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Evaluation of Aphrodisiac Activities of Four Nigerian Ethnomedicinal Plants

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Abstract

Objective: Some age-long plants are currently used as aphrodisiacs. *Allium cepa*, *Allium sativum*, *Garcinia cola* and *Cola acuminata*, used ethnomedicinally in Nigeria for enhancement of libido and erectile dysfunction, were evaluated.

Methods: Aqueous-ethanol extracts (50, 100, 150 mg/kg) were subcutaneously administered to six groups of male rats. Normal saline (5 mL/kg, ip) and testosterone (1 mg/kg, sc) were negative and positive controls, respectively. Another group received testosterone (1 mg/kg, sc) and 10 min later, the extract (100 mg/kg, sc). Eight hours thereafter, the male rats were introduced to females with pre-determined oestrous cycle and Mount (MF), Erection (EF) and Intromission (IF) frequencies, Mount (ML), Intromission (IL) and Ejaculatory (EL) Latencies, Post Ejaculatory Interval (PEI) and Lordosis were recorded.

Results: Testosterone induced increased sexual frequencies that were comparable ($p>0.05$) to those of *G. cola* but significantly ($p<0.05$) higher than those mediated by *A. cepa*, *A. sativum* and *C. acuminata*. Only *G. cola* consistently gave reduced latencies that were either significantly ($p<0.05$) lower or comparable to those of testosterone. Therefore, order of significant sexual activity was testosterone = *G. cola* > *A. sativum* = *C. acuminata* > *A. cepa*. Co-administration of testosterone with *A. cepa* and *A. sativum* bulbs significantly inhibited the effects of standard drug, *C. acuminata* showed some enhancement of effects, while *G. cola* had no effect.

Conclusion: The plants were confirmed as ethnomedicinal aphrodisiacs, while common practice of using herbal sexual stimulants with prescribed drugs may not always increase sexual performance.

Keywords: ***Allium cepa*; *Allium sativum*; *Garcinia cola*; *Cola acuminata***

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Introduction

Sexual function is an important attribute of behavioral life, especially in relationships between the opposite sexes. Libido, the capacity for sexual activity (sex drive), is frequently expressed as sex-seeking behavior and its intensity varies among individuals over a given period of time [1]. Hence, in marriages/relationships, absence of libido would mean no procreation (reproduction) and ultimately the extinction of human race [2]. Sexual problems are widespread and may adversely affect mood, well-being and interpersonal functioning [3]. Various regions of the brain have been implicated in mood and sexual behaviors. Upon sexual stimulation and arousal, neural message is sent from the brain to the spinal cord and nerves that serve the sexual organs [4,5]. In men, the body responds by releasing a cascade of chemicals that direct the flow of blood into the penis resulting in penile erection while in women, the nipples are stiffened, clitoris stimulated, vagina lubricated and the body prepares for intercourse [6].

Erectile dysfunction has been defined as the difficulty or the inability to attain or sustain an erection adequate for satisfactory sexual intercourse, in at least 50 % of the time for a period of six months [1,6]. Studies have shown that mostly menopausal women suffer from reduced libido and men from erectile dysfunction. Hence, a variety of central and peripheral disorders, including damage to nerves, arteries, smooth muscles and fibrous tissues, chronic alcoholism, smoking, and psychological factors, such as stress, anxiety, guilt, depression, low self-esteem and fear of sexual failure, and diseases such as diabetes, kidney, vascular and neurologic diseases, side effects

of antihypertensive, antihistaminic, antidepressant, tranquilizer, appetite suppressant drugs and cimetidine, together with hormonal abnormalities, such as low testosterone levels, could also be responsible for this dysfunction [7-9]. With 10% to 52% and 25% to 63% occurrences in men and women, respectively, sexual dysfunction or disorientation has assumed the status of a serious medical and social problem [10]. It is also an inevitable process of aging and the prevalence in men aged 50 years to 70 years is over 50% [11].

There exist some literature on few studies on the physiology of the human sexuality and how the brain organizes the sexual behavior [12]. The enlargement and stiffening of the penis is triggered by neurotransmitter-nitric oxide, which stimulates production of an enzyme cyclic Guanosine Monophosphate (cGMP). This enzyme in turn stimulates the relaxation of the smooth muscles surrounding the arteries of the penis, thereby allowing the inflow of blood into the penis [6]. Hence, failure in the triggering of cGMP leads to a libido problem. Success in completing the sexual act has been reported to depend on local excitation and psychic stimulus. For example, administration of a small amount of the female sex hormones, oestradiol and progesterone, will immediately activate stereotypic female copulatory/reproductive behavior, known as lordosis [13,14].

Aphrodisiac is any drug, food or food products (e.g. chocolate), topical rubefacient, etc. that stimulates sexual desire, sex drive or sexual pleasure [15]. Their use, in modifying/restoring the impaired sexual functions of humans by the ancient Greek and Arab Physicians, such as Hippocrates (460 BC), Dioscorides (70 AD), Raazi (926 AD), Ibn-e-sina (1038 AD) have been documented [16]. The continued use of plants and their products in the management of sexual dysfunction and enhancement of libido in various African and Asian folkloric medicines, and recently world-wide as supplements, has generated some scientific interests [1,17]. Ginseng root, an essential traditional Chinese medicine, is currently used as aphrodisiac by about 6 million Americans [18]. Yohimbine, an indole alkaloid, is the aphrodisiac ingredient of the bark of *Pausinystalia yohimbe* (Bielle) Pierre (*Rubiaceae*) or root of *Rauwolfia* species. *Rauwolfia* plant, used in treatment of psychiatric disorders, is native to the tropical rain forest of West Africa. The aphrodisiac activity of yohimbine plant has been known before the last century [19]. Its dried stem bark is widely used in North-eastern Nigeria for the treatment of erectile dysfunction and as an aphrodisiac, while its concoction is traditionally used to treat loss of libido. Current hypothesis on the beneficial mechanism of the action of yohimbine on sexual activities mainly points to a central mechanism of action [20].

