TO DETERMINE THE SHELF LIFE OF IBUPROFEN SOLUTION

AIM: To determine the shelf life of ibuprofen solution using accelerated stability studies.

MATERIAL REQUIREMENT

Ibuprofen, ethanol, phenolphthalein, sodium hydroxide (0.1N), glass wares, dryer etc

THEORY

Most of the drugs purchased from the retail shop contain expiration date on the label of pack. The expiration date is an assurance given by the manufacture that, if the product is taken before the expiry of the labeled date, the dosage form fulfils the specifications presented on the label regarding identity, strength, quality, and purity. The Drug Control Department ensures through regulatory controls, that every product released into the market should be evaluated to fix the expiry date.
The technical term for expiry time is shelf life.[1]By convention, shelf life is defined as the time required for a drug to reduce its concentration to 90% of the labeled concentration. The evaluation of shelf life is essential because the stability of a drug in dosage forms can be influenced by the normal environment conditions. Drugs, such as esters (for example aspirin, procaine) and amides (for example chloramphenicol), undergo hydrolytic reactions during storage under normal conditions. Similarly drug such as ascorbic acid, promethazine undergo oxidation reaction. As a result, the drug may not exhibit the desired effect and may show reduced biological response. Since degradation or decomposition involves chemical alteration (reaction) of the active ingredient, the knowledge of chemical kinetics is helpful to predict the reaction rates and further to evaluate the shelf life. Stability consideration also includes change in physical appearance of the products. In older method, a product is placed at room temperature or in refrigerator in order to mimic the shelf conditions and the stability is evaluated for a prolonged period of 2to 5 years. Such a design of experimentation is time consuming and uneconomical. The reaction rate is accelerated by carrying out the reaction at elevated temperature. Therefore, by conducting the experiment, a factor is obtained that has a linear relationship with temperature. The analytical method is such that either starting material or decomposed product alone can be analyzed, while other compound dies not interfere with the method of estimation. Therefore, a stability indicating assay procedure is essential for conducting the stability studies. [1, 2]
The results of accelerated decomposition are extrapolated to the room temperature, i.e., 25^{o}C or specific refrigerator conditions. We generally assume that the drug reaction is zero order or first order. Accelerated stability studies are an experimental design to evaluate the stability of a product by accelerating the rate of reaction.
A more comprehensive pharmacopoeial protocol (USP) involves the evaluation of
1. Chemical integrity,
2. Physical changes.
Test for sterility, resistance to microbial growth, toxicity and bioavailability studies are carried out, wherever necessary. Such studies enable the prediction of shelf life for each influence of temperature on degradation. In general, the rate or a reaction increases with

the rise in temperature. Arrhenius establishes a more quantitative relationship between temperature and rate of reaction.
The exponential equation is:
$K= Ae^{-Ea/RT}$
Where K=specific rate constant
A= frequency factor or Arrhenius factor
Ea=energy of activation, KJ/mol.K
T= absolute temperature
Arrhenius factor or frequency factor is a measure of the frequency of collision that can be expected between the reacting molecules in reaction. Energy of activation is defined as the minimum energy required by the molecule so the molecule so the molecule so the molecular collisions give useful products.
logK=log A- Ea/2.3.3RT
According to this equation, a plot can be drawn by taking logK on ay axis and reciprocal temperature (1/T) on x axis. The slope gives the energy of activation.
Ea=slope *2.303*R
Where R=8.314 J/mol.K
Ibuprofen follows pseudo-first order kinetics [1, 2, 3]

PROCEDURE

1) Standard curve preparation

I. A weight of accurately 100 mg of ibuprofen was taken & dissolved in 100 ml of 0.1 N NaOH solution.(solution A)
II. From the solution A 10 ml was pipette out & diluted to 100 ml in a volumetric flask with 0.1 N NaOH solution (solution B)
III. From solution B different volumes of 0.1 ml, 0.2 ml, 0.4 ml, 0.6 ml 0.8 ml & 1ml were taken and diluted up to 10 ml with0.1 N NaOH solution.
IV. The absorbance was measured at 223 nm in U V spectrophotometer against 0.1 N NaOH solution as blank. [4]
V. A graph was plotted by taking concentration VS absorbance.

2) Accelerated stability studies[3]

- About 100mg of ibuprofen was accurately weighed and transferred the ibuprofen into a 250 ml conical flask.
- About 1 or 2 ml alcohol was added to dissolve the ibuprofen and makeup 100ml with0.1 N NaOH solution.
- The conical flask was corked and kept in water bath at 40^{o}C
- Immediately after placing in water bath, 1ml sample of mixture was taken which represents zero time samples.
- At regular interval of 10, 20,30,40,50 and 60minutes,1 ml of samples were withdrawn from the container and makeup the volume to 10 ml with 0.1 N NaOH solution

- The absorbance was measured at 223 nm in U V spectrophotometer against a blank.
- A graph was plotted by taking time on x axis and log percent aspirin undecomposed on y axis.
- The same procedure was repeated at 60°c and 70°c
- The slopes of these graph were calculated and, Arrhenius plots were made by plotting logarithm of rate constants against the reciprocal of absolute temperature.

3) ASSAY PROCEDURE [4]

Accurately 0.4 gm was weighed and dissolved in 100ml of ethanol (95%). This solution was titrated with 0.1n NaOH using 0.2 ml phenopthalein. Performed a blank determination make any correction.
Each ml 0.1N NaOH is equivalent to 0.02063gm of ibuprofen.

