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**APHRODISIAC EFFECTS OF AQUEOUS EXTRACTS OF *Pausinystalia yohimbe*, *Cassia sieberiana* and *Cissus populnea* ROOTS IN PAROXETINE-INDUCED SEXUAL DYSFUNCTION MALE RATS: A COMPARATIVE STUDY**

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**ABSTRACT**

There is a folkloric claim that *Pausinystalia yohimbe*, *Cassia sieberiana* and *Cissus populnea* roots can be used to enhance sexual behaviour in male rats. However, there is still dearth of scientific evidence that substantiated the acclaimed efficacy of separate and combined use of the plant as sex enhancer. Therefore, the aims of this study were to compare the separate and combined effects of aqueous extracts of *Pausinystalia yohimbe*, *Cassia sieberiana* and *Cissus populnea* roots in paroxetine-induced sexually impaired male rats. Thirty five male rats were assigned into seven groups (A-G) such that rats in group A received orally 1.0 ml of distilled water for 7 days, while those in groups B - G which were induced into sexual dysfunction (administration of 10 mg/kg of paroxetine) also received equal volume of distilled water, 7.14 mg/kg body weight of PowmaxM (a reference drug), 50 mg/kg body weight of *P. yohimbe*, 50 mg/kg body weight of *C. sieberiana*, 50 mg/kg body weight of *C. populnea* and 50 mg/kg body weight of 1:1:1 mixture of the three extracts, once daily for seven days respectively. The sexual behavior indices of the male rats and the levels of their reproductive hormones were evaluated by standard procedures. The paroxetine-treatment related reductions ( $P < 0.05$ ) in the sexual behaviour indices of Mount Frequency, Intromission Frequency and Ejaculatory Frequency, levels of serum reproductive hormones of testosterone, luteinizing hormone and follicle stimulating hormone were progressively attenuated by the separate administration of the plant extracts. Furthermore, the increases in the Mount Latency, Intromission Latency, Ejaculatory Latency and Post-ejaculatory Interval were also gradually reduced, following the administration of the plant extracts. The male rat sexual behaviour indices and the levels of the male reproductive hormones following the administration of the 1:1:1 mixture of the extracts were not significantly different ( $P > 0.05$ ) from the effects of the separate extracts. All these changes compared favourably ( $P > 0.05$ ) well with those of the sexual dysfunction rats that received PowmaxM (Group G). The results obtained in the present study indicate that the extracts of these plants may have the potential for the management of sexual dysfunction in male rats. The combined use of the plants was not significantly better than the individual use of the plants thereby, each and any of the three plants readily available might be used for this purpose.

**Keywords:** Aphrodisiac; *Pausinystalia yohimbe*; *Cassia sieberiana*; *Cissus populnea*; Paroxetine; PowmaxM; male sexual dysfunction

**INTRODUCTION:**

A normal male sexual response cycle is functionally divided into five interrelated events, which include libido, erection, orgasm, ejaculation and detumescence. These events must occur in a defined sequence for a normal sexual function [1]. The disturbance during any phase of the normal sexual response cycle that prevents the male from experiencing satisfaction from sexual activity is termed male sexual dysfunction (MSD). Sexual dysfunction can occur as a result of physical causes (neurogenic disorders - spinal cord and brain injuries, nerve disorders such as Parkinson's disease, Alzheimer's disease, multiple sclerosis, and stroke; hormonal disorders - pituitary gland tumor; low level of testosterone; lifestyle – alcohol and drugs, obesity, cigarette smoking [2,3]; and non-physical causes: mental disorders (clinical depression, schizophrenia, substance abuse, panic disorder, generalized anxiety disorder, personality disorders or traits, psychological problems, anxiety, work-related stress negative feelings [3]. Although, MSD have been managed with different strategies (including surgical and non-surgical approaches), the adverse effect/limitations of treatments, together with the high cost of treatment and drugs, have led to several research works on the search for natural treatment options that will not only increase sexual potency and sexual pleasure, but also are affordable, readily available, fast acting and

with little or no side effects. In Nigeria, the use of herbal remedies in enhancing normal functioning of the male reproductive organs, and strengthening erection and sex-drive have been reported [4,5,6,7,8]. *Pausinystalia yohimbe*, *Cassia sieberiana* and *Cissus populnea* are another set of medicinal plants widely acclaimed to be of immense importance in the management of sexual dysfunction in Nigeria.

*Cissus populnea* Guill & Perr (Vitaceae), also known locally as *Ogbolo* or *Ajara* (Yoruba), *Daafaaraa* or *Latutuwa* (Hausa) and *Okoho* (Igbo) is a strong woody plant 8-10m long, by 7.5cm by diameter, which is dispersed across West Tropical Africa [9]. Phytochemical screening of the stem and root extracts revealed the presence of alkaloids, cardiac glycosides, anthraquinones, phytosteroids, tannins, flavonoids, saponins, and cyanogenic glycosides [10]. The leaves are reported to be used as thickening agent in soup for postnatal stoppage of bleeding [10], while the roots had also been reported to be used by the Yorubas to cure sore breasts of women at childbirth, and as a male coital adjunct [9]. Its stem extracts have been credited with antibacterial and antitrypanosomal properties [11-12] and as a component of a Nigerian anti-sickling herbal formula [13].

