

Histopathological effect of carica papaya seeds on reproductive organs of female

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Abstract-Carica Papaya (Papita) is a fruit eating plant but unripe fruit and seeds are said to impair the reproductive function of male and female animals including human beings,. To assess the above activity the dried seed powder of this plant was administered orally as aqueous suspension at doses of 10, 20 and 30 mg /kg / rat to adult female albino rats for 30 days. All the rats were killed, weighed and their reproductive organs- ovary and uterus were taken out. These organs were processed for pathological examination. The maximum dose (30mg/kg) caused a significant reduction in genital organs weight. There was no effect on body weight. Cellular organization of ovary and uterus was affected leading to total degeneration. Atrophic changes were found in both ovary and uterus in treated female rats. It appears that the seed powder of Carica papaya have contraceptive properties.

Keywords: Carica Papaya, Phytotherapy, Herbal drugs, Reproductive organs, Contraception.

Introduction

Carica Papaya (Papita) is a popular edible fruit plant. Various parts of this plant has been used as therapeutic agents in Ayurvedic medicine. It is said that consumption of raw (unripe) fruit with latex (milky juice) causes abortion in pregnant women. Recently, various parts of this plant such as latex of green fruit (Rosen and Milman, 1955), unripe fruit pulp (Garg and Garg, 1970, 1971) oil from unripe fruit pulp (Garg, 1974) and seeds (Sareen et.al., 1961, Bodhankar et al, 1974) had reported for control of fertility of female rats. Dar et al (1965) reported ant helmintic property in seeds. Das (1980) reported anti spermatogenic effect of seeds in male albino rats. Singh and Singh (1992) studied

anti-implantation effect of seeds in female albino rats. Singh (2008) also reported anti spermatogenic effect of seeds in male House sparrow (*Passer domesticus* Linn). From the above studies, it appears that seeds of *Carica papaya* has strong antifertility activity. No research work on its histopathological effects on female reproductive organs has been reported therefore, present study was under taken and the results are presented in this paper.

Phytochemistry

Active chemical substance from seeds of *Carica papaya* was isolated and named as carpasemine. Its melting point is 165⁰C and molecular formula is C₈H₁₀N₂S. Chemical properties of this compound together with its degradation products have been studied and some new derivatives have been prepared from it. A carpasemine have been identified as Benzlythiourea or Banzylthiocarbamide by mixed melting point with the synthetically prepared Benzylthiourea. This research was performed by Panse and Paranjape, 1943). Nineteen different carotenoids were identified in the fruit and a major being cryptoxanthene. Oxycarotenoids were higher in preportion as compared to carboxhydrocarbons. The percentage of cryptoflavin and Beta Carotene were 13 and 29.5 respectively (Subbarayan and Cama, 1964).

The mass spectrum of Pseudocarpain isolated from plant showed that it was dimeric. The fragmentation pattern observed for pseudocarpain was identical with that of carpaine but for minor difference in the relative intensities of the ions. The two alkaloids had the same gross structure. Pseudocarpain on acid hydrolyses yielded carpamic acid and pseudocarpamic acids (Govindachari et al, 1965).

Material and Method

Adult, healthy with regular cyclicity, 20 in number weighing between 100 to 125 gms female albino rats (*Rattus rattus norvegicus*) were selected from our laboratory maintained animal house for present experimental study. Four groups of female rats, each group with five rats were made 1st group served as control and 2nd, 3rd and 4th group served as experimental or treated group with seed powder doses. The dried seed powder of *Carica papaya* was dissolved in distilled water (w/v) in such a way that 10mg powder corresponded to 01ml of water. Thus, 10mg/kg/ rat administered orally to 2nd group of rat with the help of soft catheter tube fitted into a syringe. Similarly, other doses 20 and 30 mg/kg/ rat were prepared and administered to 3rd and 4th group of female rats. The gum acacia powder was added at the rate of .01mg/dose in all the doses. The 01mg/kg/rat gum acacia powder dissolved

in distilled water was given at the rate of 01ml/rate as vehicle to the control female rats in the similar manner as given to powder treated group of rats, The doses were given daily for 30 days to all the rats, control and experimental rats. Before the start of experiment, the weight of each rat was recorded. The rats were maintained under uniform husbandry condition provided with proper feed (Hindustan Levers Ltd.) and drinking water.

On day 31st, the rats of all groups were weighed and sacrificed or killed with chloroform. The ovary and uterus from each rat were dissected out, freed from surrounded tissues, blotted on filter paper and weighed quickly on a semi micro balance for histological studies. The ovary and uterus of all rats, control and powder treated were fixed in Bouin's fluid over night, washed in distilled water, dehydrated in xylene. Now the organs were transferred to the molted paraffin wax and embedded in paraffin blocks, Thus, the blocks were made. The thin sections of ovary and uterus blocks were cut at 6 micron using Rotary Microtom. Slides of ovary and uterus were stained with haemotoxylene and eosine

dyes. Thus slides of orary and uterus prepared and studied for histopathological changes and photographed. The histological changes were described. The data were statistically analyzed by student 't' test. P<0.05 was considered as significant in comparison to control group of female rats. All the experiments were conducted and supervised as per guidelines of institutional, Animal Ethical Committee, appointed by the than Principal of College.

