6.HCl$; also the sulphate, $(C_{22}H_{23}NO_6)_2H_2SO_4$.—Hydrastine is levo-rotatory, with a specific rotatory power, in chloroformic solution, of $[a]_D = -170°$ (POWER).

b.—Hydrastine, free, is tasteless and odorless. The salts have an acrid taste. Hydrastine is the true active principle of Hydrastis Canadensis (Prof. BARTHOLOW, 1885[1]). Three grains of the hydrochlorate caused the death of a frog in four minutes, and the results upon rabbits were corresponding. Like strychnine, it causes death by arrest of the respiratory movements in a tonic spasm.

c.—Hydrastine is not appreciably soluble in water or in dilute alkaline solutions. At 15° C. it dissolves in 1.75 parts of chloroform, in 15.7 parts of benzene, in 83.46 parts of ether,

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planted by berberine at any immediate day": "Drugs and Medicines of North America," vol. i. 100.

A. B. DURAND, 1851: *Am. Jour. Phar.*, **23**, 112. W. S. MERRELL, 1862: *Am. Jour. Phar.*, **34**, July. J. D. PERRINS, 1862: *Phar. Jour. Trans.*, [2], **3**, 546 (May): first separation as a colorless alkaloid. F. MAHLA, 1886: *Am. Jour. Sci.*, [2], **36**, 27. J. U. LLOYD, 1878: *Proc. Am. Pharm.*, **26**, 805. F. B. POWER, 1884: *Proc. Am. Pharm.*, **32**, 448. J. U. LLOYD, a full history: "Drugs and Medicines of North America," 1884, vol. i. 130. FREUND and WILL, a critical investigation, 1886: *Ber. d. chem. Ges.*, **19**, 2797; *Phar. Jour. Trans.*, **16**.

Upon a second colorless alkaloid in Hydrastis see A. K. HALE, Ann Arbor, 1873: *Am. Jour. Phar.*, **45**, 247 J. C. BURT, 1875: *Am. Jour. Phar*, **47**, 481. H. LERCHEN, Philadelphia, 1878: *Am. Jour. Phar.*, **50**, 470. J. U. LLOYD, 1884: "Drugs and Med. of North America," vol. i. 139. According to FREUND and WILL (1886, *loc. cit.*) hydrastine has decided chemical resemblance to narcotine ($C_{22}H_{23}NO_7$). When oxidized by permanganate or by dilute nitric acid, hydrastine was found to yield a crystalline acid identical with opianic acid, together with a crystalline base closely resembling cotarnine (compare under Narcotine, *d*).

[1] Communication, from physiological trials, in "Drugs and Medicines of North America," **1**, 156.

and in 120 parts of alcohol (Power, 1884[1]). It does not dissolve in petroleum benzin.—The ordinary *salts* are soluble in water; the tannate and picrate insoluble. The salts of hydrastine mostly have an acid reaction. The acetate, formed in solution, decomposes on evaporation.

d.—**Alkali hydrates** precipitate hydrastine, from the aqueous solution of its salts, in a bulky amorphous mass, which finally takes on crystallization, with great reduction of volume. The precipitate is but slightly soluble in excess of alkalies.—White precipitates are produced by **potassium iodide,** potassium **ferrocyanide, sulphocyanide, mercuric chloride,** and by **tannic acid** (Power). *The general reagents* for alkaloids cause precipitates—**iodine** in potassium iodide, brown; Mayer's solution, white; platinic chloride, orange-yellow; gold chloride, yellowish-red; picric acid, yellow. **Potassium bichromate** gives a yellow precipitate.—**Sulphuric acid**, undiluted, causes a yellow color, becoming red on warming, and turning to brown on adding a crystal of bichromate. Concentrated sulphuric acid and **molybdate** of ammonium give an olive-green color (Power). Concentrated nitric acid produces only a yellowish color in the cold. The hydrochloride solution, treated with chlorine, shows blue fluorescence (Mahla). Ethyl-hydrastine was obtained in hydriodide by Power,[2] who also formed a hydro-hydrastine $C_{22}H_{27}NO_6$, in the hydrochloride.

e.—Hydrastine may be separated from golden seal root as follows (Power, Lloyd: 1884): The powdered root is moistened with alcohol and percolated with the same solvent; sulphuric acid in strong excess is added to the percolate; after four hours the crystals of berberine sulphate are filtered out; ammonia is added to the filtrate until it has but a slightly acid reaction and the crystallized ammonium sulphate is filtered out; the filtrate is concentrated (by distillation) to a syrupy consistence, and the residue poured into ten times its volume of cold water. After twenty-four hours the precipitated resinous substances, oils, etc., are filtered out; ammonia-water in decided excess is added to the filtrate; and the resulting precipitate, impure hydrastine, collected and dried. The product is digested with 100 times its weight of cold water, to which sulphuric acid has been carefully added to *slight* acid reaction; after twenty-four hours the liquid is filtered and ammonia in excess added to the filtrate, the precipitate collected on a strainer, dried, and then powdered and

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[1] *Proc. Am. Pharm.*, **32**, 450.

[2] 1884: *Proc. Am. Pharm.*, **32**, 454.

extracted with boiling alcohol. On cooling the solution gives crystals of hydrastine, still dark yellow with impurities, and to be recrystallized from alcohol, repeatedly, until perfectly colorless.

f.—Quantitative.—The free alkaloid crystallizes anhydrous, $C_{22}H_{23}NO_6$, and the crystals or the well-washed precipitate by ammonia, when obtained colorless, may be dried at 100° C. for weight. The gold chloride of hydrastine, by precipitation of the hydrochloride of the alkaloid with auric chloride, and drying at 100° C., gave Prof. Power[1] 16.92 per cent. of metallic gold. The formula, $(C_{22}H_{23}NO_6 . HCl)_2AuCl_3 = 1169.2$, indicates 16.78 per cent. of gold and 67.91 per cent. of hydrastine.

The platinum chloride, obtained by precipitation of the hydrochloride solution, gave MAHLA 16.17% of platinum; the formula $(C_{22}H_{23}NO_6 . HCl)_2PtCl_4$ indicating 16.12% of platinum.

HYDROQUININE. See CINCHONA ALKALOIDS, p. 91.

HYGRINE. See COCA ALKALOIDS, p. 173.

HYOSCYAMINE. See MIDRIATIC ALKALOIDS.

IGASURINE. See STRYCHNOS ALKALOIDS.

INKS. See TANNINS.

JAPACONITINE. See ACONITE ALKALOIDS, p. 18.

KAIRINES. See CINCHONA ALKALOIDS, p. 166.

LANTHOPINE. See OPIUM ALKALOIDS.

LARD. See FATS and OILS, p. 290.

LINOLEIC ACID. See p. 249.

LINSEED OIL. See p. 284.

MADDER RED. See COLORING MATTERS, p. 189.

MAGENTA. See p. 191.

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[1] 1884: *Proc. Am. Pharm.*, 32, 453.

MALIC ACID. $H_2C_4H_4O_5 = 110$. $CO_2H.CH_2.CHOH.CO_2H$. Aepfelsäure.—Distributed widely through the vegetable kingdom. Reported already in not less than 200 plants (Husemann's "Pflanzenstoffe"). Most abundant in fruits, but found in other parts of plants.[1] Usually obtained from mountain-ash berries or from unripe apples. LENSSEN (1870) obtained 6 62% from barberry berries, only 1.58% from mountain-ash berries. Others report about 2% from the latter. It is abundant in tobacco. It is believed identical with Minispermic acid, Solanic acid, Tannacetic acid, Euphorbic acid, and perhaps with Igasuric acid. It is formed artificially from asparagin, from tartaric acid, and from succinic acid. It is not manufactured for use.

Malic acid is *identified*, more especially, by its sublimation products (*a*), the deportment of its lead precipitate when warmed and when treated with ammonia, and the formation of its calcium precipitate by alcohol, also by its reduction of dichromate with apple-odor (*d*). It is *separated* from citric, tartaric, and oxalic acids by non-precipitation in boiling calcic aqueous solutions, or by the alcohol solubility of its ammonium salt (*e*); from fruit juices by systematic treatment (*e*). *Estimated*, gravimetrically, as lead salt (*f*), or as calcium salt weighed as sulphate. Methods of preparation are indicated at *g*.

a.—Malic acid crystallizes with some difficulty, and from syrupy solution, in tufted needles or in four or six sided prisms, anhydrous, and deliquescent in the air.—*Heated* in a small retort over an oil-bath or sand-bath to 175° or 180° C., malic acid evolves vapors of maleic and fumaric acids, which crystallize in the retort and receiver. The fumaric acid forms slowly at 150° C., and mostly crystallizes in the retort in broad, colorless rhombic or hexagonal prisms, which vaporize without melting at about 200° C., to condense in needles, and are soluble in 250 parts of water, easily soluble in alcohol or ether. If the temperature is suddenly raised to 200° C. the maleic acid is the chief product. Maleic acid crystallizes in oblique, rhomboidal prisms, which melt at 130° C. and vaporize at about 160° C., condensing in hard needles, and are readily soluble in water, alcohol, and ether. The test for malic acid, by heating to 175° or 180° C., may be made in a test-tube, with a sand-bath, the sublimate of fumaric and maleic acids condensing in the upper part of the tube. Malic acid melts below 100° C., and does not lose weight at 120° C.; at

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[1] For list of plants containing malic acid see Gmelin-Kraut's "Handbuch," v. 336, Supplem. 884.

the temperature of the test water-vapor is separated—maleic and fumaric acids both having the ultimate composition of malic anhydride ($C_4H_4O_4$).—Solution of malic acid quickly moulds, with various products. Fermented with yeast or cheese, in presence of calcium carbonate, succinic acid is formed, with acids of the formic series.

b, *c*.—Malic acid is freely *soluble* in water, alcohol, and ether; the malates soluble or sparingly soluble in water, mostly insoluble in alcohol; ammonium malate soluble in alcohol.—Malic acid is dibasic, and forms normal and acid salts. Like tartaric and citric acids, it prevents the precipitation of metals by alkalies.

d.—Solution of **acetate of lead** precipitates malic acid, more perfectly after neutralizing with ammonia, as a white and frequently crystalline precipitate, which upon a little boiling melts to a transparent, waxy semi-liquid (a characteristic reaction, obscured by presence of other salts). The precipitate is very sparingly soluble in cold water, somewhat soluble in hot water (distinction from Citrate, Tartrate, and Oxalate), crystallizing out when cold; soluble in strong ammonia, but not readily dissolved in slight excess of ammonia (distinction from citrate and tartrate); slightly soluble in acetic acid and in malic acid. If the precipitate of malate of lead is treated with excess of **ammonia,** dried on the water-bath, triturated and moistened with alcoholic ammonia, and then treated with **absolute alcohol,** only the malate of ammonium dissolves (distinction from Tartaric, Citric, Oxalic, and many other organic acids, the normal ammonium salts of which are insoluble in absolute alcohol). Also, malic acid may be separated from tartaric, oxalic, and citric acids, in solution, by adding ammonia in slight excess, and then 8 or 9 volumes of alcohol, which leaves only the malate of ammonium in solution.

Solution of **chloride of calcium** does not precipitate malic acid or malates in the cold (distinction from Oxalic and Tartaric acids); only in neutral and very concentrated solutions is a precipitate formed on boiling (while calcic citrate is precipitated in neutral boiling solutions, if not very dilute). The addition of **alcohol,** after chloride of calcium and boiling, in neutral solution, produces a white, bulky precipitate of calcic malate in even dilute neutral solutions (indicative in absence of sulphuric and other acids whose calcium salts are less soluble in alcohol than in water). The precipitate dissolves in water, and is reproduced by alcohol.

Solution of **mercurous nitrate** gives a white, flocculent precipitate, slightly soluble in water (formed in solutions not very dilute), not soluble in malic acid, but dissolving in dilute acetic acid, in sodium malate solution, and in excess of the precipitant.

Silver malate precipitate darkens but slightly on boiling.—Permanganate of potassium is reduced but very slowly (distinction from Tartaric acid); somewhat more on addition of sulphuric acid.—Nitric acid, on boiling, is readily deoxidized by malic acid, brown vapor appearing.—**Dichromate of potassium** solution is reduced, even in the cold. By addition of dilute sulphuric acid, and warming, apple odor is developed, according to PAPASOGLI and POLI,[1] who distinguish between malic, citric, and succinic acids, with use of this reaction, as follows: The acid, if necessary, may be first precipitated with calcium chloride and alcohol; the precipitate, freed from alcohol, treated with dilute sulphuric acid and the calcium sulphate precipitate filtered out. The filtrate, containing sulphuric acid, is boiled with a little dichromate. If (1) the liquid remains perfectly yellow, succinic acid may be present; (2) the color becomes yellowish-green, citric acid may be present, as well as succinic; (3) if a green color appears, with odor of ripe or over-ripe apples, malic acid is indicated. [A green color without apple odor would result from Tartaric acid and from numerous reducing agents which might be precipitated by calcium chloride with alcohol.]—In the various oxidations of malic acid above mentioned, its products are formic acid, carbon dioxide and water, and, from nitric acid especially, oxalic acid. Dichromate in the cold concentrated solution produces some Malonic acid (Dessaignes, 1858), $C_3H_4O_4$, crystallizable, soluble in alcohol and ether.—Malic acid is capable of reduction to succinic acid, by hydriodic acid, at 130° C., and by other agents.

e.—Malic acid can be *separated* from Citric, Tartaric, and Oxalic acids by the solubility of its ammonium salt in alcohol, as follows:[2] Ammonia is added to neutral reaction, the solution well concentrated, and again neutralized, treated with 7 or 8 volumes of 98% alcohol, and set aside 12 to 24 hours, when it may be filtered, and the filtrate treated with lead acetate, for malate. The residue may contain ammonium citrate, tartrate, oxalate.

The separation of the same four acids may be done, through

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[1] 1877: *Gazzetta chim. ital.*, 7, 294; *Jour. Chem. Soc.*, 32, 807; *Jahr. Phar.*, 1878, 128.

[2] BARFOED, 1868: *Zeitsch. anal. Chemie*, 7, 408. In a full report upon the separations of malic acid, *loc. cit.*, p. 403.

the calcium precipitates, with approximate closeness, by the following method :[1]

Solution of Oxalic, Tartaric, Citric, and Malic acids.

(If sulphates are present, remove by just enough barium chloride with hydrochloric acid.) Add ammonium hydrate to a slight alkaline reaction; add ammonium chloride solution; then enough calcium chloride solution, and let stand from ten to twenty minutes. Filter.

Precipitate (*a*): Oxalate (complete), Tartrate (nearly complete).

(If Phosphates are present, separate from oxalate by acetic acid, and identify by molybdate.)

Filtrate (*b*): Citrate, Malate.

Wash Precipitate (*a*), digest it in the cold with sodium hydrate solution (or potassium hydrate solution), then dilute a little and filter.

Residue (*c*): Oxalate. Nearly insoluble in acetic acid.

Solution (*d*): Tartrate. Boil some time. A precipitate indicates tartrate. Test by reducing power, with dichromate, silver salt, or permanganate, and by Fenton's color test.

To Filtrate (*b*)—which must have excess of calcium chloride—add 3 times its measure of alcohol. If a precipitate occurs, filter.

Precipitate (*e*): Citrate, Malate (nearly complete).

Filtrate (*f*): (May contain benzoic, acetic, formic acids, etc.)

Wash Precipitate (*e*) with alcohol; dissolve on the filter with dilute hydrochloric acid. To the filtrate add ammonium hydrate to slight alkaline reaction, and boil for some time. If a precipitate occurs filter, hot (Filtrate *h*).

Precipitate (*g*): Citrate. Confirm by dissolving again with hydrochloric acid, neutralizing with ammonia, and boiling, to obtain a precipitate. Other tests may be applied.

Filtrate (*h*): Malate. (May contain succinate.) Try for malic acid by precipitating with strong alcohol. Test a precipitate, so obtained, by reduction of dichromate, by lead precipitate, and other tests. To separate from succinic add strong nitric acid and evaporate to dryness, when there will be oxalic acid instead of malic, the succinic acid unchanged. Test for oxalic by calcium salt.

Malic acid may be separated from Tannic acid by digesting the solution a half-hour with well-washed rasped hide, and filtering out the tannate. The filtrate may be concentrated and treat-

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[1] Except final tests, arranged from Fresenius' "Qualitative Analysis," S. W. Johnson's edition of 1875, p. 304.

ed with lead acetate, to be tested for malic acid. Or both acids may be precipitated by chloride of calcium, with a slight excess of ammonia and alcohol, and the malate then washed out of the precipitate with water.[1] Also, tannic and gallic acid may be removed by acetic ether.

For determining the presence of malic acid in Fruit Juices, the expressed juice or water extract is first precipitated by lead acetate solution, when the washed precipitate may be treated as directed under *d*, p. 334.

f.—The *estimation* of malic acid is usually done gravimetrically, as a lead salt. The alcoholic solution of malate of ammonium may be precipitated with acetate of lead, washed with alcohol, dried on the water-bath, and weighed as malate of lead. $PbC_4H_4O_5 : H_2C_4H_4O_5 :: 1 : 0.3953$. The crystals of this salt contain three molecules of water of crystallization.—The calcium normal malate precipitate, in strong alcohol, may be washed with alcohol, converted into sulphate, this washed with alcohol, dried, ignited, and weighed. $CaSO_4 : H_2C_4H_4O_5$.

g.—In the preparation of malic acid on the small scale, the lead precipitate may be decomposed by boiling with excess of very dilute sulphuric acid; filtering, neutralizing one-half the filtrate with ammonia, and mixing this with the other half of the filtrate, then evaporating to crystallize, as ammonium acid malate, $NH_4HC_4H_4O_5$, in large orthorhombic prisms.[2]

MARGARIC ACID. See Fats and Oils, p. 244.

MECONIC ACID.—$H_3C_7HO_7 = 200$. Oxychelidonic acid.—Found only in opium, which yields 3 to 4% of it. Not manufactured for use.—*Identified* by its physical properties, its products when heated, its precipitation by hydrochloric acid, and reactions with iron and other metals. It is *separated from opium* through formation of the calcium salt or lead salt.

Meconic acid crystallizes in white, shining scales or small rhombic prisms, containing three molecules of crystallization water, fully given off at 100° C. At 120° C. (248° F.) dry meconic acid is resolved into *comenic acid;* at above 200° C.

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[1] Further for these separations, and for separation from Gallic, Benzoic, and other acids, see Barfoed where last cited. Separation from Gallic acid is directed by adding calcium chloride to the slightly alkaline solution, and leaving some time, without heat, for precipitation of calcium gallate.

[2] For methods of preparation on larger scale, with first precipitation as lead salt, see "Watts's Dictionary," iii. 789; with first precipitation as calcium salt, Husemann's "Pflanzenstoffe," 537.

the comenic acid is resolved into pyrocomenic acid and other products. The sublimate of comenic acid dissolves sparingly in hot water, not at all in absolute alcohol. It crystallizes in prisms, plates, or granules. Solution of comenic acid gives a red color with ferric chloride, green pyramidal crystals with cupric sulphate in concentrated solution, and a yellowish white granular precipitate with acetate of lead. Meconic acid is soluble in 115 parts of water at ordinary temperatures, less soluble in water acidulated with hydrochloric acid, much more soluble in hot water, freely soluble in alcohol, slightly soluble in ether. It has an acid and astringent taste and a marked acid reaction. Its salts, having two atoms of its hydrogen displaced by bases, are neutral to test-paper. Except those of the alkali metals, the dimetallic and trimetallic meconates are mostly insoluble in water. Meconates are nearly all insoluble in alcohol. They are but slightly or not at all decomposed by acetic acid.

Solutions of meconates are precipitated by **hydrochloric acid,** as explained above.

Solution of meconic acid is colored red by solution of **ferric chloride.** One ten-thousandth of a grain of the acid in one grain of water with a drop of the reagent acquires a distinct purplish-red color (Wormley). The color is not readily discharged by addition of dilute hydrochloric acid (distinction from Acetic acid), or by solution of mercuric chloride (distinction from sulphocyanic acid).—Solution of **acetate of lead** precipitates meconic acid or meconates as the yellowish-white meconate of lead, $Pb_3(C_7HO_7)_2$, insoluble in water or acetic acid.—Excess of **baryta** water precipitates a yellow trimetallic meconate.—Solution of **nitrate of silver** in excess precipitates free meconic acid on boiling, and precipitates meconates directly, as yellow trimetallic meconate; if free meconic acid is in excess, the precipitate is first the white dimetallic meconate; both meconates being soluble in ammonia and insoluble in acetic acid.—Solution of **chloride of calcium** precipitates from solutions of meconic acid, and even from neutral meconates, chiefly the white monometallic meconate, $CaH_4(C_7HO_7)_2.2H_2O$, sparingly soluble in cold water. In the presence of free ammonia, the less soluble, yellow, dimetallic salt, $CaHC_7HO_7.H_2O$, is formed. Both precipitates are soluble in about 20 parts of water acidulated with hydrochloric acid.

The *separation of meconic acid from opium* is effected with least loss by precipitating the infusion with acetate of **lead** (leaving the alkaloids as acetates with some excess of lead in the filtrate). The precipitate is decomposed, in water, with hydrosulphuric acid gas, and the filtrate therefrom is concentrated (and acidulated with hydrochloric acid) to crystallize the meconic acid. The crystals are purified by dissolving in hot water and crystallizing in the cold after acidulation with hydrochloric acid.

The **calcium** meconate, precipitated in concentrated solution by Gregory's process for preparation of morphia, as by the Br. Pharmacopœial preparation of morphiæ hydrochloras, is washed with cold water and pressed. One part of the precipitate is dissolved by digestion in 20 parts of nearly boiling water with 3 parts of commercial hydrochloric acid, and set aside to crystallize the acid meconate of calcium. The crystals are purified from color and freed from calcium by repeated solution in the same solvent, used just below 100° C., and each time in a slightly diminished quantity. The acid may be further decolorized by neutralizing with potassic carbonate, dissolving in the least sufficient quantity of hot water, draining the magma of salt when cold, dissolving again in hot water, and adding hydrochloric acid to crystallize.

MIDRIATIC ALKALOIDS OF THE SOLANACEÆ.[1]—*The Natural Tropeines.* The researches of LADENBURG and others (1879–1884) place the group of alkaloids distinguished by active dilatation of the pupil of the eye as isomers of *the common formula*, $C_{17}H_{23}NO_3$. These isomers are compounds of isomeric tropines, $C_8H_{15}NO$, each in combination with the same tropic acid, $C_9H_{10}O_3$ (KRAUT, 1863). The union of the basal tropines with tropic acid is shown as follows:

$$C_8H_{15}NO + C_9H_{10}O_3 = C_{17}H_{23}NO_3 + H_2O.$$

This synthesis of atropine is realized experimentally. The alkaloids themselves are termed *tropeines.* The separation of tropic acid is of the nature of a saponification, being most easily effected by alkalies, as given in full under Atropine, *d.* The natural midriatic alkaloids having the common formula have been named, partly from their sources in plants, as Atropine, Daturine, Hyoscyamine, Hyoscine, Duboisine, and, probably as $C_{17}H_{23}NO_4$, Belladonnine. Ladenburg reduces these alkaloids in identity to the three isomers, *Atropine*, *Hyoscyamine*, and *Hyoscine* (beside belladonnine). The alkaloids of the midriatic group, like the Aconite group of alkaloids and like Cocaine, are to be treated with a clear understanding of the fundamental fact common to these groups, that *they are saponifiable bodies*—a fact that sheds most welcome light upon the long-standing difficulty of preserving these alkaloids intact during operations for their

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[1] Some authorities classify the midriatic plants under the order of Scrophulariaceæ.

separation.[1] The tropeine alkaloids, including artificial tropines like *Homatropine*, have strongly marked chemical characteristics—including a quite direct relationship to benzene, as shown by "the odor test"; and an exceptionally strong alkalinity, as shown by phenol-phthalein.

The sources of the three natural tropeine isomers already known are as follows:

Medicinal drug, and commercial alkaloid.	*Plant.*	*True alkaloids* (LADENBURG).
Belladonna, root, leaf. "Atropine." "Heavy atropine" of Merck. "Heavy daturine."	Atropa Belladonna.	Atropine (larger part). Hyoscyamine. In root, belladonnine. Total, 0.3 to 0.5 per cent. Root $\frac{1}{3}$ more than leaves.
Hyoscyamus, leaf, seed. "Hyoscyamine." "Light atropine" of Merck.	Hyoscyamus niger. H. albus.	Hyoscyamine. Hyoscine. Total, 0.1 to 0.5%
Strammonium, leaf, seed. "Daturine." "Light daturine."	Datura Strammonium.	Hyoscyamine. Atropine (a little). Total, 0.2 to 0.3%
Duboisia. "Duboisine."	Duboisia mioporoides.	Hyoscyamine.

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[1] KRAUT, 1863–65: *Ann. Chem. Phar.*, **128**, 280; **133**, 87; *Watts's Dict.*, **5**, 895. LADENBURG, in part with MEYER, SMITH, and others, 1879 to 1884. A summary to 1883 in *Liebig's Annalen*, **217**, 74; *Jour. Chem. Soc.*, 1883, Abs., 670; *Proc. Am. Pharm.*, **32**, 316; *Am. Jour. Phar.*, **55**, 463. *Jour. Chem. Soc.*, 1884, Abs., 761.

Tropine, the common base of the Atropine group of alkaloids, is a derivative of pyridine. Pyridine, C_5H_5N, is the primary member of the pyridine series, $C_nH_{2n-5}N$, and the type of the quinoline series, $C_nH_{2n-11}N$. Both series have great interest in the chemistry of natural alkaloids, many of which are found to be clearly placed in the aromatic group. There is a great deal of evidence now making it probable that alkaloids generally are hydrogenized derivatives of pyridine. See under *Cinchona Alkaloids, Constitution of,* and *Quinoline.* (LADENBURG, 1884, 1885; A. W. HOFMANN, 1884, 1885; HANTZSCH, 1884; KÖNIGS, 1884. *Review* in *Am. Chem. Jour.*, 1882-85: **4**, 64, 157; **5**, 60, 72; **7**, 200.

Ladenburg places the rational formula of tropine, as $C_5H_7(C_2H_4.OH)N(CH_3) = C_8H_{15}NO$. That is, in a *tetra*hydro-pyridine (C_5H_9N), ethylene-hydroxyl ($C_2H_4.OH$) and methyl (CH_3) take the place of H_2. And then atropine, or tropate of tropine, stands as $C_5H_7(C_2H_4.O[C_9H_9O_2])N(CH_3) = C_{17}H_{23}NO_3$.

The comparison with *Aconite Alkaloids* and *Cocaine*, mentioned in the text, is extended by the fact that they all yield either benzoic acid or a derivative of benzoic acid, by saponification—the tropic acid from atropine saponification easily changing, through atropic acid, to benzoic acid.

In belladonna root an alkaloid other than the "atropine" of commerce was found by Hübschmann in 1858, and named *Belladonnine.* Ladenburg (1884) finds belladonnine to be, probably, the tropate of oxytropine, $C_{17}H_{23}NO_4$, an oxy-atropine. Poehl (1876) found the "daturine" of strammonium to be optically levo-rotatory, while the "atropine" of belladonna was inactive, and several observers have stated that the "daturine" is the stronger of the two in physiological effect. Hager's Commentar (1883) asserts that the former reputation of "English atropine" for superiority arose from its having been made from strammonium, "daturine" being more powerful than "atropine." It will be observed that Ladenburg places the difference between "atropine" and "daturine" chiefly in the larger proportion of pure atropine in the former, and of pure hyoscyamine in the latter. Also the medicinal "hyoscyamine," the total alkaloid of the hyoscyamus, is generally reported to have more intense physiological action than the "atropine" taken as total alkaloid of belladonna (Duquesnel, 1882). Undoubtedly these differences in effect are covered by greater differences of strength, due to incomplete separation from impurities not alkaloids.

The Duboisia Hopwoodii, dried leaves and twigs of which constitute the Australian drug "Piturie," yields an alkaloid quite different from duboisine of D. mioporoides, a liquid, volatile alkaloid, not containing oxygen, resembling nicotine, not midriatic, and named *Piturine* (Liversidge, 1881). (See under Piturine.)

For Atropine, with the reactions, estimation, etc., of the midriatic group of alkaloids, see p. 344; for *Hyoscine*, p. 342; *Hyoscyamine*, p. 342; *Homatropine* (one of the artificial alkaloids of the midriatic group), p. 343.

Piturine.—C_6H_8N.[1] From the Duboisia Hopwoodii of Australia. The dried leaves and twigs of this plant constitute the drug *piturie*, used by the natives, with effects chiefly the same as those of tobacco. The yield of alkaloid is stated to be one per cent. of the dried drug. Piturine is a liquid, volatile alkaloid, of oily consistence, slightly heavier than water. It has an acrid, burning taste, a tobacco-like odor, and gives the physiological effects of tobacco. Its reaction is strongly alkaline, and it neutralizes acids. It is soluble "in all proportions" of water, alcohol, and ether. It gives precipitates with the general reagents

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[1] Liversidge, 1881: *Phar. Jour. Trans.* [3] 11, 815; *Am. Jour. Phar.*, 53, 352. The literature of this alkaloid is chiefly dependent upon the report of this author.

for alkaloids, and differs from nicotine in its reactions with mercuric chloride, gold chloride, platinic chloride, and in Palm's test for nicotine with hydrochloric and nitric acids.

HYOSCYAMINE.—$C_{17}H_{23}NO_3 = 289$. An isomer of Atropine (LADENBURG), which it closely resembles (see p. 344). For sources and relations see p. 340. It will be observed that the distinct alkaloid hyoscyamine forms a small part of manufactured medicinal "atropine," a large part of "daturine," an especially large part of "light daturine," the whole alkaloid of "duboisine," and one of the two alkaloids of the "hyoscyamine" of the market (the mixed alkaloids of Hyoscyamus niger), the other alkaloid of this drug being Hyoscine. The article sold as "crystallized hyoscyamine" is stated to consist mainly of true hyoscyamine, while "amorphous hyoscyamine" consists chiefly of the alkaloid hyoscine. "Hyoscyamine" is presented in the Ph. Fran. as free alkaloid, in crystalline form, with the "observation" that the article of commerce is commonly amorphous. There appears to be some indirect evidence that hyoscyamine (true) is a more potent midriatic than atropine (see Atropine, *b*), but the greater activity of "hyoscyamine," as total alkaloids of Hyoscyamus niger, is mainly due to the hyoscine, which is a more active midriatic than either atropine or hyoscyamine.

Hyoscyamine crystallizes in slender, colorless needles, which sometimes radiate in groups. It melts at 108° C. (226.4° F.) Its *solubilities* are nearly the same as those stated under Atropine, *c*. It responds to the distinctive tests given under Atropine, *d*, with the differences there stated for the reactions with **gold chloride,** platinum chloride, mercuric chloride, and picric acid. In treatment for tropine, with alkalies, a tropine isomeric with that of atropine, and a tropic acid identical with that of atropine, are obtained.

Hyoscyamine is well *separated* from atropine, and less easily from hyoscine, by the precipitation with **gold chloride** (see under Hyoscine). The *separation from hyoscyamus* leaf and seed, and methods of *quantitative* estimation, are given under Atropine, *e* and *f*.

HYOSCINE.—$C_{17}H_{23}NO_3 = 289$. Tropate of pseudotropine. An isomer of Atropine (LADENBURG), one of the two alkaloids obtained from Hyoscyamus niger, leaf and seed, p. 340. It has been stated that the so-called "amorphous hyoscyamine" of the market has consisted mainly of hyoscine. Hyoscine hydrobromide, and other salts, presented as such, in crystalline form, are offered for sale for medicinal uses. An ordinary dose by the mouth is $\frac{1}{85}$ grain, a full dose ^{1} grain; it is a calmative, with effects distinct from those of atropine; its midriatic effects are more rapid than those of atropine;[1] obtained by a quantity smaller than required of atropine.[2]

Hyoscine, uncombined, is in syrupy or amorphous solid state, colorless, forming, with ordinary acids, solid salts. The hydrobromide crystallizes in prisms without color; the hydriodide in pale golden prisms. The hydriodide is levo-rotatory. In *solubilities* hyoscine resembles Atropine. Hyoscine responds to the *distinctive tests* given under Atropine, *d*. The hyoscine *aurochloride* is less soluble and less lustrous than the hyoscyamine aurochloride; it crystallizes in yellow prisms and melts at 198° C. (the aurochloride of atropine, lustreless, nearly insoluble precipitate, melts at 135° C.; that of hyoscyamine, lustrous golden, melts at 159° C.—LADENBURG). The *platinochloride* of hyoscine forms small octahedral crystals, soluble in water and in alcohol (of hyoscyamine, triclinic crystals; of atropine, monoclinic crystals). **Iodine** solution in potassium iodide gives a dark-colored, oily product. **Potassium ferrocyanide** gives a white, amorphous precipitate. The precipitate with **Mayer's solution** is yellowish; with **mercuric chloride,** amorphous, sometimes oily liquid.

Treated with **barium hydrate** for *tropine*, as given under Atropine, *d*, the isomer named pseudotropine is obtained. This crystallizes in rhombohedrons, melts at 106° C., and boils at 241° C. (tropine melts at 62° C.), dissolves readily in water and in chloroform, sparingly in ether. The aurochloride melts at 198° C. The tropic acid of hyoscine is identical with that of hyoscyamine and atropine.

LADENBURG *separates* hyoscine from hyoscyamine by formation of the aurochloride, which is crystallized several times for removal of the more soluble hyoscyamine salt (atropine aurochloride, if present, being removed at first as a nearly insoluble precipitate). The crystals obtained are decomposed with hydrogen sulphide, the filtrate made alkaline with potassium carbonate and shaken with chloroform, and the resulting chloroform solution evaporated to give a residue of the hyoscine.

HOMATROPINE.—$C_{16}H_{21}NO_3$. Phenyl glycollic tropeine. One of a group of artificial alkaloids called *tropeines*, and produced by

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[1] H. C. WOOD, 1885: *Therapeutic Gazette*, 9, 1, 594. 760.

[2] By one-fifth the quantity (!) EMMERT. See also HIRSCHBERG, 1881.

Ladenburg (1880) by uniting tropine, the common base of natural atropine and hyoscyamine, with various acidulous and other radicals, p. 339. Homatropine is formed by the union of tropine, $C_8H_{15}NO$, with mandalic acid, $C_8H_8O_3$, a molecule of water being separated. Mandalic acid is formed from amygdalin by digestion with hydrochloric acid, and in other ways, and has the structure $C_6H_5.CHOH.CO_2H$, phenyl-glycollic acid. When mandalate of tropine is digested with hydrochloric acid, the elements of water are withdrawn and homatropine is produced. $C_8H_{15}NO.C_8H_8O_3 = C_{16}H_{21}NO_3 + H_2O$. Since about 1882 homatropine hydrobromide has been used medicinally. It is an active midriatic; its effects do not continue as long as those of atropine, and in the same doses it is less poisonous.

Homatropine is crystallizable in prisms from a solution in absolute ether; has a melting point of about 98° C.; is hygroscopic and very deliquescent; and it is ordinarily obtained only in the state of a thick liquid. It dissolves some in water, but is not freely soluble in water. It is freely soluble in ether and in chloroform. The hydrobromide, $C_{16}H_{21}NO_3.HBr$, crystallizes in flat, rhombic prisms forming wart-like aggregations, permanent in the air.[1] It is soluble in ten parts of water, the solution not readily suffering change. The hydrochloride is very soluble in water, and is crystallizable. The sulphate crystallizes in silky needles.

With solutions of homatropine salts **potassium mercuric iodide** gives a white, curdy precipitate; **gold chloride,** a precipitate, $C_{16}H_{21}NO_3.HCl.AuCl_3$, at first of oily consistence, soon crystallizing in prismatic forms; **picric acid**, a precipitate soon becoming crystalline. Platinic chloride gives a precipitate only in concentrated solutions, but fine crystals of the double salt are formed (with the hydrochloride).

Atropine.—$C_{17}H_{23}NO_3 = 289$. Tropate of tropine, and probably $C_5H_7(C_2H_4O.CO.CHC_6H_5.CH_2.OH)NCH_3$ (Ladenburg). For sources and chemical structure see p. 339. Forms the larger part of pharmacopœial "atropine"; a smaller portion of the "daturine" or "atropine" obtained from strammonium; and an isomer of the alkaloids hyoscyamine and hyoscine.

Atropine and its isomers (hyoscyamine, hyoscine) are *identified* as midriatics by the organoleptic test (*b*, *d*); as tropine tropates by Vitali's test, the crystallizable bromine precipitate, the phenol-

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[1] F. B. Power, 1882: a summary upon homatropine, *Am. Jour. Phar.*, 54, 145.

phthalein reaction, the test with mercuric chloride, and (if in sufficient quantity) by the odor-tests (*d*). Atropine and its *isomers are distinguished from each other* by the precipitation with gold chloride, and by differences in reactions with mercuric chloride, platinum chloride, and picric acid, that with gold chloride being serviceable for *separation.* Hyoscyamine from atropine by their melting points. Atropine and its isomers are *separated* from crude drugs, extracts, plasters, animal tissues, the urine, etc., by general and special methods given under *e;* and are *estimated in quantity*, by gravimetric, volumetric, or physiological method, as laid down under *f.* Tests for *impurities, g.*

a.—Colorless or white, lustrous acicular crystals, or a crystalline or nearly amorphous powder. In commerce sometimes yellowish. By exposure to air it acquires at length a yellowish or even violet tint. *Melts* at 114° C. (237.2° F.) (LADENBURG, 1881) (U. S. Ph.) At 115°–115.5° C. (239°–240° F.) (E. SCHMIDT, 1880). The medicinal atropine heated alone on a bath of glycerine begins to melt at about 104° C. and is entirely melted at 113° C. (SQUIBB, 1885). The artificial alkaloid melts at 113.5° C. (LADENBURG, 1883). At 123° C. gives a faint mist of microscopic sublimate, not crystalline (BLYTH). Vaporizes at about 140° C., giving white fumes and an oily sublimate.[1] Vaporizes slightly with boiling water, and even with boiling alcohol (DRAGENDORFF). When dry does not lose weight at 100° C. (DUNSTAN and RANSOM, 1886). Upon ignition it is easily dissipated, without residue.

b.—Without odor, it has a disagreeably bitter and acrid taste. The largest medicinal dose is about $\frac{1}{75}$ grain (Ph. Germ.), and it is an active deliriant poison.—Solutions for application to the eye should never exceed the strength of one per cent., and for the test of midriasis should be far more dilute than this. The cat is a favorable subject for the test. A solution in 130000 parts of water, applied to one eye of a cat, suffices for dilatation (DRAGENDORFF). With frogs a solution of 1 to 250 obtains dilatation, commencing in about five minutes (v. GRAEFE). Dr. E. R. SQUIBB (1885[2]) reports the following results upon the human eye, on applying to one eye of each person one drop of a solu-

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[1] As to the form of the crystals, formed under the microscope, see HELWIG, 1864; A. PERCY SMITH, 1886.

[2] *Ephemeris*, 2, 855. See also "Blyth on Poisons," 1885, New York, p. 339.

tion of atropine sulphate diluted nearly in the proportions here stated:

Dilution.	*Individuals under trial.*	*Commencing dilatation.*
2280 parts................	Several.	15 to 18 minutes.
4560 "	Several.	30 minutes.
9120 "	Two.	About 40 minutes.
18240 "	Two.	50 and 32 minutes.
45600[1] "	Two.	45 minutes each.
91200 "	Five.	In two, no effect; in three, effect in about 1 hour.

The same persons were not used in all experiments, and eighteen persons in all were employed. The sulphate of atropine was "about the best obtainable in the market." A sample of crude atropine fresh from an assay of belladonna leaf gave earlier dilatations, and in the last trial, by dilution to 90800 parts, gave dilatation in 45 and 50 minutes. The investigator estimated that an effect in 50 minutes was obtained by action of about 0.000000427 gramme of the alkaloid.—Atropine is excreted by the urine to some extent, being found in that fluid after administration.

In frogs the constitutional effects of atropine are peculiar, including first paralysis, and, after a day or later, tetanic spasms.

c.—Atropine is soluble in 600 parts of water at 15° C. (59° F.), or in 35 parts of boiling water; soluble in glycerine, and freely soluble in alcohol, chloroform (3 parts), ether (60 parts), amyl alcohol, and benzene (42 parts), scarcely soluble in petroleum benzin or carbon disulphide. Fixed oils dissolve it. Aqueous solutions are not very stable.—It has a decided alkaline reaction, exhibited not only with litmus-paper in common with most alkaloids, but with phenol-phthalein, a difference of atropine and its isomers from other alkaloids (Flückiger, 1886). Its special alkalinity is also shown by its reaction with mercuric chloride (see *d*).—Its salts with the stronger acids are freely soluble in

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[1] Graefe gives 1 to 28000 as the dilution for moderate dilatation commencing in $\frac{3}{4}$ to 1 hour.

water or alcohol; not soluble in chloroform or ether. At 50° to 60° C. both benzene and amyl alcohol extract a little atropine from acidulous solution (DRAGENDORFF). The sulphate crystallizes anhydrous, $(C_{17}H_{23}NO_3)_2H_2SO_4$. The salicylate is of neutral reaction, not crystallizable, deliquescent, not stable in solution. Dr. SQUIBB (1885) advises the preservation of aqueous solutions of atropine sulphate by salicylic acid, a cold saturated solution of which is taken for one half of the solvent.

d.—In evidence of the presence of atropine, the physiological test for the pupil-dilating alkaloids, chiefly atropine and its isomers (p. 340), deserves to be named first. Of bodies other than the solanaceous alkaloids it is to be observed that cocaine, digitalis and its active principles, and conine dilate the pupil of the eye. Aconitine has a variable effect of dilatation. Nicotine is stated to first dilate and then contract the pupil. SELMI (1877–1879) found certain ptomaines to dilate the pupil. The visual effect of the solanaceæ seems to have been imperfectly known prior to the last quarter of the eighteenth century.[1] The limits are given under *b*. Dilatation from a solution not stronger than 1 in 500 parts causes little inconvenience to the human eye. The eye of the cat is preferable. In testing the separated product of an analysis, an aqueous solution is obtained of the free alkaloid or its salt (sulphate), neutral or only very feebly alkaline in reaction, and not strongly saline with any metallic salts, and not alcoholic. A drop or two is let fall into one of the eyes, the time noted, and from time to time the width of the one pupil is compared with that of the other.

Vitali's test is made as follows: The dry residue is treated with a little fuming nitric acid, then dried on the water-bath, and when cold touched with a drop of solution of potassium hydrate in absolute alcohol, when, in evidence of atropine (or one of its isomers), a violet color will appear, slowly changing to a dark red. Strychnine gives a red, brucine a greenish color. The violet color is distinctive for atropine among all important alkaloids, and reaches the limit of 0.000001 gram of the alkaloid (D. VITALI, 1880). ARNOLD (1882) in this test uses, instead of fuming nitric acid, first a drop of sulphuric acid rubbed, cold, to moisten the residue, and then a solid particle of sodium nitrite. With atropine the violet does not appear till the alcoholic potash is applied (strychnine, orange-red). Colors appearing before the

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[1] See an interesting historical paper by KOBERT, 1886: *Therapeutic Gazette*, 10, 445.

alcoholic potash is added (narceine, morphine, narcotine) render the test inapplicable.

Phosphomolybdate of sodium gives a yellow precipitate, visible in dilution to 4000 parts (Dragendorff), dissolving in ammonia with a blue color.—**Iodine in potassium iodide** solution, better applied to the hydrochloride solution, gives a precipitate of the color of the iodine solution, oily at first and afterward crystalline (Ladenburg), distinct in solution of 8000 parts of water and visible in solution of 50000 parts (Jörgensen), more complete than precipitation by phosphomolybdate (Dunstan and Ransom), dissolved by boiling alcohol, from which solvent it crystallizes, blue-green, as pentahydriodide. For separation of the alkaloid from this precipitate see *e.*—**Bromine** dissolved to saturation in hydrobromic acid solution gives a yellow precipitate, at first amorphous, obtained in a solution of the alkaloid in 10000 parts of water (Wormley[1]), not dissolved by acids or fixed alkalies. The amorphous precipitation is common to most alkaloids, but the precipitate of atropine and its isomers is characteristic in this (Wormley) that it soon becomes crystalline, and under a magnifying power of 75 to 125 diameters presents distinctive forms of lanceolate leaf-like crystals, which gradually group together like the petals of a flower. These crystals may be obtained from spontaneous evaporation of one grain of a solution diluted to 25000 parts. Imperfect crystallization gives only irregular needles and granules. Repeated trials are made by dissolving in a drop of water and crystallizing anew.

Phenol-phthalein as an indicator applied to the free alkaloid, as to the chloroformic or ethereal residue, gives the scarlet color in evidence of alkalinity, this reaction being, according to Prof. Flückiger,[2] common to atropine and its isomers and homatropine, and a distinction from all alkaloids in general use.

Mercuric chloride in a 5 per cent. solution in 50 per cent. alcohol, avoiding an excess, gives a red precipitate containing mercuric oxide (Gerrard, 1884; Schweissinger, 1885; Flückiger, 1886). On standing tabular crystals of atropine mercuric chloride are obtained. With hyoscyamine the precipitate appears only after warming (Schweissinger). With this reagent most alkaloids give white precipitates; morphine and codeine, yellow ones. Of course inorganic bodies of alkaline reaction must be absent, and the alkaloid must be free.—**Potassium mercuric iodide,** or Mayer's solution, gives a whitish, curdy precipitate,

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[1] "Microchemistry of Poisons," 2d ed., 1885, 641.

[2] 1886: *Phar. Jour. Trans.* [3] 15, 601; *Am. Jour. Phar.*, 58, 129.

hardly visible in solution diluted to 4000 parts (DRAGENDORFF).—**Potassium bismuthic** iodide, a precipitate visible in solution diluted to 25000 parts (THRESH, 1880). **Gold chloride,** a lustreless precipitate, discernible in solution diluted to 20000 parts, melting at 135° C. (LADENBURG), $C_{17}H_{24}NO_3.AuCl_4$. The hyoscyamine precipitate, with gold chloride, has a golden lustre and melts at 159° C. (LADENBURG). **Platinum chloride** (with hydrochloric acid) precipitates only very concentrated solutions of atropine; the crystals of chloroplatinate are monoclinic and melt at 207° C. (hyoscyamine chloroplatinate crystals are triclinic) (LADENBURG). **Picric acid** (HAGER) with the "English atropine" (p. 341) gave an amorphous turbidity, which, after heating to dissolve it, crystallizes in rectangular plates on cooling. The "German atropine," treated in the same way, gave the rectangular plates at once. **Tannic acid** precipitates neutral and concentrated solutions of atropine.—The dilute caustic **alkalies,** and sodium and potassium normal carbonates, precipitate, from concentrated solutions of atropine, a part of the alkaloid, soluble in an excess of a caustic alkali. On heating the fixed alkali solutions ammonia is finally evolved by decomposition of the atropine. Ammonium carbonate and fixed alkali bicarbonates give no precipitates. Concentrated sulphuric acid gives no color.

Atropine, in common with its isomers, is easily *saponified*, or resolved by alkalies into its TROPINE and TROPIC ACID. (See under Midriatic Alkaloids.) The aqueous solution of alkaloid is digested with **barium hydrate** at 60° to 80° C.; then carbon dioxide is passed in and the barium carbonate filtered out; the filtrate is acidified with hydrochloric acid and shaken with ether, in two portions; the separated ether is allowed to evaporate spontaneously, when tropic acid is obtained in the residue. The aqueous solution left after removing the ether is now treated with potassium hydrate solution to an alkaline reaction, and the liquid again extracted with ether, which is allowed to separate after shaking, drawn off, and evaporated in a warm place. The residue will contain the tropine. Instead of digestion with barium hydrate, digestion with hydrochloric acid may be employed. *Tropic acid* melts at 117° C. Heated with dilute solution of permanganate it gives odor of bitter-almond oil, and on further treatment benzoic acid is formed. Tropic acid is easily changed, by loss of H_2O, to atropic acid, $C_9H_8O_2$, isomeric with cinnamic acid. *Tropine* crystallizes from anhydrous ether in the rhombic system, and melts at 62° C. It is hygroscopic, in ordinary residues assumes an oily consistence, is freely soluble in water, in alcohol, and in ether, has a strong alkaline reaction, gives an odor when heated, and forms definite salts with acids. The chloroplatinate crystallizes with orange-red color, dissolves in water, not in alcohol.

The odor test, by production of benzoic or salicylic aldehyde, is made, in several ways, by concentrated sulphuric acid alone, or by this followed by dichromate or other oxidizing agent, and is directed as follows in the Ph. Germ.: "0.001 gram [at the least] of the atropine sulphate, in a small test-tube, is heated until white vapor appears, then 1.5 grams of sulphuric acid is added, and heated until it commences to brown. Now on adding 2 grams of water an agreeable odor is perceived, and by further addition of a crystal of permanganate of potassium the odor of bitter-almond oil is obtained." This reaction, by whatever reagents, is not a delicate one, and often fails, but it is characteristic in comparison of ordinary alkaloids.

e.—Separations.—Aqueous solutions of atropine, in concentration by heat and in standing, are liable to suffer very slight waste of the alkaloid by its decomposition, but this waste is less for salts with stable acids than it is for the free alkaloid, and in ordinary evaporations is prevented by adding enough dilute sulphuric acid to neutralize or barely to acidulate the liquid.—Acidulous solutions of atropine can be washed by petroleum benzin without loss of the alkaloid, and washed by chloroform or ether with only so much loss as results from the slight miscibility of the water with these solvents. Chloroform or ether, preferably the former, or, if separations require, benzene or amyl alcohol, by agitation (in repeated portions) with aqueous solutions made alkaline, will extract the alkaloid almost without waste The certainty of complete separation is assured by a negative result in testing the aqueous solution with phosphomolybdate, or iodine in potassium iodide, or a residue on evaporating a portion by Vitali's method. Also, it is important to remember that when an acidulous solution is made alkaline a salt is formed, as ammonium sulphate, and such salt will be carried into chloroform or ether or amyl alcohol, and on evaporation of the solvent a crystalline residue of the salt will be obtained. If the salt be ammonium or other alkali sulphate, the atropine is safely separated from the residue by solution in absolute alcohol. Again, water acidulated with sulphuric or hydrochloric acid, agitated with a solution of free atropine in chloroform or other above-named solvent, gradually transfers the alkaloid to the aqueous solution. The remaining chloroformic or ethereal liquid is tested, as to the progress of the separation, by subjecting a residue from a small portion to Vitali's test. An aqueous solution so obtained may be precipitated by iodine in potassium iodide solution for estimation of the alkaloid, as directed on p. 354.

In separating the aqueous layer from an under-layer of chloroform, or from an over-layer of ether or benzene, a "separator" made for the purpose is, on some accounts, the most convenient vessel, but the use of a large, strong test-tube, or test-glass on foot, with the wash-bottle fittings for siphon-decantation, is very satisfactory. These forms of apparatus are figured and described under Alkaloids, pp. 35, 36.

For separations from belladonna root and leaves DUNSTAN and RANSOM (1884, 1885)[1] direct as follows: "Twenty grams of the dry and finely powdered *root* are exhausted by hot percolation with a mixture of equal parts by volume of chloroform and absolute alcohol; and if an extraction apparatus is used about 60 c.c. of the mixture is required. The percolate is agitated with two successive 25 c.c. of distilled water [acidulation having been found unnecessary], which [the watery layers] are separated in the usual way. These are mixed and well agitated with chloroform to remove the last traces of mechanically adherent coloring matter. The chloroform is separated, the aqueous liquid rendered alkaline with ammonia and agitated with two successive 25 c.c. of chloroform, which are separated, mixed and agitated with a small quantity of water (rendered faintly alkaline with ammonia) to remove adherent aqueous liquid. The chloroform is then evaporated and the residue dried over a water-bath until the weight is constant, which usually occupies a little less than an hour." The alkaloid is obtained in white, silky crystals, for weight, and by trial found pure alkaloid. For *the leaves* "20 grams, dried and finely powdered, are well packed in an extraction apparatus, and exhausted with about 100 c.c. of absolute alcohol. The alcoholic liquid is diluted with about an equal volume of water made slightly acid with hydrochloric acid. The chlorophyl, fat, etc., are then removed from the slightly warmed liquid by repeatedly extracting it with chloroform until nothing further is removed by the solvent. The aqueous liquid is made alkaline with ammonia, and the alkaloids extracted by chloroform, by evaporating which a residue of pure alkaloid is obtained, and dried by heating it at 100° C. until a constant weight is attained."

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[1] From the Root: *Phar. Jour. Trans.* [3] 14, 623; *Am. Jour. Phar.*, 56, 279. From the Leaves and the Extract: *Phar. Jour. Trans.* [3] 16, 237, 238; *Am. Jour. Phar.*, 57, 582, 584. Additional report, and discussion by Messrs. GERRARD, REDWOOD, and others, *Phar. Jour. Trans.*, 1886 [3] 16, 777, 786.

Dr. E. R. Squibb[1] exhausts finely powdered root or leaves of belladonna with alcohol slightly acidulated with sulphuric acid, as follows: 50 grams powdered leaves are moistened with 32 grams alcohol of sp. gr. 0.820 to which about three drops (0.1 gram) of sulphuric acid have been added. Pack in a cylindrical percolator and exhaust, most readily by a water-pump, with alcohol not acidulated, of which about 300 c.c. will be required. Of the powdered root 50 grams are moistened with 15 to 20 grams of strong alcohol acidulated with three drops of sulphuric acid, and packed rather lightly unless an efficient pump can be used in the percolation. The percolate is evaporated in a shallow dish over the water-bath until alcohol ceases to be perceptible in the vapor; the liquid is diluted while warm with 25 c.c. of water to which one or two drops of sulphuric acid have been added; the mixture stirred well and transferred to a separator, rinsing the dish with one or two c.c. of water. Wash the dish with two or three portions of chloroform, about 30 c.c. in all, stirring to take up the residue, transfer the whole to the separator, acidulate with about three drops more of sulphuric acid, and agitate the whole by active shaking for about five minutes, "not so very vigorous as to emulsify the liquids" to an extent preventing separation afterward. Emulsion occurs in the assay of the leaves, not in that of the root. "If, after standing at rest for an hour, the separation shall not have begun, add three drops more of acid, again agitate for a minute or two, and again set at rest for an hour. If the emulsion still does not begin to separate, add 10 c.c. more of water and of chloroform, again agitate and set at rest." "The stronger the alcohol used the less of this emulsifying matter is carried into the extract. An alcohol of sp. gr. 0.814 used for exhaustion of the powder never gave any trouble from emulsifying." After the chloroform layer (dark colored) is obtained and drawn off, the aqueous liquid is washed with fresh portions of chloroform, of 10 c.c. each, until the chloroformic layer is obtained nearly colorless. The total chloroformic washings are now agitated with 15 c.c. of water acidulated with a drop of sulphuric acid, and after separation by rest the aqueous layer is taken off and added to the main watery solution of alkaloidal sulphate. This is now agitated, in the separator, with 20 c.c. of fresh chloroform and as much as 6 grams of crystallized sodium carbonate, the last added in small portions to avoid frothing over, until a decided alkaline reaction is obtained. After agitation and rest the chloroformic layer is drawn off into

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[1] *Ephemeris*, 2, 849, Sept., 1885.

a tared beaker. A second treatment with 10 c.c. more of chloroform is made, this chloroform being added to the first, and the tared beaker is set in a warm place for the spontaneous evaporation of the chloroform. The beaker is then turned on its side in a warm place, and the residue, sometimes crystalline, sometimes varnish-like, is dried, to weigh as atropine.

For Hyoscyamus leaves either method above given for belladonna leaves may be employed. *Hyoscyamus seeds* are first freed from fats by exhausting the powder with petroleum benzin (DRAGENDORFF).[1] Prollius's fluid, a mixture of 88 parts of ether, 4 of ammonia-water, and 8 of alcohol, may be used to exhaust the drug in separation of atropine and its isomers. Dragendorff (1876–1877) objects to the use of chloroform upon the acidulous solution of hyoscyamus to remove impurities, on the ground that this solvent takes some alkaloid from acidified liquids. He recommends, instead of chloroform, benzin, benzene, or amyl alcohol upon the acid solution, and uses chloroform (or benzene), after making alkaline, to take up the alkaloids.

DUNSTAN and RANSOM, in the report quoted on p. 351, give a separation of the alkaloid *from alcoholic extract of belladonna leaves* as follows: "1 to 2 grams of the extract are warmed with dilute hydrochloric acid until as much as possible is dissolved. The mixture is filtered, preferably through glass wool or cotton wool, and the residue washed with hot dilute hydrochloric acid until nothing further is dissolved. The acid liquid is then repeatedly agitated with chloroform, which, when evaporated and dried at 100° C., leaves a residue of pure alkaloid." (Compare SCHWEISSINGER, 1885.)

In quantitative separation of the alkaloids from belladonna plasters (the mass of which is usually insoluble in alcohol), a weighed portion of the plaster is macerated in chloroform several hours, with addition of enough ammonia to give an alkaline reaction, the plaster-cloth is macerated again, and washed, in chloroform, then dried and weighed to obtain by difference the weight of plaster-mass taken. The chloroformic liquid and washings, with all the suspended matters liberated from the plasters, are now shaken out (in a separator) with two or three successive portions of water acidulated with sulphuric acid, the mixture set at rest, and the aqueous layer drawn off. If the partly emulsified mixture resists separation after standing some hours, it may be warmed to near the boiling point of the chloroform (by immers-

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[1] Further see DUQUESNEL, 1882: *J. Pharm.* [5] 5, 131; *Jour. Chem. Soc.*, 1882, Abs. 535.

ing the separator in warm water). Also small additions of alcohol, or of fresh chloroform and of water, may be made by turning rather than by shaking the separator. And a shallow dividing layer of persistent emulsion may be managed by transferring it to a test-tube for treatment with additional chloroform and water, or with a little alcohol. The united portions of watery solution, filtered if not entirely clear, are now made distinctly alkaline by adding ammonia, and shaken out with two or three portions of chloroform, which is drawn off clear. Films of emulsion may be washed with chloroform on a filter previously wet with this solvent. The clear chloroformic solution is evaporated in a tared beaker for weight. The residue may be purified by dissolving in absolute alcohol (by which sulphates are left behind with traces of other impurities), filtering and washing with the same solvent, and evaporating the filtrate to dryness. Or the residue from evaporation of the chloroform may be purified (according to DUNSTAN and R.) by dissolving in hydrochloric acidulated water, filtering and washing, precipitating with iodine in potassium iodide, collecting the precipitate, shaking it with sodium thiosulphate solution to liberate the alkaloid, then shaking out with portions of chloroform as before. In the above process the acidulous water solution may be washed with petroleum benzin with advantage, unless the constituents in aqueous solution are such as to form a troublesome emulsion with the benzin.

