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Aphrodisiac agents used in traditional medicine and their mechanism of action - A Review

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Abstract

Erectile dysfunction is the repeated inability to sustain erection firm enough for sexual intercourse while an aphrodisiac is an agent (food/drug) that arouses sexual activity. Various factors affect sexual performance in men, and include; psychological, hormonal abnormalities, aging, penile injury, chronic diseases, lifestyle, medications and radiation. Aphrodisiac medicinal plants could elicit their effect by providing essential nutrients such as vitamins, minerals and amino acids or could improve blood flow to the penile tissues, e.g. *Kaempferia parviflora* which could inhibit phosphodiesterase enzyme (PDE-5). Some medicinal plants stimulate or act on the central nervous system to derive their aphrodisiac effects, e.g. *Pausinystalia yohimbe* due to the presence of an alkaloid yohimbine. Medicinal plants could increase the serum level of cholesterol, testosterone, luteinizing hormone and follicle stimulating hormone and improving the overall male reproductive health. The aim of this research is to review the role of medicinal plants in the management of erectile disorders in men, which could lead to discovery of novel chemical scaffolds for the synthesis of potent aphrodisiac agents. Natural products particularly aphrodisiac medicinal plants remain an important source of new drugs, new drug leads and new chemical entities allowing the design, rational planning of new drug biomimetic, discovery of new therapeutic properties not yet attributed to known compounds and synthesis development.

Keywords: Erectile dysfunction, Aphrodisiac agents, Medicinal Plants, Phosphodiesterase inhibitors, Testosterone

1. Introduction

Erectile dysfunction may also refer to “Impotence” it is the repeated inability to sustain erection firm enough for sexual intercourse. The cause of erectile dysfunction varies among individuals. Erectile dysfunction can occur when any of the events that lead to erection is disrupted ^[1, 2] Erectile function is a balance between two contrasting forces, with orgasm happening in between ^[1]. The aim of this research is to review the role of medicinal plants in the management of erectile disorder in men and their mechanism of action. These could lead to discovery of novel chemical scaffolds for the synthesis of potent aphrodisiac agents.

Different factors could cause erectile dysfunction in men, such as damage to nerves, smooth muscles and fibrous tissues. It could also result from diseases, such as diabetes, kidney diseases, chronic alcoholic, muscle sclerosis, atherosclerosis, vascular disease and Neurologic disorders. These diseases are responsible for about 70% of erectile dysfunction in Men ^[1, 3], These factors could affect the sexual performance of individuals.

1.2 Factors Affecting Sexual Function

i. Psychological: Erectile Dysfunction can also be caused by psychological conditions and social problems such as stress, depression, and unhappy relationships. Erectile dysfunction may be caused by diseases that affect libido and the brain's perception of arousal, such as Alzheimer's, stroke, Parkinson, or brain trauma and injury to the spinal cord which may interrupt neural pathways to the sacral region, preventing or inhibiting the process of achieving erection ^[3, 4-6].

ii. Hormonal Abnormalities: Hormonal abnormalities such as low level of testosterone or androgen have been implicated in the modulation of erectile functions, and high level of prolactin which could cause hypogonadism and low blood testosterone concentration levels could lead to decrease in sex drive. Prolactin increases the production of breast milk and suppresses the secretion of Luteinising Hormone (LH) and Follicle Stimulating Hormone. The role of prolactin in men is not known. However, high level of prolactin in men may cause hypogonadism; low blood testosterone levels, decrease in sex drive (libido) and

sexual function [4, 7-9]. Any medicinal agents that could suppress the production of prolactin would enhance the production of Luteinising Hormone (LH) and Follicle Stimulating Hormone (FSH) and by extension increases testosterone concentration [3, 7-9].

- iii. **Aging:** As men age there is a natural decrease in testosterone production and this could contribute to erectile dysfunction by decreasing the sex drive [3]. Sexual dysfunction increases with age, men age between 40-70 years old could be affected by this disorder called erectile dysfunction. This could be due to alteration of nitric oxide (NO) synthesis or low level of testosterone. This could be one explanation for the increasing incidence of erectile dysfunction with aging men [10].
- iv. **Penile injury or disease:** Peyronie's diseases, priapism, anatomical defect could lead to poor sexual performance [5, 11].
- v. **Chronic diseases** such as diabetes mellitus, cardiovascular, hypertension, vascular disease, dyslipidemia, renal failure and hepatic disease could also affect erectile function. National Institutes of Health (NIH) reports that 35 to 50 percent of men with diabetes experiences erectile dysfunction [4, 10-12].
- vi. **Lifestyle:** Poor diet, relationship issues, cigarette smoking, alcohol abuse, lack of exercise and overweight could lead to poor sexual performance [11, 13, 14]. High levels of alcohol consumption could result in Zinc deficiency [14].
- vii. **Medication or drugs:** Medication may cause erectile dysfunction through similar pathophysiological mechanism. Medications are estimated to be responsible for approximately 10-25% of cases of erectile dysfunction [11, 15]. The use of many common medications such as blood pressure drugs, antihistamines, antidepressant, tranquillizer, appetite suppressant, chemotherapy, hormone replacement and antiulcer drugs such as cimetidine, could cause erectile dysfunction as a side effect [4, 11, 16-19].

viii. **Radiation:** It has been shown to reduce the number of penile nitric oxide synthase (NOS) containing nerves in rat, possibly providing an explanation for the development of erectile dysfunction due to post- pelvic irradiation in men, the side effects after radiation therapy significantly affects the quality of life of prostate cancer patients. Within 5 years of radiation therapy approximately 50 percent of patients could develop radiation induced erectile dysfunction. This could be due to neuronal damage; inflammation and neuronal nitric oxide synthase reduction resulting in erectile dysfunction [10, 19, 20].

1.3 Penis (Male Reproductive Organ)

The penis, male genital organ, has two functions; sexual and urination. It is located above the scrotum, linked to the pubic syphilis by ligaments as shown in Figure 1.0 [1, 21]. The penis is innervated by autonomic (sympathetic and parasympathetic) and somatic (Sensory and Motor). The sympathetic pathway originates from the 11th thoracic to the second lumbar spinal segments and passes through the white rami to sympathetic chain ganglia [21]. The blood supply to the penis comes from the terminal branches of the pudendal artery, which is a branch of the internal iliac artery with venous drainage following the same reverse route. Nerve supply is both Somatic (arising from root S₂-S₄) and Autonomic (sympathetic nerve root T₁₀-L₂ and Parasympathetic) which all contribute to the pelvis plexus [1]. The penis is composed of three bodies of erectile tissue running in parallel; the Corpus Spongiosum encompassing the urethra and terminating in the glands penis and the two Corpora Cavernosa (CC), which functions as blood filled capacitors, providing structure for the erect organ. The penile tissue, corpora cavernosa are highly specialized vascular structures that are morphologically adapted to their function of becoming engorged during arousal. There are three main arteries in the penis cavernosal, dorsal and bulbourethral. Novel findings revealed that pudendal arteries contribute about 70% of the total penile vascular resistance [22].

Fig 1.0: Male reproductive system

1.4 Physiology and mechanism of normal erector

Penile erection is a complex neurovascular event involving the interaction of the three physiological systems; the Central Nervous System, Peripheral Nervous System and Penile arterial and Trabecular smooth muscle [23]. Erectile function is a balance between two contrasting forces with orgasm happening in between, these are flaccidity or DE tumescence which is an active smooth muscle process with constriction of the arterial bed mainly a postsynaptic alpha sympathetic function but with contribution from other neurovascular factors including Angiotensin II, Prostaglandin EF_2 (PGF_2) and endothelins [21, 24].

Penile erection involves central and peripheral pathways. Erection is initiated after central processing and integration of tactile, visual, olfactory and imaginative stimulus upon sexual stimulation. Signals are generated to the peripheral tissues involved [22]. Stimulation of the parasympathetic and non-adrenergic, non-cholinergic nerves (NANC), promotes vascular and cavernosal relaxation, leading to an increase in blood flow and intracavernosal pressure resulting to penile erection. Also, stimulation of parasympathetic nervous system inhibits noradrenaline release and evokes acetylcholine release, which binding to muscarinic receptors in endothelial cells promotes endothelial nitric oxide synthase (eNOS), activation and consequently, production of nitric oxide (NO). Nitric oxide is formed from the amino acid precursor L-Arginine by enzymatic action of nitric oxide synthase (NOS), which exist in three main isoforms neuronal nitric oxide synthase (nNOS), inducible nitric oxide synthase (iNOS) and endothelial nitric oxide synthase (eNOS) are detected in penile tissue and these could increase the concentration of $3'5'$ -cyclic Guanosine Monophosphate (cGMP), which is released from the smooth muscle [22,129].

There are two main intracellular mechanism for relaxing the cavernosal smooth muscle granulate cyclase (cGMP) and Adenylate cyclase (cAMP) pathways. Nitric oxide upon its release diffuses locally into adjacent tissues [25]. Several central transmitters are involved in erectile control; dopamine, acetylcholine, nitric oxide, and peptides, such as oxytocin, adrenocorticotropin stimulating hormone have facilitatory role, where as serotonin may be either facilitatory or inhibitory. The balances between contracting and relaxant factors control the degree of contraction of the smooth muscle of corpora cavernosa and determine the functional state of the penis [25].

