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Aphrodisiac effect of *Hunteria umbellata* seed extract: Modulation of nitric oxide level and arginase activity *in vivo*

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ABSTRACT

Hunteria umbellata has been reported useful in managing the male sexual related disorder, but there is a dearth of information on its possible mechanism of action. Hence, this study was designed to investigate the effect of *H. umbellata* on some sexual behavior parameters in male rats, in order to ascertain its acclaimed aphrodisiac property. Twenty-four male rats were divided into four groups (n = 6). The extract (50 and 100 mg/kg body weight/day) and sildenafil citrate (5 mg/kg body weight) were administered orally by gavages for 28 days. Some sexual behavior parameters (mounting number, mounting latency, intromission number, and intromission latency), and some anxiety behavioral tests (dark-light box test and open field test) were monitored. In addition, the effect of the extract on arginase activity, nitric oxide and antioxidant level in male rats was assessed. Results revealed that administration of *H. umbellata* extract increases the mounting number, intromission number, time spent at the light compartment, nitric oxide and antioxidant level when compared with animals in the control group. Conversely, administration of *H. umbellata* caused a significant decrease in mounting latency, intromission latency, and arginase activity. Findings in this study revealed that *H. umbellata* improves sexual behavior parameters in male rats, and the results indicate that aphrodisiac effect of *H. umbellata*, identified by its effect on nitric oxide level and arginase activity, may play an important role in initiating and maintaining an erection.

1. Introduction

Erectile dysfunction, one of the male sexual disorders, is characterized by the inability to attain and maintain a penile erection necessary for satisfactory sexual performance [1]. In an attempt to overcome the problem, aphrodisiacs (foods or substances that enhance sexual erection) have become popular over the years in stimulating or increasing sexual desire and performance. The former is regulated by the central nervous system which integrates tactile, olfactory, auditory, and mental stimuli, while the latter is dependent on sexual desire, also called erectile performance or capacity. Aphrodisiacs have been reported to stimulate psychological effects, thereby elevating sexual desire and pleasure aside other mood stimulating properties [2]. Aphrodisiacs can also cause physiologically impact, for instance by increasing blood flow and enhancing erection which could be a result of alteration of hormonal levels [2]. Anxiety is one of the risk factors for sexual function and aphrodisiac are known to ameliorate anxiety-induced sexual dysfunction.

In this dispensation, increased work commitment poses severe psychological burdens on a human. This leads to the development of anxiety and it's associated psychological stress which affects the health status of an individual. Anxiety is therefore considered a common emotional phenomenon in the human population, occurring in response to physiological and/or environmental factors. It represents one of the public health problems found among people of all ages and is associated with a considerable burden of disease, suicide, physical comorbidity, and a significant decrease in the quality of life of the patient [3]. Previous studies have stated the role of anxiety in the development of erectile dysfunction [4,5].

Since the existence of human races, the use of plant-derived products in stimulating and sustaining erection has been reported useful because of their accessibility, affordability and less toxicity. Different plant species have gained popularity as a sexual stimulant in folkloric medicine in many countries [6]. *Hunteria umbellata*, a member of the Apocynaceae family, is a medicinal plant of great importance in the treatment of various human ailments [7]. In African traditional medicine, preparations from different parts of the plant have been employed in the treatment of various human diseases such as sexually transmitted infections including yaws, stomach ulcers, pains and swellings, diabetes mellitus, dysmenorrhoea and to induce or augment labor [7,8]. A decoction made from

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the dried seeds of *H. umbellata* is of pharmacological importance in the management of diabetes mellitus, obesity, stomach ache, pains and swellings, and hypertension [9,10]. In separate studies, Falodun et al. [8] and Igbe et al. [11] reported the oxytocic, antipyretic and analgesic effect of *H. umbellata*.

Previous studies have highlighted different biological activities of *H. umbellata* [8–11], but to our best knowledge, the aphrodisiac property of *H. umbellata* seed extract has not been investigated in experimental animals. Hence, this study sought to assess the aphrodisiac activity of *H. umbellata* seed extract. The study also assessed the possible effect of administration of *H. umbellata* extract on the level of nitric oxide, sexual behavior and arginase activity in experimental animals.

2. Materials and methods

2.1. Sample collection and preparation

Hunteria umbellata seeds were purchased from a retailer of herbal produce at Akure main market, Akure, Nigeria. Authentication was carried out at the Department of Biology, Federal University of Technology, Akure, Nigeria. Voucher sample was deposited at the institution herbarium with reference number FUTA/BIO/301 allotted. The seeds were gently washed under running tap water to remove any dirt and completely dried at room temperature. Hundred gram (100 g) of the dry seeds were pulverized to a fine powder using a domestic blender. 25 g of the finely powdered sample was boiled in 500 ml of distilled water in a beaker for 1 h under continuous stirring. The homogenate was allowed to cool for about 6 h before it was rapidly filtered through a piece of clean white cloth. The filtrate was lyophilized and the residue obtained was stored in an air-tight container at −4 °C. The yield obtained was 40% (w/w). From the residue, a fresh stock was reconstituted in distilled water at a concentration of 50 and 100 mg/kg body weight, whenever needed.