*Cassia sieberiana* (Caesalpinaceae), also known locally as *Aridan toro* (Yoruba), *Apagban* (Bini), *Gama fada* (Hausa) is a

savannah tree that usually grows from 2 - 12 metres tall and mostly found in the dry areas of the forest and thickets. The phytochemical screening of the plants root and stem bark extract revealed the presence of alkaloids, anthraquinones, flavonoids, triterpenoids, tannins, cardiac glycosides, saponins, reducing sugars and other carbohydrates [14]. *Cassia sieberiana* has many medicinal usages. The roots are used as a diuretic and vermifuge that can be used to treat diseases such as elephantiasis, leprosy, diarrhea, hemorrhoids, dysentery and venereal diseases [15], while the leaves have been reported to help with the symptoms of arthritis and rheumatism. The extracts are used to treat fever, malaria, diuretics, diarrhoea, leprosy, The aqueous extracts of the roots, stem, bark and the fruit pulp have been used traditionally in North-eastern Nigeria for the management of malaria [14], ulcer [16], inflammatory conditions, tiredness and joint pains [17], bilhazia, stomach pains and as a dewormer [18]. *Pausinystalia yohimbe* (K. Schumann) Pierre ex Beille (Rubiaceae), formerly known as *Corynanthe yohimbe* and sometimes spelled johimbe, is also known locally as *takitaki* (Yoruba) and the tree grows about 30m tall, with a straight bole that is rarely larger than 50-60 cm in diameter. It is a psychoactive plant which contains the tryptamine alkaloid- yohimbine that has been used primarily in the treatment of sexual dysfunction, weight (body fat) loss, and xerostomia (dry mouth) [19]. It has also been

used in studies investigating autonomic failure and orthostatic hypotension. It is widely distributed over-the-counter as an herbal aphrodisiac. It has been purported to be helpful for men with erectile dysfunction (ED) and for sexual side effects caused by some antidepressants (SSRIs) [19, 20]. In addition to yohimbine, the tree also contains 55 other alkaloids. Yohimbine accounts for 1-20% of its total alkaloid content. Among the others is corynanthine, an alpha-1 adrenergic receptor blocker [21]. Hence, the use of yohimbe extract in sufficient dosages was reported to provide concomitant alpha-1 and alpha-2 adrenoceptors blockade and thus may enhance erections than yohimbine alone [22].

We were informed from the ethnobotanical survey that using only one or two of these plants extracts separately to determine its aphrodisiac activities may not yield effective result. Therefore, the aims of this study were to compare the separate and combined effects of aqueous extracts of *Pausinystalia yohimbe*, *Cassia sieberiana* and *Cissus populnea* roots in paroxetine-induced sexually impaired male rats.

#### **MATERIALS AND METHODS:**

Dried roots of *Cissus populnea*, *Cassia sieberiana* and *Pausinystalia yohimbe* free from fungal infection or other contaminants, obtained from a farmland through the help of a herb seller at a market (Oja tuntun) in Ilorin, Nigeria, were authenticated at the University of Ilorin

Herbarium, Ilorin, Nigeria, where voucher samples (UIH 1019, UIH 619 and UIH 819 respectively) were deposited. Thirty five, healthy, Wistar, male rats and same number of female rats were housed in clean aluminum cages contained in well ventilated housing conditions (temperature:  $22 \pm 3^{\circ}\text{C}$ ; photoperiod: 12 hours light/dark phase; humidity: 45-50%). The rats were allowed free access to rat pellets (Premier Feeds, Ibadan, Nigeria) and tap water. The study was conducted following an ethical clearance from the Ethical Committee on the care and use of laboratory animals of the Department of Biochemistry, University of Ilorin, Ilorin, Nigeria. Paroxetine hydrochloride was a product of S.C. Europharm, Brasov, Romania, while PowmaxM was from Beijing Kowloon Pharmaceuticals Co., Ltd, Beijing, China. Progesterone was a product of Ningbo Tisun Medic Biochemic Co., LTD., Ningbo, Peoples Republic of China, while Estradiol benzoate was from Sigma Chemical, St. Louis, USA. Assay kits for testosterone, follicle stimulating hormone and luteinizing hormones were products of Inteco Diagnostics UK LTD., London, United Kingdom. All other reagents used were of analytical grade and were prepared in distilled water and stored in neat and airtight reagent bottles.

Preparation of aqueous extracts of *Cissus populnea*, *Cassia sieberiana* and *Pausinystalia yohimbe* roots: A known weight (300 g) of the roots of *Cissus populnea*, *Cassia sieberiana* and *Pausinystalia yohimbe* were separately