Relaxation of penile smooth muscle is necessary for erection, which allows blood to flow into the penile structures resulting in increase in cavernosal pressure. The relaxation of cavernous smooth muscle depends on the known neurotransmitter prostaglandin E_1 (PGE_1) and nitric oxide (NO). The smooth muscle relaxation during erection depends upon promoting of Ca^{2+} efflux from smooth muscle cells, as well as the sequestration of intracellular calcium in the sarcoplasmic reticulum. The relaxation of penile is mediated mainly by nitric oxide, which activates the enzyme granulate cyclase. This enzyme (granulate cyclase) increases the formation of cGMP as a second messenger and in turn promotes the efflux of Ca^{2+} ion, enabling the smooth muscle of corpora cavernosa to relax, resulting in erection. The cGMP is hydrolyzed to GMP by Phosphodiesterase 5 enzyme (PDE-5) [21, 23, 26]. The enzyme phosphodiesterase -5 degrades cGMP leading to penile smooth muscle contraction, DE tumescence, and inhibition of these enzymes enhance nitric

oxide and facilitate erections. It also increases the level of cAMP which is also an erotogenic [23,130].

DE tumescence enhance vascular drainage and this could result to decrease in the intracavernosal pressure. The flaccid state of penis is maintained by contraction of penile smooth muscle caused by intracellular accumulation of Ca^{2+} ion, affected by the stimulation of α_1 - adrenergic receptors by noradrenaline [27-30].

1.5 Pathophysiology of erectile dysfunction

Sexual dysfunction may occur due to loss of desire (libido), problems with ejaculation and failure of the testes to make normal amount of male sex hormones and this could be a very distressing condition for men. It can erode the male essence [31]. Failure of adequate venous supply or occlusion has been proposed as one of the most common causes of vasculogenic impotence. Venocclusive dysfunction may result from the following pathophysiological processes;

- The presence or development of large venous channels draining the corpora cavernosa.
- Degenerative changes or traumatic injury to the tunica albuginea (penile fracture) resulting to adequate compression of the subtunical and emissary vein.
- Brain and brain stem: Adrenocorticotrophic Hormone (ACTH), oxytocin may stimulate erection in animals, ACTH may act by inhibiting the effects of opioid and oxytocin as an excitatory neurotransmitter and is localized in pathways not only to the brains stem, but also the spinal autonomic centers [30], and on the other hand, the activating of α -amino butyric acid, α_2 - adrenergic, opiate, prolactin or neuropeptide, α - receptor, in these regions of the brain, appear to have anti-erectile function. Stimulation of parasympathetic nerves induces penile erection, while sympathetic nerves induce penile DE tumescence and terminate erection [29, 30].

1.6 Classification of conventional aphrodisiac agents

Aphrodisiac is derived from Aphrodite the Greek goddess of sex, love, sweetness and beauty. Aphrodisiac is defined as an agent (food/drug) that arouses sexual activity. From time immemorial man's endeavor has been to improve his sexual prowess because sexual relationships are the most important social and biological relationship in human life [12, 32]. Sexual health is a state of complete physical, mental and social wellbeing in all aspects related to the reproductive system. Compromised sexual abilities may lead to infertility. This may affect the personal and social life of the couples and also contribute to infertility [33]. Sexual feelings are innate part of life, sex is the most cherished, indispensable and integral part of every individual and it can be a cradle of pleasure and satisfaction. The goal of treatment is to ensure improvement in the quantity and quality of penile erection suitable for intercourse [32, 34-36].

Conventional aphrodisiac agents could be classified according to their mechanisms of action.

- Phosphodiesterase inhibitors e.g. Sildenafil, Tadalafil, Vardenafil and Papaverine as illustrated in Figure 2.0. Papaverine which is isolated from *Papaver somniferum* L. Papaveraceae [37]. Sildenafil is a drug of choice for the management of erectile dysfunction, but side effects with this drug are headache, flushing, dyspepsia, nasal congestion and priapism [38, 39, 124].

Fig 2.0: Chemical structures of some phosphodiesterase inhibitors

b. Adenylcyclase stimulant e.g. Alprostadil ^[11]

Fig 3.0: Chemical structure of Alprostadil

c. **Hormonal Replacement Therapy:** This involves the use of testosterone and its analogue to enhance the plasma concentration of testosterone which could potentiate the sexual activity in men ^[11].

Fig 4.0: Structural analogue of Testosterone

d. Others Trazodone, Yohimbine and Phentolamine, Dapoxetine and Lidocaine as illustrated in Figure 5.0. These drugs have limited efficacy ^[11, 38, 39].

Fig 5.0: Chemical structures of miscellaneous agents used as Aphrodisiac

2. Aphrodisiac agents used in traditional medicine

Biodiversities of plants can be a great source of drugs because the plant kingdom is a treasure house and source of potential new drugs, useful intermediates, leads for the synthesis of new medicinal agents ^[40, 41]. The use of local herbs has resulted in new breakthrough in the treatment or management of sexual dysfunction and has become recognized worldwide for immediate therapy. The use of plants for the treatment of erectile dysfunction is increasing every day; traditionally employed indigenous plants in folkloric medicine have been popular from time immemorial and have commanded increased attention worldwide due to their potential nutraceutical values ^[36, 41, 128]. There are various belief systems on the account of how man was created, these accounts of creation vary. Man's endeavor is to subdue in every aspect of life. The Inability of man to exercise this important biblical and social responsibility has led to the search for plants, food, minerals and animals that could enhance his sexual prowess, such substance are known as aphrodisiac ^[32, 39, 42, 43].

2.1 Mechanism of action of aphrodisiac agents used in traditional medicine

Aphrodisiac agents used in traditional medicine could act via the following mechanisms:

- Some aphrodisiac substances provide a burst of nutritional value improving the immediate health or wellbeing of the consumer and consequently improving sexual performance and libido. Such nutritional components are potassium, calcium, zinc, magnesium also play significant role in all the processes that promote penile erection ^[44-47].
- This group includes aphrodisiacs that have more specific physiological effects but are not centrally active. These agents affect blood flow, increase duration of sexual performance by numbing the genital area, due to reduction of the penile organ to stimuli; for example, Samsu oil, which contains Ginger rhizome, as a major

constituent, *Kaempferia parviflora*, Wall. Ex Baker (Zingiberaceae) *Beberis vulgaris* L. (Berberiaceae) ^[48, 49].

- Compounds that are psychoactive cross the blood brain barrier and stimulate some area of sexual arousal in the brain. Substances often used as aphrodisiac cross the blood brain barrier and mimic or stimulate some area of sexual arousal in the central nervous system ^[50]. These substances may also limit the influence of sympathetic nervous system in order to correct erectile dysfunction ^[50]. These categories include some hormones, pheromones and a wide range of neurotransmitters. Example of such plant is *Pausinystalia yohimbe* (K. Schum) W. Brandt, Rubiaceae ^[2, 51, 52].
- Increase in testicular, serum cholesterol and testosterone levels have been shown to be linked to the aphrodisiac activity of medicinal plants. This is sequel to cholesterol being a precursor for the production of several physiologically important steroids which include sex hormone, bile acid and vitamin D. Following the increase in cholesterol, testosterone concentration may increase via steroidogenesis which should normally reflect in a corresponding increase in libido ^[36, 53].

2.2 Medicinal plants with aphrodisiac properties

2.2.1 *Mucuna pruriens* (L) DC Leguminosae ^[54]

Fig 6.0: *Mucuna pruriens*

Mucuna pruriens (L) DC is a plant used as an aphrodisiac; it belongs to the family of Leguminosae which is the second largest flowering plant Figure 6.0. It improves male fertility and contains Levodopa which has been implicated in relieving the symptoms of Parkinson disease. The seeds are traditionally used as an aphrodisiac, nerve tonic, and for leucorrhoea. *Mucuna pruriens* is distributed throughout the world [55]. This medicinal plant enhanced male fertility by its action on the hypothalamus-pituitary axis. This medicinal

plant act by improving male serum testosterone, luteinizing hormone, dopamine, adrenaline and noradrenaline levels in infertile men and reduce the level of Follicle Stimulating Hormone (FSH) and prolactin Hormone (PRL). The seed contained 12.5 percent of L-dihydroxyphenylalanine, Gallic acid, ascorbic acid, glutathione could be responsible for the antioxidant properties and sit sterol may play an important role in prostate health as shown in Figure 7.0 [35, 56-60].

Fig 7.0: Chemical structures of compounds isolated from the seed of *Mucuna pruriens*

2.2.2 *Telfairia Occidentalis* Hook. F (Cucurbitaceae)

Fig 8.0: Photograph of *Telfairia occidentalis*

The seed of *Telfairia occidentalis* Hook. F (Cucurbitaceae) is cultivated widely across West Africa Figure 8.0. It is widely cultivated for its palatable and nutritious leaves. The oil from the seed increased the level of testosterone, luteinizing hormone, sperm count, motility and testicular weight compared to alcohol treated rats. The presence of arginine, Vitamin-C and Zinc play a crucial role in male reproductive parameter [61]. Pumpkin seeds besides having a pleasant flavour, are revered by the Chinese for its antidepressant properties. More importantly, pumpkin seed ingestion can improve prostate health in men, which is very important for male sexual health. It is commonly used to strengthen the prostate gland and promote healthy hormone function in men.