Although testosterone may be used for hypoactive sexual desire [21], many of the world populations now prefer the use of natural plants [22]. Many of such plants have served as lead for currently used drugs, such as quinine and quinidine from *Cinchona* spp., vincristine and vinblastine from *Catharanthus roseus*, artemisinin from *Artemisia annua*, etc. Also, lupenyl acetate was identified as the most active anti-plasmodial agent of *Gongronema latifolium*, ethnomedically used for treating malaria in Nigeria [23], while β-stigmasterol was the active anti-hyperglycemic ingredient in *Senecio biafrae* [24]. *Murraya koenigii*, an Asian spicy plant growing in Nigeria, is used by the Asians all over the world to flavor their curries and the volatile constituents responsible for this action have been reported [25]. Therefore, investigations into safer and more active natural sexual stimulants should be increased.

Cola acuminata (*P. Beaux*) Schotf & End (*Sterculiaceae*), synonym *Cola nitida* (Vent) Schoff & End and commonly known as Cola or Kola nuts and *Garcinia kola* Heckel (*Clusiaceae/Guttiferae*) also known as Bitter kola are believed to increase libido [26]. Garlic, garlic bulb and garlic clove are the common names of *Allium sativum* L while *Allium cepa* L is called white onion. They are both of the *Liliaceae* family and are known to possess aphrodisiac properties, especially milk of the white onion that has been reported to promote sperm count in man [27]. Since, these four Nigerian medicinal plants and spices are either used in whole or part of aphrodisiac preparations in Uyo, southeast Nigeria, we evaluated their aphrodisiac property, using Wistar rats, in order to justify the ethnomedicinal claims.

Materials and Methods

Plant materials and extraction

The bulbs of the indigenous brown variety of *A. sativum* and nuts of *C. acuminata* were purchased in November, 2010 from the fruit and garden market located in Urua Akpan Andem, Uyo Local Government Area of Akwa-Ibom State, Nigeria while in the same month, *G. cola* and *A. cepa* were collected from IkotEtetuk village in IkotAbasi Local Government Area of Akwa-Ibom State. They were identified by Dr. (Mrs.) Bassey, Botany Department, University of Uyo, Uyo, Nigeria. Their pericarps were removed, rinsed with distilled water, sliced into thin pieces and dried in a hot air oven at 40°C for 24 h. A 500 g of each plant material was weighed, macerated with 70% aqueous-ethanol in a Waring blender and thereafter soaked at room temperature (25°C) in 1.5 L of 70% aqueous-ethanol for 72 h, with occasional agitation. The extract was filtered and this process was repeated twice. The filtrates for each plant were separately combined and concentrated *in vacuo* to give their extracts with 10.4, 15.9, 1.8 and 7.4% yields for *A. cepa*, *A. sativum*, *C. acuminata* and *G. cola*, respectively. They were thereafter stored at 4°C until needed.

Animals

Adult and mature Wistar rats of both sexes (200 g to 250 g) were obtained from the animal house of the University of Calabar, Calabar, Nigeria. The male and female rats were kept separately, acclimatized and maintained for one month under standard conditions (12 h light/12 h dark cycle) at the animal house of the Department of Pharmacology and Toxicology, University of Uyo, Uyo. The animals were fed with growers' pellet (Bendel Feeds, Ewu, Nigeria) and water was given ad libitum. All animal experiments conformed to the guide for the care and use of Laboratory Animals published by the National Academies Press [23,24,28].

Determination of oestrous cycle of the female rats

The oestrous (sexual) cycles of the female rats were determined by a subcutaneous (sc) administration of 17β-oestradiol (15 µg/kg) to the pre-determined oestrous cycled female rats, 48 h prior to their being paired in cages with the male rats. Some 40 h later, progesterone (500 µg/rat) dissolved in 30% Tween 80 was administered (sc) to the same group of female rats and their lordosis frequency determined [29].

Characterisation of the male rats

Randomly picked male rats were paired with sexually mature receptive female rats for 30 min in a plexiglass cage at 19.00 h, using a red bulb and their sexual activities were characterized by noting the sexual behavioral indices of Mount (MF), Intromission (IF) and Erection (EF) Frequencies, Mount (ML), Intromission (IL) and Ejaculatory (EL) Latencies, Post Ejaculatory Interval (PEI) and Lordosis. The male rats with the highest scores of these indices were classified as sexually active, followed by sexually sluggish while those

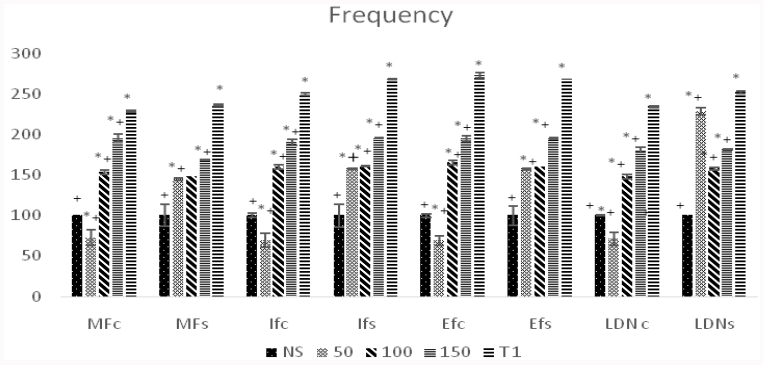

Figure 1: Comparison of the effects of *Allium cepa* and *Allium sativum* extracts (50, 100, 150 mg/kg) on sexual frequencies.
Data show the mean ± SEM of sexual frequency indices expressed as percentages of those of negative control, n=6. *: Values are significantly different ($p<0.05$, one-way analysis of variance followed by the Student-Newman-Keuls' test) from negative control; †: Values are significantly different ($p<0.05$, one-way analysis of variance followed by the Student-Newman-Keuls' test) from positive control. c: *Allium cepa*; s: *Allium sativum*; MFc, MFs; IFc, IFs; EFc, EFs; LDNc, LDNs: Mount frequency, Intromission frequency, Erection frequency and Lordosis of *A. cepa* and *A. sativum*, respectively; NS: Normal saline (negative control, 5 mL/kg); 50, 100, 150: Doses (50, 100, 150 mg/kg) of extracts given; T1: Testosterone (positive control, 1 mg/kg).