washed, sliced, oven-dried and pulverized in a blender (Mikachi Blender, Model MK-1830, China) after which the resulting powder (100 g) was extracted in 200 ml of distilled water for 48 hours at room temperature with constant shaking. A dark brown coloured extract was obtained for *Cissus populnea*, *Cassia sieberiana* and *Pausinystalia yohimbe*. The extracts were filtered separately with Whatman No. 1 filter paper (Maidstone, England) and the resulting filtrate was concentrated on steam bath to give a yield of 5.25 g, 5.75 g and 6.04 g for *Cissus populnea*, *Cassia sieberiana* and *Pausinystalia yohimbe* respectively. Calculated amounts for each extract were reconstituted in distilled water to give the required doses of 50 mg/kg body weight and also a composite mixture of the three extract in ratio 1:1:1 to also give a required dose of 50 mg/kg body weight. Induction of sexual dysfunction and assessment of mating behaviour indices in male rats: Thirty male rats were each induced with sexual dysfunction by oral administration of 10 mg/kg of paroxetine hydrochloride suspension (prepared daily in Tween-80 [BDH Chemicals, Ltd., Poole, England], suspended in 0.9% saline solution) using a metal oropharyngeal cannula [23, 24]. Healthy female rats were made receptive by sequential subcutaneous administration of oestradiol benzoate (10  $\mu\text{g}/100$  g body weight) and progesterone (0.5 mg/100 g body weight), 48 and 4 hours respectively prior to pairing [25]. Oestrus phase in female rats was confirmed by

vaginal smears examinations according to the Organisation for Economic Co-operation and Development (OECD) - 106 guidelines [26]. The oestrous female rats were then introduced into the male rats in their respective cages and observed for 30 minutes for mating behavior of Mount Frequency (MF: number of mounts without intromission from the time of introduction of the female until ejaculation), Intromission Frequency (IF: number of intromissions from the time of introduction of the female until ejaculation), Ejaculation Frequency (EF: number of ejaculations made during the observatory period), Mount Latency (ML: time interval between the introduction of the female and the first mount by the male), Intromission Latency (IL: time interval between the introduction of the female to the first intromission by the male, usually characterized by pelvic thrusting and springing dismounts), Ejaculation Latency (EL: time interval between the first intromission and ejaculation, usually characterized by longer, deeper pelvic thrusting and slow dismount followed by a period of inactivity or reduced activity), and Post-Ejaculation Interval (PEI: time interval between ejaculation and erection of the male copulatory organ for the next phase) [4]. For the interpretation of the data, male rats that showed minimum of 25% reduction in MF, IF, and EF as well as a minimum increase of 25% in ML, IL, and PEI were considered as sexually impaired and were used for the subsequent study [7, 24]. Thus, sexual dysfunction being

referred to in the present study included the testosterone-dependent behavior of mating, copulation, and ejaculation.

#### Animal Grouping and Extract Administration:

A total of 35 male rats that were acclimatized for 2 weeks were assigned into seven Groups (A-G) in a complete randomized design, with each group comprising five rats as follows: In Group A (control group) were normal rats that received distilled water. Group B were Sexual dysfunction rats administered distilled water. Group C were Sexual dysfunction rats administered 7.14 mg/kg body weight of PowmaxM (this is the reference male sexual stimulant and energy enhancing polyherbal drug made up of *Panax ginseng*, *Camelia sinensis*, *Cnidium monnieri*, *Epimedium brevicornum*, *Songaria cynomorium*, *Gingko biloba*, *Dahurian angelica*, *Salvia miltiorrhiza* root, L-arginine hydrochloride, and gamma aminobutyric acid) [27]. In Groups D, E, F and G were Sexual dysfunction rats administered 50 mg/kg body weight of *Pausinystalia yohimbe*, *Cassia sieberiana*, *Cissus populnea* and a composite mixture of the three extracts in ratio 1:1:1 respectively.

The rats in the various groups were orally administered 1.0 ml each of distilled water, PowmaxM and the extracts, once daily (08:00 - 08:45 am) for 7 days, with the aid of a metal oropharyngeal cannula. The rats were maintained on unrestricted access to rat pellets (Premier Feeds, Ibadan, Nigeria) and tap water. The male sexual behavior parameters

were monitored and results were recorded 30 minutes after dosing on days 1, 3, and 7 (between 17:00 and 21:00 h) under dim light condition at room temperature (26–28°C).

The blood from the rats was collected into clean, dry centrifuge tubes. The samples were left undisturbed for 15 min at room temperature for coagulation to take place. Clear serum was then collected using Pasteur pipette after centrifuging at  $33.5 \times g$  for 15 min using Uniscope Laboratory Centrifuge (Model SM800B, Surgifriend Medicals, Essex, UK). The sera were kept frozen for 12 h before being used for the various hormonal assays.

The concentrations of the hormones, testosterone, follicle-stimulating hormone (FSH) and luteinizing hormone (LH) in serum were quantitatively determined using the direct human serum enzyme immunoassay kits as outlined in the manufacturer's manual [28]

Data were expressed as the mean  $\pm$  SEM of five determinations. Means were analyzed using one-way analysis of variance followed by Duncan Multiple Range Test. Statistical Package for Social Sciences, version 16.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analyses. Differences were considered statistically significant at  $P < 0.05$ .

## RESULTS:

Administration of paroxetine significantly decreased ( $P < 0.05$ ) the MF, IF and EF while the ML, IL, EL, and PEI were significantly increased as compared to the control (Table 1).

The changes in all the sexual behaviour parameters investigated were more than 25 % (Table 1). Administration of the aqueous extracts of *P. yohimbe*, *C. sieberenia* and *C. populnea* to sexually impaired male rats significantly increased the MF and IF of the rats on Days 3 and 7 (Table 2). The improvement compared significantly with the reference drug (PowmaxM) but the sexual function of the rats was not restored back to normal when compared with the non-sexually impaired rats administered distilled water (Table 2).

