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RESEARCH ARTICLE

EFFECT OF *CARICA PAPAYA* FRUIT EXTRACT ON HORMONAL PROFILES OF MALE ALBINO RATS

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ABSTRACT

The present study was carried out to investigate the effect of fruit pulp extract of *Carica papaya* (seeded and seedless fruits) on male albino Wistar rats. The experimental animals were divided into three groups, One group served as control, Group- II , received papaya pulp extract from seeded fruits and Group - III received papaya pulp extract from seedless fruits. Both groups were orally administered with pulp extract (10ml/kg/body weight) for 60 days. Pituitary gonadotropins (LH, FSH) and steroid hormone (testosterone) analysis was carried out on 21st, 41st and 61st day. There was a significant decrease ($p<0.05$) in the concentration of LH, FSH and testosterone on the 20th, 40th and 60th day. These results may indicate that *Carica papaya* fruit pulp extract of seeded and seedless possess antifertility adverse effects.

INTRODUCTION

Several plants are traditionally used as birth control agents by the rural people of India. *Carica papaya* is a plant amid few whose fractions have been exploited and documented for its antifertility properties (Lohiya *et al*., 2005; Kusemiju, *et al*., 2012). *Carica papaya* seeds had been used as fertility control agents in some animal models and even on human beings (Lohiya *et al.,* 2004; Udoh and Kehinde, 1999). They contain active ingredients such as Caricin, an enzyme Carpasemine, a plant growth inhibitor and Oleanolic glycoside (Emeruwa, 1982) the last of which caused sterility in male rats (Das, 1980). However, little is known about the exact mechanism by which *Carica papaya* extract effect the testes negatively to bring about infertility in male rats. Most of the achievement in male contraception is confirmed to improving the already existing barrier and sterilization methods (Nass and Straus 2004, Fpa 2006). Recently efforts are being devoted to identity a plant based male contraceptive that is supposed by orally bioactive, non-toxic and more important cost effective based on ethano medical information (Lohiya *et al.,* 2001). The quest for the development of a male contraceptive particularly from natural sources has led to the discovery of the antifertility efficacy of the seed of some species of *Carica papaya*. The locally available and widely distributed *Carica papaya* seed have shown great promise in male contraception in animal models (Verma and Chinoy, 2001; Lohiya *et al.,* 2001; 2006; Hamman *et al.,* 2011). The present work was carried out to evaluate the claimed antifertility effect of aqueous extract of seeded and seedless papaya pulp extract in adult male Wistar rats.

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MATERIALS AND METHODS

Plant Materials used for the study

Unripe seeded and seedless *Carica papaya* fruits were commercially obtained from local market. The fruits were washed, outer skin and the inner seeds were removed. The aqueous extract of the pulp was prepared with required amount of distilled water with a blender.

Experimental animals

Healthy male Wistar strain rats weighing about 100-125g were used in the present study. The animals were bred and housed in polypropylene cages under standard environmental conditions at temperature (25 ± 2°C). The animals were fed with standard pellet diet (Goldmohur brand, M.S Hindustan Lever Ltd.,) They were maintained in layers mesh, exposed to a 12h light: 12h dark cycle and water *ad libitum*. Animals were treated humanely. Care and supervision were provided throughout the period of study. The study protocols were duly approved by the ethical committee Regn.No. CPCSCA/CA/ORG/2006/65/4. Studies were performed in accordance with the CPCSEA guidelines.

Experimental design

Group I: Control animals which received normal feed and water.

Group II: Experimental animals which received normal feed and oral administration of seeded papaya fruit juice (10ml/kg body weight/day) for a period of 60 days.

Group III: Experimental animals which received normal feed and oral administration of seedless papaya fruit juice (10ml/kg body weight/day) for a period.

The animals were acclimatized to laboratory conditions for a week with normal feed and water before the start of the experiment. The pulp extract was given daily at 9.00AM by a gastric catheter. The animals were sacrificied by cervical decapitation. Blood was collected and serum was separated by centrifugation at 3000 rpm for 10 minutes and was stored in sterilized vials for hormone analysis.

Hormone Assay

Analysis of pituitary gonadotropins (LH and FSH) and steroid hormone testosterone was performed on on 21^{st}, 41^{st} and 61^{st} day of the experimental period. The quantitative determination the hormones was done by using Chemiluminescence Immuno Assay (CLIA) detection method using microplate luminometers.

Statistical Analysis

Data was expressed as Mean ± SD. Student's t test was used for statistical comparision.

RESULTS

Male albino rats were orally administered with extracts of seed papaya fruit juice and seedless papaya fruit juice for a period of 60 days (10ml/kg body weight/day). Pituitary gonadotropins LH and FSH which are peptides in chemical nature and steroid hormone testosterone was analysed in serum samples obtained from different days of the experimental period. The results show a significant decrease in the level of pituitary gonadotropins, LH and FSH in both the groups of animals during the 20^{th}, 40^{th} and 60^{th} day when compared with the control animals (Table 1 & 2). The activity of steroid hormone testosterone decreased significantly on the 20^{th}, 40^{th} and 60^{th} day in both the experimental groups when compared with control animals (Table 3). But the decrease was more predominant in the animals which received normal feed along with seed papaya fruit juice when compared with that of the controls.