Table 1: Effect of *Allium cepa* aqueous-ethanol extract on sexual behavior indices of male rats.

Extract/Drug (mg/kg)	Frequency (number)			Lordosis (number)	Latency (sec)			PEI (min)
	MF	IF	EF		ML	IL	EL	
Normal saline	15.83 ± 1.81^{b}	13.67 ± 1.84^{b}	13.00 ± 1.87^{b}	15.00 ± 1.80^{b}	40.17 ± 5.64^{c}	1.05 ± 0.22^{b}	7.52 ± 1.19^{e}	12.03 ± 0.80^{b}
50	11.50 ± 1.08^{a}	9.50 ± 0.78^{a}	9.00 ± 0.56^{a}	10.67 ± 0.87^{a}	1.39 ± 0.44^{b}	1.46 ± 0.44^{b}	3.62 ± 0.33^{c,d}	8.78 ± 0.41^{a}
100	24.33 ± 0.72^{c}	21.83 ± 0.60^{c}	21.50 ± 0.61^{c}	22.17 ± 0.65^{c}	0.13 ± 0.01^{a}	0.29 ± 0.06^{a}	3.08 ± 0.52^{b,c}	10.05 ± 1.17^{a,b}
150	31.00 ± 1.59^{d}	26.00 ± 0.97^{d}	25.33 ± 0.78^{c}	27.17 ± 0.91^{d}	0.45 ± 0.10^{a}	0.41 ± 0.14^{a}	0.98 ± 0.25^{a}	8.68 ± 0.66^{a}
Testosterone 1	36.17 ± 0.43^{e}	34.17 ± 0.65^{e}	35.50 ± 1.22^{d}	35.17 ± 0.59^{e}	0.47 ± 0.09^{a}	0.47 ± 0.09^{a}	4.21 ± 0.35^{d}	11.61 ± 0.29^{b}
Testosterone 1 + Ext (100)	29.17 ± 0.76^{d}	24.50 ± 1.34^{c,d}	22.50 ± 1.61^{c}	26.50 ± 1.19^{d}	0.37 ± 0.09^{a}	2.21 ± 1.71^{b,c}	2.24 ± 0.31^{b}	12.74 ± 0.39^{b}

Data show the mean ± SEM, n=6. Values with different superscripts within columns are significantly different ($p<0.05$, one-way analysis of variance followed by the Student-Newman-Keuls' test). Normal saline: Negative control (5 mL/kg); MF: Mount frequency; IF: Intromission frequency; EF: Erection frequency; ML: Mount latency; IL: Intromission latency; EL: Ejaculatory latency; PEI: Post Ejaculatory Interval; Testosterone 1: Positive control (1 mg/kg); Testosterone 1 + Ext (100): 1 mg of Testosterone followed by 100 mg/kg of the extract 10 min later.

classified as sexually impotent did not mount at all [29].

Evaluation of aphrodisiac activities of the extracts

Food was withdrawn 3 h prior to the experiment. Mature and sexually active male rats were divided into six (6) groups of six (6) rats, each. Group I (negative control) was given normal saline (5 mL/kg, i.p.). Groups II-IV were given 50, 100 and 150 mg/kg (sc) of 70% aqueous-ethanol extract of *A. cepa* or *A. sativum* or *C. acuminata* or *G. cola*, respectively 8 h prior to introduction of the female rats into the plexiglass cages while group V was sc administered with testosterone (1 mg/kg, positive control). Group VI was given testosterone (1 mg/kg, sc) and 10 min later, extract (100 mg/kg, sc) was administered. Each male rat was acclimatized for 10 min in the plexiglass cage prior to the introduction of the female rat. The rats were observed for 30 min. However, a rat is disqualified if any of the following conditions occur before 30 min: Immediately after the post ejaculatory intromission, if intromission does not occur within 15 min, or post ejaculatory interval exceeds 15 min or if ejaculation latency exceeds 30 min [29].

Statistical analysis

The mean ± SEM values were compared using one-way Analysis of Variance (ANOVA), followed by Student-Newman-Keul post-hoc tests. A probability level of less than 5% ($p<0.05$) was considered significant. To plot the graphs of comparison of activities of the two *Allium* species on one hand, and of the two Kolas on the other hand, sexual behavioral index scores induced by the negative control were taken as 100% and those of the extracts/drugs given in the figures were percentages of the negative control. For the tables and other figures, values were those obtained in the experiments [29].

Results and Discussion

The indices of sexual dysfunction, especially sexual incompetence and erectile dysfunction occur in both men and women. These problems, which are not exclusive to humans, are of increasing concern. Since it has been reported that a variable percentage of male rats are sexually impotent and could not conclude ejaculation process or initiate sexual intercourse with a receptive female, rodents are therefore considered as good models for the study of sexual dysfunctions [30]. Interestingly, there have been a number of important approaches to restore sexual function in both human males and females. Among these are many plants that are traditionally employed in different cultures to improve sexual performances [31-34]. The Chinese herb of choice as treatment for impotence is Horny Goat weed (*Epimedium sagitattum*) while elixir of Maca (*Lepidium meyenii* Walpers) is employed in the Andean region for its alleged ability to improve energy and fertility [35]. Hence, in this present study, the ethnomedicinal claims of four Nigerian spices that are used as aphrodisiacs and in the management of sexual dysfunction were evaluated. These were *A. cepa*, *A. sativum* that are commonly used in preparations of spicy African and Asian cuisines, and *C. acuminata* and *G. cola* that are usually consumed as spicy nuts in Nigeria.