2.2. Chemicals and reagents

L-arginine, diaminobenzaldehyde, coomassie blue G and sulphanilamide were obtained from Sigma Chemical Co (St. Louis, MO, USA) and bovine serum albumin, nitrate, and vanadium chloride was obtained from Reagen (Colombo, Parana, Brazil). Sildenafil Citrate was obtained from Cipla Limited., Mumbai, India, and Estradiol benzoate procured from Organon Limited, Kolkata, India, whereas progesterone was obtained from Cadilla Healthcare Limited, Daman, India. Tris buffer and other reagents were of analytical grade, and distilled water was used.

2.3. Animal care

Twenty four (24) adult male Wistar albino rats (weighing 150–180 g) were procured from the Department of Biochemistry Breeding colony, University of Ibadan, Nigeria. The animals were acclimatized for two weeks and allowed to *ad libitum* access to water and commercial diet. The handling of animals was in accordance with the guidelines of the National Council for Animal Experiments Control (CONCEA) and institutional ethical committee. The animals were housed in stainless steel cages and kept in a room where 12 h light/dark cycle was maintained throughout the period of the experiment. All animal experiments were performed according to the protocols and recommendation of the Institutional Animal Ethics committee of the School of Sciences, Federal University of Technology, Akure, Nigeria (Ethical No.: FUTA/SOS/1411). The rats were subsequently divided into four groups (n = 6) such that animals in a group are ± 5 g different. Group 1, normal control, was orally administered, once daily with 1 ml of distilled water, group 2, positive control, was treated with Sildenafil citrate (5 mg/kg), while animals in group 3 and 4 were treated with 50 and 100 mg/kg body weight of *H. umbellata* respectively through oral gavage. The choice of *H. umbellata* doses (50 and 100 mg/kg) was in accordance with a previous study [10].

2.4. HPLC-DAD analysis of phenolic constituents

Samples extract at a concentration of 12 mg/ml were injected by means of a model SIL-20 A Shimadzu Auto sampler. Separations were carried out using Phenomenex C_{18} column. The mobile phase was water with 1% formic acid (v/v) (solvent A) and HPLC grade methanol (solvent B) at a flow rate of 0.6 mL/min and injection volume 40 μL. The composition gradient was: 5% solvent B reaching 15% at 10 min; 30% solvent B at 25 min, 65% solvent B at 40 min and 98% solvent B at 45 min, followed by 50 min at isocratic elution until 55 min. At 60 min the gradient reached the initial conditions again, following the method described by Shodehinde et al. [12]. The chromatography peaks were confirmed by comparing its retention time with those of reference standards and by DAD spectra (200–600 nm).

2.5. Anxiety behavioral studies

2.5.1. Open field test

The effect of the different doses of *H. umbellata* extract was carried out in the open-field to ascertain possible plant extract-induced motor impairment. In brief, the open field test was carried out in an apparatus consisted of a brightly lit arena measuring 60 × 60 x 50 cm and divided into 16 equal squares. The animals were placed in the center of the apparatus and the locomotor activity was recorded as the number of line crossings for 5 min [13].

2.5.2. Dark-light box test

Using the dark-light box test, motor, anxiety and exploration behavior in male rats were assessed. The experimental procedure was described by Crawley and Goodwin [14]. The light-dark box consisted in two equally sized compartments (25 × 33 × 24 cm), which were connected by an opening (8 × 8 cm) located at floor level in the center of the partition. The light compartment was white, while the dark compartment was black. The test was performed in a dimly lighted room. Each animal was initially confined in the white compartment for 30 s, afterward, the sliding door was open allowing the rat to freely explore the apparatus for 5 min.

2.6. Sexual behavioral protocol

In order to evaluate the sexual behaviors, estrous female rats were paired with males treated with the infusion of *H. umbellata*. Female rats were induced to estrous by administration of estradiol benzoate at a dose of 2 μg/kg body weight and progesterone, 500 μg/kg body weight at 48 and 4 h, respectively prior to the commencement of sexual behavioral studies. Behavioral observations were conducted 4 h after progesterone administration. Sexual behaviors were monitored in a separate room for 1 h in a clear plastic box (60 × 60 × 80 cm) and captured by digital video recording. The sexual behavior parameters examined were mounting number (the number of mounts without intromission from the time of introduction of the female to the male), mount latency (time from introduction of the female until the first mount with pelvic thrusting), intromission number (the number of intromissions from the time of introduction of the female until the end of the experiment), intromission latency (time from introduction of the female until the first mount with pelvic thrusting and vaginal penetration) [15,16].

2.7. Biochemical analyses

After the treatment period of 28 days, animals were sacrificed 24 h after the last dose under light ether anesthesia. Blood samples were obtained by heart puncture and centrifuged at 3000*g* for 10 min. The clear non-hemolyzed sera were stored at −20 °C till subsequent measurements. The penile tissues were quickly excised and washed in cold saline solution, blotted on filter papers to remove adhering blood, and homogenized in 100 mM sodium phosphate, pH 7.4. The homogenates were centrifuged at 10,000*g* for 20 min at 4 °C, and the supernatants were used for subsequent assays. The supernatant obtained was assayed for catalase [17], non-protein thiol [18], and total protein (Randox kit).

2.8. Measurement of nitric oxide level

Nitric oxide content in penile tissue homogenate was estimated in a medium containing 400 mL of 2% vanadium chloride (VCl_3) in 5% HCl, 200 ml of 0.1% N-(l-naphthyl) ethylenediamine dihydrochloride, 200 mL of 2% sulphanilamide (in 5% HCl). After incubating at 37 °C for 60 min, nitrite levels, which correspond to an estimative level of NO, were determined spectrophotometrically at 540 nm, based on the reduction of nitrate to nitrite by VCl_3 [19]. Penile tissue nitrite level was expressed as micromole of NO per gram of tissue.