In separation from animal tissues and other matters *under an analysis for poisons*,[1] the finely divided material is to be digested, with the addition (if need be) of water enough nearly to cover the solids and dilute sulphuric acid to strong acidulation, for an hour or two, at about 70° C. The mixture is now filtered by a filter-pump, or strained, and the residue digested some time with two successive smaller portions of slightly acidulated water, each portion being filtered or strained into the first filtrate, the filters being sparingly washed with slightly acidulated water. To the liquid is now added enough calcined magnesia to neutralize the excess of acid, still leaving a distinctly acid reaction, and the whole is concentrated on the water-bath to a thin syrupy consistence, stirring to promote evaporation and prevent any drying at the edges. The mixture is now drained into a flask; the dish is moistened with water and then rinsed with repeated small portions of alcohol into the flask, each alcoholic addition being mixed by gentle agitation of the flask, and alcohol further added

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[1] Further see DRAGENDORFF: "Gerichtl. Chemie." BLYTH: "Poisons," p. 346 (New York edition). WHARTON and STILLE, 4th ed., 1884 (Amory and Wood), p. 425. WORMLEY: "Poisons," 2d ed., 1885, p. 645.

to make in all about 3 or 4 volumes to 1 volume of the syrupy liquid. A few drops of dilute sulphuric acid are added, the whole is well shaken and set aside for some hours, then filtered, the filter washed with alcohol, and the filtrate evaporated in a flask to remove all the alcohol. The watery solution, if it be not thin and limpid, is diluted with only enough water to obtain this consistence. The acidulous liquid is now shaken out with one or more portions of petroleum benzin, or of benzene, or of both, repeating (if the layers separate well) as long as the solvent removes organic matters, and lastly the liquid is well shaken out with chloroform. The benzin and benzene solutions may be examined, if desired, for other substances : the chloroform solution is washed with a little water to which a drop of diluted sulphuric acid is added, and this aqueous solution is added to the liquid under analysis. This liquid is now made alkaline by adding ammonia, and shaken out with two or three portions of chloroform. The chloroformic solution is evaporated to dryness in a beaker or assay-flask. The residue is dissolved by warm absolute alcohol, in repeated small portions, the alcoholic solution filtered through a small filter into a small foot-glass graduated in c.c., the filter being washed several times with a little of the alcohol. Of the mixed filtrate $\frac{9}{10}$ by volume is evaporated to dryness in a tared beaker, for weight: the $\frac{1}{10}$ is evaporated in one or more small porcelain evaporating dishes, for Vitali's test, taking first two or three drops by a pipette to evaporate in the dish, then repeating the evaporation on the same spot until a concentrated residue is obtained. If this test does not reveal atropine, one edge of the residue in the beaker is carefully subjected to the same test, after which the remains of the test are fully wiped out with filter-paper, noting what fraction of the entire residue appears to have been removed. Whatever the result of this test upon either residue, the entire (remaining) residue in the beaker is now dissolved in a small measured volume of water. The solution is subjected to the physiological test, which may be made quantitative, and to the bromine test, and other precipitations, working with drop portions on a glass slide, over white or black ground, using a magnifier, comparing crystals under the microscope with those of a known solution of atropine.—It must be ascertained that none of the solvents gives any residue by evaporation.

From the urine atropine may be separated by acidulating with sulphuric acid, washing with chloroform, making alkaline by ammonia, shaking out with chloroform, and proceeding from this point as above directed in treatment of the alkaline aqueous liquid.

Atropine has been recovered from tissues after 2½ months' putrefaction (Dragendorff).

f.—Quantitative.—Pure atropine is dried at or below 100° C. and weighed as anhydrous alkaloid. In ordinary methods of separation the isomers hyoscyamine and hyoscine, so far as present in the material, will be included in the estimation, affording a statement of total (midriatic) alkaloid, as atropine. For certainty of the absence of non-alkaloidal matter the separation from the periodide precipitate is a resource (p. 354). The crystalline (or amorphous) residue by evaporation of a chloroformic solution prepared with the precautions already given is clean and suitable for gravimetric estimation.

In a physiological valuation, taking Dr. Squibb's results with atropine sulphate (p. 345) as a basis, 1 part of atropine sulphate in about 90000 parts of aqueous solution, or 1 part of free atropine in about 106000 parts of aqueous solution, by application of one drop of such solution to the human eye, should cause a perceptible difference of dilatation of the pupil within one hour. For convenience of making the solution, 0.010 gram of the alkaloidal material to be tested may be dissolved to make 10.6 c.c. (for free alkaloid), or 9.0 c.c. (for sulphate), and then 10 c.c. of either of these solutions is to be diluted to 1000 c.c. A single full drop is let fall from a dropping tube directly into the eye while the lids are held open and the head thrown back, this position being maintained without winking for half a minute after the drop is introduced. The trial may be repeated on the same individual and on different individuals. If dilatation be not obtained a stronger solution is to be tried, and trials repeated until the limit of strength for dilatation is obtained (p. 346).

Precipitation of atropine by Mayer's solution of potassium mercuric iodide is not very close, but has been used by Dragendorff[1] both in the gravimetric and volumetric way. In the final *volumetric* estimation the dilution is to be made such that there shall be 1 part of alkaloid in 350 to 500 parts of solution; the reagent diluted to one-half Mayer's strength; and an addition is directed of 0.00005 gram of alkaloid for each c.c. of total liquid. The reagent is to be added very slowly, so that the precipitate shall crystallize and be able to subside. In the volumetric way the end reaction is found by filtering from time to time a few drops through a very small filter, and adding to this filtrate a drop of the reagent, then returning this portion to the

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[1] "Werthbestimmung," 1874; "Plant Analysis," 1882 (London, 1884).

entire liquid, into which the little filter is rinsed with a few drops of water. Each c.c. of Mayer's (full strength) solution denotes 0.0125 gram of alkaloid as atropine (Dragendorff's experiments).[1]

In the gravimetric estimation by potassium mercuric iodide, Dragendorff directs precipitation of an acidulated solution of the alkaloid, 1 to 350 or 400, with excess of Mayer's solution. After standing 24 hours the precipitate is collected on a small filter and drained, washed with distilled water, dissolved in alcohol of 90 to 95%, and the alcoholic solution and washings are evaporated in a beaker and the residue dried at 100° C. Of the weight of the residue 44.9% is atropine. The results are not very close, and will vary with the extent of water-washing of the precipitate.

g.—Tests of purity.—Atropine and its salts, when heated over the flame, should vaporize without residue. It should not have a yellowish tint, and when treated with concentrated sulphuric acid, or with excess of ammonia, should not be colored. One drop of a solution in 1000 parts of water, on the tongue, should cause a bitter and acrid taste. One drop of a solution in 45000 parts of water, placed in the human eye, should cause dilatation in about 45 (not less than 60) minutes. Free atropine and its salts should correspond to the solubilities stated under *c.* If 0.001 be dissolved in 1 c.c. of water, and a drop of gold chloride solution be added, a lustreless golden precipitate should be obtained. Further in distinction from hyoscyamine and hyoscine, note the reactions with gold chloride, and the results by saponification, pp. 343, 349.

Prof. E. SCHMIDT (1884) proposes that there should be only two commercial names of the midriatic alkaloids, namely: atropine, with a melting point of 115° to 115.5° C. (239°–240° F.) (compare p. 345); and hyoscyamine, with a melting point of 108.5° C. (227.5° F.)

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[1] Only empirical data can be used. And whether this factor of Dragendorff be adopted, or one obtained with a solution of atropine, the concentration and other conditions must be held uniform. Before the addition of Mayer's solution ceases to increase the precipitate, a condition of equilibrium is reached, in which an addition of a solution of atropine salt also causes a precipitate. GÜNTHER (*Zeitsch. anal. Chem.*, **8**, 477) gave to 1 c.c. of Mayer's solution the value of 0.0193; and Mr. Mayer himself, on obscure theoretical grounds, put the value at 0.0145. The latter figure corresponds to the ratio of 1 atom of mercury to 1 molecule of atropine—$C_{17}H_{23}NO_3(HI)_2HgI_2$. But the *gravimetric* indications of Dragendorff, given in the next paragraph of the text, correspond to the ratio of 2 atoms of mercury to 1 molecule of atropine—$(C_{17}H_{23}NO_3HI)_2HgI_2$. Further upon this reaction see the author's contribution on "Estimation of Alkaloids by Potassium Mercuric Iodide," 1880: *Am. Chem. Jour.*, **2**, 294–304, at pp. 298-300: *Chem. News*, **45** 114–115; *Ber. d. chem. Ges.*, **14**, 1421.

MINERAL OILS, SEPARATION OF. See Fats and Oils, p. 274.

MORPHINE. See Opium Alkaloids, p. 362.

MYRISTIC ACID. See p. 245.

NARCEINE. NARCOTINE. See Opium Alkaloids.

OAK BARK TANNIN. See Tannins.

OLEIC ACID. See p. 246.

OLEOMARGARIN. See p. 292.

OLIVE OIL. See p. 285.

OPIUM ALKALOIDS.—Alkaloids in the concrete, milky exudation obtained by incising the unripe capsules of Papaver somniferum.

List of Alkaloids, with description of those of minor importance.
Chemical Constitution. Grouping by color tests.
Classification by deportment with sulphuric acid.
Morphine: Yield in opium; analytical outline; crystallization and heat reactions of the alkaloid and its salts (*a*); physiological effects (*b*); solubilities of the alkaloid and its salts (*c*); color tests and limits of each, precipitations (*d*); separations in general, from tissues in cases of poisoning, with limits of recovery and organs of deposition (*e*); estimation, gravimetric and volumetric, in opium by the several pharmacopœial and other methods, and in tincture of opium, with authorized standards (*f*); impurities by the pharmacopœial standards in different countries (*g*).
Narcotine: analytical outline, constants, and directions for analysis.
Codeine: description and analysis; tests for purity.
Apomorphine: description; tests; impurities.

(1) *Morphine*, $C_{17}H_{19}NO_3$. Sertürner, 1816. See p. 362.
(2) *Codeine*, $C_{18}H_{21}NO_3$. Robiquet, 1832. See p. 388.
(3) *Thebaine*, $C_{19}H_{21}NO_3$. Thiboumèry, 1835. Yield, 0.15–1.0%. Needles or quadratic plates. Of sharp and styptic taste, and tetanic poisonous effect, fatal in doses smaller than those of morphine. Soluble in 140 parts ether, soluble in benzene, amyl alcohol, and in chloroform, not in petroleum benzin. Of alkaline reaction, and neutralizes acids. Colored by sulphuric acid, blood-red turning yellow; according to Hesse (1872) green to brown-green; by Froehde's reagent, orange; by nitric acid, yellow. By boiling dilute acids, converted

into *Thebenine*, which is changed by concentrated acid to *Thebaicine*, both these products being isomers of thebaine, and amorphous.

(4) *Narcotine*, $C_{22}H_{23}NO_7$. Desrone, 1803. See p. 387.

(5) *Narceine*, $C_{23}H_{29}NO_9$. Pelletier, 1832. Yield, 0.02 to 0.1%. Crystallizable, in four-sided prisms or in needles. Of bitter taste, styptic after-taste, and purely hypnotic effect. Sparingly soluble in hot water or cold alcohol, soluble in hot alcohol; nearly insoluble in ether, or benzene, or petroleum benzin, or (Wormley) in chloroform; moderately soluble in amyl alcohol, not from acid solutions. It is of neutral reaction, but unites with acids, forming crystallizable salts. Colored by sulphuric acid, brown or black to yellow or red; by nitric acid, yellow; by Froehde's reagent, yellow-brown to blue.

(6) *Pseudomorphine*, $C_{17}H_{19}NO_4$. Pelletier and Thiboumèry, 1835. Yield, not over 0.02 per cent. Lustrous crystals. Tasteless, and of neutral reaction. Insoluble in water, alcohol, ether, chloroform, dilute acids, or alkali carbonates; soluble in caustic alkalies or lime solution. Colored by sulphuric acid an olive green; by nitric acid, orange-red. Forms acidulous crystallizable salts, difficultly soluble in water or alcohol. Hesse infers that this is the same as Oxymorphine, formed by action of nitrites on morphine, as stated under Morphine, *d*.

(7) *Papaverine*, $C_{21}H_{21}NO_4$. Merck, 1848. Yield, sometimes as high as 1 per cent. Crystalline, in white needles or prisms. In action resembles morphine, but is much feebler. It is slightly soluble in cold alcohol and in ether, freely in hot alcohol, moderately soluble in amyl alcohol, in benzene, and in petroleum benzin, soluble in chloroform both from alkaline and from acid solutions. Does not neutralize even acetic acid. Its salts are very difficultly soluble in water; its sulphate dissolves in sulphuric acid, but is precipitated on adding water. Colored by concentrated sulphuric acid deep blue-violet, soon fading; Froehde's reagent, violet to blue; sulphuric acid, with permanganate added, green turning to gray. Dilute solution not precipitated by phosphomolybdate.

(8) *Codamine*, $C_{20}H_{25}NO_4$. Hesse, 1872. Forms hexagonal prisms. Can be sublimed; melts at 121° C. Soluble in hot water, in alcohol, ether, chloroform, benzene. Sulphuric acid with a little ferric salt colors it green-blue, at 100° C. dark violet.

(9) *Laudanine*, $C_{20}H_{25}NO_4$. HESSE, 1870. Crystallizes in fine prisms, sparingly soluble in alcohol or ether, soluble in chloroform or benzene. Sulphuric acid containing ferric salt colors it rose-red, at 150° C. violet-red. In physiological effect, like thebaine, a tetanic poison, more active than morphine, less active than thebaine.

(10) *Laudanosine*, $C_{21}H_{27}NO_4$. HESSE, 1871. Crystallizable. A tetanic poison to animals. Soluble in ether, chloroform, benzene, and in alcohol, insoluble in water.

(11) *Meconidine*, $C_{21}H_{23}NO_4$. HESSE, 1870. Amorphous. Fusible at 58° C., instable. Soluble in alcohol, ether, chloroform, benzene. Colored red and decomposed by mineral acids. Alkaline in reaction.

(12) *Lanthopine*, $C_{23}H_{25}NO_4$. HESSE, 1870. Minutely crystalline. Slightly soluble in alcohol, ether, or benzene, freely soluble in chloroform. Does not neutralize acids. Sulphuric acid with ferric salt does not color it.

(13) *Protopine*. $C_{20}H_{19}NO_5$. HESSE, 1871. Crystallizable. Insoluble in water, freely soluble in ether, sparingly soluble in alcohol, chloroform, or benzene. Colored dark violet by sulphuric acid with ferric salt.

(14) *Cryptopine*, $C_{21}H_{23}NO_5$. T. and H. SMITH, 1864. Yield very minute. Hexagonal crystals. A bitter taste and pungent, cooling after-taste. Hypnotic and midriatic. Insoluble in water, ether, or benzene; soluble in hot alcohol or chloroform. A strong base. Colored by sulphuric acid, blue; on adding potassium nitrate, green.

(15) *Gnoscopine*, $C_{34}H_{36}N_2O_{11}$. T. and H. SMITH, 1878. In long needles. Slightly soluble in cold alcohol, freely soluble in benzene, chloroform. or carbon disulphide. Combines with acids. Colored yellow by sulphuric acid, turning red on addition of nitric acid.

(16) *Rhoeadine*, $C_{21}H_{21}NO_6$. HESSE, 1865. Also in Papaver Rhoeas. Crystallizable. Not poisonous. Scarcely soluble in water, alcohol, ether, chloroform, or benzene. Feebly alkaline. Does not form definite salts. Mineral acids dissolve it with a red color, and with the production of *Rhoeagenin*, isomeric with rhoeadine, a strong base, neutralizing acids. Rhoeadine is colored olive-green by sulphuric acid, yellow by nitric acid.

(17) *Hydrocotarnine*, $C_{12}H_{15}NO_3$. HESSE, 1871. A constituent of opium; also produced from narcotine. *Cotarnine* ($C_{12}H_{13}NO_3$) is first formed by oxidation of narcotine, then reduced to hydrocotarnine (C. R. A. WRIGHT, 1877 and

earlier). In monoclinic prisms. Poisonous. Soluble in alcohol, ether, chloroform, and in benzene. Slightly vaporizable. Colors yellow in cold sulphuric acid, red on heating.

Numerous *derivatives of the natural alkaloids of opium* are known. A description of one of these, *Apomorphine*, $C_{17}H_{17}NO_2$, is given at the close of this article.

Constitution of Opium alkaloids.[1]—Morphine and codeine are closely related to each other and to artificial derivatives of each. Narcotine and narceine also are chemically allied, with cotarnine and hydrocotarnine as derivatives. The relation of both these groups to pyridine, the type of alkaloids, has been shown by v. Gerichten. The immediate structure of morphine and codeine is as follows:

$$\text{Morphine, } C_{17}H_{17}NO\left\{\begin{matrix}OH\\OH\end{matrix}\right. \quad \text{Codeine, } C_{17}H_{17}NO\left\{\begin{matrix}OH\\OCH_3\end{matrix}\right.$$

The structure of narceine and narcotine:

$$\text{Narceine, } (C_{13}H_{20}NO_4)-CO-C_6H_2\left\{\begin{matrix}CO_2H\\OCH_3\\OCH_3\end{matrix}\right.$$

$$\text{Narcotine, } (C_{11}H_{11}CH_3NO_3)-CO-C_6H_2\left\{\begin{matrix}COH\\OCH_3\\OCH_3\end{matrix}\right.$$

Codeine, therefore, is morphine mono-methyl ether. The corresponding morphine mono-ethyl ether is readily formed.

And morphine is artificially converted into codeine (Grimaux, 1881) by treatment, successively, with methyl iodide and fixed alkali. Hydrocotarnine is not only found with narcotine, in opium, but is producible from narcotine by chemical treatment.

Among the products of decomposition of narcotine are meconin, opianic acid, and hemepic acid—non-nitrogenous bodies, of which the first-named is found ready formed in opium. These

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[1] C. R. A. Wright and co-workers, 1872–1877: *Proc. Roy. Soc.*, **20**; *Jour. Chem. Soc.*, **25** to **32**; on narcotine and narceine, **29**, 461; **28**, 573; **32**, 525; on morphine and codeine, **25**, 150, 504. O. Hesse, 1872: *Ann. Chem. Phar.*, Suppl. Bd., **8**, 261; *Jour. Chem. Soc.*, **25**, 721; 1884: *Liebig's Annalen*, **222**, 203; *Jour. Chem. Soc.*, **46**, 613. E. v. Gerichten, 1881–83: *Ber. d. chem. Ges.*, **13**, 1635; **14**, 310; **15**, 2179; *Jour. Chem. Soc.*, **40**, 110, 445; **44**, 221. Grimaux, 1881–83: *Ann. Chim. Phys.* [5] **27**, 273; *Jour. Chem. Soc.*, **44**, 358. Chastaing, 1881: *Compt. rend.*, **94**, 44; *Jour. Chem. Soc.*, **42**, 413. A list of opium alkaloids, with a few derivatives, arranged in order of the number of carbon atoms, is given in the Pharmacographia of F. & H., 2d ed., p. 59.

three bodies are related in structure, as benzene derivatives, as follows:

$$C_6H_2\begin{cases}(OCH_3)_2\\ CO.O\\ CH_2\end{cases}\qquad C_6H_2\begin{cases}(OCH_3)_2\\ CO_2H\\ COH\end{cases}\qquad C_6H_2\begin{cases}(OCH_3)_2\\ CO_2H\\ CO_2H\end{cases}$$

Meconin. Opianic acid. Hemepic acid.

Hesse (1872) presented a practical division of the opium alkaloids into groups, according to their deportment with pure **sulphuric acid**, as follows:

1. *a*.—Dirty dark-green.—Morphine, pseudomorphine, codeine.
   b —Dirty red-violet.—Laudanine, codamine, laudanosine.
2.—Dirty green to brown-green.—Thebaine [?], cryptopine, protopine.
3. *a*.—Dark-violet.—Papaverine.
   b.—Black-brown to dark-brown.—Narceine, lanthopine.
4.—Dirty red-violet (of shade different from that of 1 *b*).—Narcotine, hydrocotarnine.

MORPHINE. $C_{17}H_{19}NO_3$[1] $= 285$. Crystallized, $C_{17}H_{19}NO_3.H_2O = 303$. (For structure see p. 361.)—In opium, as sulphate and meconate. In all parts of the Papaver somniferum, more particularly in the leaves, stems, and seeds just before maturity. In other species of Papaver.—Of dried opium crystallized morphine forms from 3 to 20 per cent.: by the U. S. Ph. (1880) 12 to 16, average 14, per cent.; by the Br. Ph. (1885) 10 per cent. (or 9.5 to 10.5 per cent.); by the Ph. Germ. (1882) at least 10 per cent.; by the Ph. Fran. (1884) 10 to 12 per cent.; these pharmacopœial standards being further defined according to methods of assay given in each. The U. S. Ph. of 1870 specified for dried opium at least 10 per cent. morphine; the U. S. Ph. of 1860, for opium not dried, at least 7 per cent. morphine. Since 1848 the U. S. customs' service has required of opium imported at least 9 per cent. of morphine on the moist basis—equal to 11¼–12 per cent. on a dry basis. And so well has the standard of importation been maintained that, for years before the pharmacopœia of 1880 came into effect, very little opium in reputable hands in this country contained less than about 12 per cent. of morphine on a dry basis. In 1882, before the present pharmacopœia was issued, Dr. Squibb reported from 230 cases of opium an average of 12.45 per cent. in the dry state, and from

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[1] LAURENT, 1847: *Ann. Chim. Phys.* [3] 19, 361. WRIGHT, 1877, $C_{34}H_{38}N_2O_6$.

191 cases an average equal to 12.35 per cent. in the dry state; and in the same year Mr. C. W. Parsons reported the assay of 21 Turkish opiums with an average of 15.2 per cent. of morphine in the dried opium. In fact, although opium was much stronger than the national pharmacopœia required it to be, the pharmacopœia gave no authority for diluting it. Opium, not powdered, could be diluted only by the grossest sophistication. Additions to powdered opium, if made by reputable persons, were made in accordance with an assay and then declared in the brand of the article as containing a specified percentage of morphine. If made by persons without repute or scruple, the limit of the pharmacopœia would be little regarded.[1]

Morphine is recognized under the microscope by its form as free alkaloid crystallizing from solution (*a*); is identified by chemical tests with ferric chloride, sulphuric and nitric acids, Froehde's reagent, phosphomolybdate solution, etc. (*d*, p. 365); is *separated* by action of amyl alcohol on alkali solutions, and by other means (*e*); and from viscera, in cases of suspected poisoning, and with reference to the recovery of Meconic acid, as directed. Morphine is usually *estimated* gravimetrically as free alkaloid (*f*); sometimes volumetrically by Mayer's solution (p. 43), or colorometrically by iodic acid. The *estimation of morphine in opium* is indexed under *f*. The yield of morphine in opiums is stated on p. 362. The tests of purity of the alkaloid and its salts are given under *g*.

a.—Morphine crystallizes, with one molecule of water, in short, translucent, hexihedral prisms of the rhombic (trimetric) system, or in white, lustrous needles. If a few drops of a warm saturated aqueous solution, or a dilute alcoholic solution, be allowed to evaporate spontaneously on a glass slide, characteristic crystalline forms are obtained, to be recognized in analysis by comparison with forms from a known portion of morphine treated in the same way. Too rapid evaporation gives an amorphous residue. Morphine is permanent in the air and below 100° C., and becomes anhydrous at 120° C. (248° F.), losing 5.94 per cent. of the weight of the crystals. According to TAUSCH (1880) the water is expelled at 100° C., though slowly. At 150° C., in the "subliming cell" (BLYTH, 1878), morphine "clouds the upper disc with nebulæ; the nebulæ are resolved by high mag-

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[1] Further, an article by the author "On the Strength of Opium and its Preparations in this Country, as compared with the standards of the Pharmacopœias of 1870 and 1880," 1883: *Proc. Mich. State Pharm.*, I, 48.

nifying powers into minute dots; these dots gradually get coarser, and are generally converted into crystals at 188° C.; the alkaloid browns at or about 200° C." Heated on platinum foil the crystals melt, then char, and slowly burn completely away. The crystals are of sp. gr. 1.317–1.326 (SCHRÖDER, 1880).—Morphine solutions are levorotatory: $[a]r = -88.04$ (BOUCHARDAT; HESSE, 1875).

Crystallization and heat reactions of Morphine Salts.—The sulphate, $(C_{17}H_{19}NO_3)_2H_2SO_4.5H_2O = 758$, crystallizes easily in colorless, feathery needles of silky lustre, permanent in the air, losing its water of crystallization (11.87%) at 130° C. (at 100° C., Ph. Germ.)—*The hydrochloride,* $C_{17}H_{19}NO_3HCl.3H_2O = 375.4$, forms colorless, feathery needles of silky lustre, or minute white, cubical crystals, permanent in the air, parting with the water (14.38%) at 100° C. (TAUSCH, 1880, Ph. Germ.), at 130° C. (FLÜCKIGER, "Phar. Chem.")—*Morphine acetate* holds $3H_2O$, with the molec. weight 399, in a white or faintly yellowish-white, crystalline or amorphous powder, slowly losing acetous vapor in the air.—*Morphine hydrobromide,* with $2H_2O$, crystallizes in needles, becoming anhydrous at 100° C. (SCHMIDT, 1877).—*Morphine hydriodide,* $2H_2O$, forms needles and rosettes, and parts with its water at 100° C. (BAUER, 1874; SCHMIDT, 1877).

b.—Morphine is without odor, and of a bitter taste, more promptly obtained from its soluble salts. It is narcotic, hypnotic, causing contraction of the pupils, and on animals often producing convulsions and paralysis. The fatal dose is not at all uniform for different species of animals of the same size. The alkaloid undergoes change, in part, while passing through the animal body.[1] Further respecting its deposition in the various organs and recovery therefrom by analysis, see statements under *e.*

c.—Solubilities of the free alkaloid.—Morphine, crystallized, is very slightly soluble in cold water (1 to 5000–10000, CHASTAING, 1882); soluble in 500 parts of boiling water; in about 100 parts of ordinary alcohol at 15° C., or 36 parts of boiling ordinary alcohol, or 13 parts of boiling absolute alcohol. The saturated solution in cold absolute alcohol contains one part in 60, and is not precipitated by adding water (Flückiger's "Phar. Chem.") In different conditions, different quantities of solvent are required, as follows—the "nascent" condition being that of liberation from

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[1] Husemann's "Pflanzenstoffe," 1883, p. 706. ELIASSOR, 1884.

salt in aqueous solution: the ether, chloroform, and amyl alcohol, water-washed:[1]

	Ether.	*Chloroform.*	*Amyl. Alc.*	*Benzene.*
Crystallized............	6148	4379	91	8930
Amorphous powder.....	2112	1977	..	....
Nascent state...........	1062	861	91	1997

Morphine is not dissolved by petroleum ether. The solvents above-named, immiscible with water, do not take morphine from acidified solutions. Morphine is dissolved somewhat freely by aqueous fixed alkalies, and by 117 parts of water of ammonia of sp. gr. 0.97. It is a decided base, and neutralizes strong acids.

Solubilities of Morphine Salts.—*Morphine sulphate* is soluble in 23 parts of water at 15.6° C. (DOTT, 1882); in an average of 21 parts of water at 15° C. (COBLENTZ, 1882); in 24 parts water at 15° C. (U. S. Ph.); in 0.75 part boiling water (U. S. Ph.); in 702 parts of alcohol at 15° C., or 144 parts of boiling alcohol (U. S. Ph.)—*Morphine hydrochloride* is soluble in 24 parts of water at 15.6° C. (DOTT, 1882), or 0.5 part of boiling water; in 63 parts of alcohol at 15° C., or 31 parts of boiling alcohol; not soluble in ether (U. S. Ph.)—*Morphine acetate* is soluble in 2½ parts of water at 15.6° C. (DOTT, method of digestion, 1882); when freshly prepared in 12 parts of water at 15° C., or 68 parts of alcohol at same temperature (U. S. Ph.); in 60 parts of chloroform (U. S. Ph.) It is decomposed by boiling alcohol, so that, on adding water, free morphine is precipitated (Flückiger, "Phar. Chem.") *Morphine tartrate* (normal, $3H_2O$) is soluble in 9.7 parts of water at 15.6° C. (DOTT, 1882); *morphine meconate* ($5H_2O$), in 33.9 parts water at 15.6° C. (the same). The *hydrobromide* is soluble, the *hydriodide* slightly soluble, in cold water.

d.—*The color tests* for morphine, when the alkaloid is perfectly separated, are not extremely delicate, as compared with tests for other alkaloids, and are more than usually liable to error from admixture of non-alkaloidal matters.

The test with **nitric and sulphuric acids** ranks first as a means of distinction. Sulphuric acid itself (strictly free from

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[1] The author. 1875: *Am. Chem*, **6**, 84; *Jour. Chem. Soc.*, **29**, 405.

nitric acid) does not color dry morphine (free from narcotine, papaverine, p. 359), or causes only the slightest reddish coloration, unless heat be applied. On the water-bath some shade of purple to brown occurs, later deepening to a brown. Sulphuric acid and cane sugar color morphine purple-red. Minute traces of nitric acid cause a violet to purple color in the cold or on slight warming, and this application of morphine constitutes a very delicate though not distinctive test for nitric acid as an impurity in sulphuric acid. Also the sulphuric acid alone is a delicate test for certain other opium alkaloids as impurities in morphine. Nitric acid alone colors morphine red to orange or reddish-yellow —the coloration not being intense. Concentrated sulphuric acid with a very little nitric acid gives a violet color. Erdmann (1861) employed sulphuric acid with intermixture of one per cent. of nitric acid, sp. gr. 1.25—adding 8 to 20 drops to 1 or 2 milligrams of alkaloidal solid—for a violet color. Husemann[1] treated the solid alkaloidal matter with a little sulphuric acid, heated the solution above 100° C., but not as high as 150° C., and then touched with a drop or two of nitric acid of sp. gr. 1.2, for a dark violet color. Barfoed (1881) dissolves the solid alkaloid in concentrated sulphuric acid, two drops for each milligram, and heats above 100° C. for a second or two, and then adds, to a thin layer on the porcelain surface, a minute fragment of potassium nitrate, a red color giving evidence of morphine, a violet-red obtained with a good quantity, and a rose-red when but a little is present. Instead of nitric acid, other oxidizing agents, potassium chlorate, or chlorine water may be used. Of the forms of the test above mentioned the last given one is preferred. But the test without heat can be recommended as follows:

To a quantity not over a few milligrams of the dry residue to be tested, on a white porcelain surface, add a drop of pure sulphuric acid, and rub with a narrow glass rod for a few minutes, not spreading the acid more than is unavoidable. The point of the glass rod is now touched to nitric acid of sp. gr. 1.42, and drawn across the dissolved residue. A red color, violet if intense, rose-red if less distinct, and soon paling, is the evidence of morphine. The limit of quantity revealed with a good color by this form of the test is about 0.0005 gram of morphine.[2] Husemann gave, as the extreme limit, with heat, 0.00001 gram.

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[1] 1863–1876: *Arch. d. Phar.*, **206**, 231: *Zeitsch. anal. Chem.*, **15**, 103.

[2] "Control Analyses and Limits of Recovery," by the author, 1885: *Proc. Am. Assoc. Advanc. Sci.*, **34**, 111 ; *Chem. News*, **53**, 78, et seq. Respecting the color reactions of nitric acid, see further a note by the author, 1876: *Am. Jour. Phar.*, **48**, 62.

Without heat there is less danger of error due to extraneous matters.

Froehde's reagent—0.001 gram of **molybdic acid** or molybdate of soda freshly dissolved by aid of heat in 1 c.c. of concentrated **sulphuric acid** (Dragendorff), and the solution cooled—gives a bright color reaction for morphine, quite delicate, but not very distinctive. A drop of the reagent is applied to the dry alkaloidal residue, not over a few milligrams, on a white porcelain surface. Morphine gives a blue color, simply that of a certain lower oxide of molybdenum, obtained by deoxidation—violet-blue when pale, and changing, through shades of greenish-blue, finally to dark blue.[1] Kauzmann placed the limit of quantity of morphine responding to this test at 0.00005 gram; Wormley, for blue color, at 0.00007 gram. Unless other reducing agents can be excluded it is unsafe to depend upon this test alone as evidence for morphine.

The **iodic acid** test is another application of the reducing power of morphine, which promptly liberates iodine from iodic acid, and in presence of starch gives the blue color of iodized starch. It is generally applied to the aqueous solution of a salt of morphine, a single drop of which is enough. DUPRÉ (1863) directs to evaporate the morphine with a drop of starch solution to dryness, and when cold to moisten with a solution of iodic acid. WORMLEY states that 0.00007 gram of the alkaloid will give a blue color. With very dilute solutions in considerable quantities, liberated iodine may be sought for by shaking, in a test-tube, with carbon disulphide or chloroform. The reaction has been used for a volumetric method of estimation. This test, carefully applied, is scarcely exceeded in delicacy by any other, and it furnishes a confirmation to affirmative results by other tests, but the presence of morphine should never be declared upon the evidence of this test alone. The chemist should clearly understand that a multitude of reducing agents, inorganic and organic, will liberate iodine from iodic acid.

The two tests last above given depend upon *the reducing power of morphine.* Compared with other non-volatile natural alkaloids, it is a strong deoxidizing agent. To give these two tests any value, non-alkaloidal reducing agents, such as tissue substances, must be strictly removed. In any doubt as to their removal, a control analysis may be instituted, in which like tis-

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[1] FROEHDE, 1866; ALMÈN, 1868; KAUZMANN, 1869; NEUBAUER, 1870; DRAGENDORFF, 1872. "Note on Froehde's Reagent as a test for Morphia," the author, 1876: *Am. Jour. Phar.*, 48, 59. WORMLEY directs a 3 per cent. solution of molybdic acid in sulphuric acid; BUCKINGHAM, a 7 per cent. solution.

sues or other matters are treated with the same solvents in the same conditions, and the product subjected to these final color tests, in comparison with the residues liable to contain morphine.—The capacity of morphine for combination with oxygen renders the alkaloid somewhat instable, though in other respects it is a quite stable alkaloid. Among the oxidation products known are *Oxymorphine*, $C_{17}H_{19}NO_4$ (perhaps Pseudomorphine, Hesse), and Oxydimorphine, $C_{34}H_{36}N_2O_6$, formed by action of silver nitrite, potassium permanganate, or ferricyanide; and a body of the composition $C_{10}H_9NO_9$ (Chastaing, 1882). By hot sulphuric acid, at 150°–160° C., "*Sulphomorphid*," $C_{34}H_{36}N_2O_8S$, is formed, a body probably closely related to *Apomorphine sulphate*. As obtained it is a white, amorphous mass. Nitric acid converts morphine into a resinous body, which, treated with potash, yields methylamine (Anderson). Gold and silver are reduced from solutions of their salts by morphine.

Another application of the reducing power of morphine has been made in a test by a drop of ferric chloride followed by a drop of very dilute solution of potassium ferricyanide, when a blue color results from the formation of ferrous salt. It is said that a solution of morphine salt in 10000 parts of water gives a blue color by this operation. According to Wormley, narcotine and brucine give this reduction. The reaction is also a test for *Ptomaines* (which see). Long (1878[1]) observed a reaction of morphine with ammonio-cupric sulphate, giving a green color, perhaps due to reduction. When morphine is treated with concentrated sulphuric acid (p. 365), and then with potassium chromate, a green color is obtained, due to the reduction of the chromium. Therefore, in the fading purple test for strychnine, morphine, if present in sufficient quantity, gives a green color (not fading).

Ferric chloride, as a normal salt, with no free hydrochloric acid, in solution of ordinary reagent strength, gives a blue color with morphine or its salts. The solid residue, while cold, on a white porcelain surface, is moistened with a drop of the reagent, or by touching with a narrow glass rod wet with the reagent. According to Wormley, a good deep color can be obtained with 0.0007 gram (0.001 grain) of alkaloid in solid residue. A solution of morphine must be as concentrated as 1 : 600 in order to give the color. Less delicate than the tests previously given, this test is quite as characteristic as any other.[2] It is necessary,

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[1] *Chem. News*, 38; *Am. Jour. Phar.*, 50, 490.

[2] A comparison of the tests by iodic acid, Froehde's reagent, and ferric chloride, applied to morphine, grape-juice, orange-juice, and saliva, was reported by D. Brown, 1878: *Phar. Jour. Trans.* [3] 8, 70; *Proc. Am. Pharm.*, 27, 485.

however, to exclude various organic acids of aromatic composition, including the tannins, phenols, salicylic acid, etc., as enumerated under Phenol, *d.*[1] According to Selmi (1876) certain cadaver alkaloids give the blue color to ferric salts, as well as reduce iodic acid. But these cadaveric alkaloids did not give the violet color obtained by morphine on treatment with a solution of lead dioxide in glacial acetic acid, evaporating at a gentle heat.

The general qualitative reagents for alkaloids all respond to morphine. **Phosphomolybdate** gives a very nearly complete precipitate of a yellowish-white color, dissolving in ammonia with a blue color. **Potassium mercuric iodide,** or Mayer's solution, gives a less perfect precipitate, not appearing at all in solutions of 1 to 4000. The precipitate approximates to the composition $(C_{17}H_{19}NO_3HI)_4(HgI_2)_3$.[2] **Iodine in iodide of potassium** solution gives a reddish-brown precipitate, immediately visible in one drop of a solution of the alkaloid in 10000 parts of water (Wormley); under the microscope in a 1 to 100000 solution (Selmi, 1876). On standing, reddish-brown crystals form. The precipitate dissolves in alcohol, in alkalies, slowly in acetic acid. Its distinction, under the microscope, from other opium alkaloids, is given by Selmi, 1876. **Potassium iodide** gives a formation of needle-shaped crystals, somewhat characteristic, obtained only in quite concentrated solutions.—**Tannic acid** and **picric acid** give precipitates in solutions not very dilute.—Alkali carbonates and bicarbonates precipitate morphine, not soluble in excess of the precipitant. Alkali hydrates give a crystalline precipitate, dissolved by excess of fixed alkalies, and by lime solution, sparingly soluble in excess of ammonia.

Crystals of free morphine, obtained by precipitation with a little excess of ammonia, or by spontaneous evaporation of a dilute alcoholic or warm aqueous solution, examined under the microscope (in comparison with known morphine under like treatment), give valuable confirmatory evidence of the identity of the alkaloid (p. 363).

e.—Separations.—Aqueous solutions of morphine are concentrated on the water-bath without marked loss, but if the concentration require long time, or if the solution be complex, in a quantitative separation, it is better to evaporate under diminished pressure at temperature not above 60° to 75° C.—From

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[1] Chastaing (1881) claims, from the chemical proportions in which morphine unites with fixed alkalies, and other considerations, that this alkaloid is in fact a phenol.

[2] The author, 1880: *Am. Chem. Jour.*, **2**, 294.

substances insoluble in acidified water or alcohol these solvents remove morphine in its salts, and hot alcohol may be used to dissolve out the free alkaloid. Of *solvents not miscible with water*, amyl alcohol is the most satisfactory for morphine. The acidified aqueous solution may be purified, or freed from other alkaloids, by shaking out with benzene, or chloroform, or ether, and finally with amyl alcohol itself. Then the liquid is made alkaline by adding ammonia, and exhausted of morphine by repeated portions of amyl alcohol, or by a continuous liquid-extraction apparatus supplied with this solvent. It is to be remembered that amyl alcohol carries with it a little of the aqueous solution, so that the amyl alcohol solution requires water-washing, and a little waste occurs.

In separation from the tissues and contents of the stomach, or other matters, *in analysis for poisons*,[1] the solids are finely divided, in a good-sized evaporating-dish, by playing upon the material with a pair of bright, sharp shears. The divided material may then be treated as directed under Atropine, p. 354, substituting *amyl alcohol* for chloroform as a solvent of morphine. Tartaric acid may be used for acidulation instead of sulphuric, to favor the rejection of ptomaines (GUARESCHI and Mosso, 1883). If it be analysis for opium constituents, it is to be understood that Narcotine is dissolved sparingly by amyl alcohol applied to acidulous solutions, also sparingly dissolved by benzene applied to alkaline solutions, morphine remaining undissolved in both these cases. Unless morphine be found in more than traces, narcotine is not likely to be recovered with identification.

Evidence of opium, in distinction from morphine alone, is more confidently sought through tests for *Meconic acid*. This acid may be separated from the aqueous liquid, in the course for morphine, if acetic acid be added instead of tartaric acid, for acidulation. The filtered aqueous liquid is treated with lead acetate solution, just sufficient to complete a precipitate formed, and filtered. The filtrate is treated with enough hydrogen sulphide gas to throw down all the lead, then filtered, and the filtrate treated in the course of analysis for the morphine The precipitate first formed on adding the lead acetate is washed on the filter with a little water, carried through the filter-point with a thin jet of water, the lead meconate decomposed by hydrogen sulphide gas, the mixture filtered, the filtrate evaporated, the

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[1] Toxicology: Taylor on Poisons; Blyth's Poisons; Wharton and Stillé, vol. 2, 1884; Dragendorff's "Ermittelung von Giften" and "Organischer Gifte"; Wormley's "Microchemistry of Poisons," 2d edition, 1885. STRUVE, 1873: *Zeitsch. anal. Chem.*, 12, 168.

residue taken up with strong alcohol, this solution filtered and evaporated, the residue taken up with warm water, and tested, with ferric chloride and other reagents, for Meconic acid (which see).

The residue from the careful final evaporation of the amyl alcohol solution of morphine—which may be divided in several dishes for the tests and for weight as directed in analysis for atropine—is examined for its deportment in tests by (1) sulphuric and nitric acids, (2) sulphuric and molybdic acids, (3) ferric chloride, (4) iodic acid, and (5) with phosphomolybdate, as directed for each under *d*. Also, (6) a drop of the warm aqueous, or dilute alcoholic, solution is allowed to evaporate very slowly, under the microscope, for crystals of free morphine, to be recognized as stated under *a*. Other tests may be added.

The amyl alcohol used should be examined by evaporating a quantity as large as that used in the analysis, and if any fixed residue be obtained, or if a solution of a supposed residue in acidulated water give reactions with general reagents for alkaloids, then the portion of this solvent to be used must be redistilled, after adding a little tartaric acid. To decide any question as to results, a control analysis should be carried in a parallel operation upon tissue material as nearly as possible the same as that under examination for poisons. If the tissue material taken be very troublesome, or if the operator prefer, the first solution from the tissues may be an alcoholic acidulous solution, and the residue from the evaporation of this solution may be taken up by water (and a very little acid). If acetic acid be used, care must be taken that acid reaction with litmus be maintained. It is better that the temperature of evaporations be kept below 80° C., and that concentrations be hastened by a reduced air-pressure.

The recovery of morphine from the body in cases of fatal poisoning by it is by no means always possible. There are numerous recorded cases of failure of competent chemists to find this alkaloid. In the living body morphine is constantly undergoing decomposition. In the dead body it may suffer decomposition at a very slow rate, though it has been found after standing fourteen months in putrefactive liquids (Taylor). It is highly probable that morphine undergoes waste by decomposition during a prolonged analytical separation from tissues. On the other hand, when an analysis is commenced immediately after the introduction of morphine into tissue material, it can be recovered with less waste than attends some much more stable alkaloids, probably because it interposes a less degree of adhesion than they. In experiments instituted by the author[1] it was found that the loss in the *immediate* separation of morphine, in its smallest recoverable quantities, from an avoirdupois pound of tissues, was not over one hundred times the quantity needed for recognition by the test of Husemann.

In further experiments in the progress of the same investigation,[2] when 0.32 gram of morphine was administered to a cat, an analysis commenced 40 minutes afterward, the alkaloid was recovered for identification from the stomach, the kidneys, the urine, and from the blood, but not from the liver. In four experiments for quantitative recovery, using estimation by Mayer's solution, results were obtained as follows: In each instance 0.32 gram in solution was introduced directly into the stomach by a stomach-tube; and in each instance the stomach, liver, heart, and kidneys were analyzed together. In No. 4, when the animal was killed 30 minutes after the administration, and the analysis begun at once, the volumetric result indicated the recovery of 0.25 gram of alkaloid. When the animal was killed 4 minutes after the introduction into an empty stomach, symptoms having meantime occurred, and the body then left for two days, the final titration indicated the recovery of 0.208 gram. When the animal was allowed to survive the administration for 14 hours, and the analysis then at once commenced, the four organs gave only 0.05 gram of alkaloid. On the repetition of the last experiment, but with a delay of 2 days between the death and the analysis, 0.0485 gram was recovered.

f.—Quantitative.—Morphine is usually dried on the water-bath for *weight as hydrate*, $C_{17}H_{19}NO_3 . H_2O = 303$; 5.94% water.

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[1] "Control Analyses and Limits of Recovery," 1885: *Proc. Am. Asso. Adv. Sci*, 34, 111; *Chem. News*, 53, 78, *et seq.* From series, each of four graded trials, by the method of separation substantially as given in the text, and by the qualitative test with sulphuric and nitric acids, the following *limits of recovery* were fixed for *a good color test:*

From 64 grams of bread, 1 part morphine in 185185 parts.
" 64 " tissues, 1 " " 142857 "
" 64 " liver, 1 " " 142857 "

These "tissues" were membranous, as the coats of the stomach, and containing much less fat than the liver. Trial of the volumetric estimation of the recovered morphine, when larger proportions of the alkaloid were taken, indicated a much greater and much less consistent loss, as follows:

From 128 grams of tissues, 1 part morphine in 19608 parts.
" 128 " liver, 1 " " 10870 "

The experiments were performed by Mr. S. G. Steiner, at the request of the author.

[2] Mr. Steiner, with the author, in 1885, unpublished.

(See *a.*) But it is recommended to dry at a temperature not above 85° C. for the weight of the hydrate, or at near 120° C. for the weight of the anhydrous alkaloid. The last-named temperature is sustained by the anhydrous alkaloid without loss of weight.—The washing of finely crystallized morphine with saturated morphine solutions has been resorted to by Teschemacher and others, as specified further on. Stillwell (1886) proposes to estimate the meconate of lime left as an impurity in the crystallized morphine of an opium assay by dissolving and washing with hot alcohol, on a balanced filter, weighing the dried residue, and deducting this weight.

Besides this gravimetric determination of the free alkaloid there is no well-established method of estimating morphine. The method next to be named, however, is the volumetric estimation with *Mayer's solution* (see Alkaloids, Volumetric Estimation of). The solution is adjusted, if necessary by a preliminary assay, to be of the strength of 1 part alkaloid to 200 parts of the solution, and well acidified with hydrochloric or sulphuric acid (alcohol and acetic acid being always absent in this estimation). Undoubtedly the composition of the precipitate is varied somewhat by conditions of concentration and preponderance of mass, as occurs with other alkaloids, but when holding the concentration uniform by a preliminary assay (or more than one) the main conditions are fixed. Degrees of acidulation have little effect (DRAGENDORFF). The end-reaction is found by the completion of the precipitate. A filtered drop is tested on glass slide over black paper, with a drop of the reagent; and several of these test-portions rinsed from time to time, with a drop or two of water, into the solution under titration. According to Mayer (1862), and Dragendorff and Kubly (1874), 1 c.c. of Mayer's solution indicates 0.020 gram morphine hydrate or 0.019 gram anhydrous morphine. The author has obtained results usually a little too low by use of this factor, and recommends standardizing the Mayer's solution with a solution of pure morphine in acidulated water, in conditions of concentration and temperature fixed for the estimation.[1] The composition of the precipitate is given under *d*, p. 369.

An estimation of morphine, in the volumetric and colorometric way, *by iodic acid*, was given by STEIN (1871), by MIL-

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[1] DRAGENDORFF, 1874: "Werthbestimmung," p. 87. A. B. PRESCOTT, 1878: *Pro. Am. Pharm.*, **26**, 812; *Jour. Chem. Soc.*, **38**, 192. And 1880: *Am. Chem. Jour.*, **2**, 301; *Jour. Chem. Soc.*, **42**, 664. The aqueous extract of opium, deprived of morphine, yields to amyl alcohol bodies giving a considerable precipitate with Mayer's solution.

LER (1872),[1] and by SCHNEIDER (1881), and applied to the assay of opium. Aqueous iodic acid is added to a known weight of (opium) solution, and after the lapse of a few minutes the liberated iodine is washed out by shaking with carbon disulphide. The sample color thus produced is then compared with a standard color obtained in the same manner from a solution of morphine of known strength, and their intensity equalized by adding carbon disulphide to the deeper.—This method may prove useful in certain exigencies, as where estimations are habitual and there is nothing present besides morphine to reduce iodic acid. The details of the method as improved by Schneider are given where cited.

KIEFFER's[2] volumetric estimation of morphine consists in a measure of its reduction of potassium ferricyanide. VENTURINI (1886 [3]) finds this to be the most exact of the volumetric methods.

Estimation of Morphine in Opium. Processes of Morphiometric Assay.[4]—The following is the process of the *U. S. Ph., adopted in the Revision of* 1880:

"Opium, in any condition to be valued, seven grams (7); lime, freshly slaked, three grams (3); chloride of ammonium, three grams (3); alcohol [sp. gr. 0.820], stronger ether [sp.

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[1] *Archiv d. Phar.* [2] **148**, 150; *Phar. Jour. Trans.* [3] **2**, 465: *Jour. Chem. Soc.*, **25**, 180. SCHNEIDER, 1881: *Archiv d. Phar.* [3] **19**, 87; *Proc. Am. Pharm.*, **30**, 232.

[2] L. KIEFFER, 1857: *Ann. Chem. Phar.*, **103**, 271.

[3] V. VENTURINI, *Gazzetta chim. ital.*, **16**, 239; *Jour. Chem. Soc.*, **50**, 1086.

[4] In the text following are given the processes of the pharmacopœias of the United States, England, and Germany, with commentary upon their provisions, in comparison with each other. Also, the detailed process of Dr. Squibb, the directions of Prof. Flückiger respecting modifications of the method of the Ph. Germ., and the experimental criticisms of Mr. Conroy, Mr. H. Lloyd, Mr. Stillwell, and of Messrs. Wrampelmeier and Meinert, with citations from Portes and Langlois, Prollius, and the Soc. de Phar. of Paris.

Of further literature a few references are here added: PERGER, 1884: *Jour. prakt. Chem.* [2] **29**, 97; *Jour. Chem. Soc.*, **46**, 1217; *Pro. Am. Pharm.*, **33**, 298. PROCTER, 1871: *Am. Jour. Phar.*, **43**, 65. ALESSANDRA, 1882: *Phar. Jour. Trans.* [3] **11**, 994; *Pro. Am. Pharm.*, **30**, 231. A. B. PRESCOTT, 1878: with STECHER, *Pro. Am. Pharm.*, **26**, 807; *Jour. Chem. Soc.*, **38**, 191; in 1880. "Report on Revision U. S. Ph.," p. 102; with Moss, 1875: *Am. Jour. Phar.*, **47**, 460; with JOSEPH F. GEISLER, 1880: "Morphiometric Methods," *New Remedies*, **9**, 356. In 1883: "On the Strength of Opium," etc., *Pro. Mich. State Phar. Assoc.*, **1**, 48; *The Druggist*, **6**, 1. Method of TESCHEMACHER, 1877: *Chem. News*, **35**, 47. Report of T. J. WRAMPELMEIER and G. MEINERT, *Mich. State Phar. Asso.*, Oct. 14, 1886; *Am. Druggist*, New York, **15**, 203. Report of CHARLES M. STILLWELL, 1886: *Am. Chem. Jour.*, 8, 295.

A "Bibliography of the Opium Assay" is in preparation by Mr. A. Van Zwaluwenberg, Ann Arbor, and its publication is promised at an early date.

gr. 0.725], distilled water, each a sufficient quantity. Triturate together the opium, lime, and 20 c.c. of distilled water, in a mortar, until a uniform mixture results; then add 50 c.c. of distilled water, and stir occasionally during half an hour. Filter the mixture through a plaited filter, three to three and one-half inches (75 to 90 millimeters) in diameter, into a wide-mouthed bottle or stoppered flask (having the capacity of about 120 c.c. and marked at exactly 50 c.c.), until the filtrate reaches this mark. To the filtered liquid (representing 5 grams of opium) add 5 c.c. of alcohol and 25 c.c. of stronger ether, and shake the mixture; then add the chloride of ammonium, shake well and frequently during half an hour, and set it aside for twelve hours. Counterbalance two small filters, place one within the other in a small funnel, and decant the ethereal layer as completely as practicable upon the filter. Add 10 c.c. of stronger ether to the contents of the bottle and rotate it; again decant the ethereal layer upon the filter, and afterward wash the latter with 5 c.c. of stronger ether, added slowly and in portions. Now let the filter dry in the air, and pour upon it the liquid in the bottle, in portions, in such a way as to transfer the greater portion of the crystals to the filter.—Wash the bottle, and transfer the remaining crystals to the filter, with several small portions of distilled water, using not much more than 10 c.c. in all, and distributing the portions evenly upon the filter. Allow the filter to drain, and dry it, first by pressing it between sheets of bibulous paper, and afterward at a temperature between 55° and 60° C. (131° to 140° F.) Weigh the crystals in the inner filter, counterbalancing by the outer filter. The weight of the crystals in grams, multiplied by twenty (20), equals the percentage of morphine in the opium taken."

The Br. Ph., in the Revision of 1885, adopted the following process of opium assay: " Take of powdered opium, dried at 100° C., 140 grains [9.072 grams]; lime, freshly slaked, 60 grains [or 3.9 grams]; chloride of ammonium, 40 grains [2.592 grams]; rectified spirit (sp. gr. 0.838), ether (sp. gr. 0.735), distilled water, of each a sufficiency.—Triturate together the opium, lime, and 400 grain-measures [25.9 c.c.] of distilled water in a mortar until a uniform mixture results; then add 1000 grain-measures [64.8 c.c.] of distilled water, and stir occasionally during half an hour. Filter the mixture through a plaited filter, about three inches in diameter, into a wide-mouthed bottle or stoppered flask (having the capacity of about six fluid-ounces [Imp. meas., or 170 c.c.] and marked at exactly 1040 grain-measures [or 67.4 c.c.]), until the filtrate reaches this mark. To the filtered liquid (representing 100 grains [6.48 grams] of opium) add 110 grain-measures [7.1 c.c.] of rectified spirit and 500 grain-measures [32.4 c.c.] of ether, and shake the mixture; then add the chloride of ammonium, shake well and frequently during half an hour, and set it aside for twelve hours. Counterbalance two small filters; place one within the other in a small funnel, and decant the ethereal layer as completely as practicable upon the inner filter. Add 200 grain-measures [or 13 c.c.] of ether to the contents of the bottle and rotate it; again decant the ethereal layer upon the filter, and afterwards wash the latter with 100 grain-measures of ether added slowly and in portions. Now let the filter dry in the air, and pour upon it the liquid in the bottle in portions, in such a way as to transfer the greater portion of the crystals to the filter. When the fluid has passed through the filter, wash the bottle and transfer the remaining crystals to the filter, with several small portions of distilled water, using not much more than 200 grain-measures [or 13 c.c.] in all, and distributing the portions evenly upon the filter. Allow the filter to drain, and dry it, first by pressing between sheets of bibulous paper, and afterward at a temperature between 55° and 60° C. (131°–140° F.), and finally at 96° to 100° C. (194° to 212° F.) Weigh the crystals in the inner filter, counterbalancing by the outer filter." The weight represents the quantity of morphine in 100 grains [6.480 grams] of the opium.

The process of the Ph. Germ., adopted in the revision of 1882, is as follows: Opium is to be dried at a temperature not above 60° C. Of opium powder 8 grams are to be agitated with 80 grams of water, and after half a day the mixture filtered. Of the filtrate 42.5 grams are treated with 12 grams of alcohol (sp. gr. 0.834–0.830), 10 grams ether (sp. gr. 0.728–0.724), and 1 gram of ammonia water (sp. gr. 0.960), and the mixture set aside, in a stoppered flask, with frequent shaking, for 24 hours, at a temperature of 10°–15° C. The contents of the flask are then brought upon a small filter, of 80 millimeters ($3\frac{1}{8}$ inches), previously dried and weighed. The crystals recovered from the filtered liquid are washed on the filter with a mixture of 2 grams diluted alcohol (59.8% to 61.5% by weight) with 2 grams of water and 2 grams of ether, applying this mixture in two portions. The filter and contents are dried at 100° C. Deducting the weight of the filter, the weight of the alkaloid gives the quantity of morphine in 4 grams of opium.

The three pharmacopœial processes of opium assay agree in taking a stated quantity of the filtrate to represent a stated fraction of the opium taken, thereby avoiding the washing of the undissolved residue of opium, and without concentration obtaining a solution of a strength desired for crystallization. The quantity of filtrate used, in proportion to the total quantity of liquid taken with dried opium for the mixture filtered, is provided in each of these respective processes, and by the authors of similar processes, as follows:

U. S. Ph....	For	$\frac{5}{7}$	of the opium,	a vol.	of filtrate	= $\frac{50}{70}$	vol.	of liquids	taken.
Br. Ph.....	“	$\frac{5}{7}$	“	“	“	= $\frac{5}{7}$	“	“	“
Soc. Phar. Paris[1]....	“	$\frac{10}{15}$	“	“	“	= $\frac{100}{150}$	“	“	“
PORTES and LANGLOIS.[2]	“	$\frac{5}{7}$	“	“	“	= $\frac{53}{70}$	“	“	“
CONROY[3]....	“	$\frac{5}{7}$	“	“	“	= $\frac{52}{70}$	“	“	“
WRAMPELMEIER and MEINERT, 1886.[4]....	“	$\frac{5}{7}$	“	“	“	= $\frac{50}{70}$	“	“	“
Ph. Germ....	“	$\frac{4}{8}$	“	weight	“	= $\frac{42.5}{80.0}$	weight	“	“
PROLLIUS, 1877[5]... FLÜCKIGER, 1885[6]...	“	$\frac{4}{8}$	“	“	“	= $\frac{42.5}{80.0}$	“	‘	“

The U. S. and Br. pharmacopœias, and, earlier, the Pharmaceutical Society of Paris, take out of the filtrate an aliquot portion of the total *volume* of liquid introduced into the solution subjected to filtration, making no allowance for the volume of solvents being increased by taking solids into solution. Still earlier Portes and Langlois seem to have made such an allowance by the increase of 50 c.c. to 53 c.c. Mr. Conroy (1884) assumes that the “50 c.c. contain the extractive of 5 grams of opium, equal to *about* 3 grams *in the moist state* [italics added] in which it exists in opium. This, from experiments that I have tried, increases the bulk to 52 c.c.”

Recently Messrs. Wrampelmeier and Meinert have given (*loc. cit.*) report of direct experimentation on the question “whether the total liquid—that is, the 70 c.c. of water plus the

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[1] Société de Pharmacie, Paris—adoption of a modification of the process of Portes and Langlois, 1882: *Phar. Zeitung*, No. 6, from *Jour. de Pharm. d'Alsace-Lorraine; Am. Jour. Phar.*, 54, 598.

[2] PORTES and LANGLOIS, 1881: *Jour. de Pharm. et de Chim.*, 1881, 399; *New Rem.*, 11, 64; *Chem. News*, 45, 67.

[3] CONROY, 1884: *Phar. Jour. Trans.* [3] 15, 473.

[4] *Proceedings Mich. State Phar. Asso.*, 4, 127; *Am. Druggist*, New York, 15, 203.