Observations

Effect on Body and Reproductive organ weight

Table 1 depicts the changes in body and ovarian and uterine weight. The control group of rats did not reflect any change in body weight and both the reproductive organ weight. It was maintained through out experimental period. No depletion in body weight was seen at any dose level of Carica papaya seed powder treatment the weight of ovary and uterus was decreased at the doses of 20 and 30mg/kg/rat. The significant reduction in weight was noticed at 30mg/kg/dose in both the reproductive organs.

Table-1 Effect of Carica papaya seed powder on body (gms) and reproductive organs weight (Mgms) of female rats treated with 20 and 30 mg/kg doses for 30 days .05 rats were included in each group. Values are mean ± standard error

Doses (mg)	Body weight (gm)		Reproductive organ weight (Mgms)	
	Initial	Final	Ovary	Uterus
Central	100 ± 3.50	132.5 ± 3.91	50 ± 3.64	80 ± 5.65
10 mg	110 ± 2.42	130 ± 2.66	45 ± 5.20	70 ± 3.50
20mg	118 ± 3.35	126 ± 4.25	18.8 ± 1.10*	30 ± 3.7*
30mg	125 ± 1.29	120 ± 2.50	16.2 ± 1.20*	24 ± 1.60*

*Significant p values < 0.05

Effect on histology of reproductive organs

Effect on ovary

The histology of ovary of control female rats did not show any change in structural organization. The normal cellular structures revealed well developed corpora lutea, developing follicles (Primary and secondary and mature or gravid follicles) with defined ovum (egg). The germinal epithelium and vascularity appeared normal in loose stroma (**figure-1**). The dose 10mg/kg for 30 days of regular feedings of Carica papaya seed powder caused no atrophic changes in follicles of ovary. The vascularity appeared normal in loose stroma. No change in structure of developing and mature follicles.

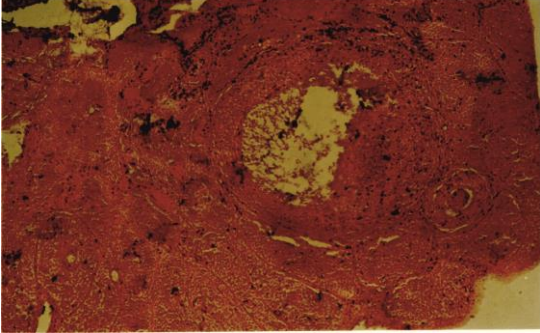
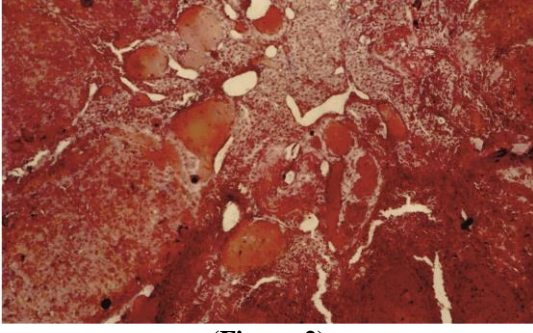
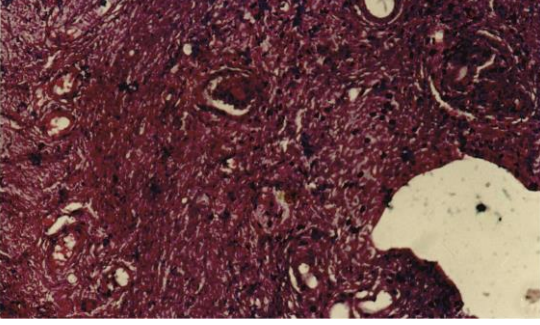

The doses 20 and 30mg /kg administration for 30 days caused serious atrophic (degenerative) changes in the ovary. Maximum untoward (degenerative) effect was noted at 30mg/kg dose. It caused mass atrophy of developing and mature follicles. Nuclear degeneration noted in all ova (Eggs) of mature follicles. No corpora lutea were observed. They also showed atrophic changes. Similarly, very less number of developing (Primary follicles) were seen towards germinal epithelium.

