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APHRODISIAC AND HYPOGLYCEMIC POTENTIAL OF ROOT BARK EXTRACTS OF *FERETIA APODANTHERA DEL* IN STREPTOZOTOCIN INDUCED DIABETIC MALE WISTAR ALBINO RATS

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ABSTRACT

Diabetes mellitus is one of the prevalent chronic diseases. Men with diabetes have a threefold higher chance of erectile dysfunction than men without the condition, which makes diabetes a known risk factor for male sexual dysfunction**.** *Feretia apodanthera* (Rubiaceae *spp*), is a dense and deciduous shrub with winding or twisting branches. The root bark of *Feretia apodanthera* del is believed to possess sex-enhancing properties in Nigerian indigenous medicine, although there is limited open-access scientific research on it. Therefore, the aphrodisiac potentials of root bark extracts of *Feretia apodanthera* del in streptozotocin-induced diabetic male wistar albino rats were investigated using standard methods. Phytochemical analysis was conducted on the aqueous, ethanol and n-hexane extracts of the root plant. Male wistar albino rats (150-200g) were induced with streptozocin (50mg intravenous injection . The rats were randomised into seven groups (A, B, C, D, E, F and G). Animals in group A (control) received 1 ml of distilled water (vehicle), B (Diabetic control) and test groups C and D were administered 100 and 200mg/kg b.w aqueous extract, groups E and F received 100 and 200mg/kg b.w ethanol extract while G received a combination treatment of 5mg/kg b.w sildenafil citrate + 100mg Metformin). Quantitative analysis reveals the significant ($p<0.05$) presence of flavonoids, tannin, saponins and cardiac glycoside in aqueous extract compared to ethanol and hexane root bark extracts of *Feretia apodanthera* del. Sexual behaviour parameter was monitored in the male rats for 7, 14 and 21 days, after 7 doses, 14 doses and 21 doses respectively once daily by pairing with a receptive female (1:1). Mount frequency, intromission frequency, ejaculation frequency and ejaculation latency were significantly ($p<0.05$ and $p<0.01$) decreased in diabetic control rats and significantly ($p<0.05$) increased mount latency and intromission latency when compared with the normal control and treated groups. Rats treated with standard drugs combination and aqueous extract (200 mg/ kg body weight) showed significant ($p<0.01$) increase in mount frequency, intromission frequency, ejaculation frequency and ejaculation latency and a significantly ($p< 0.05$) decreased mount latency and intromission latency compared to normal control and other treated groups. Hypoglycemic effect of *Feretia apodanthera del* root bark reveals that the aqueous extract significantly ($p<0.05$) decreased the fasting blood sugar and concurrently enhanced the sexual functions. These results suggest that aqueous extracts of root bark of *Feretia apodanthera del* (200 mg/kg bw) administered for 28 days possesses significant sexual behaviour and antihypoglycemic properties among other therapeutic values justifying its use in folklore medicine.

Keywords: Diabetes, aphrodisiac, mount, intromission, ejaculation, streptozotocin.

INTRODUCTION

Globally, about 529 million people have diabetes, which affects men, women, and children of all ages in every nation. By 2050, the figure is expected to increase by more than double to 1.3 billion (GBD, 2021). Diabetes is currently one of the top ten (10) major causes of mortality and disability, with a 6.1% global prevalence rate (IDF, 2022). Aphrodisiacs are substances that, when ingested, heighten or intensify sexual inclination and activity (Amy & Alina 2023). These compounds are obtained from plants, animals, or minerals while the title "aphrodite" originates from the ancient Greek goddess associated with love, passion, beauty and fertility The persistent inability to obtain and sustain an erection strong enough to allow for satisfactory sexual performance is known as erectile dysfunction (ED). Although ED is a benign illness, it negatively impacts physical and psychological well-being as well as the quality of life (QoL) of those who experience it as well as their spouses and relatives (Wespes et al., 2006). Several medical conditions, including diabetes, kidney disease, chronic alcoholism, multiple sclerosis, atherosclerosis, vascular diseases, and neurological disorders, are known to contribute to erectile dysfunction (Kok and Gerald 2003 & Romeo 2000). Among these disorders, oxidative stress and diabetes represent two of the main causes of impotence in men (Mitidieri et al., 2020). A constant or recurrent failure to obtain and sustain an erection sufficient for sexual performance is thought to afflict over 75% of diabetic men at some point in their life, generally at a younger age than non-diabetic men (Badescu et al., 2016). Additionally, erectile dysfunction risk factors associated with food, smoking, sedentary behaviour, alcohol use, and drug misuse (such as cocaine and opiate usage) may increase this pathological condition in diabetic individuals (Ramandeep, 2013).

