The effect of bilateral ovariectomy, different hormonal replacements (E + P combinations) and combined effects of ascorbic acid plus treatments of hormones were studied in female rats for five days, with respect to uterine structure, metabolism and the cyclicity of animals.

Bilateral ovariectomy manifested acyclicity, which is correlated with concomitant decrease in circulating hormonal levels. The significant decrease in uterine weights, protein levels and histoarchitecture are also attributed to the absence of the female hormones. Thus the results revealed that total ovariectomy leads to acyclicity, alteration in structural and functional integrity of uterus, which is a target organ for female sex steroids.

In ovariectomized rats treated with three different dose regimens of estrogen and progesterone, the effects were observed to depend on the dose and type of the hormone administered. The results showed that the animals were in estrus on day of autopsy. The total proteins, glycogen, cholesterol and uterine weights were increased during these
treatments due to the hormones. The ascorbate turnover was also increased, as a result of active mobilization of bound ascorbate to free form, during these treatments. Moreover, the combined treatment of ascorbic acid plus hormone also simulates to some extent, the effects, particularly the anabolic effects of the steroids on the uterus.

Thus the role of ascorbic acid and its mechanism of action have significant bearing in overcoming stress and for the maintenance of the status quo of the female reproductive organs.

Amongst all the treatments it is evident that group I treatment i.e. (0.5 µg) estrogen + progesterone (5.0 µg) and the combined treatment of group III A i.e. (estrogen more (5.0 µg) + progesterone less (0.5 µg) + 100 mg ascorbic acid) were more effective than the others.

The effect of unilateral ovariectomy on ovarian and uterine ascorbate turnover, cholesterol, protein and organ weights and uterine glycogen were investigated and compared with the intact animals. The histocytometry and cyclicity were also recorded.

The data revealed that unilateral ovariectomy resulted in compensatory hypertrophy of remaining ovary associated with histological and biochemical changes in comparison to controls. The ovarian and uterine changes were also noted and have been
correlated with the changes in ovarian steroids, serum gonadotrophins and their feedback on the hypothalamo-hypophysial-gonadal axis.

PART II

A: EFFECTS OF CARICA PAPAYA SEED AQUEOUS, ALCOHOLIC EXTRACT TREATMENT AND WITHDRAWAL

The effects of treatment of rats with aqueous and alcoholic extracts of Carica papaya seeds for 7 and 15 days were studied on the histophysiology of their ovaries and uterus; estrus cycle, fertility rate and the uterine contractility. The possible reversibility of the induced effects were also investigated.

The results revealed that the effects were more pronounced in ovary than the uterus and more so by the aqueous extracts. The changes in biochemical profile, and the histology of ovary and uterus involved alterations in the levels of protein, ascorbic acid, glutathione, cholesterol and glycogen. The increase in ascorbate turnover is an adaptation to overcome the harmful effects of the extracts.

The fertility test was 100% negative and the estrus cycle was irregular with the predominance of diestrus.

The two extracts manifested antiestrogenic or estrogenic effects depending on the duration of the treatment and also
anti-anabolic, anti-implantation and abortifacient effects. These have been related to the alterations in histophysiology of the ovary and uterus, its enhanced contractility, irregular cyclicity and reduced mating behaviour in the treated animals.

The above mentioned changes indicate a probable disruption of hypothalamo-pituitary-gonadal axis by the extracts and/or due to direct effect of the extracts at the gonadal level.

The withdrawal treatment overcame the adverse effects of the treatments in ovary and uterus and restored the fertility. Therefore, functional sterility could be induced in rats by short term treatments with *Carica papaya* seed extracts.

B: The effects of *Vinca rosea* leaf extracts on female rats were by and large, similar to those observed by *Carica papaya* seed extracts, but comparatively lesser in potency. The pattern of recovery also closely paralleled those which were observed earlier after *Carica papaya* seed extract withdrawal.

**PART III**

**STUDIES ON EFFECTS OF VARIOUS COPPER WIRE DEVICES**

The effects of extra-uterine and intra-uterine copper wire devices on female reproductive processes were studied for 20 days. The device bearing rats showed 60% and 100% negative fertility rate respectively. The data revealed that
the copper implant device brought about an increase in ascorbate metabolism of both ovary and uterus, changes in their structure and metabolism which were more marked in rats of group V. The cyclicity and fertility rate were also altered. The changes in the ovary signifies that the ovulation was not inhibited by copper IUD. The ovary contained nevertheless atretic primary, secondary and Graffian follicles, particularly in rats of groups IV and V.

The uterine changes in endometrium and myometrium of copper device bearing rats indicate sloughing with cell debris in the lumen, or proliferation of the endometrium and an inflammatory reaction. The sub-epithelial region of uterine endometrium showed nuclear pyknosis. These data suggest that the endometrium in the presence of an intra-uterine copper device requires higher levels of ovarian steroid, for maintenance.

The effects of copper on the ovary and uterus are attributed to its spermicidal and anti-implantation effects and through interference with the action of female sex steroids at their target sites. However, a local toxic action of accumulated copper on the ovary and uterus also, cannot be ruled out and the protective effect of ascorbic acid in copper toxicity has been emphasized.
PART IV

EFFECTS OF PROSTAGLANDINS:

The effects of administration of prostaglandins $E_1$ and $F_2\alpha$ ($PGE_1$ and $PGF_2\alpha$) for four days on the ovary and uterus of albino rats was studied.

The estrogen and progesterone dependent parameters were reduced but the organ weights were increased showing a growth promoting effect of prostaglandins, but they altered the redox milieu of the ovary and uterus and thereby affected their structure and metabolism.

The prostaglandins act directly on the ovary or via the hypothalamo-pituitary-gonadal axis and cause luteolysis, irregular cycles and partial antifertility effects by influencing uterine contractility.

PART V

The effects of vitamin C deficiency (for 21 days) in female guinea pigs were investigated on their ovarian and uterine histophysiology, contractility of uterus, estrus cycle and ascorbic acid localization.

The results revealed marked changes in histology and metabolism of the ovary and uterus which have been attributed to the disturbed physiology under induced stress conditions. The results also suggest a probable deficiency of sex hormones
due to reduced steroidogenesis, since the female sex hormone dependent metabolism and structural integrity of ovary and uterus were affected and accumulation of cholesterol occurred. The cyclicity was disrupted, uterine contractility was reduced and fifty percent reduction of fertility occurred.

The overall reduction in ascorbate metabolism suggests that the redox milieu of the ovary and uterus are affected since ascorbic acid is known to be involved in their metabolism via formation of its free radical.

The data elucidates the importance of vitamin C for maintenance of structure, metabolism and redox milieu of ovary and uterus conducive to their normal functioning.