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31. Annotated Bibliography on Methylpentynol

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ANNOTATED BIBLIOGRAPHY ON METHYLPENTYNOL

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Abstract.--An annotated bibliography containing 26 selected references on the biochemistry, physiology, and methods of analysis of methylpentynol.

Experiments with methylpentynol as an anesthetic for four salmonids to describe its toxicity and efficacy began in 1964 at the Fish Control Laboratory, La Crosse, Wis. The U.S. Food and Drug Administration requires these data for clearance and labeling of drugs. During the study, a number of selected references on fishery uses of the drug, and on its biochemistry, physiology, and methods of analysis were annotated.

BIBLIOGRAPHY

Bayliff, William H., and Edward F. Klima.
1962. Live-box experiments with anchovetas, Cetengraulis mysticetus, in the Gulf of Panama. Inter-American Tropical Tuna Commission Bulletin, vol. 6, No. 8, p. 333-436.

Four anesthetics--quinaldine, MS-222, methylpentynol, and tertiary amyl alcohol--were used to facilitate tagging operations. Quinaldine caused some mortalities and proved to be chemically unstable. Methylpentynol and tertiary amyl alcohol also killed some fish and acted too slowly for field use. The methylpentynol was used at a concentration of 6 milliliters per gallon. MS-222 is the most satisfactory of the chemicals tested, although there were some mortalities at the higher concentrations.

Bell, Gordon R.
1964. A guide to the properties, characteristics, and uses of some general anaesthetics for fish. Fisheries Research Board of Canada, Bulletin 148. 4 p.

The structural formulas, manufacturers, dosages, toxicities, and solubilities are presented for 11 chemicals used as fish anesthetics: carbon dioxide, chloral hydrate, chloretone, ether, methylpentynol, MS-222, phenoxyethanol, quinaldine, sodium amytol, tribromomethanol, and tertiary amyl alcohol. Methylpentynol is recommended at a dosage of 1 to 2 milliliters per liter in transportation. Bell does not recommend it as an anesthetic for surgery because immobilized fish twitch when prodded or cut. Methylpentynol immobilizes fish slowly with occasional violent struggling, but recovery is rapid in fresh water.

Carlson, Frank T.
1965. Susquehanna River Shad study. Pennsylvania Angler, October, p. 1-7.

Shad were transported in a solution containing 1 milliliter of methylpentynol per gallon of water. They were anesthetized in a 15-gallon tub of river water containing 3 milliliters of methylpentynol per gallon.

Fry, F. E. J., and K. S. Norris.
1962. The transporting of live fish. In Georg Borgstrom, Editor Fish as Food, Vol. 2, Chap. 17, p. 595-608. Academic Press, N.Y.

The authors suggest methylpentynol for use in transporting live fish.

Hirsh, Harold L., and William H. Orsinger.
1952. Methylparafynol- a new hypnotic. Preliminary report on its therapeutic efficacy and toxicity. American Practioner, vol. 3, no. 1, p. 23-26.

Patients received a 100 to 800 milligram dose of methylpentynol as a sedative with no after effects on blood pressure, pulse, respiration rate, blood and urine composition, electrocardiogram, or liver and kidney function. The authors considered methylpentynol a safe, nontoxic, efficient, rapid, and long lasting hypnotic drug in humans.

Howland, Robert M., and Richard A. Schoettger.
1969. Investigations in Fish Control: 29. The efficacy of methylpentynol as an anesthetic on four salmonids. U.S. Bureau of Sport Fisheries and Wildlife.

Methylpentynol was tested as an anesthetic against rainbow trout, brown trout, brook trout, and lake trout. Concentrations ranging from 1.5 to 8.0 parts per thousand produced anesthesia within 4 to 57 minutes respectively. They studied the effects of water temperature, water quality, and pH on the rate of anesthetization and found that only temperature had a measurable effect. The authors concluded that methypentynol is better suited as a sedative than as an anesthetic for salmonids, because fish under anesthesia are not completely immobilized.

Job, C. von.
1959. Die Beziehungen zwischen der stärke der narkotischen wirkung und der thermodynamischen konzentration bei estern des methylpentinols. Arzneimittel-Forschung, vol. 9, no. 1, p. 14-22.

