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Investigation into the aphrodisiac properties of aqueous and ethanol root extracts of *Manniophyton fulvum* in male Wistar rats

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Abstract: *Manniophyton fulvum root is a popular herb amongst traditional medicine practitioners in Nigeria for the enhancement of male sexual behavior. This study therefore investigated the aphrodisiac property of aqueous and ethanol root extracts of Manniophyton fulvum by observing the sexual behavior of male Wistar rats against a standard aphrodisiac drug (Sildenafil citrate, 25 mg/kg). The mount frequency, mount latency, ejaculation latency and post-ejaculation latency were observed in animals to evaluate their sexual activity. Results from the study showed that the 400 mg/kg body weight aqueous extract of Manniophyton fulvum induced a sexual behavior that was far more than the other extracts (200 mg/kg aqueous extract, 200 mg/kg ethanol extract, and 400 mg/kg ethanol extract) which was not comparable to those of the standard drug (Sildenafil citrate, 25 mg/kg body weight). While there was a significant ($p<0.05$) increase in mounting frequency in the experimental animals compared to the control, there was significant ($p<0.05$) decrease in the ejaculation latency and the post-ejaculation latency in the experimental animals compared to the control. The findings from this study validate the claim by traditional medicine practitioners on the aphrodisiac property of Manniophyton fulvum root extract.*

Keywords: *Aphrodisiac activity, aqueous and ethanol root extract, Manniophyton fulvum root, male Wistar rats.*

I. Introduction

Erectile dysfunction (ED) is a sexual problem, characterized by the inability to achieve or sustain an erection of the penis sufficient for satisfactory sexual intercourse [1-2]. It is linked to substantial psychological, social and physical morbidity, requiring an inclusive and empathetic approach by the health care provider [2]. The cause of ED varies from one individual to another [4]. However, we do know from previous studies, that diseases such as diabetes (in which 35–50 % of male sufferers experience ED), kidney diseases, chronic alcoholism, multiple sclerosis, atherosclerosis, vascular diseases as well as neurological diseases have all been shown to induce ED in men. Chronic use of anti-hypertensive, anti-histamines, anti-depressants, tranquilizers, appetite suppressants, anti-ulcer drugs - cimetidine among male patients have also been reported to cause ED as a side effect [2-3]. Smoking, hormonal abnormalities (low levels of testosterone) as well as psychological factors (stress, anxiety, guilt, depression, low esteem and fear of sexual failure) have also been shown to precipitate ED in men [3].

The discovery of the cGMP-specific phosphodiesterase type 5 inhibitors (Sildenafil, Tadanafil and Vardenafil) brought in what can best be described as a landmark breakthrough in the treatment of ED [4-5]. Before then, other synthetic drugs such as oral testosterone, yohimbine, papaverine hydrochloride (used under strict supervision), phentolamine and alprostadil have been recommended for treating ED, but then, all of these drugs, just like cGMP-specific phosphodiesterase type 5 inhibitors, showcase many undesirable side effects [5-6]. While testosterone is associated with liver damage [5], the cGMP-specific phosphodiesterase type 5 inhibitors, have been linked to irregularities of the heart rhythm, tremor, suicidal tendencies and mental disorders [7]. They also cause blood vessel dilatation in other areas of the body, which in the head, results in headache and fainting. Other side effects of synthetic aphrodisiac may include blurred vision, sensitivity to light (at high doses), facial flushing, and gastrointestinal upset [8]. On the socio-economic side, synthetic aphrodisiacs are very expensive and inaccessible to most ED patients [9]. All of the above have contributed difficulty to clinicians in choosing between their efficacy and the safety for their patients [7].

These plethora of known side effects associated with synthetic aphrodisiacs has led to the growing demand for a more natural aphrodisiacs, sourced from plants or herbs, with much less unwanted side effects [10].

The use of herbs as aphrodisiac is not new to many cultures, and in recent times, there have been significant increases in the use of herbal medicines to cure erectile dysfunction [11]. This is encouraged by the World Health Organization's (WHO) promotion of traditional medicines [12].

Different herbs according to different cultures and practices have been used for treating erectile dysfunction [13-14]. Before now, *Massularia acuminate* [15], *Myristca fragrans* Houtt [16], *Tribulus alatus* [17], *hermoni*

[18] have been confirmed to possess aphrodisiac properties. However, the root extract of *Manniophyton fulvum* had been used by herbalists in south-south region of Nigeria to manage erectile problem [19].

