CHAPTER I

SUMMARY

PART 1

1. Studies on the effects of aqueous extracts of *Carica papaya* seeds on male albino rats for 7 and 15 days.

2. Combined extract + ascorbic acid feeding for 7 and 15 days.

3. Withdrawal studies for 1 and 2+ months after 7 days extract treatment.

The effects of short term treatment (7 and 15 days) with aqueous *Carica papaya* seed extract, beneficial effects of ascorbic acid feeding along with treatment and reversibility of the induced effects by discontinuation of 7 day treatment for one and 2+ months were studied on the reproductive physiology of adult male albino rats of Holtzman strain. The dosage was 1 mg/0.4 ml/day/rat injected intramuscularly. The data revealed that the aqueous extract was the most potent in causing zero percent fertility within 7 days which is attributed to reduction in sperm motility and their morphology as well as their oxidative metabolism, and an androgen-deprived effect to the target organs as most of the androgen-deprived effect to the target organs as most of the androgen-
sensitive parameters were altered after treatment to a variable extent. In the whole, the cauda epididymis and the distal vas deferens were affected more by the treatment than the other organs, probably due to their differential sensitivity to androgens for maintaining their structure and metabolic functions. The treatment, however, did not alter serum testosterone, DHT and DHEA levels as well as testis weight, histology and activities of 3β and 17β hydroxysteroid dehydrogenases (HSD) and SERT testicular sperm count thereby indicating no effect on spermatogenesis, steroidogenesis nor pituitary somatotropin levels.

The androgen deprived condition especially to cauda epididymis led to alterations in its structure and metabolism and probably its microenvironment, thereby rendering its milieu hostile for sperm maturation and viability which eventually lowered the fertility rate in treated rats. The alteration in the contractile response of vas deferens in extract treated rats might also be a contributing factor in reducing fertility rate. However, the extract manifested no 5-HT like activity.

The ascorbic acid metabolism was enhanced with increased mobilization of the bound ascorbiate to its free form and its subsequent higher rate of utilization in treated rats.

To study the beneficial effects of ascorbic acid in the reproductive tissues of treated animals, 7 and 15 day Carica papaya seed extract treated rats were simultaneously fed with
ascorbic acid. The results revealed that the recovery in most of the androgenic parameters was similar to, if not more, in comparison to withdrawal treatment. A significant recovery in the ascorbic acid turnover pattern also occurred both in epididymides and vas deferens. However, the AA feeding did not alter the fertility rate of treated rats.

To ascertain whether the induced effects of Carica papaya seed extract was transient and reversible, the 7 days treatment was withdrawn for 1 and 2½ months respectively. A slight increase in the body weight was observed by both 1 and 2½ months withdrawal of treatment. The weights of all reproductive tissues recovered to almost complete normalcy after one and 2½ months discontinuation of treatment. Most of the induced effects were transient and reversible by withdrawal of treatment. Therefore, papaya seed extract is a potential post-testicular male contraceptive agent and functional sterility could be induced. The extract did not seem to have toxic effects.

The mechanism of action seems to be causing low target organ response by a probable alteration in hormone receptor interaction and/or the reduced conversion of testosterone to its potent metabolites.
1. Studies on the effects of aqueous extracts of Vinca rosea leaves on male albino rats for 7 and 15 days.

2. Castration + testosterone treatment for 7 days.

3. Extract treatment for 7 days + discontinuation of treatment for one and 2+ months respectively.

Intra-muscular injections of aqueous Vinca rosea leaf extract at a dosage of 1 mg/0.2 ml/day/rat for 7 and 15 days on adult male albino rats of proven fertility revealed that the treatment caused antianandrogenic, antiandrogenic and antifertility effects. However, the treatment did not manifest any change in the body weight except in 15 days treated animals. But a significant decrease occurred in the weights of most of the organs including pituitary excepting ventral and dorsolateral prostate. The weight of cauda epididymis and seminal vesicles were affected more than the caput, VDL and VDD tissues.

The treatment brought about significant decline in sperm density, percent motility of cauda epididymal spermatozoa of both 7 and 15 days leaf extract treated animals, besides altering their morphology resulting in zero percent fertility rate in both the treated group of animals. A significant
alteration in androgen-sensitive parameters viz., SDH, ACP and seminal vesicle fructose, an increase in cholesterol levels and a change in the ascorbic acid turnover pattern of 7 day extract treated rats was an important manifestation. That the extract possessed antiandrogenic effects were further substantiated by the results of treatments imparted to groups IV and V rats. The accumulation of cholesterol in testis points to reduced steroidogenesis.

The general histology of all the organs studied, viz., testis, caput and cauda epididymides, VDr and VDD and seminal vesicles were affected significantly in treated animals. Changes observed included nuclear pyknosis, resulting in degeneration of tissue epithelium, confluence of tubules, sperm coagulum obstructing the lumen of epididymides and vas deferens tissues of both 7 and 15 day treated rats.

However, the treatment did not bring about significant changes in the levels of testosterone, FSH and LH in 7 day leaf extract treated animals.

A significant recovery to most of the androgen sensitive parameters including body weight, organ weights, levels of FSH and fructose were obtained by combined extract + ascorbic acid feeding. The ascorbic acid turnover pattern recovered completely to normal levels in caput and cauda epididymides of 7 and 15 day combined extract + AA fed rats. The general histology of epididymides and vas deferens recovered significantly as compared to extract alone treated rats.
However, in the previous case, the combined treatment did not bring about any recovery in the percent motility, sperm count and fertility rate of these animals.

The possible reversibility of the induced effects were investigated by cessation of 7 days treatment for 1 and 2+ months withdrawal respectively. It was observed in these groups of rats that the organ weights, biochemical profile of epididymisides and vas deferens and seminal fructose levels and also the histotarchitecture recovered significantly as compared to treated rats. However, a spurt in SII activity occurred after 2+ months cessation of treatment. The ascorbic acid parameters showed almost total recovery.

The general histology of caput and cauda epididymisides and proximal and distal vas deferens also recovered significantly to control state. However, recovery in caput and cauda epididymisides was less significant by one month withdrawal and by 2-2+ months. However, in the distal vas deferens a significant increase in the muscle layer thickness was observed.

The most important manifestation was a significant spurt in the testosterone levels after one month cessation of treatment and a decline in the FSH levels were also observed. However, LH levels remained unchanged throughout the various treatments. The mechanism of action of *Vinca rosea* leaf extract appears to be directly on the testis and epididymisides.
However, it is possible that the extract might also be affecting the functions of the pituitary-gonadal axis especially in 15 day treated rats.

From the above data it is clear that both 

Carica papaya seed and 

Vinca rosea leaf extracts exhibit potent antiandro- 
genic and antifertility effects in adult male albino rats, although the former seems to be a more feasible approach.