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Anabolic, Androgenic and Anti-Cholesterolemic Effect of *Kigelia africana* Leaf Extract on Some Male Wistar Rats

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Abstract

Male erectile dysfunction (ED) refers to incompetency in reaching and retaining adequate penile tumescence for sexual intercourse, possibly due to hormonal imbalance or its inverse relationship with age. Over 152 million men globally suffer from ED and by 2025; the number of affected individuals is anticipated to be around 322 million. In this research work, the effect of petroleum ether extract of *Kigelia africana* on lipid profile and reproductive hormones of Wistar rats was examined. The leaf of *K,africana* was collected, air-dried , pulverized and extracted using 1200ml of 70% petroleum ether for 72 hours. This was then concentrated and stored in a refrigerator at 4°C. Twenty-one (21) Wistar male rats were used for this research. The animals were acclimatized for seven (7) days. Treatment was carried out as follows: group 1 (normal control) received only the vehicle (Normal saline) orally, while groups 2 and 3 received an extract of (200 and 400 mg/kg b.wt/day respectively for 2 successive weeks. The rats were sacrificed and the blood was collected by cardiac puncture for the analysis of lipid profile and reproductive hormones. The result revealed that the extract produced a significant increase (p<0.05) in serum testosterone, follicle-stimulating hormone, luteinizing hormone, TAG and HDL but a significant (p<0.05) decrease in serum total–cholesterol and LDL respectively when compared with normal control. It was speculated that the extract may possess anabolic, androgenic and anti/ hypocholesterolaemic

effect which might reduce the risk of predisposition to both cardiovascular and erectile dysfunctions possibly due the presence of phytoandrogens and phytonutrients like alkaloids and flavonoids.

Keywords: Anti-cholesterolamia, HDL, *Kigelia africana*, LDL, Libido, Phyto Androgens

INTRODUCTION

Erectile dysfunction (ED) is a neurovascular condition that involves endothelium of the corpora cavernosal arterial blood vessels in the penis and indirectly to cardiovascular diseases. The causative factors that include ED are vascular, neurogenic, psychogenic, and hormonal factors mainly in 52% of aging men 40 to 70 years of age, diabetes, hypertension, prostate and heart disease, obesity and due to certain medications, physical injury or anatomical deformity of the penis (Dasofunjo *et al.,* 2013;Mobley *et al.,* 2012;Hackett *et al.,* 2018) .Other endocrine disorders are also responsible such as adrenal insufficiency, hypogonadism, low testosterone, hypercholesterolemia, atherosclerosis, and hypothyroidism (Kalka *et al.,* 2018).

Erectile dysfunction is becoming a major calamity in Africa. It is slowly eating deep into the life of individuals' especially in married homes and is causing problems that have led to broken homes, separation and divorce not only in Africa but across the globe. The global estimated prevalence has been on the rise. It has been projected that the number of men with this condition will rise to 322 million by 2025 and 35%-47% in Nigeria (Dasofunjo *et al.,* 2020)

Reproductive hormones are involved in fertility and sexuality. They help to develop and maintain sexual characteristics and also play an important role(s) in the menstrual cycle, fertility, and pregnancy (Andrew *et al*., 2018)

Reproductive hormones play pivotal roles in the reproductive systems of both male and female pubertal development, as well as their growth and sexual character. Although, the synthesis of reproductive hormones is stimulated by the hypothalamic gonadotropin-releasing hormone (GnRH). In the female ovulatory cycle, FSH is responsible for inducing follicular growth and increasing oestrogen production, while LH, apart from enhancing

cholesterol availability for steroidogenesis, also signals ovulation following its peak mid-cycle (Kjeldsen *et al.,* 2013)

Ethno-medicinal plants have provided a major focus in global health care and are contributing substantially to the drug development processes and procedures. The hormonal profile of reproductive hormones is highly stimulated during reproduction and most African herbal therapy help in the stimulation of this hormones to help enhance reproduction (Egharevba *et al.,* 2010). A typical example of this herbal therapies used in folk medicine in the management of infertility related challenges is *Kigelia africana*.

It has been reported that *K. africana*'s medicinal uses as an anti-inflammatory, antioxidant,antidiabetic, anti inflamatory, anti-dysentery, among other uses in various communities (Fatokun , 2010 .Traditionally, *K. africana* has been used either as a single plant or in combination with other plants for increased potency and libido (Ogbeche, 2002) The leaves, stems and roots decoction are also used to manage sexually transmitted infections and sores .In folklore, the fruit of *K. africana* represents a symbol of fertility . In south eastern Nigeria, the fruits and flowers are mixed with alcohol or water and used by traditional healers for fertility treatment among women and men of child bearing age (In south western Nigeria, the bark extract have been reported to have aphrodisiac effect as it enhances sexual libido and erection in males(Dasofunjo *et al.,* 2020). Therefore, since sexual hormones and lipid profile play significant roles in reproduction. This present study determines the effect of *Kigelia africana* on serum lipid profile and reproductive hormones of male Wistar rats.