Even though the prevalence of erectile dysfunction rises proportionately with age in the general population, it is especially pronounced in men with diabetes who appear to have more severe dysfunction (Mitidieri et al., 2020). Numerous approaches to therapy are now accessible because of the prevalence of sexual insufficiency in male humans. Unfortunately, these alternatives have some major side effects such as bleeding, urethral burning, infection, and penile pain in addition to being too expensive and not easily accessible (Fatusi et al., 2003). This condition, along with the rise in the number of diabetic men seeking therapy for male erectile dysfunction, could grow worse over time if nothing is done about it (Muhammad, 2023).

Feretia apodanthera del *is* a bushy, deciduous shrub that can reach heights of 2 to 6 metres and has branches that wind or twist. It is used locally as food, medicine, and cosmetics and it is harvested from the wild. They are naturally found around clay soils and soils that experience frequent seasonal flooding. Particularly by shepherds and kids, the red fleshy pulp of ripe fruit is consumed raw as a snack and used to satisfy hunger and thirst. Feretia apodanthera is the most predominantly occurring specie of the Rubiaceae family (Le Houreo, 1978). Several plants in this family are used in traditional medicine (TM) to treat a wide range of illnesses, including gonorrhoea, dysentery dermatoses, syphilis, constipation, fever, anaemia, dementia, malaria, epilepsy, diabetes, and high blood pressure (Silué et al., 2023). Because they are easily available, inexpensive, and less poisonous, the screening of this plant and its bioactive components for sex-enhancing ef-

fects in diabetics may intensify interest in their use for aphrodisiac activity.Therefore, *Feretia apodanthera del*, is said to have sex-enhancing effects in African folk medicine but has limited open-access clinical data. This study reports findings from an inquiry into sexual activities in *Feretia apodanthera del* root bark extracts.

Materials and Methods

Animals

Experimental procedures involving animal and their care were conducted in conformity with International, National and Institutional Guidelines for care and use of Laboratory Animals in Biomedical Research promulgated by the Canadian council of Animal Care and United State National Institute of Health (NRCNA, 2011). A total of 108 apparently healthy Wister albino rats of both sexes with an average body weight 150 – 200g were obtained and kept in a well -ventilated Laboratory cage in the Animal house, Department of Pharmacology and Pharmaceutical Sciences, Ahmadu Bello University Zaria, Nigeria. The animals were allowed to acclimatize for a period of two weeks before the commencement of the experiment. They were fed daily with water and grower mash from Vital Feeds Company, Nigeria. The study was approved by animal ethics committee, Ahmadu Bello University Zaria, Kaduna State.

Drugs and Supplies

Streptozotocin (STZ), Estradiol benzoate, and Progesterone were purchased from Sigma Chemical Company St. Louis U.S.A while Metformin and Sildenafil Citrate were purchased from a Standard Pharmaceutical store at Sabon-gari Zaria, Kaduna State.Chemicals used were of analytical grade.

Sample Collection and Preparation

Fresh roots of *Feretia apodanthera* del were obtained from its natural habitat at Magami village, Gusau Local Government Area, Zamfara State, Nigeria in December 2020. The plant was identified and verified at Ahmadu Bello University's Herbarium Unit in the Biological Sciences Department, Faculty of Science building, where a voucher specimen bearing the number 930 was tagged. The bark was peeled from the roots using an iron metal and air-dried at room temperature for three weeks. Thereafter, dry samples were ground to powder using mortar and pestle. The powder was sieved through a mesh size 1mm and then stored in polythene bags for further use. 500g dried root bark powder of *Feretia apodanthera del* was extracted successively with 2.5 liters each of n-hexane, ethanol, and distilled aqueous solution in a soxhlet extractor.

Acute toxicity test

According to the Organization for Economic Cooperation and Development (OECD)'s recommendations (AOT 425), an acute toxicity research was carried out on a total of 25 healthy adult male albino rats weighing between 150 and 200g .They were divided into eight groups with three animals per group; they were tested with different doses of the extracts (10-5000mg/kg body weight). For two hours, the rats were continuously watched for behavioural and autonomic patterns, as well as for any other indications of toxicity or mortality up to seven-days (Agmo & Laan 2023). Two distinct doses-100 and 200 mg/kg body weight were chosen for additional research based on the findings observed.