2.9. Determination of arginase activity

Serum and penile tissue arginase activities were determined by measuring the amount of urea produced using α-isonitrosopropiophenone as previously described by Zhang et al. [20]. Briefly, 50 μL of homogenate was added into 75 μL of Tris−HCl (50 mM, pH 7.5) containing 10 mM $MnCl_2$ and was preincubated at 37 °C for 10 min to activate the enzyme. The hydrolysis reaction of L-arginine by arginase was performed by incubating the mixture containing activated arginase with 50 μL L-arginine (0.5 M) at 37 °C for 1 h and reaction was terminated by adding 400 μL of the acid solution mixture [$H_2SO_4/H_3PO_4/H_2O$ = 1:3:7 (v/v/v)]. For colorimetric measurement of urea, 25 μL of α-isonitrosopropiophenone (9% in absolute ethanol) was added and the mixture was heated at 100 °C for 45 min. Thereafter, the urea concentration was determined spectrophotometrically by measuring the absorbance at 550 nm. The amount of urea produced was used as an index for arginase activity.

2.10. Statistical analysis

Analysis and graphs construction was performed using the software GraphPad Prism version 5.00 (GraphPad Prism Software, Inc., San Diego, California). The results were analyzed using appropriate analysis of variance (ANOVA) followed by the Bonferroni multiple range test and data are presented as mean ± standard error of the mean (SEM).

3. Results

3.1. Anxiolytic-like activities of H. umbellata

Figs. 1 and 2 show the results of open field and light and dark box tests. Administration of *H. umbellata* extract at a dose of 100 mg/kg significantly increase ($p < 0.05$) time spent at the light compartment and decrease time spent at the dark compartment (Fig. 1A–B). Whereas, there is no significant difference in the number of crossings when compared treated group with control groups (Fig. 1C). In addition, Fig. 2A reveals an increased number of square entered in rats treated with *H. umbellata* compared with the control group ($p < 0.05$). Sildenafil citrate had no significant effect on the number of squares entered. This could be associated with the fact that sildenafil citrate acts by inhibiting PDE-5 and not a cognitive enhancing drug. The same trend was observed in the time spent at the center where extract-treated rats spent more time at the center in an open field test compared with the control group (Fig. 2B).

3.2. Effect of extract on sexual behavioral performance

Sexual behavior parameters increased significantly in rats treated with *H. umbellata* and sildenafil citrate. Extract administration caused significant ($p < 0.05$) decrease in mounting latency and intromission latency and conversely increase mounting and intromission numbers (Fig. 3A–D). Rats treated with sildenafil citrate showed better performance than *H. umbellata* treated groups.

3.3. Effect of extract on biochemical parameters

Results presented in Fig. 4 show decreased arginase activity in the *H. umbellata* treated groups compared to the control group (Fig. 4A–B). As shown in Fig. 5, administration of *H. umbellata* (100 mg/kg) caused a significant ($p < 0.05$) increase in nitric oxide level. However, there was no significant difference between sildenafil citrate and 50 mg/kg *H. umbellata.* Similarly, *H. umbellata* extract at doses of 50 and 100 mg/kg increased catalase activity in treated compared with control group ($p < 0.05$) (Fig. 6). The same trend was observed in non-protein thiol determination where *H. umbellata* extract caused a significant ($p < 0.05$) increase in non-protein thiol level compared with the control group (Fig. 7A–B).

3.4. HPLC analysis of constituents of H. umbellata

HPLC analysis of phenolic constituents of *H. umbellata* revealed abundance of gallic acid, chlorogenic acid, caffeic acid, ellagic acid, quercetin and apigenin (Fig. 8 & Table 1).

4. Discussion

Despite its use in traditional medicine of many countries to treat pain, inflammatory diseases, and diabetes, *H. umbellata* has not yet been evaluated for its aphrodisiac and anxiolytic-like activities. The present study revealed that administration of *H. umbellata* in the dark-light box test induced an increase in the exploration and the time spent in the illuminated compartment (*i.e.*, anxiolytic-like action) in a dose-dependent manner. The dark-light test has been validated as well-accepted, experimental animal model typically used to test the effectiveness of any drugs or substances with acclaimed anxiolytic properties [21], since anxiety has an ethological approach relied on innate response of fear in face of aversive situations (open and illuminated space). The time spent in the illuminated compartment has been considered the most reliable parameter for evaluating anxiolytic activity, while the number of crossings considered a sign of explorative activity [22]. Furthermore, in order to ascertain the anxiolytic effect of *H. umbellata* and locomotor activity alteration, open field test (a widely accepted animal model) was carried out to assess the autonomic activities of *H. umbellata* and the general activity of animals [23]. In this study, animals treated with *H. umbellata* at doses which produced anxiolytic effect did not alter general motor activity of the animals, suggesting that the plant may not produce undesirable side effects. Anxiety plays a role in the development of sexual dysfunction in both men and women [24]. Studies carried out by Mathew and Weiman, [25] and Masters and Johnson [26], highlighted the role of anxiety in the short-term treatment of sexual dysfunctions. In our study, we observed anxiolytic-like effect in rats treated with *H. umbellata* and this could be justified by significant increase in time spent at