The author investigated the effects of methylpentynol and some of its esters on the rat and on the isolated frog nerve. Action potentials of the isolated frog nerve are retarded and interrupted under the influence of methylpentynol. Methylpentynol blocks conduction of stimuli at a concentration of 5 grams per liter.

Kennedy, Walter A., and Edward Marley.
1959. The electroencephalographic effects of methylpentynol. Electroencephalography and Clinical Neurophysiology, vol. 2, no. 1, p. 59-64.

The authors discuss several aspects of the drug in clinical work, and cite cases of overdosage and side effects from methylpentynol. They found a correlation between the degree of electroencephalographic abnormalities and the amount of physical disturbance produced in patients given 0.5 gram of methylpentynol orally for 5 days.

Klontz, George W.
1964. Anesthesia of fishes. In Proceedings of the Symposium on Experimental Animal Anesthesiology. Brooks Air Force Base, December 14-16. 13 p.

Techniques for anesthetizing fish and a brief description are given for 15 agents: carbon dioxide, electricity, diethyl ether, secobarbital sodium, amobarbitol sodium, urethane, chloral hydrate, tertiaryamyl alcohol, tribromoethanol, chlorobutanol, 2-phenoxyethanol, 4-styrylpyridine, methylpentynol, quinaldine, and MS-222. Concentrations of 0.5 to 0.9 milliliter per liter of methylpentynol are suggested to induce anesthesia within 2 to 3 minutes. Maintenance of anesthesia is considered fair, and the recovery of fish in fresh water occurs in 5 to 20 minutes. The author also rated the maintenance of deep anesthesia as fair because fish seem to go into respiratory arrest. He considered the odor of methylpentynol quite disagreeable.

Lasagna, Louis.
1954. A comparison of hypnotic agents. The Journal of Pharmacology and Experimental Therapeutics, vol. III, p. 9-20.

The author used chloral hydrate, pentobarbital sodium, methylpentynol, and a placebo to determine which doses are most useful for inducing prolonged sleep in man. A dosage of 0.5 to 1.0 gram of methylpentynol induced sleep that was undistinguishable from that of the placebo.

Leal, Aluiso Marques, and Maria Helena Diniz.
1956. Assay of methylpentynol in galenic preparations. Revista Portuguesa de Farmacia, vol. 6, p. 14-17.

Two titrimetric methods for the assay of methylpentynol in body fluids are described.

Margolin, S., P. Perlman, F. Villani, and T. H. McGavack.
1951. A new class of hypnotics: unsaturated carbinols. Science, vol. 114, p. 384-385.

Methylpentynol was studied for use as a clinical hypnotic. The LC_{50} for mice, rats, and guinea pigs is 600 to 900 mg./kg. (milligrams per kilogram). The animals died in coma. Two hundred to 300 mg./kg. had no effect on mice, rats, and dogs. One half to 4.6 percent of a 200-mg./kg. dose fed to dogs was excreted in the urine within 24 hours. Ten minutes after an intravenous administration of 200 mg./kg. to dogs, 20 percent of the dose is found in the blood, but none is present after 2 hours. Tweny percent of an 800-mg./kg. dose is found in the muscle and liver tissues taken from rats which are still under hypnosis. No residues were found in these tissues after the effects of anesthesia wore off. Methylpentynol was not metabolized by whole blood of dogs or rats but it was metabolized by slices of kidney, liver, or brain.

Marking, Leif L.
1969. Investigations in Fish Control: 30. The toxicity of methylpentynol to selected fishes. U.S. Bureau of Sport Fisheries and Wildlife.

Toxicity of methylpentynol to rainbow trout, brown trout, brook trout, lake trout, northern pike, channel catfish, bluegills, largemouth bass, and walleyes of various sizes ranged from the 96-hour LC_{50} value of 660 p.p.m. (parts per million), for the more sensitive lake trout to 1,890 p.p.m. for channel catfish at 12° C. Larger rainbow, brook, and lake trout were considerably more resistant than smaller ones. Rainbow trout and bluegills are more sensitive to methylpentynol in warmer temperatures. Total hardnesses of 10.0 to 170.0 p.p.m. produced similar results in the static bioassays. Methylpentynol is much less toxic than other anesthetics tested in the 24-, 48-, and 96-hour static bioassays at selected temperatures and water qualities.

