

Medicinal Plants as Aphrodisiac Agents: A Current Status

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Review Article

Volume 4 Issue 3 Received Date: June 01, 2019 Published Date: July 08, 2019 DOI: 10.23880/apct-16000160

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Abstract

Modern life vogue and bound environmental exposures have resulted in male infertility. The activating factors turn out differing types of derangements that directly or indirectly cause sexual dysfunctions. Male impotence conjointly known as erectile dysfunction (ED) may be a common medical condition that affects the sexual lifetime of ample men worldwide. ED is outlined because the inability of a person to realize and maintain an erection adequate for naturally satisfactory intercourse. This literary criticism discusses regarding aphrodisiac potential of plants, its biological science name, Common name, family, parts used and chemical constituents, that are useful for investigator to development new aphrodisiac formulations. Hence, patients are seeking complementary and practice of medicine to treat sexual dysfunction. Ayurveda and different Indian literature mention the utilization of plants in numerous human ailments. India has regarding over 45000 plant species and among them many thousand are claimed to possess medicative properties.

Keywords: Sildenafil; Ayurveda; India; Chemistry; Aphrodite; Fabaceae

Abbreviations: WHO: World Health Organization; ED: Erectile Dysfunction; NO: Nitric Oxide; ML: Mount Latency; IL: Intromission Latency; EL: Ejaculation Latency; MF: Mounting Frequency; IF: Intromission Frequency; PEI: Post-Ejaculatory Interval; Pgs: Phosphodiesterase; FSH: Follicle Stimulating Hormone.

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Advances in Pharmacology and Clinical Trials

Introduction

Aphrodisiac is that the word derived from Aphrodite, the Greek god of sexual, love and sweetness. Associate aphrodisiac is outlined as an agent (food or drug) that arouses physical attraction or sexual desire [1]. The chance of bioactive aphrodisiacs which can be derived from plants, animals or minerals, has been engaging throughout recorded history [2]. Aphrodisiac are mentioned there as Vajikaranas, the word vaji that means horse and karanta meaning creating i.e. Live to excite lust by charms etc. Natural products are on the market in texts of Ayurveda for their spermatogenic and virility potential activities. Ayurvedic aphrodisiac medical specialty is classified into vajikarana (pharmacological) and rasavana (non-pharmacological products) [3]. The plant-based, ancient or traditional medicine systems still play an important role in health care, with regarding 80% of the world's inhabitants relying in the main on ancient medicines for his or her primary health care. Modern pharmacopoeia still contains a minimum of 25% drugs derived from plants and plenty of others that are artificial or synthetic analogues, designed on model compounds isolated from plants. Medicinal herbal plants produce bioactive compounds used in the main for medicinal functions [4-6]. Some well-known herbal aphrodisiacs are genus Allium sativum, Alpinia galangal, Anacardium occidentale, Anacyclus pyrethrum, Butea frondosa, Caesalpinia benthamiana, Cannabis sativa, Chlorophylum borivilianum, Citrullus lanatus, Eurycoma longifolia, Ginkgo biloba, *Hibiscus sabdariffa*, etc. Sexual relationships are some of the foremost necessary social and biological relationship in human life. According to World Health Organization (WHO) Sexual health is prime to the physical or emotional health and wellbeing of people, couples and families and to the social or economic development of communities and countries [7,8]. The National Institutes of Health Consensus Development Conference on Impotence (7 December 1992) has outlined, Male impotence conjointly known as ED may be a common medical condition that affects the sexual life of millions of men worldwide. Impotency or ED as the 'inability to realize and maintain a penial erection adequate for satisfactory sexual relationship' (Figure 1) [9]. ED is outlined because the persistent inability to get associated maintains an erection comfortable for naturally satisfactory intercourse. Male reproductive capability was found to be deficient in nearly 50% of infertile couples in step with a study carried by the WHO. Sexual disfunction may be a serious medical and social symptom that happens in 10-52% of men and 25-63% of women [10-12]. Sexual desire is controlled and regulated by the central central nervous system that integrates tactile, olfactive and mental stimuli (Figure 2) [13].





S. No.	Stages	Explanation				
1	First	Some aphrodisiac merely provides a burst of nutritionary worth rising the immediate health or well-being of the patron and consequently improving sexual performance and concupiscence (libido).				
2	Second	This cluster includes the supposed aphrodisiac have a lot of specific physiological affects however don't seem to be psychologically active. They will have an effect on blood flow; increase duration of sexual intercourse by desensitizing the sex organ space [14,15].				
3	Third	The third cluster of aphrodisiac is created up compounds that are psychopharmacological, i.e. they really cross the blood brain barriers and stimulates some space of arousal [16]. This class includes a wide range of neurotransmitters, hormones, pheromones and drugs that interfere with the traditional perform of those molecules [17]. This class is most tough to check as a result of information of each arousal and therefore the mechanisms of the psychoactive properties of drugs are restricted. Solely the foremost general data regarding arousal and therefore the brain is known [18].				

Table 1: Mechanism involved in aphrodisiac potentials.

Side Effects of Allopathic Treatments Used in Sexual Dysfunction

Side effects include drowsiness, insomnia, nasal congestion, headaches, dizziness, tachycardia, weight loss, etc. (Figure 3) [19].