The genus *Manniophyton fulvum* belongs the Euphorbiaceae family. It is distributed widely in tropical Africa from Sierra Leone to Sudan as well as South-ward to Angola [19]. In African traditional medicine, the, stem, leaf, root and bark are useful, against diarrhea, stomach ache, cough, pain and bronchitis [20]. It has been used as remedies for dysentery, hemorrhoids, hemoptysis and dysmenorrhea, and also to heal wounds [21]. The red stem sap possesses haemostatic activities, while the leaf sap is used against ear problems and caries [20]. Anti-oxidant and anti-inflammatory activity [22], antidiarrheal activity [23], antimicrobial activity [24]. and phytochemical screening showing the presence of, cardiac glycosides, saponins, sterols/terpenes, reducing sugars, anthraquinones and alkaloids [19] had been reported on *Manniophyton fulvum.* LD_{50} of its leaf extract produced toxicity at a dose of 1050 mg/kg [19].

With no scientific proof on the efficacy of *Manniophyton fulvum* root in the treatment of erectile dysfunction, and in the face of its usefulness amongst herbal medicine dealers in the south-south region of Nigeria, We hypothesize that the herb may indeed possess some properties that could boost the levels of sexual performance. This study therefore investigates the aphrodisiac activity of aqueous and ethanol root extract of *Manniophyton fulvum*in in animal model. Data from this research, if positive, will not only improve ways of managing and treating erectile dysfunction, but could well create a lead on the discovery of a new aphrodisiac agents.

II. Materials and Methods

2.1 Plant collection and identification

The fresh root of *Manniophyton fulvum* was collected from the bush beside the female Medical Hostel, Site III, Delta State University, Abraka, Nigeria and identified at the Botany Department, Delta State University, Abraka, Nigeria. The roots were washed and air dried at room temperature 27 ± 2^{o}C for several days in the Pharmacology Laboratory of the same University. Dried roots of *Manniophyton fulvum* were cut into small particles and were further reduced into a fine powder using sterile grinding machine. The powder was stored in air tight glass container protected from direct light and heat until required for analysis.

2.2 Preparation of crude extracts

Two hundred (200) grams of the powdered root specimen was weighed and extracted with 97% ethanol, and distilled water respectively, in a ratio of 1:3 of powdered root to each solvent. The root extracts was done by gentle but continuous agitation of each mixture (ethanol and distilled water) for 3 hours using an orbital shaker at 20 rpm. Each mixture was then filtered using dried Whatman filter paper and the filtrate was concentrated to dryness in a rotory evaporator set at 40^{o}C. Each solid extract was reconstituted in distilled water to obtain a stock solution of 20 and 40 mg/ml which correspond to 200 and 400 mg/kg body weight doses respectively.

2.3 Animals

Healthy male adult albino rats of Wistar strain, weighing 150- 200 g were obtained from the Animal House of the Department of Pharmacology and Therapeutics, Faculty of Basic Medical Sciences, Delta State University, Abraka, Delta State, Nigeria. Rats of either sex were isolated and kept in separate well ventilated cages at room temperature (24 ± 2°C) with a 12:12 hour light/dark cycle, and were allowed free access to clean drinking water and growers mash (Guinea Food Nigeria Ltd) *ad libitum*. The animals were acclimatized for two weeks and received human care in compliance with the ethical guide approved by the College of Health Sciences, Delta State University, Abraka, Delta State, Nigeria, in accordance with the NIH guidelines for the care and use of laboratory animals.

2.4 Acute toxicity study

The median lethal dose (LD_{50}) was determined using method described by Lorke's (1983)[25], with slight modification on dosage of extract.

2.5 Preparation of male rats

The male rats were trained, for sexual behavior, two times a day for 14 days. The male rat which did not show any sexual interest during the test period was considered as an inactive male. Thirty-six (36) sexually active male rats were selected for the testing of the aphrodisiac properties of the extracts.

2.6 Preparation of female rats

Female rats were housed in separate cages with food and water *ad libitum*. The female rats were brought in oestrous phase by treating them with Estradiol valerate (10 microgram/kilogram body weight

subcutaneously) and Hydroxyl progesterone (1.5 mg/kg body weight subcutaneously) for 48 hours and 5 hours prior to experimentation, respectively, to make them sexually acceptable and were selected for the study.