Administration of the mixture of the extracts and reference drug significantly ( $P < 0.05$ ) increased the EF of the sexually impaired male rats on Day 1 while all the extracts as well as the mixture significantly increased the EF on Days 3 and 7 (Table 3). The ML of sexually impaired male rats administered aqueous extract of *P. yohimbe*, *C. sieberenia* and *C. populnea* as well as the mixture of the extracts were significantly increased (Table 3). The increase compared significantly with the reference drug (PowmaxM) but did not compare significantly with the control rats that were administered distilled water only (Table 3). Administration of the extracts and their mixture significantly reduced the IF and EF of the sexually impaired male rats in days related manner which compared significantly with the reference drug treated rats (Table 4). This trend of reduction was extended to the PEI but did not compare significantly with non-sexually impaired rats administered distilled water group

(Table 5). The serum concentrations of testosterone and luteinizing hormone significantly decreased in sexually impaired male rats while the concentration of follicle stimulating hormone significantly increased when compared with non-sexually impaired rats administered distilled water group only (Table 6). Administration of *P. yohimbe*, *C.*

*sieberiana* and *C. populnea* separately and combined at 50mg/kg body weight significantly increased ( $p<0.05$ ) the concentrations of testosterone and luteinizing hormone in a manner similar to the reference drug while the serum concentration of follicle-stimulating hormone significantly decreased (Table 6).

Table 1: Effect of paroxetine administration on sexual behaviours of male rats

Parameters	Control	Paroxetine-treated rats	Percentage change (%)
Mount frequency (MF) (numbers)	13.36±0.86 <sup>a</sup>	5.08±0.21 <sup>b</sup>	61.97#
Intromission frequency (IF) (numbers)	11.46±0.12 <sup>a</sup>	4.88±0.23 <sup>b</sup>	57.41#
Ejaculatory frequency (EF) (numbers)	1.83±0.18 <sup>a</sup>	1.06±0.13 <sup>b</sup>	42.08#
Mount latency (ML) (seconds)	101.61±3.35 <sup>a</sup>	167.26±5.33 <sup>b</sup>	64.61+
Intromission latency (IL) (seconds)	132.33±4.11 <sup>a</sup>	196.41±3.54 <sup>b</sup>	67.37+
Ejaculatory latency (EL) (seconds)	147.18±6.53 <sup>a</sup>	226.68±5.49 <sup>b</sup>	64.93+
Post-ejaculatory interval (PEI) (seconds)	186.54±5.82 <sup>a</sup>	241.93±7.34 <sup>b</sup>	29.69+

Data are mean of five determinants ± SEM.

Values carrying superscripts different from the control for each parameter are significantly different ( $P<0.05$ )

# means percentage reduction in parameter. + means percentage increase in parameters

Table 2: Effect of aqueous extract of *P. yohimbe*, *C. sieberiana* and *C. populnea* roots on mount and intromission frequencies of paroxetine-induced sexual dysfunction male rats

Treatments	Mount frequency (numbers)			Intromission frequency (numbers)		
	Day 1	Day 3	Day 7	Day 1	Day 3	Day 7
Distilled water (control)	12.98±0.76 <sup>a</sup>	13.41±0.61 <sup>a</sup>	13.36±0.59 <sup>a</sup>	11.33±1.03 <sup>a</sup>	11.81±0.74 <sup>a</sup>	10.83±0.65 <sup>a</sup>
Paroxetine + Distilled water	5.19±0.19 <sup>b</sup>	5.33±0.22 <sup>b</sup>	5.84±0.23 <sup>b</sup>	4.93±0.31 <sup>b</sup>	5.02±0.18 <sup>b</sup>	5.47±0.22 <sup>b</sup>
Paroxetine + <i>P. yohimbe</i>	5.39±0.26 <sup>b</sup>	7.68±0.91 <sup>c</sup>	9.76±0.70 <sup>c</sup>	5.02±0.51 <sup>b</sup>	8.80±0.33 <sup>c</sup>	8.85±0.31 <sup>c</sup>
Paroxetine + <i>C. sieberiana</i>	5.54±0.34 <sup>b</sup>	7.92±0.38 <sup>c</sup>	9.28±0.54 <sup>c</sup>	5.11±0.48 <sup>b</sup>	8.85±0.35 <sup>c</sup>	9.01±0.37 <sup>c</sup>
Paroxetine + <i>C. populnea</i>	5.26±0.41 <sup>b</sup>	8.21±0.43 <sup>c</sup>	10.11±0.81 <sup>c</sup>	5.04±0.26 <sup>b</sup>	8.98±0.47 <sup>c</sup>	8.97±0.33 <sup>c</sup>
Paroxetine + extract ABC	5.29±0.28 <sup>b</sup>	9.11±0.36 <sup>d</sup>	10.18±0.76 <sup>c</sup>	5.06±0.50 <sup>b</sup>	8.57±0.58 <sup>c</sup>	9.26±0.46 <sup>c</sup>
Paroxetine + PowmaxM	5.32±0.30 <sup>b</sup>	8.57±0.50 <sup>d</sup>	9.63±0.33 <sup>c</sup>	5.05±0.49 <sup>b</sup>	9.11±0.81 <sup>c</sup>	8.89±0.35 <sup>c</sup>

Data are mean of five determinants ± SEM. Values carrying superscripts different from the control down the group for each day and parameter are significantly different ( $P<0.05$ ).