Marley, E.
1959. Pharmacology of methylpentynol and methylpentynol carbamate. British Journal of Pharmacology, vol. 14, p. 284-306.

Methylpentynol and methylpentynol carbamate are depressants of monosynaptic and polysynaptic reflexes in cats, frogs, rabbits, and guinea pigs. Small doses exerted weak ganglionic and neuromuscular blocking actions, increased aortic blood flow, diminished systolic amplitude, increased coronary flow, and stimulated respiration. Large doses depressed respiration.

Marley, E., and W. D. M. Paton.
1959. The effect of methylpentynol and methylpentynol carbamate on the perfused superior cervical ganglion of the cat. British Journal of Pharmacology, vol. 14, p. 303-312.

The output of acetylcholine in the perfused cervical ganglion is depressed by dosages of 1 to 5 milligrams of the drugs.

Marley, E., and J. R. Vane.
1958. The distribution of methylpentynol and methylpentynol carbamate in tissues and body fluids of cats. British Journal of Pharmacology, vol. 13, p. 364-371.

The authors present a modified titrimetric method for estimating methylpentynol in amounts as small as 0.1 milligram. They found no difference between plasma concentrations and whole blood concentrations of methylpentynol 10 minutes after injection. They concluded that the drug has free access to all parts of the body, and general anesthesia does not inhibit its metabolism and excretion. It enters cells easily, where it tends to accumulate.

Marley, Edward.
1958. Susceptibility to methylpentynol and methylpentynol carbamate. British Medical Journal, Medical Memoranda, August 23, p. 493.

He compared the toxicities of methylpentynol and methylpentynol carbamate in man. Methylpentynol at 0.5 gram per day for 5 days causes many toxic effects in man.

McFarland, William N.
1959. A study of the effects of anesthetics on the behavior and physiology of fishes. Publications of the Institute of Marine Science, University of Texas, vol. 6, p. 23-55.

The anesthetic effects of 21 chemicals on Fundulus parvipinnis, Gambusia affinis, Paralabrax alathratus, and Girella nigricans were investigated. The effects on behavioral patterns are observed in four major stages: sedation, loss of equilibrium, loss of reflex,

and medullary collapse. These stages are compared to the sequence of anesthesia described for higher vertebrates. Narcotic potencies are correlated with molecular weight of the drugs. Methylpentynol is rated highly potent.

McFarland, William N.
1960. The use of anesthetics for the handling and the transport of fishes. California Fish and Game, vol. 46, no. 4, p. 407-431.

The author suggested that MS-222, tertiary amyl alcohol and methylpentynol are beneficial for inducting deep anesthesia because the drugs act quickly and the fish recover rapidly. Recovery is complete, provided the respiratory movements have not ceased for more than a few minutes. A concentration of 1.5 to 2.0 milliliters per gallon of methylpentynol is considered desirable for transporting marine and freshwater fishes. Methylpentynol lowers metabolic rates and therefore increases load capacity. He suggests that fishes should be pretreated in the anesthetic to reduce metabolic rates prior to loading and transportation.

Nicholls, J. G., and J. P. Quilliam.
1956. The mechanism of action of paraldehyde and methylpentynol on neuromuscular transmission in the frog. British Journal of Pharmacology, vol. 11, p. 151-155.

Paraldehyde and methylpentynol block neuromuscular transmission by decreasing the secretion of acetyl cholinesterase at the synapse in the frog.

Norris, Kenneth S., Frank Brocato, Frank Calandrino and William N. McFarland.
1960. A survey of fish transportation methods and equipment. California Fish and Game, vol. 46, no. 1, p. 5-33.

Methylpentynol is suggested as a useful anesthetic in fish transportation.

Parkhurst, Z. E., and M. A. Smith.
1957. Various drugs as aids in spawning rainbow trout. The Progressive Fish-Culturist, vol. 19, no. 1, p. 39.