2.7 Experimental design

The rat's body weights were recorded before the commencement of treatment. Then sexually active male rats were chosen separately and divided into 6 groups with each group consisting of 6 animals. The animals in the divided groups received oral treatments are as follows:

Group I: Negative control (Normal saline) 10 ml/kg body weight.
Group II: Positive control (Sildenafil citrate) 25 mg/kg body weight.
Group III: Aqueous extract of *Manniophyton fulvum* 200 mg/kg body weight.
Group IV: Aqueous extract of *Manniophyton Fulvuum* 400 mg/kg body weight.
Group V: Ethanol extract of *Manniophyton fulvum* 200 mg/kg body weight.
Group VI: Ethanol extract of *Manniophyton fulvum* 400 mg/kg body weight.

Administration of drugs took place between 9:00am and 10:00am daily and lasted for the duration of 28 days.

2.8 Sexual behavior analysis

The sexual behavior of the experimental rats was observed in a dim light in specially designed cages that have net on all the sides and measuring 50×30×30 cm for convince and aeration. An initial period of 15 minutes was considered as acclimatization period, following which, the extracts and sildenafil citrate were administered. Thirty (30) minutes after drug administration, experimental male rats were first placed in the cage and then two female rats in estrous phase were introduced into the same cage with the male rats and the sexual activities of the male rats in each group were recorded individually for 60 minutes [26-27]. To determine the aphrodisiac effect of the extracts, the following parameters were recorded; Mount Latency, Mount Frequency, Ejaculation Latency and Post Ejaculation Latency.

2.9 Statistical analysis

The data obtained from this study were expressed as mean ± Standard error of mean (SEM) of six animals in each group (n=6). The data from all the groups were analyzed by one way analysis of variance (ANOVA) followed by post hoc Turkey's test using statistical package for social science (SPSS) version 16 for windows. p-value less than 0.05 ($p<0.05$) were considered statistically significant.

III. Results

Toxicity study

The aqueous and ethanol root extract of *Manniophyton fulvum* showed LD_{50} values of 1131.37 mg/kg and 565.69 mg/kg body weight respectively. However, some signs of toxicity observed in some animals were hyper-reactivity, convulsions, weakness, dizziness, loss of appetite, rubbing of nose and mouth on the floor of the cage, tremor and death as summarized in Tables 1a and 1b.

Mount Frequency

There was significant ($P<0.05$) increase in mount frequency of animals in Sildenafil, aqueous and ethanol extract treated groups (42.82 ± 0.40, 39.67 ± 0.20, 43.28 ± 0.05, 30.43 ± 0.21 and 33.78 ± 0.61) when compared to mount frequency of negative control group (9.70 ± 0.28). However, all extract treated groups showed significantly lower mount frequency compared to that of Sildenafil. Aqueous extract 400 mg/kg elicited greater mount frequency than other extract treated groups.

Mount Latancy

There was significant ($P<0.05$) reduction in mount latency of animals in Sildenafil, aqueous and ethanol extract treated groups (0.15 ± 0.03, 0.22 ± 0.01, 0.17 ± 0.02, 0.33 ± 0.05 and 0.25 ± 0.04) when compared to mount latency of negative control group (0.72 ± 0.01). All extract treated groups showed significantly ($P<0.05$) higher mount latency compared to that of Sildenafil. Aqueous extract 400 mg/kg showed lesser mount latency than those in other extract treated groups.

Ejaculation Latency

There was significant ($P<0.05$) reduction in ejaculation latency of animals in Sildenafil, aqueous and ethanol extract treated groups (12.43 ± 0.03, 14.52 ± 0.02, 12.81 ± 0.03, 16.60 ± 0.06, and 13.19 ± 0.08) when compared to ejaculation latency of negative control group (22.74 ± 0.16). However, all extract treated groups showed significantly ($P<0.05$) higher ejaculation latency compared to that of Sildenafil. Aqueous extract 400 mg/kg showed lesser ejaculation latency than other extract treated groups.

