EFFECT OF PAPAYA (*CARICA PAPAYA* LINN) ON PREGNANCY AND ESTROUS CYCLE IN ALBINO RATS OF WISTAR STRAIN

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Summary: The antifertility effects of *Carica papaya* were investigated by feeding adult cycling and pregnant rats with different components of its fruits. No attempt was made to force-feed the animals. The results indicate that unripe fruits of papaya interrupt estrous cycle and induce abortions. The abortifacient property seems to decrease as the fruit becomes stale or ripe. Exogenous progesterone counteracts partially the adverse effects on pregnancy and the surviving foeti are without any distinct malformations.

Key words: abortion estous cycle papaya progesterone

INTRODUCTION

The control of fertility through the agents of plant origin is an attractive proposition advocated by several systems of indigenous medicine. Some plants reported to be useful for the control of conception are known to exhibit anti-hormonal properties (13). The milky juice of the unripe fruit of *Carica papaya,* if applied to the *os uteri,* is believed to interrupt pregnancy in women. The unripe fruits and seeds are described as powerfully emmenagogue, galactagogue and abortifacient (2, 3, 10, 11). However, there appears to be no systematic information regarding the anti-fertility effects of papaya on the laboratory mammals and hence this investigation was undertaken.

MATERIALS AND METHODS

The albino rats used were of Wistar strain from among the colony maintained in the animal house but they were originally from the Central Food Technological Research Institute, Mysore (India). The vaginal smears were observed daily between 5 and 6 p.m. and those rats in pro-estrous were housed overnight with males of proven fertility. The rats showing cornified cells and sperms in their smears on the subsequent morning were separated and this day was designated as day zero (Do) of pregnancy (6). They were divided into groups and treated as follows :

Experiment Ia : The controls were fed on the normal chow throughout the experiment while the treated were given unripe fruits of papaya (Table I). No effort was made to force-feed the animals.

Experiment Ib : The animals were fed on different components of the fruit such as unripe, ripe or stale papaya, seeds and crude papain mixed with or without normal chow.

Experiment Ic : Progesterone (VPC Institute, New Delhi) 5 *mg* per 100 *g* weight of the body

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in 0.2 *ml* olive oil (16), was administered subcutaneously during treatment while the controls received an equal volume of the vehicle for the same duration. All the rats were maintained individually exposed to natural light, water *ad libitum* and on the normal chow except otherwise stated. The weight of the body and the vaginal smears were recorded daily and the animals were laparotomised on day 8 under light ether anaesthesia and outopsied on day 13 of pregnancy to note the foetal sites. The different organs such as uteri, ovaries, adrenals, thymus, thyroids and pituitaries were dissected out and weighed on a torsion balance. The weight of thyroids was noted after fixing them in Bouin's fluid and later transferring on to 70 per cent alcohol.

Experiment II : Adult cycling females were treated with papaya and their estrous cycles were studied.

RESULTS

Effect on pregnancy : The fertility of the colony is high as seen from the number of foetal sites of the controls at autopsy (Table I). A post-implantation loss of 5.6 per cent recorded in this strain compares favourably with the observations elsewhere (7). The implantation of blastocysts occurs in rats sometime during day 5 through 6 of pregnancy (17). Rats treated with unripe papaya register a marked reduction in their foetal sites and the treatment during the post-implantation days is very effective when compared with the other days. If the treatment is commenced from Do and continued upto D8 of pregnancy the implantation sites are reduced in size. The treatment from D5

Table I: Effect of feeding papaya fruit on pregnancy in Albino rats.

Treatment	*Number of rats pregnant at*		*Implantation sites M±S.E.*			*Post-implantation loss (per cent)*
	Mated	*Laparotomy*	*Autopsy*	*Laparotomy*	*Autopsy*	
Control:						
day 0-13 normal chow	15	15 (A)	15 (C)	7.5±0.6 (E)	7.1±0.6 (G)	5.6
Treated :						
Papaya 30 g/100 g b.w. from						
day 0—3	5	3	3	3.8±1.6	3.6±1.6	5.3
,, 3—5	5	3	3	3.6±1.6	3.4±1.4	5.6
,, 5—7	5	5	1	8.6±0.8	2.0±2.0	76.7
,, 6—8	5	5	3	8.5±2.0	4.8±0.8	43.5
,, 7—8	9	9	4	8.7±0.7	3.5±1.4	59.8
,, 9—10	5	5	3	8.0±0.8	4.8±2.1	39.9
,, 4—8	15	15	0	9.3±0.6	—	100.0
,, 0—8	10	2	0	0.7±0.1	—	100.0
Total	59	47 (B)	17 (D)	6.5±0.5 (F)	2.1±0.5 (H)	67.7

Comparison between control and treated groups
percentage pregnant at laparotomy A vs B $X^2 = 2.679$ $P > 0.05$
percentage pregnant at autopsy C vs D $X^2 = 24.762$ $P < 0.001$
In mated rats : Mean number of implantations at laparotomy E vs F $t = 3.736$ $P < 0.001$
,, at autopsy G vs H $t = 6.224$ $P < 0.001$
Post-implantation loss is the discrepancy between the number of implantations at laparotomy and autopsy.
M ± S.E. = Mean in relation to standard error. b.w. = body weight.

to D7 and D4 to D8 records maximum litter-destroying effect. The interruption of pregnancy occurs sometime between day 9 and 11. This can be made out from the bleeding that occurs during the vaginal smear examination. However, the termination of pregnancy does not impair the ovarian function for long since these rats come to estrous within 3 to 4 days after abortions. Further, they mate and bear normal foeti again.