Table 3: Effect of aqueous extract of *P. yohimbe*, *C. sieberiana* and *C. populnea* roots on ejaculation frequency and mount latency of sexual dysfunction male rats

Treatments	Ejaculation frequency (numbers)			Mount Latency (seconds)		
	Day 1	Day 3	Day 7	Day 1	Day 3	Day 7
Distilled water (control)	2.00±0.00 <sup>a</sup>	2.25±0.25 <sup>a</sup>	2.25±0.29 <sup>a</sup>	114.18±3.12 <sup>a</sup>	120.88±3.55 <sup>a</sup>	116.04±4.36 <sup>a</sup>
Paroxetine + Distilled water	1.25±0.25 <sup>b</sup>	1.25±0.25 <sup>b</sup>	1.25±0.29 <sup>b</sup>	160.64±4.64 <sup>b</sup>	154.23±2.11 <sup>b</sup>	152.16±5.84 <sup>b</sup>
Paroxetine + <i>P. yohimbe</i>	1.25±0.25 <sup>b</sup>	1.50±0.29 <sup>c</sup>	1.75±0.29 <sup>c</sup>	156.54±5.33 <sup>b</sup>	146.52±4.81 <sup>c</sup>	131.05±4.53 <sup>c</sup>
Paroxetine + <i>C. sieberiana</i>	1.25±0.25 <sup>b</sup>	1.50±0.29 <sup>c</sup>	1.75±0.25 <sup>c</sup>	153.61±4.98 <sup>b</sup>	142.53±4.30 <sup>c</sup>	128.10±3.61 <sup>c</sup>
Paroxetine + <i>C. populnea</i>	1.25±0.25 <sup>b</sup>	1.75±0.25 <sup>d</sup>	1.75±0.25 <sup>c</sup>	158.32±5.21 <sup>b</sup>	143.38±6.49 <sup>c</sup>	135.20±4.85 <sup>c</sup>
Paroxetine + extract ABC	1.50±0.29 <sup>c</sup>	1.50±0.29 <sup>c</sup>	1.75±0.29 <sup>c</sup>	151.19±5.91 <sup>b</sup>	143.90±5.77 <sup>c</sup>	130.13±3.91 <sup>c</sup>
Paroxetine + PowmaxM	1.50±0.29 <sup>c</sup>	1.50±0.29 <sup>c</sup>	1.75±0.29 <sup>c</sup>	153.84±4.63 <sup>b</sup>	144.37±6.85 <sup>c</sup>	125.80±1.68 <sup>d</sup>

Data are mean of five determinants ± SEM. Values carrying superscripts different from the control down the group for each day and parameter are significantly different (P<0.05).

Table 4: Effect of aqueous extract of *P. yohimbe*, *C. sieberiana* and *C. populnea* roots on intromission and ejaculatory latencies of paroxetine-induced sexual dysfunction male rats

Treatments	Intromission Latency (seconds)			Ejaculatory Latency (seconds)		
	Day 1	Day 3	Day 7	Day 1	Day 3	Day 7
Distilled water (control)	129.84±3.66 <sup>a</sup>	132.34±3.22 <sup>a</sup>	127.80±4.43 <sup>a</sup>	153.31±6.24 <sup>a</sup>	148.27±4.41 <sup>a</sup>	143.53 ±5.39 <sup>a</sup>
Paroxetine + Distilled water	173.92±4.19 <sup>b</sup>	168.90±7.10 <sup>b</sup>	165.32±5.21 <sup>b</sup>	195.39±4.89 <sup>b</sup>	186.47±6.88 <sup>b</sup>	179.92±6.36 <sup>b</sup>
Paroxetine + <i>P. yohimbe</i>	172.36±3.81 <sup>bc</sup>	151.05±5.67 <sup>c</sup>	142.50±5.88 <sup>c</sup>	188.99±5.31 <sup>c</sup>	168.37±5.33 <sup>c</sup>	153.70±4.48 <sup>c</sup>
Paroxetine + <i>C. sieberiana</i>	168.45±5.12 <sup>bc</sup>	154.56±6.11 <sup>c</sup>	139.15±4.89 <sup>c</sup>	188.34±4.63 <sup>c</sup>	164.54±4.61 <sup>c</sup>	148.95±5.97 <sup>c</sup>
Paroxetine + <i>C. populnea</i>	165.75±4.93 <sup>bc</sup>	153.26±5.34 <sup>c</sup>	141.23±5.31 <sup>c</sup>	189.63±6.14 <sup>c</sup>	166.44±8.11 <sup>c</sup>	151.46±6.27 <sup>c</sup>
Paroxetine + extract ABC	162.19±4.61 <sup>c</sup>	151.09±6.38 <sup>c</sup>	144.33±4.64 <sup>c</sup>	182.28±4.15 <sup>d</sup>	168.37±7.16 <sup>c</sup>	154.12±6.83 <sup>c</sup>
Paroxetine + PowmaxM	164.36±4.81 <sup>c</sup>	155.13±5.89 <sup>c</sup>	140.41±4.84 <sup>c</sup>	191.65±5.43 <sup>c</sup>	165.80±6.18 <sup>c</sup>	153.82±5.81 <sup>c</sup>

Data are mean of five determinants ± SEM. Values carrying superscripts different from the control down the group for each day and parameter are significantly different (P<0.05).