Post Ejaculation Latency

There was significant ($P<0.05$) decrease in post ejaculation latency of animals in Sildenafil, aqueous and ethanol extract treated groups (4.08 ± 0.03, 4.63 ± 0.06, 4.40 ± 0.08, 5.63 ± 0.06, and 5.34 ± 0.03) when compared to post ejaculation latency of negative control group (9.10 ± 0.03). However, all extract treated groups showed significantly ($P<0.05$) higher post ejaculation latency than that of Sildenafil. Aqueous extract 400 mg/kg showed lesser post ejaculation latency than other extract treated groups.

IV. Discussion

This study sought to determine the effect of aqueous and ethanol root extract of *Manniophyton fulvum* on the sexual behavior of male Wistar rats.

Acute toxicity (LD_{50}) results (Tables 1a and 1b) of 1131.37 mg/kg and 565.69 mg/kg body weight showed by *Manniophyton fulvum* aqueous and ethanol extract respectively suggests that the aqueous and ethanol extracts are slightly toxic (500 – 5000 mg/kg LD_{50} category). This is evidenced by hyper-reactivity, convulsions, weakness, dizziness, loss of appetite tremor and death demonstrated by animals. Although, the ethanol extract may possess more toxicity (LD_{50}, 565.69 mg/kg) than the aqueous extract (LD_{50}, 1131.37 mg/kg).

Findings from sexual behavioral studies showed that *Manniophyton fulvum* improves sexual performance. This is made evident by the increase in the mounting frequency with a consequent decrease in ejaculation latency and mount lantency among extract treated groups when compared to negative control (distilled water) within the observation period. The mount frequency, mount latency, ejaculation latency and post-ejaculation latency are amongst other parameters considered to be good measure of libido [28-29]. More aphrodisiac activity demonstrated by aqueous extract at 400 mg/kg may be attributed to its higher safety profile (1131.37 mg/kg). Comparatively, Sildenafil citrate, a reference aphrodisiac agent elicited more aphrodisiac activity than extract treated groups.

It is a known fact that improved libido and sexual potency are directly linked to an elevated level of testosterone in the body [30]. This fact is confirmed by Fabbri, (2001)[31] in his study with testosterone supplements that was shown to improve not just ejaculation, but also increase orgasm. It therefore follows that the enhanced sexual behavior which was manifested by the increase in the mounting frequency and the corresponding increase in the number of ejaculations may be due to an increase in the levels of testosterone. Ralebona *et al*. (2012)[32] had suggested in a study that testosterone may either be increased in the body through central influences on ACTH which increases the levels of gonadotropins or by an increase in the number of leydig cells as well as by an increase in the sensitivity of leydig cells to the action of luteinizing hormone.

V. Conclusion

The findings from this study as reflected in the result produced by the animals in the test groups compared with the animals in the standard group validate the anecdotal claim by local traditional medicine practitioner that extract of *Manniophyton fulvum* possesses aphrodisiac effect. However, more research needs to be done to ascertain the possible mechanisms by which the herb elicits its aphrodisiac property.

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Table 1a: Showing phase I acute toxicity test of aqueous and ethanol root extract of *Manniophyton fulvuum*

Doses (mg/kg) Survival rate (Phase 1)		
Concentration	**Aqueous**	**Ethanol**
50	0/3	0/3
500	1/3	3/3
1500	3/3	3/3

Table 1b: Showing phase II acute toxicity test of aqueous and ethanol root extract of *Manniophyton fulvuum*

Doses (mg/kg) Survival rate (Phase 11)		
Concentration	**Aqueous**	**Ethanol**
200	0/1	0/1
400	0/1	0/1
800	0/1	1/1
1600	1/1	1/1

Table 2: Showing effects of aqueous and ethanol root extract of *Manniophyton fulvum* on the sexual behavior parameters of Wistar rats.