Myosin, an amino acid found in pumpkin seeds, is known to be essential for muscular contractions [62].

Fig 9.0: Chemical structure of arginine

2.2.3 *Tribulus terrestris* L Zygophyllaceae

Fig 10.0: *Tribulus terrestris*

Tribulus terrestris L. Zygophyllaceae is shown in Figure 10.0. It is a common weed that grows in many countries across the globe [64]. Its extract is used as dietary supplement in the belief that it increases testosterone levels mainly for body building [65]. *Tribulus* is reported to contain protodioscin a steroidal saponin found in a number of plant species as

shown in figure 11.0. It acts by the release of nitric oxide in corpus cavernosum tissue, and also produces statistically significant increase in the levels of hormone testosterone, dihydrotestosterone and dihydroepiandrosterone in animal studies. This event is related to nitric oxide and nitric oxide synthase pathway [66, 67].

Fig 11.0: Chemical structure of Protodioscin

2.2.4 *Fadogia Agretis*

Fig 12.0: Photograph of *Fadogia agretis* Schweinf. ex. Hiern

Fadogia agretis Schweinf. ex. Hiern, Rubiaceae; is a Nigerian Shrubby which is used traditionally as an analgesic, anti-inflammatory and pro-erectile agent. The methanol extract of *Fadogia agretis* stem increased the blood testosterone concentration and this may be the mechanism responsible for

its aphrodisiac effects and various masculine behaviours. It may be used to modify impaired sexual function in animals, especially those arising from hypotestosteromia [53,68,69,132]. Benzophenone glycoside has been isolated from the aqueous fraction of the root as illustrated in Figure 13.0 [71].

Benzophenone Glycoside

Fig 13.0: Chemical structure of Benzophenone glycoside ^[71].

2.2.5 *Securidaca longepedunculata* Fresen Polygalaceae

Fig 14.0: *Securidaca* Longepedunculata ^[72]

Securidaca longepedunculata Fresen belongs to the family of Polygalaceae as shown in Figure 14. It is a savannah shrub commonly used by traditional medicine practitioners in Nigeria and South Africa. It contains xanthenes as illustrated

in Figure 15.0, which stimulate the relaxation of corpus cavernosum smooth muscle. This validates the traditional use of its root bark as an aphrodisiac agent ^[69, 72-74].

1,3,6,8-tetrahydroxy-2,5-dimethoxyxanthone

1,6,8-trihydroxy-2,3,4,7-tetramethoxyxanthone

Fig 15.0: Chemical structures of xanthenes isolated from *Securidaca longepedunculata*

2.2.6 *Pausinystalia Yohimbe* (K Schum) W Brandt Rubiaceae

Fig 16: Photograph of *Pausinystalia yohimbe*

Pausinystalia Yohimbe (K. Schum) W. Brandt Rubiaceae is a West African medicinal plant used in the management of erectile dysfunction. Yohimbine alkaloid has been isolated from the bark of yohimbe plant ^[11,50]. Its aphrodisiac activity is due to central α_2 -adrenergic antagonistic effect, which increases catecholamines and improves mood. The α_2 receptor stimulation could be responsible for the erectile dysfunction side effect in patient taking α -methyldopa for the management of hypertension. It has been postulated that yohimbine may reduce peripheral α -adrenergic tone, thereby permitting a predominal cholinergic tone. This could result in vasodilating response. Yohimbine can cause many systemic adverse effects including anxiety, insomnia, tachycardia and hypertension ^[11].

Fig 17.0: Chemical structure of Yohimbine isolated from stem bark *Pausinystalia yohimbe*

2.2.7 *Allium sativum*

Fig 18.0: Photograph of *Allium Sativum*

Allium Sativum L (Garlic) Amaryllidaceae is a common household ingredient used for the preparation of pepper soup and many traditional recipes. It contains peptides, sulphated compounds, steroids, flavonoids, volatile oils with sulphated compounds like allicin, enzymes, mineral and vitamins. The alcoholic extract of *A. sativum* increased sexual activity or behaviour through the activity of sulphated compounds, steroids, peptides, flavonoids, phenolics, and allicin, dopamine. Allicin increases blood flow to sexual organs through nitric oxide synthase ^[43].

Fig 19.0: Chemical compounds isolated from *Allium sativum*

Fig 20.0: Photograph of *Citrullus lanatus*

Citrullus lanatus (Thunb) Matsum and Nakai is a plant in the family (Cucurbitaceae) commonly known as Watermelon figure 20.0, a vine-like flowering plant originally domesticated in West Africa. It is a highly cultivated fruit worldwide, having more than 1000 varieties. It contains bioactive agents such as citrulline and β -carotene as shown in Figure 21.0, which have been used in the management of prostate cancer. Its aphrodisiac effect is due to citrulline which improves blood drive to the genital regions and plays a significant role in the relaxation of blood vessel, a major tool in high sexual performance ^[43, 127].

Fig 21.0: Chemical structure of Coralline and β -Carotene

2.2.9 *Nigella sativa*

Fig 22.0: Photograph of *Nigella sativa* plant and Seed ^[75].

Nigella sativa L. (N.S) belongs to the family of Ranunculaceae also known as the black cumin in Indonesia Figure 22.0, it is reported to have pharmacological activities such as antihypertensive through the relaxant effect of the vascular smooth muscle. Methanol extract of *Nigella sativa* act by affecting the penile response directly through the relaxation of blood vessels in the corpus cavernosum [5,126,131]. The seed has been used as aphrodisiac in ethnomedicine. The major and active component is essential oil identified as thymoquinone, which has been revealed by pharmacological studies, to possess a potent antioxidant activity which could protect organs from oxidative damage by free radical generating agents. *Nigella sativa* when administered to rats

with hypercholesterolemia increased their reproductive performance and weight of seminal vesicle, level of testosterone, sperm motility and quality. Black seed contain alkaloids; nigellicimine, nigellincine and phenols which could stimulate the secretion of testosterone and FSH, the effects in testicular have been shown to increase sperm concentration [76,77]. It also contains vitamin B₁, B₂, B₃ and minerals; Iron, Calcium, Potassium, Zinc, Phosphorus and Copper these compounds could play important role in enhancing male reproductive function [75]. The following are the chemical constituents of black seed; thymohydroquinone, thymoquinone, thymol, nigillicimine, thymohydroquinone, thymoquinone, thymol, nigillicimine, dithymoquinone, nigellicine, taraxerol as shown in Figure 23.0.

Fig 23.0: Chemical structures of compounds isolated from *Nigella sativa*

2.2.10 *Berberis Vulgaris*

Berberine is a Benzodioxoloquinolizine alkaloid, a quaternary ammonium salt. It is extracted from rhizome *Coptidis* root stalk that acts as Chinese herb such as *phellodendron*, *Andradix*, *berberidis* and *Beberis vulgaris*. Berberine is usually found in the roots, stem bark and rhizomes figure 24.0. Berberine enhances endothelial nitric oxide synthase (eNOS), mRNA expression that induces relaxation of corpus cavernosum and also helps to improve erectile function by antioxidant effect [6].

Fig 24.0: Chemical structure of Beberine [6].

2.2.11 Purple Corn

Fig 25.0: Purple Corn (*Zea mays*) [79].

Purple Corn (*Zea mays*, L) aqueous crude extract elicits aphrodisiac activity at 25, 50, and 75 mg/kg. when administered to male rat, it elicit arousal and execution of sexual behaviour without significant influences on the ambulatory behavior. This shows that the aqueous purple corn possesses aphrodisiac activity [79]. The purple corn contains the following chemical constituents; kaempferol, quercetin, morin, naringenin and hesperitin, protocatechuic acid, vanillic acid, syringic acid, 2,4,6-trihydroxybenzoic acid as shown in Figure 26.0 [79].

S/N	Name	R ₁	R ₂	R ₃
1	Kaempferol	H	H	OH
2	Quercetin	H	OH	OH
3	Morin	OH	H	OH
4	Naringenin	H	H	OH
5	Hesperitin	H	OH	OCH ₃

Name	R ₁	R ₂	R ₃	R ₄
Protocatechuic acid	OH	H	H	H
Vanillic acid	OCH ₃	H	H	H
Syringic acid	OCH ₃	H	H	OCH ₃
2,4,6-Trihydroxybenzoic acid	H	OH	OH	H

Fig 26.0: Chemical compounds isolated from purple corn

2.12 *Uvaria Chamae*

Fig 27.0: Photograph of *Uvaria chamae*

Uvaria Chamae (P Beauv) belongs to the family of Annonaceae figure 27.0. It is commonly known as fingers root or bush banana. The Ibibios of Akwa-Ibom call it Nkarika Ikot and the Annangs called Nkarika Ekpo, Igbo, Mmimiohia, Yoruba, Okoroja. It is distributed in savannah and Secondary forest from tropical African i.e. from Senegal to Central African Republic. It is a climbing large shrub or small tree native to West and Central African where it grows in wet and dry forest. The root is employed in the management of erectile dysfunction by the Ibibios of Akwa-

Ibom state, according to Nwafor, (2019), the root of *Uvaria chamae* P. Beauv exhibited excellent sexual indices. This is apparent in causing increase in mount frequency, intromission frequency, erection frequency and penile erection while causing decreases in mount latency, intromission and post ejaculatory intromission. This showed that the extract and its fractions possess the potential for sexual libido and potency [12,80]. The chemical constituents of *Uvaria Chamae* include; pinostrobin, uvaretin, nantenine, chamanetin, nornantine and corydine as shown in Figure 28.0 [80].

