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ANTIFERTILITY EFFECT OF *MOMORDICA CHARANTIA* (BITTER GOURD) FRUIT ON THE GONADS ON MALE GUINEA PIGS.

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ABSTRACT

Effect of momordica charantia fruit extract on the gonads and sex accessory glands of male guinea pigs were investigated. Sexually mature guinea pigs of proven fertility were administered orally with 1.3 mg/kg and 2.6 mg/kg body weight of ethanol extract of *M. charantia,* fruit daily for 60 days. Observation of animals during treatment showed significant loss of weight. Histological examination of the sections of testes of animals treated with 2.6 mg/kg showed degeneration of sperm cells in the tubules. The spermatogonia, primary and secondary spermatocytes and spermatids appeared normal. There was reduction in number of Leydig cells as compared to controls. Epididymes contained no sperm cells. There was increase in epithelial cell height. The prostate glands showed shrinkage of the villi and reduction of secretion. The high dose of *M. charantia* extract (2.6mg/kg) inhibited seminal vesicles secretion, whereas with a dose of 1.3mg/kg, antisecretory effect was less pronounced. The possible mechanism of action is discussed.

Key Words: Antifertility, *Momordica charantia*, gonads, male guinea pigs.

INTRODUCTION

The need for men to assume greater responsibility for fertility control has been reiterated on numerous occasions during International Women's year (WHO,1975). In Nigeria today and the rest of Africa there is poverty and illiteracy as a result of population explosion and economic recession.

While many female methods of fertility control are widely available the 'male pill' remains a distant prospect, as effective contraceptive regimens are still toxic and inconvenient. Many local plants have been identified and tested for their antiferitility properties in the male rats and guinea pigs (Parkhurst and Stolzenberg, 1975:; Bingel and Farnsworth, 1980; Udoh and Kehinde, 1999, Udoh and Ekpenyong, 2000).

Few researchers have investigated and reported remarkable antiferitility effect of *M. charantia* fruits and roots in laboratory mammals (Dixit et al, 1978; Chopra et al., 1982; Farnswort and Waller, 1984; Nascem et al, 1998). *M. charantia* (wild cucumber, wild balsam, bitter gourd) is a local plant in West Africa. It is a dicotyledonous plant in the family Cucurbitacea. The fruit is eaten and used as house remedies for treating colds. The plant contains lectins which can induce preferential killing of tumor cells. The roots have been successfully used as an abortificient. (Chopra et al, 1982) The findings from this research could serve as a model for studies on other local plants identified with male antifertility properties. Perhaps it might be possible to produce a 'male pill from our local plants.

Phytochemical components of *M. charantia*

The leaves contain a bitter substance, momordicin, resin, two resin acids.The plant contains about 0.038% alkaloid and the seed yields about 32% purgative oil (Chopra et al., 1982). The fatty acid composition of the oil from the seeds is α-elaesteroid acid (46.7%), linoleic acid (7.7%), oleic acid (15.8%) and stearic acid (29.8%) (Verma andAggarwa, 1956).

The active constituent of the fruit is momordicin. Other constituents of the fruit are charantin, 5-hydroxy tryptamine, diosgenin, β-sitosterol and eucurbitacin-like triterpenes,in addition to a vegetable protein, lectin.

Materials and methods

Ripe fruits of *M.charantia* were obtained from Akim Akim Aqua in Odukpani Local Government Area of Cross River State, Nigeria. They were identified at University of Calabar Botanical garden.

Extraction Procedure:

The ripe fruits were cut open to remove the seeds. The remaining parts of the fruits were oven dried at 60^{0}C for 48 hours and milled into fine powder with electric kitchen grinder (National).

The ground fruit sample was soxhlet extracted in ethanol at a temperature of 60^{0}C for 72hr. The ethanol was evaporated *in vacou* at 45^{0}C using rotary evaporator (Astell Hearson, U.K.) The final product was a thick brown liquid (syrup) with a sharp smell and bitter taste.