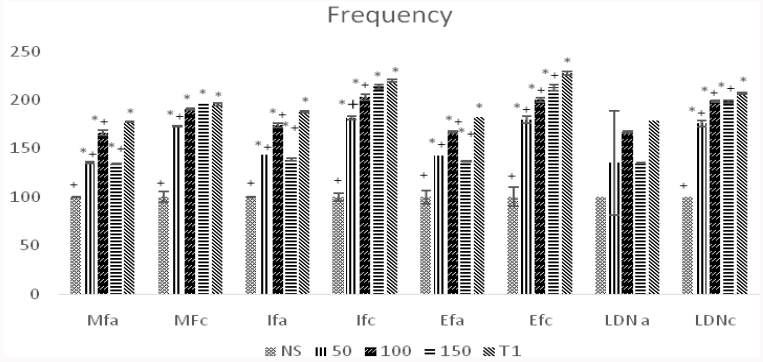

Figure 2: Comparison of the effects of *Cola acuminata* and *Garcina cola* extracts (50, 100, 150 mg/kg) on sexual frequencies.
Data show the mean ± SEM of sexual frequency indices expressed as percentages of those of negative control, n = 6. *: Values are significantly different ($p<0.05$, one-way analysis of variance followed by the Student-Newman-Keuls' test) from negative control; †: Values are significantly different ($p<0.05$, one-way analysis of variance followed by the Student-Newman-Keuls' test) from positive control. a: *Cola acuminata*; c: *Garcina cola*; MFa, MFc; IFa, IFc; EFa, EFc; LDNa, LDNc: Mount frequency, Intromission frequency, Erection frequency and Lordosis of *C. acuminata* and *G. cola*, respectively; NS: Normal saline (negative control, 5 mL/kg); 50, 100, 150: Doses (50, 100, 150 mg/kg) of extracts given; T1: Testosterone (positive control, 1 mg/kg).

Table 2: Effect of *Allium sativum* aqueous-ethanol extract on sexual behavior indices of male rats.

Extract/Drug (mg/kg)	Frequency (number)			Lordosis (number)	Latency (sec)			PEI (min)
	MF	IF	EF		ML	IL	EL	
Normal saline	13.67 ± 0.04^{a}	11.00 ± 0.30^{a}	11.00 ± 0.21^{a}	12.67 ± 0.05^{a}	40.33 ± 0.54^{e}	80.16 ± 0.19^{f}	7.55 ± 0.02^{c}	11.89 ± 0.02^{c}
50	19.83 ± 0.30^{b}	17.33 ± 0.11^{b}	17.33 ± 0.21^{b}	29.00 ± 1.40^{d}	30.50 ± 0.22^{d}	40.83 ± 0.33^{e}	3.63 ± 0.07^{a}	10.85 ± 0.10^{b}
100	20.33 ± 0.01^{b}	17.67 ± 0.11^{b}	17.67 ± 0.01^{b}	20.00 ± 0.40^{b}	13.17 ± 0.05^{c}	14.83 ± 0.34^{d}	4.85 ± 0.08^{b}	8.98 ± 0.30^{a}
150	23.00 ± 0.12^{c}	21.50 ± 0.11^{c}	21.50 ± 0.22^{c}	23.00 ± 0.12^{c}	9.12 ± 0.75^{b}	9.53 ± 0.32^{c}	3.61 ± 0.11^{a}	11.17 ± 0.04^{c}
Testosterone 1	32.33 ± 0.40^{d}	29.50 ± 0.12^{e}	29.50 ± 0.03^{e}	32.00 ± 0.52^{e}	5.03 ± 0.97^{a}	5.03 ± 0.22^{a}	4.44 ± 0.04^{b}	10.45 ± 0.48^{b}
Testosterone 1 + Ext (100)	31.50 ± 0.21^{d}	24.16 ± 0.20^{d}	24.16 ± 0.04^{d}	26.67 ± 0.60^{d}	4.09 ± 0.68^{a}	7.06 ± 0.01^{b}	3.25 ± 0.03^{a}	8.05 ± 0.32^{a}

Data show the mean ± SEM, n=6. Values with different superscripts within columns are significantly different ($p<0.05$, one-way analysis of variance followed by the Student-Newman-Keuls' test). Normal saline: Negative control (5 mL/kg); MF: Mount frequency; IF: Intromission frequency; EF: Erection frequency; ML: Mount latency; IL: Intromission latency; EL: Ejaculatory latency; PEI: Post Ejaculatory Interval; Testosterone 1: Positive control (1 mg/kg); Testosterone 1 + Ext (100): 1 mg of Testosterone followed by 100 mg/kg of the extract 10 min later.

The oestrous cycle of the female rats was determined to last for 12 h and occurred every four or five days. This corresponded to the time of their highest sexual arousal and receptiveness to the male. The oestrous cycle was induced in the female rats by administration of 17β-oestradiol, while post-administration of progesterone enhanced the effect of 17β-oestradiol, making the female rats to be highly receptive to the male rats, as indicated by their high lordosis frequency. Lordosis has been reported as the measure of the willingness of female rat to submit to male rat for copulation, which is demonstrated by the arching of the female trunk, elevation of the head and its hind quarters, thereby making it easy for the male rat to have easy intromission of their penis [29].

Effects of *Allium* spp. extracts on the sexual behavioral indices of rats

The aqueous-ethanol extract of *A. cepa* induced dose-dependent increases in the Mount (MF), Intromission (IF) and Ejaculatory (EF) Frequencies and Lordosis (LD). Testosterone (1 mg/kg, the standard drug) elicited significantly ($p<0.05$) higher frequencies than those given by the highest dose (150 mg/kg) tested of the extract (Table 1) (Figure 1). The extract elicited a dose-dependent reduction in the Ejaculatory Latency (EL) up till the highest dose tested while those of the Mount (ML) and Intromission (IL) Latencies were only dose-dependent till 100 mg/kg. The shortened ML and IL latencies induced by testosterone were comparable ($p>0.05$) to those elicited by 100 and 150 mg/kg of the extract, while its EL and Post Ejaculatory Interval (PEI) values were comparable to only 50 and 100 mg/kg, respectively of the extract (Table 1).