Fig 28.0: Chemical structures of compounds isolated from *Uvaria chamae* [80]

2.2.13 *Hibiscus Sabdariffa*

Fig 29.0: Photograph of *Hibiscus sabdariffa*

Hibiscus sabdariffa L (Hs) belongs to the family of Malvaceae. It is locally called Zobo or Roselle, Fig 29.0. Its aphrodisiac properties are based on the fact that it decreases the viscosity of the blood and stimulates internal peristalsis. Its aphrodisiac action could be ascribed to the presence of

carotenoid, vitamins, flavonoids, minerals and amino acids such as cyanidin, gallic acid, hibiscic acid, citric acid, kaempferol, quercetin-3-rutinoside and catching figure 30.0 [43, 81, 82].

Fig 30.0: Chemical structures of compounds isolated from *Hibiscus sabdariffa* [43]

2.2.14 *Musa paradisiacal* and *Musa sapientum*

Bananas are excellent source of potassium which helps in maintaining the proper function of muscles, helps to maintain blood pressure of an individual, prevents muscle spasm and reduces the risk of stroke [83]. Single banana provides about 23% of the potassium needed on daily basis [84, 85].

Bananas are excellent source of vitamins. Vitamin A aids in health of teeth, bones, and soft tissue, B₆ aids in body immune system, promotes brain and heart health. Banana contains 41% of what is needed in each day in terms of vitamin B₆. Eating banana each day helps to increase one's focus and mental activity. It also aids vitality which means it enhance the release of more energy both mentally and physically. Its aphrodisiac could be due to tryptophan.

Figure 31.0, which is bio-activated to serotonin known to make one relax, improve mood and make one feel happier [84,85]. Banana is rich in fructose and sucrose. It replenishes energy and revitalizes the body instantly [85]. It also contains zinc which plays important role in enzymes metabolism and helps the male body to produce testosterone because of its deficiency affect sexual activity [47].

Tryptophan

Fig 31.0: Chemical structure of tryptophan

2.2.15 *Eriosema Kraussianum* Fig 32.0: Photograph of *Eriosema Kraussianum*

Eriosema kraussianum, Meissnar (Leguminosae), and other *Eriosema* species are shown in Figure 32.0. The Zulu traditional practitioners have claimed that it is effective for the treatment of erectile dysfunction and impotence. Five Pyranoisoflavone, Kraussianone (1-5) as shown in Figure

33.0, have been isolated from the root stock of *Eriosema kraussianum* and were screened for smooth muscle relaxation of rabbit penile muscle. The most active of the compounds had an activity of 75% of that found in Sildenafil (Viagra), thus living up to the plants traditional use [69, 86, 87, 125].

Fig 33.0: Chemical structures of pyranoisoflavones [86].

2.2.16 *Anthocleista Djalensis* A. Chev Loganiaceae

Fig 34.0: Photograph of *Anthocleista Djalensis*

Anthocleista Djalensis plant with several medicinal properties, is a tall tree often armed with rigid spines, native to tropical West Africa Figure 34.0. The leaves, roots and stem bark are used in folkloric medicine to treat different disease conditions which include male infertility [88]. The result of the study evaluated by Okeke *et al.*, (2019), revealed that the methanol root extract of *Anthocleista djalensis* possessed fertility enhancing effect through improved sperm quantity, quality, and increased serum testosterone level. Study had shown that it has antioxidants effects, which

improve various processes of male reproductive function such as spermatogenesis and steroidogenesis. The presence of antioxidant phytochemicals in *A. djalensis* root extract and its high antioxidant properties indicate that it could possess the capacity to scavenge excess reactive oxygen species (ROS) in spermatozoa responsible for oxidative damage of sperm cells. The study lends credence to the use of the roots of the plant as a male fertility enhancer in ethnomedicine [88]. The following compounds are presence in the root bark of *A. djalensis* as shown in figure 35.0.

Fig 35.0: Chemical structures of compounds isolated from *Anthocleista Djalensis*

2.17 *Paullinia Pinnata*

Fig 36.0: Photograph of *Paullinia pinnata* [47]

Paullinia pinnata, L, belongs to the family of Sapindaceae. It is a West African medicinal plant which has been used for the management of erectile dysfunction, malaria, wound healing and dysentery. It is a woody creeper or climber with rigid stems. The leaves are pinnate with five leaflets, the terminal leaflet being the largest as shown in Figure 36.0 [47, 84, 90]. Elemental analysis of the root revealed the presence of four elements: calcium, magnesium, potassium and zinc which were significantly high. These elements have been shown to play an important role in the physiology of functional sexual activity. This also proves the use of the plant as medicinal agents for the management of erectile dysfunction [47]. The followings are chemical compounds isolated from the root of *Paullinia pinnata*, Figure 37.0.

Fig 37.0: Chemical structures of compounds isolated from *Paullinia pinnata*

2.2.18 Ginseng

Fig 38.0: Photograph of Ginseng

Ginseng is often referred to as the king of all herbs, and is said to improve the general well-being. It has been reputed as

an aphrodisiac and used for treatment of sexual dysfunction as well as to enhance sexual behaviour in traditional medicine. There are nine species of ginseng which are named by their geographical distribution e.g. Asian ginseng (*Panax ginseng*, Bail) as shown in Figure 38.0, American ginseng (*Panax quinquefolium* L), Japanese ginseng (*Panax japonicas* T. Nees), family Araliaceae, it is used to enhance sexual performance and satisfaction. Data from studies on ginseng berry extract suggest its action is nitric oxide dependent. The pharmacological component of ginseng, ginsenosides are known to induce nitric oxide synthesis in endothelial cells and perivascular nerves and to augment vascular smooth muscles cells sensitivity to nitric oxide. The release of nitric oxide causes muscle to relax, thus allowing more blood to enter the erectile bodies known as corpus cavernosum, and results in erection. Rg1 has been found for nitric oxide production in endothelial cells by glucocorticoid receptor (GR), dependent, non genomic mechanisms.

Ginsenoside Rg1 (10 mg/Kg): rats fed with 5.0% of *P. ginseng* in their diet for 60 days, have shown significant increase in blood testosterone levels, whereas 1.0% *P. ginseng* had no effect. Ginsenoside (Rg1) also led to improvement of copulatory behaviour observed and Ginsenoside Rb1 is a key ginsenoside found to increase the secretion of LH by acting directly on the anterior pituitary gland [91]. Several neurotransmitters have been implicated in

libido such as dopamine for desire, acetylcholine for arousal and gaba aminobutyric acid(GABA) for orgasm. Ginsenoside Re has been shown to increase extracellular dopamine and

acetylcholine levels in rat brain ^[91]. The compounds shown in Figure 39.0, could enhance male sexual behavior.

Fig 39: Chemical structures of compounds isolated from Ginseng

2.2.19 *Ginkgo biloba*

Fig 40.0: Photograph of *Ginkgo biloba*

Ginkgo biloba is a tree native to China, fossils record of the tree dates back 270 million years Figure 40.0 [92]. It has been used medicinally since the time of early man. Active compound in ginkgo extract possesses antioxidant, improves blood circulation, discourages clot formation, reinforces the walls capillaries and protects the nerve cells from harm when deprived of oxygen. Due to its notable pharmacological effect, it is used for treatment of Alzheimer disease,

concentration difficulties, memory impairment, cerebral insufficiency, intermittent claudication, vertigo and tinnitus. It also increases dopamine, adrenaline and acts by relaxing the blood vessels. When the blood vessels are relaxed and calm, more blood can circulate throughout the body and also help desire for sex to come quickly [93, 94]. The followings are some of the chemical constituent of *Ginkgo biloba* as shown in Figure 41.0.

Fig 41.0: Chemical structures of compounds isolated from *Ginkgo biloba* [94].

2.2.21 *Citropsis Articulata*

Citropsis articulata (Wild.Spreng.) Swingle & M. Kellerm. It belongs to the family of Rutaceae. It is commonly known as African Cherry Orange and West African Cherry Orange. The

root and bark chewed and swallowed or taken orally as beverage in tea increased the level of serum testosterone [95,96]. It contains Rutarin, Trigonelline, Seselin, Suberosin, Omubioside as shown in figure 42.0.

Fig 42.0: Chemical structures of compounds isolated from *Citropsis Articulata*

2.2.22 *Withania Somnifera*

Withania somnifera (L.) Dunn, Solanaceae, known as Indian ginseng is commonly used in Ayurvedic medicine. It is best regarded as adaptogenic tonic with aphrodisiac properties. It has the ability to combat stress induced infertility. The aqueous extract improved spermatogenesis, which may increase interstitial cell stimulating hormone and testosterone

like effect as well as induction of nitric oxide. The powdered root when given at 5g/day for 3 months inhibited lipid peroxidation, protein carbonyl content and improved sperm count and motility [97-100]. The root decoction is taken orally at a dose of one to two tablespoonful daily. It improved overall semen quality. The compounds shown in Figure 43.0, have been isolated from *Withania somnifera* [101-103].