Vascularity affected as no blood vessels observed in stroma (**figure-2**)

Effect on Uterus

The uterus of control group of rats shows normal histo architectural features. The endometrium made up of columnar epithelial cells. They show mitotic nuclei and leucocytic infiltration. The uterine cavity or lumen was wide. The uterine glands were tortuous and irregular with distended lumen. The musculature appeared well developed. The stroma and vascularity seen quite normal (**figure-3**)

The dose 10mg/kg for 30 days of administration caused no changes in histology of uterine cellular structure. No untoward effect was noted in endometrium, myometrium and luminal epithelium. The uterine cavity or lumen was fully distended. The uterine glands were normal and tortuous. Musculature and vascularity appeared normal. It was comparable to uterus of control female rats. The dose 20 and 30mg/kg for 30 days appeared very effective to cause deleterious changes in uterine histoarchitecture. The 30mg/kg dose was found to be maximally effective dose. This dose caused shrinkage and atrophy in uterine glands, reduction in uterine cavity (lumen) and height of endometrium. Musculature and vascularity were reduced (**figure-4**)

 <p style="text-align: center;">(Figure-1)</p> <p>T.S. of ovary of female rat of control group (Vehicle treated) for 30 days shows normal cellular structure with organized germinal epithelium, all types of follicles (Primary, developing to mature follicles) and corpora lutea, stroma and vascularity also appear normal x 150</p>	 <p style="text-align: center;">(Figure-2)</p> <p>T.S. of ovary of female rat of treated group with seed powder of Carica papaya at doses of 20 and 30 mg/kg/day for 30 days shows small maturing follicles with degenerated ovum. Many atretic follicles and less corpora lutea. Poor vascularity and compact stroma x 150</p>
 <p style="text-align: center;">(Figure-3)</p> <p>T.S. of uterus of female rat of control group (Vehicle treated) for 30 days shows normal histological structure with organized myometrium and endometrium. Well developed uterine glands (Tortuous) in stroma. Wide uterine lumen (Cavity) with epithelium and vascularity x 150.</p>	 <p style="text-align: center;">(Figure-4)</p> <p>T.S. of uterus of female rat of treated group with seed powder of Carica papaya at doses of 20 and 30mg/kg/day for 30 days shows atrophic changes in uterine histoarchitectures, shrinkage of musculature (Myometrium) with less developed endometrium and narrowed uterine lumen (cavity). Reduced vascularity and epithelial cell height x 150</p>

Discussion

In the present study no reduction in body weight was noted after 30 days of administration of three doses of Carica papaya seed powder as a drug. The ovarian and uterine weight was reduced significantly with increasing doses i.e. 20 and 30mg / kg/rat for 30 days ($P < 0.05$). The present study also revealed histopathological changes in female reproductive organs i.e. ovary and uterus.

The response of a drug depends upon the dose and duration of treatment. The changes in female reproductive organs weight is controlled by ovarian hormones – Estrogen and Progesteron. Formation of follicles with normal ova (Egg), ovulation, fertilization, implantation and maintenance of estrus cycle / menstrual cycle are also controlled by these hormones as described above through Pituitary gland (Lerner,

1969). The petroleum ether extract of pulp of *Carica Papaya* showed significant antifertility activity in female rat (Garg and Garg, 1971). Latex of Green fruit have been reported to possess Oxytocic activity. The seeds decreased fertility of albino female mice (Sareen et, al 1961). Various compounds isolated from seeds of this plant, only Benzylthiourea was found most potent and found to be responsible for anthelmintic and antifertility activity. It did not cause toxic symptoms even at doses of 30mg/kg in rats (Dar, et. al., 1965)

The results noted in the present study on histopathological changes in ovary and uterus due to oral administration of *Carica papaya* seed powder as aqueous solution at doses of 20 and 30mg/kg/day for 30 days are comparable of the study done by Chakraborti et.al., 1968) in which the female rats were fed with green leaves of *Aristolochia odoratissimus*. Follicular atresia and other degenerative changes were observed in this study. Similar results were reported by Kholkute and Udupa (1974) following the administration of flowers of *Hibiscus rosa sinensis* Linn. Both ponderal (organ weight) and histological changes in ovary and uterus respectively were reported (Prakash, 1979) through administration of *Embelia ribes* seeds in female albino rats. Dixit (1977) reported effect of chronically administered *Malva Viscus conzattii* flower

extract in female genital tract of female Indian gerbel (*Meriones-hurriani*, Jerdon) which is a rodent like albino rat. The dose 25mg/kg was given for 20 days. it caused degenerative changes in ovary. Corpora lutea were also affected in this study. *Carica papaya* seed also caused similar effects in ovary and uterus of female albino rats as described above. Chinoy et al (1995) revealed that when an aqueous extract of *Carica papaya* seeds were administered in female albino rats, it was found to cause contraction of rats uterus stripes. Singh et al (2000) reported degenerative effects in female genital organs of albino rats with the administration of seeds of *Randia dumetorum*. Singh (1917) also reported anti fertility and histopathological changes in female reproductive organs with the administration of leaves powder of *stevia rebaudiana*.

From the present investigation, it may be concluded that the *Carica papaya* seeds has potentiality to impair fertility of female mammals by causing histopathological changes in female reproductive organs and can be used in family planning programme

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Disclaimer Statement

Authors declare that no competing interest exists. The products used for this research are commonly used products in research. There is no conflict of interest between authors and producers of the product.

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