Compared to the negative control, *A. sativum* extract significantly increased MF, IF and EF frequencies, and Lordosis, although these increases were significantly lower than those elicited by testosterone (Table 2) (Figure 1). The extract also dose-dependently and significantly reduced the ML and IL latencies while those of the EL and PEI were not dose-dependent (Table 2). The significant increases in Lordosis, MF, IF and EF frequencies given by testosterone, *A. cepa* and *A. sativum* extracts agreed with the significant reduction in their latencies, with the exception of their effects on PEI. Hence, results of this study showed that the *Allium* extracts augmented male and female rats' sexuality, as measured by the improved behavioral indices of Lordosis, sexual frequencies and latencies (Table 1 and 2) (Figure 1), thereby justifying their aphrodisiac ethnomedicinal use.

Effects of *Cola* extracts on the sexual behavioral indices of rats

The dose-dependent improvement of Lordosis and sexual frequencies of MF, IF and EF elicited by *C. acuminata* and *G. cola* extracts was only till 100 mg/kg. At this dose, values of frequency indices given by testosterone were significantly higher than those elicited by extracts of these two kolas (*C. acuminata* and *G. cola*), with the exception of MF and Lordosis values of *G. cola* extract that were comparable to those of the standard drug (Table 3 and 4) (Figure 2). In addition, sexual frequencies and Lordosis values elicited by 100 mg/kg and 150 mg/kg of *G. cola* were comparable, while the IF and EF values of 150 mg/kg of this extract were comparable to those of testosterone (Figure 2). Furthermore, the significant reduction in the latency indices induced by *G. cola* extract was dose-dependent. The

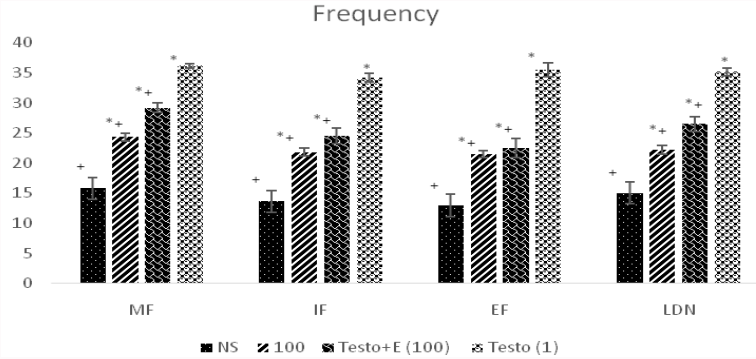

Figure 3: Effect of *Allium cepa* (100 mg/kg) on the sexual frequency indices elicited by testosterone (1 mg/kg).
Data show the mean ± SEM sexual frequency indices, n = 6. *: Values are significantly different (p<0.05, one-way analysis of variance followed by the Student-Newman-Keuls' test) from negative control; †: Values are significantly different (p<0.05, one-way analysis of variance followed by the Student-Newman-Keuls' test) from positive control. MF: Mount frequency; IF: Intromission frequency; EF: Erection frequency; Lordosis; NS: Normal saline (negative control, 5 mL/kg); 100: 100 mg/kg dose (median) of the extract given; Testo + E (100): Testosterone (1 mg/kg) flowed by extract median dose (100 mg/kg); Testo (1): Testosterone (positive control, 1 mg/kg).

Table 3: Effect of *Cola acuminata* aqueous-ethanol extract on sexual behavior indices of male rats.

Extract/Drug (mg/kg)	Frequency (number)			Lordosis (number)	Latency (sec)			PEI (min)
	MF	IF	EF		ML	IL	EL	
Normal saline	18.67 ± 0.11^{a}	16.50 ± 0.12^{a}	16.33 ± 1.08^{a}	18.16 ± 0.01^{a}	37.03 ± 0.02^{e}	63.33 ± 0.02^{f}	4.70 ± 0.21^{d}	7.55 ± 0.02^{c}
50	25.33 ± 0.23^{b}	23.67 ± 0.04^{c}	23.33 ± 0.08^{c}	24.50 ± 0.11^{b}	26.06 ± 0.11^{d}	0.78 ± 0.09^{a}	7.21 ± 0.10^{e}	3.97 ± 0.60^{a}
100	31.00 ± 0.82^{c}	28.67 ± 0.72^{d}	27.33 ± 0.22^{d}	30.33 ± 0.22^{c}	11.40 ± 0.73^{b}	11.75 ± 0.12^{d}	4.01 ± 1.36^{c,d}	3.65 ± 0.11^{a}
150	25.00 ± 0.12^{b}	22.83 ± 0.30^{b}	22.33 ± 0.11^{b}	24.50 ± 0.12^{b}	18.50 ± 0.28^{c}	19.83 ± 1.10^{e}	1.18 ± 0.06^{a}	6.20 ± 0.20^{b}
Testosterone 1	33.16 ± 0.09^{d}	31.00 ± 0.30^{e}	29.83 ± 0.05^{e}	32.50 ± 0.04^{d}	4.08 ± 0.64^{a}	4.08 ± 0.10^{b}	5.22 ± 0.29^{d}	3.21 ± 0.13^{a}
Testosterone 1 + Ext (100)	34.00 ± 0.12^{e}	30.83 ± 0.71^{e}	30.83 ± 0.01^{f}	32.50 ± 0.25^{d}	5.56 ± 0.19^{a}	5.80 ± 0.16^{c}	2.08 ± 0.40^{b}	5.21 ± 0.11^{b}

Data show the mean ± SEM, n = 6. Values with different superscripts within columns are significantly different (p<0.05, one-way analysis of variance followed by the Student-Newman-Keuls' test). Normal saline: Negative control (5 mL/kg); MF: Mount frequency; IF: Intromission frequency; EF: Erection frequency; ML: Mount latency; IL: Intromission latency; EL: Ejaculatory latency; PEI: Post Ejaculatory Interval; Testosterone 1: Positive control (1 mg/kg); Testosterone 1 + Ext (100): 1 mg of Testosterone followed by 100 mg/kg of the extract 10 min later.