Fig 43.0: Chemical structures of compounds isolated from *Withania somnifera*

2.2.23 *Kaempferia parviflora*

Fig 44: Photograph of *Kaempferia parviflora*

Kaempferia parviflora, Wall. ex Baker, belongs to the family of Zingiberaceae, it is also known as black ginger, and is found mainly in China, and north Thailand figure 44.0 The rhizome extract has an inhibitory activity against PDE-5. It relaxes the human cavernosum *in vitro* by voltage dependent

Ca^{2+} channel through the action of 3,5,7, 3',4'-pentoxyflavone and 5,7-dimethoxyflavone Figure 45.0 [6, 104, 105]. The presence of methoxy group at position 5 and 7 plays a crucial role in PDE-5 inhibition and methoxylation at position 4'- shows no benefit for PDE-5 inhibition [48, 49].

Fig 45.0: Chemical Structures of 5,7-dimethoxyflavone(a) and 3,5,7,3',4'-Pentamethoxyflavone(b)

2.2.24 *Smilax Kraussiana* Fig 46.0: Photograph of *Smilax Kraussiana*

Smilax kraussiana Meisn belongs to the family of Smilacaceae Figure 46.0. The Ibibios of Akwa-Ibom State Nigeria called it Odufat Ekpo, the common name is catbrier or greenbrier. It is a climbing shrub with prickly shoots, leaves are alternate, ovate-elliptical and is native to South Africa, used in folkloric medicine in the management of gout in Latin American countries and also to treat infertility in eastern Tanzanian tribe of South Africa and used for the management of inflammation among the Ibibio's. The root is employed in solving sexual dysfunction among the Ikono indigenes of Akwa-Ibom State ^[13]. The extract when investigated on sexual behaviour of adult albino rats showed the extract ability to decrease mount latency, intromission latency, and post ejaculation intromission. On the other hand the extract significantly increased ejaculation latency, mount latency and penile erection and the extract also exhibited antioxidant effect against DPPH. These corroborates with the use of extract in folkloric medicine ^[106].

2.2.25 *Terminalia Cattappa* Fig 47: Photograph of *Terminalia cattappa*

Terminalia Cattappa L Combretaceae: the seeds are used in ethnomedicine for the treatment of erectile dysfunction Figure 47.0. The kernel of *T. catappa* has aphrodisiac potential and maybe useful in the treatment of certain forms of sexual inadequacies, such as premature ejaculation, reduced libido and impotence. The dose of 1500 mg/kg/dose had a marked aphrodisiac action (prolongation of ejaculation latency) but no effect on libido (% mounting, % intromission, and % ejaculation). On the other hand, at high dose of 3000 mg/kg, it reversibly inhibited all parameters of sexual behaviour other than mounting and intromission frequency and corpulatory efficiency. This could be due to marked sedation. The following compounds have been isolated from the seed of *Terminalia cattappa* as shown in Figure 48.0 ^[107].

Fig 48.0: Chemical structures of compounds isolated from *Terminalia cattappa*

2.26 Rauwolfia Vomitoria

Fig 49.0: Photograph of *Rauwolfia vomitoria*

Rauwolfia vomitoria Afzel (Apocynaceae), its common name is serpent root as illustrated in Figure 47.0. The root of *R. vomitoria* is known for its antihypertensive, psychoactive properties and aphrodisiac potentials. The extract and fractions of dichloromethane, ethylacetate, butanol, and aqueous fractions showed significant effect by decreasing mount latency, intromission latency, mount frequency, post ejaculation interval and increasing ejaculation latency,

erection frequency, mount frequency and penile erection. These effects were statistically significant. These findings authenticate the use of the root of *R. vomitoria* as aphrodisiac agent in ethno medicine [96, 108-110]. The root bark of *R. vomitoria* contained the following constituents; Yohimbine 17.0, Rescinamine, Aricine, Stigmasterol shown in Figure 50.0 etc.

Source: Ajao *et al.*, (2018)

Fig 50.0: Chemical structures of compounds isolated from *Rauwolfia vomitoria*.

2.2.26 *Camelia Sinensis*

Fig 51.0: Photograph of *Camelia Sinensis*

Camellia sinensis (L.) O Kuntze it belongs to the family of Theaceae Figure 51.0. The leaves and the buds when extracted with aqueous solution, increase the sexual activity in male. This could be due to increase in blood testosterone concentration. It acts by prolongation of latency of ejaculation, shortening of mount and intromission latency and elevation of plasma testosterone level. The aphrodisiac action had a rapid onset of action and appears to be mediated via

inhibition of anxiety and elevation of serum testosterone. *Camellia sinensis* can be used as quick acting, safe, oral aphrodisiac which may be useful in premature ejaculation and impaired libido ^[111, 112].

The chemical constituents of *Camellia sinensis* include Caffeine, Theobromine, Gallic acid, Epicatechin-3-O-gallate are shown in Figure 52.0 ^[113].

Caffeine

Gallic acid acid

Epicatechin-3-O- gallate

Source: Zhu *et al.* (2013)

Fig 52.0: Chemical structures of compounds isolated from *Camelia Sinensis*

3. Discussion

The use of natural products with therapeutic properties is as ancient as human civilization and for a long time plant and animal products were the main source of drugs ^[40]. Natural products such as plant extracts either as pure compounds or as standardized extract provide unlimited opportunities for new drug discovery because of the unmatched availability of chemical diversity ^[114]. Plants used in traditional medicine contain a wide range of substances that can be used to treat chronic as well as infectious diseases ^[115]. According to the World Health Organization reports in 2010, 80% of the

inhabitants of the world rely mainly on traditional medicine for their primary health care need and it may be presumed that a major part of traditional health care involves the use of plant extracts or their active principles.

The plant kingdom is a treasure house of potential drugs, about 25% of the drugs prescribed worldwide come from plants, 121 of such compounds are in current use. About 252 drugs considered as basic and essential by the World Health Organization ^[116] about 11% are exclusively of plant origin and significant numbers are synthetic drugs obtained from natural precursors. Examples of important drugs obtained

from plants are digoxin from *Digitalis* spp., Quinine and Quinidine from *Cinchona officianalis*, L. Rubiaceae, Vincristine and Vinblastine from the *Catharanthus roseus*, (L) G.Don Apocynaceae, Atropine from *Atropa belladonna*, L. Solanaceae and Morphine, Codeine and Papaverine from *Papaver Somniferum* [40]. It is estimated that 60% of antitumor and anti-infective drugs that are already in the market or under clinical trial are of natural origin [40, 117, 118-121].

Several medicinal plants have been reported to possess aphrodisiac properties. The presence of diverse compounds such as polyphenolics, steroids, xanthenes and alkaloids play important role in biological activities of medicinal plants. These compounds could affect various biochemical or physiological processes by inhibition of an enzyme to enhance or decrease the concentration of a neurotransmitter. Pentoxifyllone, 5,7-dimethoxyflavone and papaverine isolated from *Kaempferia parviflora* and *Papaver somniferum* respectively, play a crucial role to inhibit PDE-5 causing elevation of cGMP level which is responsible for their aphrodisiac effect. Pyranisoflavone I and II, Xanthone; 1,3,6,8-tetrahydroxy-2,5-dimethoxyxanthone and 1,6,8-Trihydroxy-2,3,4,7-tetramethoxyxanthone and citrulline obtained from plants derived from *Eriosema krausianium*, *Securidaca longepedunculata* and *Citrallus lanatus* respectively, act by relaxation of corpus cavernosum smooth muscle leading to in flow of blood to genital organs [47,69,72,73]. Medicinal plants could increase blood flow to sex organs via the increase of the biological activity of nitric oxide synthase or which enhances the stimulation of LH by acting on the anterior pituitary gland example of such agents is Allicin and Rg1 found in *Allium sativum* and ginseng respectively [47,91,122]. Aphrodisiac medicinal plants could also act by the release of minerals and vitamins that are needed for optimal reproductive functions [47, 75, 89, 90].

Free radicals are the inevitable by-products of biological redox reactions. The reaction between reactive oxygen species and bio-molecules generally leads to impairment or loss of biological function. Therefore, there is much pathology in which free radicals and other forms of oxidising species play an important role. It is well known that the structure and function of proteins exposed to free radicals are altered and, depending on the free radical involved, the nature of the protein and the conditions of interaction, protein molecules can undergo scission and cross-linking, increase in susceptibility to proteolysis, and heat denaturation. Lipid peroxidation has potential importance in relation to the oxidative damage that occurs during cardiovascular diseases, such as pre-eclampsia, atherosclerosis, aging and ischaemia-reperfusion injury, and in addition, the end products of this process can cause damage to proteins and DNA [123]. Flavonoids and quinones have received the most attention as phenolic antioxidant derivatives and much is known about the structural requirements for antioxidant activity. Therefore, so many other phenolic compounds such as xanthone have been shown to act as scavengers of various oxidizing species; superoxide anion (O_2^-), hydroxy and peroxy-radicals [123].

4. Conclusion

Aphrodisiac medicinal plants used in folkloric medicine could be a source of new medicinal scaffold for the management of erectile dysfunction in men. This activity could be due to presence of polyphenols, xanthenes, steroids and alkaloid which could be responsible for the aphrodisiac effect. Natural products particularly aphrodisiac medicinal plants remain an important source of new drugs, new drug leads and discovery

of new therapeutic properties not yet attributed to known compounds.

