Environmental Sciences and Health

En.toxicity lab.
3rd stage

Lab: 3
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Duration of Toxicity Studies

Essentially three types of study have become mandatory in the course of safety evaluation of chemical. These are as follows:

1. Acute toxicity studies

Acute studies demonstrate the adverse effects occurring within a short time, usually up to 2months, following administration of a single dose of a substance or multiple doses given within 24 hr.

- Traditionally, the emphasis in these types of studies was on determining the LD50, time to death, the slope of the lethality curve, clinical sings.
- Acute lethality testing designed to determine the amount of a chemical that cause death.

3.Chronic toxicity study

Chronic Toxicity Test or long term toxicity test is defined as study of longer than 3 months duration. These types of studies are conducted in all species of laboratory animals and in some economically important animals, wild and domestic.

The most important facet of any toxicological experiment is the condition of the animals.

all toxicity studies should be conducted in:

- controlled environment.
- temperature of 22 ±3 °C
- adequate ventilation
- relative humidity between 30% and 70 %
- twelve hours light/dark cycle.
- The diet and quality of drinking water should be of standard

Protocol Design

The protocol design depends on:

- ✓ type of chemical substances and the country in which it is used.
- ✓ sexes of two species.
- ✓ rout of exposure.

- **Parameters in acute Systemic Toxicity Assessments**
- Establishing a dose- response relationship for exposures at which the probability of a known fraction of a population of a species under study will show lethality will not the objective of acute systemic toxicity studies.
- acute studies establish the following:

- Dose range for subsequent studies.
- Potency, ranking from extreme to non-toxic.
- Identifying probable physiological systems/target organs being affected.

- Behavior and death.
- • Minimal regulatory guideline requirements.

The following illustrates the additional data that can be obtained with appropriate protocol

- design:

- Clinical sign: Time of onset, duration and recovery.
- pharmacological effects; dose responses curve (EDso)
- Lethality
- estimation of median lethal dose (LD50)
- lethal dose (LD10o).

- Body weight: decreased body weight gain; body weight loss; reduced food consumption.
- Target organ identification: tissue examination; histological examinations.
- blood clinical chemistry; hematology.
- Physiological function: immunology

- electrocardiogram; electroencephalogram.
- Identification of the probable physiological systems and target organs involve in acute systemic

Calculation of Median Lethal Dose (LD50)

For each mouse, the observation was made for 24 hr and symptoms of toxicity and rate of mortality in each group were noted. At the end of study period, expired animals were counted for the calculation of LD50. The arithmetic method of Karber was used for the determination of LD50.

$LD50 = LD100 - \Sigma(a \times b)\, n$

n = total number of animal in a group.

a = the difference between two successive doses of administered extract/substance.

b = the average number of dead animals in two successive doses.

LD100 = Lethal dose causing the 100% death of all test animals.

Animal house

Procedure

- 1- preparation of dose
- 2- animal preparation
- 3- dose classification
- 4-chemical materials
- 5-design
- 6-animal house
- 7-target organ
- 8-data analysis