CONCLUSIONS

1. Oral route of administration of papaya seed extract (5 mg/kg body weight/day) in rat and an intramuscular route of same dose as above in guinea pig proved potent in bringing about the desired effects by utilizing a smaller dose.

2. The treatment most probably manifested a selective androgen deprived effect to target organs. The caput and cauda epididymides as well as vas deferens were affected more than the other reproductive organs and accessory glands.

3. The treatment brought about alterations in the micro-environment and internal milieu of the epididymis which in turn led to changes in motility, metabolism, morphology and fertilizing ability of the epididymal spermatozoa, thus causing a decrease in fertility.

4. The extract had no effect on the body weights or the reproductive organ weights in rat as well as in guinea pig.

5. The papaya seed extract seems to possess a direct effect on the epididymis, it acts as a spermicidal/spermatoxic agent on saturating/mature spermatozoa by affecting particularly their oxidative metabolism. The glycolytic pathway, however, was not affected.
6. Serum testosterone levels were not altered in rat but were decreased in guinea pig which might be due to the altered conversion of testosterone to its potent metabolites.

7. The treatment did not alter testicular histoearchitecture but a significant loss in cauda epididymal sperm motility was observed. These observations indicate that the extract has a post-testicular action.

8. Previous findings have indicated that FSH and LH levels were not altered by the treatment suggesting that the treatment did not effect pituitary-gonadal axis.

9. A possible decrease in androgen binding protein levels in epididymis which could directly block androgen action on the target tissue is also possible thus causing androgen deprived effect.

10. Polyacrylamide gel electrophoresis study revealed that the treatment brought about alterations in electrophoretic mobility of the different protein fractions.

11. Previous findings have concluded that the papaya seed extract is non-estrogenic and causes no toxic side effects.

12. Withdrawal of the treatment for two months in rat revealed that sperm motility and morphology, fertility rate and androgen dependent metabolism of target organs manifested recovery to normal levels.
13. The extract has been found to be efficacious as an antifertility agent in mice, too.

14. The mechanism of action of papaya seed extract seems to be via selective action on epididymis/vas deferens by probably altering the hormone receptor interaction and/or reduced target organ response to androgens by a likely interference with the conversion of testosterone to its metabolites.

15. Functional sterility could be induced by papaya seed extract treatment. It has proved to be an effective, reversible, safe, post-testicular contraceptive in rodents, and should be tested in non-human primate models.

16. The extracts of *Piper betel* leaf and *Euclea arundinacea* tender shoot exhibited potent antifertility activity in male rats.

17. The body and other reproductive organ weights remained unaltered after the treatment of both the extract mentioned above.

18. Cauda epididymal sperm motility significantly decreased resulting in loss of fertility.

19. Sperm count remained unaltered after the betel leaf extract but was significantly reduced after Bamboo shoot extract administration.

20. Calcium exerts an immediate as well as biphasic action
on the motility of cauda epididymal spermatozoa.

21. An appropriate level of calcium seemed necessary for optimal sperm motility.

22. The future course of work includes:

- Ultrastructural studies of caput and cauda epididymides as well as spermatozoa of treated animals to focus the alterations brought about by the treatment.

- Identification of protein fractions present in cauda epididymis to find out which particular protein fraction is affected by the treatment.

- To identify and trace any change in proteins present on the spermatozoa.

- To study the levels of androgen binding proteins in the testis and epididymis.

- To study the levels of $\Delta^4$, $\Delta^\alpha$, and $\Delta^\alpha$-hydroxy steroid dehydrogenase activities in the epididymis.

- To extract the levels of $\text{Na}^+$, $\text{K}^+$, and $\text{Ca}^{++}$ in the serum and epididymis in order to ascertain if an electrolyte balance therein has been affected or otherwise.
- To study calmodulin localization and calmodulin-binding drugs, as is now considered to be one of the major factors in sperm motility.

- Isolation and characterization of the active component in the papaya seed extract and testing of their biological activity is underway at present.