Induction of Diabetes

Male rats of weight 150-200g were selected for the experiment; they were fasted for 18h and water was supplied *ad libitum* during the fasting period. The rats were administered

with Streptozotocin (50mg/kg, I.V) in Citrate buffer (pH 4.4, 0.1M). After 3 days, blood samples were taken retro-orbitally after DM was induced by STZ to confirm the onset of diabetes. Rats with blood glucose more than 200mg/dL were included in the experiment (Sevda et al., 2017). Treatment with the extracts and mixture of Metformin and Sildenafil citrate (100mg and 5 mg/kg body weight/day) commenced 24 hours after establishment of diabetes and was continued for 21 days on daily basis.

Animal Groupings

Forty-two (42) male rats were randomly grouped into seven (1–7) consisting of 6 animals each and appropriate doses of the extracts were administered orally per day for twenty-one (21) days. Group 1: Normal control rats were given feed and water. Group 2: Diabetic rats were given feed and water only.

Group 3 and Group 4 were diabetic rats treated with 100 and 200mg/kg body weight of aqueous extract of *Feretia apodanthera*.

Group 5 and Group 6 were diabetic rats treated with 100 and 200mg/kg body weight of ethanol extract of *Feretia apodanthera*, while Group 7 were diabetic rats treated with Standard drugs mixture (Sildenafil citrate-5mg and Metformin-100mg).

Induction of Oestrus for Evaluation of Sexual Behaviour

Using the technique described by Agmo & Laan 2023, a total of 42 female rats weighing 100 and 150 grams from the same strain were employed as the stimulus for evaluating sexual behaviour. Female oestrus was induced prior to all testing sessions by giving rats 25 mg of estradiol benzoate, then 48 hours later, 250 mg of progesterone was administered. Between 4- and 8-hours following progesterone injection, female rats were used for copulatory studies. They were injected subcutaneously into each rat after dissolution with 0.1 ml of arachis oil (Kriti, India).

Test for Copulatory Behaviours

Adopting the standard procedures, the following male sexual behaviour indices were recorded or calculated for the observatory periods (Day 7, 14 and 21 respectively) i.e., after 7 doses, 14 doses and 21 doses respectively. Diabetic rats were confirmed by drawing blood samples and determining the glucose level. These rats were placed with prooestrus female rats and their sexual behaviour indices were assessed after two weeks. These parameters included *Mount frequency* (MF); the number of times the male attempted copulation but was unsuccessful in achieving intromission**.** *Intromission frequency* (IF): The number of vaginal penetrations made by the male. *Ejaculation frequency* (EF): The average amount of semen ejection by males following vaginal penetration, as indicated by rhythmic contraction of the posterior abdomen.

Additionally, other typical parameters of sexual behaviour that were manually recorded using a stopwatch include: *Mount latency* (ML): the interval between the female's introduction and the male's first mount. *Intromission latency* (IL): the interval between the female's introduction and the male's first entrance, which is typically marked by pelvic pushing and a jumping dismount. Ejaculation *latency* (EL): The phase between the first intromission and ejaculation is typically characterized by more gradual and slower dismounting longer, deeper pelvic thrusting, and a subsequent period of diminished activity. The male rats were subsequently introduced in the copulatory arena individually following their corresponding treatments. After being given 10 minutes to adjust, a female rat in oestrous was placed in the arena,

and the male rats were watched for the sexual behaviour parameters until ejaculation or, at most, for 30 minutes.

Data Analysis

The data were analysed using Graphpad prism (10.0.1). The results were expressed as mean ± standard deviation (SD). Analysis of variance (ANOVA) was conducted and the differences between the various animal groups were compared using the Duncan Multiple Range Test. P- value less than 0.05 was considered as significant ($P< 0.05$) (Dakhale, 2012).

RESULTS

Phytochemical Analysis and Oral Toxicity Test

The quantitative analysis of phytochemical constituents of aqueous ethanol and n-hexane extracts of *Feretia apodanthera del* shows significant ($p<0.05$) increase in tannins, saponins, cardiac glycoside and flavonoids . Conversely, n-hexane extracts shows significant ($p<0.05$) increase in alkaloids only. (Table 1). Furthermore, among all the quantified phytoconstituents, flavonoids showed significantly ($p<0.05$) higher concentrations across all the three extracts.

All rats tested negative for any harm or toxicity for all the three extracts (ethanol, aqueous and n-hexane) within the permissible OECD criteria, up to a level of 5000 mg/kg. The rats were subjected to a dose range of 10-5000 mg/kg b.w. There was no symptons of toxicity and mortality recorded from the rats after seven days observation period. The diabetes mellitus group's serum glucose levels were noticeably greater than that of the vehicle control.