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Treatment of animals

Sexually mature male guinea pigs *(Cava cayara)* between 6 and 8 months old and weighing betweeen 200g – 500g were used. The initial body weight of all animals in both experimental and control groups were taken before treatment and after every 30 days during treatment period. Treatment lasted for 60 days. The animals were housed in hygenic well lit and ventilated room. They were fed on Grower's mash (Sanders Feeds Ltd, Aba). Water and green foliage (calopo) were provided *ad libitum*. Weighted quantities of the extract, 1.3 mg/kg and 2.6 mg/kg body weight were mixed with palm oil as vehicle. They were administered daily by oral intubation for 60 days. The controls were given the vehicle only.

At the end of treatment period the animals from each group were sacrificed by cervical dislocation. 24 hrs after the last treatment, the testes and sex accessory glands were dissected out and fixed in Bouin's fluid for 24 hrs. The tissues were processed for histological examination (Chieli, et al, 1995). Photomicrographs were taken with Leitz (Ortholux) microscope and camera.

RESULTS

Body weight (Table 1)

There was a significance increase in body weights of animals during the first 30 days of treatment with the fruit extract ($p<0.05$), and then a significant weight loss ($p<0.05$). The weight loss was correlated with a corresponding increase in dose.

Histopathology

The testes of group B animal treated with low dose of 1.3 mg/kg showed few tubules affected particularly those at the periphery. There was degeneration of sperm in the lumen while other germ cells appeared normal. There was shrinkage and separation of tubules in some areas from the connective tissues, leaving some empty spaces in between them. The Leydig cells (L) showed reduction in number as compared to controls (Figs 1 and 2). At high dose level of 2.6 mg/kg, the effect was more pronounced (fig.3).

Photomicrographs of sections of testes and epididymes of ethanol extract of *M. charantia* treated quinea Pigs for 60 days (H & E stain) .

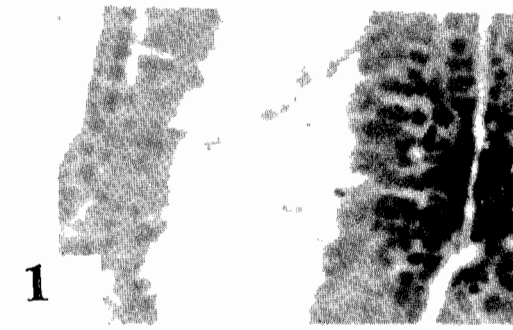

Fig 1: Single tubule of testes showing normal histology (x 640).

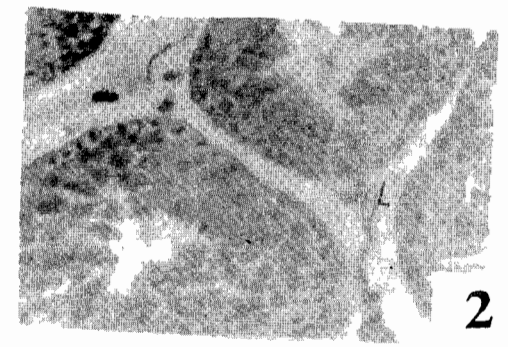

Fig.2: Tubules of 1.3 mg/kg treated guinea pigs Showing degeneration of tubules from connective tissues (x 170).

Table 1 Average weight of animals before and after treatment.

Group and no of animals	Daily Dosage	Average weight before treatment (g)	Average weight after 30 days (g)	Average weight after 60 days (g)
A (Control) 4	Vehicle	314.04 ± 1	378.78 ± 1	399.73 ± 1
(Experimental I) B - 4	1.30mg/kg	371.83 ± 1	411.88 ± 1	399 70 ± 1
(Experimental II) C - 4	2.60mg/kg	402.32 ± 1	451.07 ± 1	302.80 ± 1

Each value represents Mean ± SEM of four guinea pigs.