EVALUATION

TABLE 1
Standard curve of ibuprofen

CONCENTRATION (µg/ml)	ABSORBANCE
10	0.051
20	0.082
40	0.169
60	0.25
80	0.348
100	0.448

TABLE 2:
Ibuprofen decomposition stored at 50°C

Time (min)	Measured absorbance	ibuprofen conc. (µg/ml)	Ibuprofen decomposed, mg/ml	ibuprofen Remain Undecomposed (99.53-x)	% ibuprofen Remain undecomposed	Log% ibuprofen remain undecomposed
0	0.658	15.009	1.500	98.388	9838.8	3.9928
10	0.567	12.940	1.294	98.245	9824.5	3.9923
20	0.587	13.395	1.339	98.2	9820	3.9921
30	0.595	13.557	1.355	98.182	9818.2	3.9920
40	0.594	13.554	1.355	98.184	9818.4	3.9920
50	0.724	16.509	1.650	97.889	9788.9	3.9907
60	0.660	15.054	1.505	98.025	9802.5	3.9913

TABLE 3:
Ibuprofen decomposition stored at 60°C

Time (min)	Absorba-nce	Iibuprofen conc. µg/ml	Ibuprofen decomposed mg/ml	ibuprofen Remain Undecomposed (99.53-x)	% ibuprofen Remain Undecompose-d (99.53-x)x100	Log% Ibuprofen remain undecompo-sed
0	0.313	7.168	0.716	98.823	9882.3	3.9948
10	0.320	7.327	0.732	98.807	9880.7	3.9947
20	0.352	8.054	0.805	98.734	9873.4	3.9944
30	0.350	8.009	0.800	98.739	9873.9	3.9944
40	0.406	9.281	0.928	98.611	9861.1	3.9939
50	0.416	9.509	0.950	98.589	9858.9	3.9938
60	0.424	9.690	0.969	98.57	9857	3.9937

TABLE 4
Ibuprofen decomposition stored at 70°C

Time (min)	absorbance	ibuprofen conc. µg/ml	Ibuprofen decomposed, mg/ml	ibuprofen Remain Undecomposed (99.53-x)	% ibuprofen Remain Undecompose d (99.53-x)x100	Log% ibuprofen remain undecomp osed
0	0.381	8.713	0.871	98.668	9866.8	3.9941
10	0.420	9.6	0.96	98.579	9857.9	3.9937
20	0.440	10.054	1.00	98.539	9853.9	3.9936
30	0.431	9.85	0.985	98.554	9855.4	3.9936
40	0.447	10.213	1.021	98.518	9851.8	3.9935
50	0.460	10.509	1.05	98.489	9848.9	3.9933
60	0.471	10.759	1.075	98.464	946.4	3.9932

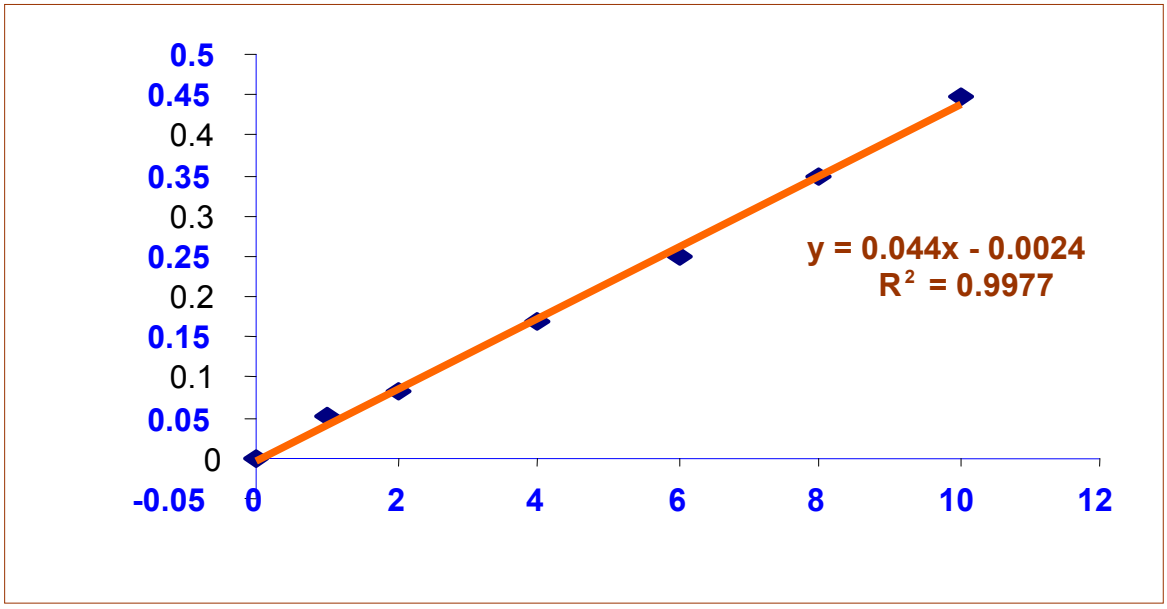

Fig-1 standard curve of ibuprofen

Figure-2 Ibuprofen decomposition profile stored at50°C, 60°C and 70°C