Table 5: Effect of aqueous extract of *P. yohimbe*, *C. sieberiana* and *C. populnea* roots on Post-ejaculatory interval of paroxetine-induced sexual dysfunction male rats

Treatments	Post-ejaculatory Latency (seconds)		
	Day 1	Day 3	Day 7
Distilled water (control)	193.61±6.27 <sup>a</sup>	185.34±5.83 <sup>a</sup>	183.06±3.61 <sup>a</sup>
Paroxetine + Distilled water	238.68±6.49 <sup>b</sup>	232.24±7.13 <sup>b</sup>	239.40±9.35 <sup>b</sup>
Paroxetine + <i>P. yohimbe</i>	236.07±5.87 <sup>b</sup>	224.67±6.06 <sup>c</sup>	194.54±8.89 <sup>c</sup>
Paroxetine + <i>C. sieberiana</i>	232.65±6.22 <sup>c</sup>	224.54±7.46 <sup>c</sup>	193.51±7.59 <sup>c</sup>
Paroxetine + <i>C. populnea</i>	235.53±5.45 <sup>b</sup>	221.14±6.93 <sup>c</sup>	190.13±8.36 <sup>c</sup>
Paroxetine + extract ABC	230.46±5.81 <sup>c</sup>	220.33±7.04 <sup>c</sup>	195.88±7.68 <sup>c</sup>
Paroxetine + PowmaxM	232.91±6.11 <sup>c</sup>	221.30±8.01 <sup>c</sup>	190.11±7.26 <sup>ac</sup>

Data are mean of five determinants ± SEM. Values carrying superscripts different from the control down the group for each day and parameter are significantly different (P<0.05).

Table 6: Effect of aqueous extract of *P. yohimbe*, *C. sieberiana* and *C. populnea* root on serum concentrations of reproductive hormones in sexual dysfunction male rats

Treatment	Testosterone (nmol/l)	Follicle-stimulating hormone (mlu/ml)	Luteinizing hormone (mlu/ml)
Distilled water (control)	6.60±0.42 <sup>a</sup>	5.60±0.22 <sup>a</sup>	3.50±0.15 <sup>a</sup>
Paroxetine+Distilled water	2.80±0.11 <sup>b</sup>	6.78±0.26 <sup>b</sup>	2.65±0.11 <sup>b</sup>
Paroxetine + <i>P. yohimbe</i>	4.80±0.27 <sup>c</sup>	4.90±0.18 <sup>c</sup>	4.50±0.16 <sup>c</sup>
Paroxetine + <i>C. sieberiana</i>	4.60±0.14 <sup>c</sup>	4.75±0.21 <sup>c</sup>	4.60±0.23 <sup>c</sup>
Paroxetine + <i>C. populnea</i>	4.50±0.15 <sup>c</sup>	4.60±0.14 <sup>c</sup>	5.50±0.35 <sup>d</sup>
Paroxetine + extract ABC	4.50±0.05 <sup>c</sup>	4.70±0.10 <sup>c</sup>	3.80±0.24 <sup>e</sup>
Paroxetine + PowmaxM	4.90±0.17 <sup>c</sup>	4.50±0.17 <sup>c</sup>	4.20±0.16 <sup>c</sup>

Data are mean of five determinants ± SEM. Values carrying superscripts different from the control down the group for each day and parameter are significantly different (P<0.05).

## DISCUSSION:

The sexual behaviour parameters of MF, IF and EF were decreased while the ML, IL, EL and PEI were prolonged following the administration of paroxetine to sexually active male rats in our present study. These alterations could be due to the capability of

selective serotonin reuptake inhibitors (SSRIs) such as paroxetine to decrease libido and cause other sexual side effects by increasing synaptic concentrations of serotonin and stimulating 5HT<sub>2</sub>, and possibly 5HT<sub>3</sub>, receptors [29]. The increase in MF and IF of sexually impaired rats following the administration of the

aqueous root extracts of *Pausinystalia yohimbe*, *Cassia sieberiana* and *Cissus populnea* shows enhanced sexual desire [30, 31]. This could be due to the action of components in the extract to reduce the synaptic concentration of serotonin as well as increase the amount of dopamine release [32]. The increase recorded in ML, IL and EL, indicators of sexual arousability and potency, in sexually impaired rats could have resulted from reduced erectile response through inhibition of the synthesis of nitric oxide in the penis leading to reduced cavernous stimulation in paroxetine-treated rats [33, 34, 35]. The action of components in the extracts and their mixture to reverse these increases in a manner similar to the reference drug (PowmaxM) indicates their potential to stimulate sexual arousability, performance, motivation, and vigour in the rats [36]. The PEI, an index of potency, libido, and rate of recovery from exhaustion after first series of mating [37], was elevated in paroxetine-induced sexual dysfunction rats which indicate loss of libido and potency [4]. Following the administration of the extracts as well as their mixture to the sexually impaired rats, the PEI was attenuated which denotes enhanced libido and potency. These recoveries from paroxetine-induced sexual dysfunction in sexually impaired rats were similar to the recovery pattern in the reference drug treated groups. The positive effects on the indices of male sexual behaviour may have been due to the actions of constituents of the extracts on

testosterone, luteinizing hormone (LH) and follicle stimulating hormone (FSH) assessed in the present study. Therefore, there is a need to further evaluate the effects of administration of the extracts on serum concentrations of these hormones [38] as they are hormonal markers of androgenicity [39].