[5] PROLLIUS, 1877: *Schweiz. Wochenschr. f. Phar.*, 1877, 381; *Proc. Am. Pharm.*, 26, 276.

[6] FLÜCKIGER, 1885: *Archiv der Phar.* [3] 26; *Am. Druggist*, 14, 149. The Ph. Germ. process was contributed by Flückiger, who presents, later, a slight modification, noticed in the text further on.

extractive matter dissolved thereby—is really more in volume than 70 c.c. or not." These experiments[1] obtained an average total volume of liquid of but 70.29 c.c., and, so far as they extend, go to support the rate adopted by the U. S. Ph.—The method of the Ph. Germ. and of Professor Flückiger, in which for $\frac{4}{8}$ of the opium a *weight* of filtrate is taken equal to $\frac{425}{800}$ the

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[1] Following is the original report of the experiments of Messrs. Wrampelmeier and Meinert (*loc. cit.*): 7 grams of powdered opium were taken, dried at 100° C., and transferred to a flask. A flask was used instead of a mortar, in order to avoid loss by evaporation. Three grams of freshly slaked lime and 70 c.c. of water were added, the whole thoroughly mixed and allowed to stand for half an hour. The mixture was then placed upon a filter and (instead of 50 c.c.) the liquid was drained off as much as possible by means of an aspirator. The filtrate was weighed, and its specific gravity taken. In order to determine how much liquid there was left in the opium on the filter, the filter was weighed with the funnel, dried at 100° C. to constant weight, and again weighed. By multiplying the loss in weight by the specific gravity of the filtrate, the weight of the liquid left in the opium was found. In the same manner the weight of the liquid left in the macerating flask which could not be brought upon the filter was determined. The weight of total liquid was then found by adding to the weight of the filtrate the weight of liquid left in the opium on the filter, and that of the liquid left in the flask, and from this the total volume—*i.e.*, the 70 c.c. plus the extractive matter dissolved thereby—was calculated by dividing by the specific gravity.

On working two samples of powdered opium in this way, the volume was found to be in the one case 70.83 c.c., and in the other it was 70.85 c.c.; whereas, according to Conroy, the volume should be 72.8 c.c. Since the U. S. Ph. directs to take opium in any form, it seemed possible that, if lump opium which contains some moisture be used, the volume of liquid might be increased. A sample of lump opium was taken which contained 11 per cent. of moisture. Seven grams were weighed off, cut into small pieces, and transferred to a flask. Then the lime and 70 c.c. of water were added, the whole thoroughly mixed by means of a stirring rod until a uniform mixture was obtained. The mixture was then allowed to stand for half an hour and finally placed upon a filter. The filtrate was weighed and its specific gravity taken, and the weight of the liquids left in the opium on the filter, and that of the liquid left in the flask, were calculated in the above-described manner. Experiments made with two samples gave the following results:

	Specific gravity of filtrate.	*Per cent. of morphine.*	*Total liquid.*
Experiment I..........	1.01270	8.3 per cent.	70.39 c.c.
Experiment II.........	1.01265	9.04 "	70.19 c.c.
Average..............................			70.29 c.c.

This gave an average increase of 0.29 c.c. Then a very moist lump opium containing 20.7 per cent. moisture was used, and the volume of liquid was found to be, in this case, 70.61 c.c. These experiments, therefore, would seem to prove that the volume of filtrate directed to be taken by the Pharmacopœia (50 c.c.) is nearly correct.

weight of the liquids used with the *dry* opium, depends upon dry opium containing $\frac{5}{8}$ of its weight (62 5%) of soluble matter. The proportion of soluble matter in opium is, at all events, quite variable.

HERBERT LLOYD[1] found that when morphine itself is subjected to the U. S. Ph. process of assay, it suffers a loss equal to from 0.060 to 0.089 gram on the yield of the 50 c.c., greater or less according to the taking of greater or smaller quantities of morphine. Of course it should be understood that an alkaloid cannot be obtained by a single crystallization, as in all established methods of the morphiometric assay of opium, without some loss; nevertheless the result becomes practically a true one when the quantity of the loss is made to equal an average balance of the quantity of impurity remaining in the crystals weighed. It appears from all evidences to be not improbable that, by the U. S. Ph. or Br. Ph. process, the loss of weight of real morphine, whatever its sources, exceeds the weight of impurity with the morphine.

The quantity of ammonium chloride introduced into the filtrate is to the quantity of dried opium represented in the filtrate, by the directions of the U. S. Ph. as well as by the process of Portes and Langlois, in the proportion of 3 : 5; by the Br. Ph. it is 2 : 5. Mr. Conroy (where cited) reports experiments showing that excess of ammonium chloride causes proportional diminution of yield. The truth of this conclusion has been confirmed by Messrs. Wrampelmeier and Meinert (1886, *loc. cit.*) From these observations and those of Lloyd (*loc. cit.*) it appears that morphine and lime exert a mutual solvent action on each other, and that other constituents of opium help to dissolve lime. The more lime the more free ammonia. And both free ammonia and remaining ammonium chloride help to dissolve the morphine.[2] It appears, therefore, that the pro-

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[1] 1885: *Am. Druggist*, New York, 14, 221.

[2] "In order to find out whether the morphine is held in solution by the excess of ammonia liberated or by the excess of ammonium chloride, the following experiments were made. By calculation it was found that, when 0 202 gram of calcium oxide is in solution, 0.399 gram of ammonium chloride is decomposed. Subtracting this from 3 grams, we find that in this case there is an excess of 2.61 grams of ammonium chloride present in the assay liquor. This amount of ammonium chloride was then dissolved in 50 c.c. of pure water and 0.500 gram of morphine added, and the solution allowed to stand for 12 hours, after which time 0.500 gram of morphine had lost 0.135 gram. The amount of ammonia which would be set free in such assay was also calculated, and a solution of 50 c.c. of pure water containing that amount of ammonia was found to dissolve, after 12 hours' standing, 0 110 gram of morphine. Thus it was shown that both ammonium chloride and free ammonia in

portion of ammonium chloride directed by the Br. Ph. is advisable.

The quantity of free ammonia liberated from the ammonium chloride in the filtrate is limited by the slight but varying solubility of the lime. The excess of lime in the primary maceration serves to improve the consistence of the mucilaginous matters of the opium, favoring solution and filtration. This use of lime in excess, which first holds the alkaloid morphine in an alkaline solution, and afterward, in the filtrate, becomes exchanged for free ammonia, ($2NH_4Cl + Ca(OH)_2 = 2NH_3 + CaCl_2 + 2H_2O$), is credited to the plan of Mohr. Whether liberated by lime from ammonium chloride, or added in water of ammonia (as by the Ph. Germ.), at all events free ammonia is employed in separating morphine from its compounds, to crystallize on standing, in all methods of morphiometric assay so far well established in use.—The crystallization of the alkaloid requires time. In the Hager-Jacobsen processes crystallization was promoted, and the crystals purified, by the addition of small quantities of ether and benzene, not too much to be taken into solution in the crystallizing liquid. The use of an excess of *ether*, much beyond ether-saturation, so as to cause an ether layer to rise above the crystallizing liquid, along with the frequent shaking up of the ether with the aqueous liquid in the closed flask during crystallization, marks an important practical advance in opium assay. This use of ether, introduced about 1881, has been adopted in each of the three pharmacopœial processes above given, also in the processes on individual authority, as hereafter presented. By this use of immiscible ether in forcible contact by agitation with the aqueous solution, crystallization is greatly quickened, and purer crystals are obtained. The effect of stirring was emphasized in 1877 by Teschemacher, who says: "The rapid and continuous stirring is most important, as the precipitation of the whole morphine *in fine powder* is thereby effected, instead of the granular or mammillated condition so frequently met with." This effect on crystalline precipitates, in numerous analytical operations, is well understood at present. The addition of *alcohol*, in the crystallizing liquid, is well understood to cause whiter and finer crystals to be obtained, but, unless counteracted with ether or by greater

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solution exert a distinct solvent action upon the alkaloid. It is therefore probable that by using about 1.000 gram of ammonium chloride instead of 3.000 grams, the amount of morphine held in solution will be greatly reduced."—Wrampelmeier and Meinert, 1886: *Am. Druggist*, New York, 15, 203.

concentration, alcohol in proportion to its quantity tends to diminish the yield of crystals. By the processes of the Ph. Germ. and Professor Flückiger, *alcohol*, *ether*, and *aqueous liquid* hold the proportions by weight 12 : 10 : 43.5 in the crystallizing liquid. By the Br. Ph. process these proportions are by volume nearly as 4 : 20 : 41 ; and by the U. S. Ph. process, as 5 : 25 : 50. That is, *for* 100 *parts by weight of aqueous solution*, the crystallizing liquid contains, *in parts by weight*, nearly as follows :

	U. S. Ph.	*Br. Ph.*	*Ph. Germ.*
Of Alcohol......	8 (sp. gr. 0.820)	9 (sp. gr. 0.838)	28 (sp. gr. 0.832)
Of Ether.......	35 (sp. gr. 0.725)	35 (sp. gr. 0.735)	23 (sp. gr. 0.726)

The directions given by Prof. Flückiger, in 1885,[1] slightly modified from those of the Ph. Germ., are as follows : "Place 8 grams of powdered opium upon a filter of 80 millimeters ($3\frac{1}{8}$ inches) diameter, and wash it gradually with 18 grams (or 25 c.c.) of ether, the funnel being kept well covered ; force out the last drops of filtrate by tapping the funnel, dry the opium on a water-bath, transfer it to a small flask containing 80 grams of water at 25° C., and shake well repeatedly. After 12 hours pour the mixture on the previously used filter, and collect 42.5 grams of the filtrate in a small flask, to which add 12 grams of alcohol [sp. gr. 0.832], 10 grams of ether [sp. gr. 0.726], and 1 gram of ammonia-water [sp. gr. 0.960], stopper well, set aside at a temperature of 12° to 15° C., and shake repeatedly. After 24 hours moisten a new tared filter of 80 millimeters [$3\frac{1}{8}$ inches] diameter with ether, pour upon it the ethereal layer in the flask, add 10 more grams [14 c.c.] of ether to the latter, and shake well. Again pour the ethereal layer upon the filter. When this has passed, pour the whole contents of the flask upon the filter, and wash the crystals of morphine twice with a mixture of 2 grams of diluted alcohol (sp. gr. 0.892), 2 grams of water, and 2 grams of ether. Dry at a gentle heat, finally at 100° C., and weigh, adding the morphine which may still adhere to the inside of the flask." Prof. Flückiger prefers to weigh the morphine in the flask instead of on the filter.

The concentration of the (*aqueous*) *solution set for the crystallization* of the morphine in an opium assay is very nearly 1 to 10, the same in each of the four processes which have been given —those of the Ph. Germ., Br. Ph., U. S. Ph , and Professor

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[1] See foot-note on p. 377.

Flückiger. In these processes 10 c.c. of water are taken for each 1 gram of opium, with little addition to alter this proportion, which is nearly retained in the crystallizing liquid.[1] In the process next to be given, that of Dr. Squibb, the plan of using an aliquot part of the digestive solution is rejected. The undissolved residue of opium is to be exhausted and washed clean, the total filtrates reaching near 20 c.c. for each 1 gram of opium. The entire solution is to be reduced in volume by evaporation, the washings separately, until brought to about 2 c.c., increased, by transfer rinsing and by ammonia-water, to about 3 c.c. of crystallizing liquid for 1 gram of the opium taken. The ether, of course, is not to be counted as solvent, since it serves as an anti-solvent in all the processes. This greater concentration of volume undoubtedly diminishes the loss[2] due to morphine left in the mother-solution, and increases the gain due to impurities held in the morphine crystals.[3] The relation between this loss and this gain, in opium assay, was mentioned on p. 379.

The process of Dr. E. R. Squibb,[4] published in 1882, is as follows: "Take of opium in its commercial condition[5] 10 grams

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[1] Wrampelmeier and Meinert (*loc. cit.*) object to the U. S. Ph. direction to triturate and digest in an open mortar, and to measure in a wide-mouthed bottle or flask, as liable to cause some concentration by evaporating. Such concentration of volume interferes with the principle of taking an aliquot part, and tends toward too high results.

[2] "About 10 per cent. of the morphine in the opium is retained in the mother-liquor after crystallizing the morphine according to the U. S. Ph."—"In order to determine how much of the alkaloid is dissolved in the mother-liquor after crystallizing the morphine, a solution was made to correspond as nearly as possible to the assay liquor, and then a certain amount of morphine was used. The amount of lime (CaO) found to be present in the mother-liquor of the lump opium was 0.202 gram. This amount of lime was taken, slaked with a little water, transferred to the flask, and 50 c.c. of distilled water were added. On adding then 0.500 gram of pure morphine it was found that some of the lime was left undissolved. Therefore, in another trial, a little less calcium oxide was used, the 50 c.c. of water and 0.500 gram of morphine added. Then, as in the U. S. Ph. process, 5 c.c. of alcohol, and 25 c.c. of ether, and 3 grams of ammonium chloride were added, and the mixture allowed to stand for 12 hours. The amount of morphine obtained was 0.442 gram, showing that of the 0.500 gram taken 0.058 gram was retained in solution in the mother-liquor."—WRAMPELMEIER and MEINERT, *Am. Druggist*, New York, 15, 203.

[3] "The precipitate of morphine obtained by Dr. Squibb's process contains insoluble matter, resinous and other organic matters soluble in alcohol, and meconate of lime, the latter constituting about 25 per cent. of the impurities present. The average amount of the impurities present in the crystals obtained by his process is 8 per cent. of the weight of the crystals."—CHARLES M. STILLWELL, *Am. Chem. Jour.*, 8, 306.

[4] 1882: *Ephemeris*, 1, 14; *Jour. Chem. Soc.*, 42, 666. Further, see WAINWRIGHT, 1885: *Jour. Am. Chem. Soc.*, 7, 45.

[5] "If of lump opium, every tenth lump of a case should be sampled by cutting out a cone-shaped piece from the middle of the lump. Then from the side

(154.32 grains). Put the weighed portion in a flask, or common wide-mouthed vial of 120 c.c. (4 f. oz.) capacity, tared and fitted with a good cork. Add 100 c.c. (3.3 f. oz.) of water, and shake well. Allow it to macerate over-night, or for about 12 hours, with occasional shaking, and then shake well and transfer the magma to a filter, of about 10 centimeters (4 inches) diameter, which has been placed in a funnel and well wetted.[1] Filter off the solution into a tared or marked vessel, then percolate the residue on the filter with water dropped on the edges of the filter and on the residue, until the filtrate measures about 120 c.c. (4 f. oz.), and set this strong solution aside. Then return the residue to the bottle by means of a very small spatula, without breaking or disturbing the filter in the funnel, add 30 c.c. (1 f. oz.) water and shake well, and return the magma to the filter. When drained rinse the bottle twice, each time with 10 c.c. (⅓ f. oz.) water, and pour the rinsings upon the residue. When this has passed through, wash the filter and residue with 20 c.c. (⅔ f. oz.) of water, applied drop by drop around the edges of the filter and upon the contents. When the filter has drained there should be about 70 c.c. (2⅔ f. oz.) of the weaker solution.[2] The filter and residue are now to be dried until they cease to lose weight at 100° C. If any residue remains in the bottle, the bottle is also to be dried in an inverted position and weighed. [The weights show the quantity of insoluble matter in the opium.] Evaporate the weaker solution in a tared capsule of about 200 c.c. (6⅔ f. oz.) capacity, without a stirrer, on a water-bath until

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of the cone a small strip is taken from point to base, not exceeding say half a gram from cones which would average 10 to 15 grams. The little strips are then worked into a homogeneous mass by the fingers, and the mass is then wrapped in tin-foil to prevent drying, until it can be weighed off for assay. When opened to be weighed off it is best to weigh off at once three portions of 10 grams each. In one portion the moisture is determined by drying it on a tared capsule until it ceases to lose weight at 100° C. Another portion is used for the immediate assay, and the third is reserved for a check assay if desirable." . . . Opium "should not be dried, but should be weighed for the assay in the condition in which it is found in the market, and in which it is to be dispensed."

[1] "If the shaking be frequent and active," "the time of maceration can easily be shortened even to three hours." The author of the process states that exceptional opiums give a magma which will not filter, and advises to treat such with ether before the assay, washing in a bottle with 30 c.c. ether, shaking well, and washing further with 10 c.c. ether and drying on a filter.

[2] "This (120 + 70 =) 190 c.c. (6⅓ f. oz.) of total solution will practically exhaust almost any sample of opium. But occasionally a particularly rich opium, or one in coarse powder, or an originally moist opium which has by slow drying become hard and flinty, will require further exhaustion. In all such cases, or cases of doubt, the residue should be again removed from the filter and shaken with 30 c.c. (1 f. oz.) of water, and returned, and be again washed as before."

reduced to about 20 grams (309 grains). Now add the 120 c.c. of stronger solution, and evaporate the whole again to about 20 grams (309 grains).

"When cool add 5 c.c. (0.17 f. oz.) of alcohol (sp. gr. 0.820), and stir until a uniform solution is obtained and there is no extract adhering undissolved on the capsule.[1] Pour the concentrated solution from the capsule into a tared flask of about 100 c.c. (3⅓ f. oz.) capacity, and rinse the capsule into the flask with about 5 c.c. of water used in successive portions.—Then[2] add 30 c.c. (1 f. oz.) of ether, and shake well. Add now 4 c.c. (0.133 f. oz.) of water of ammonia of ten per cent. (sp. gr. 0.960), and shake the flask vigorously until the crystals begin to separate. Then set the flask aside in a cool place for 12 hours, that the crystallization may be completed.[3]—Pour off the ethereal stratum from the flask, as nearly as possible, on to a tared filter of about 10 centimeters (4 inches) diameter, well wetted with ether. Add 20 c.c. (⅔ f. oz.) of ether to the contents of the flask, rinse round without shaking, and again pour off the ethereal stratum as closely as possible on to the filter, keeping the funnel covered. When the ethereal solution is nearly all through, wash down the edges and sides of the filter with 5 c.c. (0.17 f. oz.) of ether, and allow the filter to drain with the cover off. Then pour on the remaining contents of the flask and cover the funnel. When the liquid has nearly all passed through, rinse the flask twice with 5 c.c. (0.17 f. oz.) of water each time, pouring the rinsings with all the crystals that can be loosened on to the filter, and dry the flask in an inverted or horizontal position, and, when thoroughly dry, weigh it. Wash the crystals with 10 c.c. (⅓ f. oz.) of water applied drop by drop to the edges of the filter. When drained, remove the filter and contents from the funnel, close the edges of the filter together, and compress it gently between many folds of bibulous paper. Then dry it at 100° C. and weigh it. Remove the crystals of morphine from the filter, brush it off, and reweigh it to get the tare to be subtracted. The remainder, added to the weight of the crystals in the flask, will give the total yield of morphine in clean, distinct, small light-brown crystals."

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[1] "If this solution should contain an appreciable precipitate, as from rare specimens of opium it will, it must be filtered, and the filter be carefully washed through. Then the filtrate must be evaporated to 25 or 30 grams."

[2] "If it has been filtered and evaporated, add 10 c.c. (⅓ f. oz.) of alcohol and shake well."

[3] "If the shaking be frequent and vigorous, 2 or 3 hours' time will be sufficient to complete the crystallization; or if it be continuous, half an hour will be sufficient, but as a rule it is better to allow the flask to stand over-night."

As to the tests for purity of the recovered morphine, see *g*, p. 386.

To effect a complete washing of the crystallized morphine without loss, TESCHEMACHER, in 1877,[1] resorted to the use of a saturated aqueous solution of morphine and a saturated alcoholic solution of morphine as washing liquids. The "morphiated water" was simply a saturated solution, and contained 0.04 per cent. of the alkaloid. The "morphiated spirit" was prepared by mixing 1 part of ammonia-water, sp. gr. 0.880, with 20 parts of (methylated) alcohol, and digesting a large excess of morphine in this mixture for several days. It contained 0.33 per cent. of morphine. STILLWELL, 1886,[2] adopts this way of washing the crystallized morphine obtained by Squibb's process. He collects the crystals on balanced filter-papers of 4½ inches diameter. The ethereal stratum of the crystallizing liquid is poured through the filter, washing out several times with 10 c.c. of ether, rinsing the flask around without shaking it, letting settle for a few minutes, and decanting upon the filter. If the aqueous solution pass on to the filter it is of no importance. The washing with ether is followed, first, by a thorough washing with the "morphiated spirit," then by a thorough washing with the "morphiated water," and, after draining, by two more washings of 10 c.c. each of "morphiated spirit." After draining a few minutes, while the funnel is covered with a watch-glass, two additional washings, each with 10 c.c. of ether, are made. "This will remove any narcotine which may have been left from the evaporation of the ethereal solution at the beginning of the operation. The paper and contents are thus left in a condition to be rapidly dried. Let the filter and its contents stand exposed for a few minutes, and then dry at 100° C. and weigh. Twenty minutes' or half an hour's drying is usually sufficient."

The purification of the crystals from meconate of lime and any other matters insoluble in hot alcohol, as used by Stillwell, was stated on page 373.

The Estimation of Morphine in Tincture of Opium.—The following are the directions of Mr. H. B. PARSONS in application of the U. S. Ph. process of morphine estimation to laudanum.[3] Of the laudanum 75 c.c. are evaporated to dryness on the water-

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[1] E. F. TESCHEMACHER, *Chem. News*, **35**, 47; *Jour. Chem. Soc.*, **32**, 231–232.

[2] CHARLES M. STILLWELL, *Am. Chem. Jour.*, **8**, 295.

[3] "The Composition of the Laudanum generally dispensed in the State of New York," with report of forty-eight samples, 1883: New York State Phar. Asso., *New Rem.*, **12**, 194.

bath. When cool, 75 c.c. of water are added, together with 3 grams of water-slaked lime. Thorough admixture is attained by trituration at intervals during half an hour. The liquid is filtered (from calcium meconate and other insoluble matters), and 50 c.c. of the filtrate (representing 50 c c. of laudanum) is placed in an assay-flask for treatment. Now add alcohol (sp. gr. 0.820), 5 c.c. ; ether (sp. gr. 0.725 or lower), 25 c.c. ; ammonium chloride, 3 grams. Shake the mixture in the corked flask several times during the first half-hour, and occasionally afterward. After 12 or more hours' standing the crystals are gathered on a small balanced filter, slightly washed with cold water, dried at 60° C. (140° F.), and weighed. The grams of this weight, multiplied by 2 (for 100 c.c. of the laudanum) and by the specific gravity of the laudanum, equal the per cent. of morphine in the sample assayed.

Tincture of opium of the U. S. Ph., 1880, is required to be made from one-tenth its weight of dry opium (powdered opium, U. S. Ph.)

g.—Impurities.—" On adding 20 parts of colorless solution of soda or potassa to 1 part of morphine, a clear, colorless solution should result, without residue (absence of other alkaloids)" (U. S. Ph.) " The watery solution of morphine salt is readily made turbid by addition of potassium carbonate. Ammonia gives a precipitate not sensibly soluble in excess of ammonia or in ether, but soluble both in lime solution and in soda solution" (Ph. Germ.)

"Take a small portion of the crystals [free morphine from the opium assay], rub them into very fine powder, and weigh off 0.1 gram. Put this in a large test-tube fitted with a good cork, and add 10 c.c. of officinal lime-water. Shake occasionally, when the whole of the powder should dissolve (absence of narcotine)" (FLÜCKIGER, SQUIBB). " The lime-water test for the narcotine in the results of the assay is quite sufficient, since nothing, except coloring matter, is so likely or so liable to be present as narcotine. The only difficulty is to know when the lime-water has surely dissolved all it will dissolve. This is facilitated by having a very fine powder, and then good judgment is required to know the value or significance of undissolved residues when they are small" (E R. SQUIBB, 1882).

" Morphine yields a colorless solution with cold concentrated sulphuric acid, which should not acquire more than a reddish tint by standing some time" (U. S. Ph.) This test, applied with care, gives good comparative indications of the proportions of narcotine.

If 0.5 gram of morphine sulphate be dissolved in 15 c.c. of water, with the addition of 5 drops of sulphuric acid, and the solution washed with four or five portions each of 25 c.c. of stronger ether, and the united ethereal solutions be evaporated, the narcotine, if any, will be found in the residue. The amount of this residue, and the intensity of its color under action of concentrated sulphuric acid, furnish comparative evidences of the quantity, or comparative quantities, of narcotine as an impurity in the morphine salt.

NARCOTINE.—$C_{22}H_{23}NO_7 = 413$. (For structure see p. 361.)—Occurs in opium, in very variable proportions, from 1.3% to 10.9%. Some samples of French opium do not contain any recoverable by ordinary methods. T. and H. SMITH found an alkaloid, *aconelline*, in the roots of *Aconitum Napellus*, which they thought was identical with narcotine.

Narcotine is *characterized* by its deportment with pure sulphuric acid, and with sulphuric and nitric acids (*d*); *distinguished* and *separated* from morphine by its solubility in ether (*c*), even from feebly acidulous solutions. It is *estimated* gravimetrically or by Mayer's solution (*f*). Separation from opium (*e*), from morphine, under Morphine (*g*), p. 386.

a.—Crystallizes from alcohol or ether in colorless, transparent, orthorhombic prisms, or in groups of needles, which melt at 170° C., solidifying again at 130°, crystalline if cooled slowly, otherwise amorphous. Above 200° C. it splits into meconine and cotarnine (MATTHIESSEN and WRIGHT).

It is heavier than water, odorless, and forms salts of feeble combining force, mostly amorphous, and acid in reaction. The salts are soluble in water, alcohol, and ether, and are to a greater or less extent decomposed either by addition of much water or (when the acid is a volatile one) by evaporating the solutions.

b.—Narcotine in solution is bitter, when free nearly tasteless. It acts as a narcotic poison, though only in large doses (from 1.5 to 3.0 grams).

c.—Narcotine is soluble in about 25000 parts cold and 7000 parts boiling water; when freshly precipitated by ammonia, in about 1500 parts cold and 600 parts boiling water; in 120 parts cold and 20–24 parts boiling alcohol (96%); in 126 parts cold and 48 parts boiling ether (sp. gr. 0.735); in 60 parts acetic ether; in 2.7 parts chloroform; in 300 parts amylic alcohol; in 22 parts benzene; slightly soluble in petroleum benzin, which takes up only a trace from alkaline solutions (DRAGENDORFF). Chloroform removes it from acid solutions.

d.—The **alkaline hydrates, carbonates,** and **acid carbonates** precipitate narcotine (white, crystalline, insoluble in excess of precipitant). **Iodine in potassium iodide** gives a precipitate (brown), **potassio-mercuric iodide** (white amorphous), **potassium sulphocyanate** (amorphous). The other alkaloid reagents also precipitate narcotine, the precipitates not being characteristic. Concentrated **sulphuric acid** dissolves narcotine, at first colorless, becoming yellow. Upon heating gently the solution becomes orange-red, then violet to dark blue streaks appear, and finally the mixture assumes an intense violet-red color. If the heat be stopped before the violet-red color appears, the solution becomes cherry-red on cooling (HUSEMANN). If a drop of nitric acid be added to a solution of narcotine in sulphuric acid, a red color appears. FROEHDE's reagent dissolves narcotine with green color, becoming brown, finally reddish. Concentrated **nitric acid** dissolves it with a yellow color.—In the oxidation of narcotine, by nitric acid or acid chromate, or by permanganate, cotarnine and opianic acid are formed as follows: $C_{22}H_{23}NO_7 + O = C_{12}H_{13}NO_3$ (cotarnine) $+ C_{10}H_{10}O_5$ (opianic acid).[1]

e.—Narcotine is obtained, in greater part, from the residue after treating opium with water (see Morphine, *f*), by extracting with dilute hydrochloric acid, precipitating with sodium acid carbonate, extracting the precipitate with boiling 80% alcohol, and crystallizing out. It is then purified by washing with cold alcohol and recrystallizing from boiling alcohol. Narcotine may also be extracted from opium by means of ether, and crystallizes out on concentrating the ether solution. For the separation of narcotine from morphine see under Morphine, *g*, p. 386.

f.—Narcotine can be estimated gravimetrically. Also by means of Mayer's solution, of which 1 c.c. precipitates 0.0213 gram of narcotine.

CODEINE.—$C_{18}H_{21}NO_3 = 299$. (Structure, p. 361.) In opium, from 0.1 to 1 per cent.

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[1] WÖHLER, 1844: *Ann. Chem. Phar.*, 50, 19. MATTHIESSEN and FOSTER, 1860: *Ann. Chem. Phar.*, Supplement B, 1, 330; *Jour. Chem. Soc.* [2] 1, 342. ANDERSON, *Ed. Phil. Trans.*, 20 [3] 359; *Jour. Chem. Soc.*, 5, 266. Also see "Watts's Dict.," ii. 89.

Codeine is characterized by its solubilities in water, benzene, and ether (*c*), whereby it is distinguished and separated from morphine and from narcotine. Its bright color-reactions with sulphuric acid, alone and with the oxidizing agents (*d*), though somewhat distinctive from other alkaloids in general, are yet in a near resemblance to the parallel reactions of morphine and of narcotine. Tests for purity are presented (*g*) on p. 390.

a.—Codeine crystallizes from its solution in absolute ether in small, colorless, anhydrous crystals. In presence of water it crystallizes in large octahedra and prisms of the orthorhombic system having the composition $C_{18}H_{21}NO_3 . H_2O$. These become anhydrous at 100° C., and melt to an oil-like liquid in boiling water. The anhydrous alkaloid melts at 150° C., and solidifies to a crystalline mass on cooling. It rotates the plane of polarization to the left. It has a strongly alkaline reaction. It precipitates salts of some of the heavy metals. Its salts (mostly crystallizable) are very bitter and almost insoluble in ether. The *hydrochloride*, $C_{18}H_{21}NO_3 . HCl . 2H_2O$, becomes anhydrous at 121° C. It is soluble in less than one part of boiling water, in 20 parts of cold water.

b.—Codeine is odorless, slightly bitter, and resembles morphine in its physiological action. The dose is from 0.5 to 1.0 grain (0.032 to 0.065 gram).

c.—Codeine is soluble in 80 parts cold (15° C.) and 17 parts boiling water; readily soluble in alcohol, ether, and chloroform; in 7 parts amyl alcohol; in 10 parts benzene; almost insoluble in petroleum benzin. Chloroform extracts it most easily from alkaline solutions. It has an alkaline reaction, and neutralizes acids.

d.—Ammonia precipitates codeine from solutions of its salts only after standing some time, and then not completely. **Potassium hydrate** precipitates codeine (partly soluble in excess). The **alkaline carbonates** cause no precipitate in the cold. **Iodine in potassium iodide** precipitates it (brown), **potassio-mercuric iodide** (white), **potassio-cadmic iodide** (white), **phosphomolybdic acid** (yellow-brown), **tannic acid** (even from very dilute solutions, white, soluble in hydrochloric acid), **mercuric chloride** (crystalline), **platinic chloride** (from concentrated solutions, yellow), **gold chloride** (from concentrated solutions, brown), **potassium sulphocyanate** (colorless, crystalline, dissolving on warming). Concentrated **sulphuric acid** dissolves codeine without color, becoming blue on warming or after standing several days, sooner if there be a trace of nitric acid present or if a trace of ferric salt be added. Concentrated **nitric acid** dissolves it with orange-yellow color. Froehde's reagent dissolves it with dirty green color, becoming blue. If to a small portion of codeine, in a watch-glass, there be added two drops of sodium hypochlorite solution, and then four drops of concentrated sulphuric acid, after mixing with a glass rod a fine blue color is obtained (Raby, 1885).

g.—"If codeine be added to nitric acid of sp. gr. 1.200, it will dissolve to a yellow liquid which should not become red (difference from and absence of morphine)."—U. S. Ph.

Apomorphine.—$C_{17}H_{17}NO_2 = 267$. A product of morphine by the action of concentrated hydrochloric acid at 140°–150° C., or with zinc chloride at 110° C.: $C_{17}H_{19}NO_3 = C_{17}H_{17}NO_2 + H_2O$. A product of codeine, by intermediate formation of chlorocodid, $C_{18}H_{20}ClNO_2$, which splits into CH_3Cl and $C_{17}H_{17}NO_2$.—As a hydrochloride, in use in medicine.

Apomorphine is *identified* by the bright colors assumed by its solutions in various solvents (*c*, *d*), and the green color soon taken by its precipitate as free alkaloid (*d*); also by color tests (*d*). It may be *separated* by the action of its solvents (*c*). Its *purity*, in the hydrochloride, is tested, as regards presence of its decomposition products, by noting the color of its solutions (*g*).

a.—When pure, in snow-white, crystalline masses; generally found green-gray or gray-white; and by exposure to the air acquiring greenish and grayish tints. *The Hydrochloride*, $C_{17}H_{17}NO_2.HCl = 303.4$, is in "minute, colorless, or grayish-white, shining crystals, turning greenish on exposure to light and air" (U. S. Ph.) A "white or gray-white crystalline powder," "becoming green by action of air and light" (Ph. Germ.) Oxidation occurs as the green color appears.

b.—Apomorphine and its salts are bitter to the taste and without odor. In effect upon man, a prompt and non-irritant emetic. Dangerous and even fatal symptoms have followed the hypodermic administration of one-sixth of a grain. Medicinally, to an adult, $\frac{1}{60}$ to $\frac{1}{10}$ grain (0.001 to 0.006 gram) is administered by the stomach. The Ph. Germ. maximum dose is 0.01 gram. With animals, convulsions often follow administration.

c.—Apomorphine, a free base, is slightly soluble in water, readily soluble in alcohol, ether, chloroform, or benzene; the aqueous and alcoholic solutions turn greenish; the solutions in solvents immiscible in water, rose-purple to violet.—*The hydrochloride* (see *a*) is freely soluble in water or alcohol, the solutions turning green on boiling or on standing. In ether the salt is almost insoluble. The hydrochloride has "a neutral or faintly acid reaction" (U. S. Ph.); "a very faint acid reaction on moistened litmus-paper" (Br. Ph.); a neutral reaction (Ph. Germ.)—these statements concerning the degree of purity of the salt.

d.—The **alkali hydrates** precipitate apomorphine from solutions of its salts, the precipitate dissolving in excess of either alkali with such readiness that precipitation is not easily made to appear. The alkali solutions turn green. **Sodium bicarbonate** gives a precipitate, only slightly dissolved by excess of the reagent, and distinguished by turning green on exposure. Shaken up with chloroform, the precipitate dissolves in this solvent, which separates with a violet to blue color. Ether or benzene, used in the same way, takes a purple to violet color. The alkaline solution, of excess of alkali hydrate, turning green and finally black, imparts red-purple color to ether, and crimson to blue colors to chloroform, benzene, or carbon disulphide (WRIGHT, 1873).—**Potassium iodide** gives a white precipitate, soon becoming green (WRIGHT); **silver nitrate,** a white precipitate, rapidly turning black by reduction to metallic silver, a result obtained at once if ammonia be added.—**Nitric acid** gives a blood-red color; **ferric chloride** dilute solution, a pink or amethystine color; **iodine** in potassium iodide, a red color.—**Sulphuric acid** gives a violet to brown; **Froehde's reagent,** a green to violet color.—*The general reagents* for alkaloids give precipitates with apomorphine salts in solution.

g.—The watery solution of the salt [*hydrochloride*] should be colorless or not strongly colored; if a solution in 100 parts of water be emerald-green, the article should be rejected (Ph. Germ.) Respecting purity, also, see statements as to the reaction with test-papers (*c*).

ORGANIC ANALYSIS.—*The analytical chemistry of carbon compounds.* A determination of the chemical composition of organic materials.—Organic substances, in their chemical character, are known simply as compounds of carbon and as derivatives of the hydrocarbons, and are not sharply separated from inorganic substances. In the statements of chemistry the term organic has no fixed relation to vitality, or to the products of living bodies, or to organized structure of an anatomical form. Matter is made up of molecules, whether it be organic matter or not; and the molecule is strictly a chemical product, whether it contain carbon or not.[1]

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[1] Inasmuch as the molecule is the final product of chemical action, it follows that the cell is not built up into an anatomical form, from the collection of its constituent molecules, by virtue of chemical action as a typical force. In

Any operation partly or wholly to determine the chemical composition of a portion of organic matter may be termed an operation of organic analysis. Such operations widely differ from each other in scope and extent, from a simple qualitative test of the presence of a given carbon compound to an elaborate scheme for separating and estimating all the distinct substances in a complex mixture, and then determining the elemental structure of certain of these substances.

If a distinct chemical compound have been already obtained in strict purity, the determination of its elemental composition and structure is one of the first and most important of the studies necessary to its chemical acquaintance. For carbon compounds the centesimal figures of elemental composition are obtained by operations of "elementary organic analysis" or "ultimate organic analysis," as described on pages 198 to 238 of this work. Beyond the finding of true centesimal figures, and outside of analytical chemistry as a division of chemical work, there remain the important tasks of learning the real molecular weight and the actual molecular structure of the substance under investigation. Studies of structure were referred to, in consideration of rational chemical formulæ, on page 238, and require the same breadth and faithfulness of original research that are necessary, for example, in determinations of atomic weights. But mere ultimate organic analyses are routine operations, making no greater demand than that of exact execution of well-worn analytical methods. Certainly the estimation of the elements in a given carbon compound already separated in purity is a very narrow task when compared with that of the determination and separation of the several carbon compounds in a given portion of organic material.

The proper place which "elementary analysis" holds in analytical chemistry, in comparison with that of "proximate analysis," will appear in a true light if we contrast the one kind of analytical work with the other, when applied to common *inorganic* materials. Thus, there are at least eight sulphur acids consisting each of sulphur and hydrogen and oxygen, besides compounds of sulphur with hydrogen, sulphur with oxygen, sulphur with halogens, and numerous other "inorganic" compounds of sulphur. The percentage of sulphur in each of these compounds was long since established to within narrow limits of error, and their "ultimate analysis" for sulphur is now required only as an

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the organization of the cell, chemism can exert no other power than that of a "correlative force," acting in such a way as that by which heat enables certain chemical combinations to take place.

infrequent resort in indirect methods of estimating sulphur compounds. Qualitative and quantitative analyses for sulphuric acid and for other common compounds of sulphur are in constant demand, and are made with confidence, although we have no general analytical scheme for all sulphur compounds. Determinations of the presence and proportion of sulphuric acid are not spoken of as operations in "proximate analysis." Neither is the estimation of acetic acid often referred to as a "proximate organic analysis." The term "proximate" has been carefully defined, over and over again, to specify a certain kind of analyses, but *in its principal use* by chemists the term seems to have belonged mainly to such analytical undertakings as have been quite remote from realization. With this distant apprehension on the part of chemists it is not strange that laymen should forget what the precise difference is between "proximate" and "approximate" determinations in the laboratory.

To determine and to separate chemical compounds as they exist in the material under inquiry, to assort the molecules and to ascertain their structure without permitting any changes in them to elude observation, is the end to be reached in analytical chemistry, whether of inorganic or organic substances, whether for qualitative or quantitative statements, and whether the desired percentages be those of compounds in a given mixture or those of elements in a given compound. Divisions of analysis for inorganic and organic articles, or for qualitative and quantitative purposes, are only divisions of labor designed for the convenience of chemists, and are sometimes an occasion of embarrassment and delay. Like the differences between inorganic and organic general chemistry, the distinctions between inorganic and organic analysis have been overstated, quite to the discouragement of learners and to the misleading of scientific inquiry.

In any so-called branch of chemical analysis the operator may resort to separation by physical state without chemical change, or to reactions of substitution, addition, or disunion; but whatever the resource, it is required to trace the relation between the external deportment and the molecular structure of substances, and to make acquaintance with the character of the compounds under treatment.

PALMITIC ACID. See Fats and Oils, p. 244.

PAPAVERINE. See Opium Alkaloids, p. 359.

PAYTINE. See Cinchona Alkaloids, p. 92.

PHENOL.—$C_6H_5OH = 94$. Hydroxylbenzene.—The first member of a series of PHENOLS, $C_nH_{2n-7}OH$, a series of monohydroxyl benzenes. Phenols have a structure as though derived from the hydrocarbons, benzene, C_6H_6; toluene, C_7H_8, etc.—by substituting OH for H in the mono hydroxyl benzenes, 2OH for 2H in the di-hydroxyl benzenes, etc.[1]

Phenol may be obtained by the destructive distillation of resins and many other organic substances. It is formed in the dry distillation of salicylic acid, more readily if lime be added: $C_6H_4.OH.CO_2H = C_6H_6O + CO_2$. The urine of various animals contains phenol, and it is liable to occur in the urine of man. Certain albuminoid decompositions, or putrefactions, generate phenol. It often appears in the distillates from wood-tar, making an impurity, or less valued constituent, of true wood-tar creosote, which contains phenols of another series. But the phenol in use comes from no other source than the distillation of coal-tar, and bears the name of *Carbolic Acid.* The making of this article has been an industry since about 1860. Crude carbolic acid contains phenol with the cresols and some of the xylenols of the following list. Best-grade carbolic acid is nearly pure phenol. The article sold as "cresylic acid," of variable composition, contains cresols and may include xylenols.

		Melting.[2]	*Boiling.*[2]
Phenol, $C_6H_5.OH =$	C_6H_6O	42° C.	184° C.
Cresols, $C_6H_4.CH_3.OH =$	C_7H_8O		
Orthocresol, 1 : 2		31°	186°
Metacresol, 1 : 3		liquid	194°–200°
Paracresol, 1 : 4		36°	198°
Xylenols, $C_6H_3.CH_3.CH_3.OH =$	$C_8H_{10}O$		
Orthoxylenol, 1 : 2 : 4		61°	225°
Metaxylenol, 1 : 3 : 4		liquid	211°
Metaxylenol, 1 : 3 : 2		74°	212°
Paraxylenol, 1 : 4 : 2		75°	213°

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[1] KEKULÉ, 1865: "Organ. Chem.," iii. (1882), 1, 12; "Substitution Products," 25. "Watts's Dictionary," vii. 924 (ARMSTRONG), 132. Ladenburg's "Handwörterbuch." Remsen's "Organic Chemistry," 269, 233.

[2] The melting and boiling points of the isomeric cresols and xylenols have been ascertained, mainly, from the artificial compounds. The isomers have not been separated in purity from coal-tar distillates. It is not known to what extent xylenols and the several cresols occur in crude carbolic acids and in

In the distillation of coal-tar the distillate is received in fractions limited usually by boiling points, sometimes by volume-quantities, and generally in part by specific gravities, with regard also to periods of distillation. The number and limits of the fractions of distillate have varied with the progress of the industry and with local customs and special purposes.[1] After vaporization of the water and ammonia, under name of the "first runnings" or "crude naphtha," a "break" occurs, after which distillation recommences at 105° to 110° C. Beginning at this point, the first fraction is almost everywhere named "light oil," and contains the hydrocarbons of the benzene series. Formerly the distillate was generally received as "light oil" until a portion ceased to float on water (sp. gr. 1.0), when the boiling point is about 210° C. [Lunge]. At present, in many places where carbolic acid is an object, the "light oil" is cut off at 165°–170° C.; and a fraction of "middle oils," for carbolic acid and naphthalene, is received up to 230° C. "Light oil," if carried to 210° C., contains a good deal of carbolic acid; if cut off at 170° C. it contains but little. But after a "light oil" is distilled up to 210° C., a fraction named "carbolic oil" is received, up to 240° C., as a source of carbolic acid. The term "creosote oil" ("heavy oil") is very generally applied to a fraction taken either after "carbolic oil" or "middle oil," and cut off at 270° C. Carbolic acid is not made from "creosote oil," or from any distillate above 240° C., but "creosote oil" contains unknown quantities of cresols and xylenols. It is used entire, for lubricating, pickling timbers, etc., etc., and has not gained much credit for antiseptic power. Above 270° C. a final distillate named "anthracene oil" ("green oil" or "red oil") is now generally obtained as a source of anthracene, a product of great value. Formerly all distillate after "light oil" was taken in one portion as "dead oil"; and all the fractions after "light oil," sinking in water, may now be classed as "dead oils." If the distillation be stopped when "light oil" is received, the retort-residue is called "asphalt"; if "dead oils" are distilled, the residue is "soft pitch" or "hard pitch," according to the persistence of distillation. Carbolic acid, then, is obtained from distillates below 240° C., and mainly from portions taken after the "light

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cresylic acid. On artificial xylenols, Jacobsen, 1878: *Jour. Chem. Soc.*, 34, 411. On cresols, Oppenheim and Pfaff, "Watts's Dict.," viii. 581. The statements that there is one liquid cresol and one liquid xylol are of interest in view of the fact that "cresylic acid" also remains liquid at low temperatures. *Paracresol* is found to have a more powerful *local anæsthetic effect* than carbolic acid (McNeill, 1886).

[1] On this subject see Lunge's "Coal-tar Distillation," 1882.

oil," though some carbolic acid is saved in purifying the benzoles of "light oil."

The treatment of a distillate for carbolic acid usually begins with an agitation with caustic soda solution, more or less dilute (12% to 40% of hydroxide), the alkaline solution of the phenols being afterward acidulated to separate *Crude Carbolic Acid*, which rises as a liquid layer. Strong alkalies dissolve non-phenols; weak alkalies fail to dissolve all the cresylic acid. Acidulation is done by sulphuric acid (mostly in lead-lined vessels), by hydrochloric acid, and with best results by carbonic acid. Crude carbolic acid is apt to contain sulphuric or hydrochloric acid. The manufacturer sometimes improves it by washing with a little water or by distilling it. Crude carbolic acid should have a specific gravity of 1.050–1.065 at 15.5° C. (ALLEN). Watson Smith found samples of it to yield 61½ to 62½ per cent. of carbolic acids of a grade to solidify at 15° to 18° C., and 12 to 15 per cent. of water. Methods of valuation of crude carbolic acid are noted under Separations (p. 401) and Quantitative (p. 404).

All the phenols both of crude carbolic acid and of wood-tar creosote agree in giving, among other reactions, deep-colored nitro-acids with nitric acid; pale-colored bromo-compounds with bromine-water; soluble sulphonic acids by standing with concentrated sulphuric acid; and feebly chemical solutions with alkali and water, from which they are separated by acidulating. Definite, crystallizable salts are easily obtained from nitro-phenic acid, likewise from phenolsulphonic acid, but the alkali phenols, or "carbolates," are not easily obtained in purity.

CARBOLIC ACID.—*Carbolsäure.* Crystallized carbolic acid. Phenol of approximate purity obtained from coal-tar. Recognized by its sensible properties (*a*, *b*); *identified* by reactions with bromine, ferric chloride, nitric acid, etc. (*d*); distinguished from Creosote by its behavior with ferric chloride, albumen, collodion, glycerin (*d*); *separated* by distillation, solvents, etc. (*e* and *c*); *estimated*, volumetrically or gravimetrically, by bromine (*f*, p. 404). For *chemical relations and manufacture* see p. 395; *examination respecting purity* and quality, *g* and *a;* Nitro-phenic acid, p. 398; Sulphocarbolic acid, p. 405. For separation from the Urine, p. 402; in Toxicology, p. 402.

a, b.—Carbolic acid appears in a crystalline mass of interlaced needles, colorless, or, after keeping, faintly pinkish, with a characteristic and aromatic odor (feebly creosote-like—HAGER), and (when diluted with much water) a sweet taste with a burning after-taste. Only the imperfectly purified grades have an odor like that of creosote (SQUIBB). In full concentration it is caustic to the skin, which it whitens, and gives a sensation of numbness, acting as a local anæsthetic (McNEILL, 1886). Internally it is an active poison, even if so diluted as not to be corrosive, the full medicinal dose being one or two grains It is neutral in reaction. From solution in petroleum-ether separate needle-form crystals of phenol are obtained. In presence of water crystals can be formed of the composition $2C_6H_6O.H_2O$, equal to 9.57 per cent. of water (CALVERT, 1865). The best carbolic acid of the market "contains 2 to 4 per cent. of water, and some very good acid contains much more" (SQUIBB, 1883). Phenol crystallized from petroleum-ether melts at 44° C. (111° F.) (FLÜCKIGER: "Phar. Chem.," 280); perfectly pure phenol at 42.2° C., at 43.2° C. (SCHERING, HAGER). CALVERT found the hydrate to melt at 16.6° C. (62° F.) The congealing point is the more constant criterion, and, when melted, good carbolic acid of the market was found to congeal at from 29.4° to 39.5° C.; also, addition of 2 per cent. of water lowered the congealing point 7.9° C. (SQUIBB: *Ephemeris*, i. 305). Carbolic acid melts at 35° to 44° C. (*Ph. Germ.*, 1882), "at 36° to 42° C. (96.8° to 107.6° F.), and boils at 181° to 186° C. (357.8° to 366.8° F.), the higher melting and lower boiling points being those of the pure and anhydrous acid" (U. S. Ph., 1880). Phenol boils at 187° to 188° C. (LAURENT, 1841). A fine specimen of carbolic acid, congealing at 38.5° C., boiled first at 170° C., later at 183° C.; another sample, first at 173° C., later at 186.2° C. (SQUIBB, where last quoted). Both Cresol and Creosote remain liquid when exposed to a freezing mixture (ALLEN).—The specific gravity of phenol is 1.065 at 18° C. (LAURENT, 1841), 1.0627 (SERUGHAM). When melted to a liquid the specific gravity of carbolic acid is 1.060 (Ph. Germ.)

c.—It has been a general statement that phenol is soluble in 20 parts of water, a statement applied to carbolic acid by the U. S. Ph., 1880, and Ph. Germ., 1882. ALLEN[1] found the acid (Calvert's No. 1) to dissolve in 10.7 parts by weight of water for 1 part of absolute acid. Likewise, it has been a frequent statement that carbolic acid dissolves only one-twentieth (5%) of its weight of water, but according to Allen it dissolves about 27 per cent. of water (nearly $2H_2O$). With elevation of temperature a larger proportion of water can be held in solution, the mixture

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[1] 1878: *Analyst*, **3**, 320; *Jour. Chem. Soc.*, **36**, 182.

becoming turbid when cooled. A permanent liquid state is obtained by adding 5 per cent. of water, and this addition, or one of a fluid-ounce of water to a pound of the crystals, is usually adopted in dispensing. Cresols are said to dissolve in about 31 parts of water (?) The alkalies with water dissolve carbolic acid freely, but on neutralizing precipitation occurs, and very little phenol is dissolved in a saturated solution of common salt.[1] Carbolic acid is soluble in all proportions of alcohol and of glycerin, and freely soluble in ether, chloroform, benzene, carbon disulphide, volatile oils, and in fixed oils, water, if present, being partly separated by solvents not miscible with it. Petroleum benzin dissolves but little carbolic acid in the cold.

d.—**Nitric acid** reacts upon the phenols, violently unless diluted, producing yellow to brown nitro-compounds, with escape of brown nitric oxide vapors. With phenol proper it yields successive nitro-phenols, the final product being $C_6H_2(NO_2)_3OH$, tri-nitrophenic or picric acid. The color is intensified by neutralizing with potash, and the potassium trinitrophenate is sparingly soluble in water, less soluble in alcohol, and crystallizes in bright yellow needles. Some analysts add to the liquid to be tested an equal volume of sulphuric acid (not diluted) and then a minute fragment of potassium nitrate. Solution of **mercuric nitrate** with a trace of nitrous acid gives the nitric acid reaction visible in dilution of the phenol to 150000 or 200000 parts; **Millon's reagent** reveals phenol in dilution to 2000000 parts, in 20 c.c. of solution (0.00001 gram phenol) (ALMÉN, 1878). PICRIC ACID has a very bitter taste, colors the skin and fabrics of nitrogenous composition with special intensity, acts as an explosive both of itself and with reducing agents, forms true salts with bases in general, and gives constant precipitates in solutions of the alkaloids.

Bromine-water, with solution of carbolic acid, gives a curdy or crystalline, whitish precipitate, tribromophenol, $C_6H_2Br_3OH$, soluble in excess of the phenol, but permanent upon addition of enough of the reagent, soluble in alcohol, ether, carbon disulphide, etc., and in alkalies. The test is very delicate, but in very dilute solutions several hours should be given for the formation of the crystalline precipitate, when one part of phenol in 57100

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[1] Dry phenol is soluble in an equal volume of 9 per cent. soda solution. With addition of water, up to 7 volumes, the liquid remains clear, but is precipitated by 8 volumes of water. Dry "cresol" is soluble in an equal volume of the 9 per cent. soda, but with addition of the soda to 3½ volumes a precipitate occurs. Creosote requires at least 2 volumes of the 9 per cent. soda to dissolve it.—ALLEN.

parts of solution is revealed (Landolt, 1871), stellated needles appearing under the microscope. Corresponding precipitates, of nearly the same appearance, are given by the homologues of phenol, by aniline and its homologues, by the phenols of wood-tar creosote, by certain alkaloids, and by other organic substances. With "cresylic acid," or crude carbolic acid, the precipitate is amorphous and soft.[1]

Ferric chloride, as free from hydrochloric acid as possible, in solution with phenol gives a fine violet-blue color. Limit of dilution for this test, 1 part in 3000 parts (Almén, 1878). Acids and some neutral salts interfere. "On adding to 10 c.c. of a one per cent. aqueous solution of carbolic acid one drop of test solution of ferric chloride, the liquid acquires a violet-blue color which is permanent (the color thus caused by Creosote rapidly changing to greenish and brown, with formation, usually, of a brown precipitate)" (U. S. Ph.) But in more concentrated solutions this test does not clearly distinguish creosote from carbolic acid. Various organic compounds, and according to Schiff all compounds containing phenol-hydroxyl,[2] give violet to blue colors with ferric salts.

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[1] Landolt's original report upon this reaction, both in its qualitative and its gravimetric uses, is full and satisfactory. 1871: *Ber. d. chem. Ges.*, **4**, 770; *Zeitsch. anal. Chem.*, **11**, 93; *Chem. News*, **24**, 217. Of substances giving precipitates with bromine-water, in solutions not too dilute, Landolt mentions quinine, quinidine, cinchonine, strychnine, and narcotine, all giving yellow or orange precipitates, soluble in hydrochloric acid, but insoluble in alkalies [a distinction from phenol]. As not giving precipitates in dilute solutions, there are named gallic acid, pyrogallol, picric acid, bitter-almond oil, amygdalin, caffeine, brucine, and hippuric acid. Morphine gives a white precipitate, soon dissolving. Wormley, in "Microchemistry of Poisons," treats of Bromine in solution of Hydrobromic acid as a reagent for alkaloids, causing crystalline precipitates with the greater number of them.

[2] That is, all phenols, and all derivatives of phenols which still retain one or more of the OH of phenols, give an iron-bluing reaction. Schiff enumerates, as giving *blue* colors, tannins, gallic acid, pyrogallol, other tannin derivatives, arbutin; as giving *violet* colors, phenols, salicylic acid, creosote, salicylic aldehyde (oil of spiræa), methyl salicylate ($C_6H_4.OH.CO_2CH_3$), saligenin, phenolsulphonic acid ($C_6H_4.OH.SO_3H$), etc.; giving *green* colors, many tannins, æsculetin, etc.; *red and red-violet* colors, phloridzin, phloretin, tyrosin, and some others. Morphine gives the blue color, and Chastaing (1881) classes it as a phenol. The reaction is not given with nitro-compounds, nor with compounds in which the H of phenol OH is displaced.—Schiff, 1871: *Ann. Chem. Phar.*, **159**, 164; *Zeitsch. anal. Chem.*, **10**, 483; *Jour. Chem. Soc.*, **24**, 959.—Hager states that the following substances interfere with this test: organic acids, mineral acids, phosphates, acetates, borax, glycerin, alcohol, amyl alcohol.—Comparison of the reaction of carbolic acid, salicylic acid, resorcin, antipyrine, and kairine, with ferric chloride, is given by Schweisinger, 1885: *Archiv. d. Phar.*, **222**, 686; *Zeitsch. anal. Chem.*, **24**, 469. Distinction of reactions of carbolic, salicylic, gallic, and tannic acids, with ferric salts, Hager, 1880: *Ding. polyt. Jour.*, **235**, 407; *Am. Jour. Phar.*, **52**, 264.

Molybdic acid in solution in concentrated sulphuric acid is reduced by phenol with the formation of a purple color. The molybdic acid is dissolved in ten parts of the sulphuric acid, a few drops of this reagent, on a white porcelain surface, are covered by a drop of the solution to be tested, and, after a momentary yellowish-brown coloration, the purple appears. To promote the reaction the liquid may be slightly warmed, but not above 53° C. The reaction is a delicate one, but a similar color is given by many reducing agents. Creosote, free from phenol and pure, gives only a reddish-brown tint (E. W. DAVY).[1]

Quinine or **Cinchonidine**, as Sulphate or Hydrochloride, yields a characteristic crystalline compound with phenol (HESSE[2]). The solution to be tested for phenol must be neutral. To this, while hot, a neutral solution of the alkaloid salt is added, one drop at a time, and so sparingly that phenol shall be in excess, if possible. If phenol be present a white precipitate appears, either at once or in crystals as the mixture cools, soluble in hot water, sparingly soluble when cold, almost insoluble in phenol-water, easily soluble in acids, decomposed by alkalies, crystallizable from alcohol. With quinine sulphate the precipitate is $(C_{20}H_{24}N_2O_2)_2H_2SO_4C_6H_6O$. The dextro-rotary cinchona alkaloids, according to Hesse, do not form these crystallizable phenolo-compounds.

Chlorate of Potassium may be used for the following test (CHARLES RICE[3]): Ten grains of the powdered chlorate, in a five-inch test-tube, are covered with strong hydrochloric acid to the depth of about one inch, the evolution of gas is allowed to continue about one minute, when 1½ volumes of water are added, and the gas is removed from the upper part of the test-tube by blowing it out with a small bent glass tube. Pour in water of ammonia, without shaking, to form a layer about half an inch deep, and remove the cloud of ammonium chloride by blowing it out as before. Now add a few drops of the liquid to be tested, letting it flow down the side of the test-tube. If phenol be present a colored layer or "ring" will appear, rose-red to red-brown. Creosote gives the same reaction.

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[1] An adaptation of Froehde's reagent. DAVY: *Phar. Jour. Trans.* [3] 8, 1021; *Jour. Chem. Soc.*, 34, 809. The reagent for alkaloids: FROEHDE, 1866: *Archiv. d. Phar.*, 126, 54; *Zeitsch. anal. Chem.*, 5, 214; *Pro. Am. Phar. Asso.*, 15, 241. DRAGENDORFF, 1872: "Gericht. Chem. organ. Gifte." This work, p. 51.

[2] 1876: *Liebig's Annalen*, 181, 53; 180, 248; 182, 160; *Jour. Chem. Soc.*, 30, 313, 639; note by WRIGHT, 314.

[3] 1873: *Am. Jour. Phar.*, 45, 98.

Other tests are obtained by action of Ammonia and Chlorine, Ammonia and Hypochlorite, and by Millon's reagent.[1]

Pure phenol does not *reduce* Fehling's solution, and but slowly reduces silver and mercury salts, but reduces permanganate, both in acid and in alkaline solutions. With concentrated sulphuric acid, *phenolsulphonic acid*, $C_6H_6SO_4$, is slowly formed, almost without color when the phenol is pure. The phenolsulphonates of alkali metals are soluble in alcohol, and those of other metals, including barium and lead, are soluble in water, these solubilities giving separations from sulphuric acid. On distilling phenolsulphonic acid, phenol is obtained. See Sulphocarbolic Acid.