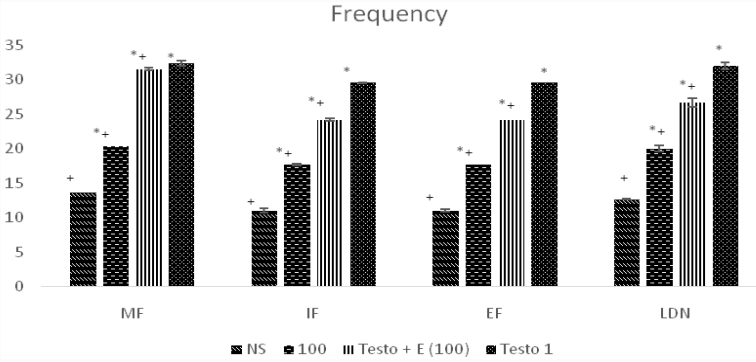

Figure 4: Effect of *Allium sativum* (100 mg/kg) on the sexual frequency indices elicited by testosterone (1 mg/kg).
Data show the mean ± SEM sexual frequency indices, n = 6. *: Values are significantly different (p<0.05, one-way analysis of variance followed by the Student-Newman-Keuls' test) from negative control; †: Values are significantly different (p<0.05, one-way analysis of variance followed by the Student-Newman-Keuls' test) from positive control. MF: Mount frequency; IF: Intromission frequency; EF: Erection frequency; Lordosis; NS: Normal saline (negative control, 5 mL/kg); 100: 100 mg/kg dose (median) of the extract given; Testo + E (100): Testosterone (1 mg/kg) flowed by extract median dose (100 mg/kg); Testo 1: Testosterone (positive control, 1 mg/kg).

ML and IL indices induced by the most active dose (150 mg/kg) of *G. cola* extract were significantly higher than those given by testosterone, while it's EL and PEI indices were comparable to those of the standard drug (Table 4). A 100 mg/kg of *C. acuminata* extract gave the least ML value of 11.4 sec that was significantly higher than the 4.08 sec given by the standard drug. Also, 0.78 sec and 1.18 sec elicited by 50 mg/kg and 150 mg/kg of *C. acuminata* extract for the IL and EL respectively were significantly lower than those of the standard drug. On the other hand, the PEI values given by 50 mg/kg and 100 mg/kg of *C. acuminata* extract and testosterone were comparable (Table 3). This study (Tables 3 and 4) (Figure 2), therefore showed that testosterone was a better aphrodisiac than the Kolas and provided justification of the ethnomedicinal use of *C. acuminata* and *G. cola* as sexual stimulants and aphrodisiacs.

Table 4: Effect of *Garcinia cola* aqueous-ethanol extract on sexual behavior indices of male rats.

Extract/Drug (mg/kg)	Frequency (number)			Lordosis (number)	Latency (sec)			PEI (min)
	MF	IF	EF		ML	IL	EL	
Normal saline	19.00 ± 1.01^{a}	16.16 ± 0.61^{a}	15.50 ± 1.54^{a}	17.66 ± 0.50^{a}	42.16 ± 1.05^{e}	50.16 ± 1.02^{e}	4.15 ± 0.24^{d}	12.99 ± 0.12^{d}
50	32.83 ± 0.21^{b}	29.33 ± 0.60^{b}	27.83 ± 0.95^{b}	31.00 ± 1.05^{b}	21.30 ± 0.04^{d}	22.16 ± 1.20^{d}	1.90 ± 0.10^{c}	10.54 ± 0.21^{c}
100	36.16 ± 0.32^{c}	32.83 ± 1.03^{c}	31.00 ± 0.69^{c}	35.16 ± 0.33^{c}	12.33 ± 1.00^{c}	13.33 ± 0.50^{c}	1.39 ± 0.15^{b}	9.50 ± 0.18^{b}
150	37.50 ± 0.37^{c}	34.50 ± 0.78^{c,d}	33.00 ± 0.97^{c,d}	35.00 ± 0.56^{c}	6.16 ± 0.45^{b}	7.66 ± 0.44^{b}	1.14 ± 0.05^{a}	7.87 ± 0.16^{a}
Testosterone 1	37.16 ± 0.43^{c}	35.50 ± 0.46^{d}	35.30 ± 0.54^{d}	36.50 ± 0.37^{c}	3.50 ± 0.46^{a}	3.50 ± 0.46^{a}	1.13 ± 0.04^{a}	7.22 ± 0.30^{a}
Testosterone 1 + Ext (100)	37.83 ± 0.33^{c}	34.83 ± 0.33^{c,d}	34.66 ± 0.23^{d}	36.33 ± 0.54^{c}	2.66 ± 0.36^{a}	3.00 ± 0.39^{a}	1.04 ± 0.01^{a}	7.52 ± 0.18^{a}

Data show the mean ± SEM, n = 6. Values with different superscripts within columns are significantly different (p<0.05, one-way analysis of variance followed by the Student-Newman-Keuls' test). Normal saline: Negative control (5 mL/kg); MF: Mount frequency; IF: Intromission frequency; EF: Erection frequency; ML: Mount latency; IL: Intromission latency; EL: Ejaculatory latency; PEI: Post Ejaculatory Interval; Testosterone 1: Positive control (1 mg/kg); Testosterone 1 + Ext (100): 1 mg of Testosterone followed by 100 mg/kg of the extract 10 min later.

