SUMMARY
The present work embodies histological and biochemical investigations on male albino rats following administration of steroidal and non-steroidal compounds. During these investigations, an attempt has been made to study separately the effects of two drugs - one steroidal and the other non-steroidal in combination with testosterone/testosterone enanthate on the male reproductive and liver functions in rats.

The two drug combinations used comprise:
(i) Norethisterone enanthate (Net-en, 100 µg in 0.1 ml olive oil/rat/day) + testosterone (T, 100 µg in 0.1 ml olive oil/rat/day); (ii) Clomiphene citrate (CC, 5 mg in 0.2 ml saline/rat/day) + testosterone enanthate (TE, 100 µg in 0.1 ml olive oil/rat/day). The two drug combinations were administered for 45 and 30 days respectively, whereafter the recovery was recorded for 30 days after cessation of the drug treatments.

The present study encompasses the histological and biochemical analysis of the testis and accessory reproductive organs viz. epididymis, seminal vesicle and prostate. Limited serum biochemistry has also been attempted. Biochemical investigations involve estimation of various metabolites and enzymes of the listed organs. Enzymes of
carbohydrate metabolism in both the testis and epididymis in particular have been studied. Spermatogenic kinetics have been studied employing the method of Leblond and Clermont (1952) and counting of cell types in the seminiferous tubules was done in stages VII-VIII tubules (Bansal and Davies, 1986).

The Net-en + T treated animals were sacrificed 15, 30 and 45 days after initiation of the treatment and then 15 and 30 days after cessation of the treatment. The CC + TE treated animals were sacrificed 15 and 30 days after initiation of the drug treatment and then 15 and 30 days after cessation of the treatment. Various groups were comprised of 8 each of both treated and control animals. The control animals received the vehicles alone.

Although body weight was not affected much in either case, there was recorded a significant reduction in the weights of testis and accessory reproductive organs. Forty-five days of Net-en treatment reduced the testis weight to 56.2% of the control and that of the epididymis, seminal vesicle and prostate fell to 68.9%, 54.5% and 70% of the control values respectively. The CC + TE treatment reduced the weights of the four organs viz. testis, epididymis, seminal vesicle and prostate to 36.3%, 60%, 49.8% and 45.9% of the control values respectively.
Both treatments were seen to inhibit testicular activity accompanied by spermatogenic arrest at spermatocyte stage. The seminiferous tubules after the drug treatments, suffered shrinkage with respect to the control; spermatids and developing spermatozoa were prominent by their absence from the tubules, specially in the later intervals.

Loss in testicular weight was accompanied by and attributed to various histological lesions which included shrinkage of seminiferous tubules and heavy desquamation of the germinal epithelium.

Shrinkage of tubules had significantly reduced the tubular diameter to 47% and 42% of the control values, after 45 days of Net-en + T treatment and 30 days of CC + TE treatment respectively. The tunica propria and tunica albuginea were prominently thickened (specially the latter) by the end of both the treatments.

Testicular atrophy comprised the gradual depletion and eventual disappearance of the elongating (step 19) spermatids from the seminiferous tubules by 30 days of Net-en + T and 15 days of CC + TE treatments. This showed that the step 19 spermatids were the first to be affected.
in both the treatments. The frequency of St\textsubscript{7} round pachytene spermatids and of the spermatocytes was also reduced. After 45 days of Net-en + T treatment, St\textsubscript{7} spermatids were negligible in number while spermatocytes were about 35% of the control value. After 30 days of CC + TE treatment, there were hardly any St\textsubscript{7} spermatids and the number of spermatocytes was also significantly reduced.

Further, there were seen, lot of desquamated cells in the tubular lumina after 30 days of Net-en + T and 15 days of CC + TE treatment. The cell debris, in the lumina, specially in the latter treatment also showed giant cells - both hypertypic mononucleated and multinucleated towards the end of both treatments. Hypertypic mononucleated giant cells comprised the degenerated pachytene spermatocytes characterized by their large-sized and karyolyzing nuclei. Multinucleated giant cells on the other hand, were conjectured to represent coalesced cap stage spermatids that failed to differentiate further as a result of treatment.