Effect on the body and organs : The controls record an increase in the weight of their body by 9 per cent due obviously to the maintenance of pregnancy. The treatment towards the post-implantation days shows a reduction in the weight of the body. However, no correlation between the loss in the weight of the body and the extent of damage to pregnancy can be made out. With regard to the variations in the weights of organs uterus alone shows significant changes. The control uterus is heavy on day 13 of pregnancy when the foetal sites are well marked. As a result of abortions occurring in the treated animals the uterine weight decreases considerably and its appearance is like that of cycling females. Abortifacient property of papaya shows a marked reduction when it becomes stale or ripe (Table II). Some of the rats treated with stale papaya fail to respond to treatment and when they are allowed to term the young ones born are without any distinct malformations. Similarly the administration of progesterone exogenously (Table III) during treatment has a favourable effect on pregnancy. These rats, also, carry normal pups.

Table II : Effect of stale, ripe papaya *etc.*, with or without normal chow on pregnancy.

Treatment	*Mated*	*Number of rats pregnant at*		*Implantation/foetal sites (M±S.E.)*		*Per cent post-implantation loss*
		Laparotomy	*Autopsy*	*Laprotomy*	*Autopsy*	
Control (Do-13) normal chow	15	15	15	7.5±0.6	7.1±0.6	5.6
*Treated (papaya D4-8)	15	15	0	9.3±0.6	—	100.0
,, stale papaya D4-8	5	5	3	6.6±0.7	3.2±1.4	51.5
,, ripe papaya D4-8	5	5	2	7.6±2.0	3.2±3.9	57.9
,, chow + papaya D4-8	5	5	5	5.6±0.9	5.4±0.8	3.6
,, seed + chow D4-8	5	5	5	5.8±0.8	5.6±1.1	3.5
,, papain + chow D4-8	5	5	5	6.8±0.8	6.2±0.6	8.8

* data as in Table I.

Table III: Effect of administering progesterone to papaya-fed pregnant rats.

Treatment	*Mated*	*Number of rats pregnant at*		*Implantation/foetal sites (M±S.E.)*		*Foetal survival per cent*
		Laparotomy	*Autopsy*	*Laparotomy*	*Autopsy*	
* Control (D-13) normal chow	15	15	15	7.5±0.6	7.1±0.6	94.4
Oil treated control	5	5	5	6.6±1.1	6.6±1.1	100.0
Papaya treated control	15	15	—	9.3±0.6	—	—
Treated: (papaya-fed + progesterone	10	10	7	7.7±0.7	4.5±1.1	58.4

*data as in Table-I
control vs treated $X^2 = 14.583$ $P < 0.001$
M±S.E. = mean in relation to standard error.

Effect on estrous cycle : Adult cycling females fed on papaya show continuous diestrous and on discontinuing the treatment they revert to the normal cycle.

DISCUSSION

The pharmacological screening of plants reputed to have anti-fertility activity has been undertaken by several investigators (3, 13-15, 19). Estrogens and estrogen-like substances are indicated in many essential oils (1, 8, 18). Emmenagogic property is a feature of estrogens. The other properties exhibited by the plant extracts are direct cytotoxic and anti-hormonal effects on pregnancy or on the cellular metabolism. The seeds of *Abrus precatorius* show adverse effects on pregnancy and the foetal growth in mice (15). Rottlerin from *Mullatuo philipinensis* is reported to interrupt the estrous cycle in mammals and it possesses hormonal and anti-hormonal properties (20). The petals of *Butea frondosa* flowers possess anti-estrogenic activity (21).

The present investigation shows that the unripe fruits of papaya induce abortions in rats. The treatment towards the post-implantation days is very effective when compared with the other days. The termination of pregnancy occurs sometime between day 9 and 11 and these rats come to estrous within 3 to 4 days after the abortions. Thus, there is rapid recovery in the uterine and the ovarian functions. Since nutritional deficiencies are known to induce the foetal wastage (12) this possibility can not be ruled out in this study. This is particularly true in the case of treatments for prolonged periods such as from day zero to 8 and D4 to 8 of pregnancy. The loss in the weight of the body may be taken as an index of the nutritional status of the animals. The percentage loss in the weight of the body does not correlate well with the extent of damage to pregnancy. When the rats show cent per cent abortions during treatment from D4 to 8 of pregnancy the loss in the weight of the body is 5 per cent while there is a gain by 10 per cent during treatment from D5 to 7 of pregnancy with a foetal loss of 72 per cent. When stale and ripe papaya is used the pregnancy-terminating effect decreases by 50 per cent though the nutritional status has not improved. No adverse effect on pregnancy is noticed when the fruit is given as a supplement to the normal diet. This may be due to the fact that the consumption of the fruit and/or its absorption may decrease when it is mixed with the normal chow.

The hormonal requirements for the maintenance of pregnancy in many mammalian species are discussed by several investgators (4, 16). The pregnancy-terminating effect of papaya can be partially countered by administering progesterone exogenously. The fruits of papaya possess anti-helminthic property (10) and it is said that anti-helminthic substances may act as anti-fertility agents (16). The fruits does not seem to possess estrogenic activity since the adult females show interrupted estrous cycle during treatment.

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