DISCUSSION

Studies on the effects of the plant products on male reproductive system and fertility are comparatively few and far fetched. The present paper will provide a number of observation regarding the effects of aqueous extract of *Carica papaya* seed and seedless fruit pulp on testicular function in male albino rats. Hormonal measurement has limited but important role in the assessment of gonadal dysfunction. The development of normal mature sperm is the key to optimum male fertility. The production of the sperm cells and testosterone in the testis are mainly regulated by follicle stimulating hormone (FSH) and lutenizing hormone (LH) which are released from the anterior pituitary.

Table 1. Effect of *Carica papaya* fruit extract on the levels of serum LH in male albino rats

Experiment Period	Control Normal feed + water	Experimental group I Normal feed +Seed Papaya fruit juice	Experimental group II Normal feed + Seedless Papaya fruit juice
20^{th} day	0.39 ± 0.007	0.25 ± 0.009*	0.28 ± 0.008**
40^{th} day	0.42 ± 0.005	0.16 ± 0.004**	0.20 ± 0.006***
60^{th} day	0.45 ± 0.006	0.10 ± 0.007***	0.17 ± 0.007**

Values are expressed as µIu /ml
Values are Mean ± SD (n=6) obsevations
Statistical significance denoted as *p < 0.05 ; **p < 0.01; ***p < 0.001 (Compared between Control Vs Experimental Group I ; Control Vs Experimental Group II)

Table 2. Effect of *Carica papaya* fruit extract on the levels of serum FSH in male albino rats

Experiment Period	Control Normal feed + water	Experimental group I Normal feed + Seed Papaya fruit juice	Experimental group II Normal feed + Seedless Papaya fruit juice
20^{th} day	3.51 ± 0.008	1.60 ± 0.002**	1.52 ± 0.004**
40^{th} day	3.57 ± 0.004	1.52 ± 0.011**	1.45 ± 0.008**
60^{th} day	4.11 ± 0.001	1.32 ± 0.010***	1.30 ± 0.010***

Values are expressed as µIu /ml
Values are Mean ± SD (n=6) obsevations
Statistical significance denoted as **p < 0.01; ***p < 0.001 (Compared between Control Vs Experimental Group I ; Control Vs Experimental Group II)

Table 3. Effect of *Carica papaya* fruit extract on the levels of serum testosterone in male albino rats

Experiment Period	Control Normal feed + water	Experimental group I Normal feed + Seed Papaya fruit juice	Experimental group II Normal feed + Seedless Papaya fruit juice
20^{th} day	549.83 ± 1.32	116.62 ± 0.01***	136.50 ± 0.01***
40^{th} day	551.66 ± 1.36	143.50 ± 0.02***	246.45 ± 0.01***
60^{th} day	560.10 ± 1.41	107.33 ± 0.01***	150.61 ± 0.07***

Values are expressed as ng /dl
Values are Mean ± SD (n=6) obsevations
Statistical significance denoted as ***p < 0.001 (Compared between Control Vs Experimental Group I ; Control Vs Experimental Group II)

FSH stimulates spermatogenesis in the Sertoli cells, seminiferous tubules, while LH stimulates the production of testosterone in Leydig cells of the testis. Many studies on the testis of rats treated with plant extracts has demonstrated the inhibitory activity on the proliferation of spermatogonia in mammals (Hulethel and Lunenfeld, 2004). The present study also showed a marked decrease in the levels of LH and FSH. Testosterone is required for the maintenance of accessory sex organ function, hence reduction in the serum level of testosterone will lead to the atrophy of testis. The low plasma testosterone concentration indicates primary testicular dysfunction. The present study showed reduction in testosterone level in rats administered orally with papaya pulp extract from seeded and seedless fruits. The decrease is correlated with the duration of the experimental animals which received the fruit pulp extract. This is in agreement with other findings by Parshed *et al* (1994) indicating significant decrease in testosterone level in rats receiving neem aqueous extract. Testosterone low level may be attributed to leydig cell failure (Dafalla *et al.*, 2012; Mahmoud *et al.,* 2003; Yama *et al*., 2011c). This may be either to be as a result of direct effect of the extract on the germinal epithelium or indirect effect through its action on the pituitary gonadotrophs that influence normal spermatogenesis.

The present study revealed reduction in the serum level of testosterone which could probably be due to the decrease of serum levels of LH and FSH observed. Leydig cells secrete testosterone by the stimulatory effect of LH. In males reduction in testosterone level may impair spermatogenesis and cause male infertility. The diminution in the activities of testicular 3β hydroxysteroid dehydrogenase and 17β hydroxy steroid dehydrogenase the key enzymes for androgen formation may be due to inhibition in pituitary gonadotropin secretion (Uttam Kumar Das *et al.,* 2006). In conclusion the data of our study suggest that the aqueous extract of papaya pulp from seeded and seedless fruits results in the diminution of plasma LH, FSH and testosterone along with inhibition in spermatogenesis. The actual mode of action of this papaya pulp extract for its hypogonadal activity is not clear and more information is necessary for better understanding of the effect of this pulp extract and its active metabolites/compounds from papaya on the functional physiology of the reproductive system. This study creates a hope to develop a new drug from an herbal product in this new era of herbal drug technology. The antifertility drug from plant will be more acceptable for economic reasons in terms of self reliance. Further studies are needed to prove whether the alternations are reversible or permanent after cessation of treatment and for understanding the exact mechanism as the present study duration suggest marked alterations in the male reproductive organs.

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