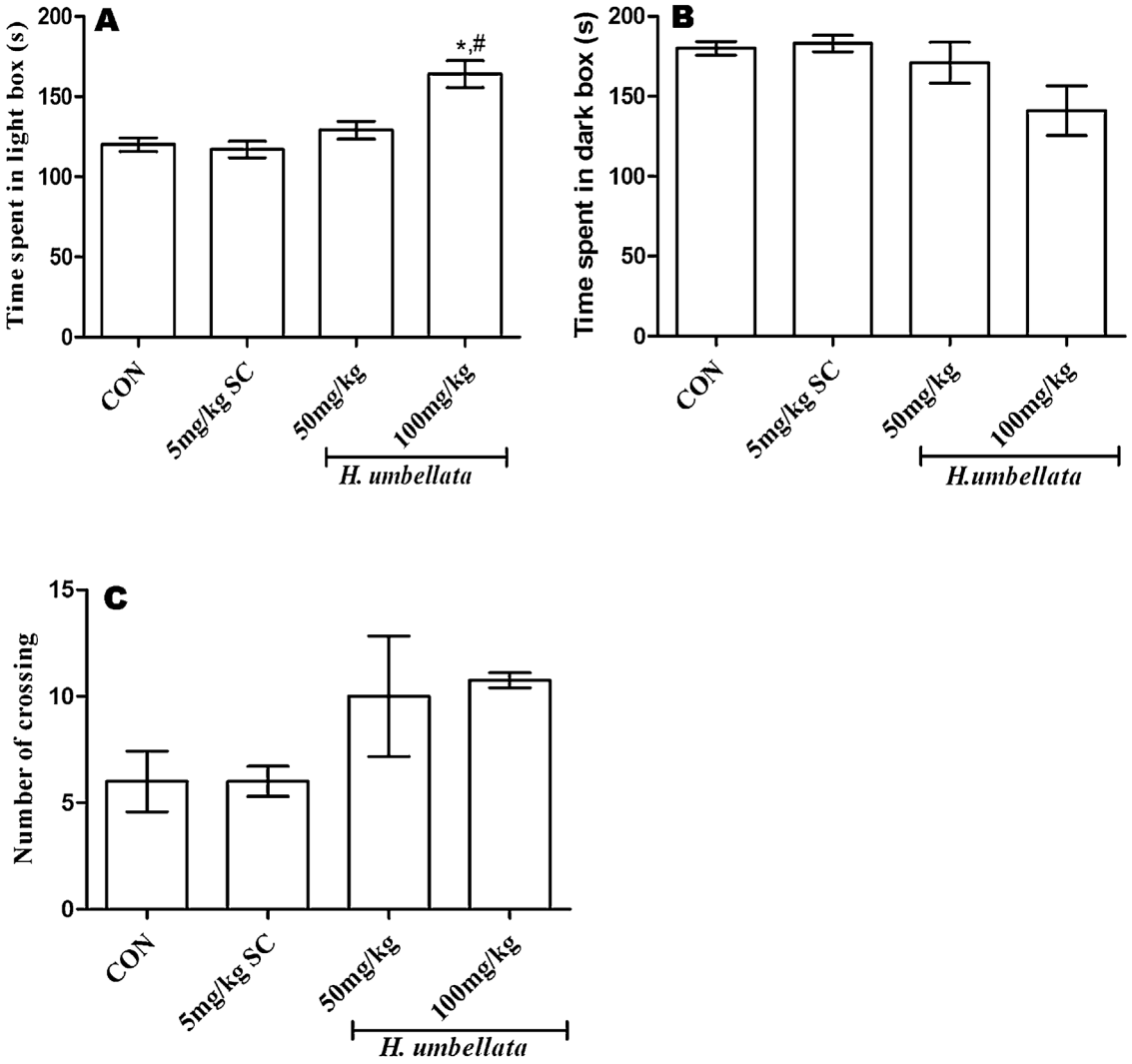

Fig. 1. Effect of administration of *H. umbellata* extract and Sildenafil citrate (SC) on time spent in light compartment (A), time spent in dark compartment (B) and number of crossing (C) during dark-light test performed in rats. Values are mean ± SEM, (n = 6). One way ANOVA followed by Bonferroni multiple range test was used for statistical significance. "*" denotes significant differences compared with the control group ($p < 0.05$) and "#"denotes significant differences compared with the SC group ($p < 0.05$).