The results obtained in the present study indicate that the extracts of these plants may have potential for the management of sexual dysfunction in male rats. The combined use of the plants was not significantly better than the individual use of the plants thereby, each and any of the three plants readily available might be used for this purpose.

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## REFERENCES

1. Guay AT, Spark RF, Bansal S, Cunningham GR, Goodman NF, Nankin HR, Petak SM, Perez J. American Association of Clinical Endocrinologist Medical Guidelines for clinical practice for the evaluation and treatment of male sexual dysfunction: A couple's problem-2003 update. *Endocrine practice*. 2003, (9)1: 77 - 95.
2. Peat I. The effects of smoking on the reproductive health of men. *Br. J. Nurs.* 2005, 14(7): 362 - 366.

3. Korenman SG. Epidemiology of erectile dysfunction. *Endocrine*. 2004, 23(2-3): 87 - 91.
4. Yakubu MT, Akanji MA, Oladiji AT. Aphrodisiac potentials of aqueous extract of *Fadogia agrestis* (Schweinf. Ex Heirn) stem in male albino rats. *Asian J. of Androl*. 2005, 7: 399–404.
5. Yakubu MT, Afolayan AJ. Effect of aqueous extract of *Bulbine natalensis* (Baker) stem on the sexual behaviour of male rats. *Int J. Androl*, 2009, 32: 629-636.
6. Nurudeen QO, Ajiboye TO. Aqueous root extract of *Lecaniodiscus cupanioides* restores the alterations in testicular parameters of sexually impaired male rats. *Asian Pac J Reprod*. 2012, 1(2): 120 - 124.
7. Yakubu MT, Nurudeen QO. Effects of aqueous extract of *Cnestis ferruginea* (Vahl ex De Cantolle) root on Paroxetine-Induced Sexual Dysfunction in Male Rats. *Asian Pac J Reprod*. 2012, 1(2): 111 – 116.
8. Ajiboye TO, Nurudeen QO, Yakubu MT. Aphrodisiac Effect of Aqueous Root Extract of *Lecaniodiscus cupanioides* in Sexually Impaired Rats. *J Basic Clinical Physiol Pharmacol*. 2014, 25(2): 241–248.
9. Burkill HM. *The Useful Plants of West Tropical Africa*, vol. 5. Families S-Z, Royal Botanic Gardens, Kew. 2000: pp. 296-297.
10. Soladoye MO, Chukwuma EC. Quantitative phytochemical profile of the leaves of *Cissus populnea* Guill. & Perr. (Vitaceae) – an important medicinal plant in Central Nigeria. *Arch. Appl. Sci. Res.*, 2012, 4(1): 200-206.
11. Koné WM, Kamanzi Atindehou K, Terreaux C, Hostettmann K, Traoré D, Dosso M. Traditional medicine in North Côte-d'Ivoire: screening of 50 medicinal plants for antibacterial activity. *J Ethnopharmacol*, 2004, 93(1): 43 – 49.
12. Atawodi SE, Ameh DA, Ibrahim S, Andrew JN, Nzelibe HC, Onyike EO, Anigo KM, Abu EA, James DB, Njoku GC, Sallau AB. Indigenous knowledge system for treatment of trypanosomiasis in Kaduna state of Nigeria. *J Ethnopharmacol*. 2002, 79(2):279 - 282.
13. Moody JO, Ojo OO, Omotade OO, Adeyemo AA, Olumese PE, Ogundipe OO. Anti-sickling potential of a Nigerian herbal formula (ajawaron HF) and the major plant component (*Cissus populnea* L. CPK). *Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives*. 2003, 17(10):1173 - 1176.
14. Abdulrazak N, Asiya UI, Usman NS, Unata IM, Farida A. Anti-plasmodial activity of ethanolic extract of root and stem bark of *Cassia sieberiana* DC on mice. *J Intercult Ethnopharmacol*. 2015, 4(2): 96 – 101.
15. Gill LS. *Ethnomedical uses of plants in Nigeria*. Uniben Press, Benin, Nigeria. 1992: Pp 143.
16. Nartey ET, Ofosuhene M, Agbale CM. Anti-ulcerogenic activity of the root bark extract of the African laburnum “*Cassia sieberiana*” and its effect on the anti-oxidant defence system in rats. *BMC Complement Altern Med*. 2012, 12(1): 247.
17. Madusolumuo AM, Nadro SM, Wurochekke, UA. Antihepatotoxic properties of *Cassia sieberiana* in