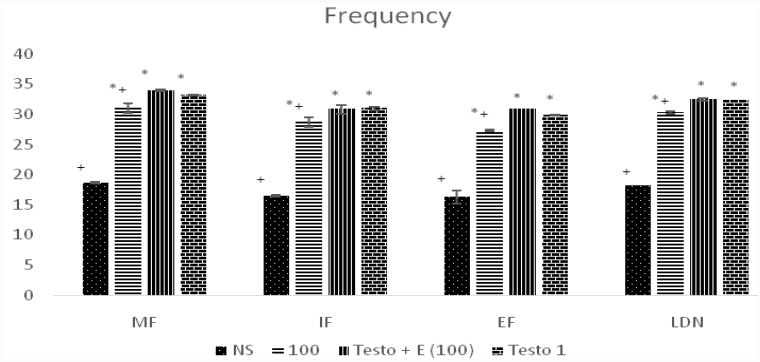

Figure 5: Effect of *Cola acuminata* (100 mg/kg) on the sexual frequency indices elicited by testosterone (1 mg/kg).
Data show the mean ± SEM sexual frequency indices, n = 6. *: Values are significantly different (p<0.05, one-way analysis of variance followed by the Student-Newman-Keuls' test) from negative control; †: Values are significantly different (p<0.05, one-way analysis of variance followed by the Student-Newman-Keuls' test) from positive control. MF: Mount frequency; IF: Intromission frequency; EF: Erection frequency; Lordosis; NS: Normal saline (negative control, 5 mL/kg); 100: 100 mg/kg dose (median) of the extract given; Testo + E (100): Testosterone (1 mg/kg) flowed by extract median dose (100 mg/kg); Testo 1: Testosterone (positive control, 1 mg/kg).

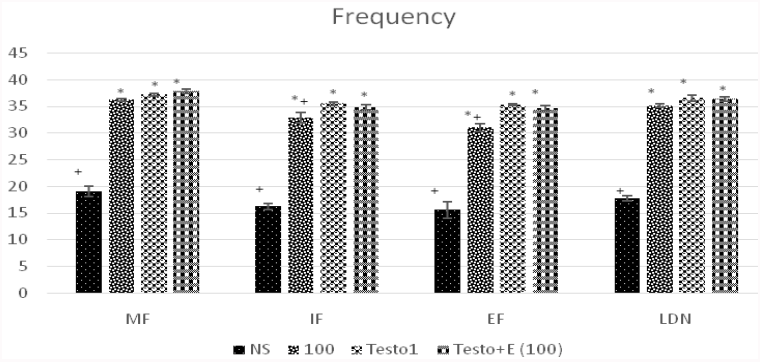

Figure 6: Effect of *Garcina cola* (100 mg/kg) on the sexual frequency indices elicited by testosterone (1 mg/kg).
Data show the mean ± SEM sexual frequency indices, n = 6. *: Values are significantly different (p<0.05, one-way analysis of variance followed by the Student-Newman-Keuls' test) from negative control; †: Values are significantly different (p<0.05, one-way analysis of variance followed by the Student-Newman-Keuls' test) from positive control. MF: Mount frequency; IF: Intromission frequency; EF: Erection frequency; Lordosis; NS: Normal saline (negative control, 5 mL/kg); 100: 100 mg/kg dose (median) of the extract given; Testo1: Testosterone (positive control, 1 mg/kg); Testo + E (100): Testosterone (1 mg/kg) flowed by extract median dose (100 mg/kg).

Comparison of the aphrodisiac effects between the *Allium* species

The values of the sexual frequency indices (MF, IF, EF and Lordosis) given by *A. sativum* were significantly higher than those of *A. cepa* at 50 mg/kg, while their indices at 100 mg/kg and 150 mg/kg were comparable. However, the MF value of *A. cepa* at 150 mg/kg was significantly higher than that of *A. sativum* (Figure 1). Moreover, the decreasing order of activity of the two extracts was testosterone >*A. sativum* >*A. cepa*. Therefore, it could be concluded that *A. sativum* was a better sexual stimulant than *A. cepa*, while the highest sexual stimulation property demonstrated by testosterone confirmed this standard hormonal drug as an orthodox aphrodisiac. Testosterone, *A. cepa* and *A. sativum* extracts specifically stimulated increases in the frequency indices (Figure 1). Also, testosterone is a commonly acknowledged aphrodisiac and its effect has been shown to be due to increased sperm production. The enhancement of spermatogenesis is

believed to promote a corresponding increase in desire for sex [21,36]. Similarly, an aphrodisiac activity that had the highest activity at lower doses has been reported for extracts of spicy *A. cepa* and *A. sativum*, in a study that the sexual indices of MF, ML, Anogenital Sniffing (AS), Genital Grooming (GG) and Chasing of Female Animal (CFA) were measured. Tadalafil was the standard drug used [37]. Furthermore, the report that white onion promotes sperm count in man [27], and similarity in the activity of the onions and testosterone by increasing sexual frequencies in rats (Tables 1 and 2) (Figure 1), may indicate that the onions (*A. sativum* and *A. cepa*) of this study may have similar mechanism of sexual stimulation as testosterone.

Comparison of the aphrodisiac effects between the *Cola* species

At all doses, the decreasing order of ability of the Kola extracts to increase the sexual frequency and Lordosis indices was testosterone ≥ *G. kola* > *C. acuminata* (Figure 2). On the other hand, the decreasing order of the Kola extracts to reduce the ML and EL latency indices was testosterone =*G. kola* > *C. acuminata*, while those of IL and PEI was testosterone ≥ *C. acuminata* > *G. kola*, especially at 50 mg/kg and 100 mg/kg (Tables 3 and 4). This may indicate that although the two Kola nuts had sexual stimulation properties, *G. kola* was a significantly better sexual stimulant and confirmed the same assertion made earlier [38]. Also, *C. acuminata* was more active in reducing the sexual latencies than increasing the sexual frequencies (Tables 3 and 4) (Figure 2). The modification of male sexual behaviors by *C. acuminata* extract, adduced to enhanced production of dopamine, was linked to its caffeine content [38]. The levels of caffeine reported in *C. acuminata*, *G. cola* and *Cola nitida* were 4.7%, 0.6% and 2.4 %, respectively [39]. Since *Cola acuminata* had a high level of caffeine and gave a significantly lower rest period in-between mating and less frequency of actual mating, *C. acuminata* may be more of an energizer [38].

Moreover, the ability of *G. cola* to significantly increase the sexual frequencies (Figure 2), may indicate that it has higher ability to increase sexual arousal (desire) and ability to copulate (sexual frequency) than that of *C. acuminata*. Therefore, the aphrodisiac mechanism of action of *G. cola* could not be due to its low caffeine content [39]. Hence, the authors of this present study agreed with an earlier suggestion that its mechanism of action in modifying sexual behaviors in male rats needs to be determined, especially now that its aphrodisiac ethnomedicinal claim is confirmed [38]. Also, this study (Tables 1-4) (Figure 1 and 2), suggests that the sexual frequencies may be a more responsive model than the latencies in measuring aphrodisiac activity.