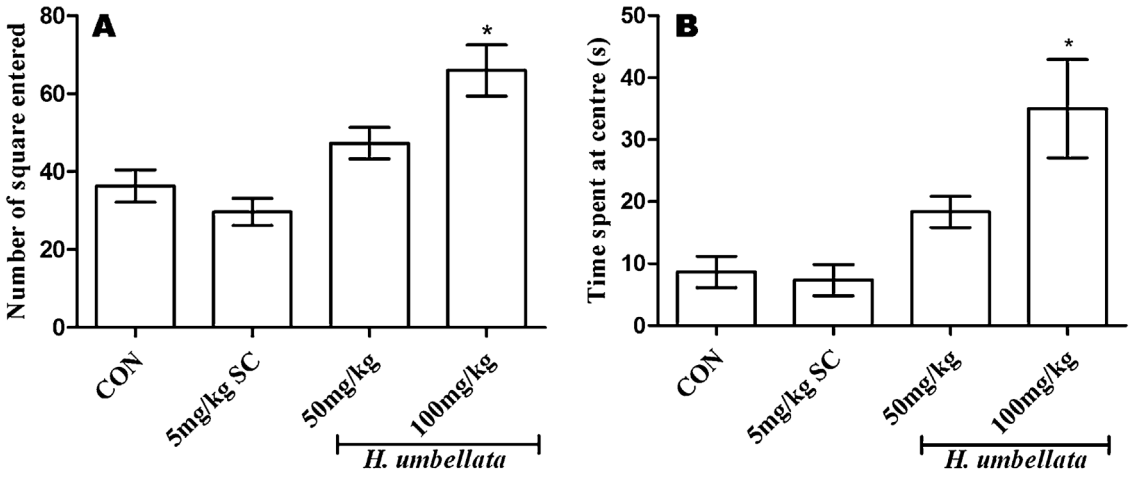

Fig. 2. Effect of administration of *H. umbellata* extract and sildenafil citrate (SC) on number of square entered (A) and time spent at center (B) during open field test performed in rats. Values are mean ± SEM, (n = 6). One way ANOVA followed by Bonferroni multiple range test was used for statistical significance. "*" denotes significant differences compared with the control group ($p < 0.05$).

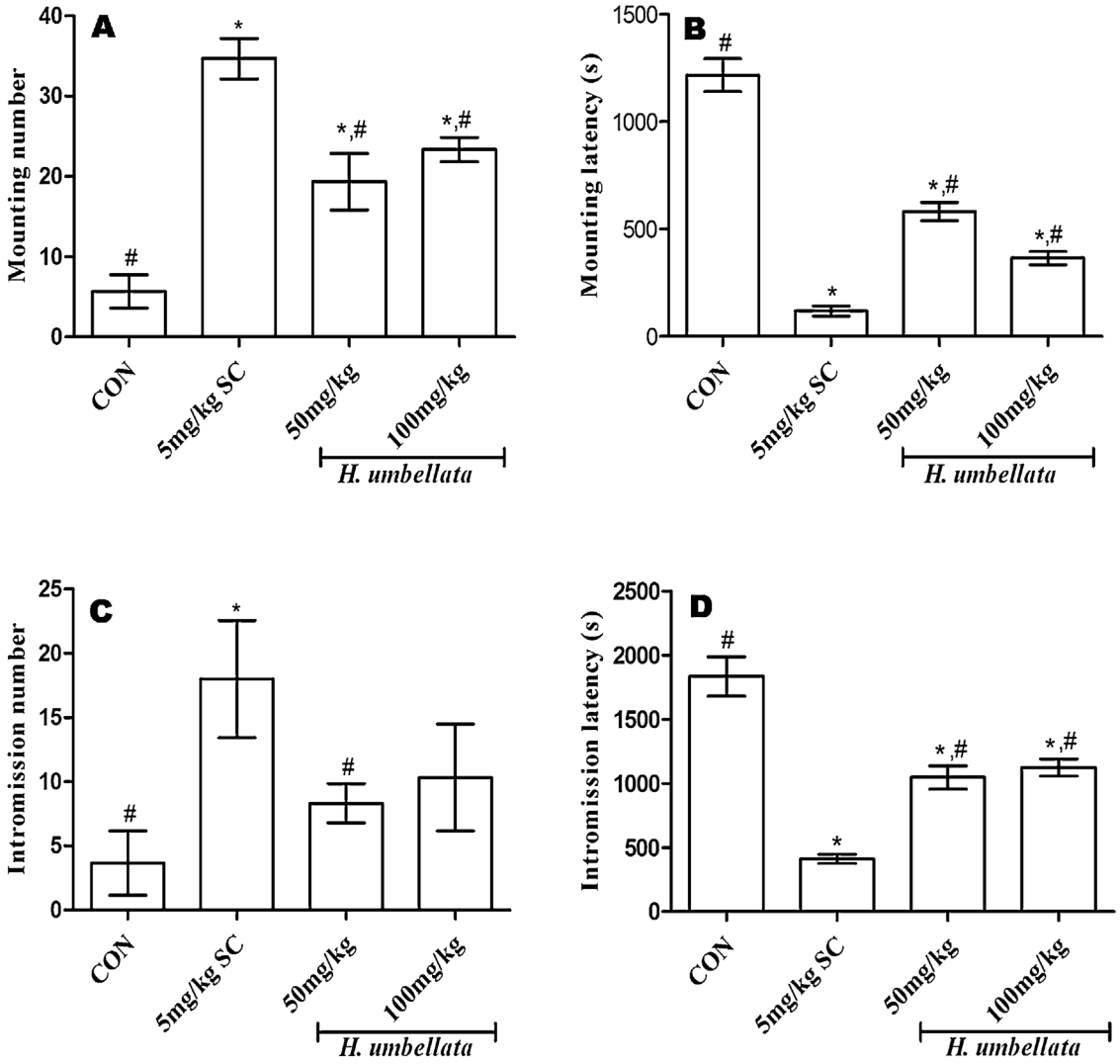

Fig. 3. Effect of administration of *H. umbellata* extract and Sildenafil citrate (SC) on mounting number (A), mounting latency (B), intromission number (C) and intromission latency (D) during sexual behavioral test performed in rats. Values are mean ± SEM, (n = 6). One way ANOVA followed by Bonferroni multiple range test was used for statistical significance. "*" denotes significant differences compared with the control group ($p < 0.05$) and "#"denotes significant differences compared with the SC group ($p < 0.05$).

