CHAPTER V

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The present study was carried out with special reference to the following:

1. To investigate the contraceptive efficacy of papaya seed extracts, viz. Methanol, Butanol, Mixture of Aqueous : Benzene (1:1) and Aqueous : Alcohol : Benzene (4:2:1) on female mice (Mus musculus).

2. To study the effects of papaya seed extracts on the structure (Histology and ultrastructure) and functions of reproductive organs of female mice.

3. To investigate, if these papaya seed extracts had any side effects on the structure and metabolism of some vital organs and serum parameters. The estrogenicity and LD₅₀ was also checked.

4. To study the reversibility of the induced effects.

Studies on effects of papaya seed extracts as an antifertility agent on female albino mice:

Healthy, adult female albino mice (Mus musculus) were administered different papaya seed extracts (Methanol, butanol, Aqueous : Benzene (1:1) and Aqueous : Alcohol : Benzene (4:2:1) at a dose of 20 mg/kg body weight for 15 and 30 days in order to investigate the effects on its fertility rate. The control and treated animals were maintained on a standard chow and water ad libitum. The treated animals were sacrificed alongwith the control animals and utilised to study various parameters.

The results revealed that:

1. Body and organ weights remained unaffected in all groups of animals. Serum electrolyte balance remained unaffected by the extract treatments as serum Na⁺.
K⁺ and Ca²⁺ levels remained unaltered.

2. The extract treatments did not reveal any estrogenic effects since, estrogen dependent changes in ovariectomized immature female mice were not observed in treated rats when compared to the estradiol treated standard group of animals.

3. The study also elucidated that all the papaya seed extracts did not affect ovarian structure, ovulation and steroidogenesis as is evident from the unaltered levels of 3βHSD, 17βHSD, Cholesterol, Serum FSH, LH, estradiol and progesterone.

4. The changes in uterine biochemical profile and alterations in its histology suggested that the extracts altered the internal milieu of uterus in treated mice which might not be conducive for nidation and implantation. Therefore, the extracts manifested anti-implantation effects.

5. The above mentioned changes together with the absence of implantation resulted in 100% negative fertility rate in treated animals.

6. The study also elucidated that all the extract treatments did not manifest any toxic side effects on the vital organs as is evident from unaltered levels of serum SGOT, SGPT, protein and cholesterol as well as unaltered histology of liver and kidney. The LD₅₀ studies revealed that extracts were non-toxic.

7. In order to ascertain the reversibility of the induced effects, the treatment was withdrawn for a period of 30 days after 15 and 30 days of respective treatments and the data revealed significant recovery in all the induced effects.

8. The fertility rate was restored back to normal suggesting that the effects of the extract treatments were transient and reversible after withdrawal of treatment.
Therefore, functional sterility could be induced in female mice by different papaya seed extracts.

From the work presented in this part of the thesis, the following conclusions could be drawn:

(i) All the papaya seed extracts on oral administration were effective in bringing about a contraceptive effect.

(ii) The extracts manifested a non-estrogenic effect, since estrogen dependent changes were not observed in the extract treated mice.

(iii) The body and organ weights remained unaffected by the treatment which suggests that the extracts did not promote body weight gain.

(iv) Ovarian cholesterol, 3BHSD, 17βHSD, serum FSH, LH, estradiol and progesterone levels remained unaltered suggesting that the extract did not alter steroidogenesis, ovulation or hypothalamo-pituitary gonadal axis as well as cyclicity.

(v) Ovarian histology as well as ultrastructure remained unaltered suggesting that the ovarian structure was not affected.

(vi) Nucleic acid metabolism of ovary and uterus was not affected.

(vii) Uterine histology and secretions were altered with changes in protein, glycogen and phosphorylase which rendered the uterine milieu non-conducive for implantation and resulted in 100% negative fertility rate in the treated mice.

(viii) The extract treatments maintained the electrolyte balance as evident from the unaltered levels of Na⁺, K⁺ and Ca²⁺ in serum.

(ix) The liver histology, protein, glycogen, phosphorylase levels were not altered. The serum transaminases (GOT and GPT) levels remained unaffected, hence
liver functions were not altered.

(x) The kidney histology, protein, creatinine levels remained unchanged suggesting that kidney functions were not affected after treatment.

(xi) From the above data it was evident that the extracts tested were non-toxic as is also revealed by the LD$_{30}$ value of 18 and 20 g/kg body weight which is much higher than the LD$_{50}$ dose of 5g/kg body weight recommended by the WHO as of non toxic nature for a plant product.

(xii) A significant recovery was observed in the fertility potential of the animals and all affected parameters of uterus by the withdrawal of the treatment for 30 days.

(xiii) These animals appeared to be normal and comparable to those of the untreated mice with proven, fertility. Hence, all the seed extracts were effective in inducing functional sterility in the rodent model used.

(xiv) Hence, it could be concluded that different papaya seed extracts were effective at very low doses, were non-estrogenic, non-toxic, had reversible effects, and could be used as an oral female contraceptive agent in rodents.

**Future lines of work**

* Isolation, characterization and identifications of the active component(s) in the papaya seed extract and testing of their biological activity. Some studies in this direction are being carried out.

* Since the contraceptive efficacy of the papaya seed has been established and tested in different rodents, phase I trials should be initiated to test their effect in non-human primates which is presently underway.