Student's-test:

A & B (not significant)

A & C (significant: $p<0.05$)

B & C (significant; $p<0.05$)

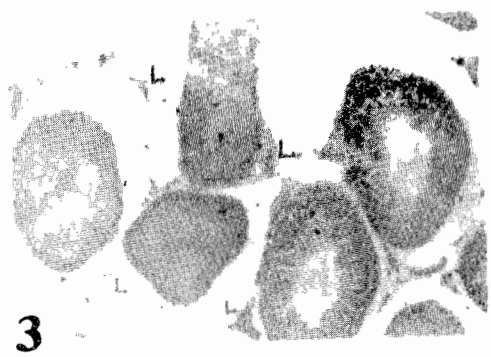

Fig. 3: Tubule of 2.6 mg/kg treated guinea pigs showing pronounced shrinkage and separation of tubules. (X 640).

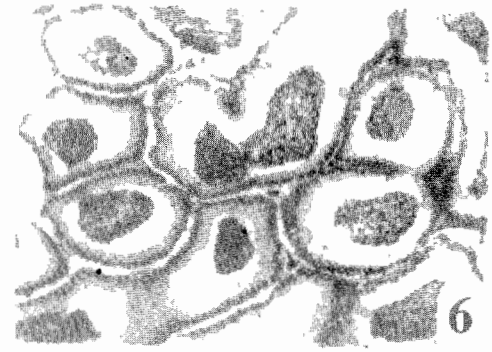

Fig. 6. Epididymal tubules of 2.6 mg/kg treated guinea pigs showing intense clumping and shrinkage of sperm cells (x170)

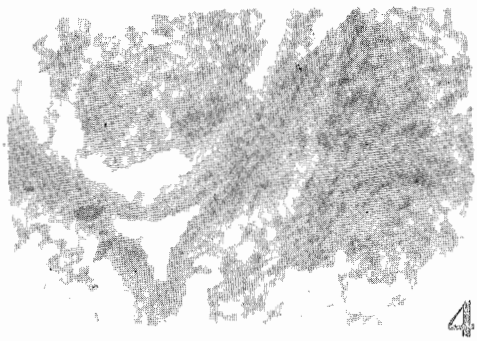

Fig. 4: Tubules of control epididymis showing normal histology.Note the lumens filled with sperm cells (x 640).

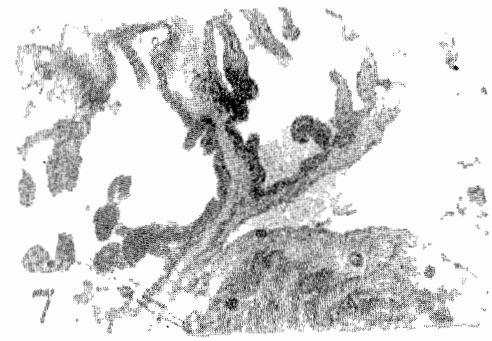

Fig 7: Prostate glands of control guinea pig showing normal histology. Note the tubules filled with secretion (x 640).

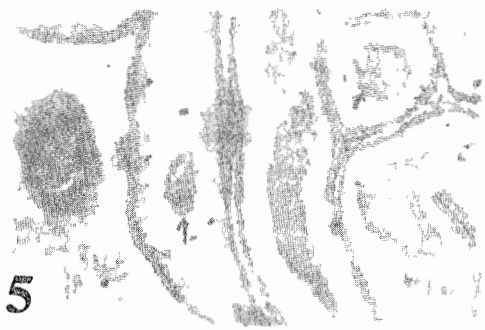

Fig.5: Epididymal tubules of 1.3 mg/kg treated guinea pigs showing clumping of sperm cells in the lumen (arrows) (x 170).

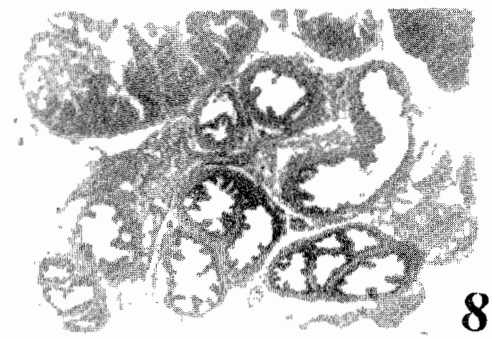

Fig. 8: Prostate of 2.6 mg/kg treated guinea pigs showing shrinkage and atrophy of the villi as well as arrest of secretion (x170).