MATERIALS AND METHODS

Materials

Study area: The study was carried out at the Department of Medical Biochemistry Laboratory, University of Cross River State, Cross River State, Nigeria from January - August ,2022

Plant Material

Fresh leaf of *K.africana* was collected from UNICROSS community, Okuku, Cross River State, Nigeria. The leaf was taken to the University of Calabar, Department of Botany for

identification and authentication. The voucher number of 206 has been deposited for future reference at the department's herbarium.

Experimental animals

Twenty- one (21) Wistar male rats were obtained from the animal holding unit of the Department of Medical Biochemistry, University of Cross River State. The animals were allowed to acclimatize for 7 days, in a well-ventilated room at room temperature and relative humidity of 29°C and 70% respectively with 12 hours natural light-dark cycle. They were allowed food and water *ad libitum*. Good hygiene was maintained by daily cleaning and removal of faeces and spills from their cages.

Method

Preparation of extract of *K. africana* leaf

The leaves of *K.africana* were collected around UNICROSS and air- dried at room temperature for a period of 21days until constant weight was obtained. The dried leaves were then pulverized to powdered form by a machine blender and sieved. Thereafter, 400g of the pulverized plant material (*K. africana*) was dissolved in 1200ml of 70% petroleum ether for 72 hours. This was followed by vacuum filtration and extracts were concentrated using an evaporator water bath at 40°C to obtain solvent -free extract, and stored in a refrigerator at 4°C.

Experimental design

Treatment was carried out as follows: group 1 (normal control) received only the vehicle (Normal saline) orally, while group 2 and 3 received an extract of (200 and 400 mg/kg b.wt/day respectively for 2 successive weeks.

Blood sample collection

Blood was collected from experimental animals by cardiac puncture under plane sterile tubes for analysis, preceded by centrifuging and separation of the blood plasma with standard pipette. The specimens were labelled with the identification alphabets/ number. The samples were kept at room temperature until processing, which occurred within 30 minutes of collection for the analysis of lipid profile and reproductive hormones.

Hormonal and lipid profile assay

Serum testosterone was estimated using Rapid Lab Kit (United Kingdom) for the enzyme-linked immunosorbent assay (ELISA) for the quantitative determination of testosterone. The serum LH and FSH were estimated using Dialab Kit (Austria) for ELISA for the quantitative determination of FSH in the serum. Serum total cholesterol, triglycerides, HDL and LDL was determined using Randox cholesterol Kit based on the cholesterol oxidase method as described by (I-Hua et al., 2019)

Statistical analysis

The data obtained were analyzed using a one-way analysis of variance (ANOVA). The SPSS software version 20.0 was used to establish statistical significance at $P<0.05$.

RESULTS

This research work reveals the effect of extract of *K. africana* leaf on serum lipid and reproductive hormone profile of Wistar rats.

The extract produced a significant increase ($p< 0.05$) in serum FSH, LH and testosterone at both 200 and 400 mg/kg body weight of *Kigelia africana* extract in a dosage -dependent manner when compared with the normal control (Figure 1).

The extract of *K. africana* leaf on the serum lipid profile of male Wistar rats. The plant extract of *Kigelia africana* produced a significant ($p<0.05$) increase in serum TAG, HDL but a significant ($p<0.05$) decrease in serum LDL and T.cholesterol when compared respectively when compared with the control (Figure 2).

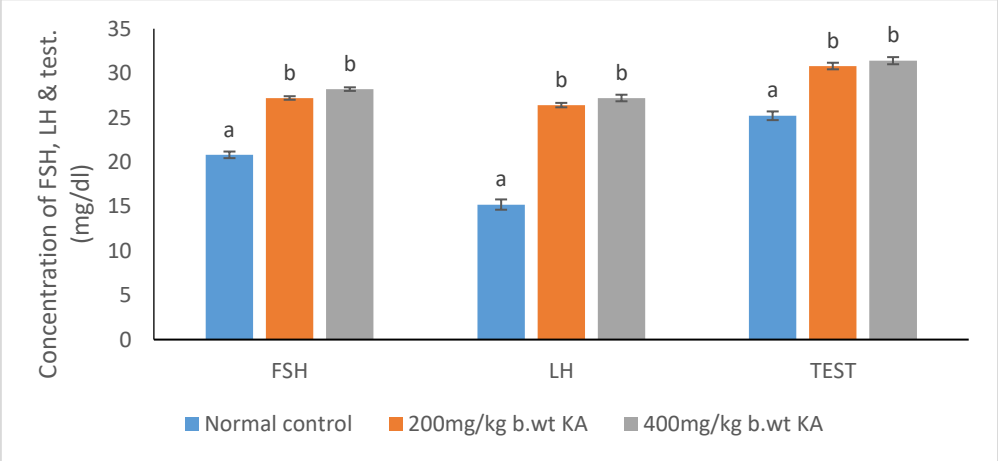

Figure 1: Effect of extract of *K. africana* leaf on serum reproductive hormones of male Wistar rats.