5. References

1. Mutambirwa S and Segone A. The Physiology of erection and its relationship to the management of erectile dysfunction, CME. 2013;31(5):1-2.
2. Singh R, Ali A, Gupta G, Semwal A and Jeyabalan G. Some medicinal plants with aphrodisiac potentials: A current status, Journal of acute disease., 2013, 179-188.
3. Lasker GF, Maley JH and Kadowitz PJ. A review of the pathophysiology and novel treatments for erectile dysfunction, Advances in Pharmacological Science, 2010, 1-10.
4. Singh R, Ali A, Jeyabalan G and Semwal AJ. An overview of the current methodologies used for evaluation of aphrodisiac agents, Journal of acute disease, 2013, 85-91.
5. Singh R, Gupta AK and Kakar K. Traditional medicinal as scientifically proven aphrodisiacs, International Journal of Health and Biological Sciences. 1(1):29-36.
6. Goel B and Maurya NK. Aphrodisiac herbal therapy for erectile dysfunction Archives of Pharmacy Practice. 2020;11(1):1.
7. Pardridge WM. Serum bioavailability of sex steroid hormones, Clinical Endocrinology Metabolism, 1986;5:259-278.
8. Morales A. Androgen supplementation in practice: The treatment of erectile dysfunction associated with hypotestosteronemia. In: Oddens BJ, Vermeulen A, (Editors), Androgen and aging male London: Parthenon Publishing Group 1996; 233-245p.
9. Aversa A and Fabbri A. New oral agents for erectile dysfunction: what is changing in our practice? Asian Journal of Andrology. 2001; 3:175-179.
10. Sullivan ME, Thompson CS, Dashwood MR, Khan MA, Jeremy JY, Morgan RJ and Mikhailidis DP. Nitric oxide and penile erection. Is erectile dysfunction another manifestation of vascular disease? Cardiovascular Research 1999;43(3):658-665.
11. Lee M. Erectile dysfunctions. In: Pharmacotherapy: A Pathophysiologic Approach, 6th Edition, Dipiro JT, Talbert RL, Yee CG, Matzke GR, Wells BG and Posey LM (editors). Mcgraw-Hill Companies Inc, New York, 2005, 1515-1533.
12. Nwafor PA. My interswitch from fertility regulating plants contraceptives to aphrodisiacs. 69th Inaugural Lecture of the University of Uyo, Uyo, The University of Uyo Press Ltd, Uyo, Nigeria, 2019, 1-138.
13. Schlichthorst M, Sanci LA and Hockings JS. Health and lifestyle factors associated with sexual difficulties in men - results from a study of Australian men aged 18 to 55 years, BMC Public Health. 2016;16:1043.
14. Shalmy AV, Shalnaya MG, Grabeklis AR, Shanaya AA and Tinkov AA. Zinc deficiency as a mediator of toxic effects of alcohol abuse, European Journal of Nutrition. 2018;57(7):2313-2322.
15. Keene LC and Davies P. Drug-related erectile dysfunction. Adverse drug reaction, Toxicol Review, 1999;18:5-24.
16. Clayton AH, Pradko JF, Croft HA, Montano CD, Leadbetter RA, Bolden-Watson C *et al.* Prevalence of sexual dysfunction among newer antidepressants, Journal of Clinical Psychiatry. 2002;63(4):357-366.

17. Olaniyi AA. Essential Medicinal Chemistry, 3rd Edition, Hope Publisher, Ibadan, Nigeria., 2005, 353-355.
18. Gamaniel KS. Antipsychotic drugs. In: Akubue, I (Editor), Textbook of Pharmacology, Africana First Publishers Limited, Onitsha, Nigeria, 2005, 362-385.
19. Vozenesensky M, Annam K and Kreder KJ. Understanding and managing erectile dysfunction in patients treated for cancer, American Society of Clinical Oncology. 2016;12(4):297-304.
20. Mahmood J, Shamah AA, Creed TM, Pavlovic R, Matsuri H, Kimura M *et al.* Radiation- Induced erectile dysfunction: Recent advances and future directions, Advances in Radiation Oncology. 2016;1:161-169.
21. International Journal of Impotence Research. Anatomy and physiology of erection: Pathophysiology of erectile dysfunction, Nature publishing Group. 2003;15(7):S5-S8.
22. Nunes KP and Webb RC. Mechanism in erectile function and dysfunction: In: Nunes KP (Editor.) An overview erectile dysfunction-disease associated mechanism and novel insights into therapy. Intech Shanghai, China, 2012, 1-214.
23. Wagner G and Mulhall J. Pathophysiology and diagnosis of male erectile dysfunction BJU International. 2001;88(suppl. 3):3-10.
24. Anderson KE and Michel MC. Mechanism of penile erection and basis for pharmacological treatment of erectile dysfunction Pharmacological Reviews, 2011;63(4):811-859.
25. Mullhall JP, Daller M and Traush AM. Intracavernosal forskolin: Role in management of vasculogenic impotence resistant to standard 3-agent pharmacotherapy, Journal of Urology. 1997;158(5):1752-1758.
26. Burnett AL. Role of nitric oxide in the physiology of erection, Biology of Reproduction. 1999;52:485-489.
27. Hedlund H and Anderson KE. Effects of some peptides on isolated human penile erectile tissue and cavernous artery, Acta Physiologica of Scandinavica. 1985;124:413.
28. Saenz, D-T.I, Kim, N, Lagan, I, Krane, R. J, Goldstein, I. Modulation of Adrenergic activity in penile corpus cavernosum. Journal of Urology 1989; 142; 1117-1121.
29. Naylor AM. Endogenous neurotransmitters mediating penile erection, British Journal of Urology. 1998;81(3):426-431.
30. Chuang AT and Steers WD. Neurophysiology of penile erection. In: Carson CC, Kirby RS, Goldstein I, (Editors). Textbook of Erectile Dysfunction. Oxford, Isis Medical Media, 1999, 51-57.
31. Essien GE, Effiong GS and Nwafor PA. Evaluation of aphrodisiac potential of methanol extract of Garcinal kola seed in male rodents, European Journal of pharmaceutical and medical research. 2017;4(8):60-65.
32. Singh R, Singh S, Jayabalan G and Ali A. An overview on traditional medicinal plants as aphrodisiac agents, Journal of Pharmacognosy and Phytochemistry. 2012;1(4):43-56.
33. Sharma P, Bhardwaj P, Arift T, Khan I and Singh R. Pharmacology, phytochemistry and safety of aphrodisiac medicinal plants, A review. Research and Review Journal of Pharmacology and Toxicological Studies. 2014;2(3):1-18.
34. Abudayyak M, Nath EO and Ozhan G. Toxic potentials of ten herbs commonly used for aphrodisiac effect in Turkey, Turkish Journal of Medical Science. 2014;45:496-506.
35. Biswas TK, Pandit S and Jana U. In search of spermatogenetic and virility potential drugs of Ayurvedic leads: A review Andrology. 2015;4(2):1-4.
36. Erhabor OJ and Idu M. Aphrodisiac potentials of the ethanol extract of Aloe barbadensis Mill root in male wistar rats, BMC Complimentary and Alternative Medicine. 2017;17:360.
37. Porst H, Padma-Nathan H, Giuliano F, Anglin G, Varanese L and Rosen R. Efficacy of Tadalafil for the treatment of erectile dysfunction at 24 and 36 hours after dosing: A randomized, controlled trial Urology. 2003;62:121-125.
38. Lue TF. Erectile dysfunction, English Journal of Medicine. 2000;342:1802-1813
39. Singh B, Gupta V, Bansal P, Singh R and Kumar D. Pharmacological potential of plants used as aphrodisiacs, International Journal of Pharmaceutical Sciences Review and Research. 2010;5(1):104-113.
40. Rates SMK. Plants as source of drugs Toxicon, 2001;39:603-613.
41. Lakshmi SM, Nagasree BY, Sreelekha K, Madhavi N and Reddy CS. Aphrodisiac agents from medicinal plants: An Ethno-Pharmacological and phytochemical review, Journal of Pharmacy Research. 2012;5(2):845-848.
42. Ojewole JAO. African traditional medicines for erectile dysfunction, elusive dream or imminent reality, Cardiovascular Journal of Africa. 2007;18(4):213-215.
43. Enema OJ, Umoh UF, Umoh RA, Ekpo EG, Adesina SK and Eseyin OA. Chemistry and Pharmacology of aphrodisiac plants, A review. Journal of Chemical and Pharmaceutical Research. 2018;10(7):70-98.
44. Jeon YH, and Al E. Phosphodiesterase - Overview of protein structures, potential, therapeutic applications and recent progress in drug development Cell Molecular Life Science 2005;62(1):198-220.
45. Ghofrani HA, Osterloh IH and Grimminger F. Sildenafil: from angina to erectile dysfunction, pulmonary hypertension and beyond nature review drug discovery. 2006;5(8):689-702.
46. Androgue HJ and Madias NE. Sodium and potassium in the pathogenesis of hypertension, New England Journal of Medicine. 2007;356:1966-1978.
47. Samuel FM, Tetteh G, Daniel H, Gyorgy D, Kwadwo NA, Daniel B and Mohamed A. Bioinorganic elemental content of the Ghanian, aphrodisiac medicinal plant, Paullinia pinnata Linn (Sapindaceae), African Journal of Pharmacy and Pharmacology, 2016;10(11):206-211.
48. Chen D, Li H, Li W, Feng S and Deng D. Kaempferia parviflora and its methoxyflavones: Chemistry and biological activities evidenced based complementary and alternative medicine, 2018, 1-15.
49. Pitakpawasutthi Y, Palanuvej C and Ruangrunsi N. Quality evaluation of Kaempferia parviflora rhizome with reference to 5,7-dimethoxyflavone, Journal of Advanced Pharmaceutical Technology and Research. 2018;9(1):26-31.
50. Gundidza GM, Mmbengwa VM, Magwa ML, Ramalivhana NJ, Mukwevho NT, Ndaradzi W and Samie A. Aphrodisiac properties of Zimbabwean medicinal plants formulations, African Journal of Biotechnology. 2009;8(22):6402-6407.
51. Patel DK, Kumar R, Parasad SK and Hemlata S. Pharmacologically Screened aphrodisiac plant-A review of current scientific literature, Asian Pacific Journal of Tropical Biomedicine., 2011, 131-138.