The epididymes at low dose level also showed the tubules that partially were empty. In a few tubules there was reduction of sperm density due to clumping (figs. 4 & 5). At high dose of 2.6 mg/kg the effect was more intense. Many tubules were affected. There was shrinkage and clumping of sperm and increase in epithelial cell height (fig. 6)

The prostate glands at low dose showed some empty tubules without secretion. The smaller tubules were

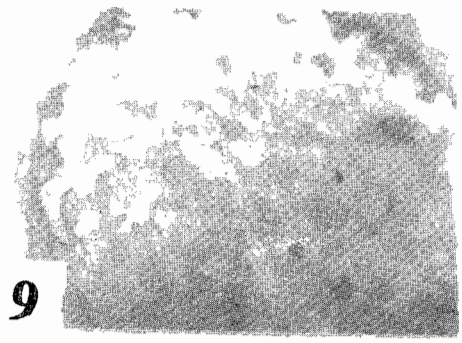

Fig. 9: Seminal vesicles of control guinea pigs showing normal histology with lumen filled with secretion. (x 170).

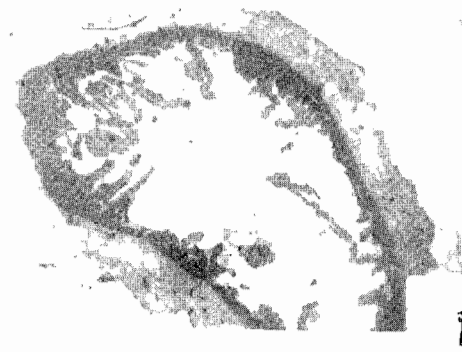

Fig.10: Seminal vesicle of 2.6 mg/kg treated guinea pigs showing complete inhibition of secretion in the lumen. (x170).

more affected than the larger ones, which appeared normal. At high dose there were shrinkage and atrophy of the epithelium as well as inhibition of secretion (figs. 7,8).

The seminal vesicles at low dose, showed the effect was similar to that of prostate. There was slight reduction in secretion in the lumen, while epithelial lining appeared normal. The effect at high dose was pronounced. The tubules were empty of secretion i.e total inhibition of secretion while epithelial lining appeared normal (figs. 9, 10).

DISCUSSION

Momordica charantia fruit extract demonstrated some level of pathological changes in the gonads of male guinea pigs. Another study of its effect on the body weight of animals showed a reduction in the rate of body weight gain (see Table 1) . This was in accord with that previously reported for gossypol acetate administration in rat and man (Chang and Griffin 1980; Udoh et al, 1992). The fruit extract of *M charantia* given to guinea pigs at a high dose of 2.6 mg/kg day caused severe degeneration of spermatozoa and a mild effect was observed in the animal that received a low dose 1.3 mg/kg/ day. Degeneration of sperm cell following treatment of *M. charantia* fruit extract was similar to that reported for papaya seeds extract – treated rats and Mucuna seeds extract treated guinea pigs respectively (Udoh and Kehinde, 1988; Udoh and Ekpenyong, 2000). The degeneration of the sperm cells following the administration of *M. charantia* fruit extract was dose and duration related. However the sperm cells were more susceptible to the effect of *M. charantia* than other germ cells. Furthermore, the administration of *M. charantia* to these animals caused reduction in the number of Leydig cells. The observation allowed the suggestion that the crude drug from *M. charantia* induced its action either directly via the testicular cells or indirectly via the physiology of the pituitary –gonald axis.

The disruption of secretory tubules and the connective tissue of the testis following the administration of the fruit extract of *M. charantia* might result in a reduced androgen concentration. An extended study on the histology of epididymis revealed pathological changes, which could be responsible for retardation of Leydig cells function and production of androgen. This defect might interfere with spermatogenpsis and the life span of spermatozoa. These observations were similar to that of gossypol acetate (Udoh et al, 1992). Administration of the fruit extract of *M. charantia* also induced epithelial cell hyperplasia in the epididymes. Similarly, the high dose of the crude drug treatment caused shrinkage and atrophy of the epithelium of prostate and seminal vesicles. These effects were also similar to what was reported about gossypol acetate (Udoh et al, 1992).

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