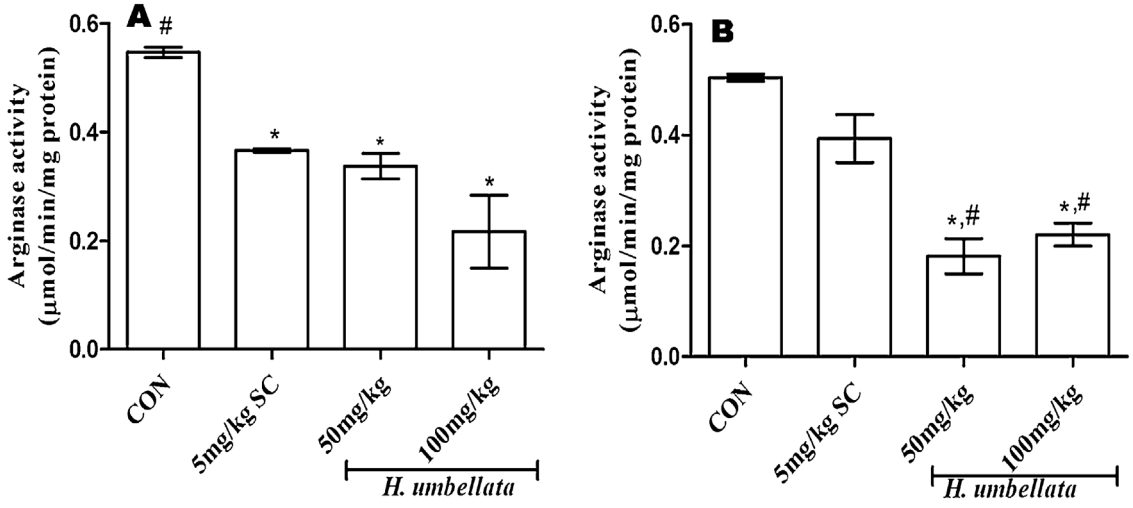

Fig. 4. Effect of administration of *H. umbellata* extract and Sildenafil citrate (SC) on (A) penile tissue and (B) serum arginase activities in rats. Values are mean ± SEM, (n = 6). One way ANOVA followed by Bonferroni multiple range test was used for statistical significance. "*" denotes significant differences compared with the control group ($p < 0.05$) and "#"denotes significant differences compared with the SC group ($p < 0.05$).

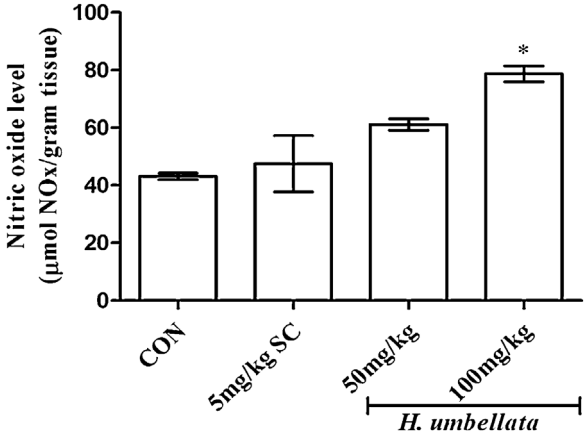

Fig. 5. Effect of administration of *H. umbellata* extract and Sildenafil citrate (SC) on penile tissue nitric oxide level in rats. Values are mean ± SEM, (n = 6). One way ANOVA followed by Bonferroni multiple range test was used for statistical significance. "*" denotes significant differences compared with the control group ($p < 0.05$).

Table 1
HPLC analysis of phenolic composition of *H. umbellata*.

Compounds	Concentration (mg/g)
Gallic acid	0.59 ± 0.03
Chlorogenic acid	1.27 ± 0.01
Ellagic acid	5.83 ± 0.04
Quercetin	2.94 ± 0.01
Apigenin	0.45 ± 0.03

Values represent mean ± standard deviation of replicate readings.

the light compartment during light-dark box test and increased exploratory activity in the center part of the open box during open field test. However, this activity could be attributed to their inherent phytoconstituents especially phenolic and flavonoid compounds possibly through inhibition of neurotransmitter degrading enzymes.

In our findings, we examined the possible effect of *H. umbellata* on sexual behavior markers in experimental male rats. Interestingly, *H. umbellata* extract significantly increased the mounting latency and intromission frequency in male Wistar albino rat, when compared with the control group. *H. umbellata* also decreased mounting latency significantly compared to the control group. The increase in sexual function justifies the role of *H. umbellata* in Nigerian traditional medicine for the management of male sexual dysfunction [27,28]. However, this could be related to an increase in the levels of several anterior pituitary hormones and serum testosterone which in turn stimulates synthesis of dopamine receptor and sexual behavior [29].

