CHAPTER 1

Acute Oral Toxicity Study of Deltamethrin 1% + Triazophos 35% EC in Rat

The hazards associated with pesticide's injudicious use present a serious problem. Therefore, new and more safer and biodegradable chemicals are being developed. With a new substance, the customary starting point is toxicological evaluation utilizing lethality as an index. An acute toxicity test is the first toxicological experiment done on the compounds synthesized by the chemist; those are biological active molecule **(Sood, 1999).**

The characteristic of exposure and the spectrum of effects come together in a correlative relationship customarily referred to as dose-response relationship. This position is the most fundamental and pervasive concept in toxicology. Indeed, an understanding of this relationship is essential for the toxic material. It is this relationship that **Trevan (1927)** envisioned in his introduction of the lethal dose as an index (LD_{50}). The lethal dose (LD_{50}) is the statistically derived single dose of the substance that can be expected to cause death in 50 percent of the animals **(Eaton and Klassen, 1996).** The results of the acute toxicity tests are used as guidance for the dose selection and to design the further experiments.

Determination of the LD_{50} has become a public issue because of increasing concern for the welfare and protection of the laboratory animals However the LD_{50} is essential for characterizing the toxic effect of chemicals and determining their hazards to human Information is obtained on the types of toxic effect the chemical produces, onset of toxicity, the duration of toxicity etc. This information is essential for the rational treatment of humans exposed to the chemical, for the design of experiments and to assess the toxicity of repeated exposure of chemical **(Eaton and Klassen, 1996).**

Test material used in present study is a combination of the synthetic parathyroid (deltamethrin) and organophosphate insecticide (triazophos) Deltamethrin and triazophos have different mechanism of toxicity (triazophos is a cholinesrterase inhibitor while the deltamethrin cause prolonged Na^+ channel depolirasation); both insecticides are detoxified via carboxylase. Toxicological effects of deltamethrin on various animal models have been

studied. There are indications that potentiation of toxicity may occur when deltamethrin is combined with some organophosphorus compound **(Environmental Health criteria 97, 1990).** Organophosphate accentuates the effect of deltamethrin **(Haines *et al.*, 2001).** Hence, it was necessary to find out the LD_{50} for the combination product and to evaluate the potentiation effect of deltamethrin due to organophosphate

MATERIAL AND METHOD

Four groups of animals comprising 5 males and 5 females were given a single dose of Deltamethrin 1% + Triazophos 35% EC through oral gavage at the dose levels of 0 (G1: control), 120, (G2: Low dose) 168 (G3: Mid dose) and 235 (G4: high dose) mg /kg body weight. All the animals were starved for overnight prior to dosing and 3 - 4 hours post dosing. Deltamethrin 1% + Triazophos 35% EC was dissolved in distilled water and administered at the dose volume of 10-mL/kg-body weight. Control group animals were maintained in similar condition with the treatment of distilled water. All the animals were observed frequently for the overt sign of toxicity and mortality on the day of dosing and once daily for a period of 14 days. The LD_{50} was calculated using probit analysis method **(Finny, 1971).**

RESULTS

The mortality rate was increased with the increase of dose levels **(Table 1.1, Figure 1.1).** The mortalities observed were 40 80 and 90 per cent at the dose levels of 120, 168 and 135 mg/kg body weight. Percent mortality was plotted against the log dose **(Figure 1.2).** LD_{50} was calculated using Probit analysis method **(Finny, 1971)** and was found to be 128.32-mg/kg body weight with 95% confidential limit (94.32 – 173.64 mg/kg body weight).

Toxic signs of poisoning observed are presented in **Table 1.2.** Lethargy, tremor, abdominal breathing, convulsion, lacrimation, exophthalmos, gasping, nasal discharge, salivation, and diarrhea observed due to treatment of deltamethrin 1% + Triazophos 35% EC. The symptoms were started immediately post treatment. Surviving animals return to normalcy at or before 48 h post treatment showing rapid excretion of the test substance.

DISCUSSION

Toxicological effects of deltamethrin on various animal models have been studied and LD_{50} value was reported as 139 to >5000mg/kg body weights depending on vehicle/solvent **(Environmental Health criteria 97, 1990). Tomlin, (1997)** reported LD50 value of deltamethrin at various concentrations (1080 mg/kg body weight for 15g/L EC; 535 mg/kg body weight for 25g/L EC). In present study, LD_{50} value of deltamethrin (10g/L EC) found to be 128.32-mg/kg body weight is much lesser than above value suggests the increased toxicity of deltamethrin due triazophos an organophosphate insecticide.