- acetaminophen treated rats. Nig. J. Biochem. Mol. Biol. 1999, 14: 21-25.
18. Tamboura HH, Bayala B, Lompo M, Guissou IP, Sawadogo L. Ecological distribution, morphological characteristics and acute toxicity of aqueous extracts of *Holarrhena floribunda* (G.don) Duran and Schinz, *Leptadenia hastate* (Pers.) decne and *Cassia sieberiana* (Dc) used by veterinary healers in Burkinafaso. Afr. J. Trad. C AM. 2005, 2 (1):13-24.
  19. McGuffin M, Hobbs C, Upton R. American Herbal Products Association's Botanical Safety Handbook. CRC Press. 1997: p. 83.
  20. Wildman REC, Medeiros DM. Advanced Human Nutrition. CRC Series in Modern Nutrition 22. CRC Press. 2000, p. 390.
  21. Doxey JC, Lane AC, Roach AG, Virdee NK. Comparison of the alpha-adrenoceptor antagonist profiles of idazoxan (RX 781094), yohimbine, rauwolscine and corynanthine. Naunyn-Schmied Arch Pharmacol. 1984, 325 (2): 136–144.
  22. Saenz DT, Kim NN, Goldstein I, Traish AM. Regulation of pre-synaptic alpha adrenergic activity in the corpus cavernosum. Int J Impotence Res. 2000, 12 Suppl 1: S20–25.
  23. Chan JS, Waldinger MD, Olivier B, Oosting RS. Drug-induced sexual dysfunction in rats. Curr Protoc Neurosci 2010; Chapter 9:Unit 9.34.
  24. Malviya N, Jain S, Gupta VB, Vyas S. Effect of garlic bulb on paroxetine-induced sexual dysfunction in male rats. Asian J Pharm Biol Res. 2011; 1: 218-221.
  25. Amin KM, Khan MN, Rahman SZ, Khan NA. Sexual function improving effect of *Mucuna pruriens* in sexually normal male rats. Fitoterapia 1996, 67: 53-58.
  26. Organisation for Economic Co-operation and Development (OECD). Guidance or Genetic Document Histological Evaluation of Endocrine and Reproductive Tests in Rodents. Preparation, Reading and Reporting of Vaginal Smears; 2009.
  27. Powmax M For Men Tablet - Uses, Side-effects, Reviews, and Precautions TabletWise - Nigeria. (n.d.). Retrieved August 01, 2019, from <https://www.tabletwise.com/nigeria/powmax-m-for-men-tablet>
  28. Tietz NW. Clinical Guide to Laboratory Tests. 3rd edition, W.B. Saunders Company; Philadelphia. 1995; Pp 215
  29. Michael A, O'Keane V. Sexual dysfunction and depression. Hum Psychopharmacol Clin Exp. 2000, 15: 337 – 345.
  30. Tajuddin AS, Latif A, Qasmi IA, Amin KM. An experimental study of sexual function improving effect of *Myristica fragrans* Houtt. (nutmeg). BMC Complement Altern Med. 2005, 5(1):16.
  31. Yakubu MT, Akanji MA, Oladiji AT. Alterations in serum lipid profile of male rats by oral administration of aqueous extract of *Fadogia agrestis* stem. Res. Journal Med. Plant. 2008, 2: 66-73.
  32. Hull EM, Lorrain DS, Du J, Matuszewich L, Lumley LA, Putnam SK, Moses J. Hormone-neurotransmitter interactions in the control of sexual behavior. Behav Brain Res. 1999, 105(1): 105 - 116
  33. Angulo J, Peiró C, Sanchez-Ferrer CF, Gabancho S, Cuevas P, Gupta S, Tejada IS. Differential effects of serotonin reuptake inhibitors on

- erectile responses, NO-production, and neuronal NO synthase expression in rat corpus cavernosum tissue. *Br J Pharmacol.* 2001, 134(6): 1190 - 1194.
34. Angulo J, Bischoff E, Gabancho S, Cuevas P, de Tejada IS. Vardenafil reverses erectile dysfunction induced by paroxetine in rats. *Int J Impot Res.* 2003, 15: 90 – 93.
35. Ahn GJ, Kang KK, Kim DS, Ahn BO, Kim WB, Kang SK, Lee BC, Hwang WS. DA-8159 reverses selective serotonin reuptake inhibitor- induced erectile dysfunction in rats. *Urology.* 2005, 65(1): 202 – 207.
36. Ratnasooriya WD, Dharmasiri MG. Effects of *Terminalia catappa* seeds on sexual behaviour and fertility of male rats. *Asian J Androl.* 2000, 2: 213 - 219.
37. Tajuddin AS, Latif A, Qasmi IA. Effect of 50% ethanolic extract of *Syzygium aromaticum* (L) Merr. & Perry. (Clove) on sexual behaviour of normal male rats. *BMC Complement Altern Med.* 2004, 4:17–24.
38. Yakubu MT, Akanji MA, Oladiji AT. Male sexual dysfunction and methods used in assessing medicinal plants with aphrodisiac potentials. *Pharmacog Rev.* 2007, 1(1): 39-46.
39. Walton S, Cunliffe WJ, Kaczkes K, Early AS, McGarrigle HH, Katz M, Reese RA. Clinical, ultrasound and hormonal markers of androgenicity in acne vulgaris. *Br J Dermatol.* 1995. 133:249–253.