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Oral administration of leaf extracts of *Momordica charantia* affect reproductive hormones of adult female Wistar rats

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PEER REVIEW

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Comments

Considering the tremendous increase in acceptance and public interest in natural therapies globally, this study is useful as it contributes to the much desired documentation of the adverse effects or toxicity potentials of herbal remedies. Data from this study revealed dose-related decrease in plasma level of the female reproductive hormones, oestrogen and progesterone, in Wistar rat. This information will contribute to promoting safe use of this plant as an herbal remedy.
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ABSTRACT

Objective: To determine the effect of graded doses of aqueous leaf extracts of *Momordica charantia* on fertility hormones of female albino rats.
Methods: Twenty adult, healthy, female Wistar rats were divided into four groups: low dose (LD), moderate dose (MD) and high dose (HD) groups which received 12.5 g, 25.0 g, 50.0 g of the leaf extract respectively and control group that was given with water *ad libatum*.
Result: Estrogen levels reduced by 6.40 nmol/L, 10.80 nmol/L and 28.00 nmol/L in the LD, MD and HD groups respectively while plasma progesterone of rats in the LD, MD and HD groups reduced by 24.20 nmol/L, 40.8 nmol/L and 59.20 nmol/L respectively.
Conclusion: Our study has shown that the antifertility effect of *Momordica charantia* is achieved in a dose dependent manner. Hence, cautious use of such medication should be advocated especially when managing couples for infertility.

KEYWORDS
Momordica charantia, Estrogen, Progesterone, Fertility

1. Introduction

It is estimated that 80% of the world population uses medicinal plants in the treatment of diseases[1]. This rate is higher in African countries where up to 90% of the population relies on the use of medicinal plants to help meet their primary health care needs[1,2]. Traditional medicines were used for fertility regulation in ancient times[3]. Since then, large numbers of plant species have been screened for their antifertility efficacy; including their use in plummeting female fertility and contraception[4,5].

Previous researches have evaluated antifertility effect of different herbs. Ethanolic and aqueous extracts of *Calotropis procera*, *Rivea hypocrateriformis* and methanolic leaf extract of *Cissampelos pareira* were found to disrupt the estrus cycle in mice[6-8], while the ethanolic extract of *Nelumbo nucifera* and *Cuminum cyminum* seeds have antiestrogenic properties[8,9]. A significant reduction in implantation was observed with benzene and aqueous extracts of *Hibiscus rosa sinensis* and *Moringa coneanensis* respectively[8]. Some others have also been used as abortifacients[8].

Momordica charantia (*M. charantia*), a tropical plant

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known widely for its hypoglycemic effect, has been extensively used for diabetic studies in herbal medicine[10]. It is also used as anti-viral, anti-bacterial and anthelmintic agent to treat a number of infections and diseases[11]. Its antifertility effect on male animals has been extensively evaluated by other workers[12,13]. However, there still exists paucity of researches on the effect on the female reproductive system. Since previous workers used single doses[14,15], we intended to explore the effect of *M. charantia* on female rats using graded doses.

Also, a study carried out in a fertility clinic in Iran documented that about half (43.3%) of the attendants preferred to use herbal remedies; most of them being women[16]. Less than 2% reported to their physician they were concurrently taking herbal medication. The reason for this was that most of them (98.7%) claimed they were not asked or they forgot.

As most people in developing countries (including Nigeria) consume herbal medications without adequate knowledge of the pharmacologic actions and side effects of such medications[17], it is therefore important to evaluate the effect of *M. charantia* on female reproductive hormones (estrogen and progesterone) in order to advice patients especially infertile couples on abuse of herbal medications.

2. Materials and methods

2.1. Sources, maintenance of animals

Twenty adult, healthy, female Wistar rats were used for the study. They were acquired from the animal house of the Department of Physiology, Faculty of Basic Medical Sciences, Olabisi Onabanjo University, Nigeria. The rats were divided randomly into 4 groups: low dose (LD), moderate dose (MD), high dose (HD), and control (C) groups respectively. All the animals were housed in well ventilated cages made of wood and wire gauze. Wood shavings were used as beddings to keep each compartment dry. Here, normal standard ambient conditions of temperature between 28-31 °C, relative humidity between 50%-55% and a photoperiodicity of 12 h natural light and 12 h dark were maintained. The animals were allowed to acclimatize for 2 weeks for proper adaptation to their new environment and were weighed weekly. They had access to pelletized feed purchased from Animal Care Feed Mills in Ogere, Nigeria and water *ad libitum*.

