Chapter 4.
Summary and Conclusions
Chapter I:

Diabetic mellitus is a serious disease and neglect can lead to dangerous complications. It afflicts about 3% of the Indian population. Diabetes mellitus is now being increasingly diagnosed as awareness of the disease has great impact on the individuals life style in the physical economic and social aspects.

Two major types of diabetic are recognized. Insulin dependent diabetes mellitus (IDDM) and Non-insulin dependent diabetes mellitus (MDDM).

Induction of diabetes in animal can be carried out by various ways by using different chemical diabetogenes include alloxan, uric acid, dehydroascorbic acid dehydrois ascorbic acid thinolones, streptozotocin, magnesium and cyclophosphamide. Out of these alloxan attain great importance in producing insulin deficiency.

Several drugs have been and being used for their blood sugar lowering activity, cure of diabetes and anti diabetic property.

In the present investigation effects of hyperglycaemia on testicular functions (alloxan 150 mg/kg b.wt.) have been examined in male albino rats.

The objectives were:
A) Effect of hyperglycaemia (alloxan 15 mg/kg body wt ) with the help of sperm dynamics.
B) Biochemical alteration in the reproductive tract and organs of vital importance.
C) Haematological and serum analysis study for the possible side effects if any, after induced hyperglycaemia.
D) Changes in the histoarchitecture of reproductive as well as vital organs.
E) Changes in the testicular cell population dynamics.
Alloxan was injected intraperitoneally to male albino rats at the dose level 15 mg/kg body weight.
A. Hyperglycemia and gonadal function:
1. Alloxan injection to intact rats caused reduction in the weights of testes, epididymides, vas deference. Seminal vesicle and ventral prostate.
2. Sperm density in cauda epididymides and testes and motility counts in cauda showed remarkable decrease after 48 hours of alloxan injection.
3. Histometry showed degenerative changes in testes and sex accessory organs alloxan treated rats. The seminiferous tubules were shrunken and Leydig cell nuclei were reduced in diameter.

B) Tissue Biochemistry:
1. Protein and sialic acid contents of tests and sex accessory organs were significantly reduced after alloxan injection to intact rats. Adrenal ascorbic acid was depleted in alloxan treated male rats. Similar changes in seminal vesicle fructose contents were observed.

C) Serum Biochemistry:
a) RBC and WBC haemoglobin and haematocrit values in alloxan treated rats did not change significantly and remained within the normal limits. Blood sugar was significantly increased at 48 hours of alloxan injection intraperitoneally.
b) Serum cholesterol was increased after alloxan treatment.
c) Serum phospholipids concentrations did not alter after alloxan injection at 48 hours.
d) Serum triglyceride levels were significantly after alloxan treatments.
e) Serum HDL cholesterol was within normal range.
f) Serum transminase (SGOT, SGPT) activity did not change after alloxan treatment.

D) Histopathology:
Treatments of alloxan have remarkably altered the histological structure spermatogenesis was inhibited at spermatocyte stage. Lumen of vas deferentia were devoid of sperms. Epididymies showed reduced number of spermatooza. The secretary activities of seminal vesicle and ventricular prostate were also altered.
E) Testicular Cell population dynamics :

Alloxan treatment to intact rats caused significant reduction in different germ cell population i.e. spermatogonia, Spermatocyte and spermatids. Similarly immature and mature Leydig cell number were also reduced after treatment.

The mechanism of action of alloxan discussed.

The decreased weights of testes and other sex accessories is suggestive of reduced androgen levels.

Increased blood sugar point out the nature of alloxan action that damage of β Cell and prevent insulin synthesis.

Histological quantitative results indicate that alloxan may have affected the intratesticular androgen levels either by inhibiting Leydig cell function or by inhibiting hypothalamus pituitary axis hence impaired androgen synthesis have been achieved resulting in infertility.

Reduction in Leydig cell nuclei and seminiferous tubule diameter support the view of reduced androgen synthesis.

Depletion in adrenal ascorbic acid also suggest the impaired androgen synthesis.

Reduced fructose, protein, sialic level suggest the decreased level of androgen, since these parameters are androgen dependent.

From the foregoing account it is evident that effect of induced physiological change in the form of hyperglycemia caused adverse effect on testicular function in male rats. In conclusion hyperglycemia leads to testicular dysfunction in male rats via affecting Leydig cell.
Chapter II and III:

The possible disruption of endocrine system by the environmental chemicals and the effect on human health which may result have become major topic of discussion and research in the past few years. An endocrine disruption is an exogenous substance that cause adverse health effect in an intact organism or its progeny subsequent to change in endocrine function. A large number of man made chemicals that have been released into the environment as well as few natural ones have the potential to disrupt the endocrine system of animals including humans. Among these are the persistant bio accumulative organohallogen compounds that includes some pesticides, fungicides, insecticides and herbicides. Many wildlife population are already affected by these compounds. In the present investigation effect of malathion insecticide on pancreas and testicular functions have been examined in male albino rats.

The objective were:

A) Effect of malathion on biochemical alternation in testis.
B) Effect of malathion on biochemical alternation in pancreas.
C) Changes in the histoarchitecture of the testis and pancreas.

A) Tissue Biochemistry (Testis):
I) Increase in acid and alkaline phosphatase in the testis after oral dose of pesticides.
II) Increase in total, soluble and insoluble protein.
III) Decrease in testosterone concentration of the testis.

B) Tissue Biochemistry (Pancreas):
I) Increase in acid phosphatase.
II) Increase in alkaline phosphatase.
III) Pesticide dose to male rats caused depletion in pancreatic insulin.

C) Histopathology:

Malathion dose have remarkably altered the histoarchitecture of testis and pancreas.

In pancreas there is decrease in number of insulin granules as compared to control rats, also cytoplasmic vacuolation in beta
cells and exhibited the degeneration of smooth endoplasmic organelles.

In the testis degenerative changes were found in the germ cells usually associated with sertoli cell vacuolation and retraction. There was a disorganised appearance of the germinal epithelium in the affected tubules. The proper development of spermatocytes was affected by the sertoli cells dysfunctioning which acts as a nurse cell for developing spermatocytes.

From the above observation it is concluded that malathion caused the chemical injury to vital and reproductive organs of male albino rats, may interfere with carbohydrate metabolism causing hyperglycemia by decreasing the concentration of insulin and also acts to altered the sertoli cell structure and appeared to affect the process of spermatogenesis. This insecticide altered the secretion of testosterone responsible for secondary sexual characters resulting into sterility in male albino rats.