Effects of extracts on sexual behavioral indices elicited by a standard drug

The rural dwellers of the African, Asian and Latin America continents consult traditional practitioners as their first choice of medical care and only visit the hospital or qualified medical personnel when there is no relief [40]. They use combinations of plants or plant parts in treatment and management of diseases, including malaria. The efficacies of such combinations have been evaluated and the results obtained often justified some of these actions. The increased effects observed with the decoctions over the activities of the individual herbal extracts suggested synergism in their activities [40-42].

Moreover, herbal drugs are secretly taken together with prescribed orthodox drugs, even on the hospital beds and in convalescing homes. Such practices have raised some concerns, especially among the orthodox medical practitioners. However, the proponents of this practice, of which traditional medical practitioners are chief, have mostly justified their actions by citing the WHO approved ACT (Artemisinin Combination Therapy) for treatment of malaria, and other combinations of orthodox drugs used in treating diabetes, tuberculosis, peptic ulcer, cancer, HIV-AIDS, among others [40,42]. Hence, the continued investigation of the effects of co-administering herbal and orthodox drugs is imperative [42]. Earlier on in our studies, we had indicated that combination of standard drugs with plant extracts enhanced or inhibited effect of the orthodox drugs on the extracts [37,38]. However, we now believe that such combinations of orthodox or standard drugs and herbs or plant extracts should only be interpreted as possible modulating effects of such practice on activities of the standard drugs. This position was rightly captured in our last paper (Figures 3 and 4) [42].

Administration of 100 mg/kg of *A. cepa* and *A. sativum* (median dose) significantly inhibited the sexual frequency indices and Lordosis of testosterone. However, *A. sativum* (100 mg/kg) had no effect on the MF index value elicited by testosterone, as the MF value of the extract-testosterone combination was comparable with that of testosterone (Figure 3 and 4). Also, *A. cepa* extract significantly enhanced and inhibited the effects of testosterone on EL and IL, respectively, while *A. sativum* significantly enhanced and inhibited the effects of testosterone on PEI and IL, respectively. The values of the other latency indices given by *A. cepa* and *A. sativum* testosterone combinations were comparable with those of the standard drug (Tables 1 and 2). Therefore, although both plant extracts were confirmed as sexual stimulants in this study, similar to earlier report of same [37], co-administration of these *Allium* species with testosterone would significantly inhibit increased sexual activities elicited by the standard drug (Figure 3 and 4). On the other hand, concomitant administration of these *Allium* species and tadalafil (5 mg/kg) was reported to produce no significant effects on the sexual activities elicited by tadalafil, the standard sexual stimulant used in the study [37].

Hence, in achieving the maximal sexual stimulation given by testosterone, co-administration of testosterone and the *Allium* species is contraindicated. In northern Nigeria, many of the adult citizens take both orthodox sexual stimulants with Burantashi, a locally prepared aphrodisiac. Also, a local delicacy named "Suya" (grilled red meat) is often habitually consumed with large quantities of onions. Therefore, people that enjoy taking Suya and large quantity of onions need to be cautioned not to eat this delicacy at the same time that they are on orthodox aphrodisiacs, as such practice or habit may not give the desired enhanced sexual stimulatory effect.

Concomitant administration of the median dose of *Cola acuminata* or *G. cola* extract and testosterone had no effect on Lordosis and sexual frequencies elicited by testosterone. Also, *Cola acuminata* enhanced EL, inhibited IL and PEI and had no effect on the ML latencies of testosterone, while *G. cola* had no effect on the latencies of the standard drug (Figures 5 and 6). Hence consumption of *C. acuminata* and *G. cola* at the same time when testosterone is being used as an orthodox sexual stimulant would give no beneficial effect to the use of the standard drug. Similarly, both *C. acuminata* and *G. cola* were reported not have any effect on the sexual stimulation given by tadalafil [38].

Furthermore, concurrent administrations of chloroquine and *Citrus aurantifolia* fruit extract, pyrimethamine and *Chrysophyllum albidum* stem bark extract, chloroquine and *C. albidum* leaf or stem bark extract in the suppressive, prophylactic and curative antimalarial models, respectively were reported non-beneficial or contraindicated in malaria chemotherapy. These plant extracts were reported to have inhibited the prophylactic, suppressive and curative activities of choloroquine and pyrimethamine [40,42]. Similarly, co-administration of chloroquine with *Nauclea latifolia* or *Artocarpus altilis* or *Enantia chlorantha* significantly reduced the curative activity of this orthodox drug while only *N. latifolia* inhibited the prophylactic activity of pyrimethamine and suppressive activity of chloroquine [40]. It was further suggested that these co-administrations may lead to increased resistance of the plasmodium parasites, increased toxicity to man, loss of man hours due to the terrible sickness or death for immune compromised patients [42]. The current study therefore clearly showed that extreme caution should be exercised in choosing which orthodox and herbal drugs should be concomitantly administered for enhanced aphrodisiac effects of the standard drugs [40,42].

Conclusion

Generally, testosterone was more active as a sexual stimulant than each of the plant extracts tested, thereby confirming it as an orthodox and proven aphrodisiac. In most cases, the plant extracts significantly enhanced the sexual frequencies but gave varied effects on their latencies. Nevertheless, order of significant activity of the extracts was testosterone = *G. cola* > *A. sativum* = *C. acuminata* > *A. cepa*. These results confirmed their ethnomedicinal use as aphrodisiacs. Co-administration of testosterone with *A. cepa* and *A. sativum* bulbs significantly inhibited the effects of the standard drug, while *C. acuminate* and *G. cola* had no effect on this orthodox drug. Therefore, common practice of using herbal sexual stimulants with prescribed drugs to increase sexual performance may not always be beneficial.

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