

Acute Toxicity (Lethal Dose 50 Calculation): Medicine as a life saver or destroyer

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Abstract

Lethal dose (LD 50) has been calculated. Different-testing methods have been used. The observed values have been plotted by Dose-Response against measured response & dose. Different LD value shows that all substances are poison. It depend on the amount of dose whether a substance is poison or remedy. In Our research paper we will discuss the different doses, their routes of administration, Lethal, Chronic & Acute toxicity on rats & mice. For the calculation of LD50, Hodge, Sterner, Gosselin, Smith & Hodge scale was used. In this study, different doses (about 10 to 10,000 mg/kg) of the extract were administered by different route to the different groups of rats and mice. Experiments were carried out to observe the toxicity & possible death of animal like rat & mice continuously for 24 hour to calculate LD₅₀ for different drugs.

1. Introduction

According to Swiss doctor Paracelsus knows as “father of toxicology” (-1500 AD) & Orfila (-1800 AD) helped to understand the fundamental concept of toxicology. He said that “all substance are poisons”. [1]. whether the dose is poison or non-poison, it depends upon the right dose. If water is taken in excess, it can be toxic though water is non-toxic [2-3]. Jean Stas isolated plant poisons from human tissue in 1850 successfully. Toxicity is a level to which a substance is poisonous or can causes injury or death. Test of toxicity can be carried out by the count of death or impaired health issues of laboratory organism, when they comes into the contact with different concentration of a substance [3-4]. The extract is provided to animal either by mouth or by skin rubbing or by injected to blood vein & muscles. In our research paper we have exposed our test on different species including dogs, cat, guinea-pig, rabbit & monkeys. In each case, the LD₅₀ (Amount of a substance that can be responsible to cause death in 50% of the population when given by a particular route) [5-6] value in the experiment indicates the weight of dose administrated per kg bodyweight of the animal. This states the exposure of LD₅₀ eg. Nearly 50% of the death of tested animals are caused when 5 mg of the dose administered by mouth of rat at every 1 kg body weight of the rat. [7].

2. Testing Method

Toxicity experiment is performed in vivo (within the whole living organism) or in vitro (testing on cell, microorganism, biological molecules & tissues). Hodge & Sterner Scale & Gosselin Smith & Hodge Scale are used [11].

The dose response complexities are based on observed data from experimental animal, human, & clinical cell studies. The measured dose (in milligrams, micrograms or gram per kilogram according to the body weight) is plotted on the X axis & the response is plotted on the Y axis.

3. Dose Response Complexities

In the present paper several measures used to expressed toxic doses with their degree of effect on an biological organism, these are as-

- Threshold Dose – Minimum dose having no side effect on exposure
- NOEL- No effect was observed
- NOAEL – No observed adverse administered
- PET – Personal exposure limit, confirmed by under US OSHA regulations [8-9].

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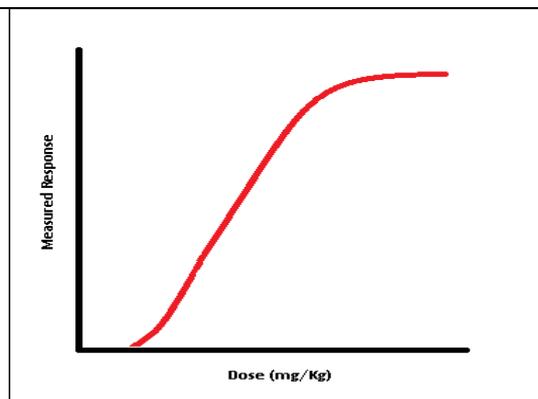


Fig. 1: Dose response curve

3.1 Dose Response Curve

Dose response curve (figure 1) of threshold dose, having no adverse effect on human body because human body can protect our self against many toxic agents. In this way human body can take some toxic substance (at a dose that is below the threshold) & still remain healthy [10].

In this there is no toxicity occurs on body at a amount of dose 10 mg when administrated by any route whereas at a amount of dose 50 mg, 100 % of the population experience toxic effect.

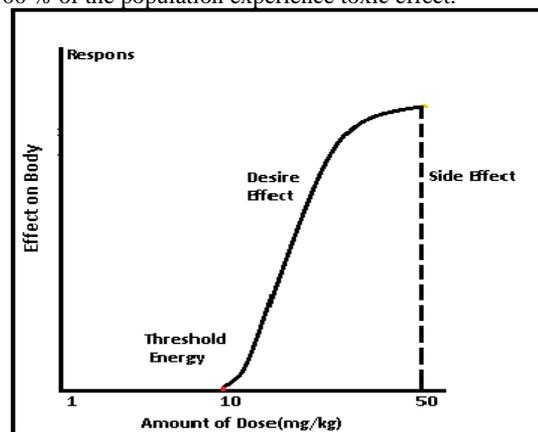


Fig.2: Dose and its effect on body

4. Result & Discussion

In the experiment different chemicals with their different dose & route of exposure (ex oral, dermal, inhalation) were taken. On behalf of this, toxicity of a dose depend upon the amount of dose & route of exposure, eg. An LD₅₀ dose of dichlorvos which is used as insecticide in household gives different result on different species.