"Carbolic acid coagulates albumen or collodion (difference from creosote). . . . One volume of liquefied carbolic acid, containing five per cent. of water, forms, with one volume of glycerin a clear mixture which is not rendered turbid by the addition of three volumes of water (absence of creosote and cresylic acid)."—U. S. Ph., 1880.

e.—Separations.—Carbolic acid can be obtained *by distillation* from acid or neutral liquids without loss. Less volatile than water, the phenols are yet carried over, slowly, with vapor of water, and the operation requires conditions similar to those needful for distillation of the essential oils. In alkaline aqueous solutions the phenols are held nearly or quite secure from vaporization, so that these solutions can be *concentrated* on the water-bath without loss of phenol, though as to the limits of the retention of phenol by hot alkalies when very dilute further proof is desirable. Potassium hydrate is the best alkali. Alcohol and other more volatile neutral bodies are easily removed by evaporation or distillation from alkaline mixtures of carbolic acid. Before distilling phenol, therefore, alkaline liquids and mixtures —such as "carbolate of lime" and "soda-phenol"—should be acidified by adding an acid, in most cases sulphuric acid, sometimes hydrochloric or phosphoric acid. But phenol may be distilled, with water, from a neutral mixture. Dry distillation,

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[1] Detailed reports upon qualitative tests for phenol have been given as follows: WALLER, 1881: *School of Mines Quarterly*, 1881, Jan.; *Chem. News*, **43**, 151. ALMÉN, 1877: *Archiv. d. Phar.* [3] **10**, 44; *Jour. Chem. Soc.*, **32**, 360. ALLEN, 1878: *Analyst*, **3**, 319; *Jour. Chem. Soc.*, **36**, 182. HIRSCHSOHN, Phenol and Thymol, Dorpat, 1881: *Phar. Jour. Trans.* [3] **12**, 21; *Am. Jour. Phar.*, **53**, 459; *Jour. Chem. Soc.*, **40**, 942. Regarding Detection and Estimation in the Urine—BAUMANN, 1882: *Zeitsch. physiolog. Chem.*, **6**, 183; *Jour. Chem. Soc.*, **42**, 106. ENGEL, 1881: *Ann. Chim. Phys.* [5] **20**, 230; *Jour. Chem. Soc.*, **40**, 114.

without addition, in glass vessels over the flame, is directed by ALLEN for recovering from the siliceous material of "carbolic acid powders."

In analysis of animal tissues, or indeterminate organic mixtures, in cases of poisoning, the finely cut material is digested, after slight acidulation with sulphuric acid, to obtain an aqueous solution of all the phenol. If concentration of the extract is undertaken before distilling, the analyst must choose a method suited to the material and conditions. Extraction with ether has been recommended in this case, and it may serve if there is little fat. The ether solution may be shaken with very slightly alkaline water, the ether-layer and dissolved ether evaporated off, and the aqueous solution acidified and distilled. In any case the last distillate is divided into aliquot parts by volume, for qualitative and quantitative determinations, the bromine reaction being most serviceable.[1] Phenol is eliminated freely by the kidneys.

In the Urine phenol appears in salts of phenylsulphuric acid, chiefly $KC_6H_5SO_4$, formed by union of the excretory phenol with the sulphates of the urine. Therefore it is a clinical result that the sulphates of the urine, as noted by the precipitation of barium, diminish in measured proportion to the increase of excretory phenol. The later investigations[2] carefully distinguish the urinary form of phenol, above named, from its isomer, phenolsulphonic acid (see Sulphocarbolates). When much phenol is excreted, and in cases of phenol poisoning, the urine sometimes, but not invariably, has a greenish-brown color. Baumann separates the sulphates from the phenylsulphates and determines the sulphuric acid of the latter and of other ethersulphuric acids as follows: 25 to 50 c.c. of the urine is acidified with acetic acid, diluted with an equal volume of water, treated with an excess of barium chloride solution, and warmed three-quarters of an hour on the water-bath, for the full precipitation of all the simple sulphates. The filtrate is boiled with hydrochloric acid to decompose the conjugated acids and throw down their sulphuric acid as barium sulphate, which is then washed with hot

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[1] For *the Toxicology of Carbolic Acid*, including analysis, see Wharton and Stillé, "Med. Juris.," 4th ed. 1884, vol. 2, p. 96. Blyth's "Poisons," London, 1884. ENGEL, 1881: *Ann. Chim. Phys.* [5] 20, 230; *Jour. Chem. Soc.*, 40, 114. BISCHOFF, On distribution in the body, 1883: *Ber. d. chem. Ges.*, 16, 1337; *Jour. Chem. Soc.*, 44, 1020.

[2] BAUMANN, supported by CLOËTTA and SCHAER.

alcohol to remove resins, etc., and prepared for weighing. The phenylsulphates are more easily decomposed by mineral acids and heat than the phenolsulphonates. From the weight of barium sulphate obtained by decomposition of the phenylsulphates the quantity of excretory phenol is calculated:

$$BaSO_4 : C_6H_6O :: 232.8 : 94.0 :: 1 : 0.40378.$$

The phenol of the urine may also be estimated by distilling at length, adding hydrochloric acid to liberate phenol from the phenylsulphates, and determining the phenol, in the distillate, by the volumetric method with bromine.

In separation by solvents, ether, hot water, and alkaline water are most serviceable, but carbon disulphide, benzene, and chloroform may be employed. Petroleum benzin takes up but traces. Ether extracts the phenols from aqueous solutions not alkaline, and from other materials not acted on by the ether. It is to be applied in repeated portions till no more phenol is obtained. Liquids are to be shaken with the ether in a test-glass or stoppered cylinder, when the ether-layer is allowed to rise and is taken off. This is well done, exactly as water is expelled from an ordinary wash-bottle, the delivery tube (not too large) playing up and down in the stopper to take up the ether (p. 36). Or, with use of a separator, the watery layer may be drawn away. The ether may be removed by spontaneous evaporation, or in a current of warm air driven by a bellows or drawn by a filter-pump, with very little loss of the phenol. But to prevent this loss it is well, if the operation permits, to add enough water, made slightly alkaline with potassium hydrate, to take up the phenol from the ether-solution. Hot water extracts carbolic acid from fats, a very thorough application being needful. From animal tissues acidulated hot water has been mostly used, sulphuric acid acidulation being preferred. JACOBSEN (1885) extracted with benzene or ether.[1] Materials not at all acted on by alkalies may be most efficiently exhausted of phenol by water alkaline with about nine per cent. of potassium hydrate. The water solutions, neutral or acid, if pure enough to require no further separation, are ready for precipitation of phenols by bromine, as directed for the Quantitative work.

In the valuation of Crude Carbolic Acid the per cent. of tar-oils is briefly found (ALLEN) by shaking, in a graduated tube

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[1] W. JACOBSEN, 1885: Dorpat Dissertation: *Zeitsch. anal. Chem.*, 25, 607.

or jar, with a nine per cent. caustic soda solution, and reading off the resulting layers of undissolved liquid (substances besides phenols and water). But some naphthalene and other non-phenol bodies are dissolved by the alkali, which therefore must be as dilute as will barely dissolve the phenols. An equal volume of petroleum benzin previously added, and accounted for, diminishes the solution of "tar-oils" by the alkali. An assay *by distillation* of the crude carbolic acid is used at works (Charles Lowe[1]), the phenol distillates being compared in solidifying points with known mixtures of good carbolic and cresylic acids.

Phenols may be separated or estimated in special cases by conversion into *phenolsulphonic acid.* The latter may be obtained in its soluble barium salt, and the barium precipitated as a sulphate, one molecule of barium sulphate denoting one molecule of the phenol, the same as from the phenylsulphate above given. The formation and characteristics of the phenolsulphonates are to be observed, as given under Sulphocarbolates.

f.—Quantitative.—For chemical estimation the precipitation with **bromine** appears to be best suited. The precipitate was stated by Landolt[2] to be $C_6H_3Br_3O = 330.4$; and when it was washed with water, and dried in a desiccator, this author obtained fair gravimetric results. The precipitate, however, is not easily washed, and it both melts and vaporizes on the water-bath. **The volumetric** method is more satisfactory. Waller[3] employs an aqueous solution of bromine by which the solution estimated is exactly compared with a solution of phenol of known strength. Koppeschaar uses a standardized solution of $5KBr + KBrO_3$, added in excess, then acidulates, and titrates back with thiosulphate solution (also used to standardize the bromide), with use of iodide as an indicator.[4] Seubert,[5] estimating phenol *in Surgical Dressings*, found it necessary to filter before adding the iodide, as tribromophenol liberates iodine from iodide. Weinreb and Bondi[6] report that the precipitate is *not* $C_6H_3Br_3O$, but $C_6H_2Br_4O$ or $(C_6H_2Br_3OBr)$, and that Koppeschaar's correct results were indebted to the reaction with the iodide of potassium used as an indicator (in presence of the pre-

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[1] Allen's "Commercial Organic Analysis," 1879, i. 311.

[2] *Ber. d. chem. Ges.*, 4, 770; *Chem. News*, 44, 217. See Weinreb and Bondi, below.

[3] 1881: *Chem. News*, 43, 157.

[4] 1876: *Zeitsch. anal. Chem.*, 15, 233; *Jour. Chem. Soc.*, 31, 746. Degener, 1878: *Jour. pr. Chem.* [2] 17, 390; *Jour. Chem. Soc.*, 34, 918.

[5] 1882: *Arch. Phar.* [3] 18, 321; *Jour. Chem. Soc.*, 42, 106.

[6] 1885: *Monat. f. Chem.* (1885), 6, 506; *The Analyst*, 11, 39.

cipitate), whereby $C_6H_3Br_3O$ is at last formed, when (as Seubert states) iodine is liberated. CHANDELON[1] uses bromine dissolved in dilute alkali solution, as hypobromite, the estimation being applied *to the Urine*, as well as to surgical dressings. As to estimations in the urine and in dressings, the method of BAUMANN has been given under p. 402. The directions given by Dr. Waller, in the method first above named, are as follows :

Solutions required: (1) Ten grams pure crystallized phenol [of the dryness desired as a standard] in water to make 1 liter, a solution not suffering alteration for some months. (2) A solution of bromine in water. (3) Diluted sulphuric acid, of 15 to 20 per cent. strength, saturated with alum. This is needed to enable the precipitate to settle. Of the sample 10 grams are introduced into a liter-flask, water is added, with agitation, to make one liter, the solution mixed and some of it filtered (through a dry filter). Of the clear filtrate 10 c.c. are run into a six or eight ounce glass-stoppered bottle, and about 30 c.c. of the alum solution are added. In another bottle of the same kind 5 c.c. or 10 c.c. of the standard phenol solution are taken, again with about 30 c.c. of the alum solution. Bromine solution is now added, from the burette, to the bottle containing standard phenol solution, till no more precipitate forms, the bottle being stoppered and shaken after each addition, for the separation of the precipitate, and the end-reaction being further indicated by appearance of a yellow color in the clear solution when a very slight excess of the bromine is reached. Near the end the precipitate forms slowly. The solution from the sample is titrated in the same way. Then, c.c. of bromine-water required for 10 c.c. standard phenol sol. : c.c. bromine-water required for 10 c.c. from sample :: 100 : x = percentage of the standard phenol in the sample.

g.—Impurities in Carbolic Acid.—Alkaline dilutions are revealed by their alkaline reaction, and by giving a precipitate when neutralized by adding dilute sulphuric acid. If an article presented as liquid carbolic acid, pure or impure, is freely miscible with water, it may be either the very dilute carbolic acid water or an alkaline mixture. Regarding the Tar Oils see p. 404. Concerning the quality of "Carbolic Acid of America," E. M. HATTON, 1886: *Proc. Am. Pharm.*, **34**, 70.

SULPHOCARBOLATES.—Salts of phenolsulphonic acid, C_6H_4.

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[1] 1882: *Bull. Soc. Chim.* [2] **38**, 69; *Jour. Chem. Soc.*, **44**, Abstracts, 124. Further, CLOETTA and SCHAER, 1881–82: *Jour. Chem. Soc.*, **42**, 106.

$OH . SO_3H$ ($C_6H_6SO_4 = 174$, monobasic). *Phenolsulphonates.* Sulphophenates. Phenolsulfosäuresalz.—There are two phenolsulphonic acids easy of production and liable to occur in sulphocarbolates of commerce—namely: (1) Phenol orthosulphonic acid, having $OH : SO_3H = 1 : 2$, produced by continued contact of phenol and concentrated sulphuric acid in equal parts at ordinary temperatures, and the proper constituent of medicinal sulphocarbolates. (2) Phenol para-sulphonic acid, $OH : SO_3H = 1 : 4$, produced by heating the ortho acid. Phenol disulphonic acid, $C_6H_3 . OH . (SO_3H)_2$, is formed by heating phenol with excess of sulphuric acid.[1] Cresolsulphonic acid and xylolsulphonic acid are formed when crude carbolic acid or other mixtures of cresol and xylol are digested with concentrated sulphuric acid.

In preparing phenolorthosulphonic acid equal parts of phenol and concentrated sulphuric acid are mixed, after twenty-four hours water is added, and, in some way, the (unavoidable) free sulphuric acid is removed. This may be done by saturating both the phenolsulphuric and sulphuric acids with barium carbonate and filtering; or by carefully saturating only the sulphuric acid, so that the filtrate shall precipitate neither a barium salt nor a sulphate; or by saturating both acids with sodium carbonate, evaporating, dissolving the phenolsulphate in alcohol, and crystallizing from the filtrate. The higher the temperature of action of the sulphuric acid, and the greater the excess of this acid, the more of phenolparasulphonic acid will result, and its production is not wholly avoided in any case.

The potassium phenolorthosulphonate melts at 240° C., and crystallizes in needles with two molecules of water; the potassium phenolparasulphonate melts above 260° C. and crystallizes, anhydrous, in hexagonal plates.[2] Phenolsulphonates are decomposed with reproduction of sulphuric acid, by boiling with nitric acid or with hydrochloric acid, and slowly by boiling with water. The nitric acid reacts vigorously, as with phenol, forming nitrophenic acids. Even in water solution at ordinary temperatures free phenolsulphonic acid suffers gradual decomposition.

The metallic sulphocarbolates are all measurably soluble in water, the barium and lead salts included (separation from sulphates). The sodium salt is $NaC_6H_5SO_4 . 2H_2O$. The alkali

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[1] Sulphuric acid, $HO(SO_3H)'$ or $HO(SO_2)''OH$
Phenolsulphonic acid, $HO . C_6H_4 . SO_3H$ [$C_6H_6SO_4$]
Phenoldisulphonic acid, $HO . C_6H_3 . (SO_3H)_2$
Phenylsulphuric acid, $C_6H_5O . SO_3H$ [$C_6H_6SO_4$]

[2] "Watts's Dictionary," viii 1538.

sulphocarbolates are soluble in much alcohol (another separation from sulphates). Further, the sulphocarbolates are *identified* by giving the chief reactions of phenol—those with nitric acid, bromine, and ferric chloride—and by giving the reactions of sulphates only after decomposing with boiling nitric or hydrochloric acid.

PHYSETOLEIC ACID. See Fats and Oils, pp. 246, 250.

PICRACONITINE. See Aconite Alkaloids, pp. 18, 20.

PITURINE. See Midriatic Alkaloids, p. 341.

PLANT ANALYSIS.—*The chemical analysis of vegetable tissues.* Phytochemical analysis.

Systematic methods of chemical analysis of plants have been presented as follows:

Frederick Rochleder, M.D., professor of organic chemistry in the University of Prague, 1858: Würzburg, Germany. English translation by William Bastick, London, 1860: *Phar. Jour. Trans.* [2] 1, 562. Same translation revised by Professor John M. Maisch, Philadelphia, 1860: *Am. Jour. Phar.*, 33, 81, *et seq.*; reprinted in 80 pages, 1862.

Dr. G. C. Wittstein, München, 1868: "Anleitung zur chemischen Analyse von Pflanzentheilen auf ihre organischen Bestandtheilen," 355 pp., Nördlingen. An English translation, "The Organic Constituents of Plants and their Chemical Analyses," by F. von Mueller, Ph.D., F.R.S., Melbourne, 1878, pp. 332. The "plant analysis" is included in Part II., 49 pages.

Henry B. Parsons, Ph.C., assistant chemist in the Department of Agriculture, Washington, 1880: "A Method for the Proximate Chemical Analysis of Plants," *American Chemical Journal*, 1, 377–391; *Am. Jour. Phar.*, 52, 210; *Phar. Jour. Trans.* [3] 10, 793; *Jour. Chem. Soc.* (abstract), 38, 754; *Ber. d. chem. Ges.*, 13, 1370; *Chem. News* (in full), 41, 256, 267: *Year-book of Phar.*, London, 1880, 50: *Jahres. d. Pharm.*, 1880, 99; Allen's "Commercial Organic Analysis," London, second edition, 1885, i. 356 (tabulated abstract); Lyons's "Pharmaceutical Assaying," Detroit, 1886, p. 37 (tabulated abstract).—*Given in full in the following pages.*

Georg Dragendorff, professor of pharmacy in the University of Dorpat, Russia, 1882: "Die qualitative und quantitative Analyse von Pflanzen und Pflanzentheilen," 285 pp., Göttingen. An English translation by Henry G. Greenish, London, 1884: "Plant Analysis: Qualitative and Quantitative," 280 pp. A French translation in Fremy's "Encyclopédie Chimique," Paris, 1885, tome viii. (from the author, without credit to previous publication). *An outline of Dragendorff's scheme is given in the following pages.*

Good examples of plant analysis, chiefly according to Dragendorff's scheme, have been presented by Helen C. DeS. Abbott, Philadelphia. In 1884, analysis of "Fouquiera splendens," *Proc. Am. Assoc. Adv. Sci.*, 33, 190; *Am. Jour. Phar.*, 57, 81. In 1885, analysis of "Yucca angustifolia," *Proc. Am. Assoc. Adv. Sci.*, 34, 125 (abstract).

Other examples are found in reports of results by Parsons's scheme as follows: John Hoehn, Ann Arbor, 1882, analysis of "cheken leaves," *Contributions Chem. Lab. Univ. Mich.*, 1, 39 (abstract). William Heim, Ann Arbor, analysis of "Piscidia erythrina," *ibid.*, 1, 38 (abstract); *Ther. Gazette*, 1882, p.

254. Henry Palmer, Ann Arbor, analysis of "Viburnum lentago," *Proc. Mich. State Phar. Assoc.*, 3 (1885), 158.

Results of plant analyses by Mr. Parsons himself are extant as follows: Analysis of "damiana" (Turnera aphrodisiaca), 1880: *New Remedies*, 9, 261; *Phar. Jour. Trans.* [3] 11, 271. Of "Eupatorium perfoliatum," 1879: *Am. Jour. Phar.*, 51, 342; *Archiv der Phar.* [3] 15, 557. Of "Berberis aquifolium (var. repens)," 1880: *New Remedies*, 11, 83; *Phar. Jour. Trans.* [3] 13, 46; *Ber. d. chem. Ges*, 15, 2745. Of "Ustilago maidis (corn smut)," 1880: *New Remedies*, 11, 80; *Phar. Jour. Trans.* [3] 12, 810. Plant analyses in the Reports of the Department of Agriculture at Washington, for 1880, 1881, 1882, as accredited to Mr. Parsons by the chemist, Dr. Collier. See also an excellent article by Mr. Parsons on "Some Constituents of Plants," 1879: *New Remedies*, 8, 168.

PARSONS'S METHOD FOR THE CHEMICAL ANALYSIS OF PLANTS.[1]

Prefatory.—It must be premised that no one method is applicable in all cases, and that the operator will so modify and adapt the proposed processes as to best attain the truths he seeks. If the present scheme shall serve merely as an example, to be improved upon as discoveries multiply, it will at least have served to stimulate to the more thorough study of a much-neglected yet very important branch of analysis. The student, when first entering upon the study of plant analysis, is perplexed and disheartened, owing to the lack of any elementary treatise in which he may find directions for the quantitative estimation of the various plant constituents. The works of Rochleder and Wittstein, while giving most valuable assistance in the investigation of special constituents and their separation from large quantities of the crude herb, still fail to give clear and practicable directions for the quantitative estimation of each constituent. Von Mueller's latest enlarged edition of Wittstein's "Plant Analysis" gives a scheme, most excellent in many respects, yet cumbered with tiresome methods of extraction and manipulation, which serve to unnecessarily lengthen the time required for making the analyses, without increasing the accuracy of results obtained.

Too many American analyses of plants have been summarized thus: "The plant contains gum, resin, tannin, a volatile oil, and a peculiar bitter principle, to which may be ascribed its medicinal activity." The foreign journals bring occasionally most excellent examples of accurate examinations of vegetable substances; as instances may be cited the examination of ginger, by J. C. THRESH,[2] and of ergot,[3] aloes,[4] and other articles by Prof. DRAGENDORFF. To these sources the student must look for his best models (p. 407 and above).

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[1] The publications of this method are cited above, p. 407. Mr. Parsons disclaimed any aim to originality, in the resources used in the scheme (presented at request of the author of this work), but submitted the plan as an outgrowth of his own experience, in a varied practice of chemical analysis of plants and vegetable tissues.

[2] *Phar. Jour. Trans.* [3] 10, 81, Aug., 1879; *Am. Jour. Phar.*, 1879, 51, 519.

[3] *Phar. Jour. Trans.* [3] 6, 1001, June 17, 1876; *Am. Jour. Phar*, 1876, p. 413; 1878, p. 335.

[4] "Werthbestimmung," 1874, p. 110.

In following the plan now presented, the use of the apparatus for continuous percolation is strongly urged for the extractions with benzene, alcohol, and other volatile solvents. A very simple and inexpensive "*extraction apparatus*" has been described by various American and foreign chemists.[1]

"In any convenient water-tight vessel is a worm of block-tin pipe, having an internal diameter of 9 mm. and a length of about 2.5 meters. The lower (external) part of this worm is fitted by an ether-soaked velvet cork to a glass percolator having a diameter of 4 cm., a length of 20 cm. to the constriction, and 5 cm. below. Within this percolator is a smaller tube, flanged at the top and bottom, and suspended by fine platinum or copper wires. This tube has a diameter of 2.5 to 2.8 cm. and a length of 14 cm.; the bottom is covered by filter-paper and fine washed linen,[2] tied on by linen thread. The weighed sample of the finely powdered herb is placed within this tube for extraction. A light glass flask, weighing about 30 grams, is fitted by an ether-soaked cork to the outer percolator." Having introduced the solvent into this glass flask, the connections are made secure, and heat is applied by a water-bath to the flask. If the liquid is too slowly volatilized the addition of a little common salt to the water in the bath serves to remove the trouble.

Next in importance is the use of a good tared filter. The form originally presented by F. A. GOOCH [3] leaves little to be desired. It may be made by perforating with fine holes the bottom of an ordinary platinum crucible, and fitting it accurately to a perforation made in a large rubber cork; this cork connects it with a receiving vessel, which in turn is connected with a Bunsen's pump. Fine asbestos suspended in water is poured into the crucible, the air exhausted from the receiving vessel, and thus a firm, thin layer of asbestos is deposited on the bottom of the crucible. After ignition and weighing, the crucible is ready for the reception of any precipitate which it is desired to separate and weigh.

The use of these two pieces of apparatus will eliminate two grave sources of error, viz., incomplete extraction of soluble matters, and inaccuracies introduced by the use of tared paper filters.

The other necessary apparatus is simple, and includes one or more platinum crucibles and evaporating dishes, accurate burettes and graduated cylin-

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[1] B. TOLLENS: *Zeitsch. anal. Chem.*, 17, 320 (1878); *New Remedies*, 7, 335, Nov., 1878. W. O. ATTWATER: *Proc. Am. Chem. Soc.*, 2, 85 (illustrated). S. W. JOHNSON: *Am. Jour. Sci.*, 13, 196. H. B. PARSONS: *New Remedies*, 8, 293 (illustrated), Oct., 1879. F. SOXHLET, 1879: *Ding. polyt. Jour.*, 232, 461; *Zeitsch. anal. Chem.*, 19, 365. MEDICUS, 1880: *Zeitsch. anal. Chem.*, 19, 163; *New Remedies*, 9, 167 (illustrated).

[2] In place of the linen and filter-paper may be substituted fine brass or platinum wire gauze. Asbestos suspended in water may then be poured in to form a fine felt. The tube can then be dried and weighed, and the amounts extracted may be found by the loss of weight of the tube and substance. A little experimentation will show the operator how to prepare and use the tube. It is but an adaptation of the Gooch's Filter here recommended.

[3] *Proc. Am. Acad. Sci.*, 13, 342 (1878); *New Remedies*, 7, 200 (Oct., 1878); *Am. Chem. Jour.*, 1, 317 (illustrated).

ders, a good balance sensitive to at most 0.0005 gram, and the ordinary glass and porcelain-ware found in all laboratories.

It is assumed that whoever attempts the analysis of a plant is informed as to the normal constituents to be sought, and that he has had considerable experience in inorganic analysis and in the identification of the principal classes of proximate constituents which he now undertakes to estimate quantitatively. Accordingly, tests for identification will not be here presented; they should, however, never be omitted. The necessity of recording in detail all physical and chemical peculiarities with every weight that is taken is self-evident.

I. *Preparation of Sample.*

The air-dry specimen should be carefully examined, and all extraneous substances removed. The entire sample should then be ground, or beaten in an iron mortar, until it will all pass through a sieve having from 40 to 60 meshes to the linear inch. After thoroughly mixing this sample, take of it about 100 grams, which should be further pulverized until it will all pass through a sieve having from 80 to 100 meshes to the linear inch. From this smaller portion remove all iron, derived from mill or mortar, by use of a magnet. Then place in a clean, dry bottle, which should be labelled and securely corked. This small sample is for the analysis; the larger portion should be reserved for the separation of those proximate principles which seem, from the analysis, to be worthy of more extended investigation.

II. *Estimation of Moisture.*

Dry rapidly, at 100° to 120° C., two or more grams of the sample; the loss of weight equals moisture and occasionally a little volatile oil. In some cases it is best to dry at a lower temperature, and at other times the drying should be conducted in a stream of hydrogen or carbonic anhydride.[1]

III. *Estimation of Ash.*

In a weighed crucible gently ignite two or more grams of the sample until nearly or quite free from carbonaceous matter; the heat should not be permitted to rise above faint redness, or loss of alkaline chlorides may occur. Weigh this residue as *crude ash*, and in it determine:

a.—Amount Soluble in Water.—This portion may contain chlorides, sulphates, phosphates, and carbonates of potassium and sodium; also slight amounts of chlorides and sulphates of calcium and magnesium.

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[1] On treatment of fresh plants for drying, and on methods of powdering, see Dragendorff's "Plant Analysis," London edition, p. 6.

b.—Insoluble in water; Soluble in Dilute Hydrochloric Acid.—The residue from *a* should be treated with a slight excess of hydrochloric acid, and evaporated in a porcelain dish over a water bath until all free acid has been expelled; it should then be again moistened with hydrochloric acid, water added, and be filtered from any remaining insoluble substances. This treatment removes carbonates (with decomposition) and phosphates of calcium and magnesium, sulphate of calcium, and oxides of iron and manganese.

c.—Insoluble in Water; Insoluble in Dilute Hydrochloric Acid; Soluble in concentrated Sodium Hydrate.—Boil the residue from *b* with a solution containing about 20 per cent. of sodium hydrate. This treatment removes combined silica of the ash. The residue still insoluble is sand and clay which adhered to the specimen; this residue should be separated, washed thoroughly, and weighed.

Always determine the amounts removed by the above treatment by weighing the dried, undissolved residues. The ash, as thus estimated, usually includes a little unconsumed carbon, together with more or less carbonic anhydride, most or all of which was not originally present in the plant, but was produced by the combustion of the organic matter. For most purposes it is unnecessary to estimate and exclude from the ash this carbonic anhydride; where great accuracy is desired, a complete quantitative analysis should be made, the amount of each base and acid being determined, and in the statement of results only those should be included which existed originally in the plant. For this purpose it is necessary to burn from 20 to 100 grams of the sample; for further directions consult text books on agricultural and inorganic analysis.

IV. *Estimation of Total Nitrogen.*

In half a gram or more of the sample determine total nitrogen by combustion [p. 230 or 229]. If later in the analysis no other nitrogenous substances are discovered, calculate the total amount of nitrogen to albuminoids by multiplying by 6.25 [or 6.33]. When other nitrogenous compounds are present, their content of nitrogen should be determined directly or by difference; after proper deductions have been made, the remaining nitrogen should be calculated to albuminoids.

V. *Estimation of Benzene Extract.*

In a suitable extraction apparatus completely exhaust 5 grams of the sample with pure coal-tar **benzene** (sp. gr. 85–88, boiling at 80° to 85° C., leaving no residue when evaporated). The extraction requires from four to six hours' continued action of the solvent. Carefully evaporate this liquid to dryness in a weighed dish, and record its weight as *total benzene extract.* This extract may contain volatile oils and other aromatic compounds, resins, camphors, volatile or non-volatile organic acids, wax, solid fats, fixed oils, chlorophyll, other colors, volatile or fixed alkaloids, glucosides, almost no ash.

To the weighed extract add water, again evaporate on the water-bath, and complete the drying in an air-bath at 110° C. In absence of other vaporizable substances the loss of weight approximates the amount of *volatile oil.* If the presence of a volatile alkaloid is suspected (from a characteristic odor or an alkaline reaction), add a drop of hydrochloric acid to prevent its volatilization. Camphors are partially dissipated by this treatment; hence, when they are present, this evaporation should be dispensed with.

Treat now the residue with a moderate amount of warm water, allow to stand until cool, then filter through fine paper by aid of a Bunsen's pump. In half of the aqueous filtrate determine *total organic matter* and *ash;* test the remaining half for *alkaloids*, *glucosides*, and *organic acids* by salts of lead, silver, barium, and calcium. Care must be taken not to mistake a slight amount of suspended matter, frequently resinous, for other substances actually soluble in water.

The still undissolved residue should be again removed from filters and dishes by solution in benzene, the benzene solution being again evaporated to dryness. Treat this residue with warm, very dilute hydrochloric acid, allow to cool, and filter through paper. The filtrate should be tested for *alkaloids* and *glucosides.* The amount extracted by acid, if any, may be determined by weighing the still undissolved residue. Treat this residue with several considerable portions of 80 *per cent. alcohol* (sp. gr. 0.8483 at 15.6° C.), allowing at least an hour for each treatment. Filter through paper and determine by evaporation the matter dissolved; this usually consists of *chlorophyll* with one or more *resins*, which may sometimes be separated by use of *petroleum benzin*, *chloroform* or similar solvents. *Purified animal charcoal* removes *chlorophyll* and *some resins* from alcoholic solution, while certain other resins are not removed. If *camphors* were present in the plant, the greater portion will be found in the alcoholic liquid.

The substances undissolved by 80 per cent. alcohol may be *fixed oil, solid fat*, *wax*, and very rarely a *resin;* their separation may be attempted by refrigeration and pressure, or by use of ether, chloroform, etc.

Recapitulation (*portion soluble in benzene or chloroform*).

1. Loss by evaporation, with precautions: *volatile oil.*
2. Soluble in water: *alkaloids*, *glucosides*, *organic acids.*
3. Insoluble in water: Soluble in dilute acids: *Alkaloids*, possibly *glucosides.*
4. Insoluble in water. Insoluble in acids. Soluble in 80 per cent. alcohol.
    - *a.* Removed by animal charcoal: *chlorophyll*, *some resins.*
    - *b* Not removed by animal charcoal: *some resins.*
5. Insoluble in water: Insoluble in dilute acids: Insoluble in 80 per cent. alcohol: *Wax*, *fats*, *fixed oils.*

It is frequently advantageous to extract the plant with petroleum benzin (sp. gr. 0.66 to 0.70, boiling at about 50° C., wholly volatile) before treatment with benzene; by reference to the accompanying table of comparative solubilities (p. 422) it will be seen that this treatment may serve to separate fixed and volatile oils, and some resins and colors, from certain solid fats, wax, other resins and colors.

Where *benzene* of sufficient purity cannot be had, pure *chloroform* is the best substitute. The use of ether is objectionable in this place, as its solvent properties are less distinctly marked than are those of benzin, chloroform, and benzene; in other words, more plant constituents are sparingly soluble in ether than in the above-mentioned solvents. Consequently many substances which should properly be extracted by 80 per cent. alcohol will be sparingly dissolved if ether were used, while benzene, chloroform, and benzin would have no perceptible solvent action upon them; tannic acids may be cited as instances illustrating this point.

VI. *Estimation of* 80 *per cent. Alcohol Extract.*

That part of the plant not dissolved by benzene should be dried at 100° C., and then completely exhausted by 80 per cent. alcohol (sp. gr. 0.8483 at 15.6° C.) This requires from 12 to 14 hours' continuous treatment with the solvent. Remove, dry, and weigh any crystals or powder that may separate upon concentrating and cooling the alcoholic percolate. Make the clear liquid to a definite volume (say 200 c.c.) by adding more 80 per cent. alcohol.

AN ALIQUOT PART (usually 20 c.c.) of this volume of liquid is evaporated to dryness for weight (m) of organic matter with ash, the residue then ignited for weight (n) of ash, to find by difference ($m - n$) *the amount* (o) *of organic matter in VI.* ANOTHER EQUAL ALIQUOT PART (20 c.c.) is evaporated to remove all alcohol, treated with water, filtered, and the filtrate and washings evaporated to dryness to find the weight (p) of organic matter and ash that are soluble in water, the residue then ignited for weight (q) of ash that is soluble in water. Then $p - q = r$, *the amount of organic matter* (*in VI.*) *soluble in water.*

If the plant contain much sugar or much tannin, it will be desirable to proceed now, in separation by water, as directed further on for "*the second way.*" Otherwise proceed *in separation by absolute alcohol,* in "*the first way,*" as follows: THE REMAINING ALIQUOT PART (160 c.c.) of the clear alcoholic liquid should be evaporated carefully to dryness, the residue pulverized and treated with several considerable portions of absolute alcohol (sp. gr. 0.7938 at 15.6° C.)

A. *Soluble in Absolute Alcohol* (*from the portion* by 80% alcohol).

- *a. Soluble in water.*
  - *a′. Precipitated by subacetate of lead.*
    Tannin and most organic acids; some extractives; some inorganic acids of the ash. Weigh in Gooch's filter, ignite cautiously, and again weigh; loss equals organic matter precipitated.
  - *a″. Not precipitated by subacetate of lead.*
    Alkaloids, glucosides, some extractives and colors. Determine weight by difference between *a* and *a′*.
- *b. Insoluble in water.*
  - *b′. Soluble in dilute hydrochloric acid.*
    Alkaloids, glucosides (rarely), some extractives. Determine weight by difference between *b* and *b″*.
  - *b″. Insoluble in dilute hydrochloric acid.*
  - *b‴. Soluble in dilute ammonium hydrate.*
    Most acid resins, some colors. Determine weight by difference between *b″* and *b⁗*.
  - *b⁗. Insoluble in dilute ammonium hydrate.*
    Neutral resins, some colors, albuminoids (in some seeds).
    Redissolve in alcohol, evaporate, and weigh.

B. *Insoluble in Absolute Alcohol* (*from portion* by 80% alcohol).

c. Soluble in water.

c′. Precipitated by subacetate of lead.

Some colors, extractives, albuminoids (rarely), organic acids, and inorganic acids of the ash. Weigh in Gooch's filter, ignite cautiously, and again weigh; loss equals organic matter precipitated.

c″. Not precipitated by subacetate of lead.

Alkaloids, glucosides, glucose, sucrose, some extractives. Determine by difference between *c* and *c′*. Remove Pb by H_2S, H_2SO_4, Na_2CO_3, or other means, and titrate for sucrose and glucose.

d. Insoluble in water.

d′. Soluble in dilute hydrochloric acid.

Some alkaloids and glucosides. Determine by difference between *d* and *d″*.

d″. Insoluble in dilute hydrochloric acid.

Few resins, some extractives and color substances. Dissolve in alcohol, evaporate, and weigh in a tared dish.

"*The second way": primary division of constituents in VI., by solubility in water.*—In some cases it may be preferable to use the following *method for analysis of the* 80 *per cent. alcohol extract;* it is more desirable when the plant examined contains a considerable amount of sugars, tannic acid, etc.

Alcohol Extract, dilute to 200 c.c. with 80 per cent. alcohol.—1. In 20 c.c. determine *total organic matter* and *ash*. Then, 2, in 20 c.c. determine *total organic matter* and *ash* that are *soluble in water*, and, by difference, *total organic matter insoluble in water*, as directed in "the first way."

3. Evaporate the remaining 160 c.c. to dryness, treat with water, filter, and make the filtrate measure 160 c.c. Reserve the insoluble matter on the filter for examination (10).

4. In 20 c.c. of the aqueous solution *estimate the tannin.*[1]

5. Precipitate 20 c.c. by normal acetate of lead, and determine, as before described, the amount of organic matter after drying at 100° to 120° C. This precipitate will contain, if the substances are present in the plant, *tannic, gallic,* and most other *organic acids*, some *colors*, rarely *albuminous substances*, some *extractives*, and most *inorganic acids* of the ash. Determine, by difference, the amount not precipitated by this treatment.

6. In 20 c.c. determine in like manner the amount precipitated by basic acetate ("subacetate") of lead. This reagent precipitates a greater number of *acids, colors,* and *extractives* than are precipitated by the normal acetate, hence it is frequently possible to estimate such substances by subtracting the amount precipitated by one reagent from the amount precipitated by the other. To the filtrate add a slight excess of dilute hydrochloric acid, boil gently for half an hour, and determine in the liquid *total glucose* by use of Fehling's solution.

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[1] For this estimation methods are given in the article on Tannins in this work. Mr. Parsons advised the gravimetric method of Carpeni (1875: *Jahr. der Chem.*, 989; *Chem. News*, 31, 282). Precipitate by ammoniacal acetate of zinc, use a Gooch's filter, wash the precipitate with very weak ammonia, dry at 120° C., weigh, ignite cautiously, again weigh. The loss by ignition equals tannic acid, in absence of certain interfering substances.

7. Precipitate 20 c.c. by subacetate, exactly as in 6, and use the precipitate as a duplicate to check the amount there estimated. To the filtrate add a very slight excess of solution of carbonate of sodium, filter from the carbonate of lead, wash well with water containing a little alcohol, and in the filtrate estimate *actual glucose.* If the glucose thus found is appreciably less than that in 6, subtract it from that amount; this glucose may be due to the presence in the plant of *sucrose* or some *glucoside.* If due to sucrose, the amount of the latter may be found by multiplying this residual glucose by 0.95; if to a glucoside, a fit subject for an extended investigation is presented. The properties, formula, and decomposition products of the newly found glucoside should be carefully studied.

8. Precipitate 20 c.c. with subacetate of lead, as in 6 and 7, employing the precipitate as material from which to separate organic acids, after removal of lead by sulphuretted hydrogen. Acidulate the filtrate with sulphuric acid, add an equal volume of alcohol, allow to stand two hours, filter, wash the precipitate with 50 per cent. alcohol, and evaporate the filtrate until all alcohol has been dissipated. Test the acid solution for *alkaloids, glucosides, sugars, extractives.*

9. Reserve the remaining 40 c.c. for duplicating any unsatisfactory determinations.

10. The residue mentioned in 3 as insoluble in water may contain *resins, albuminoids* (especially from seeds), *colors, alkaloids, glucosides.* Dilute acids remove *alkaloids* and some *glucosides;* dilute ammonia water will remove some *resins, colors,* and *glucosides.* Any still insoluble residue probably contains *albuminous* or *resinous* substances.

VII. *Estimation of Cold Water Extract.*

That part of the plant remaining insoluble after treatment with alcohol should be dried at 110° C. and completely extracted by cold water. When the plant contains considerable mucilaginous matter this is best removed by placing the substance in a flask or graduated cylinder, and then adding a measured volume of cold water. Allow to macerate, with frequent agitation, for from 6 to 12 hours, then filter through fine washed linen, and evaporate an aliquot portion of the solution. In this residue determine *total organic matter* and *ash.* This residue usually contains little but *gum;* in analysis of fruits and fleshy roots, *pectin bodies, salts of organic acids,* rarely a substance resembling *dextrin,* and small amounts of *albuminous substances* and *coloring matter.* Usually the separation of these substances is very difficult. The unevaporated liquid should be used for such qualitative reactions as are necessary to show the nature of the substances extracted. The insoluble residue should be well washed with water, transferred to a crucible, and completely dried at 110° C. This residue should then be weighed.

VIII. *Estimation of Acid Extracts.*

The dried residue insoluble in cold water should be transferred to a beaker containing 500 c.c. of water and 5 c.c. of concentrated sulphuric acid (sp. gr. 1.84). Boil for 6 hours on a gauze support, adding water to keep the volume of liquid unchanged; if the substance be very starchy a longer boiling may be necessary. This treatment will convert *starch* and its *amorphous isomers* to dextro-glucose, and will occasionally remove some *salt of an organic acid*, with usually traces of *albuminous* and *indeterminate* substances.

The *total amount extracted* may be found by washing, drying at 110° C., and weighing the yet insoluble residue, and subtracting the weight from the one taken after extracting with cold water. The amount of *starch and isomers* may be found by determining in a given volume of the acid filtrate the amount of *glucose*, using Fehling's solution; the glucose thus found multiplied by 0.9 equals starch and isomers. The *total extract* minus *starch and isomers* equals *acid extract not starch.* This includes a small amount of *ash*, which may be approximately determined by evaporating and igniting a known volume of the solution.

Where it is wished to separate the extracted matter from the sulphuric acid, boil the liquid with an excess of powdered barium carbonate until no acid reaction remains. Filter and evaporate to dryness. The residue consists chiefly of hydrated dextro-glucose ($C_6H_{12}O_6.H_2O$), with some ash.

IX. *Estimation of Alkali Extract.*

Wash well and dry at 110° C. the residue from treatment with acid, and record its weight. Boil this residue for two hours with 500 c.c. of a solution containing 20 grams of sodium hydrate to the liter. Filter through fine washed linen, and wash the residue thoroughly with hot water, alcohol, and ether. Transfer it to a weighed crucible, dry at 110° to 120° C., and weigh the residue as *crude fibre* and *ash;* this weight subtracted from the previous one shows the *total alkali extract.* This extract is largely *albuminous matter* and various modifications of *pectic acid*, Fremy's "*cutose*," and various *coloring*, *humus*, and *decomposition compounds*, in small amounts. Most of the extracted substances may be precipitated by excess of an acid with or without the presence of alcohol.

X. *Cellulose.*

The crude fibre from IX. should be treated with from 50 to 100 c.c. of U. S. Ph. solution of chlorinated soda and allowed to stand twenty-four hours. If not then bleached white, slightly acidulate with hydrochloric acid and set aside for another day. Filter through fine linen or Gooch's filter, wash with hot water, dry at 110° to 120° C., and weigh, ash-free, as *cellulose.* The loss of weight by this treatment state as *lignose* and *color.*

Recapitulation of Parsons's Method.

I. Sampling, pulverization, and preservation of an air-dry portion in constant condition for an analysis.

II. Estimation of *moisture* by loss at 100°–120° C.

III. Estimation of *Ash.*

- *a.* Portion of the ash soluble in water.
- *b.* Insoluble in water; soluble in dilute hydrochloric acid.
- *c.* Insoluble in water or in the acid; soluble in sodium hydrate solution.

IV. Estimation of *the total nitrogen.* For check on results; for calculation of albuminoids after estimation of alkaloids, etc.

V. ESTIMATION OF PORTION SOLUBLE IN BENZENE (OR CHLOROFORM).

1. Portion of benzene extract vaporized with benzene: *volatile oils* (*camphors*).
2. Portion of benzene extract soluble in water: *alkaloids, glucosides, organic acids.*
3. Not soluble in water, soluble in dilute acid: *Alkaloids,* possibly *glucosides.*
4. Not soluble in water or the acid. Soluble in alcohol of 80%.
   - *a.* Removed by animal charcoal: *chlorophyll, some resins.*
   - *b.* Not removed by the charcoal: *some resins.*
5. Not soluble in water or the acid, or in alcohol of 80%: *Waxes, fats, fixed oils.*

VI. ESTIMATION OF PORTION SOLUBLE IN ALCOHOL OF 80% (after removal of V.) The solution is made up to a definite volume (200 c.c.) IN TWO EQUAL ALIQUOT PARTS (20 c.c. each) residues are obtained to furnish (1) *the amount of organic matter*, (2) *the amount of organic matter soluble in water*, thence *the amount of organic matter insoluble in water.*

IN "THE FIRST WAY" the constituents of VI., in the remaining 160 c.c., are primarily divided according to their solubility in absolute alcohol, then by further treatment, as follows:

A. *Soluble in absolute alcohol.*

a. Soluble in water. Weight obtained.

a'. Precipitated by subacetate of lead.

Tannin and most *organic acids;* some *extractives;* some inorganic acids of the ash. Weight of all obtained.

a''. Not precipitated by subacetate of lead.

Alkaloids, glucosides, extractives, colors.

$a - a' = a''$.

b. Insoluble in water. Weight obtained.

b'. Soluble in dilute hydrochloric acid.

Alkaloids, rarely glucosides, extractives.

$b - b'' = b'$.

b''. Insoluble in dilute hydrochloric. Weight taken.

b'''. Soluble in dilute ammonium hydrate.

Most acid *resins*, some *colors.*

$b'' - b'''' = b'''$.

b''''. Insoluble in the ammonia. Weight taken.

Neutral *resins*, some *colors*, *albuminoids.*

B. *Insoluble in absolute alcohol.*

c. Soluble in water.

c'. Precipitated by subacetate of lead.

Colors, *extractives*, rarely *albuminoids*, organic and inorganic *acids.* Weigh.

c''. Not precipitated by subacetate of lead.

Alkaloids, glucosides, glucose, sucrose, extractives.

$c - c' = c''$. Estimate sugars.

d. Insoluble in water.

d'. Soluble in dilute hydrochloric acid.

Alkaloids, glucosides. $d - d'' = d'$.

d''. Insoluble in dilute hydrochloric acid.

Few *resins*, extractives, colors. Weigh.

IN "THE SECOND WAY" the constituents of VI., taken in the remaining 160 c.c. of 80% alcohol solution, are primarily divided according to their solubility in water, then by other treatment, as follows: (3) Evaporate to dryness, add water, reserve the residue (10), and make the filtrate up to 160 c.c.

(4) In 20 c.c. estimate *tannin.*

(5) In 20 c.c. estimate total precipitate by lead normal acetate. *Tannins, acids* (inorganic and organic), *colors,* extractives.

(6) In 20 c.c. estimate total precipitate by lead basic acetate. Compare precipitate with that in (5). In filtrate estimate the *total glucose* of sugars and glucosides.

(7) In 20 c.c. duplicate the precipitation of (6). In filtrate estimate the *actual glucose.* Compare with total glucose.

(8) In 20 c.c. triplicate the precipitation of (6). Examine the precipitate for *alkaloids*, *glucosides*, *sugars*, extractives.

(9) Use the remaining 40 c.c. for additional examinations.

(10) The residue left in operation 3 may be tested for *resins*, *albuminoids*, *colors*, *alkaloids*, *glucosides.*

VII. ESTIMATION OF THE PORTION SOLUBLE IN COLD WATER (after removal of V. and VI.) Examine as directed in the text, making up the filtrate to a definite volume, and taking aliquot parts (1, 2, 3, 4, etc.) for determinations and tests. In (1) determine total solids, and then the ash, to find the *total organic substances. Gums*, *pectous substances*, *salts of organic acids*, *dextrins*, *soluble starches*, *albumens*, *colors.* Examine by solubilities, iodine test, estimation of nitrogen, etc.

The residue from solution VII., dried at 110° C., is weighed.

VIII. ESTIMATION OF PORTION SOLUBLE IN BOILING DILUTE ACID (after removal of V., VI., and VII.) The weight of the washed residue obtained for estimation of *the total solids* of VIII. *Starches* estimated by determination of glucose with Fehling's solution, first examining for interfering extractives of a reducing power. An aliquot portion of the liquid, freed from the sulphuric acid, is tested in portions qualitatively. Small amounts of albuminoids may be found.

IX. ESTIMATION OF PORTION SOLUBLE IN ALKALI-WATER (after removal of portions V. to VIII.) Take weight of insoluble washed residue, for estimation of *total solids. Albumens*, forms of *pectin*, *humus*, decomposition products, colors.

X. ESTIMATION OF THE RESIDUE LEFT BY SOLVENTS V. to IX. *Cellulose*, *lignose*, colors, ash. Estimate from separation by chlorinated soda solution.

Remarks.[1]

It is advisable to determine always, in addition to what has already been directed, the *amounts extracted directly from the sample by water, ether, alcohol of various percentages, methyl alcohol, benzin, chloroform, carbon disulphide, etc.* In each extract estimate *total organic matter* and *ash*, and determine qualitatively, and quantitatively when possible, its constituents, by treating with such solvents and reagents as are indicated. Each extract being composed of certain distinct substances, it is necessary to account for them in every case.

The amounts present of some constituents may be found by subtracting the weight extracted by some one solvent from the weight extracted by some other. It will be seen that this is a method of limited applicability, which can only be applied in those cases where the difference between the solvent action of the two liquids is very sharply defined. Certain special methods for the estimation of single constituents may be used, care being taken that all interfering substances be first removed. The methods of preparation of known substances as given in Husemann's "Pflanzenstoffe," and to a considerable extent in "Watts's Dictionary," may serve as suggestions for work. Treatment with benzene, 80 per cent. alcohol, and water, removes from nearly all plants the constituents of greatest chemical and medicinal interest, but in analyses of grains, fodder, and food materials, those compounds extracted by dilute acids and alkalies have great value. There are substances in plants, seemingly isomers of starch and cellulose, which have properties more or less resembling those of cellulose, and are changed by boiling with dilute acids to glucose. In absence of an established nomenclature it has seemed best to use the terms "starch isomers" or "amylaceous cellulose" for these substances,[2] while those constituents, *not albuminous*, which are removed by dilute alkali have been termed "alkali extract." These substances have been investigated by various chemists, but no definite and authoritative nomenclature has yet been adopted. Thomsen gives the name "holz-gummi,"[3] *wood-gum*, to a white substance extracted from plants by dilute sodium hydrate, while Fremy regarded these various compounds as modifications of pectic acid, pectin, and "cellulose bodies."[4] Starch also may exist in some seeds (as of sweet corn) in a form soluble in water.[5]

It will be seen that the field for investigation is limitless, and that there is great need for improved methods for proximate analysis. The analyst will find that a study of any common plant will require of him much more than unthinking, mechanical habits of manipulation, while every careful investigation will reveal to him some constituents deserving more full and accurate study.

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[1] *By Henry B. Parsons.*

[2] U. S. Dept. of Agric. Report, 1878, p. 189.

[3] *Jour. prak. Chem.*, 10, 146.

[4] *Compt. rend.*, 83, 1136; *Jour. Chem. Soc.*, 31, 229 (1877).

[5] U. S. Dept. of Agric. Report, 1878, pp. 153–155.

TABLE OF COMPARATIVE SOLUBILITIES.

Substances.	*Water.*	*Absolute Alcohol.*	*80 per cent. Alcohol.*	*Abs. Ether.*	*Chloroform.*	*Benzene.*	*Petrol. Benzin.*	*10 per cent. Ammonia.*	*Ammonio-cupric Hydrate.*	*Sulph. acid, Sp. gr. 1.78.*	*Fehling's Solution.*	*Lead Subacetate.*
Volatile oils	Sp.	Sol.	Sol.	Sol.	Sol.	Sol.	Sol.	Sol.	....	....	....	....
Fixed oils	Ins.	Ins. ?	Ins.	Sol.	Sol.	Sol.	Sol.	Sol. ?	....	....	....	....
Wax	Ins.	Sp.	Sp.	Sp.	Sp.	Sol.	Sp. ?	Ins. ?	....	....	....	....
Solid fats	Ins.	Sp.	Sp.	Sp. ?	Sp. ?	Sol. ?	Sp. ?	Ins. ?	....	....	....	....
Chlorophyll	Ins.	Sol.	Sol.	Sol.	Sol.	Sol.	Sp.	Ins.	....	....	....	....
Soft resins	Ins.	Sol.	Sol.	Sol.	Sol.	Sol.	Sol.	Ins. ?	....	....	....	....
Hard resins	Ins.	Sol. ?	Sol	Sol. ?	Sol. ?	Sol. ?	Sol. ?	Sol. ?	....	....	....	....
Glucose	Sol.	Ins.	Sp.	Ins.	Ins.	Ins.	Ins.	Sol.	...	....	Reduced.	Not prec.
Sucrose	Sol.	Ins.	Sp.	Ins.	Ins.	Ins.	Ins.	Sol.	....	....	Not reduced.[2]	Not prec.
Tannin	Sol.	Sol.	Sol.	Sp.	Ins.	Ins.	Ins.	Sol.	....	....	Reduced.	Prec.
Glucosides	Sol. ?	Sol. ?	Sol. ?	Sol. ?	Sol. ?	Sol. ?	Sol. ?	Sol. ?	....	....	Reduced.[2]	Not prec.
Alkaloids	Sol. ?	Sol. ?	Sol. ?	Sol. ?	Sol. ?	Sol. ?	Sol. ?	Sol. ?	....	....	....	Not prec.
Albuminoids	Sol. ?	Sol. ?	Sol. ?	Ins.	Ins.	Ins.	Ins.	Ins. ?	....	....	....	Prec.
Gums	Sol.	Ins.	Ins.	Ins.	Ins.	Ins.	Ins.	Sol. ?	....	....	Not reduced.	Prec.
Pectin	Sol.	Ins.	Ins.	Ins.	Ins.	Ins.	Ins.	Sol. ?	....	....	....	Prec.
Pectic acid	Ins.	Ins.	Ins.	Ins.	Ins.	Ins.	Ins.	Sol.	....	....	....	Prec.
Organic acids	Sol. ?	Sol. ?	Sol.	Ins. ?	Ins. ?	Ins. ?	Ins. ?	Sol.	....	....	....	Prec. ?
Salts of org. acids	Sol. ?	Sol. ?	Sol. ?	Ins. ?	Ins. ?	Ins. ?	Ins. ?	Sol. ?	....	....	....	Prec. ?
Starch	Ins.	Ins.	Ins.	Ins.	Ins.	Ins.	Ins.	Ins.	....	...	....	....
Cellulose	Ins.	Ins.	Ins.	Ins.	Ins.	Ins.	Ins	Ins.	Sol.	Sol.	....	....
"Para cellulose"	Ins.	Ins.	Ins.	Ins.	Ins.	Ins.	Ins.	Ins.	Ins.[1]	Sol.	....	....
"Meta cellulose"	Ins.	Ins.	Ins.	Ins.	Ins.	Ins.	Ins.	Ins.	Ins.	Sol.	....	....
"Vasculose"	Ins.	Ins.	Ins.	Ins.	Ins.	Ins.	Ins.	Ins.	Ins.	Ins.	....	....
"Extractives"	Sol.	Ins. ?	Sol. ?	Ins.	Ins.	Ins.	Ins.	Sol. ?	....	....	Reduced?	Not prec. ?
Colors	Sol. ?	Ins. ?	Sol. ?	Ins.	Ins.	Ins.	Ins.	Sol. ?	....	....	....	Prec. ?

[1] "Para cellulose" soluble in ammonio-cupric hydrate after boiling with dilute hydrochloric acid.

[2] Glucosides reduce Fehling's solution after boiling with dilute acid; same with sucrose.

An interrogation-point shows that some marked variations or exceptions occur.

Sp., sparingly soluble. Sol., soluble. Ins., insoluble.

OUTLINE OF DRAGENDORFF'S METHOD OF PLANT ANALYSIS.[1]

For the systematic analysis 30 to 50 grams may usually be taken. From 2 to 5 grams are dried at 100°–110° for total moisture; and usually another portion, not above 30° C., for amount of loss. The material for the systematic analysis to be powdered, sampled, mixed, and very finely pulverized for solvents. Very hard bodies are dried at 100° to 110° C. before pulverizing. Fatty bodies may be first treated with the petroleum benzin. For ignition pulverize very fine, and if need be, after partial ignition, pulverize again. To promote combustion ammonium nitrate may be added, or ignited and weighed ferric oxide may be introduced. Powdered glass or washed sand may be intermixed. The carbon dioxide of the ash is to be determined. Special methods are used for the full quantitative estimations of distinct substances.

I. SOLUTION BY PETROLEUM BENZIN (petroleum-ether, petroleum spirit).—This solvent to boil to the last at 45° C. and leave no residue. Use 10 c.c. for each gram of the dry plant powder. Macerate eight days, shaking daily. Aromatic fresh plants may be treated, without previous drying, by fine division, and by percolation with the solvent. Receive in a graduated separator, and take off aliquot volumes for examination and for weight of total dissolved substances.

To evaporate the solvent from essential oils and other volatile matters, almost without waste of the latter, place[2] the solution in a small, shallow dish, which is to be set within a wide-mouthed jar, this being so connected that a current of dried air is drawn over the surface of the solution. The air is drawn through chloride of calcium tubes, one of which is placed before and one beyond the jar containing the solution, so that there can be no backward diffusion of moist air. The jar is closed air-tight by a stopper admitting entrance and discharge tubes, the entrance tube reaching nearly to the surface of the benzin solution. The air is drawn at the desired rate by an aspirator, one acting by the discharge of water from a large closed bottle or jar.

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[1] References to publication of Dragendorff's work are given on p. 407. This outline is by no means a substitute for Dr. Dragendorff's book on the chemistry and analysis of plants. But the outline of his plan of separations is presented for the convenience of a compact form, and as suggestion for instituting various analytical operations on vegetable tissues.

[2] This method of evaporation in a current of dry air was used by OSSE, who reports control-analyses by it, 1876: *Archiv d. Phar.* [3] 7, 104; *Jour. Chem. Soc.*, 29, 759; Dragendorff's "Plant Anal.," by Greenish, p. 21.

Fats may be treated with alcohol and observed with the microscope.[1]

Glycerides may be saponified for separation [see pp. 274, 265, etc.]

Alkaloids subjected to general tests [pp. 33, 42, 53].

Ethereal oils tested by solubilities, sensible properties, reactions.

Volatile acids recognized by acidity or by forming salts.

Chlorophyll, by optical examination.[2]

II. SOLUTION BY ETHER.—This solvent to be prepared as nearly as possible free from alcohol and from water (so as not to take up tannin). It is applied to the drug or vegetable matter previously exhausted by petroleum benzin, washed with the latter, and dried. For 1 gram use 5 to 10 c.c. of the ether. Macerate in a graduated cylinder seven or eight days. Take off aliquot volumes for examination. Evaporate the ether by a current of dried air, as directed for the benzin. Test portions by solubilities in (*a*) *water*, (*b*) *alcohol* (absolute), (*c*) *alkali*. The ether-soluble portion may contain *benzoic*, *salicylic*, and *gallic acids*, *salicin* and other *glucosides*, *alkaloids*, *resins*, *hematoxylin*, etc. For estimation of total ether-soluble fixed substances an aliquot part is evaporated and dried at 110° C. [Further see the articles Alkaloids, Benzoic Acid, etc. Resins are found in the part insoluble in water. Compare p. 278.]