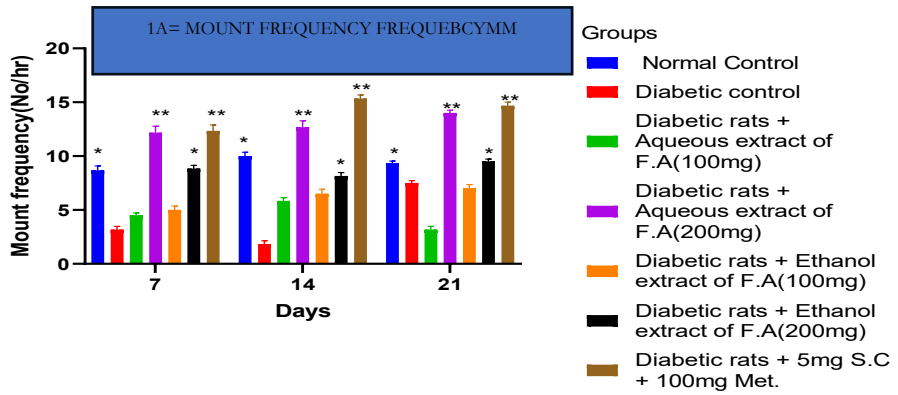
Table 1: The Quantitative Analysis of the Phytochemical Constituents in Root Bark Extracts of *Feretia apodanthera del*

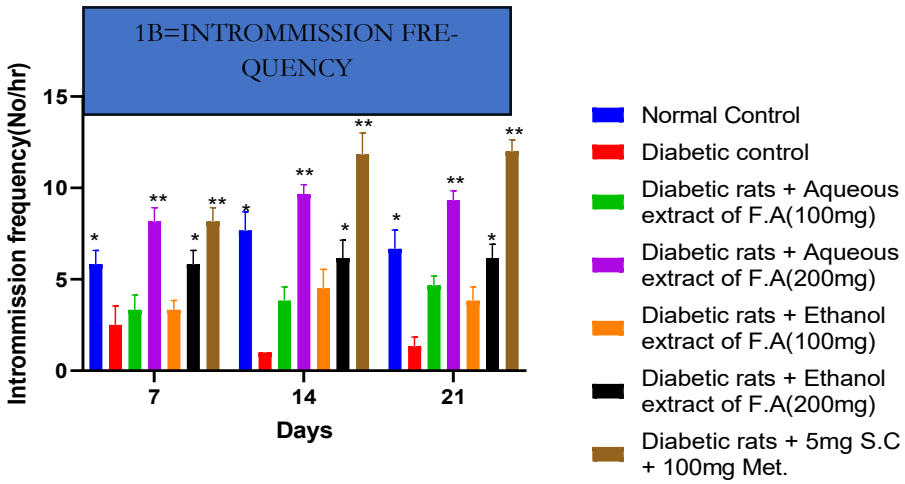
PARAMETERS	AQUEOUS EXTRACT	ETHANOL EXTRACT	n-HEXANE EXTRACT
TANNINS (mg/g)	0.480 ± 0.010^{a}	0.223 ± 0.006^{b}	0.047 ± 0.028^{c}
C. GLYCOSIDES (mg/g)	4.060 ± 0.010^{a}	2.560 ± 0.105^{b}	0.620 ± 0.100^{c}
ALKALOIDS (mg/g)	0.030 ± 0.017^{c}	0.06 ± 0.010^{b}	0.150 ± 0.010^{a}
FLAVONOIDS (mg/g)	7.180 ± 0.012^{a}	4.210 ± 0.123^{b}	2.920 ± 0.100^{c}
SAPONINS (mg/g)	0.963 ± 0.015^{a}	0.480 ± 0.012^{b}	0.260 ± 0.005^{c}

Values are Means ± SD of triplicate determinations (n=3). Values with the same superscript letter across the same row are significantly different ($P<0.05$).

Effect of Extracts of Root Bark of *Feretia apodanthera del on* Frequencies of Sexual Behaviour Parameters in STZ induced Diabetic Male Rats.

Mount, intromission, and ejaculation frequencies show a significant ($p<0.05$) decrease in the STZ induced diabetic rats compared with the normal control and induced treated groups for all the observed days at 7, 14, and 21 (Figure 1). Among the induced treated groups, the animal group treated with aqueous extract (200mg/kg body weight) and a combination of standard drug combination group showed significant ($p<0.01$) increase in mount, intromission and ejaculation frequencies when compared with normal control and other treated groups. Aqueous and ethanol (100 and 200mg /kg bw) extracts treated group showed a significant ($p<0.05$) and dose-dependent increase in frequencies for all the observed days. At day 21, there was no significant($p>0.05$) difference between the group treated with aqueous extract (200mg/kg b.w) and standard drugs (5mg S.C + 100mg Met) combination group on the sexual frequency parameters. Diabetic induced extract treated group showed significant ($p<0.05$ and $p<0.01$) increase in all the frequencies of sexual behaviour in a dose dependent manner for the observed time frame (Figures 1A, 1B and 1C).