52. Semwal A, Kumar R and Singh R. Nature's aphrodisiac- A review of current scientific literature, International Journal of Recent Advances in Pharmaceutical Research. 2013;3(2):1-20.
53. Yakubu MT and Ogunro O. Effect of Fadogia agretis stem in alloxan-induced diabetic rats, Bangladesh Journal of Pharmacology. 2014;9:356-363.
54. Odugbemi T and Akinnsulire O. Medicinal plants pictures. In: Odugbemi, T (editor) Outlines and Pictures of Medicinal Plants from Nigeria University of Lagos Press, Nigeria, 2006, 163-255.
55. Natarajan K, Narayanan N, Ravichandran N. Review on Mucuna – The wonder plant, International Journal of pharmaceutical science review research. 2012;17:86-93.
56. Shukla KK, Mahdi AA, Ahmad MK, Jaiswar SP and Shankwar SN. Mucunapuriens reduces stress and improves the quality of semen in infertile men, Evidence Based Complementary and Alternative Medicine. 2007;7:137-144.
57. Shukla KK, Mahdi AA, Ahmad MK, Shankwar SN and Rajender S. Mucuna pruriens improves male fertility by its action on the hypothalamus pituitary gonadal axis, Fertilisation and Sterilization. 2009;92:1934-1940.
58. Kasture S, Pontis S, Pinna A, Schintu N and Spina L. Assessment of symptomatic and neuroprotective efficacy of Mucuna pruriens seed extract in rodent model of Parkinson's disease Neurotoxicology research. 2009;15:111-122.
59. Lampariello LR, Cortelazzo A, Guerranti R, Sticozzi C, and Valacchi G. The Magic Velvet Bean of Mucuna pruriens, Journal of Traditional and Complementary Medicine. 2012;2(4):331-339.
60. Yadav MK, Upadhyay P, Purohit S, Pandey BL and Shah H. Phytochemistry and pharmacological activity of Mucuna pruriens: A review, International Journal of Green Pharmacy. 2017;11(2):69-73.
61. Eseyin OA, Sattar MA and Rathore HA. A review of the pharmacological and biological activities of the aerial parts of Telfaria occidentalis Hook F (Cucurbitaceae), Tropical Journal of Pharmaceutical Research. 2014;13(10):1761-1769.
62. Lim PHC. Asians herbals and aphrodisiacs used for managing erectile dysfunction Translational Andrology and Urology 2017;6(2):167-175.
63. Rath M, Muller I, Kropf P, Closs EI and Munder M. Metabolism via arginase or nitric oxide synthase: Two competing arginine pathways in macrophages, Frontier in Immunology and Inflammation, 2014. doi.org/10.3389/fimmu.2004.00532.
64. Semerdjieva IB and Zheljazkov VD. Chemical constituents, biological properties, and uses of Tribulus terrestris: A review Natural Product Communications, 2019, 1-26.
65. Pokrywka A, Obmęski Z, Malczewska-Lenczowska J, Fijałek Z, Turek-lepa E and Grucza R. Insight into Supplements with Tribulus terrestris used by athletes, Journal of Human Kinetics. 2014;4(1):99-105.
66. Do J, Choi S, Choi J and Hyun JS. Effects and mechanism of action of a Tribulus terrestris extract on penile erection, Korean Journal of Urology. 2013;54(3):183-188.
67. Nimrouzi M, Jalat A, Zarshenas MM. A panoramic view of medicinal plants traditionally applied for impotence and erectile dysfunction in Persian medicine, Journal of Traditional and Complementary Medicine. 2018;10(1):7-12.
68. Yakubu MT, Akanji MA and Oladeji AT. Aphrodisiac potentials of the aqueous extract of Fadogia agretis (Schweinf. Ex. Hiern) stem in male albino rats, Asian Journal of Andrology. 2005;7(4):399-404.
69. Malviya N, Jain S, Gupta BV and Vyas S. Recent studies on aphrodisiac herbs for the management of male sexual dysfunction - A review drug research. 2011;8(1):3-8.
70. Avula B, Bae J, Raman V, Fantoukh OI, Wang Y, Osman AG *et al.* Quantification of phenolic compound from Fadogia agretis and dietary supplement using UHPLC-PDA-MS, Planta Medica. 2019;85(02):145-153.
71. Osman GAM, Ali Z, Fantoukh O, Raman V, Kamdem RST and Khan I. Glycosides of ursane-type triterpenoid, benzophenone and iridium from Vangueria agretis (Fadogia agretis) and their anti-infective activity activities, Natural product research. 2018;34(2):683-691.
72. Maxwell DLP, John CA, Wannang NN, Steven GS and Naanlep TM. The histopathological effects of Securidaca longedunculata on heart, liver, kidney and lungs of rats, African Journal of Biotechnology. 2007;6(5):591-595.
73. Meyer JJ, Rakuambo NC and Hussein AA. Novel xanthenes from Securidaca longepedunculata with activity against sexual dysfunction, Journal of Ethnopharmacology. 2008;119(3):599-603.
74. Yusuf HK. Aphrodisiac of Nigerian medicinal plant Securidaca longepedunculata (wild wisteria or uwar Magunguna), in an albino rat model Jorind. 2014;12(2):253-256.
75. Forouzanfar F, Buzzaz BSF and Hossien Z. Black Cumin (Nigella sativa) and its constituent (Thymoquinone): A review on antimicrobial effects, Iranian Journal of Basic Medical Sciences. 2014;17(12):929-938.
76. Ping NC, Hashim NH and Adli DSH. Effect of Nigella sativa (Habbat ussauda), oil and nicotine chronic treatments on Sperm parameter and testis, histological features of rats, Evidence based complementry and alternative medicine, 2014. doi.org/10.1155/2014/218293.
77. Farkhondeh T, Samarghandians S and Borji A. An overview on cardioprotective and antidiabetic of Thymoquinone, Asian Pacific Journal of tropical Medicine. 2017;10(9):849-854.
78. Islam MT. Biological activities and therapeutic promises of Nigella sativa L, International Journal of Pharmaceutical Science and Scientific Research. 2016;2(6): 237-252.
79. Lao F, Sigurdson GT and Gnesti MM. Health benefit of purple corn (Zea mays, L) Phenolic compounds, Comprehensive review in food science. 2016;60:1-14.
80. Abu T, Rex-Ogbuku EM and Idibiye K. Secondary metabolite of Uvaria chamae P. Beauv (Annonaceae) and their biological activities, International Journal of Agriculture, Environment and Food Science. 2018;2(4):177-185.
81. Orisakwe OE, Hussaini DC and Afonne OJ. Testicular effects of subchronic administration of Hibiscus sabdariffa, calyx aqueous extract in rats reproductive toxicology. 2004;18(2):295-298.
82. Shivali NM and Kamboj P. Hibiscus sabdariffa Linn- An overview, Natural Product Radiance. 2009;8(1):77-83
83. Shruthi D. Medicinal uses of Banana (Musa paradisiaca), Drug invention today. 2019;12(1):104-107.