III. SOLUTION BY ABSOLUTE ALCOHOL (following solvents I., II.)—For 1 gram of the material 10 c.c. of the solvent. Macerate five to seven days, restoring loss, then filtering through paper wet with alcohol. Evaporate an aliquot volume, and dry at 110° C. for weight. Evaporate other portions, without heat, in vacuum, and dry over sulphuric acid. A residue, obtained as last directed, is to be treated with water, in measured proportion, filtered, the filtrate evaporated to constant weight at 110° C., for weight of all water-soluble matters in III. Other portions of the aqueous solution are taken for the estimation of *tannins* and for *sugars*. A portion of the residue (III.), undissolved by water, is gently dried and treated with ammonia water dilute (1 : 50), the ammonia solution acidulated with acetic acid, and the precipitate, if any, after concentration, examined for *phlobaphene*, which may be estimated in this way [see Phlobaphene, under Tannins]. Portion III. may contain *resins*, *alkaloids*, *glucosides*, *bitter principles*.

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[1] See HEINTZ: *Ann. Phys. Chem.* (Pogg.), **92**, 588; *Phar. Jour. Trans.* [1] **15**, 425. GREENISH: *Phar. Jour. Trans.* [3] **10**, 909. This work, p. 297.

[2] Dragendorff, English ed., p. 19.

The water-soluble portions of II. (the ether-extract) and of III. (the alcohol-extract) may be treated by immiscible solvents, applied first to the watery liquids made acidulous with sulphuric acid, and then applied to the same liquids made ammoniacal with ammonia. [See this work, pages 33 and after; and the author's "Outlines of Proximate Organic Analysis," p. 136.] As immiscible solvents, petroleum benzin, benzene (boiling constant at 81° C.), and chloroform are recommended. The following results are indicated: *By petroleum benzin from acid solution*—Absinthin, Capsicum, Hop bitter, Piperin, Salicylic acid. *By benzene from acid solution*—Absinthin, Berberine, Caffeine, Caryophyllin, Cascarillin, Colchicine, Colocynthin, Cubebin, Daphnin, Elaterin, Ericolin, Gratiolin, Menyanthin, Populin, Quassin, Santonin. *By chloroform from acid solution*—Æsculin, Benzoic acid, Cinchonine, Colchicine, Convallamarin, Digitalein, Helleborin, Narceine, Physalin, Picrotoxin, Quinidine, Theobromine, Saponin, Senegin, Solanidin, Syringin. (Before making alkaline, the dissolved chloroform is washed out with a little petroleum benzin.) *By petroleum benzin from alkaline aqueous solution*—Brucine, Capsicum, Conine, Emetine, Lobeline, Morphine, Nicotine, Sabadilline, Sabatrine, Sparteine, Strychnine (traces), Trimethylamine. *By benzene from alkaline solution*—Aconitine, Atropine, Cinchonine (traces), Codeine, Delphinine, Gelsemine, Hyoscyamine, Physostigmine, Pilocarpine, Narcotine, Quinidine, Taxine. *By chloroform from alkaline solution*—Cinchonine, Morphine (traces), Papaverine, Narceine. *By amyl alcohol from alkaline aqueous solution* (following previous solvents)—Morphine, Salicin, Solanine.

[Tests for a glucoside, by fermentation, are indicated in the article Tannins in this work. Estimation of alkaloids, p. 44, and under the several alkaloids.]

IV. SOLUTION IN WATER.—The residue insoluble in absolute alcohol (III.) is dried and treated with 10 parts of water, by 48 hours' digestion, then filtered through the filter previously used. The filter should be washed with water, and the washings examined separately. An aliquot volume (10 to 20 c.c.) of the filtrate is evaporated, and dried at 110° C., for weight of total substances in IV. To another aliquot portion, 10 to 20 c.c., add 2 c.c. absolute alcohol, leave 24 hours in a cool place, filter on a tared filter, wash with 66% alcohol, dry, and weigh. Find the weight of ash in each of the two portions last weighed. In IV. may be found *pectous substances*, *albumens*, *inulin*, *dextrines*, *sugars*, *acids*, *saponin*. A precipitate by lead acetate will contain the acids, with mineral acids. Sugars here are to be estimated. A portion, before and after obtaining IV., may be subjected to estimation of nitrogen, when consideration is given to the presence of ammoniacal salts, amides, alkaloids, nitrates, etc. (Dragendorff, paragraph 97). Albumen is estimated by precipitation with tannin or from the amount of nitrogen.

V. SOLUTION IN ALKALI WATER.—For 1 part residue not dissolved in IV. take 10 parts of a 0.1 to 0.2% solution of sodium hydrate. Macerate 24 hours. Filter an aliquot volume, saturate with acetic acid, add alcohol of 90%, leave 24 hours in the cold. Collect the precipitate on a tared filter, wash with 75% alcohol, dry, and weigh. Ignite and weigh the ash. *Albumens* and *pectous substances* are contained.—The residue insoluble in alkali is apt still to retain traces of nitrogen compounds.

VI. SOLUTION IN ACIDULATED WATER (after removal of I. to V.)—The residue not soluble in V., washed, is treated with a 1% solution of hydrochloric acid. It is found by a microscopic examination of the original material, whether it contains *starch* or not. *Oxalate of calcium* may be separated and estimated. digesting with the acid for 24 hours at 30° C. In a measured quantity of the liquid, neutralize with ammonia, add acetate of sodium to react with all the hydrochloric acid, and set aside for the calcium oxalate to form, for gravimetric determination (as calcium carbonate).

VII. THE INSOLUBLE RESIDUE from VI. is washed, dried, and weighed. Treated with chlorine, and weight of residue found, the difference represents *lignin* and incrusting substances; the remainder contains the *cellulose*, which is examined microscopically, and the *ash*.

PROTOPINE. See OPIUM ALKALOIDS, p. 360.

PSEUDACONITINE. See ACONITE ALKALOIDS, p. 19.

PSEUDOMORPHINE. See p. 359.

PTOMAINES. *Cadaveric Alkaloids.* Ptomaine.—Alkaloid-like bodies formed in the putrefactive decomposition of animal tissues. The formation may commence shortly after death. It may be caused or promoted by digestion with acids (COPPOLA, 1885), especially when the mixtures are acidulated with sulphuric acid. BRIEGER (1885) enumerates the following products of the putrefaction of the human body:

Choline, $C_5H_{15}NO_2$.
Neuridine, $C_5H_{14}N_2$.
Cadaverine, $C_5H_{16}N_2$, boiling at 115°–120° C., with water at 100° C.
Putrescine, $C_4H_{12}N_2$, boiling at about 135° C.
Saprine, $C_5H_{16}N_2$.
Trimethylamine, C_3H_9N.
Mydalein.
A ptomaine boiling at 284° C.

Of the above, only Choline is poisonous.

From putrefactive albumen and gelatine Brieger (1885) had obtained:

Neurine, $C_5H_{13}NO$.
Muscarine, $C_5H_{15}NO_3$.
An ethylenediamine, $C_2H_4(H_2N)_2$.
Neuridine, $C_5H_{14}N_2$.
Gadinine, $C_7H_{17}NO_2$.
Triethylamine, dimethylamine, and trimethylamine.

Of these the first three named are extremely poisonous. The greater number of cadaveric ptomaines are non-poisonous.

Concerning their *chemical constitution*, Brieger (1885) calls attention to the fact that most of the characteristic ptomaines are diamines; that they are chemically more simple in composition than are the vegetable alkaloids; that many of the ptomaines are derivatives of hydrocarbons of the ethylene series, and are in distinction from true alkaloids representing the pyridine group.

Ptomaines are for the most part obtained from tissues in the operations of separation by the immiscible solvents. In evaporations they are liable, in part, to be vaporized. They are easily decomposed and are affected by atmospheric oxidation. They respond to the greater number of the general reagents for precipitation of alkaloids.

Cadaverine hydrochloride, $C_5H_{16}N_2 . 2HCl$, gives reactions as follows (Brieger, 1885): With phosphomolybdic acid, a white crystalline precipitate. With iodide of potassium, or with iodine in iodide solution, brown needles; with potassium bismuth iodide, reddish needles; with picric acid, yellow needles; with potassium chromate and concentrated sulphuric acid, a red-brown precipitate, soon vanishing. Free cadaverine gives with potassium mercuric iodide a resinous precipitate; with potassium iodide, a brown precipitate; with tannic acid, a white precipitate. Free or in salt it promptly reduces a mixture of ferric chloride and potassium ferricyanide, giving a blue color.

Putrescine hydrochloride, $C_4H_{12}N_2.2HCl$, with phosphomolybdic acid gives a yellow precipitate; with potassium mercuric iodide, an amorphous precipitate soon crystallizing in needles; with iodide of potassium, or iodine in iodide solution, a brown crystalline precipitate.

Ptomaines are mostly quite strong reducing agents, and the reaction of ptomaine sulphates with ferric chloride and potassium ferricyanide (Brouardel and Boutmy, 1881) has been announced as characteristic of the animal alkaloids, but this is not admitted by Brieger. The latter states that the reduction of the ferricyanide mixture, with formation of a blue color, is obtained by cadaverine, saprine, mydaleine, and some other ptomaines, not by choline, neuridine, or putrescine. Brieger further states that he has not found a distinctive reaction for ptomaines. They are all precipitated by phosphomolybdic acid, a reaction they share with ammonia, as well as with the vegetable alkaloids (p. 46). The reduction of ferricyanide with ferric salt, forming prussian blue, is not given promptly by many vegetable alkaloids, but is given at once by morphine and veratrine (Brouardel and Boutmy), at once by colchicine (Beckurts, 1882), and is given slowly and feebly by aconitine, brucine, conine, digitaline, nicotine, strychnine, papaverine, narceine, codeine (Beckurts).

Leucomaines.—Animal alkaloids, more or less septic, formed in tissues and organs of the living body:

Xanthocreatinine, $C_5H_{10}N_4O$.	From muscular tissue. Resembles creatinine.
Cruscocreatinine, $C_5H_8N_4O$..	Resembles creatinine.
Amphicreatinine, $C_9H_{19}N_7O_4$.	
Pseudoxanthine, $C_4H_5N_5O$...	Resembles xanthine.
Mytilotoxine, $C_6H_{15}NO_2$.....	From mussels; poisonous.
Betaine, $C_5H_{11}NO_2$.........	From mussels; non-poisonous.

The first four above given were found by Gautier (1886); the last two by Brieger (1886).

Neurine was obtained by Marino-Zuco (1885) from fresh eggs, blood, brains, liver, etc., by the method of Stas, and more abundantly by the method of Dragendorff, and formed from the lecithin of the tissues by action of acids on them, not formed from the albuminoids. These leucomaines mask the reactions for the vegetable alkaloids. By repeatedly extracting (shaking out) from alkaline solution, with ether or chloroform, it was found that the neurine was left behind.—From the liver and spleen, in addition to neurine, a violet fluorescent base was obtained.

Respecting cheese-poison, reported upon by VICTOR C. VAUGHAN in 1884 as a poisonous ptomaine, and now announced by him as diazobenzene salts, see Tyrotoxicon, in this work.

The literature of ptomaines and leucomaines is mainly embraced in that of physiological and pathological chemistry. Among the publications of interest in analytical chemistry and toxicology, an index is here made of the following:

DUPRÉ and BENCE JONES, 1866: Respecting a frail alkaloid-like body found in the organs and liquids of the bodies of man and of animals, *Zeitsch. Chem. und Phar.*, 1866; *Phar. Centralh.*, **16**; *Ber. d. chem. Ges.*, **7**, 1491.

SONNENSCHEIN and ZÜLZER, 1869: On bases obtained from muscular tissue, *Berlin klin. Wochenschr.*, 1869, 123.

RORSCH and FASSBANDER, 1871: On a body giving reactions for alkaloids, found in analyses of liver, etc., for poisons, *Ber. d. chem. Ges.*, **7**, 1064.

SELMI, chiefly about 1878: On toxicology, 1876, *Gazzetta chim. ital.*, **4**, 1; *Jour. Chem. Soc.*, **27**, 607. On alkaloids of cadaveric putrefactions, 1873 to 1880: *Ber. d. chem. Ges.*, **6**, 142; **8**, 1198; **9**, 195; **11**, 808, 1838; **12**, 279; **13**, 206. "Sulle Ptomaine ad alkaloidi cadaverici," Bologna, 1878. On alkaloids in the cadaver, 1879, *Gazzetta chim. ital.*, **9**, 35; *Jour. Chem. Soc.*, **36**, 734. On a poisonous alkaloid from a cadaver containing arsenic, 1879: *Gazzetta chim. ital.*, **9**, 33; *Jour. Chem. Soc.*, **36**, 734. On an alkaloid found in the brain and liver, and in the wild poppy, 1876, *Gazzetta chim. ital.*, **5**, 398; *Jour. Chem. Soc.*, **29**, 938. On pathological bases, 1881, *Gazzetta chim. ital.*, 1881, 546; *Jour. Chem. Soc.*, **42**, 741.

TH. HUSEMANN, 1881: The ptomaines in toxicology, *Archiv der Phar.* [3] **16**, 415; *Am. Jour. Phar.*, **54**, 152.

H. BECKURTS, 1882: Distinctions between cadaver and plant alkaloids, *Archiv der Phar.* [3] **17**, 104; *Am. Jour. Phar.*, **54**, 221. *Zeitsch. anal. Chem.*, **24**, 485.

BROUARDEL and BOUTMY, 1881: Distinctive reactions of ptomaines, *Ber. d. chem. Ges.*, **14**, 1293; *Compt. rend.*, **92**, 1056.

MARINO-ZUCO, 1884: Ptomaines in toxicology, *Gazzetta chim. ital.*, **13**, 431, 441; *Jour. Chem. Soc.*, **46**, 342, 343.

ARNOLD, 1884: Ptomaines in toxicology, *Archiv der Phar.* [3] **21**, 435; *Jour. Chem. Soc.*, **46**, 469.

GARNIER, 1883: Ptomaines in toxicology, *Jour. de Phar.*, **7**, 377; *Am. Jour. Phar.*, **55**, 404.

L. BRIEGER, Berlin, 1884–87: "Ueber Ptomaine," Berlin, 1885.

Zeitsch. physiolog. Chem., **3**, 135; **9**, 1. "Weitere Untersuchungen über Ptomaine," Berlin, 1885–86. *Ber. d. chem. Ges.*, **17**, 2741; *Zeitsch. anal. Chem.*, **24**, 484. A new ptomaine producing tetanus, *Ber. d. chem. Ges.*, **19**, 3119; *Jour. Chem. Soc.*, **52**, 284.

MAAS and others, 1884: Ptomaines in boiled meat, *Chem. Cent.*, 1884, 975; *Jour. Chem. Soc.*, **48**, 676.

V. C. VAUGHAN, 1884–85: A ptomaine from poisonous cheese, *Zeitsch. physiolog. Chem.*, **10**, 146; *Jour. Chem. Soc.*, **50**, 373. Michigan State Board of Health Reports. (See "Tyrotoxicon," in this work.)

COPPOLI, 1885: Ptomaines formed by processes of analysis of tissues for poisons, *Gazzetta chim. ital.*, **14**, 124, 571; *Jour. Chem. Soc.*, **48**, 278, 913.

GAUTIER, 1885–86: Leucomaines, *Bull. Soc. Chim.*, **43**, 158; *Jour. Chem. Soc.*, **48**, 676. On alkaloids of bacterial origin, etc., Paris, 1886. Ptomaines and Leucomaines, 1886, *Jour. Phar.* [5] **13**, 354; *Jour. Chem. Soc.*, **50**, 634.

LADENBURG, 1885: *Ber. d. chem. Ges.*, **18**, 2956, 3100.

OLIVERI, 1886: Supposed ptomaines of cholera, *Gazzetta chim. ital.*, **16**, 256; *Jour. Chem. Soc.*, **50**, 1049.

PURPURINE. See COLORING MATERIALS, p. 190.

PURPUROGALLIN. See p. 431.

PYROGALLOL. $C_6H_6O_3 = C_6H_3(OH)_3 = 126$. *Pyrogallic Acid.*—Manufactured from gallic acid or from gallotannin by sublimation. One part of gallic acid with two parts of powdered pumice-stone may be heated to 210°–220° C. in a stream of carbon dioxide. To obtain colorless, sublimed in a vacuum at 210° C. Used as a reducing agent in photography; also to a limited extent in hair dyes, either by itself or to reduce silver.

Pyrogallol is *identified* by its reactions with alkalies and iron salts, and its formation of purpurogallin. It is *separated* from tannic acid by its not precipitating with gelatin. It may be *estimated* in a lead compound.

Pyrogallol crystallizes in lustrous plates or needles of white or yellowish-white color, a very bitter taste, without odor, and a neutral or very feebly acidulous reaction. It gives a brown color to the skin. The crystals are changeless in dry, pure air, darkening in ammoniacal air. It melts at 115° C., boils at 210° C., and at about 250° C. blackens with production of metagallic acid. (See Gallic Acid, p. 321.) It dissolves in three parts of water, freely in alcohol and in ether, not in absolute chloroform. The watery solution darkens on standing, sooner if heated, quickly coloring by addition of alkalies, with formation of alkali carbonate and acetate, absorption of oxygen taking place to an extent proportional to the coloration, which is destroyed by oxalic acid. The alkalies cause reddish-yellow to red-brown tints; lime solution, a violet to purple color; all becoming gradually brown to black.

Ferroso-ferric salts, slightly oxidized ferrous salts the better, give a clear blue color. If there be much ferric salt the color soon turns to red, and with ferric salt alone the color is reddish at first. If the very dilute solution of ferric salt and pyrogallol be gradually treated with ammonia, the color changes first from red to blue, and then back to bright red. (The reaction is like that of purpurogallin, given below.) By gradually adding then acetic acid or other organic acid, the blue is first restored, then a red color again appears. Hydrochloric acid and most inorganic acids give at once a red color. The blue color is produced by bicarbonates as well as by ammonia,[1] also by free alkaloids (SCHLAGDENHAUFFEN).—In presence of gum arabic, blood, saliva, and various other organic substances, pyrogallol, in solution, exposed to the air, gradually forms PURPUROGALLIN, $C_{20}H_{16}O_9$ (STRUVE). The same product is obtained at once by adding a strong solution of permanganate acidulated with sulphuric acid. Purpurogallin has a red color of much intensity, imparted to solutions, from which it crystallizes in yellow to red needles, and by sublimation is obtained in garnet-red crystals. It is sparingly soluble in water, and its solution, with an alkali, gives a transient blue color of great intensity.[2]

Pyrogallol is a most forcible reducing agent, promptly reducing salts of silver and mercury, and Fehling's solution, and reducing ferric salts in the iron reactions above given. It is

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[1] JACQUEMIN, 1874 and 1876–77: *Ann. Chim. Phys.* [4] 30, 566; *Jour. Chem. Soc.*, 27, 1016; *Jour. Chem. Soc.*, 31, 340. A very dilute solution of ferric chloride and pyrogallol is used as an indicator, more delicate than litmus, for the estimation of ammonia or of bicarbonates (as in mineral waters). The solution is made of equal volumes of a solution of 5 grams pyrogallol to the liter, and a solution of 2 grams ferric chloride to the liter. It deposits purpurogallin, and needs to be filtered from time to time. Of the solution 10 c.c. are added to 250 c.c. of water for alkalimetry.

[2] As to ethers of pyrogallol, and their color products, see "Watts's Dict.," viii. 1710. Pyrogalloquinone, *ibid.* 1713. Reaction with mercuric chloride and alkaloids, *ibid.* 1709.

attacked by nitric acid, with red products. Its dry mixtures with many oxidizing agents are explosive. In aqueous solution, with alkali, it removes nearly all the oxygen from a confined portion of air.

A gravimetric estimation may be made by adding to an alcoholic solution of pyrogallol an alcoholic solution of lead acetate, faintly acidulated with acetic acid, quickly washing the precipitate with alcohol, drying on a water-bath, and weighing. $Pb(C_6H_5O_3)_2 : 2C_6H_6O_3 :: 457 : 252 :: 1 : 0.5514$.

QUINAMINE. See Cinchona Alkaloids, p. 92.

QUINICINE. See p. 94.

QUINIDINE. See p. 154.

QUININE. See p. 125.

QUINOIDINE. See p. 94.

QUINOLINE. See p. 165.

QUINOLINE RED. See Coloring Materials, p. 182.

RACEMIC ACID. $H_2C_4H_4O_6 = 150$. Paratartaric Acid. *Traubensäure.* Separable Inactive Tartaric Acid.—An isomer of tartaric acid, found in some varieties of grapes, and differing from dextrotartaric acid in the form of crystallization, in optical powers, and in its solubilities as free acid and as calcium salt. It crystallizes in the triclinic system, with one molecule of water, becoming anhydrous at 100° C. It is soluble in about 5 parts of cold water and in 48 parts alcohol of 0.809 specific gravity. Its solution is optically *inactive*, not rotating the plane of polarized light, but it is *separable* into dextrotartaric and levotartaric acids, as follows: When the racemates of two bases, as sodium and ammonium, in molecular proportions, are crystallized from solution together, crystals of a double salt, as $NaNH_4C_4H_4O_6$, are obtained, and these crystals, rectangular prisms, have certain hemihedral faces, and are divided into pairs, right and left, by the position of the hemihedral faces. The one crystal of a pair coincides with the reflection of the other from a mirror. When the two kinds of crystals are separated by hand-picking, the one kind is found to be the salt of dextrotartaric acid, identical with ordinary tartaric acid, while the other kind is a salt of another tartaric acid isomer, whose solution rotates the light plane to the left, and is termed Levotartaric Acid, or antitartaric acid.—Racemic acid, free, forms a precipitate with calcium sulphate solution on standing, and a precipitate with calcium chloride solution quite readily; also, the calcium precipitate, dissolved by hydrochloric acid, is precipitated again by ammonia (distinctions from dextrotartaric acid).

RHOEADINE. See OPIUM ALKALOIDS, p. 360.

RICINOLEIC ACID. See FATS AND OILS, pp. 246, 248, 289.

RESIN, COMMON, SEPARATION OF. See FATS AND OILS, p. 278.

ROSIN OILS. See p. 280.

SAFFLOWER RED. See COLORING MATERIALS, p. 191.

SAFFRANINS. See p. 183.

SALICYLIC ACID.—Salicylsäure. Acide Salicylique. $C_7H_6O_3 = 138$ (monobasic and with alkalies feebly dibasic). In structure, $C_6H_4.CO_2H.OH$, in which $CO_2H : OH = 1 : 2$, *ortho-hydroxybenzoic acid.*—There is but one salicylic acid, but it is one of three isomeric hydroxybenzoic acids (or phenol-carboxylic acids), namely, the ortho, meta, and para compounds, with the respective positions of 1 : 2, 1 : 3, and 1 : 4, for $CO_2H : OH$.

Sources.—Free salicylic acid occurs very sparingly in nature, having been found in the flowers of Spiræa ulmaria, in Viola tricolor and other species of viola, and in the Gloriosa superba of the East Indies. The ethereal salt, salicylate of methyl, $C_6H_4.CO_2(CH_3).OH$, is known as "wintergreen oil." Methyl salicylate forms the larger part (over 99 per cent., PETTIGREW, 1884; 90 per cent., CAHOURS, 1843) of the oil of gaultheria, U. S. Ph.; according to Pettigrew the whole of the "oil of birch," from Betula lenta bark, commonly sold as "wintergreen oil"; and nearly or quite the whole of the oil of Andromeda Leschenaultii, of abundant growth in Hindostan, and the volatile oil of Monotropa Hypopitys of northern Europe. It is also found in the oils of several species of Gaultheria and in oil of Polygala pauciflora; sometimes in oil of cloves, and in oil from buchu leaves.

Salicylic acid may be prepared from methyl salicylate by boiling with potassium hydrate solution until the oil is dissolved, and as long as methyl alcohol is given off, and then acidulating with hydrochloric acid, when the salicylic acid precipitates. Since 1874 salicylic acid has been extensively manufactured from carbolic acid by Kolbe's method.[1] Dry sodium phenol, C_6H_5ONa, is treated with dry CO_2, at a temperature increased to 180° C. and finally to about 225° C., whereby disodium salicylate, $C_6H_4.CO_2Na.ONa$, is formed in the retort, and half the phenol taken is distilled over. Small portions of para-hydroxybenzoic acid and traces of a phenol-dicarboxylic acid are formed (Ost, 1879). If potash be used instead of soda the product is the para-hydroxybenzoic acid. But impurities of greater proportion in salicylic acid made from carbolic acid probably result from the impurities in the latter, namely, from the cresols homologous with phenol (the "cresylic acid") present in carbolic acid (see Phenol). Each of the three cresols, C_7H_8O, treated with sodium and carbon dioxide, forms a cresotic acid, $C_8H_8O_3$. The cresotic acids so formed are sometimes termed the homosalicylic acids, and are direct homologues of salicylic acid, having the rational formula, $C_6H_3(CH_3).CO_2H.OH$, with the positions $CO_2H : OH : CH_3 =$ respectively 1 : 2 : 3, and 1 : 2 : 4, and 1 : 2 : 5.[2]

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[1] Concerning recent manufacture of salicylic acid through formation of diphenyl carbonate, at the works of Aktien (late Schering) in Berlin, see *Jahr. chem. Tech.*, 1884, 504; HENTSCHELL, *Jour. prakt. Chem.*, 27, 39, and *Jour. Soc. Chem. Ind.*, 3, 115, 646.

[2] These three cresotic acids are but three isomers among ten known isomeric hydroxytoluic acids (or cresol-carboxylic acids) obtained from various sources. *Beilstein's Organisch. Chemie.* 1883, p. 1457. In part in "Watts's Dict.," viii. 2023. Concerning certain of these acids and xylene products, *Am. Chem. Jour.*, 3, 424; 4, 186. Concerning three hydroxyxylenic acids, GUNTER, 1884: *Ber. d. chem. Ges.*, 17, 1608; *Jour. Chem. Soc.*, 1884, Abs.. 1347. It will be observed that the occurrence of homologues in salicylic acid from coal-tar corresponds to the existence of homologues in carbolic acid and in the benzoles, as follows:

1. Benzene	C_6H_6.	2. Phenol	C_6H_6O.
Toluene	C_7H_8.	Cresols (see p. 394)	C_7H_8O.
Xylenes	C_8H_{10}.	Xylenols	$C_8H_{10}O$.
3. Benzoic acid	$C_7H_6O_2$.	4. Salicylic and two other hydroxybenzoic acids	$C_7H_6O_3$.
Toluic acids	$C_8H_8O_2$.	Cresotic and other hydroxytoluic acids	$C_8H_8O_3$.
Xylenic acids	$C_9H_{10}O_2$.	Hydroxyxylenic acids	$C_9H_{10}O_3$.

The question of the occurrence of the homologues and isomers of true salicylic acid, in the article made from carbolic acid, is further treated under *Impurities* (*g*). At all events, the crude sodium salicylate of Kolbe's process is acidulated with hydrochloric acid, and the resulting crude salicylic acid is purified in various ways, by crystallizations from dilute alcohol or hot water, by dialysis of the sodium salt, and by filtration through purified animal charcoal. Dr. Squibb (1877) employed sublimation of the acid by heat from steam. For some years the "natural salicylic acid" has been manufactured from "wintergreen oil" in this country, for medicinal purposes, with claims for superior purity.—The essential oil of the flowers of Spiræa ulmaria, *Salicylol*, is the aldehyd of salicylic acid. The glucoside *Salicin*, the active principle of Salix, readily liberates the corresponding alcohol, saligenin. From all these substances, from indigo, and from coumaric acid, salicylic acid can be obtained by heating with potassium hydrate under suitable conditions, and by other chemical treatment.

Salicylic acid is *identified* by its crystalline form and physical deportment (*a*), its reaction with ferric salt and with nitric acid, and the odor of its methyl ester (*d*). From Benzoic acid it is distinguished by the odor of the respective products with sodium amalgam in presence of water, and with lime by heating when dry (*d*); from Cinnamic acid by the permanganate oxidation of the latter to benzoic aldehyde. It can be *separated* and its valuation secured (*e*) by distillation from its salts (1), or of the free acid (3); by solvents not miscible with water (2); by dialysis (4); and *in special methods* from Wine and Beer (p. 440), Canned Fruits, Milk (p. 440), and the Urine (p. 441). *Quantitatively* it is estimated (*f*) by the colorometric method, or weighed as free acid. It is *examined respecting impurities* and requirements of quality (*g*) with regard to its modes of manufacture (p. 434) and its chemical isomers (p. 443), by application of recognized special tests (p. 444). For Salicyluric Acid see p. 445; Salicylate of Sodium, p. 445; other salicylates, p. 437.

a.—Salicylic acid is furnished, according to its grade, in fine, needle-shaped crystals, or in a loose or granular powder, obscurely crystalline or nearly amorphous. White when pure, it is frequently blemished with a yellowish, or pinkish, or brownish tinge. The dialyzed acid is said to keep perfectly white. The "recrystallized" acid is a good pharmacopœial brand; the "precipitated" acid is of a lower grade; the "sublimed" acid is said to acquire color and carbolic odor. The crystals are monoclinic (Marignac, 1855). From moderately warm aqueous solution it is obtained in four-sided prisms, from hot aqueous solution in needles, from alcoholic solution by spontaneous evaporation in large four-sided columns, from a drop of ether-solution evaporated on a glass slide in star form or feathery groups of radiate needles requiring to be magnified 50 to 100 diameters (Hager).—Sp. gr. 1.483 at medium temp., taking water at 4° C. as 1 (Schroeder, 1879). Permanent in the air. Melts at 156° C. (312° F.) (Hübner, 1872; Köhler, 1879). Sublimes unaltered by heat from steam at 60 to 80 lbs. pressure, not above 145° C. (293° F.), the product having no carbolic odor (Squibb, 1883). Suddenly heated, at 220°–230° C. (428°–446° F.), it is resolved into phenol and carbon dioxide, leaving no residue, and when sublimed without care the sublimate is contaminated with phenol and gives a carbolic odor. In boiling its aqueous solution it vaporizes unaltered with the steam. Heated with concentrated hydrochloric or dilute sulphuric acid, under pressure, at 140°–150° C., it is dissociated into phenol and carbon dioxide. Alkali salicylates oxidize readily.

b.—Pure salicylic acid is odorless and has a sweetish, acidulous, acrid taste. The acid of commerce sometimes has the odor of phenol or of cinnamic acid. Salicylic acid is not caustic, but is somewhat irritant to mucous surfaces, the more so by inhalation in dust. It is medicinal in ordinary doses of 10 to 60 grains. If more than 150 grains be given within twenty-four hours some disturbance usually follows. The alkali salicylates have the effect of the acid, as does also methyl salicylate (Gaultheria oil) (H. C. Wood and H., 1886). In hypodermic injections about 0.2 per cent., or the strength of a cold saturated aqueous solution of the acid, is employed. For external application 1 to 10 per cent. solutions are used. Salicylic acid is removed from the system with moderate rapidity, most largely by the urine, in part by the bile, and in traces by the saliva. Gaultheria oil becomes free salicylic acid in the living body (Wood, 1886: *Ther. Gazette*, **10**, 73). In the urine salicylic acid is excreted as salicyluric acid, with unchanged salicylic acid. Other reported excretory products are phenol, salicin, and indican.—Salicylic acid, in proportion of about 0.1 per cent. (½ grain to the fluid-ounce), preserves ordinary vegetable infusions. For fruit juices, cider, etc., 0.05 to 0.3 per cent. is requisite, but 0.01 to 0.02 per cent. exerts a degree of conserving power. To preserve hypodermic and alkaloidal solutions Dr. Squibb uses the full or half strength of a cold water saturated solution (0.2 or 0.3%).[1] As an antizymotic, or antiseptic, the salicylates have much less power than the free acid, and a sufficient quantity of bisulphate of potassium may be added to complex liquids, with salicylic acid, to prevent its combination with the bases of acetates, etc. The use of salicylic acid in foods has been forbidden in some countries.

c.—Salicylic acid is sparingly soluble in water: at 15° C. (59° F.) it requires 444 parts; at 20° C. (68° F.), 370 parts; at 30° C. (86° F.), 256 parts; at 100° C. (212° F.), 13 parts (Bourgoin, 1879). Heated with water under pressure, the acid dissolves water and liquefies (Alexejeff, 1883). In alcohol of 90% it dissolves in 2.4 parts at 15° C. (59° F.); in absolute alcohol, in 2 parts at 15° C. It dissolves, at 15° C. (59° F.), in 2 parts of ether, in 3.5 parts of amyl alcohol, freely in methyl alcohol, in 80 parts of benzene, in 80 parts of chloroform, in 60 parts of glycerin, and in about 60 parts of ordinary fixed oils. It dissolves in carbon disulphide and in volatile oils.[2]

Salicylic acid has an acid reaction; it causes effervescence from carbonates; it forms moderately stable monobasic or normal salts (as $C_6H_4.CO_2Na.OH$), those of the alkali metals being neutral to litmus (when pure), and instable dibasic salts (as $C_6H_4.CO_2Na.ONa$) of alkaline reaction. For conserving certain alkaloids the salicylate is a very favorable salt. Of the normal salts, those of alkalies, calcium, barium, magnesium, zinc, and copper dissolve in water, the lead salt in hot water, but the silver salt does not readily dissolve. The basic salts of non-alkali metals are not soluble in water. Salicylate of quinine, $C_{20}H_{24}N_2O_2.C_7H_6O_3.\frac{1}{2}(H_2O)$, is neutral and soluble in 900 parts of cold water or 20 parts of alcohol; salicylate of atropine is neutral and very soluble in water.—With the alkali salts of the weaker acids salicylic acid dissolves freely in water, making comparatively concentrated solutions, which, however, are really solutions of salicylates. Borax, acetate of potassium, and acetate of ammonium are used, also alkali phosphates and citrates, with water, as solvents. With borax a crystallizable union is obtained, $NaC_7H_5O_3 + C_7H_5(BO)O_3$, of acid reaction. With half its

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[1] Robinet and Pellet, 1882: *Compt. rend.*, **94**, 1322; *Jour. Chem. Soc.*, **42**. 1010. Bersch, 1882: "Biedermann's Centralblatt," p. 340; *Jour. Chem. Soc.*, **42**, 1010. Heinzelmann, 1884: "Biedermann's Centralblatt," p. 503; *Jour. Chem. Soc.*, **46**, 764. "Hager's Phar. Praxis," Ergänzungsband, 43. Squibb's *Ephemeris*, 1882–85: **1**, 414; **2**, 833.

[2] Langbeck (1884) reports widely varying solubilities of salicylic acid in different essential oils, and uses this difference to distinguish volatile oils from each other: *Repert. anal. Chem.*, **12**, 177; *Jour. Soc. Chem. Ind.*, **3**, 547.

weight of borax, and 2½ times its weight of glycerin, a 25 per cent. solution of salicylic acid may be obtained. The combination with boric acid, borosalicylic acid, $C_7H_5(BO)O_3.C_7H_6O_3$, is soluble in 200 parts of cold water (Hager). Glycerin salicylate can be formed (Göttig, 1877).—Solutions of salicylic acid and its salts are not easily preserved, and acquire color by standing.

d—**The stronger acids** precipitate salicylic acid from solutions of its salts in less than 200 to 400 parts of water.. **Silver nitrate** solution, with solutions of salicylates, not with solution of salicylic acid, forms a white precipitate of silver salicylate, $C_7H_5AgO_3$, dissolved by boiling water, also by nitric acid and alcohol. **Ferric chloride** solution, with solutions of salicylic acid or its salts, gives (according to dilution) a violet-blue to violet-red color of great intensity. The alcoholic solution of free acid is most favorable. A little less delicate than the sulphocyanide reaction (E. F. Smith, 1880), it reveals salicylic acid diluted to 100000 parts (Almén, 1878). The reaction is prevented by alkalies, and hindered by alkali acetates, phosphates, borates, potassium iodide, and by oxalic, tartaric, citric, phosphoric, and arsenic acids, not by dilute acetic, boracic, sulphuric, or nitric acid, nor by glycerin, alcohol, ether, common salt, or nitre (Hager, 1880). The ferric violet reaction is given by salicyluric acid and oil of spiræa, not by para or by meta oxybenzoic acid; and red to blue ferric colors are given by bromo and nitro salicylic acids and salicyl-sulphonic acid. (See Carbolic acid, ferric reaction.)—**Bromine** water gives a crystalline precipitate, $C_7H_4Br_2O_3$, very slightly soluble in water, freely soluble in alcohol. Solution in 40000 parts of water gives crystals seen under the microscope (Almén, 1878).—**Nitric acid,** if concentrated, in the cold, and if dilute, by warming, forms nitro-salicylic acids, then by more intense action forms nitrophenic (picric) acids, the latter recognized by its intense red-brown color. The reaction is most promptly obtained by Millon's reagent, fuming acid mercuric nitrate. and gives color in dilution with 1000000 parts of water (Almén, 1878).—**Copper sulphate,** with neutral solution of salicylate, gives a green color. —**Glucose** with from two to three times its weight of salicylic acid, the mixture warmed with excess of sulphuric acid (concentrated), gives a fine blood-red color. Nearly the same color is given by benzoic acid in this test; a brown to blood-red color by hippuric acid (Phipson, 1873).—**Sodium amalgam,** warmed in a slightly acidulated solution, gradually reduces salicylic acid to its aldehyde, oil of spiræa, $C_6H_4.COH.OH$, recognized by its odor (compare with Benzoic acid).—A mixture of equal volumes of sulphuric acid and **methyl alcohol,** distilled from a small portion of residue containing salicylic acid or salicylate, yields a distillate odorous of wintergreen oil, methyl salicylate, $CH_3.C_7H_5O_3$. Ethyl salicylate, formed in a corresponding way, has a similar odor.—**Heated with lime,** salicylic acid gives the odor of phenol, obtained also by heating salicylates alone (see *a*). Salicylic acid reduces permanganate of potassium solution, but does not reduce potassium cupric tartrate.—Sulphuric acid, not diluted, in contact with salicylic acid at a gentle heat, produces *salicyl-sulphonic acid* (Remsen, 1875),

$$C_6H_3(SO_3H).OH.CO_2H = C_7H_6SO_6,$$

a quite stable acid, forming both monobasic and dibasic metallic salts, all soluble in water, mostly insoluble in alcohol.

e.—Separation.—(1) Evaporation on the common water-bath carries away free salicylic acid, and is inapplicable to its aqueous solutions. To prevent waste by evaporation, either bicarbonate of sodium or ammonia-water is added to obtain a permanent neutral or very slightly alkaline reaction during the concentration. Long evaporation now endangers loss by decomposition. If a dry residue be desired, the choice of ammonia for saturation of the acid has this advantage: if the evaporation be concluded and the residue dried at a gentle heat, the excess of ammonia is expelled. After acidulating the residue the salicylic acid may be separated by suitable solvents, or dissolved to estimate by the colorimetric method.—Alcohol, ether, chloroform, benzene, etc., may be evaporated or distilled from salicylic acid without its waste.

(2) Shaking with chloroform, ether, amyl alcohol, or benzene is very generally employed to remove salicylic acid from watery solutions. If the acid be not wholly free from combination with all bases, it must be liberated by addition of sufficient acid, preferably dilute sulphuric or phosphoric. The solvent must be applied, in successive portions, as long as a portion, evaporated, responds to the ferric chloride test for salicylic acid. Ether has been much used; chloroform is preferred by Malenfent (1885); chloroform or benzene by Dragendorff (1878). When the solvent emulsifies and fails to separate from the watery layer, as may occur, the concentrated aqueous solution (not acidulous) may be acidified and mixed with about twice its weight of ground gypsum, enough to take up the liquid, the stiffened mass dried at a low heat, pulverized, the powder shaken with ether or other

solvent, the mixture filtered and the residue washed (Cazeneuve, 1879). After evaporation of the solvent, the residue, if free from other solids, may be weighed as salicylic acid, or, whether pure or not, dissolved in water and estimated by the colorimetric method.

(3) Distillation with water, from acidulous watery solutions, by boiling, has been much used to obtain the salicylic acid in the distillate, for colorimetric estimation.[1] Denny found this method ineffective in examination of foods.[2]

(4) Dialysis of salicylic acid has been resorted to for its estimation in wine and beer, milk, and animal fluids (Muter, 1876; Aubry, 1880). Muter recovered from milk 90% by dialysis. Animal membrane is the best dialytic septum for this purpose.

In separation from wine, cider, and beer the alcohol may first be removed by evaporation to one-third volume, at 70°–80° C. (Rémont, 1881). After extraction with chloroform or benzene, in repeated portions, the residue from evaporation of the solvent may be dissolved in another solvent (as with benzene if chloroform were first used), this solution evaporated, and the residue taken up in hot water to a definite volume in ratio to that of the wine, for colorimetric estimation. Dialysis is sometimes used in preliminary treatment. A simple test may be readily made by shaking 50 c.c. of wine with 5 c.c. of amyl alcohol; after standing the layer of solvent is taken off and diluted with an equal volume of alcohol, then tested with a few drops of ferric chloride solution for the violet color (Weigert, 1880).

In examination of canned fruits Mr. Denny used the following method:[3] The expressed liquids, with sparing washings, were boiled and filtered through glass wool. To 50 c.c. of the filtrate, acidulated, 5 to 8 c.c of amyl alcohol were added, the whole shaken, the amyl alcohol drawn off, diluted with an equal volume of ethyl alcohol, and this liquid tested with ferric chloride.

In examination of milk for salicylic acid Rémont (1883) takes 20 c.c. of the milk, adds two or three drops of sulphuric acid, and agitates to break up the coagulum, when the mass is shaken with 20 c.c. of ether and set aside in a stoppered tube. 10 c.c. of the ether layer are taken in a test-tube marked at 10 c.c., the ether evaporated, and the residue of butter is boiled with alcohol of 40% strength, and the liquid, when cold, made

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[1] *Archiv der Pharm.* [3] 21, 296; *Jour. Chem. Soc.*, 1884, Abs., 372.

[2] *Contributions Chem. Lab. Univ. Mich.*, 1883, 2, 81.

[3] *Contributions Chemical Laboratory, Univ. Mich.*, 1883, p. 80.

up to 10 c.c. and assumed to contain nearly the salicylic acid in 10 c.c. of the milk. 5 c.c. of the solution are then filtered into a graduated tube for colorimetric estimation. But the colorimetric standard recommended is one obtained by adding a known quantity of salicylic acid to pure milk—0.1 to 0.2 gram to the 20 c.c.—in a parallel operation. Pellet (1882) takes 200 c.c. of milk, with 200 c.c. of water, and at 60° C. adds 1 c.c. acetic acid and an excess of mercuric oxide (½ c.c. each of acetic acid and mercuric nitrate solution—Girard, 1883). When cold, the whey is filtered out, agitated twice with 100 c.c. of ether, the ether solution washed, passed through a dry filter, and evaporated. The residue is taken up in dilute alcohol for colorimetric estimation.

In examination of *butter*, 10 to 50 grams may be boiled with alcohol diluted to 40 or 50 per cent. strength, and the filtered solution, concentrated to a definite volume, titrated in the colorimetric way.

For the detection of salicylic acid *in the urine*, unless highly colored, it may be tested directly by adding the ferric chloride, in a deep test-tube observed from above. Salicyluric Acid (see p. 445) gives the same ferric reaction as salicylic acid. The precipitate of ferric phosphate may be filtered out and more of the reagent added to the filtrate for better result. And if the urine be high-colored, it is to be made alkaline with alkali carbonate, treated with an excess of lead nitrate solution, shaken strongly, filtered, and the filtrate tested with the ferric chloride. But in most cases the direct test gives the best result (Siebold and Bradbury, 1881). In 1878 Robinet recommended preparing the urine by precipitation with sufficient lead acetate solution, adding ferric chloride to the filtrate, and then (Pagliani, 1879) adding dilute sulphuric acid, drop by drop, till the red color of ferric acetate just disappears, when the violet test-color will be seen, with least interference from the sulphuric and acetic acids. If the filtrate be too dark, basic acetate of lead solution may be used instead of the normal acetate, otherwise results are closer after use of normal acetate.[1] With 0.002 per cent. of salicylic acid in urine a distinct reaction can just be reached; with 0.005 per cent. a very distinct color is obtained (Bornträger).

f.—Quantitative.—Salicylic acid in crystals may be weighed

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[1] Bornträger, 1881: *Zeit. anal. Chem.*, 20, 87; *Jour. Chem. Soc.*, 40, 472. (In the Chem. Soc. Abstract, Bleiessig is given as "impure acetate" of lead in distinction from Bleizucker, "pure lead acetate.")

as $C_7H_6O_3$. Neither the free acid nor any of its salts is insoluble enough to be precipitated for estimation. The sublimate by carefully limited heat (see *a*) could be weighed, instead of the crystals. But a colorimetric method by ferric chloride, in comparison with depth of color from known solution of salicylic acid, was given by Dr. Muter, in 1877, as follows:[1]

The solutions required are . (1) of pure salicylic acid (by dialysis and recrystallization) 1 gram in water to make 1000 c.c.; (2) of ferric chloride such a dilute solution that 1 c.c., treated with 50 c.c. of the standard solution of salicylic acid, just cease to give increase of intensity of color before the last drop or two of last-named solution is added.—If commercial salicylic acid is to be valued, dissolve 1 gram in water to make 1 liter, and take 50 c.c. in a Nessler tube (or a seven or eight inch test-tube). Of any solution recovered by separation, take 50 c.c., or a quantity to dilute to 50 c.c., in the tube mentioned. Add 1 c.c. of the ferric chloride solution to the 50 c.c. of the solution to be estimated. In one or more tubes of same width take now, in each, 1 c.c. of ferric chloride solution and as many c.c. of the standard solution of salicylic acid as deemed necessary, and dilute to 51 c.c. After five minutes, or if acetic acid be present after ten minutes, compare the color in the tubes. Repeat the trial with the standard solution until a depth of tint is obtained the same as that from the solution under estimation. Then, in the trial giving equality of tint, the c.c. of the standard salicylic acid solution $\times$ 0.001 $=$ grams of salicylic acid in the portion taken for estimation. And if the solution under estimation be that of 1 of commercial acid made up to 1000, then c.c. of standard acid $\times$ 2 $=$ per cent. desired.

Salicylic acid, with ferric chloride, has been proposed (Weiske, 1876) as an indicator in acidimetry. It is much less definite than litmus (Mohr, "Titrirmethode"). The violet color deepens in intensity as the neutral point is approached, but as soon as this point is passed the color pales to reddish-yellow. Apparently the titration of salicylic acid, with volumetric solutions of soda, using ferric chloride as an indicator, should give fairly good results, more trustworthy if the volumetric alkali be standardized by a known solution of pure salicylic acid—an $\frac{N}{100}$ solution $=$ 1.38 gram salicylic acid in a liter. Each c.c. of alkali normal solution $=$ 0.138 gram of salicylic acid.

g.—Impurities, and tests of purity.—Color may be due to coal-tar compounds, or to iron as ferric salicylate. *Carbolic*

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[1] *Analyst*, I, 193.

acid is for medicinal purposes a quite dangerous impurity, but so obvious that it is not likely to be neglected by the manufacturer or tolerated by the purchaser, and it is more liable to arise in minute quantities from decomposition of an article not pure enough to be stable. *The cresotic acids* (see *Sources*, p. 434) are probably the most abundant, and it may be feared the most serious, impurities in the salicylic acid made from carbolic acid. In 1878 Mr. Williams,[1] by investigations not completed, reported from 15 to 25 per cent. of "secondary" or allied acids, much more soluble than true salicylic acid but less soluble than para-hydroxybenzoic acid, in "the best" artificial salicylic acid of the market. In 1883 Dr. Squibb[2] said that the better grades of well-crystallized acid of the market contained 4 to 5 per cent. "of something which is not salicylic acid" but is inferred to be homologous acid, and "not present in so large a proportion as when Mr. Williams wrote." The homosalicylic or cresotic acids are described as "deceptively like salicylic acid," and "behaving with solvents and reagents almost exactly like salicylic acid."[3] On the contrary, the two isomeric hydroxybenzoic acids are so much more soluble in water than true salicylic acid that they must be well removed from the recrystallized acid.[4] Williams and others remove sali-

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[1] *Phar. Jour. Trans.* [3] 8, 785; *Pro. Am. Pharm.*, 26, 536.

[2] *Ephemeris*, 1, 412.

[3] "Watts's Dict.," 3d sup., pp. 584, 2024.

[4] The following table gives properties, so far as found, for (1) the two isomers of salicylic acid; (2) those of the next homologues of salicylic acid which are found to be formed from cresols by Kolbe's method, and have been termed cresotic acids; and (3) three reported homologues removed two places from salicylic acid, or xylenol products. (See the foot-note under *Sources.*)

	Melting, C.	*Vaporizing.*	*Solubility in water (parts).*	*In alcohol.*	*In chloroform.*	*Ferric reaction.*
1. *Hydroxybenzoic acids:*						
Salicylic acid (ortho).	156°	With steam.	444	2.4	80	Violet.
Metahydroxybenzoic.	200°	Not with steam.	108 at 18° C.	....	....	No color.
Parahydroxybenzoic.	210°	......	126 at 15° C.	Freely.	Little.	Yellow pre.
2. *Hydroxytoluic acids:* $CO_2H : OH : CH_3 =$ (Cresotic or "homosalicylic acids")						
1 : 2 : 3..........	160°	With steam.	....	...	Freely.	Violet.
1 : 2 : 4..........	173°	" "	....	...	...	"
1 : 2 : 5..........	151°	" "	....	Easily.	Easily.	"
3. *Hydroxyxylenic acids:*						
E. Gunter, 1884. (1).	170.5°	Not with steam.	....	....	....	No color.
(2).	144°	With steam.	....	....	...	Blue.
(3).	153°	......	....	...	....	No color.

cylic acid from its homologous acids, in a purification of the artificial salicylic acid of the market, by the comparative insolubility of the calcium salicylate, as follows: The acid is treated in boiling water solution with carbonate of calcium in excess, the solution of salicylate crystallized by cooling of the filtrate, the salt recrystallized repeatedly, and finally acidified with hydrochloric acid, to obtain true salicylic acid. The mother-liquors from the calcium salicylate, acidified with hydrochloric acid, gave the homosalicylic acids, not fully examined. *Hydrochloric acid* and chlorides are obviously incidental impurities. The pharmacopœia of France (1884) places glycerin among the impurities, and as falsifications names sugar, starch, silica, calcium sulphate, potassium disulphate, etc.

Carbolic acid is likely to be revealed by the odor on opening a bottle. Closer examination may be made by warming about a gram (15 grains) in a (dry) test-tube immersed for a quarter of an hour in water a little below boiling temperature, when no odor of carbolic acid should be obtained. Carbolic acid may be separated and concentrated by making a solution with excess of sodium carbonate and water, shaking with ether, and evaporating the ethereal solution (Ph. Germ., 1882). A test by the chlorate of potassium and hydrochloric acid reaction for phenol, adopted in the U. S. Ph., 1880, has been said to give a pinkish coloration with the best obtainable medicinal grades of acid (SQUIBB, 1883). ALMÉN (1877) employs chlorinated soda solution and ammonia, avoiding an excess of the chlorinated solution, and adding, last, ammonia to an alkaline reaction—a blue color, red in acidulous and blue in alkaline reaction, reveals 1-5000th of phenol at once, 1-50000th after twenty-four hours.

For organic matters, indeterminate, treatment with sulphuric acid, without heat, is official in the U. S. and German pharmacopœias.[1] One part of the salicylic acid (0.2 to 0.3 gram) (3 to 5 grains), with 15 parts concentrated sulphuric acid (U. S. Ph.), 6 parts (Ph. Germ.), 6 to 10 parts (Hager), the mixture standing 15 minutes (U. S. Ph.), without specification of time (Ph. Germ.), should give no color (U. S. Ph.), should be nearly without color (Ph. Germ.), with the 6 to 10 parts of sulphuric acid should give a colorless or pale yellow solution, brown colors indicating insufficient purity (Hager, in "Commentar").—For organic matters and iron an evaporation of the alcoholic solution has been prescribed by Kolbe (1876, and von Heyden, 1879), and

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[1] This test was advised by HAGER in 1876: *Phar. Centralh*, 17, 434; and with additional confidence in 1883: "Commentar," 194.

is official in the pharmacopœias, U. S., Br., Germ. "A saturated solution in absolute alcohol, when allowed to evaporate spontaneously in an atmosphere free from dust, should leave a perfectly white crystalline residue, without a trace of color at the points of the crystals (absence of [certain] organic impurities; also of iron)" (U. S. Ph.) Prof. Kolbe directs to dissolve 3 to 5 grams (50 to 75 grains) of the acid in the smallest possible quantity of absolute alcohol, and pour the clear solution on a watch-glass over a white surface. Mechanical impurities will be perceptible at once. The solution is left to evaporate in an atmosphere free from dust, especially from iron, and crystals in efflorescence are obtained. If points of crystal-borders are brown, resinous, or phenol-like, impurity is indicated; if light yellow, organic dye; if violet or pink, iron. Hager insists that this test is much less trustworthy than that with concentrated sulphuric acid.—*For hydrochloric acid* and chlorides, "a solution in 10 parts of alcohol, mixed with a few drops of nitric acid, should not become turbid on addition of a few drops of test solution of nitrate of silver."—*For non-volatile matters* test is readily made by vaporization, which should leave no residue. Hager directs to heat 0.15 to 0.2 gram (2 to 3 grains) in a test-tube $\frac{3}{4}$ inch wide, by moving it through the flame, when at last no stain should be left. In the vaporization odor of phenol is usually developed.

SALICYLURIC ACID.—$C_9H_9NO_4=C_6H_4.CO.NH.CH_2.CO_2H.OH$.—Occurs in the urine after administration of salicylic acid (*b*, p. 436). Crystallizes in fine needles. Melts at 160° C., and decomposes at 170° C., with vaporization of salicylic acid. Sparingly soluble in cold water, easily soluble in alcohol, soluble in ether, less soluble in a mixture of ether and benzene than salicylic acid is (BECK, 1876), and thereby separated. Forms stable salts. With ferric chloride gives deep violet color.

SALICYLATE OF SODIUM.—$C_6H_4.CO_2Na.ONa.\frac{1}{2}(H_2O) = 338$.—For description and tests of purity see U. S. Ph., 1880. Its reaction is not acidulous if it be wholly free from uncombined salicylic acid. Even when kept in tight bottles, as required, the salt is liable to acquire color by storing. According to Hager, this is due to formation of phenol. Both the ammonia and the carbon dioxide of the air induce decomposition to the extent of giving color. In operating with the salt, traces of iron in filter-paper and in waters must be avoided. The aqueous solution is instable, and darkens on standing. Mr. Martin (1883) states that the addition of thiosulphate (hyposulphite) of sodium, 1 part to 128 parts of the salicylate, prevents the coloration of the latter in aqueous solution.—Carbolic acid as an impurity may be recognized by its odor, the better on warming, not above about 90° C. It may be separated for identification by shaking the aqueous solution, exactly neutralized, with ether, and evaporating the latter at ordinary temperature.

SALICYLURIC ACID. See p. 445.

SANDAL RED. See Coloring Matters, pp. 189, 191.

STEARIC ACID. See Fats and Oils, p. 240.

STRYCHNOS ALKALOIDS.—The alkaloids found in the Strychnos nux-vomica, S. Ignatii, S. colubrina, and Upas Tieute, of the natural order Loganiaceæ.

Strychnine, $C_{21}H_{22}N_2O_2$. Pelletier and Caventou, 1818, p. 447.
Brucine, $C_{23}H_{26}N_2O_4$. Pelletier and Caventou, 1819, p. 463.
Igasurine. Desnoix, 1853; existence called in question by Schützenberger, 1858: *Ann. Chim. Phys.* [3] 54, 65. Shenstone, 1881: *Jour. Chem. Soc*, 39, 453.

Constitution of Strychnine and Brucine.—Brucine has the elements of dimethoxy-strychnine, $C_{21}H_{20}(OCH_3)_2N_2O_2$. Shenstone,[1] and later Hanssen,[2] have shown it well-nigh certain that brucine actually is dimethoxy-strychnine, and are working upon the problem of artificial conversion of the one into the other. Hanssen finds the body $C_{16}H_{18}N_2O_2$ to be common to both strychnine and brucine, and to be changed by oxidation with sulphuric and chromic acids into $C_{16}H_{18}N_2O_4$. The announcement of Sonnenschein,[3] in 1875, that brucine is converted into strychnine by treatment with nitric acid, carbon dioxide being evolved, has not been confirmed, and this conversion is denied by Hanriot (1884).[4] The physiological relations of brucine and strychnine have been investigated by Brunton,[5] with comparison, also, with methyl-strychnine, a product under trial as to its effects.

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[1] 1883–85: *Jour. Chem. Soc.*, 43, 101; 47, 139; *Ber. d. chem. Ges*, 17, 2849.

[2] 1884–86: *Ber. d. chem. Ges.*, 17, 2849; 18, 777, 1917; 19, 520; *Jour. Chem. Soc.*, 48, 276, 819, 1146; 50, 564.

[3] F. L. Sonnenschein: *Ber. d. chem. Ges.*, 8, 212; *Jour. Chem. Soc.*, 28, 771.

[4] *Compt. rend.*, 97, 267; *Jour. Chem. Soc.*, 46, 88.

[5] 1885: *Jour. Chem. Soc.*, 47, 143.

Yield of Strychnos Alkaloids.—Total alkaloids: 1.65 to 2.88 per cent. (Dragendorff, 1874[1]). More than is generally supposed, the richest specimens reaching nearly 4 per cent. (Dunstan and Short, 1883–85, by their own method[2]). Dr. A. B. Lyons, in 1885,[3] stated the results of twelve specimens, from 2.68 to 4.89 per cent., giving a mean of 3.16 per cent. *Of strychnine alone,* 0.96 to 1.39 per cent. in the results of a few lots (Dragendorff, 1874). As a generally accredited statement, from analyses older than the recent methods, strychnine is found in Ignatius bean as high as 1.5 per cent.; in nux-vomica seeds with an average of 0.5 per cent. The statements of Dunstan and Short are given in foot-note below. Methods of analytical separation of strychnine from brucine, in use, are not well assured.

Constituents of Nux-vomica, other than the Alkaloids.—In combination with the alkaloids, *Strychnic or Igasuric Acid,* so named, is in fact an iron-greening tannic acid (Höhn, *Arch. der Phar.*, **202**, 137).—A glucoside, *Loganin,* $C_{35}H_{34}O_{14}$, was discovered in nux-vomica by Dunstan and Short in 1884.[4] In the seeds of Strychnos nux-vomica, and in pharmaceutical preparations made therefrom, it is present in small proportion: in the pulp of the fruit of Strychnos nux-vomica it was found to the extent of 4 or 5 per cent. Loganin, warmed with sulphuric acid, gives a fine red color, which on standing develops into a purple—a color-result not unusual to glucosides. By boiling with dilute sulphuric acid a glucose and a body named loganetin were formed.

Strychnine.—$C_{21}H_{22}N_2O_2 = 334$. Crystallizes anhydrous. Constitution, p. 446; Yield in nux-vomica, given above.