Cessation of the treatments resulted in the recovery of the testicular tissue. Testicular damage was reversible to some extent 30 days after cessation of both the treatments. The testis weight improved in both the cases though it was still significantly lower than in the controls. The
spermatids though mature sperms were still absent. The recovery seemed to be more pronounced after CC + TE treatment.

The histological lesions in the various epididymal segments in response to the drug treatments comprised slightly decreased epithelial cell height in the caput as against the considerable increase in the epithelial cell height in the cauda region following both the treatments. Variations in the epididymal luminal contents were also witnessed. Initiation of the treatments resulted in a significant fall in the epididymal sperm concentration accompanied by shrinkage of tubules in both the caput and cauda regions. As the treatments were prolonged, epididymal lumina became virtually devoid of spermatozoa. As the sperm concentration gradually decreased with passage of time following the drug treatments, there were observed increasing amounts of cell debris consisting of immature degenerating germ cells of testicular origin in the epididymal lumina. This debris was more pronounced in the caput after 15 days of CC + TE treatment than at any time during Net-en + T treatment. Tubules of the cauda epididymis, 45 days after Net-en + T treatment, revealed PAS positive
luminal cell debris which was not the case following CC + TE treatment. In the later intervals of both the treatments, the epididymal tubules, specially those of the cauda region appeared highly shrunken with reduced and empty lumina. Basement membrane, specially of cauda, was also thickened following both the treatments.

The seminal vesicle and prostate histology was not much affected by either of the drug treatments. The seminal vesicle suffered only a marginal reduction in the epithelial cell height accompanied by a decrease in the number of villi/folds. Similarly, the prostatic epithelium also appeared somewhat shrunken, concurrent with reduced number of alveolar folds.

Post-treatment recovery 30 days after the cessation of the treatments, revealed almost complete reversibility of the histological damage in the seminal vesicles and prostate, whereas epididymal lumina were still devoid of spermatozoa. The weight of the epididymis remained significantly less than the control 30 days after cessation of both the treatments.

Biochemical estimations revealed a significant increase in the total lipids, cholesterol and glycogen
contents of testis and epididymis following both drug treatments. Contrary to this there was recorded a significant fall in the phospholipids and proteins in both cases. Whereas acid phosphatase activity was significantly elevated in testis and epididymis following the drug treatments, the reverse was true of alkaline phosphatase which fell significantly instead. Separation of energy yielding and impairment of carbohydrate metabolism following both the treatments could be inferred from the reduced activities of the dehydrogenases (succinate and lactate), adenosine triphosphatase, glucose-6-phosphatase, glycogen phosphorylase, fructose-1,6-diphosphatase, hexokinase, glucose-6-phosphate isomerase and elevated activity of amylase. Impairment of carbohydrate metabolism is also indicated by the accumulation of glycogen in the experimental animals. The biochemical parameters recovered to varying extents after cessation of both the drug treatments. In the seminal vesicles and prostate there was witnessed an increase in the total lipids as well as phospholipids following both the drug treatments. Though cholesterol, proteins and glycogen increased in the seminal vesicle, these metabolites fell significantly in the prostate. Acid phosphatase activity in both prostate and seminal vesicle
was elevated as against low alkaline phosphatase activity following the drug treatments. Cessation of treatment reversed the biochemical changes.

After both the treatments, serum revealed no significant changes in total proteins, albumin and A/G ratio, cholesterol and glucose. Bilirubin levels fell after an initial rise during Net-en + T treatment but rose significantly during CC + TE treatment. Acid phosphatase activity was lowered while alkaline phosphatase and transaminases activities were elevated.

Both the steroidal and non-steroidal drug treatments effectively impaired male reproductive functions at dose levels at which there were no adverse side-effects. Further experimentations and investigations would not be unfruitful for the establishment of these compounds as prospective male contraceptives.