Arginase (an enzyme that converts L-arginine to ornithine and urea) has been implicated to play a prominent role in the pathophysiology of male sexual dysfunction [30]. This study showed inhibition of arginase activity in experimental animals treated with *H. umbellata*. These findings also revealed the important role of arginase in the pathogenesis of male sexual dysfunction and further explained the significance of arginase inhibition as a potential therapeutic approach for treating male sexual dysfunction through increased bioavailability of nitric oxide (NO) as a result of increased nitric oxide synthase (NOS) activity. Because of the important role of arginase in the overall regulation of NO bioavailability, coupled with the fact that it is associated with pathologies arise from endothelial dysfunction [31], reduced arginase activity will result in elevating NO bioavailability through activation of endothelial nitric oxide synthase (eNOS) [32]. It has been reported that arginase inhibition restores normal endothelial function in the vasculature of several experimental models of erectile dysfunction, diabetes, hypertension, and atherosclerosis [33–35]. In one of our earlier studies, we reported the *in vitro* inhibition of arginase by *H. umbellata* aqueous extract [36]. However, our finding in this *in vivo* study clearly supports the important role of arginase in vascular endothelial dysfunction and regulation of NO bioavailability. However, the inhibitory effect of the extract on arginase could be associated with inherent phenolic compounds, which had been previously described [36,37].

Nitric oxide (NO)/cGMP signaling pathway has been reported to relax corporal cavernosal smooth muscle, which is of pharmacological importance in penile erection [38]. Simultaneous administration of L-arginine and inhibition of arginase has been reported to increase sexual function in human participants [39],

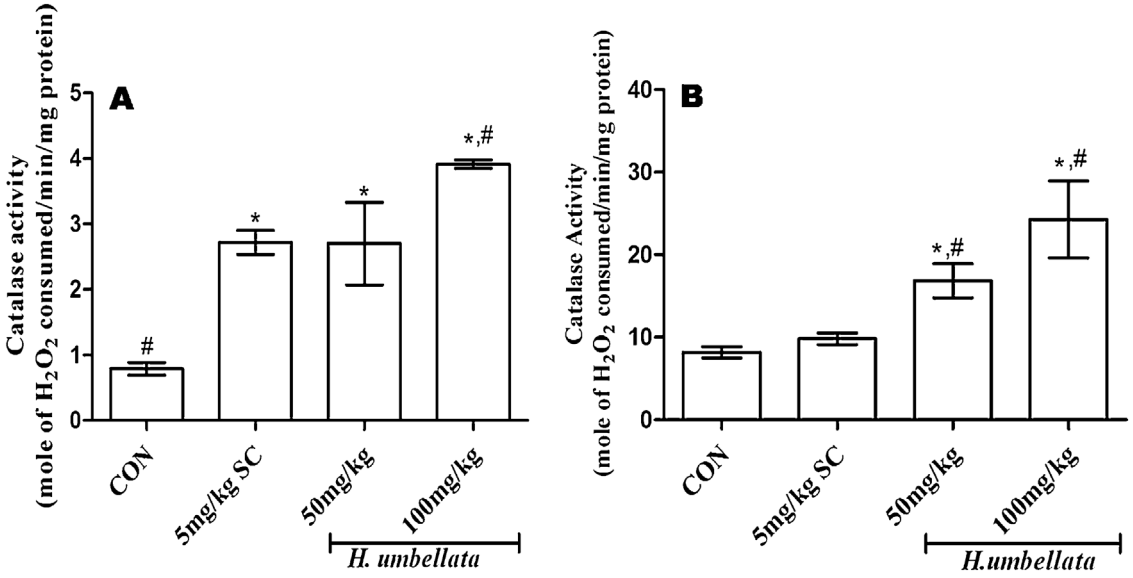

Fig. 6. Effect of administration of *H. umbellata* extract and Sildenafil citrate (SC) on (A) penile tissue and (B) serum catalase activity in rats. Values are mean ± SEM, (n = 6). One way ANOVA followed by Bonferroni multiple range test was used for statistical significance. "*" denotes significant differences compared with the control group ($p < 0.05$) and "#"denotes significant differences compared with the SC group ($p < 0.05$).

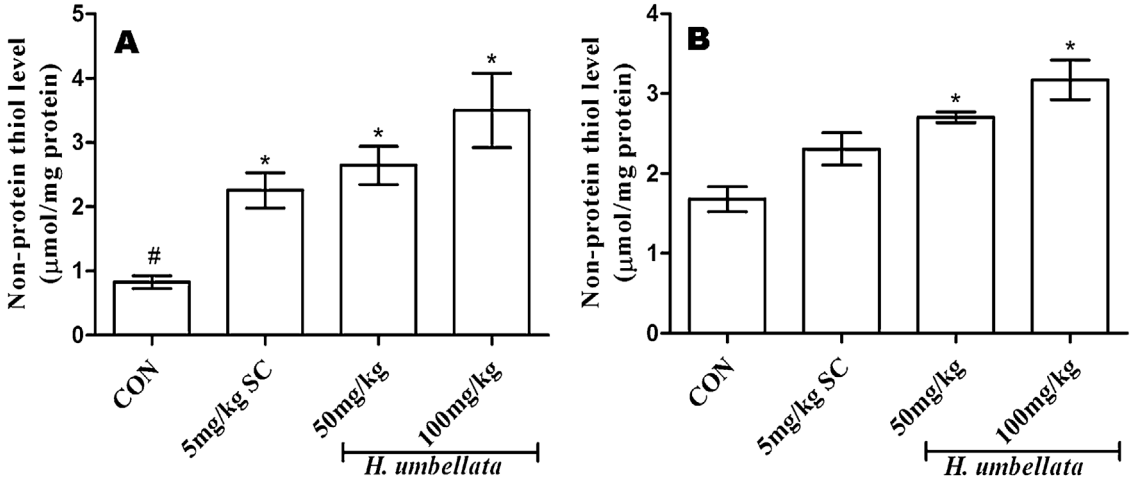

Fig. 7. Effect of administration of *H. umbellata* extract and Sildenafil citrate (SC) on (A) penile tissue and (B) serum non-protein thiol level in rats. Values are mean ± SEM, (n = 6). One way ANOVA followed by Bonferroni multiple range test was used for statistical significance. "*" denotes significant differences compared with the control group ($p < 0.05$) and "#"denotes significant differences compared with the SC group ($p < 0.05$).