Strychnine is *identified* by the chemical tests of the fading purple, and the crystallization of the dichromate and free alkaloid, and by the physiological tests of tetanic effect and bitterness (*b* and *d*). Microscopic recognition, *a* and *d*. Its *limits of quantity* are indicated by the limit of response in the fading-purple test (*d*) and in the physiological tests (*b*). *Solubilities,*

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[1] "Werthbestimmung," p. 64.

[2] *Phar. Jour. Trans.* [3] **12**, 1055; **15**. 157; *Am. Jour. Phar.*, **55**, 467. In the seeds of Ceylon nux-vomica these authors report as follows (*Phar. Jour. Trans.* [3] **15**, 1):

No. 1,	1.52	per cent. strychnine,	2.95	per cent. brucine,	4.47	per cent. total.
" 2,	1.78	" "	3.16	" "	4.94	" "
" 3,	1.71	" "	3.63	" "	5.31	" "
" 4,	1.68	" "	2.86	" "	4.54	" "

[3] *Proc. Mich. State Phar. Assoc.*, **2**, 173.

[4] *Phar. Jour. Trans.* [3] **14**, 1025; *Am. Jour. Phar.*, **56**, 431.

c, p. 451. *Separations* (*e*) by solvents immiscible with water (p. 456), from Nux-vomica (p. 456), from preparations of the latter (p. 457), from Brucine (p. 458), from tissues and foods in cases of poisoning (p. 458), from the urine (p. 460), from alcoholic beverages (p. 460). Limits of recovery from tissues, etc., p. 461. In what organs found in cases of poisoning, *b*; how long after death recoverable, *e* (p. 461). *Estimated* gravimetrically and volumetrically, *f*. Tests for impurities, *g*.

a.—Colorless or transparent octahedra, or needles, or prismatic crystals; or a crystalline white or dull white powder. By spontaneous evaporation of a few drops of an alcoholic solution, on a glass slide, a characteristic microscopic field is obtained, and recognized by comparison with a field from known strychnine under parallel treatment. The crystals may also be obtained on diluting a few drops of the alcoholic solution with particles of water applied to the slide by a pointed glass rod.

Strychnine melts at about 300° C. In the "subliming cell" at 221° C. (BLYTH, 1878). A microscopic sublimate of needles is obtained at 169° C. (BLYTH, 1878). Sublimes in part unchanged, giving a sublimate recognized under the microscope (HELWIG, 1864).[1]

Strychnine Sulphate, $(C_{21}H_{22}N_2O_2)_2H_2SO_4 . 6H_2O = 874$ (COLEMAN, 1883), is efflorescent in dry air; at about 135° C. melts and (near 200° C., RAMMELSBERG, 1881) parts with its water of crystallization (12.36%). Crystallizes in prisms. Crystals with $7H_2O$ have been reported, and crystals with $5H_2O$ are obtained from alcoholic solution.—*An acid sulphate*, $C_{21}H_{22}N_2O_2 . H_2SO_4 . 2H_2O$, crystallizes in fine needles.—*The nitrate*, normal, crystallizes anhydrous, in groups of silky needles.—*The hydrochloride*, normal, with $1\frac{1}{2}H_2O$, crystallizes in soft needles or in prisms, and readily effloresces.

b.—The bitterness of strychnine is stated to be perceptible in a solution diluted to 600000 or 700000 parts. The bitter taste is followed by some degree of metallic after-taste.—In effect, strychnine is a tetanic poison, to animals as well as man. Locally it has a very slight degree of irritation. Its tetanic effects are due to its action on the gray nerve-tissue of the spinal cord. It is in some part antagonized by chloral hydrate, aconite, hydrocyanic acid, and nicotine, but these do not serve as antidotes to its poisonous action.

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[1] BLYTH: *Jour. Chem. Soc.*, **33**, 316. HELWIG: *Zeitsch. anal. Chem.*, **3**, 46.

The smallest known fatal dose for an adult person is half a grain. With adults in ordinary varying degrees of susceptibility, the administration of from ½ to 2 grains (0.03 to 0.13 gram) is likely to cause death, unless this result be prevented by special conditions or by treatment. Recovery has occurred in cases of poisoning by doses of from 3 to 20 grains, and may occur irrespective of the quantity taken. The Ph. Germ. places the maximum single medicinal dose of the nitrate at 0.01 gram (⅙ grain); the maximum daily quantity, 0.02 gram.

With frogs Marshall Hall found distinctive effects from the immersion of the animal in a solution of strychnine at a limit of 0.0002 grain (0.000013 gram); Harley, by injection into the lungs of very small frogs, obtained spasms from as little as 0.00006 grain (0.000004 gram). By carrying the solution, about 2 grains in amount, into the stomach of a frog (Rana Halecina) fresh from the pond, and of from 15 to 50 grains weight, Wormley obtained, from 0.0002 grain (0.000013 gram) of strychnine, distinctive symptoms in from 10 to 30 minutes; from 0.002 grain (0.00013 gram), symptoms in 3 or 4 minutes, and death in 15 to 30 minutes; from 0.02 grain (0.0013 gram) of strychnine, immediate spasms and death in about 8 minutes. With 0.00007 grain (0.000005 gram) of strychnine, symptoms were obtained in some of the very small animals in 50 minutes; in other animals no symptoms were obtained.

No chemical change of strychnine, in its course through the living body, has as yet been demonstrated. In some part, or at some rate, it may suffer oxidation or conversion in the body, as Plugge and others have believed. In a considerable part, at least, it is in many cases excreted, unchanged, *in the urine.* In other cases of poisoning, analysis of the urine has failed to reveal it. **Kratter** (1882) found strychnine in the urine in half an hour after the administration of ⅛ grain (0.0075 gram) of strychnine nitrate; and it continued to be so excreted for 24 hours. When administered several times in succession, it was 3 days after the last ingestion before the alkaloid disappeared from the urine. **Hamilton** (New York, 1867) reported the finding of strychnine in the urine on the morning after the patient was poisoned. **Rautenfeld** (1884, Dorpat) repeatedly obtained strychnine, in crystalline form, from the urine. **McAdam** found it in the urine of a dog nine minutes after the administration of half a grain, and before symptoms of poisoning appeared. Usually, however, it is not to be found in the urine of animals quickly killed by it. In two cases of dogs, with death after, respectively, 40 and 100 minutes, **Wormley** failed to find the poison in the urine.—*In the liver* it is retained to an extent greater than has been found in any other organ (Dragendorff and Masing, Husemann, Anderson). In other organs and in the tissues of poisoned animals its recovery by analysis is very uncertain. When death of the animal very shortly follows the administration, it is in many cases to be found in the blood. Dragendorff concludes from experiments under his direction that strychnine very quickly leaves the blood and becomes retained in the liver.[1] G. A. Kirchmaier, in experiments made under the observation of the author, found that strychnine was by no means uniformly recovered, even to a qualitative extent, from the blood of animals quickly poisoned with the alkaloid, nor from any of their organs remote from the point of introduction.[2] (As to limits of analysis, in recovery of the alkaloid, see under Separations, *e.*)

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[1] "Meine Erfahrung über diesen Gegenstand lässt vermuthen, dass das Strychnin sehr schnell dem Blute entzogen und in der Leber zurückgehalten werde, von wo aus es nur sehr langsam wieder in die allgemeine Saftcirculation gelangt, um mit dem Harn aus der Körper entfernt zu werden. Es lässt sich wenigstens bei Hunden und Katzen nicht dafür einstehen, dass man, selbst wenn der Tod bald nach Darreichung das Giftes erfolgt, im Blute oder den blutreichen Organen (ausschliesslich der Leber) das Gift nachweisen könne. Bei Versuchen, die unter meiner Leitung angestellt wurden, erhielt G. P. Masing bald ein positives, bald ein negatives Resultat, ohne Anhaltspunkte für eine Erklärung dieser Verschiedenheiten zu gewinnen" ("Ermittelung von Giften," p. 249).

[2] Experiments by administration to cats, with dissection and analysis beginning not later than 12 hours after death occurred from the action of the poison: G. A. Kirchmaier, 1883: *Contributions Chem. Lab. Univ. Mich.*, **2**, p. 91.

	Strychnine given.	*How administered.*	*Time before death.*	*Dissection.*
No. 1.....	One-fourth grain.	Injection into the back.	2 minutes.	In ½ hour.
" 2.....	One-sixth grain.	" " "	2¼ "	" "
" 3.....	One-eighth grain.	" " breast.	4½ "	" "
" 4.....	One thirty-second grain.	In saphenous vein.	8 "	In ¾ "
" 5.....	" "	By the stomach.	11 "	In 12 hours.
" 6.....	One-sixtieth grain.	" "	20 "	At once.

In cases Nos. 3 and 4 chloroform was administered before the poison was given.

	Liver.	*Kidneys.*	*Blood.*	*Heart.*	*Muscle.*	*Muscle near puncture.*	*Stomach.*
No. 1.	Not found.	Not found.	Not found.	Not found.	Not found.	Found.	Not found.
" 2.	" "	" "	" "	" "	" "	"	" "
" 3.	Found.	" "	Found.	Found.	" "	....	" "
" 4.	Not found.	" "	"	Not found.	....	....	" "
" 5.	" "	" "	....	....	....	....	Found.
" 6.	" "	" "	....	....	....	....	Not found.

c.—Strychnine is *soluble* in 67000 parts of water at 15° C.; in 8333 parts at ordinary temperature (Wormley); in 2500 parts of boiling water; in 110 parts of alcohol at 15° C.; in 207 parts of absolute alcohol or 400 parts of common whiskey (Wormley); in 12 parts of boiling alcohol; in about 500 parts diluted alcohol of sp. gr. 0.941 and in 2617 parts of sp. gr. 0.970 (Prescott and Smith, 1878); in 1400 parts of absolute ether at ordinary temperature (Wormley), or in 1250 parts of commercial ether (Dragendorff); in 6 to 8 parts of chloroform; in 140 parts of benzene (sp. gr. 0.878); slightly soluble in petroleum benzin (Dragendorff), requires 12500 parts (Wormley); soluble in 122 parts of amyl alcohol; in 300 parts of glycerin (Cass and Garst); somewhat soluble in certain essential oils; sparingly soluble in ammonia-water, not soluble in solutions of fixed alkalies. Fine octahedral crystals are obtained from the benzene solution.

Strychnine in alcoholic solution gives a decided alkaline reaction to test-papers; and it forms stable salts, mostly of a neutral reaction.—*Strychnine sulphate* (*a*, p. 448) is *soluble* in 42.7 parts of water at 15° C. (Coleman, 1883); very freely soluble in boiling water; in 60 parts of alcohol at ordinary temperature, or 2 parts boiling alcohol; insoluble in ether, or chloroform, or benzene, or amyl alcohol; soluble in 26 parts of glycerin.—*Strychnine nitrate* is soluble (Ph. Germ.) in 90 parts of cold or 3 parts of boiling water, and in 70 parts of cold or 5 parts of boiling alcohol.—*The hydrochloride* is soluble in 50 parts of cold water.

d.—Qualitative tests.—The fading purple: If strychnine or one of its ordinary salts, purified from non-alkaloidal matter, in a film of dry residue or a particle of dry mass, on a white porcelain surface, be moistened with pure concentrated sulphuric acid, in the cold, no coloration occurs. If now a just visible fragment of crystallized potassium dichromate, taken on the end of a narrow glass rod, be placed for a moment in the moistened film of the test material, and then drawn out through it, a distinct purple to blue color appears, soon changing to reddish-yellow tints, and fading away into the slight colors due to the dichromate itself. The area of moistened film, taken at first, need not be over a fourth of an inch in diameter, and the liquid is drawn in one direction only, toward the side of the dish, as the dichromate is carried through it, in repetition of the trial.—The reaction is obtained by the sulphuric acid and an oxidizing agent, and lead peroxide, ceroso-ceric oxide, manganic hydroxide, potassium permanganate, and potassium ferricyanide have severally been used for this purpose.[1] The permanganate, cerium oxide, and ferricyanide are usually mixed with the sulphuric acid before the test: one part of permanganate in 2000 parts of the acid, etc. But if this be done the film must be separately tested with sulphuric acid alone. The proportion of oxidizing agent must be minute in testing for minute quantities of the alkaloid. The color given by the oxidizing agent itself, in the sulphuric acid, must be observed. If traces of non-alkaloidal matters are present, a portion of similar matters is subjected to the same test, and any shades of color developed are to be taken into the account. Dichromate in sulphuric acid has a slight color, from the yellowish-red of the dichromate itself to the chromic sulphate formed by reduction. Permanganate presently becomes green in sulphuric acid. These tints do not resemble the fading purple, and in use of the proper minute quantities of the oxidizing agent they do not obscure the strychnine reaction, or not until the extreme limit of recognition of the latter is reached.—It is to be remembered that the evidence of strychnine depends upon the joining of three results: (1) no coloration by the sulphuric acid, (2) a blue or purple color when the oxidizing agent takes effect, (3) the fading of the blue or purple color.—The use of a good hand-magnifier adds efficiency to the test, but all the results should be unmistakable to the eye without special aids.

By the manipulation with the dichromate as above given in detail, and applied to a residue from 1 c.c. of solution, a good and strong color can be obtained from 0.0000025 gram (0.000037 grain) of strychnine.[2]

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[1] As to special effects of vanadic acid in this test, **Mandelin**, 1883. As to a certain product of this oxidation, see p. 446.

[2] In detailed experiments the following results were obtained (G. A. **Kirchmaier**, 1883: *Contributions Chem. Laboratory Univ. of Mich.*, **2**, 89; A. B. **Prescott**, 1885: "Control Analyses and Limits of Recovery," *Chem. News*, **53**, 78):

Experiment.	*C.c. strychnine solution evaporated.*	*Strychnine sulphate in grams.*	*The fading purple.*
No. 1............	5.0	0.0000125	Distinct.
" 2............	4.0	0.00001	"
" 3............	3.0	0.0000075	"
" 4............	2.0	0.000005	"
" 5............	1.0	0.0000025	Good. Play of colors less marked.
" 6............	0.8	0.000002	Faint.
" 7............	0.6	0.0000015	Uncertain.

The solution was evaporated in a common evaporating-dish. Doubtless

WORMLEY[1] obtained very satisfactory evidence, by the use of the dichromate, from 0.0000013 gram (0.00002 grain) of strychnine; 0.000007 gram giving evidence as satisfactory as could be obtained from any larger quantity, and 0.0000007 gram, when deposited within a narrow compass, giving a distinct coloration. S. J. HINSDALE (1885) prefers the ceroso ceric oxide as an oxidizing agent, and reports a good play of colors from the 0.0000007 gram (0.00001 grain) of the alkaloid. It is to be understood that the limit of delicacy of the color test is wholly dependent upon the concentration of the alkaloid. A barely visible fragment of crystal of strychnine gives a good play of colors, but if dissolved in a few c.c. of alcohol, and the solution evaporated in a common dish, the residue would give probably a negative, possibly an uncertain, result. These statements of the smallest quantity of pure and unmixed alkaloid capable of identification give no answer whatever to the question as to the smallest quantity of the poison, existing in a stomach or a portion of food or a plant, capable of recovery and identification. *The limits of recovery* receive attention, with methods of Separation, under *e*, p. 461.

Interferences with the color test—(1) Substances diminishing the delicacy of the reaction. *Brucine* in equal quantity with strychnine prevents the coloration, unless the quantity of each be very minute, less than 0.001 grain, but a mixture of 0 0001 grain of each gives satisfactory evidence of strychnine (WORMLEY). "The 0.01 grain of strychnine with 0.001 grain of brucine yields a very marked reaction, although somewhat masked" (*Ibid.*) *Morphine* is nearly as influential as brucine in diminishing or preventing the color test. A residue from a solution of 0 01 grain each of strychnine and morphine gave WORMLEY[2] little indication of the presence of strychnine; but a similar mixture of 0.001 grain of each of these alkaloids gave good evidence of strychnine; while even a minute quantity of a mixture of three parts morphine to one part of strychnine gave a negative result.—The absence of both these alkaloids, therefore, should be assured, if need be, by use of separative solvents, as directed under Separations (*e*). Of inorganic salts, nitrates and chlorides have been named as diminishing the reaction. Organic matters

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had the residue from the 0.8 c.c. of No. 6, or even that from the 0 6 c.c. of No. 7, been brought within an area of two or three millimeters diameter, and moistened with much less than a drop of sulphuric acid, a good play of colors would have been obtained in trials 6 and 7.

[1] "Micro-chemistry of Poisons," 1885, p. 564.

[2] 1860: *Chem News*, I, 243.

acting as reducing agents undoubtedly hinder or prevent the reaction, and sugar is especially influential in this regard. While it is the rule that the test is to be applied in the absence of substances not alkaloids, in practice it is sometimes difficult to be certain whether these matters are present or not. This question can be decided by a control-test as follows: Obtain by itself a narrow film of residue, equal to that tested for the result of analysis, by evaporation of a little of the recovered solution in a porcelain dish by itself. Add thereto (aside from the portions under analysis) say 1 c.c. of a solution containing in each c.c. from 0.0000025 to 0.000005 gram of strychnine sulphate (p. 452), and evaporate again. Or evaporate the 1 c.c. *with* the small portion of solution under analysis. This residue, with the added known quantity of strychnine, should give a distinct fading-blue coloration, as distinct as can be obtained by a test upon a residue from 1 c.c. of the strychnine solution unmixed.—(2) Substances giving, in part, the same results obtained from strychnine in the fading-purple test, and presenting the so-called "fallacies" of this test. The greater number of these substances give a color with sulphuric acid alone, and therefore their results are at once excluded from all indication of strychnine. Among these substances may be named papaverine, thebaine, cryptopine, berberine, amygdalin, veratrine, and cod-liver oil. Aloin gives a greenish color, fading to yellow. Aniline, colorless with sulphuric acid alone, on adding the oxidizing agent presents yellowish or greenish tints slowly deepening to blue, which deepens, and (instead of fading) finally becomes blue-black to black. Gelsemine, colorless alone with sulphuric acid, on adding dichromate or other oxidizing agent gives a reddish-purple to cherry-red color, somewhat resembling that of strychnine. Hydrastine, but faintly yellowish with sulphuric acid, on adding the dichromate gives red to green color (LYONS, 1886). Curarine, the non-crystallizable principle of worara, obtained from botanical sources allied to those of strychnine, is the only substance besides strychnine which has been found to give the threefold result of the fading-purple test (WORMLEY).—The use of the permanganate, as an oxidizing agent, is more exposed to fallacy than the other oxidizing agents. If the oxidizing agent be mixed with the sulphuric acid, and no parallel trial be made with sulphuric acid alone, the reaction of cod-liver oil may well be assumed as an indication of strychnine.

The physiological test is to be placed second in order of the value of evidence. The data for this test with the frog, and the limits of quantity revealed by it, are given under *b*, p. 449. For the test the alkaloid is obtained in a neutral aqueous solution of a salt, as the sulphate.—*The taste* of a graded dilute solution gives corroborative proof as to the presence and limit of quantity of strychnine (*b*, p. 448).—According to WORMLEY, a grain of a 1-50000th solution of the alkaloid unmixed with other matters has a quite perceptible bitter taste; and a drop of a 1-10000th solution, even in mixture with a very notable quantity of foreign matter, usually has a decided bitter taste.

Potassium dichromate solution, added to solutions of strychnine salts not very dilute, gives a crystalline yellow precipitate of strychnine dichromate, $(C_{21}H_{22}N_2O_2)_2H_2C_2O_7$ (DITZLER, 1886), its slow formation being promoted by stirring. The crystals include octahedra and often bush-like groups. A drop of the solution, on a glass slide, may be treated with a drop of the dilute reagent, the mixture stirred with a fine pointed glass rod, and from time to time examined under a microscope with a low power. The precipitate is not soluble in excess of the reagent or in quite dilute acids. Solutions of strychnine salts in 1000 parts water do not yield an immediate precipitate, but from this and much more dilute solutions crystals can be obtained as directed above.

The general reagents for alkaloids give precipitates of strychnine. The precipitate with Mayer's solution, **potassium mercuric iodide,** appears in a solution of a salt of the alkaloid in 150000 parts of water. The precipitate by **phosphomolybdate** dissolves in ammonia without coloration. The precipitate by **iodine** in **potassium iodide** solution is obtained in very dilute aqueous solutions (1 : 100000), reddish-brown, and soluble in alcohol. From the alcoholic solution somewhat characteristic crystals can be obtained. **Alkali hydrates** give crystallizable precipitates, soluble in excess only in the instance of ammonia. The ammoniacal solution gives fine crystals of the free alkaloid (*a*, p. 448).

Strychnine is noted, among alkaloids, for its stability under ordinary influences of decomposition. By action of chlorine or bromine, monochlorstrychnine or bromstrychnine is readily formed, as a substitution compound: by action of iodine, iodated hydriodides are formed, as addition compounds. By treatment with methyl iodide, the salt of methyl-strychnine, $C_{21}H_{21}(CH_3)N_2O_2.HI$, is easily obtained, as also is ethyl-strychnine by the same means. The conversion of strychnine into brucine remains under investigation. See Constitution of strychnos alkaloids, p. 446.

e.—Separations.—Strychnine may be concentrated by evaporation of its solutions at 100° C., without loss or decomposition.—In separation by solvents immiscible with water, chloroform and benzene take it up most abundantly as a free alkaloid (from alkaline aqueous solutions).—According to Dragendorff, petroleum benzin, though dissolving strychnine but very sparingly, may be profitably used to take it up from alkaline solutions as a means of [qualitative] separation from alkaloids soluble in chloroform or benzene and not soluble in petroleum benzin.[1] From acidulous solutions strychnine is not taken by any of the ordinary solvents immiscible with water (except as traces of the aqueous solution itself may be carried in solution with ether, chloroform, and amyl alcohol).

From the Nux-vomica, in total alkaloids.—The method of Messrs. DUNSTAN and SHORT,[2] which has met with general approval, is as follows: Of the finely powdered nux-vomica seeds 5 grams are packed in the percolator of a continuous extraction apparatus, and treated actively with 40 c.c. of alcoholic chloroform containing 25 per cent. of alcohol, until exhausted, which is usually accomplished in two hours or less. The chloroformic solution is agitated (in a separator) with 25 c.c. of a ten per cent. diluted sulphuric acid, the layer of chloroform drawn off and shaken again with 15 c.c. of the diluted acid, and the chloroform layer drawn off. The formation of the chloroform layer is much facilitated by gently warming the mixture. The mixed acid solutions should be quite free from undissolved chloroform, and entirely clear. Chloroformic turbidity may be removed by adding a little chloroform and agitating slowly by gradually inverting the separator. If need be, the mixed acid solutions should be filtered, through a filter wet with the dilute acid, and the filter washed with a very little of the dilute acid. The total acidulous watery solution is now made alkaline with ammonia, and shaken out, in the separator, with 25 c.c. of chloroform. The clear chloroformic layer is slowly drawn off into a weighed or balanced beaker. If not readily obtained clear by subsiding, the chloroformic solution may be run through a small double filter wet with chloroform, washing the filter with a little chloroform. The chloroform is gently evaporated, a constant weight

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[1] Wormley states that strychnine requires 12500 parts petroleum benzin for solution. Even if this hold good for the alkaloid freshly liberated, it still would require only 0.1 c.c. of the solvent to carry a quantity of the alkaloid easily identified by the color test.

[2] 1883: *Phar. Jour. Trans.* [3] **12**, 665. Given here with very slight additions in details.

of residue is obtained at 100° C. or on the water-bath, for which one hour is usually enough, and the weight of residue taken, for the quantity of total alkaloids.

From preparations of Nux-vomica, in total alkaloids.—Dunstan and Short present directions substantially as follows for standardizing an alcoholic percolate of nux-vomica in preparation of a fluid extract of uniform alkaloidal strength.[1] The operation may be applied to the medicinal *tincture* or *fluid extract.*

Take of the liquid 25 c.c., or one fluid-ounce, or other suitable quantity by weight or volume, according to the purpose. Evaporate nearly to dryness over the water-bath. Treat the residue with water acidulated with sulphuric acid, in the proportion of 30 c.c. of a 7.5 per cent. sulphuric acid for each 6 to 7 grams of nux-vomica represented (1 f. oz. for each 100 grains), adding at the same time, for same quantities, about 7 c.c. (2 fluid-drachms) of chloroform. Agitate and warm gently. When the chloroformic layer has separated draw it off, add to the aqueous liquid ammonia to cause an alkaline reaction, and agitate with 15 c.c. (or ½ f. oz.) of chloroform, warming as before. Draw off the chloroformic solution into a weighed dish, evaporate, dry over a water-bath for one hour, cool, and weigh for total alkaloids.—*For the Solid Extract* the same authors dissolve 10 grains (or 0.6 gram) in ½ f. oz. (15 c.c.) of water, with the aid of heat, add 60 grains (4 grams) of sodium carbonate previously dissolved in ½ f. oz. (15 c.c.) of water, and agitate with ½ f. oz. (15 c.c.) of chloroform, warming to obtain a separation. The chloroformic solution of alkaloids is carefully drawn off, and agitated with ½ f. oz. each of diluted sulphuric acid and water (or 30 c.c. of 5 to 7 per cent. sulphuric acid). The clear acidulous watery solution is made alkaline by adding ammonia, and agitated with ½ f. oz. (15 c.c.) of chloroform. When the liquids have separated the chloroform is evaporated off in a weighed dish, the residue dried for an hour over the water-bath and weighed as total alkaloids.—In applying this process to the residue from (say 25 c.c. of) the alcoholic preparations, Dr. A. B. Lyons[2] directs to shake out the acidulous liquid, first, with two successive portions of ether (25 c.c.), then with one portion of a mixture of one volume of chloroform with three volumes of ether, the shaking not to be too violent. The aqueous liquid made alkaline is extracted by the same ether-chloro-

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[1] 1884: *Phar. Jour. Trans.* [3] 13.

[2] 1885: *Proc. Mich. State Phar. Asso.*, 2, 183.

form mixture, applying it in two successive portions (30 and 20 c.c.)

Separation of Strychnine from Brucine.—(1) *By dilute alcohol of sp. gr.* 0.970 (about 21% weight, 26% vol.) In 1878[1] the author communicated results as follows: Solution requires

For strychnine, 2617 parts of 21% (weight) alcohol, 500 parts of 39% alcohol.
For brucine, 38 parts of 21% (weight) alcohol, 22 parts of 39% alcohol.

When one part each of strychnine and brucine were digested one hour at ordinary temperature with 100 parts of alcohol of sp. gr. 0.970, filtered, and the undissolved alkaloid washed with 100 parts of the same alcohol, the residue of strychnine gave no qualitative test for brucine, but the brucine left on evaporating the filtrate gave a slight color test for strychnine (even in presence of the excess of the brucine).

(2) *By precipitation with ferrocyanide* (DUNSTAN and SHORT, 1883). The sulphates of the alkaloids in aqueous solution acidified with sulphuric acid are precipitated with potassium ferrocyanide. The strychnine is entirely precipitated, both when alone and when in the presence of brucine, while the brucine is not precipitated unless in concentrated solution. SCHWEISSINGER (1885) did not obtain good results by this method.

Separation from Tissues and Foods in analysis for poisons.—A weighed quantity (one part) of the material is placed in an evaporating-dish or wide beaker, finely divided under the points of a pair of sharp, bright shears, with moistening if need be to bring to a soft and homogeneous pulp, about an equal quantity of water containing about one per cent. of sulphuric acid is added, and the mass digested, with stirring, on the water-bath for 15 minutes. Four or five parts of well-rectified 90% alcohol are added, and the whole digested, with frequent stirring, at a little below the boiling temperature of the alcohol, for about an hour. The edges are to be kept free from dried residue. It is then cooled and strained through close muslin, or filtered through open filter-paper by the help of a filter-pump. The residue is digested, successively, with two smaller portions of alcohol, keeping the reaction of the mass constantly acid, the filtrates from all being received together in a wide mouthed flask, and the strainers or filters well washed with the alcohol. The filtered liquids are concentrated to a syrupy consistence, with

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[1] *Pro. Am. Pharm.*, **26**, 806; *Year-book of Phar.*, 1879, 97.

occasional gentle rotation of the flask, preventing dried residues on the edges. Four or five parts of absolute or nearly absolute alcohol are added, the mixture shaken by rotating the flask, and, when cold, filtered into another flask, and the filter well washed with the absolute alcohol. The entire filtrate is evaporated on the water-bath to remove all the alcohol, when about two parts of water are added. If the reaction be not sharply acid to litmus, it is made so by adding a drop or two of diluted sulphuric acid. The mixture is filtered, and the residue and filter well washed with small portions of water, receiving the entire filtrate in a small separator, or strong tube having a good cork. It is now shaken out with chloroform, in one or more portions, or as long as this solvent continues to extract anything. The clear chloroform layer is drawn off by the separator, or forced out of the tube as water is delivered from a wash-bottle, the tubulated stopper fitted for that purpose having an adjustable delivery tube brought to the conical bottom of the container. The chloroform solution is washed once or twice with a little faintly acidulous water, and the washings added to the aqueous liquid. The chloroform solution is reserved for any tests desired. The aqueous solution is made distinctly alkaline by adding ammonia, and exhausted by shaking out with from three to five portions of the chloroform. The united chloroformic liquids are to be obtained perfectly clear. A zone of partial emulsion next to a supernatent watery layer may be resolved by introducing into the zone a c.c. or so each of fresh chloroform and of water, and tapping the separator. If need be, the chloroform so added may be made slightly alcoholic. Also, a little portion of emulsified chloroform may be washed with chloroform on a filter wet with the same solvent. Now an aliquot part of the total chloroformic solution (from the alkaline liquid) may be evaporated for preliminary tests. The residue so obtained is usually colored and loaded with substances not alkaloids. When no other alkaloid than strychnine is sought, the residue from evaporation of the (remaining) chloroform solution may be purified as follows: The residue is treated with concentrated sulphuric acid, one or two drops, or only enough to moisten the whole, covered and heated on the water-bath, or, better, heated in an oven at 100° C., avoiding any higher temperature, for an hour or so. To the carbonized mass, when cold, barium carbonate is added, to neutralize nearly all the acid, still leaving an acid reaction. The little mass is now exhausted with small portions of water, and the solution and washings filtered into a small separator. The aqueous solution is now made alkaline by adding ammonia, and exhausted by repeatedly shaking out with chloroform in small portions. The entire chloroform solution is received in a graduated cylinder, and aliquot parts are evaporated in small porcelain and glass dishes, for the several tests, and for trial as to qualitative limits, also, if desired, for volumetric estimation. The residues will contain some ammonium sulphate, the crystals of which are likely to be seen in microscopic examinations. To obtain a portion free from ammonium salts and from sulphates in general, treat one of the residues with water and barium carbonate, evaporate to dryness, take up with warm alcohol, filter, and evaporate the alcoholic solution, for another residue.

Strychnine may be separated from the Urine by evaporating the acidulated liquid to a syrup, stirring with strong or absolute alcohol, filtering and washing well with the same alcohol, concentrating the filtrate to a syrup, which is dissolved in water enough to make a limpid solution. This is washed (while acidulous) with chloroform; then made alkaline by adding ammonia, and washed with one or more portions of chloroform. The chloroformic solution is evaporated, either all together or in aliquot portions, for direct tests upon the residue or for further purification, as directed on p. 459. As to the occurrence of strychnine in the urine, following administration, results are stated under *b*, p. 449.

Recovery from Alcoholic Beverages.—Messrs. GRAHAM and HOFMANN, in 1852, made extensive analyses of the *ales and beers* of Great Britain for strychnine, as follows: Half a gallon of the ale was shaken with 2 oz. of animal charcoal, and, after standing 12 to 24 hours, filtered through paper. The drained charcoal was boiled half an hour in purified alcohol, and the filtered alcohol distilled off. The watery residue was made alkaline with potassa, and agitated with an ounce of ether [chloro form]. The residue from evaporation of the ether was tested. Taking ½ grain of the alkaloid in ½ gallon of the malt liquor, the operators invariably obtained the color test in the final residue.—Probably a preferable procedure would be the treatment directed above for separation from the urine.—With distilled spirits, such as whisky, the same operation (last referred to) is advisory, the alcohol being first distilled off, when the slight quantity of residue usually renders the operation a very simple one.—Single cases of the detection of strychnine in beer in Eastern Europe have been reported. There is no evidence, and no probability, that strychnine has ever been used in the sophistications of distilled spirits.

Limits of Recovery from complex organic matter.—From the experiments of Mr. Kirchmaier, with the author's co-operation,[1] it appeared that the limits of analytical separation, by a process essentially the same as that just detailed, were as follows: With 50 grams of meat, the loss of strychnine was for one part of meat, 0.00000795 part of strychnine; or for one part of the alkaloid, 125786 parts of the tissue-material.[2] That is to say, in separating strychnine from an avoirdupois pound of tissues the loss of alkaloid is from one thousand to two thousand times the least quantity needed for certain identification (p. 452).

The deposition of strychnine in various organs of the living body receives statement under *b*, at p. 450. It is capable of recovery from partly decomposed organs some time after death, subject to limitations not yet very definitely established. No other alkaloidal poison resists destruction in the interred body any better than strychnine, probably none other resists as well. Yet it is by no means indestructible when contained in putrefactive tissue. The data obtained by adding strychnine to tissues, and recovering it after some months of putrefactive decomposition, are but imperfectly applicable to cases of poisoning by the alkaloid, because of the attenuation that results from absorption and elimination. Wormley states[3] that "the longest period in which the analysis furnished positive evidence of its presence in the exhumed human body is 43 days after death (*Ann. d'Hyg.*, 1881, 359)." But in the case of Magoon, in New Hampshire, 1875, Drs. Hayes and E. S. Wood, of Boston, found strychnine in the body of a woman advanced in years, exhumed one year and three days after death; and the analysts reported 0.15 grain in the stomach, 0.23 grain in the liver, and presence of the alkaloid in the intestines. Death had occurred in less than an hour after administration of an unknown quantity of the poi-

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[1] "Control Analyses and Limits of Recovery in Chemical Separations," 1885: *Chem. News*, 53, 78. *Contributions from the Chem. Lab., Univ. of Mich.*, 2, 91.

[2]

Experiment	4,	5	grams	meat,	0.00016	strychnine,	good	color-test.
"	5,	"	"	"	0.00012	"	faint	"
"	6,	"	"	"	0.00008	"	very faint	"
"	7,	"	"	"	0.000064	"	negative	"
"	8,	50	"	"	0.0004	"	good	"
"	9,	"	"	"	0.0002	"	faint	"
"	10,	"	"	"	0.00016	"	negative	"
"	3,	5	"	bread,	0.0001	"	good	"
"	4,	"	"	"	0.0008	"	faint	"
"	5,	"	"	"	0.0006	"	very faint	"
"	6,	"	"	"	0.0004	"	negative	"

[3] 2d ed. "Micro-Chem. Poisons," 1885.

son, in a tumbler of hot liquid of extreme bitterness. In 1875 Prof. Wormley made analysis of the stomach and liver seven months after death, and the chemical tests gave no evidence of strychnine, although the final residues had a bitter taste. Death had occurred within two hours, and the symptoms and other proofs were such that there was a conviction for poisoning (*Ohio* v. *Dresbach*, 1881). Buchner, Gorup-Besanez, Wislicenus, and Ranke (1881) made a series of experiments upon seventeen dogs, killed, each, by 0.1 gram of strychnine, and buried from 100 to 330 days before analysis. In no case did the chemical tests show the presence of strychnine, though the physiological test, with frogs, obtained tetanic convulsions, and the residues had a bitter taste.

f.—Quantitative.—Strychnine is estimated *gravimetrically* by weight of the anhydrous alkaloid, dried at 100° C. A *volumetric* estimation (less exact than the gravimetric) is obtained by Mayer's solution, each c.c. of which represents 0.0167 gram of strychnine ($\frac{1}{20000}$ of 334, in grams). The end of the reaction is distinct, and the precipitate settles fairly well in acidulated water, but settles better in a concentrated solution of potassium chloride (Dragendorff, 1874), when each c.c. of the entire solution dissolves 0.00216 gram of the precipitate (*ibid.*) The composition of the precipitate as $C_{21}H_{22}N_2O_2HIHgI_2$ was nearly sustained by the determinations of mercury and of iodine communicated by the author in 1880.[1] This chemical formula corresponds to 36.47% strychnine in the precipitate. Dragendorff gives a gravimetric trial by washing, drying, and weighing the precipitate, whereby there was a loss of only 1.8% on the basis of this formula. Though more constant than the greater number of alkaloidal iodomercurates, the precipitate is not the most favorable form for gravimetric purposes. And in the volumetric determination the solution is to be made of 200 parts to 1 of the alkaloid.

g.—Tests for Impurities.—"Strychnine should not be reddened at all, or at most but very faintly, by nitric acid (absence of more than traces of brucine)." May be colored yellowish but not red when rubbed with nitric acid (Ph. Germ.) Not colored by nitric acid (Br. Ph.)—A more strict exclusion of brucine is effected by washing the free alkaloid with dilute alcohol (sp. gr. 0.970) to separate the brucine, as described on p. 458, the residue

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[1] Chem. Lab. Univ. Mich.: *Am. Chem. Jour.*, **2**, 297–99; *Jour. Chem. Soc.*, **42**, 664.

from evaporation of the filtered dilute alcohol being tested with nitric acid.[1] Of ten samples of commercial strychnine, treated in this way, all but two gave tests for brucine.

BRUCINE, $C_{23}H_{26}N_2O_4 = 394$. Crystallizes with $4H_2O$, 15.45%.—For constitution of the alkaloid see p. 446; yield in nux-vomica, p. 447.

Brucine is *identified* by its color-tests with nitric acid and other additions, its dichromate precipitate, its crystalline forms, and its physiological effects as a convulsent (*d*). It is distinguished from strychnine by a negative result in the "fading-purple" test, and the positive reactions with nitric acid, etc. (*d*). It is *separated* with strychnine, and from strychnine, as described on pages 456, 460; and is *estimated* gravimetrically or volumetrically (*f*).

a.—Transparent or colorless, oblique, four-sided crystals, or in groups of delicate needles, varied in form according to the solvent and the conditions. The crystals effloresce in dry air, and on the water-bath the alkaloid soon becomes anhydrous. It melts at 151° C. (BLYTH, 1878), at 115.5° C. [when anhydrous?] (GUY). It gives a decomposition-sublimate in the "subliming cell" at 150° C. and above (BLYTH), at 204° C. (GUY).

b.—Brucine is extremely bitter. In effects in general it resembles strychnine, but a far greater quantity is required for the same effect. T. L. BRUNTON (1885) found that it is excreted far more rapidly than strychnine, so rapidly that when given by the stomach to animals pure brucine has little effect. Given hypodermically it causes death by convulsent action. WORMLEY states that the effect of brucine is that of strychnine, with $\frac{1}{12}$ the intensity.

c.—Effloresced brucine dissolves in 850 parts cold or 500 parts boiling water, the crystals being considerably more soluble. Very soluble in alcohol, absolute or aqueous. As to its solubility in certain strengths of dilute alcohol, see page 458. Almost insoluble in ether, soluble in chloroform, benzene, or amyl alcohol.—The ordinary salts of brucine are soluble in water and in alcohol, not in ether.

d.—**Nitric acid** gives a red color with brucine. For the proper intensity the acid should be concentrated, near 1.42 specific gravity, and the alkaloid should be dry and placed over a

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[1] The author and A. D. Smith, 1878: *Proc. Am. Pharm.*, **26**, 807.

white ground. If the alkaloid be concentrated at one point, and minute in quantity, it may be treated with less than a drop of the acid, added at the point of a sharp glass rod. On standing, or heating, the color changes to yellowish; on evaporating to dryness the red color returns in the residue. About 0.0000013 gram (0.00002 grain) is the limit of quantity for distinct coloration, with the best concentration.—**Sulphuric acid** alone applied to the dry alkaloid causes a faint rose color. If in a drop of the rose solution of the concentrated acid a minute fragment of **potassium nitrate** be placed, an orange-red color is obtained. If the concentration be of the best, about the 0.00003 gram is sufficient for a sensible reaction.—If the dry alkaloid or its salt be treated with a drop or just wet with nitric acid, as above directed, warmed till the color turns to the yellow, then cooled and touched with a drop or less of good solution of **stannous chloride,** a purple to violet color is obtained. Excess of either the nitric acid or the tin salt is to be avoided. The heating is only necessary to bring out the full delicacy of the reaction. Sodium sulphide solution (by saturating caustic soda solution with H_2S) may be used instead of stannous chloride. The reaction with tin salt may be recognized with the 0.00001 gram of the alkaloid. Of the three allied color-tests just described, the last is the most characteristic, and the agreement of the three furnishes quite conclusive proof of identity, with distinctions from morphine, narcotine, and other alkaloids.—In the sulphuric acid and dichromate test made for strychnine, brucine slowly reduces the chromic acid, with colors changing from dull orange to greenish, without the least resemblance to the "fading purple." Froehde's reagent gives a red to yellow color. A solution of brucine in dilute sulphuric acid, touched with very dilute dichromate solution, gives a red color changing to duller tints. **Mercurous nitrate** (free from excess of nitric acid) gives a reaction somewhat like that of nitric acid, but developed only on heating, the color being carmine, and permanent on evaporating to dryness.

Solution of a brucine salt, with solution of **potassium dichromate,** yields a yellow crystalline precipitate of brucine chromate, in groups of bent needles, formed in quite dilute solutions, and somewhat characteristic. The precipitate dissolves in nitric acid with a red color.

The general reagents for alkaloids give the customary precipitates with brucine. Very dilute solutions give the precipitate with **iodine** in potassium iodide solution. The precipitate formed by **phosphomolybdate** is of an orange tint, dissolving in ammonia to a yellow-green solution. *The caustic alkalies* cause a precipitate, gradually becoming crystalline, and somewhat soluble in ammonia.

The physiological test of brucine, with the frog, is qualitatively nearly the same as that for strychnine (pp. 454, 449), but a very much larger quantity of brucine is required for the same effect.

e.—Separations.—Brucine may be obtained from an aqueous or other solution by evaporation at 100° C., without loss.—The aqueous solution of its salts may be washed with any of the ordinary solvents immiscible with water, its salts not being soluble in these solvents. On making the aqueous liquid alkaline, chloroform or benzene serves well as a solvent, and amyl alcohol also takes it up. Petroleum benzin dissolves it to some extent.

The separation of brucine with strychnine, from nux-vomica and from its preparations, is described under Strychnine, p. 456. The separation from strychnine is given at p. 458. In analysis for poisons, brucine will be obtained with strychnine by the methods detailed at pages 458, 460.

f.—Quantitative.—Brucine is estimated gravimetrically in the same manner as strychnine (p. 462), the residue of free alkaloid being dried at 100° C. to a constant weight, when it can be weighed as anhydrous.—In the volumetric method with Mayer's solution, Mayer's factor for 1 c.c. of the solution was 0.0233 gram of the alkaloid.

SULPHOCARBOLIC ACID. See PHENOL, p. 405.

TANNINS.—*Tannic Acids.* Gerbsäuren. — Vegetable educts of an astringent taste, amorphous or obscurely crystalline solids, not volatile without change, of very slight acid power, and freely soluble in water and in alcohol. They give blue or green precipitates with ferric salts, and thick precipitates with gelatin, albumen, and starch paste. In most cases they precipitate the alkaloids, likewise tartrate of antimony and potassium, and are dissolved but sparingly by dilute mineral acids. They are all strong reducing agents, giving reductions with Fehling's solution, with permanganate, and with salts of silver and of gold. The greater number of them convert animal membrane into leather. They are darkened and decomposed by alkali hydrates. In solutions they are instable.

There are many diversities of character and composition of tannins. The best known of these differences may be stated as follows:

(1) *Glucoside-tannins.* When boiled with dilute mineral acids, yield (*a*) a crystallizable acid or its anhydride, or (*b*) a phlobaphene (a resin-like body), along with a glucose.[1]	(1) Tannins *not glucosides.* For determination whether a glucoside or not, see below.
(2) *Iron-bluing* tannins. With ferric salts give blue to black precipitates or colors. The ferroso-ferric solutions, slightly basic, give the best reactions. Mineral acids dissolve and decolor.	(2) *Iron-greening* tannins.[2] With ferric (basic) salts give greenish precipitates or colors. Brown colors sometimes obtained. Tints varied by conditions.
(3) Tannins *not tanning agents.* Do not form leather, nor preserve animal membrane, though precipitating solutions of gelatin (Wagner[3]).	(3) *Tanning materials.* Change animal membrane into leather, not putrescible. Also precipitate solutions of gelatin.
(4) Tannins which, in subliming, or in fusing with potassium hydrate, *yield a trihydroxyphenol*, C_6H_3	(4) Tannins which, in subliming, yield a dihydroxyphenol, $C_6H_4(OH)_2$, and, on fusing with potash, yield an

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[1] "I have arrived at the curious result that tannic acid, when acted upon by acids, yields, together with gallic acid, *sugar*, so that henceforth tannic acid may be classed with the conjugate sugar compounds."—Strecker in a letter to Hofmann in 1853. In 1872 Schiff found the product to be primarily digallic instead of gallic acid.

[2] Of the iron-greening tannins examined only willow-tannin was found to be a glucoside.—Stenhouse, 1861. "Tannins in the green parts of plants, according to their nature, affect iron solutions differently; that which colors iron green is apparently an oxidation product of that which colors iron blue, and the author thinks that the latter, under the influence of transpiration, breaks up into the former modification and sugar."—E. Johanson, 1879: *Jour. Chem. Soc.*, **26**, 161, from *Arch. Pharm.* [3] **13**, 103–130. Regarding iron colors with phenol-hydroxyl, see Schiff as quoted under Carbolic Acid, in reaction with Ferric Chloride, p. 399.

[3] *Zeitsch. analyt. Chem.*, **5**, 1. Wagner states that the pathological tannins of the galls of species of Quercus and Rhus do not form true leather or preserve animal membrane from putrefaction. Löwenthal (1877: *Zeitsch. anal. Chem.*, **16**, 47) found that precipitates of gelatin with gallotannin and sumach-tannin, standing under water for two years, still gave no odor of putrefaction.

$(OH)_3$, such as Pyrogallol (Hlasiwetz).

acid, as Protocatechuic acid, $C_6H_3(OH)_2CO_2H$ (Hlasiwetz).

(5) *Pathological tannins.* Formed in punctured vegetable tissues. Gallotannins (Wagner, 1866[1]). Including sumach-tannin (Stenhouse, 1861).

(5) *Physiological tannins.* From uninjured vegetable tissues (Wagner). Include various glucosides and iron-bluing tannins.

In testing for glucoside tannins, the solution, not very dilute, is first tried as to its deportment with ferroso-ferric solution, gelatin solution, cinchona sulphate solution, and Fehling's solution. Sulphuric acid equal to one or two per cent. is now added to a portion, and the liquid is boiled for an hour or two. Or hydrochloric acid is added, to give about the same percentage of real acid, the liquid sealed up in glass tubes and heated at 100° C. for an hour or longer. A portion of the liquid is now dropped into cold water, to see whether sparingly soluble fermentation products may precipitate, so that they can be removed by filtration. Otherwise the liquid may be shaken with successive portions of ether, or chloroform, or acetic ether (Dragendorff). The liquid is now nearly or quite neutralized by the addition of fixed alkali hydrate, and tested, as at first, with ferroso-ferric solution, gelatin solution, cinchona sulphate solution, and Fehling's solution, noting if these results differ from those obtained before boiling. The production of glucoses may be further investigated, by a fermentation test, with yeast (see under Sugars), and by optical examination as to rotatory power.

Tannins are precipitated by lead acetate, copper acetate, and zinc ammonio chloride, and by the salts of nearly all the non-alkali metals. *The removal of tannins* from solutions may be effected by digesting the liquid with recent ferric hydrate, zinc oxide, copper oxide, or lead oxide, and filtration. Also by maceration with animal membrane or rasped hide; or by filtration through purified animal charcoal. Gelatin gives better precipitates in solution saturated with ammonium chloride or sodium chloride, and the addition of sulphuric or hydrochloric acid further helps the separation of the precipitates. Separations by acetic ether, and non-precipitation, are given under Gallotannin.

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[1] See note on p. 466.

Estimation of Tannins and Valuation of Tanning Materials. (1) Method of Löwenthal.[1] Titration by a permanganate solution, before and after removal of the tannin by gelatin in solution saturated with sodium chloride and acidified. Both titrations made in presence of much indigo solution, which regulates the oxidation and serves as an indicator. The method employs the following-named solutions: (*a*) Permanganate of potassium solution: 1.333 or (Kathreiner) 1.000 gram of the crystallized salt to 1 liter. (*b*) Indigo solution: 6 grams pure precipitated indigo, and 50 c.c. concentrated sulphuric acid, per liter. There should be added sufficient of the indigo to require for itself two-thirds of all the permanganate used (Kathreiner). (*c*) The solution of Glue and common salt is made by macerating 25 grams of good transparent glue in cold water, then heating to dissolve, making up to 1 liter, and saturating with good common salt. It should be filtered clear when used. (*d*) The acidulated solution of Common Salt is a saturated solution with addition of 25 c.c. of sulphuric acid in a liter.—In the analysis 20 to 25 grams of bark, or 10 grams of sumach or valonia, are boiled with portions of water until fully exhausted, and the solution, when cold, made up to 1 liter. Of this 10 c.c. are diluted to 800 or 1000 c.c., 25 c.c. of the indigo and acid solution are added, the mixture treated with the permanganate solution, drop by drop from the burette, with constant stirring, until the blue color changes to a clear yellow, showing no green tint, and the number of c.c. of permanganate is noted. Another 25 c.c. of the indigo and acid solution are diluted to the same volume made before, and the titration with permanganate repeated, when this result is subtracted from that first obtained, to obtain the quantity of permanganate required for the 10 c.c. of tannin solution. The tannin, as well as gallic acid, if present, are mainly oxidized before the indigo, and therefore oxidized

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[1] 1877: *Zeitsch. anal. Chem.*, 16, 33; *Jour. Chem. Soc.*, 31, 745. Kathreiner, 1879: *Dingler's polyt. Journ.*, 227, 481; *Zeitsch. anal. Chem.*, 18, 112; a report fully sustaining this method, and defending it against a criticism in Mohr's Titrirmethode. H. R. Procter, 1877: *Chem. News*, 36, 58; *Jour. Chem. Soc.*, 32, 807, "the most practical method of tannin analysis yet discovered." Neubauer, *Zeitsch. anal. Chem.*, 10, 1 (1871), after an elaborate review of methods, gives preference to this. B. Hunt (1885: *Jour. Soc. Chem. Ind.*, 4, 263) reports at length upon this process, and advances modifications, some of which are given in a foot-note further on. Without these modifications Mr. Hunt finds that a considerable quantity of gallic acid may cause too high a result for tannin. Löwenthal made the first report of titration with permanganate in presence of indigo in 1860: *Jour. f. prakt. Chem.*, 81, 150. The volumetric use of permanganate was introduced by Monier: *Compt. rend.*, 46, 447.

promptly while the permanganate is concentrated. A portion of 100 c.c. of the tannin solution is now treated with 50 c.c. of the glue and common salt solution, and, after stirring with 100 c.c. of the acidulated solution of common salt, again stirred, set aside several hours, and filtered[1] The filtrate should be perfectly clear. Of this filtrate 50 c.c. (containing 20 c.c. of the tannin solution) are mixed with 25 c.c. of the indigo solution, and the mixture is titrated with the permanganate solution. Another 25 c c. of the indigo solution, diluted as in the last trial, and titrated, will give the number of c.c. of permanganate to deduct for reduction by indigo. The remainder will be the number of c.c. of permanganate taken by substances other than tannin in 20 c.c. of the tannin solution. Therefore one-half of this number of c.c. will be the number to deduct for decoloration of the permanganate by substances other than tannin in 10 c.c. of the original tannin solution. In the removal of the tannin, both the gelatin solution and the acid and salt solution must be added in sufficient quantity to give a perfectly clear filtrate.[2] The acid and salt solution must not be brought in contact with the gelatin solution before the latter is fully mixed with the tannin solution. The permanganate is to be added slowly, in a white porcelain dish, giving for reduction as much as four minutes with the original solution, and six minutes with the filtrate. It is better to let the gelatin precipitate stand as much as half an hour before filtering; if filtered earlier the filtrate will consume more permanganate (Hewitt). In preparing the solution from oak-bark or from galls a few drops of acetic acid may be added for preservative effect, and with each portion of water the material may be boiled ten or fifteen minutes. It must not be forgotten that tannins are instable. Duplicate titrations should be made, and should agree to within 0.1 or 0.2 c.c. of permanganate.

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[1] B. Hunt (1885) proceeds as follows: 100 c.c. of the tannin solution is treated (in a flask taken dry) with 50 c.c. of a solution of 2 grams of gelatin in 100 c.c. (freshly filtered). The flask is shaken, and 50 c.c. of a saturated solution of common salt (containing 50 c.c. of undiluted sulphuric acid per liter) is added, together with a little kaolin or barium sulphate. The solution filters clear.

[2] Löwenthal finds only a very small and nearly constant reduction of permanganate by gelatin solution, and ascribes this slight reduction to certain oxidizable substances with the gelatin. He infers that these oxidizable substances are precipitated by tannin before all the gelatin is precipitated. By adding 20 c.c. of the gelatin solution the indigo solution consumed 0.4 c.c. more of permanganate solution. Different kinds of gelatin give only a little difference of results. Kathreiner proposes to deduct one-half of the permanganate found to be consumed by the given quantity of gelatin solution (*Zeit. anal. Chem.*, 16, 33, 18, 114).

The following schedule of quantities may be changed at discretion:

For 10 c.c. tannin solution, with 25 c.c. indigo solution	a c.c.
For the same again	a' c.c.
For 25 c.c. indigo solution, diluted as before	b c c.
For oxidizable substances in 20 c.c., tannin sol.	$a + a' - b = m$.
For 50 c.c. filtrate from 100 c.c. tannin sol., 50 c.c. glue sol., and 100 c.c. acid and salt solution	c c.c.
For another 50 c.c. of the filtrate	c' c.c.
For 50 c.c. indigo solution, diluted as last above	b' c.c.
For oxidizable substances other than tannin in 20 c.c. tannin solution	$\frac{c + c'}{2} - b' = n$.
For tannin in 20 c.c. original solution	$m - n$ c.c.

So far we have only the permanganate value of the original solution, and, from this, of the material taken to be estimated. The permanganate value serves to compare articles containing the same tannin with each other, as oak-bark with oak bark, galls with galls, etc. A comparison of oak-bark with galls must be taken with some reservation, as different tannins cannot be assumed to act with the same equivalent. The permanganate solution may be compared with a standard solution of the purest gallo-tannic acid to be obtained, or with any article of tannin of known value. The conditions of time, temperature, and dilution must be kept constant in all comparisons, both in extracting the material and in titrating the solutions. According to the experiments of Neubauer, in 1871,[1] 63 grams of crystallized oxalic acid (equivalent to 31.4 grams of absolute potassium permanganate) correspond to 41.57 grams purified gallo-tannin.[2] That is, 10 c.c. decinormal oxalic acid solution reduce as much permanganate as 0.04157 grams of Neubauer's purified tannin. Oser has found that the same quantity of oxygen is required for 1 part of gallo-tannin and for 1.5 parts of oak-bark tannin. Then 10 c.c. decinormal oxalic acid solution correspond to 0.06235 grams oak-bark tannin. These factors serve provisionally, Neubauer's for galls, sumach, and myrabolans; Oser's for oak-bark,

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[1] *Zeitsch. anal. Chem.*, 10, 3.

[2] This is near the ratio of $4(H_2C_2O_4.2H_2O)$ to $C_{14}H_{10}O_9$; 504 to 322; 63 to 40.25. The ratio to Schiff's natural tannin glucoside is that of $8(H_2C_2O_4.2H_2O)$ to $C_{34}H_{28}O_{22}$; 63 to 49.25.

valonia, and chestnut. No interference in this estimation (with the specified dilutions) by presence of acetic acid, citric acid, tartaric acid, malic acid, cane-sugar, dextrin, gum, fat, caffeine, or urea (Cech[1]). Other agents for removal of the tannin in connection with Löwenthal's process have been tried. SIMANDS (1883) proposes to use the gelatigenous tissue of bones, prepared by digesting bone in dilute hydrochloric acid and washing away the earthy chlorides. The tannin solution is macerated with the prepared tissue until the tannin is removed. NEUBAUER[2] removes tannin by purified animal charcoal, which he finds not to remove pectous substances. Löwenthal originally used chlorinated lime instead of the permanganate.

(2) Method of GERLAND, improved by RICHARDS and PALMER.[3] Volumetric precipitation by potassium antimony tartrate in presence of ammonium acetate. Either acetate or chloride of ammonium causes a much closer precipitation of tannin, and prevents precipitation of gallic acid. The standard solution of Tartrate of Antimony and Potassium contains 6.730 grams of the salt dried to a constant weight at 100° C. in one liter. Of this 1 c.c. corresponds to 0.010 of digallic acid. The solution of Ammonium Acetate was prepared by Richards and Palmer by saturating glacial acetic acid with stronger water of ammonia. The material for analysis is dissolved or exhausted so as to furnish a solution of 150 c.c. to 300 c.c. in volume and strong enough to contain 0.3 to 0.9 gram of tannin. The entire solution from the weighed portion of material is now divided into three (or four) aliquot parts. To one division the standard solution of antimony is added from the burette, in probable excess, and to a second division a quantity sure not to be an excess is added. To each liquid the acetate of ammonium solution is added, in proportion of 1 c.c. (of the strong solution just specified) to about 25 c.c. of total liquid. The precipitates are left to settle, and as soon as clear liquids appear a drop is taken from each division and tested on a hot porcelain plate with a drop of

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[1] *Zeitsch. anal. Chem.*, 7, 134.

[2] 1871: *Zeitsch. anal. Chem.*, 10, 1.

[3] GERLAND, 1863: *Chem. News*, 8, 54; *Zeitsch anal. Chem.*, 3, 419. GAUHE (1863: *Zeitsch. anal. Chem.*, 3, 131) reports upon the method, with objection on ground of the difficulty of fixing the end of the reaction, and advises to test a filtrate of the titrated liquid for antimony by zinc and hydrochloric acid upon platinum foil. RICHARDS and PALMER, 1878: *Sill. Am. Jour. Sci.* [3] 16, 196, 361—modifications, in the substitution of ammonium acetate instead of chloride, and in testing for excess of antimony. These authors report elementary analyses of the precipitates.

solution of sodium thiosulphate. If the antimony have been added in excess the orange precipitate of antimonious sulphide will appear. By continued tests of the second division the point of least excess of antimony capable of recognition is found approximately. This point is then fixed with exactness by tests of the third division (and, if provided for, the fourth division). The loss by taking out test-drops is reduced to a minimum in the final titrations. It is better to carry the titrations to a decided orange tint for excess of antimony, and then subtract 0.5 c.c. from the reading of the antimony solution as a correction for this excess. The c.c. × 0.01 = the grams of tannin counted as digallic acid. Gallic acid does not interfere in this method, owing to the ammonium acetate. Various colors occurring in tanning materials enter into the precipitates, some of them uniting with the antimony instead of the tannin, and therefore appearing as tannin in the results. Two classes of color substances are indicated by the experiments of Richards and Palmer, one closely allied to quercetin, and both related to tannins and tanning agents. With this method, as with Löwenthal's, true comparisons between different tanning agents, as between oak-bark and hemlock-bark, are not likely to be obtained. The formula of the typical precipitate of digallic acid is presented by the authors last named as $Sb_2(C_{14}H_8O_9)_3 . 6H_2O$. It therefore demands $2KSbOC_4H_4O_6 (2 \times 323 = 646)$ to $3C_{14}H_{10}O_9 (3 \times 322 = 966)$. The authors' analyses of precipitates of pure tannins support the formula very well.

