CONCLUSION

Mitomycin C (MC) is popularly known as an antibiotic as well as antineoplastic drug. A large number of works have been carried out with MC on different aspects which suggests that apart from its therapeutic value the drug also produces some positive deleterious action over different organs in animals. So far literatures are available regarding the mode of action of the drug it is clearly indicated that the drug possibly mediate its action through the inhibition of DNA synthesis. Later on the inhibitory action of the drug over DNA synthesis have been confirmed by different workers (Chapter I). However, in this connection it should be mentioned that the drug showed more pronounced effect specially over the proliferating tissue cells. Previously a number of reports have been published concerning the action of the drug over testis and now it is generally accepted that in high doses (5 mg/kg Body wt.) MC brought about a severe degeneration in the testicular epithelial cells. Till now, the explanation of MC induced alteration of testicular epithelium was primarily evaluated on the basis of it's direct action on the genetical materials. The effect of MC in low doses for a prolonged period is still obscure in male rats. Recent observation in female rats treated with MC in low doses showed a significant diminution of ovarian steroidogenesis. It is established that the regulation of structural and functional activity of the testis is controlled under the influence of pituitary gonadotrophin which stimulates the secretion of
testosterone from the interstitial cells of the testis. However, the effect of MC treatment on the status of testicular steroidogenesis is not yet clear in spite of its deleterious action on the seminiferous epithelium. In the present experiment the overall action of MC on testicular physiology have been studied in different conditions. Moreover, a detailed investigation have been made to evaluate the testicular steroidogenic capacity along with its spermatogenic activity in rats after treatment with MC in low doses for various lengths of time.

In the Chapters III and IV, MC was administered both in mature and immature rats and the testicular steroidogenic capacity was assessed on the basis of radioimmunoassay (of testosterone) in case of mature rats along with histochemical and biochemical studies of the testicular tissue. A significant fall of plasma testosterone level along with similar reduction of glucose-6-phosphate dehydrogenase and $\Delta^5$-3$\beta$-hydroxysteroid dehydrogenase in MC treated rats clearly indicate the reduction of testicular steroidogenesis in this condition. There are other parameters such as weight of testes and sex accessories, DNA content of the testicular tissues and Leydig cell nuclear area also corroborated the above findings. Furthermore, the accumulation of cholesterol and ascorbic acid in the testicular tissues suggest the hypofunctioning condition of the gonad. The consideration of the above findings it is logical to assume that MC has got a potent inhibitory action over testicular steroidogenesis. In this connection it may be mentioned that testicular steroidogenesis is controlled by the stimulation of pituitary gonadotrophin (LH) and
as in the present investigation the weight of pituitary also declined in MC treated rat, it is reasonable to suggest that this drug might disturb the normal secretory pattern of pituitary. On the other hand the direct action of the drug over the Leydig cell could not be excluded as the drug has got a potent inhibitory action over the DNA synthesis (Chapter III and IV) and LH stimulation of testosterone synthesis accompanied with increased synthesis of DNA. However in the Chapter V an in vivo experiment was conducted using MC and HCG together to assess the involvement of pituitary in the reduction of testicular steroidogenesis. The results of the in vivo experiment clearly showed a significant improvement of testicular steroidogenesis. For further clarification regarding the mode of action of MC concerning testicular steroidogenesis an in vitro experiment was carried out only with MC and the histo-chemical results clearly indicates the direct inhibitory action over the steroidogenic enzymes in the testicular tissues. Therefore, the consideration of the in vivo and in vitro results suggest that the drug probably affects testicular steroidogenesis both directly and indirectly i.e. through the suppression of pituitary gonadotrophin secretion.

The involvement of hypophyseal gonadal axis in the regulation of testicular histology and spermatogenic activity have been well documented. Considering the above facts an experimental design have been oriented (Chapter VII) to examine the histological and spermatogenical status of the testis in the rats treated with MC
(500 μgm/kg Body wt.) alone and together with either HCG or testosterone. In the present set of experiment the testicular involution along with spermatogenic arrest were consistent as that of previous reports and in this connection it is noteworthy that the dose of the drug used were far less in comparison to the previous works. A gross improvement of the testicular histology and spermatogenic activity in MC treated rats were observed after administration of either testosterone or HCG. Therefore it is logical to interpret that MC (500 μgm/kg Body weight treated every alternate day) inhibits the testicular steroidogenesis and it probably exert its action by both ways i.e. through the suppression of pituitary gonadotrophin secretion and directly over the Leydig cells through the inhibition of DNA synthesis.