2.2. Weighing of the rats

Weighing of rats was done using a weighing balance. Their weights ranged between 150 g and 200 g.

2.3. Identification and preparation of M. charantia leaf extract

The leaves of *M. charantia* were purchased from the local market in Sagamu, Nigeria. It was authenticated by a botanist in the Department of Plant Sciences, Olabisi Onabanjo University. Samples were air-dried and grounded to powder and weighed. To obtain sample for the LD group, 12.5 g of the powdered specimen was boiled in 5 000 mL of distilled water for some minutes, simmered, cooled and then sieved before administration to the LD group. In MD and HD groups 25.0 g and 50.0 g of powdered specimen were used respectively.

2.4. Dosage, route and duration of administration of test solutions

The dosage of aqueous extract of *M. charantia* was calculated based on the weight of the animals and administered orally via a cannula daily for thirty days. The controls were given distilled water instead of *M. charantia*.

2.5. Experimental procedure

The animals were anesthetized using diethylether, scarificed and dissected. A deep incision was made at the ventral surface aiming for the heart in order to collect blood samples. Blood obtained from the animals were put in EDTA bottles to prevent clotting. Samples were centrifuged at 3000 r/min for 10 min to obtain plasma. Estimation of estrogen (B-estradiol) and progesterone levels was done as previously described in one study by Lilaram and Nazeer Ahmed R[5].

2.6. Statistical analysis

Results were expressed as mean±standard deviation. Analysis was carried out on SPSS version 16 using analysis of variance (ANOVA). The level of significance was considered at $P<0.05$.

2.7. Ethical considerations

All procedures involving animals in this study conformed to the guiding principles for research involving animals as recommended by the Declaration of Helsinki and the Guiding Principles in the Care and Use of Animals (World Medical Association & American Physiological Society, 2002) and were approved by the Departmental Committee on the Use and Care of Animals in conformity with international acceptable standards.

3. Results

3.1. Effect of aqueous extract of M. charantia on plasma progesterone levels

Oral administration of aqueous extracts of *M. charantia* caused a significant decrease in progesterone in a dose dependent manner in LD, MD and HD groups when compared with the control (Table 1).

Table 1

The effect of administration of aqueous extracts of *M. charantia* on progesterone levels in adult Wistar rats.

Sample groups	Dose (g)	No. of rats	Progesterone values (nmol/L)
Control (C)	–	5	67.60±29.48
Low dose (LD)	12.5	5	43.40±11.82*
Medium dose (MD)	25.0	5	26.80±6.83*
High dose (HD)	50.0	5	8.40±3.85*

*: Statistically significant, $P<0.05$ compared with the control.

3.2. Effect of aqueous extract of M. charantia on plasma estrogen levels

Oral administration of aqueous extract of *M. charantia* caused a significant decrease in estrogen in a dose dependent manner in LD, MD and HD groups when compared with the control (Table 2).

Table 2

The effect of administration of aqueous extracts of *M. charantia* on estrogen levels of adult Wistar rats.

Sample groups	Dose (g)	No. of rats	Estrogen values (nmol/L)
Control (C)	–	5	44.80±28.60
Low dose (LD)	12.5	5	38.40±12.22*
Medium dose (MD)	25.0	5	34.00±4.18*
High dose (HD)	50.0	5	16.80±14.10*

*: Statistically significant, $P<0.05$ compared with the control.

4. Discussion

The focus of this study was to determine the effect of graded doses of aqueous leaf extracts of *M. charantia* on plasma estrogen (B-estradiol) and progesterone, two important fertility hormones in females. Our results have shown that aqueous extracts of *M. charantia* significantly decreased plasma levels of estrogen and progesterone of the female Wistar rats in a dose dependent manner.