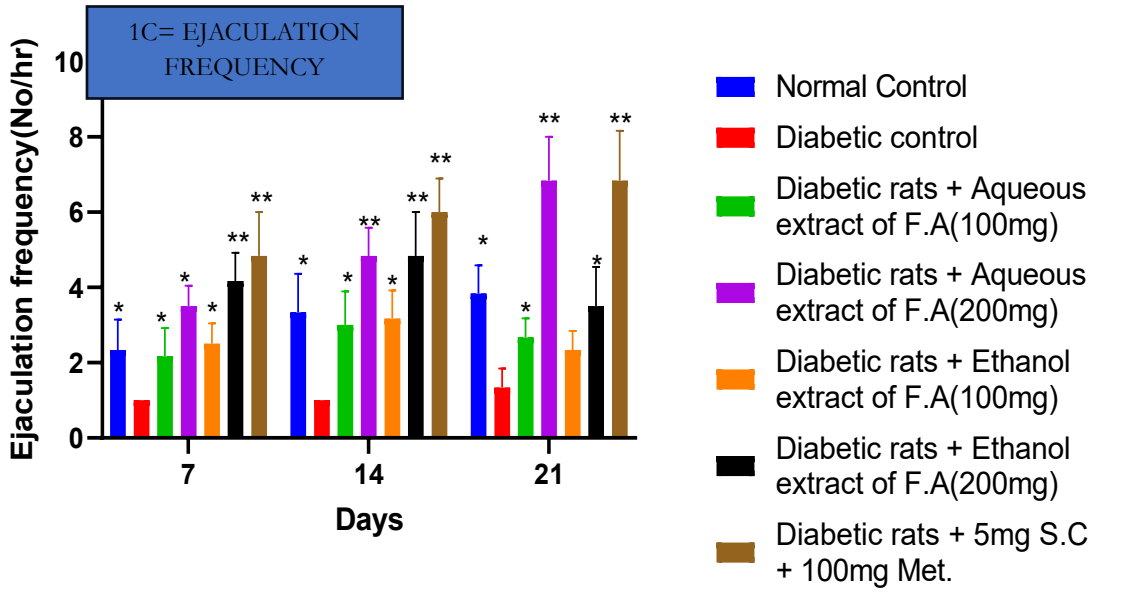


Figure 1.0: The Effect of Root Bark Extracts of *Feretia apodanthera* on the **Mount frequency(A), intromission frequency(B) and Ejaculation Frequency(C)** in STZ induced Diabetic Male Wistar albino Rats. Values are represented as means ±SD (n=6). Bars carrying single asterisk (*) shows significant different from the control ($p < 0.05$) while bars with double asterisk (**) shows significant difference from the control at ($p < 0.01$). SC-Sildenafil citrate and Met- Metformin.

Effect of Extracts of Root Bark of *Feretia apodanthera del on* Latencies of Sexual Behaviour Parameters in STZ induced Diabetic Male Rats.

Mount and intromission latencies showed a significant ($p< 0.05$) increase in the STZ induced diabetic rats compared with the normal control and induced treated groups for all the observed days -7, 14, and 21 (Figure 2). All the induced treated groups, and normal control showed no significant ($p>0.05$) difference in ejaculation latency periods for all the observed periods. Groups induced and treated with (200mg/kg body weight) extracts and standard drug combination group significantly ($p<0.05$) decreased in the mount and intromission latencies compared with the normal control and other treated groups (Figures 2A and 2B respectively). However, diabetic control group shows significant ($p<0.05$) decrease in ejaculation latency compared to normal rats and treated groups. Groups treated with 200mg/kg b.w aqueous extract and standard drug combination shows no significant ($p>0.05$) difference in the latency periods (Figure 2C).

