

Acute toxicity and LD50

By

Dr. Rawnak Aladab

Department of pharmacology and
toxicology

Duration and frequency of exposure

- Toxicologists usually divide the exposure of experimental animals to chemicals into 4 categories: **acute, subacute, subchronic, and chronic.**
- **Acute exposure:** is the exposure to a chemical for less than 24 hours
- Exposure routes are intraperitoneal, I.V, S.C, oral intubation and dermal application.

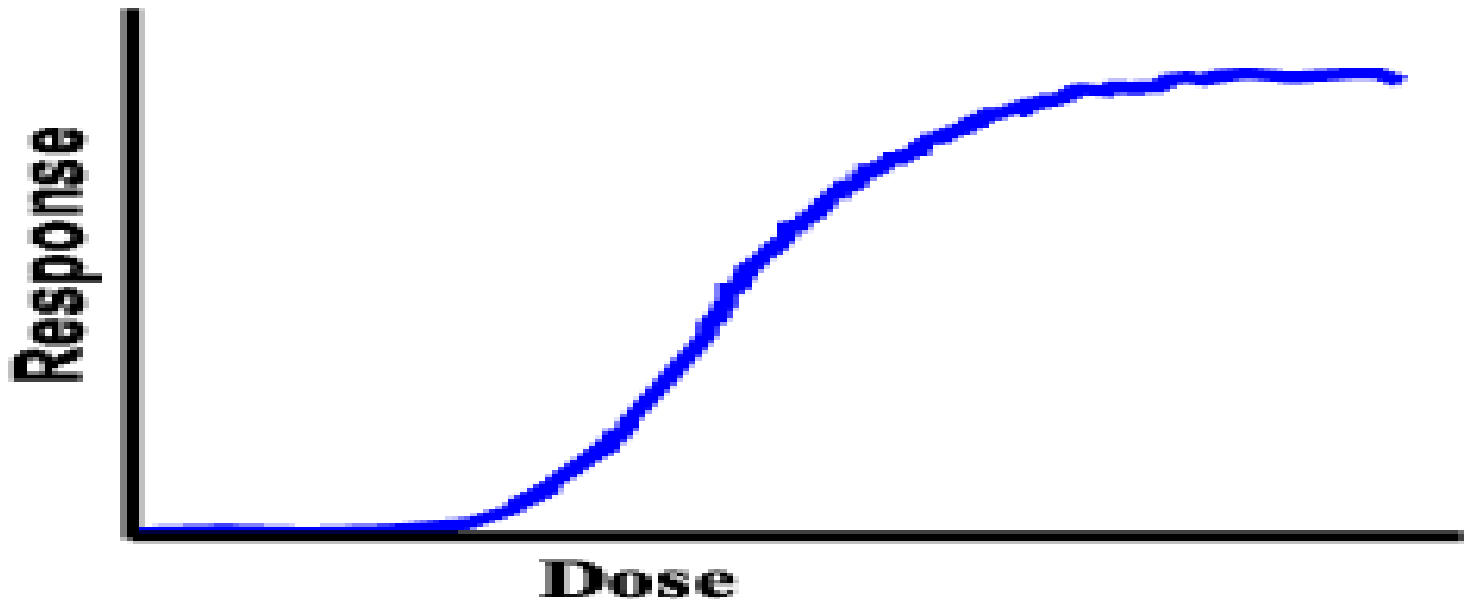
- acute exposure refers to **a single** administration, repeated exposures may be given within a 24-hour period for some **slightly** toxic or practically **nontoxic** chemicals.
- Acute exposure by inhalation refers to continuous exposure for less than 24 hours, most frequently for 4 hours.

- **Repeated exposure** is divided into 3 categories: subacute, subchronic, and chronic.
- *Subacute exposure* refers to repeated exposure to a chemical for 1 month or less
- *subchronic* for 1 to 3 months
- *chronic* for more than 3 months
- These 3 categories of repeated exposure can be by any route, but most often they occur by the **oral** route with the chemical added directly to the diet.

Dose–Response Relationship

- The relationship between the degree of response of the biological system and the amount of toxicant administered, considered the most fundamental concept in toxicology.

Dose Response Curve



There are 2 types of dose– response relationships:

- (1) The *individual* dose–response relationship.
Is characterized by a dose related increase in the severity of the response. The dose relatedness of the response often result from an alteration of a specific biochemical process.
- (2) A *quantal* dose–response relationship.
which means quantal or “all or non” that is at any given dose an individual in the population is classified as either “responder or non responder”.

Effective dose “ED”

Is a statistical approach that is widely used for estimating the response of a population to a toxic exposure.

Generally, the midpoint, or 50%, response level is used, giving rise to the “ED 50 ” value.

Lethal dose 50%(LD50): dose that is lethal to 50% of a population of test animals

Reported by mg of toxicant per kg of body weight

Smaller the LD50= more toxicity of chemical

Greater the LD50= less toxicity of chemical

LD50 of Nicotine=1 mg/kg

Ethyl alcohol=10000mg/kg

50% of the
population
dies

50% of the
population
lives

LD50 toxicity
definition

Acute Toxicity Testing

- The objectives of acute toxicity testing are to:
 - (1) an estimate of the intrinsic toxicity of the substance, times expressed as an approximate LD (eg, LD 50)
 - (2) provide information on target organs and other clinical manifestations of toxicity
 - (3) identify species differences and susceptible species
 - (4) establish the reversibility of the toxic response
 - (5) provide information that will assist in the design and dose selection for longer-term (subchronic, chronic) studies.

- The LD 50 and other acute toxic effects are determined after 1 or more routes of administration in 1 or more species. The species most often used are the **mouse** and **rat**. both adult male and female animals. Food is often withheld the night before dosing.
- The number of animals that die in a 14-day period after a single dosage is tabulated. In addition to mortality and weight, daily examination of test animals should be conducted for signs of intoxication, lethargy, behavioral modifications, morbidity, food consumption.

- **Many factors** influence toxicity and thus may alter the estimation of LD 50 in any particular study, factors such as animal strain, age, and weight, type of feed, caging, pretrial fasting time, method of administration and duration of observation have all been shown to influence adverse responses to toxic substances.

- Because of this inherent variability in LD50 estimates it is necessary to characterize the LD50 within an order of magnitude range such as 5-50mg/kg, 50-500 mg/kg and so on.

Acute inhalational studies

- When animals are exposed acutely to chemicals in the air they breathe or the water they (fish) live in, the dose the animals receive is usually not known.
- **lethal concentration 50 (LC 50)** is the concentration of chemical in the air or water that causes death to 50% of the animals.

Acute dermal studies

- **The acute dermal toxicity** test is usually performed in rabbits. The site of application is shaved. The test substance is kept in contact with the skin for 24 hours by wrapping the skin with plastic material. At the end of the exposure period, the wrapping is removed and the skin is wiped to remove any test substance still remaining. Animals are observed at various intervals for 14 days, and the LD 50 is calculated.

Thank you

