

The Calculation of Median Lethal Dose (LD₅₀) And Maximum Permissible Dose (MPD) Values of Sodium Arsenite In Female Swiss Albino Mice

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Abstract: Sodium arsenite is an environmental pollutant and is responsible for both knowing poisonings and accidental exposures that can cause harmful health issues and possibly death. Median lethal dose (LD₅₀) is a statistically obtained dose of a compound that can be predicted to cause death in 50% of the mice when administered by a specific route as a single dose and mice noticed for a specific time period. In the present research, different doses i.e., 6, 9, 12, 15, 18, 21 and 24 mg/kg body weight of Sodium arsenite was given orally by gavage method to the seven different groups of Swiss albino mice. Signs and symptoms of toxicity and probable death of mice were observed for 3 hours and then at 6, 12, 24, 48 and 72 hours to calculate the Median lethal dose (LD₅₀) and maximum permissible dose (MPD) of Sodium arsenite. The LD₅₀ was found to 18 mg/kg body weight after oral administration in Swiss albino mice. Finally, MPD of Sodium arsenite by oral route in mice was found to be 1.8 mg/kg body weight.

Keywords: Sodium arsenite, Swiss albino mice, LD₅₀, MPD

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I. Introduction

Arsenic, an unimportant trace element, tasteless, odorless environmental pollutant, a potent toxin, human carcinogen, modulator of antioxidant defence system, mutagen and xenobiotic metalloid, has recently emerged as a major pollutant of drinking water in a number of districts of Bihar [1], West Bengal [2], India [3], Bangladesh [4], Northern Chile, Thailand, Taiwan, China, Mongolia, Mexico, Argentina, Finland and Hungary[5]. There had been a large number of *in vitro* and *in vivo* studies made, dedicated to determining the genotoxicity of inorganic arsenicals [6 & 7]. *In vitro* studies on human fibroblasts, leukocytes, lymphocytes, and hamster embryo cells have exhibited that arsenic induces chromosomal aberrations and sister chromatid exchange [8]. Identical studies using human, mouse and hamster cells investigated a potential enhancement of DNA damage, DNA repair enhancement or the inhibition of DNA synthesis. Toxicity is an extremely essential aspect of any biochemical/pharmacological experiment. On the other hand, we elaborate any Metallo/a metal supplement evaluation of toxicity of that specific compound is very essential. The toxicity of a compound can be calculated by several methods. Commonly it is calculated on the test animals like mice, rats, and other animal models. Acute toxicity of a compound can be studied by the assessment of LD₅₀ i.e., the dose of a test compound that will kill 50% of the animals of a specific test species in a given period under controlled and standardized laboratory conditions. LD₅₀ is a primary screening step for the evaluation of the toxic properties of a compound. The test species had given an increasing dose of Sodium arsenite and LD₅₀ value is determined based on the mortality of the test species. However, LD₅₀ of Sodium arsenite is reported in mice [9, 10, 11 & 12] but sufficient data for LD₅₀ of Sodium arsenite in Swiss albino mice is not practicable. Hence, an experiment was made to calculate the oral LD₅₀ and MPD of Sodium arsenite in Swiss albino mice using water as a vehicle.

II. Materials And Methods

Sodium arsenite, CAS Number: 7784-46-5 from Biosol (Canada) were used throughout the experiment. In the present experiment, 3 months old normal female Swiss albino mice (*Mus musculus*) were selected. These mice were kept in the polypropylene cages containing paddy husk at temperature $26 \pm 2^\circ\text{C}$; the humidity was maintained at $50 \pm 10\%$ and in controlled light (12 hrs light and 12 hrs dark). Animals were maintained in ideal conditions as per the ethical guidelines of the CPCSEA, (CPCSEA Regd. No. 1129/bc/07/CPCSEA, dated 13/02/2008) Government of India and the Institutional Animal Ethics Committee (IAEC). Seven doses of Sodium arsenite which were near to the comparable LD₅₀ i.e., 6, 9, 12, 15, 18, 21 and 24 mg/kg body weight were administered orally by gavage method. Signs and symptoms of toxicity and probable death of mice were