A methylpentynol concentration of 2,400 p.p.m. caused sluggishness and relaxation in rainbow trout. The trout are ready for spawning in 3.5 minutes at a water temperature of 43° F. Somewhat longer exposures are not harmful. Trout remained in good condition 75 days after spawning. There was an 84.1 percent hatch from those fish spawned with drugs, and an 84.0 percent hatch from controls.

Pepeu, Giancarlo, and Nicholas J. Giarman.
1960. Effect of methylpentynol on acetylcholine in the rats brain. Nature, vol. 186, p. 638.

The authors found that methylpentynol did not interfere with the synthesis of acetylcholine in the rat brain, nor did it inhibit cholinesterase activity. Male rats were given intraperitoneal injections of methylpentynol in a dosage varying from 200 to 500 milligrams/kilogram.

Perlman, Preston L., and Carol Johnson.
1952. The metabolism of Dormison (3-methyl-pentyne-ol-3, methyl-parafynol) and methods for the estimation of Dormison in biological materials. Journal of the American Pharmaceutical Association, vol. 41, no. 1, p. 13-16.

The authors described a tritrimetric method for estimating methylpentynol in biological fluids and tissue. They studied the metabolism of methylpentynol in dogs. Methylpentynol is metabolized by destruction of the ethinyl group, which metabolizes quite rapidly. This is revealed by the rapid decline in the blood level of methylpentynol and the slow level of elimination of the chemical in the urine, and in vitro by the disappearance of the ethinyl group by metabolizing rat tissues. They found no evidence of storage or accumulation of the drug in tissues.

Perlman, Preston L., David Sutter, and Carol B. Johnson.
1953. Further studies on the metabolic deposition of Dormison (3-methyl-1-pentyn-3-ol) in dogs and man. Journal of the American Pharmaceutical Association, vol. 42, no. 2, p. 750-753.

Dogs eliminated 17-27 percent of the administered methylpentynol conjugated with glucuronic acid; 1 percent unchanged in the urine, and none by way of the lungs or feces.

In man, up to 10 percent is eliminated unchanged, and 17-27 percent as conjugates of glucuronic acid. The peak levels for elimination of the drug are reached within 48 hours.

Quilliam, J. P.
1959. Paraldehyde and methylpentynol and ganglionic transmission. British Journal of Pharmacology, vol. 14, p. 277-283.

Paraldehyde and methylpentynol block transmission of the impulse at preganglionic nerve terminals in cats. The author suggests that this is caused by a decrease in the secretion of acetycholine from the preganglionic nerve terminals.

Schafferzich, S., and Beverly J. Brown.
1952. Anticonvulsant activity and toxicity of methylparafynol (Dormison) and some other alcohols. Science, vol. 116, p. 663.

The authors used phenobarbitol, 2-methyl-2-propanol, 2-methyl-2,4-pentamediol, 3-pentanol, 2-methyl-2-butanol, and methylpentynol as an anticonvulsant in treatment of epilepsy. Rats were not effected by 0.17 percent methylpentynol in their drinking water for 4 months. The LD_{50} of methylpentynol to rats is 300 to 900 milligrams per kilogram. They concluded that methylpentynol is the least safe of those chemicals studied.

Sheldon, J. M.
1965. Plastic bag transport of salmon and steelhead by air and car. The Progressive Fish-Culturist, vol. 27, no. 2, p. 86.

The author used methylpentynol, 0.67 milliliter per gallon of water, as a sedative to transport salmon and steelhead in plastic bags. Three milliliters of 10 percent Dow-Corning Antifoam emulsion was added to prevent excessive foaming.

Smith, J. N., and R. T. Williams.
1954. The metabolism of aliphatic alcohols. The glucuronic acid conjugation of chlorinated and some unsaturated alcohols. Biochemistry Journal, vol. 56, p. 618-621.

They studied the conjugation of glucuronic acid with a number of chlorinated and other aliphatic alcohols in the rabbit. About 50 percent of the methylpentynol is conjugated with glucuronic acid and excreted in the urine.

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