Acute toxicity test

By Dr. Dharam Singh

Acute toxicity tests are conducted to determine the short term adverse effect of a chemical/ drug when administered in a single or multiple doses during a 96 hr exposure period on animal species under controlled laboratory condition. Acute toxicity tests provide information on:

1. The potential for acute toxicity in humans;

2. An estimate of safe acute doses for humans;

3. The potential target organs;

4. Time course of drug induced clinical observations;

5. Time course of chemical induced laboratory observations;

6. Species differences in toxicity;

7. Acute toxicity tests provide preliminary information relevant to single or multiple doses.

8. Evaluating relative toxicity of various toxicants;

9. Assessing doses/concentrations for chronic exposure

10. Estimating the upper limit of xenobiotics producing toxic effects.

11. Determining most sensitive species of organisms and indicator species,

Median lethal concentration (LC_{50}): Median lethal concentration has been defined as statistically derived expression of a single dose of a toxicant that can be expected to kill 50% of the test animals. In simple form, the amount of toxicant which proves lethal to 50% of the total population of test animals is known as LC_{50} or amount of toxicant which brings 50% mortality in the total population of the test animal under specific period is known as median lethal concentration.

Experimental design:

1. Selection of test animals

2. Selection of species

3. Selection of chemical

4. Selection of sex

5. Selection of exposure system

6. Number of animals

7. Selection of dose / body weight

8. Section of medium

9. Section of exposure period

10 Selection of test procedure

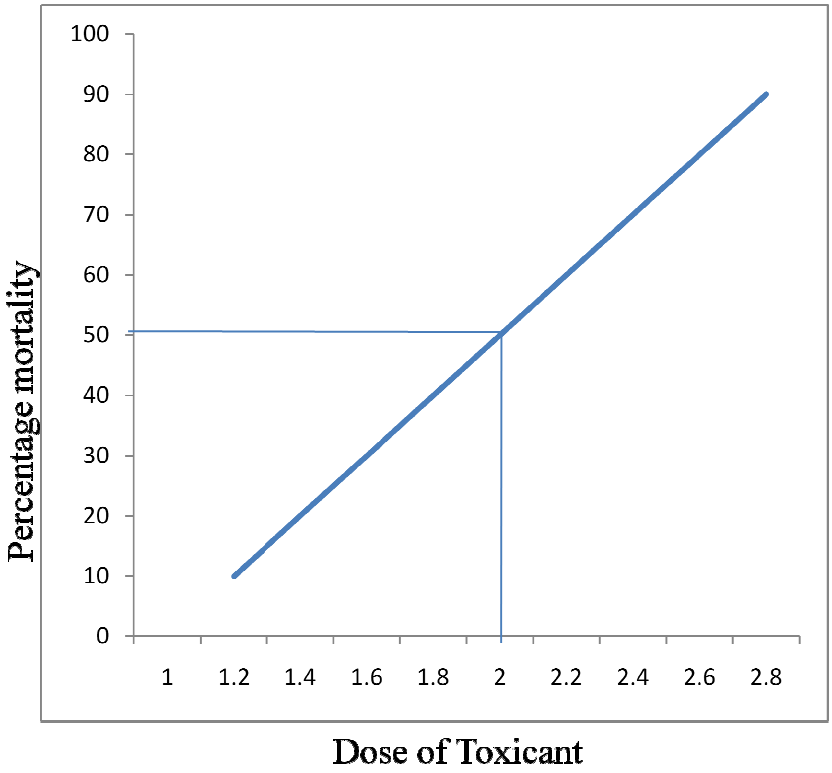
11. Section of feeding

Determination of LC_{50} (96 hr) according to Hamilton, Russo and Thurston, 1977). A hypothetical data use

No. fish	Weight of fish	Length of fish	Dose (ppm)	Exposure period				
				24 hr	48 hr	72 hr	**96 hr**	Mortality %
10	15 gm	12 cm	1.0	0	0	0	0	0 %
10	15 gm	12 cm	1.2	0	0	0	1	10 %
10	15 gm	12 cm	1.4	0	0	1	1	20 %
10	15 gm	12 cm	1.6	0	0	1	2	30 %
10	15 gm	12 cm	1.8	0	0	2	2	40%
10	15 gm	12 cm	2.0	0	1	2	2	50 %
10	15 gm	12 cm	2.2	1	1	2	2	60 %
10	15 gm	12 cm	2.4	1	2	2	2	70 %
10	15 gm	12 cm	2.6	2	1	3	2	80%
10	15 gm	12 cm	2.8	1	2	1	5	90%

Calculation of LC_{50}: On the basis of data obtained from careful observation of mortality (at different concentrations) from aquatic toxicity test. LC_{50} values may be calculated by two methods:

A) Graphical interpolation: To calculate time dependent LC_{50} values, graph is plotted between the concentrations of toxicant and present mortality of test animals (Fish) observed at each concentration. The observed curve is known as concentration-mortality curve (1.1) The dose is read 50% mortality and this is reported as LC_{50} values for particular exposure duration under certain set of laboratory conditions.



B) Statistical method: The based on data obtained from acute lethality test, time-dependent LC50 values and their 95% confidence limits can be calculated by any of a variety of statistical methods (Litchfield and Wilcoxon, 1949; Goulden, 1959; Swaroop, 1957; Hamilton et al., 1977; Finney, 1971, Abbott, 1925). In probit analysis method, the logarithmic values are read for each concentration exposed and probit values are read for present mortality. In case of mortality in control groups, the data are corrected by Abbott's formula:

$$\textbf{Corrected mortality} = \frac{\textbf{\% test mortality - \% control mortality}}{\textbf{100 - \% control mortality}} \textbf{ X 100}$$

Use of LD_{50} / LC_{50} values:

1. Classification of chemical according to their relative toxicity
2. Evaluation of hazard from accidental overdose
3. Planning sub- acute and chronic toxicity studies in animals
4. Providing information about a) the mechanism of toxicity, B) the influences of age and environmental factors, C) the variations in response among different animal species and strains.
5. Providing information about the reactivity of a particular animal population.
6. Controlling to the overall information required in planning therapeutic trails of drugs in humans.
7. Quality control of chemical, to detect toxic impurities and physico-chemical changes affecting bioavailability.