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EFFECT OF CARICAPRYL-99 SEED ALKALOID EXTRACT ON THE SERUM LEVELS OF SEX HORMONES AND PITUITARY GONADOTROPHINS IN MALE ALBINO RATS

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Summary: Activity of alkaloid extract of caricapryl–99 seeds (*Carica papaya* Linn seeds) on the serum levels of steroid hormones was studied in adult male albino rats. Three tolerated doses obtained from the graph of percectage toxicity (10, 50 and 150 mg/kg) were separately administered orally, daily for three days to three groups of male rats (n=5) while group four of 5 rats received the vehicle (corn oil) as control. The results showed that 10mg/kg/d caused increase serum levels of FSH and estrogen but decrease in the serum levels of LH and testosterone compared to control; 50mg/kg/d elevated the serum levels of FSH, estrogen but inhibited testosterone; while 150mg/kg/d pretreatments caused a significant decrease ($p<0.01$) in the serum levels of FSH, LH and testosterone. The results permitted the conclusion that caricapryl-99 treatment inhibited the serum level of the androgen, testosterone which might result in a male infertility.
Key words: *Alkaloid extracts, Caricapryl, infertility and pituitary gonadotrophins, male rats.*

Introduction

The need for fertility regulation in men cannot be overemphasized. While chemical methods for fertility regulation in woman are readily available (Chinoy and Padman, 1996; WHO, 1996) the "male pill" remains a distant prospect as effective contraceptive regimens are still toxic and inconvenient. Acceptable male contraceptive methods should reduce the burden traditionally placed almost exclusively on the female partner. Caricarpyl-99 seeds (Caricaceae) have been used in Nigerian herbal medicine for treatment of typhoid fever, malaria and other bacterial infections. However, our previous investigation into the activity of the seed extract in male rats showed that the seed extract treatment induced seminiferous tubules hypertrophy which could lead to male reproductivc dysfunction. (Udoh *et al*, 2005a) Phytochemistry showed that the seed extract contained alkaloid glycosides, saponins, flavonoids, reducing compound, polyphenol, phlobatanins and hydroxymethl-anthraquinones. (Udoh and Kehinde, 1999)

These observations led to the histological examination of the sections of pituitary gonadotrophs of rats treated with the seed extract. The result showed hypertrophy and hyperplasia of the cell morphology, whereas the gonads (testes) sections showed gradual degeneration of germ cells, Sertoli and Leydig cells. (Udoh et al, 2005c) Further observation of the effect of the extract on the fertility in male and female rats showed that extract treatment prevented ovum fertilization as well as reduced sperm count in male rats. (Udoh and Udoh, 2005b; Udoh *et al,* 2005a)

Therefore, this study was to investigate the effect of the seed extract on serum levels of testosterone, LH/ICSH, estrogen and FSH in male rats.

Materials and methods

Preparation of plant extracts

The ripe fruits of *C. papaya* were obtained from the University of Calabar vicinity around the month of June and July. The ripe seeds were removed, washed and oven dried at 80^0 C for 48h. They were milled into fine powder using electric blender (Osterizer).

The powdered sample (100g) of *C. papaya* was wrapped in a thimble and placed in a 500 cm^3 extractor (M&G England). The sample was extracted in absolute ethanol at 60^0 C. The extract was evaporated to a paste form at 40^0C for 8h to a paste form. The paste plant extract was preserved in the refrigerator (Thermocool, TEC).

Treatment

Twenty adult male albino rats weighing between 190 – 200g were divided into 4 groups (n=5). Group 1 received corn oil (0.5ml) daily as controls, groups 2, 3 and 4 received 10, 50 and 150mg/kg/d for 3 days respectively following the method adopted by Udoh et al, 2005c; Udoh, 2007. 24h after treatment the rats were sacrificed and blood sera were prepared for hormonal assays.

Hormonal Assays

Serum samples were assayed for the following; Follicle stimulating hormones (FSH), Luteinizing/intestitial cell stimulating hormone (LH/ICSH), testosterone and estrogen (estradiol). The method used was microwell enzyme-linked immunoassay (ELISA) using analytical grade reagents (Syntron Bioresearch Inc. USA)

Statistical Analysis

All data for control and experimental groups were subjected to statistical evaluation, using student t-test and analysis of variance (ANOVA) for significant differences between the controls and experimental groups at $p<0.05$.

Results

Testosterone serum level

Caricapryl-99 seeds extract (10, 50 and 150mg/kg/d) repeated treatment daily for 3 days caused a significant ($p<0.05$) decrease in the serum level of testosterone in male rats. The level of decrease was dose related (Table 1).

Luteinizing hormone (LH) serum level

Repeated treatment of male rats with the alkaloid extract for 3 days caused a dose related decrease in the serum level of LH (table 1). The level of decrease was statistically significant ($p<0.05$).

Estrogen serum level

The alkaloid extract of (10, 50 and 150mg/kg/d) caused an increase in the serum level of estrogen in male rats. Doses of 10 and 50 mg/kg/d administered daily for 3 days caused a sharp rise in the serum level of estrogen (Table 1). Whereas the highest dose of 150 mg/kg/d induced gradual increase (Table 1).

Follicle-stimulating hormone (FSH) serum level

Pretreatment with the alkaloid extract daily for 3 days caused an increase in the serum level of FSH in males compared to control (Table 1). The increase in the serum level of FSH in male rats was statistically significant ($p<0.05$).

Discussion

The results of the study revealed a decrease in the serum level of testosterone. This observation was similar to the earlier findings of Udoh et al, 2005c; Udoh and Kehinde, 1999; Udoh and Ekpenyong, 2001. In their report dietary intake of the seed extract caused reduction in body weight gain compared to control, testicular atrophy, spermatogenesis arrest and degeneration of spermatozoa. The reduction in the serum level of testosterone could probably be due to the decrease of serum levels of LH/ICSH observed in this investigation.

Leydig cells secrete testosterone by the stimulatory effect of LH (Udoh and Udoh, 2005b; Udoh et al, 2005a; Udoh *et al*, 2005c). In males, reduction of testosterone level might impaire spermatogenesis and cause male infertility.

This study further observed a dose dependent increase in the estrogen serum level. This increase might probably be due to the conversion of testosterone to estrogen (Carr and Blackwell, 1993; Chinoy and Padman, 1996).

TABLE 1: Effect of Caricapryl-99 Seeds extract on Sex hormones levels and pituitary gonadotrophins in male albino rats

Groups	*Testosterone (ng/ml)*	*LH/ICSH (µIu/ml)*	*Estrogen (pg/ml)*	*FSH (µIu/ml)*
10mg/kg (5)	1.68 ± 0.86	0.60 ±0.01	81.6 ±0.02*	1.73 ±0.03*
50mg/kg (5)	1.33 ±0.16*	0.43 ±0.01*	60.0 ±0.01*	2.00 ±0.7*
150mg/kg (5)	0.96 ±0.3*	0.33 ±0.07*	43.33 ±0.05*	0.46 ±0.03*
Controls (5)	2.53 ± 0.39	1.27 ±0.03	26.6 ±0.10	0.96 ±0.03

*Values are expressed as mean ± SEM. Number in parenthesis represents number of animals for treatment group, *p<0.05, t-test.*

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