The linear coefficient (r) determines the applicability of the data to the method of analysis **(Chau and Chau, 1989).** If the "r" value is usually 0.90, this method if analysis is accepted for animal toxicology studies. In the current study an acceptable value of 0.992 was obtained for linear coefficient. The slope (s) of the probit regression line for the deltamethrin 1% + triazophos 35% EC is the present study was found to be 0.43. This smaller value indicates modest response of changes in the dosage of deltamethrin 1% + triazophos 35% EC in rats. This further substantiated by wide of confidence limit around LD_{50} value.

Muscarinic receptors are found primarily in smooth muscle, the heart and the exocrine gland. Stimulation of this receptor by inhibition of acetylcholinesterase produces sign of cholinergic poisoning that include bronchial secretion, increased salivation, lacrimation diarrhea and constriction of the pupil. Accumulation of acetylcholin in CNS causes tremor, ataxia, convulsion, and depression of respiratory and circulatory centers. The most likely cause of death in fatal organophosphate poisoning is asphyxia associated with respiratory failure **(Saunders and Harper, 1994).** Synthetic pyrethroids are neuropoisons acting on peripheral and central nervous system causes tremor, increased salivation and paralysis **(Environmental Health criteria 97, 1990).**

The severity of toxic signs of poisoning exhibited by treated animals and the increased toxicity (LD_{50}) suggest that triazophos potentiate the toxic effect of the deltamethrin.

TABLE 1.1 Doses, Mortality and LD_{50} with 95% Confidence Interval

Group	Dose (mg/kg b.wt.)	Mortality (%)	LD_{50} Value	Fiducial Limit (95% Confidence Interval)
G1	0	0	128.32	94.82 – 173.64
G2	120	40		
G3	168	80		
G4	235	90		

TABLE 1.2 Clinical Signs Observed During Acute Study

Clinical Sign	Number of Animals showed Clinical Sign							
	Male (N = 5)				Female (N = 5)			
	G1	G2	G3	G4	G1	G2	G3	G4
Normal	5	-	-	-	5	-	-	-
Lethargy	-	5	1	-	-	5	-	-
Abdominal breathing	-	5	2	2	-	4	4	2
Tremor	-	1	3	5	-	4	5	5
Lacrimation	-	2	1	1	-	2	3	1
Exophthalmos	-	1	3	5	-	2	2	5
Salivation	-	2	2	3	-	2	3	4
Diarrhea	-	1	-	-	-	1	-	-
Convulsion	-	1	2	3	-	1	2	3

Numerals indicate number of animals showing clinical sign

FIGURE 1.1 Dose Response Curve

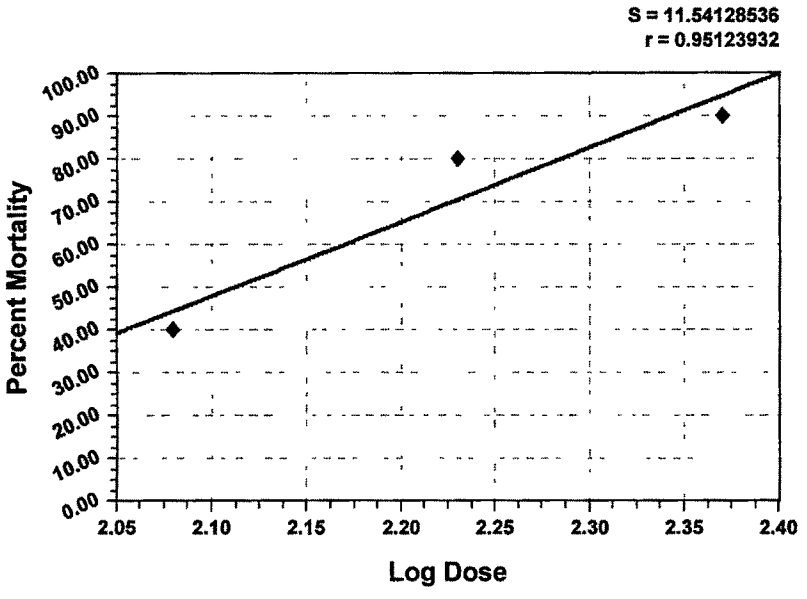

FIGURE 1.2 Median Effect Plot