(3) **Hager's** method with copper oxide.[1] The addition of oxide of copper to take up the tannin, which is estimated from the increase in weight of the oxide, or (as in Hammer's plan) by the decrease in specific gravity of the solution. The powdered material is extracted first with water and then with alcohol, the concentrated solution treated with alcohol and filtered, the filtrate evaporated to remove all the alcohol, diluted with water, filtered, and the solution made up to a determinate volume, of which the specific gravity may be taken. Recently ignited oxide of copper, equal to at least five times the weight of the tannin to

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[1] **Fleck**, in 1860, used precipitation with acetate of copper and volumetric estimation of the excess of copper in solution, by potassium cyanide. **Sackur**, *Gerberzeitigung*, 31, 32, directed the ignition of the copper precipitate, and **Wolff**, 1862: *Zeitsch. anal. Chem*, 1, 103, from twenty-eight analyses gave 1 to 1.304 as the ratio between ignited copper oxide and tannin in the precipitate formed by acetate of copper. To exclude gallic acid Fleck treated the precipitate with ammonium carbonate solution. Hager, in his "Untersuchungen," vol. ii. p. 115, gives the method here presented.

be found, is now added, the mixture warmed for an hour, and set aside, with occasional agitation, for a day. The filtrate may now be made up to the determined volume, the specific gravity taken, and the table consulted for percentage of tannin corresponding to difference of gravity. The precipitate may be washed clean, dried on the water-bath, and weighed, the increase in weight showing the quantity of tannin. Gallic acid will be included. The method seems open to danger of loss of tannin by decomposition, especially with oak-bark tannin.

(4) The method of Hammer[1], has been much used for commercial analyses, but gives untrustworthy results. The water solution of the material, made up to a determinate volume, is macerated with dried rasped hide, in quantity at least five times as much as the tannin to be found, until the tannin is wholly removed from solution. The filtered liquid is made up to the volume before noted, and the specific gravity is to be taken both before and after the removal of the tannin. Difference in specific gravity + 1 = specific gravity for per cent. A table of percentages of gallotannin is given at p. 477. Pectous substances are absorbed by the rasped hide, a cause of error unless the pectous substances are removed by precipitation with alcohol, which is then evaporated.

(5) The method of Wagner[2] gives insufficient results with oak-bark, but is serviceable for various manufactured forms of tannins. It is a volumetric precipitation by an alkaloid. 4.523 grams of good sulphate of cinchonine, with 0.5 gram sulphuric acid and 0.1 gram acetate rosaniline or fuchsine, are dissolved in water to make one liter. Each c.c. of this solution precipitates 0.01 gram tannic acid. One gram of solid material is obtained in clear solution of about 50 c.c. measure. To this the standard solution of cinchonine is added, the color being thrown down in the precipitate. By a quick agitation the precipitate soon settles. When the tannic acid is all precipitated, the aniline color appears in solution. One gram having been taken, each c.c. of the volumetric solution indicates 1 per cent. of tannic acid. Gallic acid is not precipitated by cinchonine. Clark[3] has tried a modification of this method for cases of colored liquids which

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[1] 1860: *Jour. f. prakt. Chem.*, 3, 159.

[2] 1866: *Zeitsch. anal. Chem.*, 5, 9. As to limits and deficiencies of this method see Braun, 1868: *Zeitsch. anal. Chem.*, 7, 139.

[3] Contributions from Chem. Lab. of Univ. of Mich., 1876: *Am. Chem.*, 7, 44.

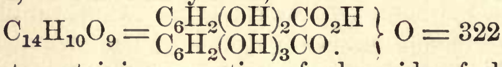
obscure the aniline red. It is the use of the standard solution of cinchonine in some excess, filtering, washing sparingly, and titrating back in the filtrate with Mayer's potassium mercuric iodide solution. This solution may be compared with the cinchonine solution, or the factor of 0.0124 gram of cinchonine sulphate for each c.c. of Mayer's solution may be used.

Among the many other methods for determination of tannins are those with use of Acetate of Lead as a precipitant, with alcohol;[1] bone gelatin solution with alum;[2] and ferric acetate solution with sodium acetate.[3] Upon the adaptation of the several methods of estimation to the several well-known different tannins, see GÜNTHER, 1870.[4]

For estimation of tannin in *leather* HAGER's method may be employed. For the most part gallic acid is obtained from leather instead of tannic acid.[5]

Of distinctly known tannins, or tannic acids, the limits of this work permit only the following to be described.

GALLOTANNIN.—Nutgall-tannin. Gallusgerbsäure. Chiefly Digallic acid, or Gallic anhydride,



$$C_{14}H_{10}O_9 = \left.\begin{matrix} C_6H_2(OH)_2CO_2H \\ C_6H_2(OH)_3CO \end{matrix}\right\} O = 322$$

(SCHIFF), but containing a portion of glucoside of digallic acid. Gallotannic Acid. The TANNIC ACID of the pharmacopœias and of commerce.

Gallotannin is *identified as a tannin* by its sensible properties (*a*, *b*), its reactions with gelatin, alkaloids, iron salts, and permanganate (*d*); *identified as gallotannin* by its fermentation product (*c* and p. 467), its product by heat (*a*), its color with iron salts, with molybdate, and the total bearing of its qualitative tests (*d*); *estimated* by the method of Löwenthal, Gerland, or Wagner (pp. 468–73); *separated* from metallic compounds, iron inks, and the fruit acids, by acetic ether (*c*) or by calcium acetate (p. 21); removed, along with tannins in general, by metallic oxides, gelatin, hide, or bone-black, as described on p. 467. May be prepared from galls as stated on p. 477.

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[1] SCHMIDT, 1874: *Jour. Chem. Soc.*, 28, 1183. ALLEN, *Chem. News*, 29, 169, 189.

[2] One of the earliest methods: FEHLING, MÜLLER: *Liebig and Kopp's Jahresber.*, 1853, 683; *Ding. polyt Jour.*, 151, 69; *Zeitsch. anal. Chem.*, 5, 232.

[3] HANDTKE, 1853: *Jour. f. prakt. Chem.*, 58, 345

[4] *Pharm. Zeitsch. f. Russland*, 1870. *Zeitsch. anal. Chem.*, 10, 354.

[5] As to the chemical examination of leather, see MARQUIS, *Zeitsch. anal. Chem.*, 5, 236 (from *Pharm. Zeitsch. f. Russland*); Hager's "Untersuchungen," ii. 116.

a.—Gallotannin is obtained in light yellowish, lustrous scales, colorless when purified. Not crystallizable, permanent in the air when kept dry, but turning yellowish in the light. Obtained as $C_{14}H_{10}O_9$ at 140° to 145° C. (Löwe, 1872). By a gradual heat (in a test-tube) it melts, darkens, and at 210° to 215° C. mostly breaks into pyrogallol, $C_6H_6O_3$, and carbon dioxide, the former subliming in white crystals. With sudden heat, at about 250° C., it chars with formation of metagallic acid, $C_6H_4O_2$, in the residue.

b.—Tannic acid is odorless or of a faint characteristic odor, and of a purely astringent taste and effect. It does not appear to be absorbed as tannic acid; at all events it is converted in the system into gallic acid, which is found as its product in the blood and urine. It diffuses through membranes very slowly, according to Graham at $\frac{3}{100}$ the rate of common salt. It may be dialyzed from alcoholic solution (Löwe, 1872).

c.—Dissolves in water very readily, with acid reaction, but decomposes gradually in the solution with formation of gallic acid, turning yellow to brown in the light. Freely soluble in aqueous alcohol, with a slight formation of ellagic acid by standing in the aqueous tincture; moderately soluble in aqueous or water-washed ether, without decomposition, but probably with formation of ethyl tannate which dissolves in the water; sparingly soluble in absolute alcohol; but slightly soluble in pure ether, chloroform, benzene, or petroleum benzin; soluble in six parts of glycerin. **Acetic ether** dissolves tannin freely, and if the solvent be strictly free from alcohol, in slightly acidulous solution, it separates the tannin from aqueous solutions and from the fruit acids. If the tannin be in metallic combination, sufficient oxalic or sulphuric acid is first added. With an iron ink, oxalic acid is added to wholly change the color. The acetic ether is shaken in a tube, and drawn off, in portions repeated as necessary, and the ethereal liquid washed with water in the same way. Gallic acid, if present, is obtained with the tannin. With the non-alkali metallic bases, and with the alkaloids, gallotannic acid forms compounds which are stable but of indeterminate proportions, mostly insoluble in water. With **the alkali hydrates,** in presence of air, it begins at once to decompose, solutions turning yellow to brown, and some gallic acid being formed. **Dilute mineral acids** partly precipitate gallotannic acid, unchanged, but on boiling dissociation to gallic acid occurs ($C_{14}H_{10}O_9 + H_2O = 2C_7H_6O_5$), glucose appearing in the solution so far as the gallotannin contained glucoside (p. 467). The change to gallic acid also takes place in presence of the ferment of nutgalls and water, when the wetted powder is set aside for some weeks.

d.—Concentrated **sulphuric acid** sparingly dissolves gallotannin, with yellow-brown color turning first to purple-red and then to black on warming. **Nitric acid** rapidly oxidizes it, with formation of oxalic acid ; chlorine, bromine, iodine, and chromic acid act violently upon it ; it promptly reduces **permanganate,** reduces silver nitrate on warming, reduces mercuric chloride and gold chloride, and reduces **alkaline copper solution.** It turns brown to green with alkali hydrates and with atmospheric oxidation. It is very perfectly *precipitated* by solutions of **gelatin, albumen,** and **gelatinized starch** (distinctions from gallic acid) ; by **cinchonine sulphate** and solutions of **alkaloids** generally (distinction from gallic acid), some of the alkaloidal precipitates dissolving easily in hydrochloric acid, and nearly all dissolving with acetic acid ; by **tartrate of antimony and potassium,** this precipitate being increased by ammonium chloride solution (in which that of gallic acid is soluble) ; and by **lime** and **baryta** solutions added in excess, the precipitates slowly darkening in color. Tannin gives no precipitates with calcium salts until alkali be added, the least excess of which darkens the precipitate and the solution. **Ferric chloride** and other ferric salts, and, still better, the basic ferroso-ferric solutions, give a blue-black precipitate, dissolving to a green solution by excess of the iron salt. With excess of the tannin solution the precipitate is permanent, and subsides so as to leave a clear liquid. The precipitate dissolves readily on addition of hydrochloric acid, strong acidulation even destroying the color, when the addition of acetate of sodium will cause a reproduction of the blue-black precipitate, which is not easily soluble in acetic acid. The green solution obtained from excess of ferric salt with acetate of sodium does not give a precipitate, but shows a reduction to ferrous salt. When the tannin is in sufficient excess, boiling destroys the blue-black color, the iron being reduced to ferrous salt. Sufficient sulphurous or hydrosulphuric acid removes the color in the same way. **Ferrous salts** (strictly free from ferric) give a white precipitate, only in concentrated solutions.—**Acetate of lead** gives a complete precipitate. **Molybdate of ammonium** with tannin presents a red color removed by oxalic acid. **Potassium ferricyanide** in solution with ammonium hydrate causes a deep red color in solutions of tannin (a delicate reaction, A. H. ALLEN).

Gallotannin, in solution very slightly acidulated with acetic acid, is not precipitated by adding calcium acetate solution and then to the liquid twice its volume of alcohol—a separation from tartaric, citric, malic, and oxalic acids (Barfoed[1]).

e.—Gallotannin is *obtained from nutgalls* by treating the powder, first exposed to a moist atmosphere for twenty-four hours, with water-washed ether to form a soft paste, covering this for six hours, and then expressing. This treatment is repeated, and the expressed liquids spontaneously evaporated to a syrup, which is spread on glass and dried (U. S. Ph. of 1870, Br. Ph.) Another method requires maceration of the powdered galls in a mixture of 12 parts ether and 3 parts of alcohol of 90%. The expressed liquid is washed with a third of its volume of water, and again with a little water, and the aqueous liquid, containing the tannin, is evaporated on the water-bath.

A water solution of gallotannic acid at 17.5° C. (63.5° F.) contains as follows:

Percentage.	*Specific gravity.*	*Percentage.*	*Specific gravity.*	*Percentage.*	*Specific gravity.*
20	1.0824	13	1.0530	6	1.0242
19.5	1.0803	12.5	1.0510	5.5	1.0222
19	1.0782	12	1.0489	5	1.0201
18.5	1.0761	11.5	1.0468	4.5	1.0181
18	1.0740	11	1.0447	4	1.0160
17.5	1.0719	10.5	1.0427	3.5	1.0140
17	1.0698	10	1.0406	3	1.0120
16.5	1.0677	9.5	1.0386	2.5	1.0100
16	1.0656	9	1.0365	2	1.0080
15.5	1.0635	8.5	1.0345	1.5	1.0060
15	1.0614	8	1.0324	1	1.0040
14.5	1.0593	7.5	1.0304	0.5	1.0020
14	1.0572	7	1.0283	0	1.0000
13.5	1.0551	6.5	1.0263		

For Hammer's table of specific gravity and percentage of tannin, see Fresenius's "Quantitative Analysis."

Sumach Tannin.—From the fruit, leaves, and branches of Rhus glabrum, R. coriaria, and other species of Rhus. Sten-

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[1] "Organ. qual. Analyse." Kopenhagen, 1881. S. 58–61.

HOUSE (1861[1]) reported it identical with gallotannin. GÜNTHER (1871)[2] found the tannins of Sumach, Myrobalan, and Divi-divi to be nearly the same—all agreeing closely with gallotannin, and not at all with oak-bark tannin. He found them all to yield gallic acids by glucosic fermentation, and pyrogallols by sublimation, and to react like gallotannin with salts of lead, copper, and iron, with gelatin, antimony tartrate, and permanganate. LÖWE (1873[3]), from examination of Sicilian sumach, *R. coriaria*, the variety chiefly used for tanning, declared it to be identical with gallotannin, and found by elementary analysis (as Günther had done) numbers nearly those of digallic acid. Sumach tannin is a tanning material much used, a fact of interest in view of its agreement with gallotannin. Wagner's classification of the latter as a non-tanning agent appears to be opposed by various evidences.

OAK-BARK TANNIN. Quercitannic acid. Quercitannin. Eichenrindengerbsäure. From bark of various species of Quercus. Found also in Black Tea (ROCHLEDER). Also the tannin of the Elm and the Willow (JOHANSON, Dorpat, 1875). It is a glucoside, with boiling dilute sulphuric acid readily breaking up with formation of oak-red, amorphous, and an uncrystallizable sugar, no gallic acid appearing (GRABOWSKI, 1868); gives up water and forms an anhydride (ETTI, 1884); boiling with caustic alkalies yields a different anhydride (the same). The oak-red is a phlobaphene, found by itself in the oak-bark. It does not yield pyrogallol in sublimation, but when heated with potash it furnishes protocatechuic acid and phloroglucin, the products also being obtained from oak phlobaphene. Oak-bark tannin is freely soluble in water and in alcohol, in ether sparingly soluble. It gives the ink color with the basic ferroso-ferric solutions, and, less intensely, with ferric solutions. It gives precipitates with acetates of lead, copper, and iron, and with gelatin; is taken up by oxides of lead, copper, and zinc, by rasped hide, and by animal charcoal. It promptly reduces Fehling's solution, or the permanganate, and chlorinated lime and other oxidizing agents act very promptly upon it. This tannin is the most important of tanning agents, and the methods of the estimating tannin (pp. 468, 473) have been mainly framed in reference to valuation of oak-bark. At the same time it is one of the least stable of the tannins, and its extraction without notable waste is a task of

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[1] *Proc. Roy. Soc.*, **11**, 401.

[2] Inaug. Dissertation. Dorpat., *Zeitsch. anal. Chem.*, **10**, 359.

[3] *Zeitsch. anal. Chem.*, **12**, 128; *Jour. Chem. Soc.*, **27**, 171.

difficulty. Dragendorff recommends[1] to extract the bark with alcohol, distil the spirit in partial vacuum, add water, filter quickly, and estimate at once. Löwenthal's method has the preference for this tannin.

Catechutannin.—From Acacia catechu and other East Indian trees. The catechu, or cutch, of commerce contains 40% to 55% of tanning material, and furnishes Catechutannic acid and Catechin. I. Catechutannic acid (Mimotannic acid, Catechin red) is obtained, nearly free from catechin, by treating catechu with cold water. It is precipitated by concentrated sulphuric acid. Boiled with dilute acids it forms a dark-brown, resinous body, mimotannihydroretin (Löwe, 1869). Gives a changeable brownish-green color with ferric salts. Precipitates tartrate of antimony and potassium (Löwe), alkaloids, gelatin, and albumen, and changes animal membrane to leather. Precipitates lead acetate (with red color), dichromate of potassium (brownish-red), and acetate of copper (with a leather color). It reduces silver nitrate and gold chloride. According to Etti (1876), catechuic acid, or, as he terms it, catechin-red (which may be termed a phlobaphene), is the first anhydride of catechin, and is formed from it by drying over sulphuric acid, or by boiling with sodium carbonate solution. $C_{38}H_{34}O_{15}$ (catechutannic acid) $+ H_2O =$ $2C_{19}H_{18}O_8$ (catechin). II. Catechin (Catechuic acid or Tannin-genic acid). Dissolved from catechin by boiling water, and extracted by ether from dilute alcoholic or concentrated aqueous solutions, crystallizing in needles (Etti, preparation, "Watts's Dictionary," vii. 415). It gives a green color with ferric salts, reduces silver salts, turns purple with concentrated sulphuric acid, and precipitates albumen, but not gelatin, nor alkaloids, nor tartrate of antimony and potassium. Fused with potash it is resolved into protocatechuic acid ($C_7H_6O_4$) and phloroglucin ($C_6H_6O_3$).

Morintannin or morintannic acid. From Fustic, prepared from Morus tinctoria. Crystallizable, with an intense yellow color. With ferric salts it gives a greenish precipitate; with lead acetate, a yellow precipitate; with copper sulphate, a yellowish-brown precipitate; with stannous chloride, a yellowish-red precipitate.

Cinchotannin or cinchotannic acid. From cinchona barks, of which it forms at the most 3% to 4%. In clear yellow masses, very hygroscopic, and becoming electric when rubbed, soluble in

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[1] "Die Analyse von Pflanzen," u. s. w., 1882, p. 167.

ether, as well as in water and alcohol. It readily changes to a red-brown, resinous body, insoluble in water. By hot dilute acids it forms sugar and cinchona-red, the latter dissolving in ammonia, this solution being precipitated by acids, also by barium chloride (with a red color) (Rembold, 1867). With aqueous alkalies, in exposure to the air, red solutions are formed. Ferric salts form a green precipitate; tartrate of antimony and potassium, a gray-yellow precipitate; and acetate of lead, a clear yellow precipitate. Precipitates are likewise formed with solutions of gelatin, albumen, and starch. Its natural compounds with cinchona alkaloids are difficultly soluble in water, but dissolve easily in acidulated water. On fusing with potassium hydrate, protocatechuic and acetic acids are formed.

Caffetannin or caffetannic acid. From coffee (Coffea arabica). In brittle masses, forming a yellow-white powder. But slightly soluble in ether. By boiling with dilute sulphuric acid, or by digesting with alkali hydrate solutions in the air, viridic acid is formed, with a blue-green color. Viridic acid is identified by giving a blue precipitate with lead acetate, and a crimson color with concentrated sulphuric acid (Rochleder, *Ann. Chem. Phar.*, 63, Cech, *ibid.* 1868, 142). By long boiling with potash, caffeic acid is formed, and crystallizes from the neutralized solution (Rochleder, Hlasiwetz). Ferric chloride gives a dark-green color. In fusion with potassium hydrate, protocatechuic acid and acetic acid are formed. In dry distillation pyrocatechol is obtained.

Tannin of Tea. Dissolves from tea very sparingly in cold water, and but slowly in boiling water, black tea withholding its tannin from solution much longer than green tea. Complete solution requires brisk boiling for half an hour, with two or three successive portions, each of fifty parts of water.[1] The average quantity may be stated at 11 or 12 per cent. of total tannin in black teas, and 15 or 16 per cent. in green tea, with widely separated extremes.[2] The character of tea tannin has not been well

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[1] Experiments with twelve kinds of tea gave solutions of the tannin, which yielded, in tannin percentage of air-dry tea, an average for the twelve, as follows: In steeping 5 minutes, 0.08 per cent.; 10 minutes, 0.55 per cent.; 20 minutes, 1.53 per cent.; 30 minutes, 2.49 per cent., the digestion being done over a water-bath.—Report by the Author, *Physician and Surgeon,* 1880, p. 339.

Fuller determinations are reported by Mr. Geisler in Tables III. and IV. in the article "Teas of Commerce" in this work.

[2] Dragendorff (1874) reports green tea at 12 and black tea at 9.4 per cent. A. H. Allen (1875), as averages, about 20 per cent. in green tea (with great variations), and 10 per cent. in black tea. Eder (1881), green tea, from nine

established. Stenhouse (1861) found a little gallic acid in both green and black teas, but no formation of either sugar or gallic acid by boiling with dilute sulphuric acid. He precipitated the tannin in strong decoction by adding a half-volume of sulphuric acid. Rochleder (1847) found BOHEIC acid (boheatannic acid), giving a brown color with ferric salts, along with iron-bluing tannin. In black tea he reported finding quercitannic acid.[1] The tannin of black tea gives a brown with ferric salts, or in alcoholic solution a green color. Green tea in infusion gives a blackish color with ferric salts, or blue-black in alcoholic solution. Tea tannin precipitates alkaloids generally (cinchonine very closely), gelatin, albumen, and lead acetate.

TANNIN OF HOPS. Of the hop-cones, 3.67% (BOWMAN, 1869). Investigated by ETTI (1876, 1878) with results as follows: I. HOP TANNIN. Easily soluble in water and in dilute alcohol, not in ether. Acts as a glucoside: $C_{25}H_{24}O_{13}$ (hop tannin) $+ 3H_2O =$ $C_7H_6O_4$ (protocatechuic acid) $+ 2C_6H_6O_3$ (phloroglucin) $+$ $C_6H_{12}O_6$. Easily dissolved by water or dilute alcohol, not by ether. Gives a dark-green color with ferric salts, a dirty green precipitate with copper sulphate, a yellow precipitate with lead acetate, a reddish-brown color with alkali hydrates, a brownish-yellow precipitate with lime solution, and a precipitate with albumen, but, unless previously heated, dry, on the water-bath, does not precipitate gelatin. Reduces alkaline copper solutions. By heating on the water-bath, is changed to II. PHLOBAPHENE OF HOP [having characteristics of a tannin] and also obtained directly from the hops. According to Etti, a glucoside ($C_{50}H_{46}O_{25}$), yielding protocatechuic acid, phloroglucin, and glucose. The Phlobaphene dissolves in alcohol and in alkalies, and is precipitated from alkaline solutions by acidulation. It reduces alkaline copper solutions. It precipitates gelatin completely.

TANNIN OF HEMLOCK-BARK. Abies Canadensis. Extensively used as an American tanning material. The bark sometimes yields 13–14% tannin.

ALDER TANNIN. From Alnus glutinosa. With acids does

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samples, 12.4 per cent.; black tea, from twenty-five samples, 10.1 per cent. A report by the Author, in 1876, gave 12 per cent. as the average of twenty kinds of green and black tea. Much higher figures have been given: WIGNER, 1875, 33 per cent. to 45 per cent. But the best present data are those given by Mr. GEISLER in the article on "Teas of Commerce" in this work.

[1] The results certainly indicate that the sweating operations in manufacture of black tea so act upon the tannin as to convert a smaller part into other substances and modify the remainder.

not yield sugar (Stenhouse). From the wood, an iron-greening; from the bark, an iron-bluing tannin. Used for tanning.

Chestnut tannin. From species of Castanea. Boiled with dilute sulphuric acid, yields chestnut-red, a phlobaphene or resin-like precipitate of cherry-red color. With ferric chloride gives a deep green color. Does not precipitate tartrate of antimony and potassium. Fused with potash, forms protocatechuic acid, $C_6H_3(OH)_2CO_2H$, and phloroglucin, $C_6H_3(OH)_3$.

For other tannins see Dragendorff's "Die Analyse von Pflanzen," article 165, pp. 162–168; Husemann's "Die Pflanzenstoffe," by general index; *Jour. Chem. Soc.*, Abstracts, etc.

Inks.—The black inks and writing fluids in most general use have gallotannin, taken as *nutgalls*, and iron as oxidized in the air from ferrous sulphate, as their essential basis. The gallic acid of the galls is quite as serviceable as the tannic acid, in fact both are required, and inks are made with use of tannic and gallic acids and iron. The color compound of iron with gallic acid and gallotannin in inks is mostly not in solution, but is in very fine suspension, usually with help of a slightly viscid menstruum, by use of a gum. Besides galls and their products, *logwood* is next most used in inks, both with galls and without. It contains a tannin, as well as the color substance hæmatoxylin. Logwood and alum or other salt form the basis of purplish inks. Logwood and chromate of potassium make a clear liquid ink that has been much esteemed. Chrome alum has also been used with logwood. Sumach has been used instead of galls. Some of the nutgall inks contain a little acetic acid, added as vinegar. Some of the gallic inks have the addition of sulphindigotic acid or of sodium sulphindigotate (indigo-carmine). Aniline dyes of various colors are used as a part or the whole of the color of black and colored inks.[1]—*Blue inks* are made of prussian blue and oxalic acid, or "soluble prussian blue" and a little oxalic acid, also of anilines. *Red inks* are made of cochineal, or its product, carmine, with ammonia or carbonate of ammonia. Cream of tartar and sodium carbonate are also used as solvents of carmine. Brazil-wood is employed for another class of red inks, and red to violet inks made from aniline dyes have been common.—*India ink* and China ink consist of finely divided carbon, and are wholly insoluble, but very durable inks of good service for the pen have been made by a suspension of india ink in dilute hy-

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[1] A black ink very highly recommended is made of nigrosine (an aniline black), potassium dichromate, and gelatin. Directions in *New Rem.*, 1883, 12, 27. Modified for copying ink, *ibid.*, 1883, 12, 250 (Aug.)

drochloric acid or in potassium hydrate solution.—*Copying inks* are made by addition of glycerin to any ink, the glycerin taking the place of an equal volume of water.—All inks containing tannin, logwood, etc., are liable to mould, and essential oils are often added as preservatives. Salicylic acid is a good preservative, and carbolic acid usually prevents decomposition.—For *indelible inks* for marking linen, solution of silver nitrate, with a little india ink, has been used. Gold and platinum have been used in the same way, staining by reduction. Aniline marking inks are in use. Molybdenum chloride is also taken as the coloring agent of a marking ink.—*Printer's ink* is finely divided carbon in mixture with linseed oil, with lesser additions of turpentine, resins, etc.—*Hectographic ink* is of aniline color (methyl-violet 1, water 7, glycerin 2).—As to the composition of inks, see the article by Prof. Silliman in "Johnson's Cyclopædia"; also "Watts's Dictionary," iii. 272, viii. 1090; and an Inaugural Dissertation of O. L. Wilson, Univ. Mich., 1881.

CHEMICAL EXAMINATION OF WRITINGS, *and the discharge of Ink-Stains.*—Such examination may give some indication of the nature of the ink used, and may serve to show whether two portions of writing were written by the same ink or not, and at the same period of time or not, also whether ink-marks have been discharged by chemical agents. A minute inspection is first made under a magnifying-glass, or a microscope of a power of not more than ten diameters. Differences of lustre, color, shade, and absorption into the paper are to be noted, and, when lines cross each other, which lies uppermost. In the chemical treatment the reagents most used are, *first*, a solution of oxalic acid, one part in fifteen parts of water, and, *second*, hydrochloric acid of 12.5%. These may be applied by a quill pen through the writing, and the result noted as the reagent dries. Writing with gallic inks, of not over two days' standing, is discharged by the oxalic acid in one application to a light gray; when older the ink color resists longer and a deeper gray remains. Logwood ink-writings, under oxalic acid, mostly turn to reddish tints. Aniline ink-marks are not altered by oxalic acid. Alizarin ink-marks turn bluish. By treatment with the hydrochloric acid (not warmed), fresh gallic ink-marks, not over one day old, turn yellow; older marks, yellow-gray. Logwood ink-writings turn reddish or reddish-gray; those of alizarin ink turn greenish; and those of aniline inks, reddish to brownish-gray. Following treatment with acids and drying, moist vapor of ammonia, or blotting-paper wet with solution of ammonia, may be applied.

Under this alkali the marks darken again in different degrees and colors, those of logwood inks turning of a dark violet to violet-black. In distinguishing between ink-marks as to their age, treatment with ammonia solution of ten per cent. is often quite decisive, old ink-marks dissolving away with more difficulty.

Other reagents employed are dilute sulphuric acid, dilute nitric acid, sulphurous acid solution, sodium hydrate solution, chlorinated lime solution, stannous chloride solution, and stannic chloride solution. The reagent may be absorbed by blotting-paper a few seconds after its application, or allowed to dry. After treatment with ammonia, solution of gallic acid or solution of cupric chloride may be employed. Control-tests, with writings of known inks and ages, should not be neglected. Obviously it may be possible to show that given marks were or were not made with the same inks, when not possible to identify the constituents of the inks.

The falsification or alteration of writings is undertaken by erasing or by application of bleaching agents. After erasing the spot is often rubbed over with powder of alum or of sandarac, or is coated with a little gelatinous sizing. The bleaching agents used are commonly oxalic acid, citric acid, hydrochloric acid, chlorine-water or chlorinated lime solution, and bisulphite of sodium. In the investigation the sizing material of the paper must be considered, as well as any coloring agents used in its manufacture. Moistened litmus-paper, or other indicator, may be applied to indicate the presence of fixed acids. Application of ammonia vapor or alcoholic solution of ammonia may restore colors discharged by acids. Tests for iron salts left after discharge of iron ink-marks may be made by alcoholic solution of gallic and tannic acids, or by water solution of one of the cyanogen reagents. Copper salts may also be tested for. Among other experiments, the application of iodine vapor, over a beaker, has been resorted to. To reveal faded marks of iron ink the paper may be moistened with solution of potassium sulphocyanide, and exposed to vapor of hydrochloric acid.[1]

To remove ink-stains from white cotton or linen fabrics, solution of oxalic acid or dilute hydrochloric is most used, and does well with stains of nutgall ink. After hydrochloric acid, granulated tin or zinc may be applied to favor reduction and removal of iron. For colored cloths of cellulose fibre, and for

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[1] Further upon the chemical examination of ink writings see Hager's "Untersuchungen," ii. 599; and W. THOMPSON, 1880: *Chem. News*, 42, 32. Also "Rogers on Expert Testimony," 1883, p. 182.

woollens, repeated washings with citric acid may be tried, but some colors will be changed by it. Strong solution of pyrophosphate of sodium has been employed, and may be used after treatment with tallow. Aniline ink-stains are in some cases removed by strong alcohol acidulated with acetic acid.[1]

TARTARIC ACID. $H_2C_4H_4O_6 = C_2H_2 \left\{ \begin{matrix} (OH)_2 \\ (CO_2H)_2 \end{matrix} \right. = 150.$

Ordinary Tartaric or Dextrotartaric Acid. *Weinsäure.*—Very widely distributed in fruits and other parts of plants, chiefly as potassium acid tartrate, calcium normal tartrate, and free acid. Manufactured from the grape-wine deposits of acid tartrate by forming calcium tartrate, and transposing this with dilute sulphuric acid. Largely used, as free acid and as acid tartrate of potassium (cream of tartar), in calico printing, and in baking powders, effervescent carbonates, medicinal preparations, etc. The normal tartrate of potassium and sodium, the normal tartrate of potassium, and the basic tartrate of antimony and potassium are in common use.

Tartaric acid is distinguished by the form of its crystals, its odor when heated, and its blackening by sulphuric acid (*a*); by its precipitations as potassium acid salt, calcium salt, and lead salt, by Fenton's color test, and by its extent of reducing power (*d*). Methods of separation, as a free acid, and from its salts, by solvents and precipitants, are noted in *e*. It is *estimated*, as free acid or acid tartrate, volumetrically and gravimetrically (*f*); in Liquors of Citric and Tartaric Acids, by precipitation and titration; in Tartars, Argols, and Lees, by various methods; in Fruit Juices, from a lead precipitate (p. 488); in pure watery solutions, by specific gravity. Impurities, *g*. *Cream of Tartar* and calcium tartrate, p. 496. Examination of Cream of Tartar, p. 498. *Baking Powders*, constituents, p. 500; valuation, pp. 501–504.

a, b.—Dextrotartaric acid is found in commerce in large, hard, fragmentary, permanent, water-white crystals, or in an opaque-white, fine powder. The crystals, $H_2C_4H_4O_6$, are monoclinic, oblique rhombic prisms, hemihedral, the most perfect ones showing two corners truncated on the same side while the two opposite corners are not cut off. They are pyro-electric, shining in the dark, after friction. The specific gravity is 1.764. The dry acid melts at 135° C., forming a clear liquid, which at 170° C. is converted into metatartaric acid, deliquescent and un-

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[1] For directions for removal of stains and spots of many kinds see *New Remedies*, March, 1882, **11**, 74; *Am. Jour. Phar.*, Dec., 1880, **52**, 632; *New Remedies*, Jan., 1883, **12**, 24.

crystallizable, and at about 200° C. forms anhydrides, some of which do not dissolve readily in water. At a higher temperature the mass blackens and evolves vapors with a strong odor of burnt sugar or caramel. Concentrated sulphuric acid dissolves dry tartaric acid in the cold without color, the mixture charring when warmed.

c.—Tartaric acid is *soluble* in less than its weight of cold water, in about three parts of alcohol (of absolute alcohol, four parts—Bourgoin, 1878), in 250 parts of absolute ether,[1] soluble in methyl alcohol and in amyl alcohol, insoluble in chloroform and in benzene. The water solution rotates the plane of polarized light to the right. Decomposition soon occurs in water solution, with a fungoid growth containing nitrogen.

The normal tartrates of potassium, sodium, and ammonium, and the acid tartrate of sodium, are freely *soluble* in water; the acid tartrates of potassium and ammonium are sparingly soluble in water; the normal tartrates of non-alkali metals are insoluble or only slightly soluble in water, but mostly dissolve in solution of tartaric acid. Tartrates are insoluble in absolute alcohol. Aqueous alkalies dissolve most of the tartrates (those of mercury, silver, and bismuth being excepted), generally by formation of soluble double tartrates, such as $K_6Fe_2(C_4H_4O_6)_6$, a scale preparation of the pharmacopœia. For this reason tartaric acid prevents the precipitation of salts of iron and many other heavy metals by alkalies. Alkali normal tartrates also hinder the precipitation of lead and barium sulphates, manganese sulphide, and ferrous ferricyanide.[2] Hydrochloric, nitric, and sulphuric acids transpose tartrates.

d.—**Lime solution,** added to free tartaric acid solution until the reaction is alkaline, gives a precipitate without warming (distinction from citric acid, which precipitates only when heated). With a neutral tartrate the precipitation is obtained by adding much of the lime solution or by boiling. **Calcium chloride** solution is precipitated, not by free tartaric acid, but by neutral tartrates, in solutions not very dilute, and when neither the tartrate nor the lime salt is in large excess. The precipitate, calcium tartrate (see p. 498), when freely formed is voluminous and amorphous, and dissolves in about 1000 parts of cold water, in an excess either of the tartrate or the calcium salt, in acetic acid (distinction from oxalate), and in ammonium

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[1] J. Nessler, 1879: *Zeitsch. anal. Chemie*, 18, 230.

[2] Spiller, 1858: *Jour. Chem. Soc.*, 10, 110.

chloride. On standing, or in dilute solutions at its first formation as a delayed precipitate, it assumes a crystalline form, much less easily seen than the amorphous form, and less easily dissolved by any of the solvents above named, hardly soluble by acetic acid. The calcium tartrate precipitate is soluble in cold strong **potassa solution** (distinction and partial separation from citrate or oxalate); the precipitate reappearing when the liquid is heated, and again dissolving as it cools. This reaction is best obtained with the washed calcium tartrate precipitate; an excess of calcium chloride in the mixture interferes.—**Calcium sulphate** solution is not precipitated by free tartaric acid (difference from oxalic acid), but gradually gives a slight precipitate with tartrates (difference from citrates).

Solution of **potassium acetate**, or citrate, precipitates free tartaric acid, as potassium hydrogen tartrate, $KHC_4H_4O_6$. The precipitate forms slowly, in trimetric crystals, which subside, the formation being favored by stirring with a glass rod. The precipitate dissolves in alkalies by formation of normal tartrates. In this test a neutral or alkaline liquid is to be strongly acidulated with acetic acid, which does not at all dissolve the precipitate. If a free mineral acid be present, only so much the more reagent potassium acetate is to be added. The precipitate is soluble in about 180 parts water at common temperatures and in 15 parts boiling water, insoluble in alcohol, and not appreciably soluble in fifty per cent. alcohol. Two volumes of ordinary alcohol may be added to one volume of the aqueous solution, with strong acetic acidulation, to hold other salts in solution. This precipitate is a *separation* from citric, malic, and oxalic acids, and from salts of many inorganic acids as well. In the latter case care must be taken that the alcohol does not throw down inorganic salts of potassium. Further, see p. 490.

Tartaric acid is distinguished from citric acid, in crystal, and the former is detected in a crystalline mixture of the two acids, as follows:[1]

A solution of 4 grams of dried potassium hydrate in 60 cubic centimeters of water and 30 cubic centimeters of 90 per cent. alcohol is poured upon a glass plate or beaker-bottom to the depth of about 0.6 centimeter (one-fourth inch). Crystals of the acid under examination are placed, in regular order, three to five centimeters (one to two inches) apart, in this liquid, and left without agitation for two or three hours. The citric acid crystal dissolves slowly but completely and without losing its

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[1] Hager's "Untersuchungen," ii. 103.

transparency. The tartaric acid crystal (or the crystal containing tartaric acid) becomes, in a few minutes, opaque white (in a greater or less degree), and continues for hours and days slowly to disintegrate without dissolving and with gradual projection of spicate *crystals*, fibrous and opaque.

Solution of **lead acetate** precipitates free tartaric acid or tartrates, as white normal tartrate of lead, very slightly soluble in water, insoluble in alcohol, but slightly soluble in acetic acid, readily soluble in tartaric acid, in ammonia, and in tartrate of ammonium solution, and freely soluble in ammoniacal solution of tartrate of ammonium (distinction from Malate), somewhat soluble in chloride of ammonium.

A color test is made, after removal of heavy metals or oxidizing agents, by adding, to the acid or its alkali salt, a little ferrous sulphate solution, then a little hydrogen peroxide, or chlorinated soda solution, or acidulated permanganate solution (the first of these three being the best)—avoiding an excess of the oxidizing agent—lastly an excess of potassium or sodium hydrate solution, when a fine violet color gives evidence of the presence of tartaric acid.[1]

Solution of **silver** nitrate precipitates solutions of normal tartrates (not free tartaric acid) as white argentic tartrate, soluble in ammonia and in nitric acid. On boiling the precipitate turns black, by reduction of silver, some portion of which usually deposits as a mirror-coating on the glass. The *reduction* to the specular metallic form may be obtained, from even slight quantities of tartaric acid, as follows: Acidulate the solution with nitric acid, add some excess of silver nitrate solution, filter out any precipitate (not tartrate), and add very dilute ammonia-water to slight alkaline reaction. If a precipitate of silver tartrate appears, add the ammonia till it is nearly all redissolved, filter, heat to near the boiling point for a minute, and set aside in a warm place. (Citric acid does not effect this reduction, or only on long boiling.) Free tartaric acid does not reduce silver from the nitrate.

Permanganate of potassium solution is reduced very slowly by free tartaric acid, but quickly by alkaline solution of tartrates, with precipitation of manganese dioxide, brown (a distinction from Citrates, which reduce permanganate but very slowly, and then form green solution of manganate, more than precipitate of dioxide).—**Dichromate** of potassium solution is

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[1] Fenton, 1881: *Chem. News*, 43, 110; *Jour. Chem. Soc.*, 40, 655; *New Remedies*, 10, 147.

readily reduced by tartaric acid, with appearance of a green color and slight effervescence. For use of this test in distinction from malic, citric, and succinic acids, see under Malic acid, at *c*. In the detection of tartaric acid in Citric acid of commerce, CAILLETET[1] directs to take 10 c.c. of saturated dichromate solution, add 1 gram of the acid to be tested, and stir, not warming. After ten minutes' standing he found pure citric acid to remain orange-colored; that with 1 per cent. tartaric acid, coffee-colored; with 5 per cent. tartaric acid, black-brown. Among the products of the oxidation of tartaric acid by permanganate and chromate are formic acid, carbon dioxide, and water.—Copper sulphate with potassium hydrate is not reduced by tartaric acid.—Gold chloride solution is reduced only in solution made alkaline with potassium hydrate, when a black precipitate of aurous chloride is formed.

e.—Tartaric acid may be *separated* from tartrates by adding its equivalent quantity of sulphuric acid and extracting with alcohol (in which most sulphates are insoluble). Free tartaric acid may be taken out of water solutions by agitation with amyl alcohol, which, after standing, is decanted. From the other fruit acids (citric, malic, oxalic), and most inorganic acids, it is best separated by its precipitation as bitartrate (*b*), also approximately separated by its calcium reactions (*b*, and in detailed scheme under Malic acid, *d*). From tannin and gallic acid as noted under Gallotannin, p. 477. From acids whose lead salts are soluble in water, by treatment with lead acetate, followed by hydrogen sulphide, etc.

f.—*Quantitative.*—Free tartaric acid, if unmixed with other acids or salts which neutralize alkalies, may be *estimated volumetrically* by standard alkali solutions, the point of saturation in normal tartrate being sharply defined by the tint of litmus or by phenol-phthalein. Weighing 0.750 gram, the number of c.c. of decinormal alkali solution required equals the number per cent. of the acid. Each c.c. of normal alkali neutralizes 0.075 gram of acid.—The *acid tartrate of potassium*, obtained by precipitation, as directed below, may also be exactly estimated by acidimetry, when each c.c. of normal alkali solution required indicates 0.150 gram of tartaric acid. Another way, properly used in some cases but having no advantage if the acid tartrate be pure, is to gradually ignite the dried precipitate of acid tartrate, at a low red heat,

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[1] *Jahresb. d. Phar.*, 1877, 316; from *Jour. de Phar. et de Chim.* [4] 25, 573; *Zeitsch. anal. Chem.*, 17, 499.

till vapors no longer rise, cool and treat the charred mass (containing all the potassium as carbonate) thoroughly with water and a slight excess of volumetric acid from the burette, boil, and filter, and wash well, and titrate back with volumetric alkali. Each c.c. of normal acid, after deduction of the number of c.c. of corresponding alkali solution used, indicates (the same as when measuring the acid precipitate with alkali) 0.150 gram of tartaric acid in the bitartrate. Much care is needed to avoid loss during ignition.

Tartaric acid is capable of estimation volumetrically by oxidizing agents. A method with use of dichromate for this purpose has been proposed (compare Citric Acid, *c*). The use of permanganate for titration of tartaric acid in metallic salts has been reported by F. W. CLARKE, 1881.[1]

The *gravimetric determination* most generally applicable is that by *precipitation as potassium hydrogen tartrate*, though this precipitate is more easily and surely treated volumetrically. The reagent is the acetate of potassium, or, if iron or aluminum be present, citrate of potassium (WARINGTON); and if the tartaric acid is in neutral salts, acetic acid should be added with the acetate (or citric acid with the citrate) to a decided acid reaction, and enough to fully prevent the formation of the freely soluble normal tartrate. In simple mixtures the acetate is better than the citrate, and excess of either is to be avoided. By use of alcohol the precipitate may be made complete, and may be washed without loss. The moist precipitate, just washed volumetrically clean, may be titrated (either with the filter or transferred) with standard alkali, as directed above, or, after washing gravimetrically clean and drying at 100° C., the precipitate may be weighed. $KHC_4H_4O_6 : H_2C_4H_4O_6 :: 1 : 0.797$. The strength of alcohol, in the precipitation and in the washing, should be at least 50% by weight, unless some other agent is depended upon to diminish the solubility of the precipitate. If no interference is apprehended the strength may be 60 to 65%.[2] If sulphates

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[1] *Am. Chem. Jour.*, 3, 201.

[2] The author has found the precipitate to be washed continuously with 50 per cent. alcohol without weighable loss FLEISCHER, 1870: *Zeitsch. anal. Chem.*, 9, 331; *Am. Chem.*, 1, 352. using the precipitate for the determination of potassium, finds it insoluble in 50 per cent. alcohol. (If sodium be present, to avoid its precipitation he directs to add ammonium chloride.) CASSAMAJOR, 1876: *Am. Chem.*, 7, 84, finds that alcohol of about 60 per cent. is needed to preserve the precipitate from waste. Strong acidulation with acetic acid has no solvent effect on the precipitate. WARINGTON found tartaric acid to have no solvent power, citric acid a slight solvent power, and hydrochloric acid much solvent power, when applied, in water, to the precipitate.

are present they are liable to be precipitated by the alcohol, and will interfere with the gravimetric treatment of the precipitate. A sulphate of aluminium, or iron, or any other salt that will neutralize an alkali, will interfere likewise with the volumetric treatment; but a sulphate of calcium, or any salt that does not neutralize an alkali, may be permitted to go into the precipitate if this is to be volumetrically determined. Further, as ascertained by WARINGTON and applied in his methods, given below, the precipitate is but little soluble in chloride of potassium solution.

For determination of tartaric acid *in complex Liquors of Citric and Tartaric Acids*, occurring in the manufacture of these acids, WARINGTON[1] directs as follows: A quantity of the liquor containing from 2 to 4 grams of tartaric acid, and of 30 to 40 c.c. in volume, is treated with citric acid unless free sulphuric acid is present, then treated with a saturated solution of normal potassium citrate, added in measured quantity drop by drop with constant stirring. If free sulphuric acid is present no precipitate appears until this is satisfied, when the streaks of bitartrate form on the sides of the vessel. An excess of reagent is avoided, and 4 c.c. are enough for the maximum of 4 grams of tartaric acid. If there is a great deal of sulphuric acid, a fine precipitate of potassium sulphate may appear before the precipitation of bitartrate. The occurrence of a gelatinous precipitate shows that not enough citric acid was added, and it is better to begin again. After standing twelve hours the precipitate is collected on a small filter, preferably a vacuum filter, and washed with two or three small portions of a five per cent. solution of potassium chloride, then with portions of alcohol, successively of 50%, 70%, and 80% to 90% strength, till the washings are no longer acid to litmus. The gradual increase of strength of alcohol, and the previous use of aqueous solution of potassium chloride, are to prevent the precipitation of salts other than the bitartrate, such as the gelatinous phosphates of aluminium and iron, which may clog the filter, and some of which may interfere with the titration. The filter and contents are now transferred to a beaker, and the bitartrate estimated volumetrically with standard alkali. Warington also gives a method of washing the precipitate only with a saturated solution of bitartrate of potas-

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[1] Pages 977–980 of the important report on the analytical work of Citric and Tartaric Acid Manufacture, 1875: *Jour. Chem. Soc.*, **28**, 925–994. Continued. on Determination of Tartaric Acid in Lees, by GROSJEAN, 1879: *Jour. Chem. Soc.*, **35**, 341; 1883: **43**, 334; *Jour. Soc. Chem. Indus*, **2**, 338.

sium, "till the acidity of the drain-water is no greater than the acidity of the wash-water," as found volumetrically. The drained filter may be weighed, dried, and weighed again, to find the amount of bitartrate solution in the drained filter, so that a correction can be made for the bitartrate retained in the wash-liquid. If there be potassium sulphate in the precipitate, it will interfere with use of this wash-liquid by causing a precipitation of bitartrate from its solution.

The methods of estimation of the total tartaric acid in tartar, argol, and lees, were summarized by WARINGTON in 1875[1] essentially as follows:

A.—The tartaric acid of the acid tartrate of potassium is found by acidimetry, or calculated from determination of the potassium with platinum salt after calcining. The calcium is determined gravimetrically after calcining, and from this is calculated the tartaric acid of the neutral calcium tartrate.

B.—The calcined tartar is exhausted with water, the dissolved potassium carbonate and the undissolved calcium carbonate are separately estimated with standard acid and alkali, and the tartaric acid is calculated from both the acid tartrate of potassium and the normal tartrate of calcium.

C.—The tartaric acid of bitartrate is found by acidimetry. Another portion is calcined and the total alkali (including lime) found by alkalimetry. The number of c.c. of alkali for the bitartrate, subtracted from the number of c.c. of corresponding acid solution for the ash, leaves the number of c.c. of this acid required for the lime, that is, the bases in normal tartrates.

D.—The whole of the tartaric acid is converted into normal tartrates by exact neutralization with soda, the whole evaporated to dryness, calcined, the neutralizing power of the ash determined, and the total tartaric acid calculated therefrom. It is an estimation of the carbonates formed in calcining neutral salts.

With a pure tartar (having only the bitartrate, the calcium tartrate, color, and sand) any one of these methods will give nearly correct results of total tartaric acid. Methods A, B, and C give the tartaric acid in the bitartrate, as well as the total. Calcium carbonate in the tartar interferes with methods A and B, the carbonate, if not crystalline, being acted upon by the bitartrate in obtaining a solution in A. Calcium sulphate also causes

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[1] *Jour. Chem. Soc.*, 28, 959.

error in methods A and B. But methods C and D are trustworthy in presence of carbonates and sulphates (unless sulphides are formed by ignition, as they will be if nitrogenous organic matter is present with sulphates). If crystallized carbonate of calcium is present, in method C it must be dissolved with the tartar by adding a measured quantity of standard hydrochloric acid, before the acidimetry, afterward deducting the standard alkali needed to neutralize the hydrochloric acid. In method D, any calcium carbonate must be dissolved by first adding enough hydrochloric acid. In any of the four methods the presence of organic acids other than tartaric, such as malic acid, or acid products of a change in tartaric acid, introduces error. Of the four methods, Warington gives preference to method C, though in presence of carbonates it does not show exactly how much of the total tartaric acid is in the bitartrate. If there be free tartaric acid there must be more than a corresponding quantity of normal tartrate, when this method is to be used. *The details of method C* are given as follows[1]: Five grams of the powdered tartar are heated with a little water, long enough to dissolve any calcium carbonate, and, if presence of crystallized carbonate be apprehended, 5 c.c. of standard hydrochloric acid are added and a covered beaker used. Standard alkali is then added to the extent of about three-fourths of that required for a good tartar and for the hydrochloric acid, and the liquid is brought to boiling. When cold the titration is finished. From the amount of alkali (minus that required by hydrochloric acid) the tartaric acid in the bitartrate is stated (p. 489). Two grams of the powdered tartar are weighed into a platinum crucible with a well-fitting lid; the crucible is placed over an argand burner; heat is applied very gently to dry the mass, and then more strongly, till inflammable gases cease to be evolved, keeping the heat at low redness or below. The black ash is next removed with water to a beaker, and some excess—20 c.c. if the tartar is a good one—of normal acid solution is added from the burette, rinsing the crucible with the acid and then with water. After boiling and filtering the excess of acid is titrated with standard alkali, bringing the filter and its contents into the beaker at the last. From the neutralizing power of a gram of burnt tartar is subtracted the acidity of a gram of unburnt tartar, both expressed in c.c. of standard alkali, and the difference is the neutralizing power of the bases existing as neutral tartrates, then to be calculated into tartaric acid. One c.c. of normal

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[1] *Jour. Chem. Soc.,* **28, 961.**

alkali is the equivalent of 0.075 gram of tartaric acid in normal tartrate.

Warington's *method of direct estimation* of total tartaric acid of argols and lees, known as "the oxalate method," is secure against the errors arising from presence of carbonates and sulphates, the formation of sulphides, and action of vegetable acids not tartaric. It provides a removal of the calcium by precipitation with potassium oxalate, a precipitation of all the tartaric acid as potassium bitartrate, and volumetric estimation of the latter.[1] This method, supplemented by a simple acidimetry to show nearly the quantity of acid in bitartrate, may be adapted to various troublesome analyses of adulterated cream of tartar.—A quantity of the material, in powder, sufficient to contain about 2 grams of tartaric acid, is placed in a small beaker, covered with water, and heated on the water-bath till thoroughly softened. Sufficient solution of potassium oxalate (of about 25% strength) to unite with all the calcium and give an excess of about 1½ gram of oxalate is then added, and the heat maintained, with frequent stirring, for half an hour. The solution, if strongly acid, as it usually will be, is now nearly neutralized by carefully adding solution of soda by drops, the reaction being left distinctly acid, and digestion on the water-bath continued half an hour. The volume of liquid is now made about 30 c.c., and the whole filtered (while hot) with a vacuum filter. Mr. Grosjean uses Cassamajor's filter,[2] in an ordinary funnel, and very little vacuum. The residue is washed ten times, each with 2 or 3 c.c. of water, and the washings separately concentrated to bring the whole filtered liquid to 50 c.c. Five grams of potassium chloride are now added and dissolved, and the solution treated, while cold, with a quantity of citric acid equal to, or a little greater than, the quantity of tartaric acid to be found. The liquid is stirred continuously for ten minutes and set aside half an hour, then collected on a vacuum filter and washed twice with a five per cent. solution of potas-

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[2] WARINGTON, *ibid.*, p. 973. GROSJEAN, 1879: **35**, 341: "This method, with individual variations, is, I believe, now exclusively employed in fixing the value of lees and inferior argol sold in the London market." A similar plan, of simpler execution, with use of carbonate of potassium (instead of oxalate) to precipitate calcium and bring all the tartaric acid into solution as normal salt, and with acetic acid and alcohol as precipitants, is given by GOLDENBERG and others, 1883: *Zeitsch. anal. Chem.*, **22**, 270; *Chem. News*, **48**; *New Rem.*, **12**, 242. The precipitation by potassium carbonate has been employed gravimetrically for the calcium.

[2] 1875: *Am. Chem.*, **5**, 438; *Chem. News*, **22**, 45.

sium chloride, then twice with fifty per cent. alcohol, and lastly with strong alcohol till the washings are no longer acid to litmus. The whole washing may be done with a five per cent. solution of potassium chloride carefully saturated with potassium bitartrate, continued till the washings neutralize no more standard alkali than the wash-liquid, in the end making a correction for the acid in the liquid remaining in the filter. The precipitate and filter, transferred to a beaker, are titrated with standard alkali (p. 489). If by inattention too much reagent oxalate of potassium have been used, acid oxalate of potassium may be crystallized in the precipitate. In the analysis of good tartar by this method the filtering of the oxalate precipitate may be omitted, and the citric acid added to the cold neutralized mixture. In this case the oxalate of calcium, vegetable matter, and sand, in the bitartrate precipitate, do not affect the titration.

In estimating tartaric acid in Fruit Juices, as a general method providing for the other fruit acids, FLEISCHER[1] directs as follows: Filter clear, if necessary by the addition of alcohol, and washing on the filter with alcohol or hot water. The liquid is fully *precipitated with lead acetate solution*; the precipitate drained on the filter and washed with aqueous alcohol, and then treated thoroughly with excess of ammonium hydrate (free from carbonate) and filtered. The residue contains lead salts of any phosphoric, sulphuric, and oxalic acids of the fruit; while tartaric, citric, and malic acids are in the filtrate. The latter is treated with some excess of ammonium sulphide, then acidulated with acetic acid, and filtered. This filtrate, boiled to expel hydrogen sulphide, is treated with potassium acetate and alcohol, as above directed, for estimation of the tartaric acid by acidimetry of the precipitate. The filtrate contains the citric and malic acids, which are now precipitated by addition of calcium chloride, ammonium hydrate, and a little alcohol. The precipitate of citrate and malate may be freed from malate by washing it with boiling solution of calcium hydrate. The citrate may be dissolved in acetic acid, and precipitated by lead acetate, to weigh as lead citrate.

f.—Tartaric acid, in pure water solution, has percentages corresponding to specific gravities, as follows:[2]

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[1] 1874: *Zeitsch. anal. Chem.*, **13**, 328, in full from *Archiv d. Pharm.* [3] **5**, 97; *Amer. Chem.*, 6, 154; abstracted in *Jour. Chem. Soc.*, **27**, 1181, and in *Pro. Am. Phar. Assoc.*, 1875, 380. See also A. H. ALLEN: *Phar. Jour. Trans.* [3] 6, 6; *Jahresb. d. Chemie*, 1875, 969.

[2] SCHIFF. See also GERLACH: *Zeitsch. an. Chem.*, viii. (1869) 295.

1.0167	sp. gr. at 15° C.	3.67	per cent.
1.0337	“ “ “	7.33	“
1.0511	“ “ “	11.00	“
1.0690	“ “ “	14.66	“
1.1069	“ “ “	22.00	“
1.1654	“ “ “	33.00	“

g.—Impurities.—Tartaric acid is liable to contain a trace of Sulphuric acid, from the manufacture, but more than slight traces of this impurity render the crystals deliquescent. Minute traces of calcium sulphate and of lead tartrate may also be left from manufacture. Falsifications with alum, borax, and sodium nitrate are mentioned. The powder is more liable to adulterations. The solubility in least quantities of alcohol (p. 486) serves as a test for absence of saline impurities

THE ACID TARTRATE OF POTASSIUM. Bitartrate of Potassium. Cream of Tartar. Tartar. *Der gereinigte Weinstein.—Purity and strength of normal tartars.*—Manufactured from the Argols and to a less extent from the Lees of grape-wine fermentation, by dissolving out with hot water and crystallizing the solution, the operation being repeated several times. Argols and lees contain calcium tartrate, and smaller proportions of aluminium, iron, and magnesium oxides and salts, phosphates, sand, and vegetable matter. They also frequently contain “plaster,” chiefly calcium sulphate, and sometimes including calcium carbonate and Spanish earth. The quantity of calcium tartrate varies from 6% to 20%[1] in lees, from 5% to 10% or 15%[2] in argols, and from 2% to 9% or 10%[3] in legitimate tartars of the market. The cream of tartar of the U. S. Ph. of 1880 (1882) is required to bear a limit test for calcium, defined as proof of “absence of more than 6 per cent. of tartrate of calcium.” The limit test of the tartar of the German Pharmacopœia is very close in its conditions of time and concentration, and is defined by the experiments of BILTZ[4] as excluding calcium tartrate above ⅓%. The article “kalkfreier Weinstein” (lime-free tartar) is mentioned as

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[1] WARINGTON, 1875: *Jour. Chem. Soc.*, 28, 951.

[2] General report of New York importers.