Legend: Values are expressed as mean+SEM (n = 7). Different letters in the same parameter are statistically significant ($P<0.05$). Legend: Normal control = group which received normal saline; 200mg/kg b.wt KA = group treated with 200mg/kg b.wt *K. africana* and 400mg/kg b.wt KA = group treated with 400mg/kg b.wt *K. africana.*

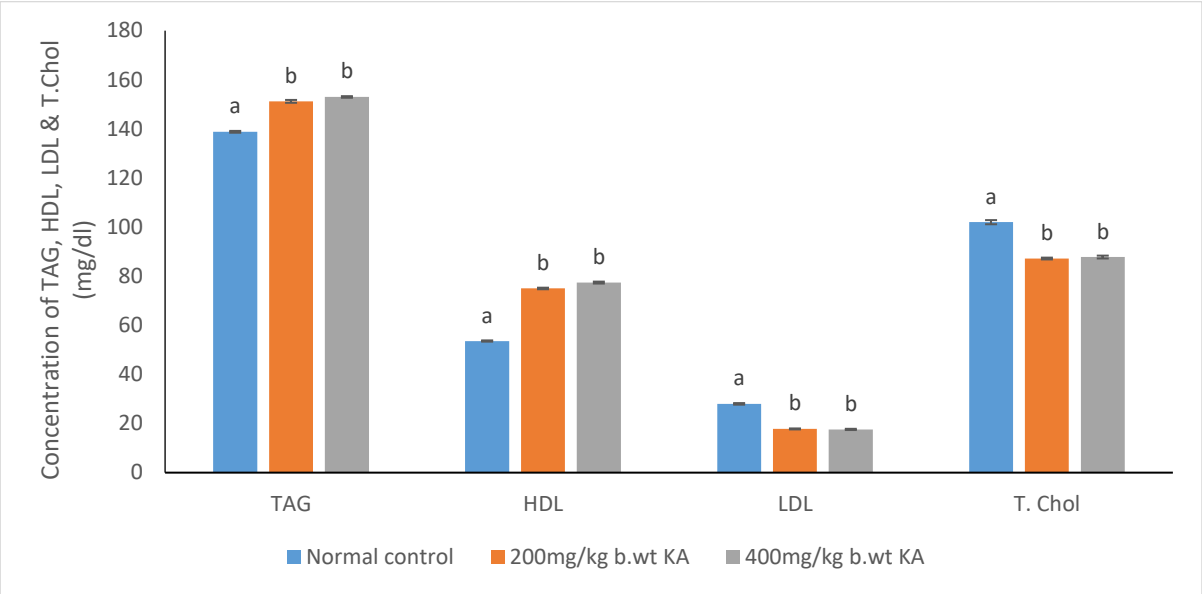

Figure 2 Effect of extract of *K. africana* leaf on serum lipid profile of male Wistar rats.

Legend: Values are expressed as mean+SEM. (n = 7). Different letters in the same parameter are statistically significant ($P<0.05$). Legend: Normal control = group which received normal saline; 200mg/kg b.wt KA = group treated with 200mg/kg b.wt *K. africana* and 400mg/kg b.wt KA = group treated with 400mg/kgb.wt *K. africana*

DISCUSSION

The recent shift from orthodox medicines to ethno botanicals and pharmacognosy or plants with medicinal potentials is a major contributory factor to a decline in the prevalence of degenerative diseases or management of the disposable risk factor in most developing nations especially in the continents of Africa, Asia and beyond (Igbodara and Omole, 2012; Dasofunjo *et al.*,2022).

Reproductive hormones are involved in fertility and sexuality. Reproductive hormones are usually made in the ovaries (in females) and testes (in males). Female reproductive hormones include oestrogen and progesterone. They help to develop and maintain female sexual characteristics and play an important role in the menstrual cycle, fertility, and

pregnancy. Male reproductive hormones, such as testosterone, help develop and maintain male sexual characteristics and enhance spermatogenesis in the testes (Koehler *et al.,* 2019).