observed for 3 hours and then at 6, 12, 24, 48 and 72 hours to calculate the median lethal dose (LD₅₀) of Sodium arsenite. After 72 hours the number of decreased mice in each group was calculated and percentage mortality was determined. For calculating the LD₅₀ value of Sodium arsenite for mice, the standard method was used. Seven groups of mice (10 mice in each group) having almost equal weight. A dose lower than LD₅₀ was used in the further experiment and the dose at which mice showed no deaths and no side effects during the treatment period as considered the Maximum Permissible Dose (1/10th of the oral LD₅₀ of Sodium arsenite). The experiment was repeated 5 times based on which values of LD₅₀ and MPD were calculated. Sodium arsenite was in crystal form. We know that the EC (Emulsified Concentration of Sodium arsenite) was 57.6 % (w/w) and Specific gravity (Sp. gr.) was 1.87. Distilled Water was chosen as the preferred vehicle. For the Per Kg methodology, the dose given should be w/v. So for making this solution (w/v) in 100 ml is equal to EC x sp. gravity. If this 0.1 ml is diluted with 600 ml of Distilled water because the calculated LD₅₀ value was 18 mg / Kg body weight. As per the toxicological rules (CDRI, Lucknow, established) –"Any solution or solute should be dissolved in 10 ml as Stock Solution (Minimum) which is to be administered to 1 Kg mice model ".So, 1 ml is equal to 108/600 mg of Sodium arsenite. Therefore, 10 ml is equal to 108/600 x 10 mg of Sodium arsenite is equal to 108/60 mg of Sodium arsenite = 1.8 mg / 10 ml (w/v) was as a stock solution.

III. Results

The following table shows Mortality (in %) of Swiss albino mice when treated with Sodium arsenite.

Sl.No.	Groups	Sodium Arsenite concentration (mg/kg body weight)	Mortality (%)
01	Group - A	6	No death
02	Group - B	9	No death
03	Group - C	12	20
04	Group - D	15	35
05	Group - E	18	50
06	Group - F	21	70
07	Group - G	24	90

At high dose, mortality of mice was the maximum. No death was found for the first weak in 9.0 mg/kg body weight, but after 8th day onward the death rate increased. With 6.0 mg/kg body weight dose, no death occurred even during the second week. Thus, LD₅₀ of Sodium arsenite was calculated as 18 mg/kg body weight. After that, experiments were set up with the dose of 1.8 mg/kg body weight which corresponding to 1/10th of the oral LD₅₀ of Sodium arsenite supported by [13]; 1.7 mg/kg body weight by [10]; 1.5 to 4.4 mg/kg body weight by [11]. Finally, the maximum permissible dose (MPD) of Sodium arsenite was selected as 1.8 mg/kg body weight.

IV. Discussion

Basically, at low doses of 6 and 9 mg/kg body weight didn't cause any toxic impact. But, at high doses i.e., 12, 15, 18, 21 and 24 mg/kg body weight mice appeared general signs of toxicity. Symptoms of burring the heads in paddy husk, abnormal movement, slowness, sleepiness and hair falling were showed by the Sodium arsenite treated mice. The number of reduced mice was noted for each dose level of Sodium arsenite, which is recorded in the above Table. Different kinds of literature regarding the toxicity of Sodium arsenite for Swiss albino mice was evaluated by different authors i.e., according to [9] the value of LD₅₀ in the range of 12-15 mg/kg/body weight; as explained by [10] the value of LD₅₀ was 17 mg/kg/body weight; [11 & 14] reported the value of LD₅₀ in the range of 15-44 mg/kg/body weight; as stated by [12] the value of LD₅₀ was 42 mg/kg/body weight and according to [15] the value of LD₅₀ was 56 mg/kg/body weight. In the present study, lethal dose 50% (LD₅₀) of acute toxicity and maximum permissible dose (MPD) of Sodium arsenite were determined via the oral route. The LD₅₀ of the Sodium arsenite was estimated to be 18 mg/kg/ body weight for Swiss albino mice, which was recorded in the respective table. This was supported by the [10] for an oral dose of LD₅₀ of Sodium arsenite for Swiss albino mice having 17 mg/kg/body weight and on the other hand [11 & 14] were supported 15 to 44 mg per body weight.

The ten-fold lower concentration of LD₅₀ was stated by [13]. i.e., 1.2 to 1.5 mg/kg body weight by [9]; 1.7 mg/kg body weight by [10]; 1.5 to 4.4 mg/kg body weight by [11 & 14]; 4.2 mg/kg body weight by [12] and 5.6 mg/kg body weight by [15] were taken as sublethal dose/maximum permissible dose (MPD). In the present study, the maximum permissible dose (MPD) was found to be 1.8 mg/kg body weight, which was supported by [10] having MPD 1.7 mg/kg body weight and [11 & 14] having MPD 1.5 to 4.4 mg/kg body weight.

V. Conclusion

Median lethal dose (LD₅₀) and Maximum permissible dose (MPD) of Sodium arsenite in Swiss albino mice give useful pharmacological, toxicological and practical knowledge for researchers. The author's data of the present research conclude that the LD₅₀ of Sodium arsenite, practically safe when given orally. This research is the experimental work in the future, this study is present a start to continue the research by administering Sodium arsenite though orally in animal models.

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