Summary

The heighest Wisdom has but one science, the science of the whole, the science explaining the whole creation and mans place in it.

- Leo Tolstoy
Pesticides have become an indispensable part of the modern agricultural practices and one of the vital factors in increasing food production. Although, the use of pesticides have helped to increase the agricultural production but their indiscriminate use has adverse effect on the non-target organisms including human beings.

Most of the organochlorine compounds are quite stable and persist in the environment for longer periods. Persistence is a primary character of the pesticides and the usefulness of this character is dichotomus. Persistence (residual activity) can be an important attribute and obviates the need for expensive and time consuming retreatment. But persistence is obviously undesirable, when it is carried beyond the period of pest attack, especially where harmful concentrations are retained in food or in the environment. Because of this advantage, the organochlorine insecticides are still being extensively used in many parts of the globe, particularly in developing countries. Hence, a widely used organochlorine compound, Aldrin was selected as a test compound in this present investigation.

Adult Wistar strain albino rats 70 ± 5 days and weight (114 ± 5g) have been selected as experimental animals. The rats were maintained at laboratory conditions (27 ± 2°C); 12 hrs light and 12 hrs darkness).
Before taking a look into the complicated physiological aspects, the determination of toxicity of the chemical was suggested. Healthy adult albino rats have been taken and dose response studies were assessed. Rats were exposed to different lethal concentrations of aldrin for 48 hrs have shown 50% mortality (LD$_{50}$) at 60 mg/kg body weight (Table 1.1 & Fig.1.1, 1.2). The graphical representation of percent mortality versus log concentration and probit mortality versus log concentration showed a typical sigmoid curve (Fig.1.1) and a straight line (Fig.1.2) respectively were in agreement with the principle of probit analysis (Finney, 1964). The toxicity of aldrin was neither high nor low when compared to certain OC and OP compounds (Tables 1.2 & 1.3).

Since the natural ecosystems do not get contamination by lethal concentration, a sublethal concentration (1/6th of LD$_{50}$ i.e. 10 mg/kg body weight), was used to study the effect of aldrin. Adult albino rats were divided into 4 groups having six animals in each. The second, third and fourth group of animals were termed as experimental animals. To the animals of second group single dose of aldrin was administered orally. Double doses were given to the third group of animals and multiple dose were given to fourth group of animals. The first group of animals were considered as controls after giving isovolumetric quantities of corn oil and acetone. After the stipulated
period, both control and experimental animals were killed and the tissue like brain, liver, kidney and intestine were isolated for biochemical and histological investigations. The blood was drawn from the orbital venous plexus by puncturing with the help of a pastuer pipette, for hematological investigations.

In the present investigation, a decreasing trend was observed in the specific activities of Mg\textsuperscript{2+} ATPase and Na\textsuperscript{+} - K\textsuperscript{+} ATPase in brain, kidney, liver and intestine. The decrement was enhanced with the increase of aldrin dose administration (Tables 2.1 & 2.2; Figs.2.1 & 2.2). ATPases play an important role in the maintenance of cell membrane permeability and energy transformation in the biological system. Decrease in ATPase activities could indicate variation in ion transport across the cell membrane suggesting a possible interference in energy metabolism to show that organochlorine diminished ATPase activity by forming an inhibitory complex. The decreased levels of ATPases in the present investigation may be due to structural damage of mitochondria in the experimental animals.

The activities of SDH, MDH decreased while that of LDH and GDH increased progressively with dose of aldrin administration (Table 3.1 to 3.4 and Fig.3.1 to 3.4). The architectural damage brought about in the experimental animals were reflected in the decrease of key oxidation enzyme profiles. Since pesticides are known
to cause architectural changes in mitochondria (Miroslaw, 1973; Varilos et al., 1976), the increased histopathological lesions from single dose to multiple dose (Chapter 6) might have resulted in malfunctioning of oxidative metabolism. The increased levels of LDH and decreased levels of SDH and MDH showed a shift in normal balance of glycolysis in favour of anaerobiosis. The appreciable elevated levels of GDH activity was observed in aldrin intoxicated animal tissues (Table 3.4 & Fig.3.4). As GDH plays an important role in detoxification of ammonia (Campbell, 1973) increased glutamate dehydrogenase activity in the present investigation may be used in the direction of reductive deamination i.e. glutamine to glutamate ratios and glutamine synthetase activity levels. As the changes in permeability properties of mitochondria and lysosomal damage are also known to elevate GDH activity (Johnson and Farrington, 1969), aldrin used in the present investigation might have effected both lysosomes and mitochondria.