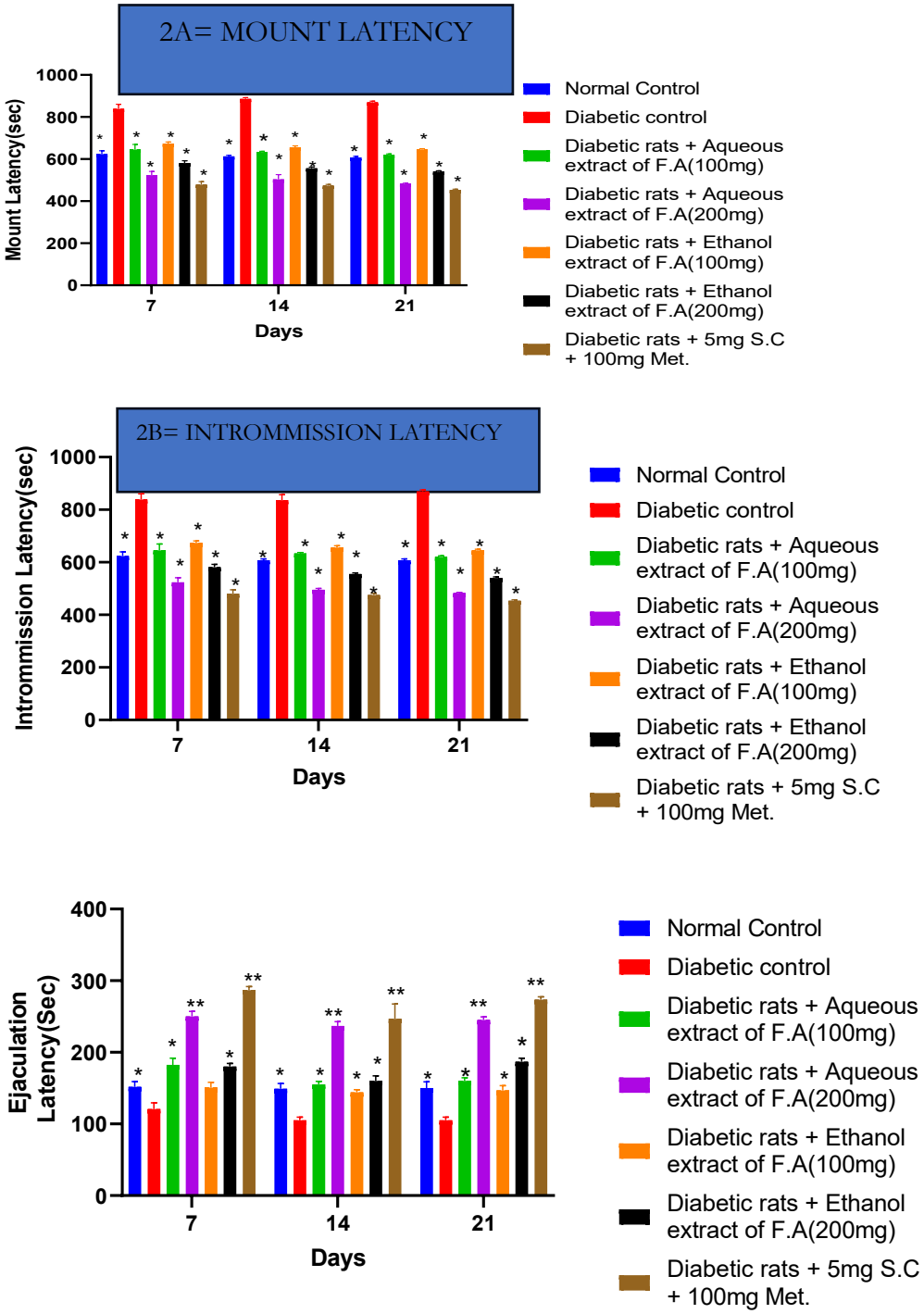


Figure 2.0: The Effect of Root Bark Extracts of *Feretia apodanthera* on the **Mount latency(A), Intromission Latency (B) and Ejaculation Latency(C)** in STZ induced Diabetic Male Wistar albino Rats. Values are represented as means ±SD (n=6). Bars carrying single asterisk (*) shows significant difference from the control ($p < 0.05$) while bars with double asterisk (**) shows significant difference from the control at ($p < 0.01$). SC-Sildenafil citrate and Met- Metformin.

Effects of Root bark extracts of *Feretia apodanthera del* on Fasting blood Sugar (FBS) levels in STZ induced Diabetic Male Rats

The diabetic control group had a slight percentage increase (1.02%) in fasting blood sugar while rats in the normal group and other treatment group showed significant ($p<0.05$) decrease in fasting blood sugar (Table 2). Amongst the treated groups, rats treated with 200mg/kg bw aqueous extract had the highest percentage decrease (33%) in blood glucose. All the extracts treated, and the standard drugs group showed significant decrease in day-1 compared to day-21 except for the diabetic control group (Table 2).