- Oral LD₅₀ for rat is 50 mg/kg if it applying on skin (Dermal) then it is 75 mg/kg
- Oral LD₅₀ for rabbit is 10 mg/kg.
- Oral LD₅₀ for pigeon is 23.7 mg/kg.

- Oral LD₅₀ for dog is 100 mg/kg.
- Oral LD₅₀ for pig 157 mg/kg.

The above data show that when dichlorvos is ingestion in pigs or dogs than it is less toxic compare to rats.

Different experiment shows that LD₅₀ has different rating on toxicity rating. Table I, expressed that dichlorvos is toxic to a certain extent when pass down the throat (oral LD₅₀) & highly toxic if inhaled (LC₅₀) in the rat. Table II, expressed that dichlorvos can be very toxic when pass down the throat (oral LD₅₀) by a rat [11].

Table 1: Rating of Toxicity by Sterner & Hodge Scale

		Administration Routes			
		Oral LD ₅₀	Inhalation LC ₅₀	Dermal LD ₅₀	
S.No	Toxic Level	(Rate Dose) mg/kg	(4 hours exposure to Rat) ppm	(single application to skin of rabbits) mg/kg	Resulted LD 50 For Human
i	Extremely Toxic	0 or 1	0 -10	0 -6	1 Drop
ii.	Very Toxic	0-50	10-100	6-42	3.5 ml (one table spoon)
iii	Fairly Toxic	50-500	100-1000	42-348	30 ml (1 fluid ounce)
iv	Considerable non Toxic	500-5000	1000-10000	348-2700	600 ml
v	Non-toxic	5000-15000	10000-100000	2700-23000	One litre
iv	Harmless	>15000	100000	>23000	One litre

Table 2: Rating of Toxicity by Hodge, Gosselin & Smith Scale [11]

Human Oral LD		
Toxic Level	Dose	For 70-kg Person (150 lbs)
i. Super Toxic	<5 mg/kg	1 grain (a taste - < 7 drops)
ii. Extremely Toxic	5-50 mg/kg	4 ml (btw 7 drps and 1 tsp)
iii. Fairly Toxic	50-500 mg/kg	30 ml (btw 1 tsp and 1 fl ounce)
iv. Considerable non Toxic	0.5-5 g/kg	30-600 ml (<1 pint)
v. Less Toxic	5-15 g/kg	600-1200 ml (<1 quart)
vi. Non-Toxic	>15 g/kg	>1200 ml (>1 quart)

Several piece of evidence indicate that the “poisons is in everything & nothing is without poison” [11].

The dosage makes it a poison or a remedy. Everything is toxic at some dose level like:-

- The caffeine is non-toxic in human diet, but just 50 times this amount could kill a human being [12].
- When water-miscible large dose of vitamin E & vitamin A is injected into the muscles its causes some adverse effect of acute toxicity like boredom, sleepiness, distaste, vomiting, & headache.[13].
- A chemical theobromine is found in chocolate. Humans stomach can consume around 1000mg/kg of their body weight of theobromine, this is completely a large figure & virtually impossible for a human to eat. An average 200gram bar of milk chocolate contains 300miligram of theobromine this is the median lethal dose for human. Apart from this for the domestic pet like dog LD₅₀ of chocolate is around 300mg/kg of their body weight, & for cat it is around 200mg/kg of their body weight & can therefore easily die as a result of eating enough chocolate.
- 13 Shot of alcohol (one shot= 45 ml) causes death.
- Water is precious for life but consuming large amount of water causes kidney failure can leads to chronic toxicity. The

American Chemistry Society recently released that about 6 liters of water enough to kill a 165-pound person.[15]

- For Vitamin D, fish, egg, & sunlight is the good source & it is a necessary nutrient for good health like its help to improve immune system, respiratory system, muscle & cardiovascular function Its deficiency can create bone deformity in children & bone weakness in adult .According to National Academy of Sciences & American Academy of Pediatrics the recommended intake of vitamin D is 200 International Unit per day, although it becomes toxic when taking in large amount. It can lead to serious health problem including cancer, asthma, diabetes, high blood pressure, skin diseases; liver failure causes death [16].
- Paracetamol medicine is consider to be most toxic if taken in excess amount .its affects the placenta of pregnant ladies & liver cells of human being. [15]
- Cyanide is known to be the most toxic substance but if a amount of 0.8 mg/kg of nicotine is taken, it is similar or even more toxic then Cyanide. [17].
- Journals, Researchers, Standard textbooks & experimental databases, warns that the LD of nicotine for adults is maximum 60 mg & less than 30.Smoking 10 cigarettes per day or 10 ml of a dilute nicotine-containing solution is quite enough to kill an adult. Even tobacco chewing is injurious to health as it contain nicotine. [18]
- Opium is highly unpredictable lethal dose. if it is taken orally(half gram) or by smoking(1/10 gm) it is less toxic but if taken in the form of tea it is 300times stronger than other doses & is of high risk & highly toxic. (<http://www.opiumabusetreatment.com>)

5. Conclusions

Dose play a very significant role in toxicology .According to Aptilly “the dose makes the poison” describe the importance of the dose. Although chemicals naturally present in our body or injected by any route like food & drink may be toxic if consumed in sufficiently large quantities.

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