

Toxicology: The Basis for Development of Antidotes

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Editorial

Toxicology is the study of poison. Sources of poisons include animals, microorganisms, plants and chemicals. Although, Paracelsus who was a lecturer at the University of Basel, Switzerland in 1520s had hypothesized that the ability of an agent to cause poisoning is dependent on the dose of that agent. It was on this basis the median lethal dose (LD_{50}) was introduced in 1920. LD_{50} is the dose which has proven to cause death to 50% of the test group of animals [1]. It is an initial assessment of toxic manifestations and is one of the initial screening experiments usually performed with carcinogenic, anticarcinogenic, venomous, anti-venomous, toxicogenic, anti-toxicogenic, immunogenic and anti-immunogenic compounds. An antidote is any is any substance that counteracts a poison by, (a) chemically destroying the poison, (b) mechanically preventing absorption, or (c) physiologically opposing the effects of the poison in the body after absorption [2]. The data from median lethal estimation serve as the basis for classification and labelling; provide initial information on the mode of toxic substance; help arrive at a dose of a new compound and help determine LD₅₀ values that may indicate potential types of drug activity [3]. The different methods used in determination of LD₅₀ include Arithmetical method of Karber [4], Lorke method [5], arithmetical method of Reed and Muench [6], graphical method of Miller and Tainter [7], graphical method of Litchfield and Wilcoxon [8], revised up-and-down procedure [9], a modified arithmetical method of Reed and Muench [6] and arithmetic-geometric-harmonic method. All the methods employ summation of the doses of toxicant that caused death in the test group of animals.

However, for Reed and Muench method, the sum of cumulative dead and cumulative survived of each dose is taken. The percent survival to two doses adjacent to LD_{50} is calculated and the LD_{50} determined [10]. In another report, LD_{50} is calculated using the data on percent mortality instead of percent survival [11]. Having noted the marked difference between the estimated LD₅₀ from percent survival and percent mortality using Reed and Muench method, Saganuwan [1] modified and validated the method using the average of median lethal dose (LD_{50}) and median survival dose (MSD_{50}) which gave a relatively ideal LD₅₀. The method was also validated by other authors with precision and accuracy. Kue et al. [12] used quick chick embryo chorioallantoic membrane (CAM) as an alternative predictive model in acute toxicological studies for cyclophosphamide, cisplatin, vincristine, carmustin, campothecin, aloin, mitomycin-C, actinomycin-D, melphalan and paclitaxel. The authors used the method of Reed and Muench modified by Saganuwan [1], and determined LD₅₀ of all the anticancer agents and there was significant correlation between the ideal LD_{50} for the CAM and LD_{50} for mice. Signifying the versatility of the revised Reed and Muench method using CAM model as a replacement for toxicological studies in rodents.

World Health Organization (WHO) [13] has patented sodium silicate complex (SSC) which comprises trimeric sodium silicate (Na₂SiO₃)₃ and sodium silicate pentahydrate (Na₂SiO₃)5H₂O. SSC has antivenomous activity against Crotalus atrox, Agkistrodon contortrix contortrix and Agkistrodon piscivorus leucostoma venoms using two enzymatic assays, gelatinase and hide powder azure assays at pH of 14. The LD50 of SSC was determined in mice after 48 hrs. The calculations for the LD50 were generated by a program on the NNTRC hompage (ntrc.tamuk.edu/LD50calculator.xls), which was based on the method developed by Saganuwan [1]. The anti-lethal dose assay was performed to determine the effective dose of LIPH that neutralized LD₅₀s of the snake venoms using the method of Sanchez et al. [14]. But Cao et al. [15], identified a Bacteriovorax sp. isolate as a potential bacterium against snake head fish-pathogenic Aeromonas veronii using the modified method of Reed and Muench [1]. Aeromonasis is a serious problem in world aquaculture caused by Aeromonas veronii which affects quality of fish such as Ictadarus punctatus, Colisa lalia, Misgrunus anquithcaudatus, Acipenser baelii, Astronotus ocellatus and Lewcassi longinostris leading to severe losses and marketing [15]. Kothari et al. [16] reported that a bivalent conjugate vaccine containing PspA families 1 and 2 has the potential to protect against a wide range of Streptococcus pneumonia strains and Salmonella typhimunum using method developed by Saganuwan.

Since LD_{50} was used to determine toxicity level of snake venom and anti-venom, anticancer drugs, *Aero monas veronii* pathogen and bivalent conjugate vaccine against *Streptococcus pneumonia* strains and *Salmonella typhimunum* using the method of Reed and Muench as modified by Saganuwan, there is every reason to believe that toxicology could be the basis for development of antidotes against cancers, snakes venoms, microbial pathogen and systemic immunogens [16].

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