Table 2 : Hypoglycemic Effect of Root Bark Extracts of *Feretia apodanthera del* in STZ Induced Diabetic Male Rats

Treatment group	Initial FBS (mmol/l)	Final FBS (mmol/l)	% change in FBS
NC	7.12 ± 1.02[a]	7.08± 0.37[a]	0.56
DC	16.70± 4.37[a]	16.87± 0.50[b]	1.02
STZ + AE (100mg)	15.45 ±0.60[a]	13.47± 0.76[a]	12.7
STZ + AE (200mg)	14.90± 2.32[b]	9.90± 1.96[a]	33.55
STZ + EE (100mg)	14.95± 0.10[b]	11.27± 1.37[a]	21.60
STZ + EE (200mg)	16.98± 2.61[b]	14.02± 2.12[a]	17.43
STZ + STD DRGS	18.77± 1.56[b]	15.49± 1.87[a]	19.27

Values are represented as means ±SD (n=6). Bars carrying different superscript letters across the rows shows significant difference ($p < 0.05$). NC- Normal control, DC-Diabetic control, STZ-Streptozotocin, AE-Aqueous extract, EE-Ethanol extract, STD DRGS- Sildenafil citrate(5mg) + Metformin (100mg).

DISCUSSION

Numerous traditional herbal remedies, such as the root bark of *Feretia apodanthera* del, were used as sex enhancers without any supporting scientific evidence (Silué et al., 2023). To understand the scientific basis for these folkoric claims, we investigated the effects of aqueous, ethanol, and n-hexane extracts of *Feretia apodanthera del* roots bark on aphrodisiac potentials in male diabetic rats. Pilot studies (not reported) showed significant potential for aqueous, and ethanol extracts only. Extracts derived from n-hexane did not show any significant activity; the rats showed no significant difference in sexual behaviours, hormonal parameters and antihypoglycemic effects upon treatment with n-hexane extracts, thus, were not considered for subsequent studies. Numerous plants with medicinal qualities work as aphrodisiacs through a variety of mechanisms, including the rise of androgens and gonadotropins, vasodilation, and nitric oxide production. Sexual behaviour may change in response to therapies that change the amount of circulating sex hormones (Jennings & Lecea 2020). The present result

yielded information concerning the ability of *Feretia apodanthera* del roots bark extracts to improve male sexual behaviour in diabetic male rats. Quantitative analysis showed that flavonoids and cardiac glycosides have a significant concentration in aqueous and ethanol extracts. Previous research has revealed that high intake of flavonoids specific food is associated with amelioration of erectile dysfunction (Cassidy, 2016). Likewise, flavonoids and isoflavonoids have shown a great potential in preventing hypogonadism in males (Martin & Touaibia 2020). Acute toxicity test shows that the root bark extracts of *Feretia apodanthera* was reasonably safe to use orally, having LD_{50} value higher than 5,000 mg/kg. Owolabi et al., (2020) documented similar result for ethanol extracts of *Feretia apodanthera del.* Despite its short comings, LD_{50} is a helpful measure for determining a substance's safety margin.

In this investigation, treatment of the male rats with the aqueous and ethanol extracts of *Feretia apodanthera del* roots enhanced the mount, intromission, ejaculation frequencies and ejaculation latency of the diabetic male rats with 200 mg/kg body weight producing better results than 100 mg/kg body weight. Animal preceptive and precopulatory activities were prior to these sexual actions. For instance, keen observation shows that responsive female rats in this study exhibited intense proceptivity and receptivity as evidenced by their ear-wiggling, darting, hopping, and lordosis, whilst the precopulatory activity of the male rats treated with the extract likewise indicated that the animals were typically aroused. The male animals near proximity to the females as they ran after them in pursuit of them implied impending copulation. Two helpful measures of energy, libido, and potency are the mount frequency and intromission frequency. It has been reported that while the number of mount (MF) indicates sexual motivation, the growth in the number of intromission (IF) demonstrates the effectiveness of erection, penile orientation, and the ease with which ejaculatory reflexes are triggered (Agmo, 2003).

