

Chapter I

An acute toxicity test is the first biological experiment done on the new molecule and chemical. Determination of the median lethal dose (LD_{50}) is essential for characterizing the toxic effect of chemicals and determining their hazards to human. The toxicity of a compound is best evaluated by studying the median lethal dose. The value obtained forms a basis for labeling of substances and is a primary approach towards hazard assessment. In the present study an attempt was made to evaluate the median lethal dose of deltamethrin 1% + triazophos 35% EC following a single dose. Four groups of rats were used, group I was served as control, while other three groups were administered deltamethrin 1% + triazophos 35% EC by oral gavage at various dose levels. Severe toxic symptoms like lethargy, abdominal breathing, tremors, lacrimation, exophthalmos, excessive salivation, diarrhea and convulsion, were observed in the rats which were followed by mortality. The mortalities observed for various doses of both sexes were 40, 80 and 90% at 120, 168 and 235 mg/kg body weight, respectively. The acute oral median lethal dose (LD_{50}) value calculated for deltamethrin 1% + triazophos 35 % EC was 128.32 mg/kg body weight with lower fiducial limit 94.82 mg/kg body weight and upper fiducial limit 173.64 mg/kg body weight. The severity of toxic signs and the increased toxicity suggest that triazophos potentiate the toxic effect of the deltamethrin.

Chapter II

Many of the standard safety evaluation toxicological studies such as sub chronic, chronic, reproductive toxicity designed to characterize the various aspects of toxicity that can be understood only after a prolonged multi-dose exposure of xenobiotics. Hence, a repeated dose reproduction (one generation) toxicity study was performed to evaluate the systemic effects and the effect on the reproductive system, due to the exposure of deltamethrin 1% + triazophos 35 % EC in albino rats. One group was exposed as control, while other three groups were treated with deltamethrin 1% + triazophos 35 % EC at the dose levels of 10, 20 and 30 mg/kg body weight. The dose volume administered was maintained 10mL/kg body weight. Male animals were dosed 70 days prior to mating than during mating and thereafter till sacrifice. Female animals were dosed 14 days prior to mating; dosing was continued

throw during mating, throughout gestation and lactation period. Treated male and female rats from the same dose group were allowed for cohabitation. The pregnant females were isolated and housed individually and observed further during gestation and lactation period.

At the terminations of the experiment, haematological and biochemical parameters were studied. The rats bled at the end of the treatment period for the analysis of biochemical parameter revealed increase in the serum levels of glucose, BUN, total protein, cholesterol, ALT, AST and ALP levels in male and female rats. Dose dependent increase in sodium (Na^+) and potassium (K^+) level and decrease in chloride (Cl^-) level was found in both the male and female rats. Treatment of deltamethrin + triazophos exhibited treatment related inhibition of the serum cholinesterase value in male and female rats.

Haematological parameters revealed increased WBC count. However, a certain decline was observed in other haematological parameters viz. erythrocyte count (RBC), hemoglobin (Hb) haematocrit (HCT), Mean corpuscular haemoglobin concentration (MCHC). Moreover, a dose dependent decrease in platelet count and increase in clotting time was also noticed in treated rats.

Gross evaluation carried out at the termination of the experiment revealed treatment-related changes in liver (mottling/hepatomegaly) and kidney (blotched/patchy congestion). Histopathological evaluation revealed lesion in liver such as altered eosinophilic foci, necrotic foci, hypertrophic foci, patchy haemorrhagic spot, congestion of sinusoid, congestion of central vein and mono nuclear cells infiltration; and kidney revealed lesions of nephropathy such as dilated pelvis, papillary atrophy, nephritis and hyperplasia of pelvis.

Chapter III

Reproductive dysfunction includes effects resulting from paternal or maternal exposure that may interfere with the conception, development, birth and maturation of offspring to healthy adult life and the data for the such experiment can be arrived from repeated dose exposure of chemicals. Repeated dose exposure of deltamethrin 1% + triazophos 35% EC caused decreased body weight and feed consumption in male rats. Female rats showed decreased bodyweight and feed consumption during pre-mating, gestation and lactation period at 30mg/kg-body weight.

In the current study, definite alterations were observed in sperm motility, epididymal counts, testicular sperm head count and sperm morphology of rats subjected to deltamethrin 1% + triazophos 35% EC.. Result showed concomitant inhibition of sperm motility with the

increase in dose levels Morphological examination of sperms revealed various morphological alterations such as no head, no hook, blunt hook, no tail, broken tail etc.

Relative organ weights of reproductive organs were recorded and no alteration was observed except in case of uterus, which showed an increase in both absolute and relative weight at 30 mg/kg body weight.

Litter examination during lactation period revealed decreased pup number, total pup weight and average weight of pups at 30 mg/kg body weight. Pup mortality was found to be higher at 30 mg/kg body weight. However sex ratio was unaffected with the treatment.

Various reproduction indices such as fertility index, survivals index, gestation index, lactation index and parturition index were calculated. Fertility index in male as well as female rats was found to be reduced at high dose group. Live births and survival index were decreased at high dose group. However no changes in gestation index, lactation index and parturition index were observed.

At the end of experiment on day 21, gross and visceral examination of pups did not reveal any treatment-related changes. Histopathological assessment of male rats showed lesions in prostate (hyperplasia and poorly active), testis (focal and diffuse degenerative exhibited by seminiferous tubules exhibited degenerative changes/atrophic changes) and epididymis (lumina of ductus epididymis completely devoid of spermatozoa, leaving epithelium intact and showing hyperplasia (2 - 4 layers). The lumina of some of the ductus epididymiis contain tissue detritus, focal vacuolation of epithelial lining of ductus epididymis)

Dams sacrificed on day 21 of postpartum showed histopathological lesions in ovary (inflammatory changes/angiectasis), uterus (endometrial glandular hyperplasia/luminal dilation) and mammary gland (undeveloped). The changes were inconsistent and not treatment related.