Group	Mount Frequency	Mount Latency (min)	Ejaculation Latency (min)	Post Ejaculation Latency (min)
Distilled water 2 ml/kg	9.70 ± 0.28	0.72 ± 0.01	22.74 ± 0.16	9.10 ± 0.03
Sildenafil citrate (25 mg/kg)	42.82 ± 0.40*	0.15 ± 0.03*	12.43 ± 0.03*	4.08 ± 0.03*
AE.MF (200 mg/kg)	39.67 ± 0.20*[a]	0.22 ± 0.01*[a]	14.52 ± 0.02*[a]	4.63 ± 0.06*[a]
AE.MF (400 mg/kg)	43.28 ± 0.05*[b]	0.17 ± 0.02*[a b]	12.81 ± 0.03*[a b]	4.40 ± 0.08*[a b]
EE.MF (200 mg/kg)	30.43 ± 0.21*[a bc]	0.33 ± 0.05*[a bc]	16.60 ± 0.06*[a bc]	5.63 ± 0.06*[abc]
EE.MF (400 mg/kg)	33.78 ± 0.61*[a bd]	0.25 ± 0.04*[a bd]	13.19 ± 0.08*[a bd]	5.34 ± 0.03*[abcd]

Values are expressed as mean ± Standard error of mean, n=6. ***P<0.05**: Significant when compared with Distilled water (2 ml/kg). **[a]P<0.05**: Significant when compared with Sildenafil citrate (25 mg/kg). **[b]P<0.05**: Significant when compared with AE.MF (200 mg/kg). **[c]P<0.05**: Significant when compared with AE.MF (400 mg/kg). **[d]P<0.05**: Significant when compared with EE.MF (200 mg/kg).

References

[1]. NIH Consensus Development Panel on Impotence. NIH Consensus Conference. Impotence. *Journal American Medical Association*. **270**: 1993, 83-90.

[2]. M. Monga, The aging penis: erectile dysfunction. *geriatric nephrology urology*., **9**(1), 1999, 27-37.

[3]. National Institutes of Health (NIH). Erectile Dysfunction. The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) 2004. Mar 9, (Eds: Melman A, Hirsch M. NIH Publication, December 2003; No. 04-3923. http://kidney.niddk.nih.gov/kudiseases/pubs/impotence/index.htm).

[4]. LI. Lipschultz, and E.D. Kim, Treatment of erectile dysfunction in men with diabetes, *Journal American Medical Association*, **281**(5), 1999, 465-466.

[5]. Food and Drug Administration (FDA). Announces Revisions to Labels for Cialis, Levitra and Viagra". 2007. Retrieved on 08-06-2015 from http://www.fda.gov/bbs/topics/NEWS/2007/NEW01730.html.

[6]. WC. Evans, Trease and Evans Pharmacognosy. (15th ed.). 2002. London: W. b. Saunders.

[7]. R. Akash, R. Akash, D. Hrishikesh, P. Amith, and S. Sabah. "Case report: association of combined nonarteritic anterior ischemic optic neuropathy (NAION) and obstruction of cilioretinal artery with overdose of Viagra". *Journal of Ocular Pharmacology and Therapeutic*. **24** (4), 2005, 315–7.

[8]. SK. Kulkarni, and DS. Reddy. Pharmacotherapy of male erectile dysfunction with sildenafil. *Indian. Journal of Pharmacology*., **30, 1998,** 367-378.

[9]. T. Parker-pope, The Cost of Treating Erectile Dysfunction, Retrieved on the 05-06-2015 from http://well.blogs.nytimes.com/2009/08/28/the-cost-of-treating-erectile-dysfunction/.

[10]. NH. Indurwade, PS. Kawtikar. SB Kosalge, and NV Janbandhu, Herbal plants with aphrodisiac activity. *Indian Drugs*. **42**, 2005, 67.

[11]. LJ. Harnack, SA. Rydell, J. and J. Stang, Prevalence of use of herbal products by adults in the Minneapolis/St Paul, Minn, metropolitan area. *Mayo Clinic Proceedings*, **76**(7), 2001, 688-94.

[12]. WHO, Guidelines for the Assessment of Herbal Remedies. Geneva: Traditional Medicine Programme of the World Health Organization. 1991.

[13]. PG. Adaikan, K. Gauthaman, RN. Prasad, and SC Ng, Proerectile pharmacological effects of *Tribulus terrestris* extract on the rabbit corpus cavernosum. Annals of the Academy of Medicine, *Singapore*. **29**(1), 2000, 22-6.

[14]. K. Maud, and O. Hannington, Traditional herbal remedies used in the management of sexual impotence and erectile dysfunction in western Uganda, *African Health Sciences*, 5(1), 2005, 40–49.