Administration of *M. charantia* reduced estrogen levels by 6.40 nmol/L, 10.80 nmol/L and 28.00 nmol/L in the LD, MD and HD groups respectively. The pituitary-gonadal axis is important for the maintenance of the reproductive system hence any distortion to this axis can be deleterious[14,18,19]. Follicule stimulating hormone stimulates maturation of the Graafian follicle while leutinizing hormone causes it to synthesize testosterone which is then converted to estrogen by aromatase[20]. Thus, the declining estrogen levels observed in our study maybe due to inhibitory effect of *M. charantia* on pituitary gonadotropins, direct toxic effect on follicular and theca cells as seen with the seminiferous tubules in males rats[13,19], ultimately resulting in variations in the estrous cycle described by other workers[14,15,18].

Administration of *M. charantia* reduced plasma progesterone of rats in the LD, MD and HD groups by 24.20 nmol/L, 40.8 nmol/L and 59.20 nmol/L respectively. High estrogen levels are important for the luteinizing hormone surge that induces ovulation. The subsequently formed corpus luteum secretes progesterone that favors implantation and establishment of pregnancy[21]. A decline in estrogen prevents ovulation hence low progesterone levels. Also a direct toxic effect on the corpus luteum may be a possible mechanism for decline in progesterone levels. The attendant effect of this is spontaneous abortion and failure of implantation reported by other workers[18,21].

There was no recovery period in our study; however, other researchers have suggested a reversal of the antifertility effect of *M. charantia* upon withdrawal of its administration[14,18,21]. We therefore conclude that cautious use of herbal medication should be encouraged and a thorough drug history should be obtained from patients seeking treatment for infertility and recurrent spontaneous abortions so as to exclude medication induced causes.

Conflict of interest statement

We declare that we have no conflict of interest.

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Comments

Background

There has been a tremendous increase in acceptance and public interest in the use of herbal medicines and other forms of natural therapies globally in recent times. Although many plants have shown promising therapeutic potential with the efficacy of a good number of them clearly established, the safety of many of them has not been adequately investigated and documented. In this regard, the present study is important and quite relevant.

Research frontiers

The pathogenesis of most conditions of infertility remains unclear. Several efforts are directed towards characterizing possible disruptors of endocrine and reproductive functions to provide information on safety. The present study attempts to identify possible interference of *M. charantia* with female reproductive function by determining the effect of graded doses of the aqueous leaf extracts on plasma levels of estrogen and progesterone in adult female Wistar rats.

Related reports

M. charantia is a tropical plant that is popularly used to treat diabetes in folklore medicine in addition to its use for treatment of various forms of infectious diseases. Previous studies on the plant have evaluated its antifertility effect on male animals. Only very few studies have been conducted in female animals and only single doses of the plant extract were used in most of the studies. To a very large extent,

there still exists paucity of information on the effect on female reproductive system.

Innovations and breakthroughs

The study demonstrated dose-dependent reduction in plasma levels of oestrogen and progesterone and suggested an antifertility potential of the plant. This provided preliminary information on the leaf extract of *M. charantia* as a possible disruptor of female reproductive function in experimental model and suggested an antifertility potential. This study should provide a basis for subsequent and detailed studies on the effects of the plant on endocrine and reproductive functions and characterizing bioactive compounds responsible as well as their mechanism of action.

Applications

As the global use of herbal medicines continues to grow, public health issues and concerns surrounding their safety are also increasingly recognized. Knowledge of their potential adverse effects is limited owing to few scientific investigations to determine their safety. Data from this study make available additional information on the risks associated with the use of *M. charantia* and related herbal products. This will go a long way in raising awareness and contributing to protection of public health and promoting safety.

Peer review

Considering the tremendous increase in acceptance and public interest in natural therapies globally, this study is useful as it contributes to the much desired documentation of the adverse effects or toxicity potentials of herbal remedies. Data from this study revealed dose-related decrease in plasma level of the female reproductive hormones, oestrogen and progesterone, in Wistar rat. This information will contribute to promoting safe use of this plant as an herbal remedy.

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