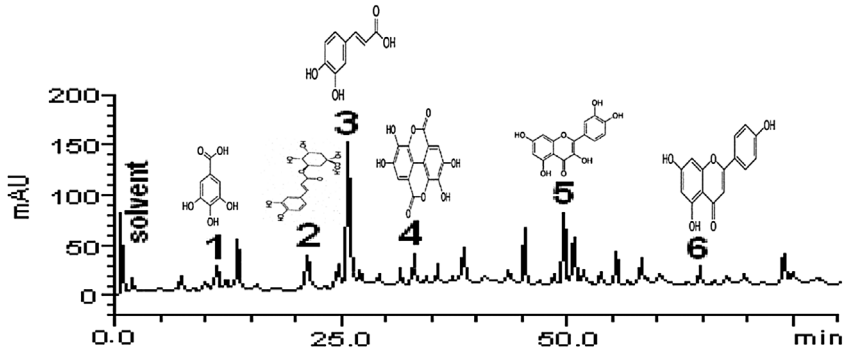

Fig. 8. Representative of high performance liquid chromatography (HPLC) phenolic profile of *H. umbellata*. Gallic acid (peak 1), chlorogenic acid (peak 2), caffeic acid (peak 3), ellagic acid (peak 4), quercetin (peak 5) and apigenin (peak 6).

which further explains the role of NO in initiating a penile erection. Neuronal nitric oxide synthase uses arginine to produce NO that diffuses into the endothelial cells of corporal cavernosal smooth muscle, where it stimulates soluble guanylate cyclase to generate cGMP from guanosine triphosphate. cGMP, the intracellular second messenger, relaxes the penile smooth muscle through the activation of protein kinase C. Arginase competes with eNOS and nNOS for arginine and thereby decrease the level of cGMP [38]. Inhibition of arginase elevates cGMP level in penile smooth muscle, thereby enhances erection. It would be reasonable to attribute the increased NO level observed in animals treated with *H. umbellata* to arginase inhibition. Since NO level is directly related to nitrite level, coupled with a short half-life of NO which makes it difficult to quantify, nitrite level is therefore used as a marker to quantify NO level [40].

There exist an association between oxidative stress and endothelial dysfunction [41]. Reactive oxygen species interfere with the NO pathway and causes vascular damage due to the formation of peroxynitrite ($ONOO^*$) [42,43]. Antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx) are the first line of defense against oxidative damage to the cell [44]. Antioxidants protect biological systems against reactive oxygen species and the breakdown products of peroxidized lipids, oxidized protein, and DNA. Oxidative stress in erectile dysfunction has been related to decreased antioxidant status, as a result of increased production of free radicals [45]. Furthermore, Brown and Hu [46] reported that increased levels of antioxidants caused a significant decrease in the level of superoxide through an increase in the level of dihydrobiopterin (BH_4), a cofactor needed for stimulation of endothelial nitric oxide synthase activity. Therefore, we can infer from our findings that the antioxidant effect of *H. umbellata* extract might contribute to the increased level of NO as observed in this study. This agrees with the previous finding where antioxidant improves erectile function in aged and diabetic rats [47–49]. In addition, the antioxidant property of some of the active compounds (ellagic acid, chlorogenic acid, and quercetin) present in *H. umbellata* has been reported [49–51]. These compounds have polyhydroxyl groups that can chelate metals and scavenge radicals, which could be the underlying mechanism behind the antioxidant activity of *H. umbellata* reported in this study.

Nonprotein thiol, a multifunctional intracellular non-enzymatic antioxidant, is considered to be the major thiol-disulfide redox buffer of the cell. It performs many vital physiological functions, including protection of cells from reactive oxygen species, detoxification of exogenous compounds, and amino acid transport with the help of the -SH group, which is essential for its antioxidant activity against some forms of reactive oxygen species in the cells [52]. Lowered thiol level observed in the control group could be as a result of increased utilization of this antioxidant compound for scavenging free radicals. Thiol group (-SH) forms complexes with metals that involves in free radical generation through the free SH group. However, treatment with *H. umbellata* enhances the level of thiol and effectively provides thiol groups necessary for -SH mediated detoxification reactions. The antioxidant mechanism of this extract could be attributed to the structure of some of its conju-

gated polyphenols, which possess the radical-trapping ability and potent ability to scavenge reactive oxygen species [53,54].

5. Conclusion

Conclusively, data generated in this study explained the possible mechanisms behind the acclaimed aphrodisiac effect of *H. umbellata*. This could be supported by the activities of *H. umbellata* reported in this study; especially its effect on sexual behavior indices, nitric oxide level and arginase activity in experimental male rats. Therefore, *H. umbellata* could be exploited in the management of erectile dysfunction. However, further *in vivo* studies using anxiety-induced sexual dysfunction model are recommended to ascertain the effect of *H. umbellata* on anxiety-induced sexual dysfunction, which is the limitation of this study.

Conflict of interest

Authors have no conflict of interest to declare.

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