Some reproductive hormones may also be synthesized in the laboratory and used to manage certain medical conditions (Huhtanemi,2014)

Testosterone is the primary male hormone responsible for regulating sex differentiation, spermatogenesis and fertility (Humi *et al*.,2018). It also responsible for the development of both primary and secondary sexual characteristics and may stimulate erythropoiesis (Janeson, 2015). Testosterone levels tend to drop with increasing age; due to this, men tend to experience a decrease in testicular size, a drop in libido, lower bone density, muscle mass decline, increased fat production, and decreased erythropoiesis which leads to possible anaemia (Humi *et al*.,2018). Testosterone levels has been reported to be directly proporional to LH and FSH levels such that increase in the levels of the gonadotropins results in a corresponding increase in testosterone (Dasofunjo *et al*.,2020). From the results obtained in this present research work, there was a significant increase in serum testosterone in all the graded doses of *Kigelia africana* extract when compared with the control which suggest that the extract might have possessed a sex- enhancing potential possibly due to the presence of phytoconstituent or phyto androgens.

Follicle-stimulating hormone (FSH) is a hormone produced by the anterior pituitary in response to gonadotropin-releasing hormone (GnRH) from the hypothalamus ((Stamatiades and Kaiser, 2018). FSH plays a role in sexual development and reproduction in both males and females. FSH is tropic to the Sertoli cells alongside with androgens maintain the gametogenic function of the testes (Dasofunjo *et al.,* 2020). In mammals, oestrogen levels or inhibin B, inhibits FSH secretion via negative feedback (Boepple *et al*., 2008). From this present study, the observed significant increase in serum FSH in all the graded doses of *Kigelia africana* extract when compared with the control suggests that the extract might improve sexual drive and development.

Luteinizing hormone is tropic to the Leydig cells and stimulates the secretion of testosterone, which in turn feeds back to inhibit LH secretion (Obi *et al.,* 2012). LH release is stimulated by gonadotropin-releasing hormone (GnRH) and inhibited by oestrogen in females and testosterone in males. LH has various functions, and they differ between women and men. In both sexes, LH contributes to the maturation of primordial germ cells. In men, LH causes the Leydig cells of the testes to produce testosterone. In women, LH

triggers the creation of steroid hormones from the ovaries (Okonkwo *et al.,* 2021). Moreso, it helps to regulate the length and order of the menstrual cycle in females by regulating both ovulation and implantation of an egg in the uterus. Therefore, from this present study the significant increase observed in serum LH suggest that the extract may act on the hypothalamic-pituitary axis or triggers the Leydig cells to produce testosterone and may also triggers ovulation in female.

This present study on the effect of *Kigelia africana* on reproductive hormones such as testosterone (TSH), follicle- stimulating hormone (FSH), and luteinizing hormone (LH) of male Wistar rats agrees with findings from recent studies conducted by (Ngwu and Okoye, 2019; Dasofunjo *et al*., 2013).

Assessment of the alteration of the lipid profile of major lipids like total cholesterol (T.C), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C) and triacyl glycerides (TAG) might reveal a clinical basis to understanding the metabolism of lipids and it role in inhibiting predisposing humans to atherosclerosis, coronary heart diseases and other cardiovascular- related disorder (Dasofunjo *et al*., 2023). The observed significant increase in serum level of HDL-C from this present work suggest that the petroleum ether extract of *Kigelia africana* may be used to increase the production of apolipoprotein A_1 (Apo A_1), thereby resulting in the synthesis of HDL. This might be useful in preventing the pre-disposition to coronary related diseases and may aid steroidogenesis and or spermatogenesis.

More so, the observed decrease in serum cholesterol may be due to a decrease in the concentration of acetyl-CoA arising probably from impaired –oxidation stem of fatty acids, since acetyl CoA is a key substrate in the biosynthesis of cholesterol or due to a decrease in absorption from the intestine suggest that the extract may reduce/lowers serum cholesterol levels or removes cholesterol from the system in other to improve sexual drive.

Likewise, the observed hypotriglyceridemic effect following the administration of the extract of *Kigelia africana* may be due to a decrease in fatty acid synthesis which may enhance catabolism of LDL, activation of lipid catabolism and tissue lipase and in activation of acetyl-CoA carboxylase and production of triglycerides precursors such as acetyl-CoA and glycerol-phosphate (Ukpnukpong *et al.,* 2013).It also suggests that the plant extract may contain phytonutrients which lowers the serum triglyceride level due to its lytic role .This

hypo triglyceridaemic potential of the extract might be responsible for its continual usage in folk medicine.

More so, the observed reduction in low density lipoprotein cholesterol (LDL-cholesterol) following the administration of the extract at 200 and 400 mg/kg body weight suggest that the extract possesses cholesterol- lowering or clearing ability or a hypocholesterolemic agent which might be a tool in the management of atherosclerosis and cardiovascular dysfunctions.

CONCLUSION

The biochemical implication of this study are indications that the extract may possess anabolic, androgenic and anti/ hypocholesterolaemic effect or cholesterol clearing/lowering ability which can reduce the risk of predisposition to both cardiovascular and erectile dysfunctions

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