I. INTRODUCTION

Arthropod infections in livestock can cause intense irritation leading to poor condition, weight loss, reduced milk yield or hide or damage to fleece damage. In addition many species of ectoparasites are responsible for transmission of disease to the animals themselves or are vectors for a number of diseases to animals and man. Ectoparasites elicit allergic reactions to venoms and toxins, decreased resistance to other diseases, reduction in egg production and feed conversion efficiencies in food producing animals, reduction in reproductive efficiency and transmission of other disease agents (Loomis, 1986).

Pesticides play an important role in the control of ectoparasites in animal health and thus improve the growth and productivity and preventing vector borne diseases. Insect pest management has assumed tremendous importance in the developed and developing countries. But, at the same time, the indiscriminate use of pesticides has led to toxicities in animal and man.

The sales and use of ectoparasiticides for the control of ectoparasites of domestic animals constitute a major sector of the global animals health industry.

Available chemicals used in the treatment of ectoparasites in veterinary practice act either systematically, following uptake of the agent from the hosts tissues or by direct contact with the target parasites following external application. Topically applied chemicals have direct effect on the target parasites present on the surface of the skin (Taylor, 2001).

Chemicals used to control external parasites are known as ectoparasiticides. Ectoparaciticides used for the control and treatment of ectoparasites can be grouped as botanicals (plant derived agents), amidines (formamidines), macrocyclic lactones ( avermectins/ milbemycins), carbamates, nitroguanidines, organochlorine, organophosphate,
phenylpyrazole, pyrethrine and synthetic pyrethroids and miscellaneous such as insect growth regulators, benzoylephenyl ureas, triazine and pyrimidine derivatives, juvenile hormone analogues (Taylor, 2001).

Amitraz is the main member of amidine group which acts at octopamine receptor sites in ectoparasites resulting in neuronal hyperexcitability and death (Nathanson, 1985). Amitraz is an effective insecticide, used against animal ectoparasites. It is a broad spectrum acaricide/insecticide, widely used for cattle, sheep goats and pigs. It has rapid action on the control of animal ectoparasites, such as mites, ticks and fleas etc., and the compound persists on hair and wool long enough to control all stages of the parasite. It is available as a spray or dip for use against mites, lice and ticks in domestic livestock (Taylor, 2000). Amitraz has also been shown to have an excellent action against attached ticks (Baker et al., 1973; Harrison and Palmer, 1981). Amitraz has been shown to be effective in controlling lice and mange in pigs and psoroptic mange in sheep (Curtis, 1985). In small animals, amitraz is used for the treatment and control of ticks and canine demodicosis (Farmer and Seawright, 1980) and sarcoptic mange (Curtis, 1999). Amitraz is also formulated in collars for tick control in dogs.

Amitraz has been shown to possess parasiticidal activity against these strains resistant to other chemical classes such as: organophosphorus and organochlorine compounds as well as carbamates.

Cypermethrin is a Type-II synthetic pyrethroid, first synthesised in 1974 and marketed in 1977 as a highly active synthetic pyrethroid insecticide effective against a wide range of pests in agriculture, public health and animal husbandry. Cypermethrin has a low solubility in water, but is highly soluble in a wide range of organic solvents (WHO, 1989).

There are many potential benefits of combination pesticide products, such as broadening the ectoparasite spectrum, prolonged duration of activity and a convenient administration to treat multiple parasitic infestations.
Additionally, combination products can be used as a strategy to manage variation in parasite susceptibility (Mercella, 1999). Among the strategies proposed for resistance management in insects are to use a pyrethroid and a non-pyrethroid insecticide in combination (Hougard et al., 2003).

Toxicity studies on cypermethrin and amitraz have already been carried out on individual pesticides earlier in this department.

The toxicity and pharmacological efficacy studies of the pesticide combination containing cypermethrin and amitraz was carried out in the present investigation with the following objectives:

1. To study the acute oral toxicity and to determine the median lethal dose in male and female rats.
2. To study the subacute toxicity with Repeated dose 28-day oral toxicity in male and female rats.
3. To study the Immunotoxicity effects with repeated dose 28-day oral toxicity in male and female rats.
4. To study the health hazards likely to arise from repeated dermal exposure with 28-day dermal toxicity in male and female rats.
5. To study the possible hazards likely to arise from the exposure of the eyes and associated mucous membranes with acute eye irritation study in rabbits.
6. To study the possible allergic action likely to arise from repeated exposure with Skin Sensitization in guinea pigs.
7. *In vitro* pharmcolgoical efficacy against different stages viz., eggs, larvae, adult male, unengorged female and engorged female *Rhipicephalus sanguineus* ticks by immersion test.
8. *In vivo* pharmacological efficacy in naturally ticks infested dogs.

9. *In vivo* pharmacological efficacy in natural ticks infested cattle.

10. *In vivo* pharmacological efficacy in natural ticks infested sheep.