[15]. MT. Yakubu, MA. Akanji, AT. Oladiji, and AA. Adesokan, Androgenic potentials of aqueous extract of *Massullaria acuminate* Bullock ex holy stem in male Wistar rats. *Journal of Ethnopharmacology*., **118** (3), 2008, 508-513.

[16]. N. Tajuddin, S. Ahmad, A. Latif, and IA Oasmi, Aphrodisiac activity of 50% ethanol extracts of *Myristica fragrans* Houtt (nutmeg) and *Syzygium aromaticum*. *BMC Complement, Alternative. Medicine*., **5** (16), 2003, 1472-6882.

[17]. WH. El-Tantawy, A. Temraz, OD. El-Gindi, and A. El-Gindi, Free serum testosterone level in male rats treated with *Tribulus alatus* extract. *International Brazilian Journal of Urology*. **33**, 2007, 554-559.

[18]. T. Colman-Saizaarbitoria, P. Boutros, A. Bahsas, Y. Mthison, M. Garrido, and A. Isaeral, Ferrutinin stimulates nitric oxide synthase activity in median eminence of the rat, *Journal of Ethnopharmacology*., **106**(3), 2008, 327-332.

[19]. PO, Agbaire, JOT. Emudainohwo, and BO. Peretiemo-Clarke, Phytochemical screening and toxicity studies on the leaves of *Manniophyton fulvum. International journal of Environmental Science* and Technology. *Vol 3 (1), 2013 1-6.*

[20]. JOT. Emudainohwo, Antibacterial properties of ethanol and aqueous root extract of *Manniophyton fulvum. Archive of Biology Science and health*. Vol 2 (1), 2014, 27 – 34.

[21]. HM. Burkill, The useful plants of West Tropical Africa. (2nd ed.). *Families E–I. Royal Botanic Gardens, Kew, Richmond*, United Kingdom. **2**, 1994, 636.

[22]. R. Nia, DH. Paper, G. Franz, EE. Essien, M. Muganza, and G. Hohmann, Anti-oxidant and Anti-inflammatory activity of *Manniopyton fulvum*. Acta Hortic. 678, 2005, 97-101

[23]. EA. Ojieh, CE. Adegor, IS Ovuakporaye, and OL Ewhre, Preliminary Phytochemical Screening and Antidiarrheal Properties of *Manniophyton fulvum***.** *IOSR Journal of Dental and Medical Science*. 10 (2), 2013, pp 46-52.
[24]. AE. Uduak, and KA. Kola, Antimicrobial Activities of Some Euphorbiaceae Plants Used in the Traditional Medicine of Akwa Ibom State of Nigeria. *Ethnobotanical Leaflets 14,* 2010, *654-64.*
[25]. D. Lorke, A new approach to practical acute toxicity testing. *Archive of Toxicology*. **54**, 1983, 275-287.
[26]. G. Singh, and T. Mukherjee, Herbal Aphrodisiacs. *Indian Drugs***. 35**(4), 1998, 175-182.
[27]. A. Subramoniam, V. Madhavachandran, S. Rajasejharan, and P. Pushpangadan, Aphrodisiac property of *Trichopus zeylanicus* extract in male mice. *Journal of Ethnopharmacology*., **57**, 1997, 21-27.
[28]. RL. Meisel, and BD, Sachs, The physiology of male sexual behaviour. In: Knobil, E. and Neill, J.D. (Eds.). *The Physiology of Reproduction*. (2nd ed.)., New York: Raven Press, **2**, 1994, 3-105.
[29]. M. Abdulwaheb, E. Makonnen, A. Debella, and D. Abebe, Effect of *Catha edulis* foresk (khat) extract on male rat sexual behaviour, *Journal of Ethnopharmacology*.,**110, 2007,** 250-256.
[30]. TM. Mills, CM. Reilly, and RW. Lewis, Androgens and penile erection: a review. *Asian Journal of Andrology*.**17, 1996,** 633-638.
[31]. AAA. Fabbri, New oral agents for erectile dysfunction: what is changing in our practice. *Asian Journal of Andrology*. **3**(3), 2001, 28-38.
[32]. N. Ralebona, CR. Sewani-Rusike and BN. Nkeh-Chungag, Effects of ethanolic extract of Garcinia kola on sexual behaviour and sperm parameters in male Wistar rats. *African Journal of Pharmacy and Pharmacology*. Vol. 6(14), 2012, pp. 1077 – 1082.