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Single dose acute toxicology in preclinical trial: The basic step in drug discovery and development

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The dose, in preclinical trial, refers to the amount of test material administered at once to study subject for pharmacological evaluation. Acute toxicity study of three different pesticides (Dichlorvos, Chlorpyrifos and Cypermethrin) with five level of doses each (10, 30, 50, 70 and 90) mg/kg body weight, were evaluated on15 Balb c mice for a maximum period of 5 days. The main clinical signs and symptoms developed after treatment with five levels of doses prepared from chloropyrifose was salivation, lacrimation, miosis (pinpoint eyes), trembling and breathing difficulty with hypo-activity which was significantly manifested within about 30 minutes to 2 hours after treatment depending on the amount of dose administered orally. Distended stomach, tremor and restlessness, breathing difficulty, salivation and bulging eyes was the clinical signs of toxicity developed after treatment with the five levels of doses prepared from Cypermethrin pesticide which was also administered orally. The Balb c Mice treated with five levels of doses prepared from dichlorvos pesticide developed slow respiration immediately after oral administration. The dose had never limited the toxic property of test chemicals but the magnitude of adverse effect and length of time at which the undesired effect manifested in treated Balb c Mice. Even if the higher dose (90 mg/kg) from each test chemical was lethal within 24 hours, the second and third highest doses (70 & 50 mg/kg) which was prepared from Cypermethrin caused lethal effect in the second day after dosing orally. This implies that the undesired effect of test chemicals was due to its toxic reaction rate (r) in the biology of treated Balb c Mice. Blood samples from each treated Bulb c Mic were drawn from the tail and facial vein using micro tubes labeled with numbers and quantitative immunoglobulins test had been conducted using architect system – Abbot before treatment as reference test and four hours after treatment for comparison. The toxic reaction rate and toxic severity of each test substances was then calculated using the formula [r =-(± lg plasma concentration)] in mg/sec and (s = x 100) in %/sec respectively and recorded in different tables. The study revealed that the value of toxic reaction rate (r) determines the margin of safety whereas the value of toxic severity (s) of test chemicals predicts the length of time at which lethal effect of test substance might be manifested in treated Balb c Mice. Tested doses with calculated value of toxic reaction rate (r) less than zero had no lethal effect to treated Balb c Mice. This means that the administered test chemicals had negligible adverse effect at the organismal level rather than at the cellular level. A test substance said to be toxic not only when it causes death but also pharmacological mechanism against the biology of an organism. If the higher dose kills treated organism, the lower dose is most likely to have a higher risk of ill health in the long run. There is no scientific ground to categorise a single test material as safe dose (ED_{50}) and lethal dose (LD_{50}). It is most likely to be a waste of time and resources to categorise a single test chemical as effective dose (ED_{50}) and lethal dose (LD_{50}) at a period of time during the experiment and proceed to the next phase of preclinical trial with inadequately validated data. The presentation will have more details on single dose acute toxicology in preclinical trial.

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