[3] ALLEN, 1880: *The Analyst*, 5, 116, found by experiments with mixtures of pure potassium bitartrate and excess of pure calcium tartrate that the quantities of calcium tartrate left after a single crystallization of filtrates from boiling water solutions varied, in proportion to the water used (25 to 75 parts), from 5.82 per cent. to 9.02 per cent. WARINGTON, *Jour. Chem. Soc.*, 28, 958, gives a general statement of the amounts of acid in calcium tartrate, equivalent to a range of 2 to 8.8 per cent. of calcium tartrate.

[4] *Notizen zur Pharm. German.*, 1878, p. 251.

being "as far as possible free from calcium."[1] Undoubtedly tartars of almost any required degree of purity can be obtained, upon order, from certain manufacturers, while very little tartar with less than 2% calcium tartrate appears to be in use in Europe or in this country. Tartar with not over 5% or at most 6% calcium tartrate, if not otherwise imperfect, is to be accepted at present as a good article for ordinary uses. Ten per cent. of calcium tartrate must be about the utmost quantity in legitimate tartars, those, however poorly or cheaply manufactured, not adulterated by addition. "Crystallized tartar"—that in larger crystals, subsiding in the crystallizing liquid—does not very much differ in purity from the small crystals, the "cream" of the liquid.

The strength of tartars is their acidity due to acid tartrate, and is stated in parts per cent. of this salt. According to WARINGTON[2] the best tartars of South Italy have from 91.0% to 94.7% of bitartrate; good ordinary Italian tartars, 87.8% to 90.3%; and Vinaccia tartars, from 79.0% to 85.3%. The first named of these, termed Venetian tartars, are the best of those not presented as lime-free tartars. The French tartars do not equal the Venetian.

The adulterations common in cream of tartar (ground or in crystals) are terra alba, chalk, alum, and tartrate of calcium. Tartaric acid, acid phosphate of calcium, starch or flour, and barium sulphate have been found. Two lots (with alum or an inert adulterant) adulterated with oxalic acid were found in 1886 in New York Of 27 suspected samples, the New York State Board of Health, in 1882, found 16 to be adulterated, and 8 to contain 3.27% to 93% of terra alba, of which 5 samples had over 70%. The tartrate of calcium did not exceed 10.39% in any case.[3] Large proportions of calcium compounds have been reported by various analysts, and reported in some cases as calcium tartrate. Calcium carbonate is so promptly changed to tartrate in solution of the bitartrate that it is not unlikely that an addition of some form of calcium carbonate has repeatedly given rise to an analyst's report of much calcium tartrate.[4] When the addi-

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[1] Hager's *Pharm. Praxis*, II. 279 (1878).

[2] By calculation from the figures in *Jour. Chem. Soc.*, 28, 958.

[3] E. G. LOVE, 1882: *Sanitary Engineer*, March 30, 1882, p. iv.; *The Analyst*, 7. 142.

[4] C. G. STONE, Univ. Mich , 1877: *New Rem.*, 6, 274—of 12 samples, 6 had from 6.1 per cent. to 8 per cent. calcium tartrate, and 6 did not have over 6 per cent. of this salt; 2 had 61 and 64 per cent. of calcium sulphate.

LONGWELL, Univ. Mich., 1882: *Phys. and Surg.*, 4, 404—of 11 samples, highest calcium as tartrate, 7.8 per cent.; 4 samples, calcium as carbonate, 49.5 to 63.4 per cent. RIEGER, Univ. Mich., 1883, unpublished—of 10 samples, 4 stated with 41.5 to 68.1 per cent. calcium as tartrate.

tion is calcium sulphate, the sulphuric acid would remain and would seldom fail to be reported as sulphate of one base or the other, but the acid of the carbonate may escape unnoticed in treating with water. Tartrate of calcium, inert in ordinary uses of cream of tartar, is a by-product of value for production of tartaric acid. That it is added to tartars, in proportions several times greater than they can derive from the argol, does not appear to be established by any evidence at the author's hand. The composition of crystallized *Tartrate of Calcium* is $CaC_4H_4O_6.4H_2O$. It loses about 17% of its weight on the water-bath, and nearly all its water at 200° C., but it can be estimated as carbonate after igniting and treating with ammonium carbonate. It is soluble in about 6000 parts of water at 15° C., and in about 350 parts of boiling water. It is somewhat soluble in ordinary free acids, in solution of the bitartrate of potassium, in solution of ammonium chloride, and in cold potassium or sodium hydrate solution.

Determination of the Purity and Strength of Cream of Tartar.—Tests for sulphates, chlorides, salts of heavy metals, and the six per cent. limit of calcium tartrate are given in the U. S. Pharmacopœia. Free tartaric acid can be tested for, and estimated, by treating the fine powder with alcohol, evaporating the alcohol from the filtrate, testing for acid, and, if found, estimating it volumetrically. In a nitric acid solution of the tartar phosphoric acid may be tested for with molybdate. If sulphates are present, the ash, or the thoroughly-charred mass, in hydrochloric acid solution, should be tested for aluminium, which may be done (in absence of phosphate) by adding ammonium chloride and a slight excess of ammonia-water.[1] If aluminium be found in any considerable quantity, ammonia may be tested for, as further evidence of alum. Terra alba, or chalk, or other earthy addition will be left undissolved after treatment of the powdered tartar with warm potassium hydrate solution (which, not too hot, dissolves calcium tartrate). The residue, filtered out and washed, is examined for carbonates, sulphates, calcium, barium, silica, etc. Then the operation may be made a quantitative one, and the collected residue washed, dried, and weighed. But in case of terra alba (calcium sulphate) alcohol should be added before filtering, and dilute alcohol used in washing. Starchy matters will be shown, after heating in water, by the iodine test. Now, in absence of alum, free tartaric acid, acid phosphate, or other foreign substance that can neutralize an alkali, *the strength*

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[1] In presence of the tartrate ammonia does not fully precipitate aluminium.

of the tartar, in percentage of bitartrate of potassium, may be found by acidimetry (p. 489). Weighing out 4.7 grams of the powder, sixty to eighty c.c. of hot water are added, and normal solution of alkali run in from the burette, with stirring and heat if necessary to dissolve the tartar before the titration is completed, until the neutral point is indicated by litmus or by phenol-phthalein. The number of c.c. × 4 = the number per cent. of bitartrate. One c.c. of normal alkali equals 0.188 gram of bitartrate. Should the percentage of real tartar be too low, it will be the more necessary to analyze the neutral substances making up the complementary percentage.

If further work be required, in most cases *the calcium* is next to be determined. In absence of alum and of earthy additions, the total calcium may be estimated (without calcining the tartar) as follows: Five grams of the tartar and 2 grams of anhydrous sodium carbonate are boiled with water and well digested, the mixture filtered, the residue washed, dried, and weighed as calcium carbonate.

$$CaCO_3 : CaC_4H_4O_6.4H_2O :: 1 : 2.6.$$
$$\text{Or} \quad CaCO_3 : CaC_4H_4O_6 :: 1 : 1.88.$$

The percentage of crystallized calcium tartrate, added to that of potassium bitartrate, in a legitimate tartar, should give a sum not far from 100.

When earthy additions or alum have been found it is better to ignite a portion of the tartar. Two or three grams, weighed, are dried in a covered crucible, and gradually ignited until vapors cease to rise, when small portions of ammonium nitrate (or potassium nitrate) are added, until by the continued calcination a white ash is obtained. This is cooled, exhausted with hot water, washed, with the rinsings, on a filter, and the residue titrated as follows: Both the filter and the crucible are placed in a beaker, an excess of standard hydrochloric acid added from a burette, the liquid heated and brought back to the neutral point with standard alkali. Each c.c. of normal acid solution used (after deduction of the alkali used) represents 0.050 gram of calcium carbonate, or 0.130 gram of crystallized calcium tartrate, or 0.094 gram of anhydrous calcium tartrate. When calcium sulphate is present, some reduction to sulphide will occur in the ignition, and a corresponding portion of calcium of reduced sulphate will be included in the estimation.—If there be a residue of the ash insoluble in hydrochloric acid (terra alba, silicious matter), it may be washed, dried and weighed, and afterward subjected to analysis.

If alum is to be estimated, in absence of other sulphates, it may be easily done by a gravimetric estimation of sulphuric acid as barium salt, precipitating in a strongly acid solution, and igniting the precipitate in the usual way.

To obtain the quantity of calcium tartrate when other calcium salts are present, the powdered tartar may be treated with warm potassium hydrate solution (as directed on p. 498), adding alcohol if there is sulphate, washing the residue on a filter, evaporating the filtrate, first neutralized with hydrochloric acid, and precipitating with oxalate of ammonium in presence of a little free acetic acid.[1] The precipitate is weighed as carbonate, after ignition. A more complete analysis may be conducted by determining the total tartaric acid by Warington's direct method (p. 494), the acidity due to acid tartrate by simple acidimetry, the total calcium soluble from the ash by hydrochloric acid, and the ash not calcium carbonate. Unless irregular constituents are present, the tartaric acid in excess of that in the acid tartrate may be calculated into normal tartrate of calcium, and any excess of calcium beyond that in the calcium tartrate calculated into carbonate or sulphate, or as the qualitative examination indicates.

Baking-Powders.—These have so far been presented to the public either as cream of tartar baking-powders, or without statement of their constituents, or as acid phosphate powders (Horsford's). They consist of sodium bicarbonate with an acidifying agent, potassium bitartrate, or alum, or tartaric acid, or acid phosphate of calcium. Ordinary carbonate of ammonium has been used, alone, as a baking-powder, and more used for a part with acidifying agents. A proportion of starch or flour, as "filling," is found in nearly all baking-powders, and is necessary to the permanence of tartar and tartaric acid powders. From 13 to 18 per cent. of starch is not too much for the permanence of a cream of tartar baking-powder, but filling beyond 20 per cent. must be held an unquestionable dilution.[2] There

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[1] The precipitation of calcium from tartars, as an oxalate, is in most cases more trustworthy if done in the presence of a little free acetic acid. The solution should not be very dilute, and twelve to twenty-four hours should be given to the precipitation.

[2] Dr. E. G. Love, acting for the New York State Board of Health, in 1882 (*Sanitary Engineer*, March 30; *The Analyst*, 7, 142) found, of 84 baking-powders upon sale, 49 were cream of tartar powders, 3 were tartaric acid powders, 20 were alum powders, 3 were acid phosphate powders, 8 contained both cream of tartar and alum, and 1 had alum with acid phosphate. Flour or starch was found in all but 11. Ammonia was found in 35. [The alum reported in 29 of them was doubtless ammonia alum.] *Eight* were reported adulterated—*six* with terra alba, *one* with tartrate of lime (in the tartar), and *one* with insoluble calcium phosphate.

has been dispute as to the injurious effect of alum baking-powders, but, at all events, they are seldom if ever sold to the public with any statement or admission that they contain alum.

The proportion of carbon dioxide extricated on boiling a baking-powder with water is termed its "strength," and is stated in percentage of weight, or in cubic inches (at 60° F., 30 in. bar.) from an avoirdupois ounce. In the case of a cream of tartar powder we have:

$$\begin{array}{llll} NaHCO_3 & + KHC_4H_4O_6 & & = KNa\,C_4H_4O_6 + CO_2 + H_2O \\ 84 & +188 & = 272 & \qquad\qquad 44 \\ 30.88\% & +69.12\% & = 100.00\% & \qquad\qquad 16.17\% \end{array}$$

At 60° F. and 30 inches pressure 34.18 grains of carbon dioxide measure 100 cubic inches; therefore 16.17 grains measure 34.18 cubic inches. That is to say, 100 grains, of a mixture 30.88% absolute bicarbonate and 69.12% absolute bitartrate, will furnish 16.17 grains or 34.18 cubic inches of the gas. And 1 av. oz. of the same chemically pure mixture will furnish 149.54 cubic inches of the gas. If we have a baking-powder holding, for example, 84% of the equivalent soda and tartar, then no more than 84% of 149.54 cubic inches of gas can be obtained from one av. ounce. Less than the theoretic yield of gas may be obtained (1st) because reaction of the tartar upon the soda may have transpired in the mixture (not fully dry), (2d) because of deficient quality of the soda, or of the tartar, or of both, and (3d) because of wrong proportions of tartar to soda. With the proportions of filling before mentioned, cream of tartar baking-powders, in moderately dry air, will not appreciably lose carbon dioxide. Powders made with tartaric acid lose gas more readily, and the same has been stated of the acid phosphate powders.[1]

The examination of baking-powders should begin with a qualitative analysis. In answer to special questions, tests may be briefly made for sulphates, ammonia, aluminium, residue insoluble in boiling water (besides gelatinized starch), and calcium in watery solution, as well as in acid solution of any residue not dissolved by water. Phosphate may be tested for in acid solution by molybdate. Free tartaric acid would be found in a filtered alcoholic solution. The reaction to test-paper after boiling thoroughly in water is of first importance. This is neutral in

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[1] In 1881 Dr. E. G. LOVE reported the yield of gas in cubic content from *sixteen* different brands of American Baking-Powders (*The Analyst,* 6, 65). From one ounce the highest yield was 127.4 cubic inches of gas, and the lowest was 75.0 cubic inches, except one (old) which was 32.7 cubic inches. Ten furnished over 100, and four over 120, cubic inches of gas.

well-made powders: it is seldom found to be acid, but is sometimes found to be alkaline.

In the *estimation of the carbon dioxide*, only that quantity of gas which is liberated by water, with warming at the end to boiling point, and without adding an acid, can be counted as "strength." However, if an alkaline reaction have not been found after boiling with water, the use of an acid to liberate the gas will introduce no inaccuracy in finding the "strength." The writer prefers to estimate the carbon dioxide by the method of increase of weight of absorption tubes, using water without acid and with gentle heat finally to boiling, to liberate just the gas counted as strength. Methods by diminution of weight due to escape of the dried gas seldom give trustworthy results, at least in the writer's observation. If a Scheibler's apparatus for measuring the volume of the gas be at hand, it may be used, with addition of hydrochloric acid in the usual way; but if it be a powder showing an alkaline reaction after boiling with water, a correction must be made, from results of alkalimetry after boiling with water, for statement of the "strength."

With a true cream of tartar baking-powder (free from alum) a most serviceable valuation can be made by a simple *alkalimetry of the ash* (A), together with alkalimetry of the liquid obtained by boiling the baking-powder with water (B) in case this liquid be alkaline, or acidimetry of the same (C) in case it be found acidulous. Using *decinormal* volumetric solutions of acid and alkali,

In A, 1 c.c. of acid = 0.0136 gm. soda tartar ($NaHCO_3 + KHC_4H_4O_6$)
In B, 1 c.c. of acid = 0.0084 gm. excess of soda ($NaHCO_3$)
In C, 1 c.c. alkali = 0.0188 gm. excess of tartar ($KHC_4H_4O_6$)

If the powder be found to have an excess of alkali, to estimate this weigh 0.840 gram, boil with water, add from the burette some excess of decinormal solution of acid, boil again, and bring back to the neutral point by adding decinormal alkali from a burette. The number of c.c. (B) of decinormal acid, beyond that taken to neutralize the decinormal alkali used, equals the number per cent. of excess of sodium bicarbonate (that is, the number of parts of such excess in 100 parts of baking-powder). If the baking-powder have an excess of acid, weigh 1.880 gram, boil, and add from the burette decinormal solution of alkali to neutralize. Then (as above) c.c. (C) = parts excess of potassium bitartrate in 100 parts baking-powder. Whether the boiled liquid have been found alkaline, acid, or neutral, *for the* *ash* weigh 1.360 gram of the baking-powder, heat it in a covered capsule very gradually, so as not to permit the puffy mass to reach the cover, at last continuing a red heat for fifteen or twenty minutes after the vapors have ceased to rise. Cool the capsule, boil it (cover and all) with a little water, in a beaker, gently rubbing up the black ash with a glass rod. If no separation of calcium of the tartar is to be undertaken, the decinormal acid may now be added at once, in excess, the mixture boiled, and (being acid after boiling) filtered and washed till the washings do not change blue litmus-paper. The filtrate and washings are titrated back to the neutral point with decinormal alkali. If the powder have been found neutral after boiling at the beginning, the c.c. of decinormal acid, minus the c.c. of decinormal alkali, = the parts of absolute equivalent-soda-tartar ($NaHCO_3 + KHC_4H_4O_6$) in 100 parts of the baking-powder. If the powder have shown an excess of alkali, then $\frac{34}{21}$ ($= \frac{136}{84} =$ 161.9%) of the number of c.c. *B*, found as above, is to be deducted from the number of c.c. required for the ash. If the powder have shown an excess of acid, deduct $\frac{34}{47}$ ($= \frac{136}{188} =$ 72.34%) of the number of c.c. *C* (decinormal alkali) from the number of c.c. of decinormal acid used for the ash. In each of these cases the remainder = parts of equivalent soda-tartar in 100 parts of baking-powder. Then the per cent. of sodium bicarbonate in the baking-powder is 30.88% (p. 501) of the per cent. of equivalent-soda-tartar, plus the per cent. of excess of "soda," if any. And the total per cent. of potassium bitartrate is 69.12% of the per cent. of soda tartar, + any per cent. of excess of "tartar" found.

If it be desirable—from the qualitative indications—to estimate *the calcium tartrate* in the alkalimetry of the ash, the black ash from the capsule must be exhausted and washed with boiling water until the washings no longer show an alkaline reaction—to litmus or to phenol-phthalein—when the total filtrate is titrated, as above directed. The residue, filter, capsule. and all, is now digested, cold, with standard hydrochloric acid, or, if there be not a large quantity of calcium, digested warm with standard sulphuric acid and sufficient water, filtered, washed (compare on p. 499), and the filtrate titrated back for alkalimetry of the calcium carbonate, referred to tartrate. 1 c.c. of decinormal solution of acid, neutralized by the washed ash, indicates 0.0130 gram of crystallized (or 0.0094 gram of anhydrous) calcium tartrate (p. 498). The quantity of calcium tartrate found is to be added to the total quantity of potassium bitartrate found (% of latter ÷ 100 × 1.36), the sum being the quantity of cream of tartar (not lime-free) used in the 1.36 gram of baking-powder. Statements are then made of the percentage of cream of tartar in the baking-powder, and of the percentage of calcium tartrate in the cream of tartar. These percentages may be calculated, directly from numbers of c.c. found, as follows: 1.36 gram baking-powder having been calcined, 95.6% of the c.c. for $CaCO_3$ (m) + % of total $KHC_4H_4O_6$ previously found = % (n) cream of tartar (not lime-free) in the baking-powder. And $m \div n =$ % of crystallized calcium tartrate in the cream of tartar used.—The calcium tartrate may be determined gravimetrically, as given on page 500, or on page 499, the precipitate of carbonate being ignited to remove starch, if necessary.

For estimation of constituents of baking-powders, used also in adulteration of cream of tartar, see pp. 498 to 500.

TEAS OF COMMERCE.—The prepared leaf of the *Thea*, native to the Himalayas and Assam, long cultivated in China and Japan, and now cultivated in India. The kinds of tea known in commerce are distinguished in the first place by the age of the leaf employed. Thus, the youngest leaf is found in "flowery pekoe"; the next in age, successively in "orange pekoe," "pekoe," "souchong," and "bohea." Without distinction of the age of the leaf, "green teas" differ from "black teas" according to the mode of preparation. The treatment of the fresh tea leaf in manufacture of tea is always an elaborate operation, and includes exposure to a roasting temperature. For black teas the leaves are withered a little, rolled to liberate the juices, left in balls for the proper extent of fermentation, then sun-dried and subjected to a careful firing in a furnace. For green teas the fresh leaves are first withered in hot pans, then rolled to free the juices, slightly roasted in the pans, sweated in bags, and returned to the pans for a final slow roasting, with stirring, for eight or nine hours, beginning at the temperature of 160° F., and falling to 120° F. at the close. The outline of operations here given is one of modern simplification, somewhat as conducted by planters in India, and considerably less elaborate than the methods of the Chinese. In black teas the greater extent of fermentation and the sharper "firing" appear to reduce the quantity of tannin, and certainly leave the tannin and the other extractive matters in a less readily soluble condition. Teas contain essential oil, which is undoubtedly affected by the curing process.

An extended investigation of teas imported into the United States was made in 1884 by Mr. Geisler, of New York, who is engaged in the analytical chemistry of foods, and his report is of great scientific and practical value. The tabular summaries of the report, and Mr. Geisler's[1] principal conclusions bearing upon the methods of infusion in the preparation of tea as a beverage, are presented on pages 506 to 508.

In Table I., showing the principal constituents of commercial teas, it will be noticed that there is no uniform relation existing between the composition of teas in general and the value of the same. Teas of the same kind from the same district would no doubt show a more uniform relation as to composition and price.

The percentage of extract, determined by half-hour boiling of the tea leaf in one hundred parts of distilled water, bears, at least in Oolong and Congou teas, a more uniform relation to the price than the other constituents determined, although the *total* extract obtained by exhausting the leaf is very irregular. This is quite in accord with a fact which dealers in tea are aware of—namely, that the finer and more valuable qualities of tea of any line consist of young and tender leaves, while the medium and poorer grades contain older and tougher leaves. The younger a leaf is the more tender and succulent will it be, and it therefore follows that it gives up its extractive matter more readily to water, which is all the more important in the customary household method, where boiling water is poured upon the leaves and allowed to draw for only a given length of time.

The percentages of theine, tannin, and soluble ash are too irregular to show any relation between their per cents. and the price of the tea. It appears from these analyses, however, that the finer the quality of the tea the more theine, soluble ash, and extractive matter will it contain ; still, the same is not uniformly true. The percentages of extract (total) and insoluble leaf are still more irregular when compared with the price of the tea.

The results in Table III. are of greater interest, since they show the principal constituents of tea which are actually taken up by water in the ordinary preparation of tea as a beverage.

In order that the results would be strictly comparable, the infusions of the different teas were all prepared under precisely

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[1] JOSEPH F. GEISLER, Ph.C., chemist to the New York Mercantile Exchange. 1884: *Am. Grocer*, Oct. 23. The discussion of the results following (pp. 510, 511) is taken wholly from Mr. Geisler's report. "Although the chemical composition of tea has frequently been made the subject of analytical inquiries with a view of ascertaining the relation existing between the chemical composition and the commercial value of tea, the amount of work previously done relative to teas of this market is very meagre."

TABLE I.

Results of the examinations of commercial teas obtained direct from importers and wholesale houses.	GREEN TEAS.						JAPANS.		CONGOU TEAS.										
	Finest Nankin Moyune Gunpowder.	*Finest Moyune Young Hyson.*	*Fine Moyune Gunpowder.*	*Common Moyune Gunpowder.*	*Pingsuey, 1 (Rejected by Gov't Inspector).*	*Pingsuey, 2 (Rejected by Gov't Inspector)*	*Japan Basket-Fired.*	*Japan Pan-Fired.*	*Finest Moning Congou.*	*Fine Moning Congou.*	*Superior Moning Congou.*	*Superior Medium Moning Congou.*	*Medium Moning Congou.*	*Medium Moning Congou.*	*Medium Moning Congou.*	*Common Moning Congou.*	*Common Moning Congou.*	*Good common Kaisow Congou.*	*Good common Kaisow Congou.*
Price per lb. wholesale.	75c	65c	39c	18c	..	..	37½c	39c	65c	45c	27c	23c	22c	20c	19½c	16c	15½c	20½c	17¼c
Moisture..............	4.695	5.398	7.34	7.01	6.32	7.78	4.00	3.933	8.29	7.65	8.43	7.85	8.14	8.78	8.70	9.15	8.67	8.615	7.79
"Extract" hf. hr. boiling in 100 pts. water.	44.7	40.2	39.2	35.37	32.1	33.25	42.00	43.2	32.14	31.42	29.0	27.84	28.4	27.6	27.9	23.94	23.48	30.26	30.52
Total "Extract".....	47.04	50.0	46.9	43.3	..	..	50.70	50.1	35.28	35.41	37.06	34.9	36.41	34.32	31.7	32.23	27.48	36.88	36.26
Tannin...............	19.11	?	16.23	11.91	11.87	13.74	15.08	14.20	11.64	13.11	13.89	10 11	11.74	12.38	12.26	10.60	8.44	12.30	10.52
Theine.......	2.86	2.06	1.96	2.20	1.52	1.54	2.81	2.22	2.84	2.87	2.77	1.97	2.56	1.97	2.38	1.70	2.01	2.68	2.68
Insoluble Leaf	48.26	44.6	45.76	49.61	..	..	45.30	45.96	56.41	56.94	54.3	57.22	55.45	56.90	59.6	58.60	63.85	54.5	55.95
Total Ash............	8.248	6.072	5.68	6.085	6.7	8.53	5.345	5.779	5.43	5.61	5.82	5.71	5.56	5 587	5.52	6.48	6.14	5.65	5.73
Insoluble Ash.........	3.229	2.532	2.117	2.712	4.68	6.38	1.859	2.236	1.90	2.38	2.54	2.62	2.57	2.58	2.64	3.71	3.86	2.40	2.29
Soluble Ash..	5.019	3.54	3.563	3.37	2.02	2.15	3.486	3.543	3.52	3.22	3.28	3.09	3.00	3.00	2.88	2.76	2.28	3 24	3.43
Ash Insoluble in Acid.	.656	.555	.213	.541	..	..	.267	.461	.32	.455	.630	.45	.42	.45	.42	1.31	.962	.360	.32

The terms "extract" and "extractive matter" as here used imply that portion which is extracted from the leaf by boiling water, and contains theine, tannin, albuminous compounds, gum, dextrin, coloring matter, mineral matter, besides other less important constituents, such as gallic acid, bohcic acid, quercetin, quercetinic acid, and oxalic acid, which are present only in small quantities, if present at all. The amount of extractive matter thus obtained will vary with the condition of the leaves, the amount of water, and the length of time of boiling.

Soluble and insoluble, unless otherwise qualified, refer to the behavior of the substance to the action of water.

Ash and mineral matter are the residues left on burning the leaves to constant weight.

TABLE I. (*Continued*).

Results of the examinations of commercial teas obtained direct from importers and wholesale houses.	INDIAN (ASSAM) TEAS.						OOLONG TEAS.												
	Indian Tea, 1.	*Indian Tea, 2.*	*Indian Tea, 3.*	*Indian Tea, 4.*	*Indian Tea, 5.*	*Indian Tea, 6.*	*Extra choicest Formosa Oolong.*	*Choicest Formosa Oolong.*	*Choicest Formosa Oolong.*	*Superior Formosa Oolong.*	*Superior Formosa Oolong.*	*Good Medium Formosa Oolong.*	*Superior Medium Amoy Oolong.*	*Medium Amoy Oolong.*	*Common Amoy Oolong.*	*Finest Formosa Oolong.*	*Superior Formosa Oolong.*	*Medium Amoy Oolong.*	*Common Amoy Oolong.*
Price per lb. wholesale.	23.13c	22.82c	21.48c	23.17c	21.25c	21.21c	65c	65c	53c	31c	30c	27c	24c	21½c	21c	75c	28c	20c	14c
Moisture.......	6.189	5.606	5.877	5.83	5.849	5.56	6.3	5.09	6.22	5.86	5.16	5.56	5.47	6.05	6.65	5.383	6.094	5.86	6.88
"Extract" hf. hr. boiling in 100 pts. water.	39.625	39.662	37.94	39.249	37.80	38.4	44.0	40.33	41.26	37.94	37.3	37.04	37.1	34.10	34.27	40.91	35.64	37.37	35.18
Total "Extract"......	41.92	41.32	41.49	45.64	44.05	43.21	48.87	46.56	45.18	41.09	42.6	44.2	44.9	40.8	40.6	43.27	41.5	42.3	41 2
Tannin	18.868	16.286	14.728	13.06	13.04	13.26	19.91	17.07	20.07	17.34	16.16	16.64	18.07	13.55	16.35	16.43	14.73	14.70	11.93
Theine.....	3.31	2.528	1.88	2.301	3.24	3.06	2.78	2.86	..	1.68	3.5	2.40	..	2.34	2.22	2.43	1.606	2.92	1.15
Insoluble Leaf.........	51.886	53.07	52.628	48.53	50.10	51.23	44.8	48.35	48.59	53.05	52.15	50.15	49.6	53.15	52.75	51.33	52.4	51.83	51.90
Total Ash..............	5.427	5.531	5.619	5.776	5.79	5.749	5.56	5.61	5.945	5.802	5.87	5.937	5.44	5.517	5.91	6.07	5.983	5.84	6.11
Insoluble Ash..........	2.183	2.223	1.936	2.173	2.12	2.102	1.842	2.28	2.61	2.30	2.83	2.75	2.387	2.917	3.10	2.87	2.28	2.56	3.17
Soluble Ash............	3.244	3.308	3.683	3.603	3.667	3.647	3.71	3.32	3.33	3.50	3.04	3.187	3.05	2.60	2.81	3.201	3.59	3.38	2.93
Ash Insoluble in Acid..	.137	.296	.127	.190	.149	.170	.327	.35	.495	.422	.41	.537	.387	.527	.675	.664	.266	.502	.838

TABLE II.

Averages calculated upon the air-dried tea, unless otherwise stated.	*Moisture.*	*Half Hr. Extract.*	*Total Extract.*	*Insoluble Leaf.*	*Tannin.*	*Theine.*	*Total Ash.*	*Soluble Ash.*	*Insoluble Ash.*	*Ash Insol. Acid.*	*No. of Analyses.*	
INDIAN.											6	1,554 Packages.
Maximum....	6.189	39.66	45.64	53.07	18.86	3.3	5.79	3.68	2.22	.296		
Minimum..............................	5.56	37.80	41.32	48.53	13.04	1.8	5.42	3.24	1.93	.137		
Average......	5.81	38.77	42.94	51.24	14.87	2.7	5.62	3.52	2.12	.178		
Average for tea dried at 100° C.........	..	·41.13	45.58	54.36	15.77	2.86	5.96	3.73	2.24	.188		
OOLONG.											13	
Maximum...............	6.88	44.02	48.87	53.15	20.07	3.50	6.11	3.71	3.17	.838		
Minimum............	5.09	34.10	40.6	44 8	11.93	1.15	5.44	2.60	1.84	.266		
Average..........	5.89	37.88	43 32	50.7	16.38	2.32	5.81	3 2	2.68	.507		
Average dried at 100° C...............	..	40.22	46.03	53.84	17.39	2.46	6.17	3.39	2.84	.538		
CONGOUS.											11	
Maximum.............................	9.15	32.14	37.06	63.85	13.89	2.87	*6.48	3.52	3.86	*1.31		
Minimum..............	7.65	23.48	27.48	54.5	8.44	1.70	5.52	2.28	1.90	.32		
Average...............	8.37	28.40	34.35	57.2	11.54	2.37	5.75	3 06	2.68	9 teas .425		
Average dried at 100° C................	..	30.98	37.48	62.4	12.59	2.58	6.26	3.33	2.92	.463		

* Averages calculated upon the air-dried tea, unless otherwise stated.

TABLE III.

Showing the percentage of extract, tannin, theine, and ash obtained from various teas by pouring one hundred (100) parts of boiling hot distilled water upon the leaves and allowing to "draw" ten (10) minutes.	*Indian Tea.*	*Indian Tea.*	*Finest Nankin Moyune Gunpowder.*	*Common Moyune Gunpowder.*	*Japan Basket-Fired.*	*Japan Pan-Fired.*	*Choicest Formosa Oolong.*	*Choicest Formosa Oolong.*	*Superior Formosa Oolong.*	*Medium Amoy Oolong.*	*Medium Amoy Oolong.*	*Choicest Moning Congou.*	*Superior Moning Congou.*	*Medium Moning Congou.*	*Good Common Kaisow Congou.*	*Common Moning Congou.*
Price per lb., wholesale..........	23 13-100c.	22 81-100c.	75c.	18c.	..	..	65c.	53c.	30c.	24c.	21½c.	45c.	27c.	19½c.	17¼c.	15½c.
Per cent. extract, macerating 10 minutes in 100 parts water......	29.15	28.57	37.32	28.07	31.75	34.37	33.62	33.30	29.00	27.4	24.5	24.25	21.55	21.02	23.25	19.50
Per cent. extract, macerating 10 minutes in 100 parts water, less per cent. ash..................	25.35	24.17	32.72	24.05	27.47	30.70	29.62	29.32	25.34	23.67	21.25	20.12	17.85	17.80	19.95	15.62
Ratio (per cent.) of extract, by drawing 10 minutes, to total extract by exhaustion............	73.56	72.04	73.19	79.36	75.59	79.59	75.90	73.69	68.60	60.99	60.5	70.6	57.83	68.6	64.12	72.2
Per cent. tannin, drawing 10 minutes in 100 parts water......	11.48	9.50	16.79	9.26	11.23	13.41	12.91	13.75	9.63	10.12	7.53	5.46	4.44	5.55	4.05	4.50
Ratio (per cent.) tannin, drawing 10 minutes in 100 parts water, to total tannin in leaf	60.85	58.38	87.8	77.74	74.51	94.39	75.60	68.51	59.6	56.00	55.6	41.7	31.98	45.2	38.49	52.9
Per cent. theine dissolved by drawing 10 minutes in 100 parts water........................	3.30	2.75	2.95	1.675	2.175	2.07	2.50	2.42	2.12	1.92	1.70	2.87	2.77	2.32	2.35	1.95
Per ct. ash, dissolved by drawing 10 minutes in 100 parts water...	3.80	4.40	4.60	4.02	4.27	3.67	4.00	3.97	3.66	3.72	3.25	4.13	3.70	3.22	3.30	2.88
Ratio (per cent.) of ash, obtained by drawing 10 minutes, to total Ash from leaf.....	70.02	79.55	55.77	66.14	79.98	63.59	71.30	66.49	62.30	68.47	58.90	73.7	63.5	58.28	59.86	46.80
Alkalinity of ash, expressed as "potassium oxide"...........	1.48	1.28	1.664	1.299	1.613	1.639	1.362	1.198	1.393	1.434	1.31	1.46	1.47	1.32	1.51	1.26

the same conditions. The results cannot be considered absolute, but, as they vary only between narrow limits, they are sufficiently accurate to illustrate the behavior of these various teas when subjected to the customary household method of pouring boiling water upon the leaves and allowing it to draw.

The results of this table (III.) give the percentages of "extract," theine, tannin,[1] ash (mineral matter) dissolved, the alkalinity of the ash expressed as potassium oxide, and the ratio (per cent.) of "extract" and tannin to the total amount of these two in the leaf. The percentages are calculated upon the air-dried leaf. A comparison of the results for the five Oolong teas shows the finer grades to have yielded more extract, theine, and ash than the poorer grades.

The decline, from the fine to the poor grades of the various teas, in the amount of theine dissolved, is something noteworthy, as showing the fine grades to yield nearly all their theine, while the poorer grades do so only to a limited extent. The percentages of tannin are quite irregular. Further, the table shows that there is more mineral matter extracted from the leaf than is indicated by the term "soluble ash" in Table I., the difference being .62 per cent. as an average of fourteen determinations.

The ratio of tannin to the "extract," and the ratio of either one to the total tannin and "extract" of the leaf, varies quite uniformly with the value of the tea, the per cent. of tannin falling or rising with the percentage of "extract." See Table IV.

It will also be noticed that the Congou teas yielded low percentages of "extract" and tannin, showing that the time allowed for drawing in these teas should be greater than ten minutes, if a full yield of these constituents is desired. If this is uniformly true of Congou teas, they would certainly be suitable for people to whom the large quantity of tannin of the other varieties is objectionable. The tannin extracted from the best green tea was unusually large, being 16.79 per cent.

Both Indian teas show a good yield of "extract," theine, tannin, and soluble mineral matter. Although these results are quite satisfactory in showing the difference in the drawing qualities of various-priced teas, they are not sufficiently uniform to make the results of an analysis the basis for calculating the price of a tea. It is evident that the essential oil plays a more important part than any other constituent of the tea in determining its commercial value.

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[1] The percentages of tannin are somewhat greater than would be obtained in using a hard water.

TABLE IV.

Showing the per cent. of extract, tannin, theine, and ash dissolved from tea by distilled water and Croton water, by allowing to draw from three minutes to over one hour. (One hundred parts of boiling water were poured upon one part of tea.)	**FINEST FORMOSA OOLONG.**					
	3 m. Distilled water.	*5 m. Distilled water.*	*5 m. Croton.*	*10 m. Distilled.*	*10 m. Croton.*	*1 h. 15m. Distilled.*
Per cent. extract, total	25.97	28.37	27.47	30.87	30.25	33.75
Per cent. extract, less ash	22.25	24.50	23.85	26.70	26.12	29.42
Per cent. tannin	9.755	11.23	10.18	13.46	10.60	14.94
Per cent. theine	1.95	2.65	2.02	2.75	2.82	2.85
Alkalinity of ash as potassic oxide	1.029	1.22	1.076	1.22	1.152	1.28
Per cent. ash	3.725	3.805	3.625	4.175	4.125	4.325

Table IV. illustrates the difference in the drawing quality of an extra choice Oolong tea when treated either with distilled or Croton water. It shows that in ten minutes' "drawing" the theine was practically extracted, and that the Croton water extracted less tannin than the distilled water, while there was no noteworthy difference in the percentages of extract and ash when the distilled water and Croton water were allowed to draw for the same length of time. Hard waters dissolve less tannin than soft waters under the same conditions. This will also be noticed in the above table. And Table IV. serves to illustrate the rapidity with which the constituents of the tea leaf are dissolved, and that the choice of the water and the proper length of time for drawing are very important factors in preparing a good cup of tea.

Practical conclusions.—Though varying widely for different teas, the total soluble (extractive) matter averages about 33 per cent., but the average is considerably lower for the infusion of tea prepared by the ordinary household method. The volatile oil gives the flavor and aroma, the tannin and extractive matter the astringency, strength, and body to the infusion. Theine, being almost tasteless, is not taken into account by "tea-tasters," though, physiologically, the most important constituent of the tea.

Besides the above, the appearance of the leaf, as well as the color of the infusion and any peculiar foreign taste or smell imparted to the same, have considerable bearing in the "teataster's" method of valuation. A strict relation between the chemical composition of the tea and the commercial value of the same is therefore scarcely to be looked for, although the former would disclose at once that tea which is physiologically the best.

The principal constituents of tea are the volatile oil, theine, tannin, albuminous compounds, gum, etc., and the soluble mineral matter, containing considerable potash and phosphoric acid.

The fertility of the soil, the nature of the climate, the processing and manipulation the leaves undergo after being plucked, and the care with which the tea is handled thereafter are all instrumental in influencing the chemical composition and the quality of the tea. Uniformity in composition cannot be expected. The principal difference between Green, Oolong, and Congou teas is caused by the processing and manipulation; but, whatever the *modus operandi* of the latter, it cannot make good tea out of leaves which have not had the proper conditions of soil and climate to further the production of those constituents which are characteristic of tea. In the ordinary analysis of the tea only the more important constituents are determined, in order to establish the presence or absence of foreign matter. The results thus obtained are scarcely applicable to the commercial valuation of tea, since much is there determined which does not enter the *infusion* of tea. It is the quality of the infusion which is of importance to the consumer, and not the total composition or appearance of the leaf. Tea is essentially something for the epicurean. To discriminate between qualities of teas of nearly the same grade requires a delicate and sensitive palate. Expert tea-tasters are guided chiefly by the strength, flavor, aroma, and quality of the infusion in judging and classifying tea as to its quality.

THALLINE. See CINCHONA ALKALOIDS, p. 168.

THEBAINE. See OPIUM ALKALOIDS, p. 358.

THEINE. See CAFFEINE, p. 77.

THEOBROMINE.—$C_7H_8N_4O_2 = 180$. A dimethyl xanthine, $C_5H_2(CH_3)_2N_4O_2$. See Caffeine, p. 77.—Found, without caffeine,[1] in the seed of the Theobroma Cacao, or "chocolate

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[1] SCHMIDT (1883) found a little caffeine in cacao.

nut" (Woskresensky, 1841), and, as a smaller accompaniment of caffeine, in the seed of the Sterculia acuminata, the "cola nut." The dry cacao seed freed from husk, the "cocoa nibs," contains about 1.5 per cent. of theobromine (Wolfram, 1879); while the husks, the "cocoa shells," furnish from 0.3 to 0.7 per cent. in average yield (Wolfram, Donker, 1880).

a.—Theobromine crystallizes in the trimetric system, appearing in permanent, anhydrous white needles and club-shaped groups, to the unaided eye as a crystalline powder. Sublimes without decomposition, yielding distinct microscopic crystals of sublimate at 170° C. (Blyth, 1878). Sublimes at 290° to 295° C. (Keller, 1854).

b.—Theobromine has a very bitter taste, slowly produced. Its physiological effects are like those of caffeine, but are obtained by smaller doses (Mitscherlich, 1859). It is excreted in the urine.

c.—Theobromine is slightly soluble in water or alcohol, its solution requiring 1600 parts water at 17° C. (62.6° F.), and 148 parts water at 100° C. (Dragendorff); 4284 parts absolute alcohol at 17° C., and 422 parts boiling absolute alcohol (Treumann, 1878), in 1400 parts cold alcohol (Mitscherlich, 1859). It is but very slightly soluble in ether, one part requiring 17000 parts cold ether or 600 parts boiling ether (Mitscherlich). It dissolves in 105 parts boiling chloroform (Treumann); is somewhat soluble in amyl alcohol; but slightly soluble in benzene; insoluble in petroleum benzin.—Theobromine is a weak base. It forms crystallizable salts; but on contact with water they give up acid and become basic salts, and those of volatile acids give up the acid at or below 100° C. Theobromine dissolves in hydrochloric and in other acids; but the hydrochloride, $C_7H_8N_4O_2 . HCl . H_2O$, and the nitrate, $C_7H_8N_4O_2 . HNO_3$, do not dissolve at all freely in water alone without free acid. Theobromine dissolves in ammonia-water. Respecting combinations, see report of Messrs. Schmidt and Pressler, 1883.[1]

d.—Theobromine responds to *the murexoin test* with the same intensity as Caffeine (p. 79), forming amalic acid when warmed with **hydrochloric acid** and **potassium chlorate** and evaporated to dryness on the water-bath, and giving purple-colored murexoin when the cold residue is touched with ammonia.—**Phosphomolybdate of sodium,** added to the acidulous

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[1] *Liebig's Annalen*, 217, 287; *Jour. Chem. Soc.*, 44, 872.

solutions of theobromine, gives a yellow precipitate, obtained in dilute solutions.—Platinum chloride does not precipitate, except in concentrated solutions, when crystals are obtained, $(C_7H_8N_4O_2)_2HClPtCl_6 . 4H_2O$. In like manner gold chloride yields yellow crystals, in tufts of needles, $C_7H_8N_4O_2 . HCl . AuCl_3$.—When an ammonia solution of theobromine is treated with **silver nitrate** solution, a gelatinous precipitate is obtained, and on boiling this granular crystals of argentic theobromine are obtained, $C_7H_7AgN_4O_2$. And when this compound is treated with anhydrous **methyl iodide,** at 100° C., for twenty-four hours, caffeine (methyl theobromine) is formed, with silver iodide (STRECKER, 1861). Again, when theobromine, alcoholic solution of potassium hydrate, and methyl iodide, in equivalent quantities, are heated together at 100° C. in sealed tubes, caffeine is formed, with potassium iodide (SCHMIDT and PRESSLER, 1883).

$$C_7H_7AgN_4O_2 + CH_3I = C_7H_7(CH_3)N_4O_2 + AgI$$
$$C_7H_8N_4O_2 + CH_3I + KOH = C_7H_7(CH_3)N_4O_2 + KI + H_2O.$$

Potassium mercuric iodide produces no precipitate in the acidulous solutions of theobromine, and iodine in potassium iodide solution causes little precipitation (distinctions of caffeine and theobromine from most other alkaloids).

e.—Theobromine may be *separated* from non-volatile matters, like caffeine, by sublimation at a gradually increasing heat beginning at 170° C. From most alkaloids by its slight solubilities, and from caffeine by its smaller solubilities in benzene (SCHMIDT), or water, or ether.

f.—The quantitative estimation of theobromine in cacao is made by SCHMIDT and PRESSLER (1883) as follows: The crushed cacao is freed from oil by pressure, half its remaining weight of slaked lime is added, and the mixture is boiled repeatedly with alcohol of 80 per cent. strength. The residue on evaporation of the alcohol is recrystallized from the same solvent, and is obtained as a white, crystalline powder. It may be dried at 100° C. and weighed.

TROPEINES. See MIDRIATIC ALKALOIDS, p. 339.

TURKEY-RED OIL. See FATS AND OILS, p. 287.

TYROTOXICON.—"*Cheese Poison.*" The putrefactive product obtained in 1885 by Professor Vaughan, and recently announced by him to be diazobenzene, $C_6H_5.N:N$, in combination with acids.[1]

a.—Tyrotoxicon, obtained from milk products as directed under *e*, was found to agree with diazobenzene butyrate, $C_6H_5.N_2.C_4H_7O_2$, in crystallizing in needles, which gradually decompose in moist air. Potassium diazobenzene, $C_6H_5.N_2.OK$, obtained from tyrotoxicon,[2] appeared in fine six-sided plates. Tyrotoxicon compounds, at 100° C., explode with violence.

b.—The crystals have a penetrating, old-cheesy odor. A minute portion placed upon the tongue produces "dryness of the throat, nausea, vomiting, and diarrhœa." In children the effects agree with the symptoms of cholera infantum. Ten drops of a concentrated aqueous solution of tyrotoxicon from milk three months old, placed in the mouth of a small dog three weeks old, in a few minutes caused "frothing at the mouth, retching, vomiting of frothy liquid, rapid breathing, muscular spasm over the abdomen, and after some time watery stools." Similar effects were obtained with cats, and subsequent dissection showed the mucous membrane of the stomach and intestines to be blanched and soft. Of diazobenzene butyrate, artificially prepared,[3] 0.010 to 0.025 gram given to cats caused severe symptoms, the same as above detailed, and 0.100 gram caused death, the mucous membrane of the stomach not being reddened, but left pale and soft.

c.—"Tyrotoxicon is soluble in water, alcohol, chloroform, and ether." "Purified tyrotoxicon is insoluble in ether, and it probably owes its solubility in ether at this stage to the presence of impurities." The ordinary salts of diazobenzene are more or less freely soluble in water, sparingly soluble in alcohol, and are for the most part precipitated from alcoholic solutions by ether.

d.—The diazobenzenoid compounds are identified by the reaction of LIEBERMANN,[4] namely, by the bright colors they give

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[1] VICTOR C. VAUGHAN, 1884–85: "A Ptomaine from Poisonous Cheese," *Zeitsch. physiolog. Chem.*, 10, 146; *Jour. Chem. Soc.*, 50, 373. Michigan State Board of Health Reports, 1885 and after. "Tyrotoxicon: Its presence in poisonous cheese, ice-cream, and milk," Am. Assoc. Adv. Sci., Buffalo Meeting, August, 1886, *Jour. Analyt. Chem.*, 1, 24. "The Chemistry of Tyrotoxicon and its action upon the lower animals," with report of determination of diazobenzene, *ibid.*, 1, 281.

[2] By method of GRIESS, 1866: *Ann. Chem. Phar.*, **137**, 54.

[3] By the method of GRIESS, *loc. cit.*

[4] LIEBERMANN, 1874: *Ber. d. chem. Ges.*, 7, 247; *Jour. Chem. Soc.*, **27**, 693: that sulphuric acid holding nitrous acid in solution gives color-reactions

when treated with concentrated sulphuric acid and phenol. "With equal parts of sulphuric acid and carbolic acid the prepared [artificial] diazobenzene nitrate gave a green coloration; while with the same reagents tyrotoxicon gave a color which varied from a yellow to an orange-red. But the diazobenzene nitrate dissolved in the whey of normal milk and extracted with ether, or in the presence of other proteids, gave the same shades of color as the tyrotoxicon did, and the potassium compound of tyrotoxicon prepared by the method to be given later produced the same shade of green as did the artificial diazobenzene. This color test may be used as a preliminary test in examining milk for tyrotoxicon. It is best carried out as follows: Place on a clean porcelain surface two or three drops each of pure sulphuric acid and pure carbolic acid. This mixture should remain colorless, or nearly so. Then add a few drops of the residue left after the spontaneous evaporation of the ether. If tyrotoxicon be present a yellow to an orange-red color will be produced. This test is to be regarded as a preliminary one; for it may be due to the presence of a nitrate or nitrite.[1] The tyrotoxicon must be purified according to a method to be given further on before the absence of nitrate or nitrite can be positively demonstrated."

The explosion of tyrotoxicon may be obtained, in evidence of its identity, by exposure of the platinochloride to a temperature approaching 100° C., as in the discovery of this property by Prof. Vaughan. A solution of the tyrotoxicon in absolute alcohol is treated with a little platinum chloride, and heated in an open dish upon the water-bath, when, as the alcohol is nearly or quite all vaporized, the explosion results. The known diazo platinum compound is $(C_6H_5.N_2.Cl)_2PtCl_4$, and in explosion is resolved into $2C_6H_5Cl + N_2 + 2Cl_2 + Pt$.

The aurochloride of tyrotoxicon is obtained, in precipitate or in golden plates, as follows: "In the filtrate from milk which is rich in tyrotoxicon, after neutralization with sodium carbonate,

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with phenols generally, the produced colors containing nitrogen but *not* in the form of the nitro, and probably not in that of the nitroso group.

All diazo compounds, also the diazo-amido compounds, share with the nitroso compounds (Hofmann) and the nitrites (Liebermann) the power to give with sulphuric acid and phenol red to blue colors of the utmost intensity (E. Fischer, 1875).—The color-products so obtained are azo-benzenoid bodies, well known as azo dyes, represented by the tropœolines (this work, p. 186; O. N. Witt, *Jour. Chem. Soc.*, 35, 179). The azo compounds, it will be remembered, contain the group NN interposed between two benzenoid (or other carbonaceous) groups. Thus, $C_6H_4.N_2.SO_3$ (diazobenzene sulphonic acid)$+C_6H_5OH = C_6H_4.SO_3H.N_2.C_6H_4.OH$ (oxy-azo-benzene sulphonic acid).

[1] "The coloration with nitrates and nitrites is darker than with diazobenzene."

filtration and acidifying with hydrochloric acid, gold chloride produces a precipitate which is insoluble in water, but soluble in hot alcohol, from which it separates, on cooling, in golden plates." "The gold compound is decomposed by frequent treatment with hot alcohol."

The potassium compound of tyrotoxicon—believed to be potassium diazobenzene, $C_6H_5.N_2.OK$—was prepared as follows: "The aqueous residue [see *e*] was acidified with nitric acid, then treated with an equal volume of potassium hydrate and the whole concentrated on the water-bath. . . . On cooling the mass crystallized . . . in six-sided plates, along with the prisms of potassium nitrate. The crystalline mass obtained from the tyrotoxicon was treated with absolute alcohol, filtered, the filtrate evaporated on the water-bath, the residue dissolved in absolute alcohol, from which it was precipitated in a white, crystalline form with ether."

The decompositions of tyrotoxicon are so far found by its discoverer to agree with the well-known decompositions of diazobenzene salts. Warmed with water the latter break up into carbolic acid and nitrogen, thus:

$$C_6H_5.N_2.NO_3 + H_2O = C_6H_5.OH + N_2 + HNO_3.$$

Warmed with alcohol, aldehyde and hydrocarbons result as follows:

$$C_6H_5.N_2.NO_3 + C_2H_6O = C_6H_6 + N_2 + C_2H_4O + HNO_3.$$

With the acids of the halogens changes occur as follows:

$$C_6H_5.N_2.NO_3 + HCl = C_6H_5Cl + N_2 + HNO_3.$$

The reducing agents in general cause immediate decomposition. Hydrogen sulphide reacts promptly.

e.—The following directions for the separation of tyrotoxicon from milk or cheese are taken from the last article of Dr. Vaughan: "Milk or other fluid to be tested for this poison should be kept in well-stoppered bottles; for if the fluid be exposed to the air the tyrotoxicon may decompose in a few hours. The filtrate from the milk, or the filtered aqueous extract of cheese, should be neutralized with sodium carbonate, then shaken with half its volume of pure ether. Time should be given for the complete separation of the ether. . . . After complete separation the ether should be removed with a pipette and allowed to evaporate spontaneously in an open dish. The residue from the ether may be dissolved in distilled water and again extracted with ether; but repeated extractions with ether are to be avoided, for as the tyrotoxicon becomes purified it becomes less soluble in ether. To a drop of an aqueous solution of the ether residue apply the preliminary test with sulphuric and carbolic acids. To the remainder of the aqueous solution of the ether residue add an equal volume of a saturated solution of caustic potash, and evaporate the mixture on the water-bath. The double hydrate of potassium and diazobenzene [$C_6H_5.N_2.OK$] will be formed if tyrotoxicon be present." The recognition of potassium diazobenzene is stated on page 517.

f.—An estimation of tyrotoxicon is indicated by the experiments of Vaughan, in converting the potassium compound (*d*), prepared as directed (*e*), into potassium sulphate for weight. The white, crystalline precipitate, by the ether, "was collected, washed with ether, dried, and the per cent. of potassium estimated as potassium sulphate."[1]

$$K_2SO_4 : 2C_6H_5N_2OK : 2C_6H_5N_2NO_3 :: 174 : 320 : 334.$$

ULTIMATE ANALYSIS of Carbon Compounds. See p. 201.

VALERIC ACIDS. $C_5H_{10}O_2 = 102$ (monobasic). Primary Pentoic Acids.—Four pentoic acids are theoretically possible, as oxidation products of the four primary pentoic alcohols, and are all known, as follows:

(1) Normal valeric acid, $CH_3.CH_2.CH_2.CH_2.CO_2H$. Made from normal butyl cyanide, etc.
(2) Isovaleric acid. Inactive valeric acid. $(CH_3)_2CH.CH_2.CO_2H$. Isobutyl-carboxyl. Chief valeric acid of valerian oil. Obtained by oxidation of the chief alcohol of fusel oil.
(3) Methyl-ethyl acetic acid. Active (dextro-rotatory) valeric acid. $CH_3.C_2H_5.CH.CO_2H$. In small proportion in valerian oil, according to some observers. Obtained by oxidation of the lesser pentyl alcohol (13%) of fusel oil.
(4) Methyl-propyl acetic acid, $CH_3C_3H_6.CO_2H$. Made from methyl-propyl-carbinol.

Ordinary Valeric Acid. Isovaleric Acid. Inactive Valeric Acid. The second of the pentoic acids above named. Baldriansäure.—A constituent of "valerian root," the rhizome and rootlets of Valeriana officinalis, and a part of the volatile oil of valerian. Reported as found in digitalis, Artimisia Absin-

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[1] Per cent. of potassium calculated, 24.42; found, 23.92.

thium, Anthemis nobilis, Sambucus nigra, Viburnum opulus, and other plants. Manufactured by oxidation (distillation from dichromate and sulphuric acid) of isoamyl alcohol (isobutyl carbinol), the principal alcohol of fusel oil.

Valeric acid is *recognized* by its odor and the odor of amyl valerate (*b*), its solubilities (*c*, *d*), and physical properties (*a*). It is *separated* by distillation or by shaking out with ether (*e*). It may be estimated volumetrically (*f*). Tests of purity (*g*).

a.—Isovaleric acid, absolute, is a colorless oil, of specific gravity 0.937 at 15° C.; 0.931 to 0.933 at 20° C. (water at same) (LANDOLT, 1862). It boils at 175° C. (FRANKLAND and DUPPA, 1867). It forms a hydrate, $C_5H_{10}O_2.H_2O$, of sp. gr. 0.950, boiling at 165° C., and gradually dehydrated by distillation.

The metallic valerates are easily fusible salts, congealing with an opaque white surface, and crystallizing by careful concentration of solutions.

b.—Isovaleric acid has an acidulous, burning taste, and a biting effect on the tongue. The odor is characteristic, unpleasant, reminding of rancid cheese. The metallic valerates are nearly odorless, and of a sweetish, sharp taste. Ethyl and amyl valerates have fragrant, heavy fruity odors. Amyl valerate is used to present an odor of apples.

c.—Isovaleric acid is soluble in about 30 parts of water at ordinary temperatures, the hydrate somewhat more soluble. By saturation of the solution with calcium or sodium chloride the valeric acid is almost wholly thrown out of solution. It is soluble in all proportions of alcohol, ether, chloroform, or glacial acetic acid.

The valerates of the alkali metals are deliquescent and freely soluble in water and in alcohol; of the alkaline-earth metals, moderately soluble in water and in aqueous alcohol. Aluminium valerate is not soluble in water; basic ferric valerate, insoluble; zinc valerate, in 90 parts of water or 60 parts of 80% alcohol; bismuth valerate (basic), insoluble in water; lead valerate, (normal) soluble in water, (basic) sparingly soluble; mercuric valerate, soluble; mercurous valerate, slightly soluble; cupric valerate, moderately soluble; silver valerate, slightly soluble, in water.—To test-papers free valeric acid has the acid reaction; the alkali valerates, neutral reaction.

d.—Isovaleric acid is characterized by its odor as a free acid, and by the odor of its amyl ester. This is formed by distilling with a little ordinary amyl alcohol and twice its quantity of sulphuric acid. Precipitates are obtained, with alkali valerates, on adding aluminium sulphate or silver nitrate, not by addition of lead normal acetate. Cupric acetate, with concentrated free valeric acid, yields oily droplets of anhydrous valerate of copper, which, on standing, crystallize as hydrate (distinction from butyrate, which in solution not very dilute gives an immediate precipitate of butyrate of copper).

e.—Separation.—Isovaleric acid is separated from non-volatile matters, and obtained from its salts, by distillation, adding diluted sulphuric acid if necessary to liberate it. From other volatile acids fractional saturation and distillation may be employed, having regard to boiling points.—Separation from aqueous solutions is effected by ether more readily than by distillation. The aqueous solution, in which the valeric acid is liberated, if need be, by adding potassium bisulphate, is saturated with sodium sulphate and shaken out with portions of ether.

f.—Quantitative.—The valeric acids may be estimated volumetrically with standard solutions of alkali, using either litmus-papers or phenol-phthalein as the indicator of saturation. Each c.c. of normal solution of alkali indicates 0.102 gram of real valeric acid; each c.c. decinormal solution, 0.0102 gram. And if 5.1 grams of material be taken, c.c. of N alkali × 2 = per cent. of acid; if 1.02 grams be taken, c.c. of $\frac{N}{10}$ = per cent.

g.—Tests of Purity.—"Purified by distillation, valeric acid is a colorless liquid, oleaginous, of a peculiar disagreeable odor. It dissolves in 30 parts of water at 20° C., and in all proportions of alcohol or ether. Its specific gravity at 0° C. is about 0.955. It boils at 175° C."(Ph. Fran.)—"A specific gravity above 0.950, and solubility in less than 25 parts of water, indicates presence of water, acetic or butyric acid, amyl alcohol or aldehyde. The last two are known by their insolubility in ammonia-water. If half of a mixture of equal parts of butyric and valeric acids be neutralized with alkali, and the whole distilled together, the butyric acid goes over, and will be found soluble in not above 10 parts of water" (Flückiger's "Phar. Chem.")

VAPOR TENSION, Determination of. See p. 237.

VINEGAR. See Acetic Acid, p. 14.

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