Haematological parameters were altered in aldrin intoxicated rats in the present investigation. Aldrin produced a gradual decrease in RBC, Hb, PCV and increase in WBC, MCH and MCV. In differential count also, a gradual increase was observed in neutrophils, eosinophils and monocytes. Decrease was found in basophils and lymphocytes (Table 4.1 & Fig.4.1). The changes in haemogram indicates that the pesticides used in the present
investigation, alters the biochemical pathway and causes cellular damage.

Teratological defects in the albino rat fetuses following maternal treatment with aldrin were observed (Table 5:1 & Plate 5. Figs. A to E). Aldrin treatment influenced the implantation and caused an increase in embryo lethality. The embryo resorption was significant in experimental animals. The visceral and skeletal weights also showed significant reduction in experimental animals. The stunted growth in the present investigation is a clear indication that the aldrin used in the present investigation might have inhibited the organogenesis and fetal development. The prominent teratological abnormalities found in the present investigation includes-syndactyly, wrinkled and degenerated skin in the dorsal region of the dead fetuses, missing of last sternebrae and malformation of humerus bone. The changes were more pronounced in multiple dose administered rats than those of single and double dose. Since teratogens are known to cause adverse effects on pregnant animals, the abnormalities found in the present investigation may be due to damage or death of certain cells of a developing organism.

Histopathology has been used as an important diagnostic tool in biomedical pathology for many years and has been a cornerstone in the large field of biomedical pathology. An attempt made in the
The present investigation has shown moderate degenerative changes in the microvilli, severe necrosis in villi leading to fragmentation of tips, separation of circular muscular layer from submucosa etc., in intestine (Plate 6. Figs. A-E). The liver showed cytoplasmic degeneration, pushing of nucleus to the periphery of hepatocytes, hypertrophied nuclei and fragmentation of nuclei in experimental animals (Plate 6. and Figs. F-K).

Aldrin induced pathological changes in the kidney include moderate necrotic changes in epithelial layer of glomerular regions and proximal convoluted tubules, atrophied and fragmented glomeruli, necrosis in distal convoluted tubules etc (Plate 6. Figs. L-P). The experimental animals showed marked pathological changes in testis which includes necrosis in germinal epithelial layer, degenerative changes in seminiferous tubule, clumped spermatozoa, reduced number of spermatids, reduced size in lumen of seminiferous tubules and degenerative changes in interstitial cells etc (Plate 6. Fig Q-V). The brain tissue prominently showed changes in granular layer cells. These cells showed swelling in double dose and reduced in number and size were noticed in multiple dose cerebellum of experimental rats (Plate 6. figs.W-Zm). All the pathological changes were more pronounced in multiple dose aldrin intoxicated animals. These changes would definitely cause poor absorption of nutrients,
changes in normal metabolism, failure of excretion, reduced reproductive potentiality etc. Since OC compounds are lipophilic in nature, the lipid accumulation in hepatocytes may be the reason for pushing of nucleus to the periphery of hepatocytes. The degenerated interstitial cells may also result in the failure of testosterone in males. The irreparable architectural changes found in multiple dose aldrin exposed animals were more than those of single and double dose.

To conclude, aldrin caused to serve energy crisis, hematological, teratological changes besides irreparable architectural changes in certain vital tissues of experimental rats. All these changes were more pronounced in multiple dose aldrin administered rats clearly indicates that the frequent exposure of non-target organisms including human beings to pesticides may result vulnerability and eventual death. In nature's conservationist point of view, pesticides should not affect the non-target life adversely but should degrade in the ecosystem at a faster rate, otherwise problems like biomagnification and cumulative effects will arise.