84. Kumar SKP, Bhowmik D, Duravivel S and Umadevi M. Traditional and medicinal uses of banana, *Journal of Pharmacognosy and Phytochemistry*. 2012;1(3):51-56.
85. Rajesh N. Medicinal benefits of *Musa paradisiaca* (Banana), *International Journal Biology Research*. 2017;2(2): 51-54.
86. Selepe AM, Drewes ES and Heerden VRF. Total synthesis of Pyranoisoflavone Kraussianone 1 and related Isoflavones, *Journal of Natural Products*. 2010;78(10):1680-1685.
87. Drewes SE, Horn MM, Munro OQ, Dhlamini JTB and Rakuambo NC. Pyrano-isoflavone with erectile-dysfunction activity from *Eriosema kraussianum* *Phytochemistry*. 2002;59:739-747.
88. Okeke UB, Igbinaduwa PO and Ozolua RI. Effects of *Anthocleista djalensis* (Chev), methanol root extracts on some fertility parameters in male rats, *Nigerian Journal of Pharmaceutical Research*. 2019;15(2):187-192.
89. Annan K, Dickson RA, Amponsah IK, Jato J and Naomi IK. Pharmacognostic evaluation and physicochemical analysis of *Paullinia pinnata* L, (Sapindaceae) *Journal of Pharmacognosy and Phytochemistry*. 2(2):203-208.
90. Mariame E, Aboudoulattiff D, Povi LE, Kodjo A, Kossi M, Essohana P and Eklug-Gadegkeku C. Repeated toxicological study and cardiotoxicity of hydroalcoholic root extract *Pauliniapinnata* L (Sapindaceae), *Journal of Applied Pharmaceutical Science*. 2016;6(03):024-028.
91. Leung KW and Wong AT. Ginseng and male reproductive function Spermatogenesis. 2013;3(3):1-10.
92. Evans WC. Trease and Evans *Pharmacognosy* 15th Edition Elsevier Limited, United Kingdom. 2002;193:327-336.
93. Yeh KY, Wu CH, and Tsai YF. Ginkgo biloba extract enhances non contact erection in rats: The role of dopamine in the paraventricular nucleus and the mesolimbic system *Neuroscience*. 2011;189:199-206.
94. Rimikiene L, Kubiliene A, Zevzekovas A, Kazlauskienė D and Jakstas V. Variation in flavonoid composition and radical - scavenging activity in *Ginkgo biloba* L. due to the growth location and time of harvest, *Journal of Food Quality*. 2017, 1-8.
95. Vudriko P, Baru MK, Kateregga J and Ndukui JG. Crude ethanolic leaf extracts of *Citropsis articulata*: A potential phytomedicine for treatment of male erectile dysfunction associated with testosterone deficiency, *International Journal of Basic and Clinical Pharmacology*. 2014;3:120-123.
96. Ajao AA, Sibiya NP and Mofeetee AN. Sexual prowess from nature: A systematic review of medicinal plants used as aphrodisiacs and sexual dysfunction in Sub-Saharan Africa, *South African Journal of Botany*, 2018, 1-18.
97. Iuvone T, Esposito G, Capasso F and Izzo AA. Induction of nitric oxide synthase expression by *Withania somnifera* in macrophages, *Life Sciences*. 2003;72(14):1617-1625.
98. Misra DS, Maiti RK, Bera S, Das K and Ghosh D. Protective effect of composite extract of *Withania somnifera*, *Ocimum sanctum* and *Zingiber officinale* on Swimming-induced reproductive endocrine dysfunction in male rat, *Iranian Journal of Pharmacology and Therapeutics*. 2005;4:110-117.
99. Mali PC, Chouchan PSN and Chaudhary R. Evaluation of antifertility activity of *Withania somnifera* in male albino rats fertility and sterility, 2008, S18.
100. Chauhan NS, Sharma V, Dixit VK and Thankur M. Review on plants used for improvement of sexual performance and virility, *Biomed Research International*, 2014, 1-19.
101. Afolayan AJ and Yakubu MT. Erectile dysfunction management options in Nigeria, *Journal of Sexual Medicine*. 2009;6:1090-1120.
102. Mahdi AA, Shukla KK, Ahmad MK, Rajender S, Shankhwar SN, Singh V and Dahela D. *Withania somnifera* improves semen quality in stress related male fertility, *Evidenced-Based complementary and alternative medicine*, 2011; 1-9.
103. Gavande K, Jain K, Jain B and Mehta R. Comprehensive report on *Phytochemistry and Pharmacological prominence of Withania somnifera* *Pharmaceutical and Bioscience Journal*. 2015;3(2):15-23.
104. Li H, Jiang H and Liu J. Traditional Chinese medical therapy for erectile dysfunction. *Translational Andrology and Urology*. 2017;6(2):192-198.
105. Stein RA, Schmid K, Bolivar J, Swick AG, Joyal SV and Hirsh SP. *Kaempferia parviflora* ethanol improves self-assessed sexual health in men: A pilot study, *Journal of Integrative Medicine*. 2018;16(4):249-254.
106. Nwafor PA and Oniyide VK. Aphrodisiac effects of methanol extract of *Smilax kraussiana* root in experimental rats, *African Journal of Biomedical Research*. 2017;20:65-73.
107. Ratnasooriya W and Dharmasiri M. Effect of *Terminalia catappa* seeds on sexual behaviour and fertility of male rats, *Asian Journal of Andrology*. 2000;2(3):213-219
108. Okereke SC, Ijeh II and Arunsi UO. Determination of bioactive constituent of *Rauwolfia vomitoria* Afzel (Asofeyeje), roots using Gas Chromatography Mass Spectrometry (GC-MS) and Fourier Transform Infrared Spectrometry (FT-IR), *African Journal of Pharmacy and Pharmacology*. 2017;11(12):25-31.
109. Etim EI, Johnson EC, Bassey US and Nwafor PA. Phytochemical and aphrodisiac studies of ethanol root extract of *Rauwolfia vomitoria* Afzel (Apocynaceae), *Journal of Pharmacy and Bioresources*. 2018;15(2):160-165.
110. Okolie N, Isreal E and Falodun A. In vitro evaluation of antioxidant potential of *Rauwolfia vomitoria* root extract and its inhibitory effect on lipid peroxidation as indication of aphrodisiac properties *Pharmaceutical Chemistry Journal*. 2011;45:476-480.
111. Li X and Zhu X. Tea: Types, Production and Trade. In: *Encyclopedia of Food and Health*, 2016, 1-5.
112. Ratnasooriya WD and Fernando TSP. Effect of black tea brew of *Camelia sinensis* on sexual competence of male rats, *Journal of Ethnopharmacology*. 2008;118(3):373-377.
113. Zhu HB, Li BM, Liu C and Chen RY. Chemical constituent of *Camelia Sinensis* Var (assamica), *ZhongguoZhongyao Za Zhi*. 2013;38(9):1386-1389.
114. Cosa P, Vlietinck AJ, Berghe DV and Maes L. Anti-infective potential of natural products, How to develop a stronger in vitro proof-of-concepts, *Journal of Ethnopharmacology*. 2006;106:290-302.
115. Duraipandian V, Ayyanar M and Ignacimuthu S. Antimicrobial activity of some ethnomedicinal plants used by Paliyar Tribe from Tamil Nadu, India, *BMC Complementary and Alternative Medicine*. 2006;6:35-41.
116. WHO. WHO model list of essential medicine, World Health Organization, Geneva, Switzerland, 2010.

117. Hamburger M and Hostettmann K. Bioactivity in plants, the link between phytochemistry and medicine, *Phytochemistry*. 1991;30(12):3864-3874.
118. Newman J, Cragg GM and Snader KM. The influence of natural products upon drugs discovery, *Natural Product Report*. 2000;17(3):215-234.
119. Newman J, Cragg GM and Snader KM. Natural products as source of new drugs over the Period 1981-2002, *Journal of Natural Products*. 2003;66(7):1022-1037.
120. Butler M. The role of natural product chemistry in drug discovery, *Journal of Natural Product*. 2004;67(12):2141-2153.
121. Yuan H, Ma Q, Ye L and Piao G. The traditional medicine and modern medicine from natural products *Molecules*. 2016;21:259.
122. Pallavi KJ, Singh R, Singh S, Singh K, Farswan M and Singh V. Aphrodisiac agents from Medicinal plants: A Review, *Journal of chemical and pharmaceutical research*. 2011;3(2):911-921.
123. Foitie J and Bohle DS. Pharmacological and biological activities of xanthones, Anti-infective agents in medicinal chemistry. 2006;5:15-30.
124. Cahil KB, Quade JH, Carleton KL and Cote RH. Identification of amino acid residues responsible for the selectivity of Tadalafil binding to two closely related phosphodiesterase PDE-5 and 6, *Journal of Biological Chemistry*, 2012, 1-22.
125. Abdillahi HS and Staden JV. South African plants and male reproductive health: Conception and contraception, *Journal of Ethnopharmacology*. 2012;143:475-480.
126. Akintude JK, Jimoh YO and Boligon AA. Essential oil from *Nigella sativa* seed differentially ameliorates steroidogenesis, cellular ATP and prostrate functions in antipsychotic drug-induced testicular damage of rats, *Journal of Clinical Toxicology*. 2018;8:371.
127. Nimesh SS, Ashwlayan VD, Barman P. Medicinal plants as aphrodisiac agents: A current advances in *Pharmacology and Clinical trial*. 2019;4(3):2-10.
128. Jain N, Goyal S and Ramawat KG. Biotechnological approaches to aphrodisiac plants of Rajasthan, India, *Desert Plants*, 2010, 479-495.
129. Bella AJ, Brant WO and Lue TF. Physiology of penile erection and pathophysiology of erectile dysfunction 15-20p. In: Bertolotto, M. (editor) *Color Doppler us of the Penis. Medical radiology diagnostic*, Springer, Berlin, 2008, 300.
130. Dean CR and Lue TF. Physiology of penile erection and pathophysiology of erectile dysfunction, *Urology Clinic North America*. 2005;32(4):379.
131. Aminoyoto M and Ismail A. Penile erection responses of *Nigella sativa* seed extract on isolated rat corpus cavernosum. *IOP Conferences Series: Earth and Environmental Science*, 2018, 1-10.
132. Yakubu MT, Akanji MA, Oladeji A.T. Aphrodisiac potentials of the aqueous extract of *Fadogia agretis* (Schweinf. Ex. Hiern) stem in male albino rats, *Asian Journal of Andrology*. 2005;7(4):399-404.