Consequently, the rise in MF and IF after the administration of 200 mg/kg of aqueous and ethanol extracts of *Feretia apodanthera del* roots bark on day 7 and at all doses thereafter on the other observation days points to increased libido (Tajuddin et al., 2010). Research has shown that increase in libido may have resulted from higher serum testosterone levels and other anterior pituitary hormone concentrations, which in turn encourage the stimulation of dopamine receptors and sexual behaviour (Calabrò et al., 2019). Furthermore, the rise in IF caused by the extracts in this study implies that the mechanism of penile erection was actively involved since intromission cannot occur without a sufficient erection and coordinated action of the penile muscles (Nimbi et al., 2020). Consequently, *Feretia apodanthera del* extracts may improve potency by promoting or maintaining erection. It is possible that not every male rat mount in this study led to intromission, based on the heterogeneity in the values of MF and IF. The increase in ejaculation frequency caused by *F. apodanthera del* extracts at 200 mg/kg body weight on days 7, 14, and 21 is a sign of the plant's improved aphrodisiac activity rats.

Sexual motivation is predicted by mount latency (ML) and intromission (IL). Sexual motivation has a negative correlation with ML and IL. As a result, the reduction in mount and intromission latencies seen in this study on days 14 and 21 at doses of 100 and

200 mg/kg body weight of the extract may indicate stimulation of sexual desire and arousability. It can also be a sign of the male rats' increased sexual propensity. All of these provide additional evidence for the extracts' ability to improve sexual function at these dosages. Additionally, the extended ejaculation latency caused by the conventional drug combinations (Sildenafil Citrate + Metformin) and 200mg/kg body weight of aqueous extract of *Feretia apodanthera del* on days 7, 14, and 21 provides evidence that the animals' copulatory performance was improved. It can also suggest that the coitus was longer than usual. Furthermore, the male copulatory organ was in touch with the vaginal opening as seen by pelvic thrusting during intromission and expulsion in the extract-treated rats in this investigation, which may have activated or strengthened lordosis in the female rats (Angoa-Pérez and Kuhn 2015). The antioxidants present in the *Feretia apodanthera del* extracts, notably total polyphenols, and flavonoids, may have a central and peripheral pathway contributing to the aphrodisiac effects of the substance (Owolabi et al., 2018). Additionally, the presence of alkaloids with ergogenic qualities may operate centrally by stimulating steroidogenesis in animal testes or by causing dilatation of the blood arteries through the generation of nitric oxide, enabling erection. Alkaloids relax the smooth muscles of the corpus carvenosum in the penal tissue of rats in a peripheral manner (Ashrafi et al., 2023). The present study also investigated the hypoglycemic effect of root bark extracts of *Feretia apodanthera del* in diabetic rats. STZ induces diabetes by rapid depletion of beta cells mass which leads to reduction in insulin release and hyperglycemia. Interestingly, administration of root bark extracts of *Feretia apodanthera del* significantly recovered fasting blood sugar (FBS) in diabetic rats. The extracts might be producing its hypoglycemic action by extrahepatic pancreatic action, possibly by stimulating glucose utilization in tissue or increase in the expression of insulin receptors in the liver plasma membranes. Numerous studies noted that DM negatively impacted male reproductive health, presumably by increasing oxidative stress and decreasing endogenous antioxidants (Park & Park 2021). Therefore, lowering oxidative stress brought on by free radicals and reactive oxygen species (ROS) may be a possible and likely mechanism for *Feretia apodanthera del* to alleviate sexual dysfunction in diabetic rats. *Feretia apodanthera del* may act through several routes given the ability of the aqueous extract to improve sexual function while also reducing diabetes. All the sexual parameters may have significantly improved due to *Feretia apodanthera del's* numerous mechanisms. The herb is clearly identified as a potent stimulant by the dose-dependently increased activity in the aqueous extract treated group that was comparable to the positive control group. However, more investigation will be helpful to identify the precise mechanism of action of the extracts in alleviating sexual dysfunction.

CONCLUSION

The present research demonstrated that *Feretia apodanthera del* has boosting properties that raise sexual arousal, or the feeling of excitement or desire experienced during a sexual encounter. Male rats' erection, genital grooming, and orienting behaviours were stimulated more effectively by aqueous extracts at a dose of 200 mg/kg body weight. *Feretia apodanthera del* is helpful in alleviating male sexual dysfunction, including erectile dysfunction along with pre-ejaculation. Hence, it is a promising aphrodisiac plant for diabetes related sexual dysfunction in men.

Author Contributions: Conceptualization;

Abdullahi Rilwan, and Dorcas Bolanle James: Methodology and Investigations: Abdullahi Rilwan, Ahmad Hamza Balarabe, Kabiru Usman and Adekola M.B. Original draft preparation: Abdullahi Rilwan. Review and Editing: Dorcas Bolanle James. Supervision: Dorcas Bolanle James and Nzelibe Humphrey. All authors have read and agreed to the published version of the manuscript.

Conflict of Interest: The authors declared no conflict of interest.

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