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Some Medicinal Plants with Aphrodisiac Potential

Some of the traditional plants have tested to possess a conventional similarly as scientifically proven aphrodisiac

which will enhance passion, increase physical attraction, enhance sexual performance and facilitate to extend the intensity of sexual love [20]. A short report of aphrodisiac plants in (Table 2) [21-26].

Scientific name (Family)	Common name	Pharmacology	Mechanism of action	Chemistry	Class of isolates
Allium sativum (Amaryllidaceae)	Garlic	The alcoholic extract of <i>A.</i> satium increased sexual behaviour through the activities of sulphated compounds, peptides, flavonoids & phenolics	Allicin increases blood flow to sexual organs through nitric oxide (NO) synthase	Peptides, sulphated compounds, steroids, flavonoids, volatile oils with sulphated compounds like alliin, enzymes, minerals & vitamins	Peptides, steroids, terpenes, flavonoids, volatile oils & vitamins
Alpinia galanga (Zingiberaceae)	Greater galangal, blue ginger	Methanolic extract of <i>A.</i> galangal showed increase in serum testosterone levels at 300 mg/kg/day		Spectroscopic analysis of sample has revealed the presence of 1'S'-1'- acetoxychavicol acetate, 1'S'- 1'acetoxyeugenol acetate, 1'S'- 1' hydroxychavicol acetate, trans-p- hydroxycinnam- aldehyde, trans-p-coumaryl alcohol, trans-p hydroxycinnamyl acetate, β- bisaboline & β-selinene	Coumarin, terpenoids, flavonoids, volatile oils, & phenols
Anacardium occidentale (Anacardiaceae)	Cashew	In a study to determine the aphrodisiac activity of the oils from <i>A. occidentale</i> seeds & shell, the result showed significant increase in sexual parameters		2-hydroxy-6- pentadecylbenzoic acid, the ethanolic extract of the nuts of <i>A. occidentale</i> contains phytochemicals such as phenols, carbohydrates, proteins & xanthoproteins as well as volatile oils, 2,6- dihydroxybenzoic acid from cashew apple, myristicin, kaempferol, rhamnetin, cyanidin, peonidin, delphinidin which are flavonoid compounds. Other isolated compounds are 2- hydroxy-6-pentadecylbenzoic acid, cardinal & salicyclic acid	Carbohydrates, phenols, flavonoids, steroids, & proteins
Anacyclus pyrethrum (Asteraceae)	Arkakara	Administration of 50 mg/kg & 100 mg/kg of aqueous extract in albino rats showed significant anabolic & spermatogenic effects. In a separate study, petroleum ether extract had marked influence on body weight & accessory	This could be partly explained by its vasorelaxant properties which may be caused by an increase in NO production in vascular bed & a decrease in its	Alkyl amides, pyrethrins, inulin, sesamine, hydrocaroline, pellitorine, volatile oils such as it is also composed of 2-phenyl ethylamine, anacylin, β-biotol, salvia-4 (14)-en-1-one. Eudesma-4(15),7- diene-1-ol and β-himachalol; the	Amides, & Volatile oils

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		control organs weight co	destruction	essential oil also contains	[]
		sexual organs weight as compared with arachis oil	destruction	germacreme D, germacreme-	
		compared with arachis on		4(15),5,10(14) trien-1-a-ol,	
				caryophyllene oxide, cedryl	
				acetate, eudesma-4(15),7-	
		m		diene-1-β-ol & spathuleno	
		The extract (400 mg/kg			
		body wt./day) was		Fixed oil 18%, Water soluble	
		administered orally by		albuminoid substances 19%	
		gavage for 28 days.		and glucose 6%. Fatty acids	
		Mount latency (ML),		isolated from this oil are orleic	
		intromission latency (IL),		linoleic, lenorlenic, palmitic,	
		ejaculation latency (EL),		stearic, arachidic, behenic and	
		mounting frequency (MF),		lingo cleric acid. Q-hydroxy-1-	
		intromission frequency		methyo allophonic acid, 15-	
	Flame of	(IF), ejaculation frequency		hydroxy pentasonic acid and	
	the	(EF)		1carboxy methoxy-2-carboxy	Amino acids,
Butea frondosa	forest,	& post-ejaculatory interval		hydrazine have been isolated	alkaloids, & fixed
(Papillionaceae)	bastard	(PEI) were the parameters		from the seed coat. Seed has	oils
(1 upinionaccuc)	teak	observed before and		shown the presence of	
	teak	during the sexual		alkaloid monspermine from	
		behaviour study at day 0,		the alcoholic extract of the	
		7, 10, 14, 21, & 28. The		seeds are identified palasonin	
		extract reduced		& palasonin-N-Phenyl imidine.	
		significantly ML, IL, EL and		Aqueous methanolic extract	
		PEI (p < 0.05). The extract		contains a triazine compound,	
		also increased significantly		4-arbomethoxy-3-dioxo-	
		MF, IF and EF (p < 0.05).		hydro-1,2,4-triazine	
		These effects were		4.Carboxymethoxy 3.6 dioxo-	
		observed in sexually active		hydro 1, 2, 4, triazine	
		and inactive male rats			
				The petroleum ether extract of	
				the bark has yielded cassane	
				diterpenes with antibacterial	
		The methanolic extract		activity such as	
		exhibited an accelerator		deoxycaesaldekarine C,	
		effect by decreasing the		benthaminine I &	
		latent time. The oral		benthaminine	
Caesalpinia	_	administration of aqueous		2, the aqueous extract	Terpenes,
benthamiana	Bail	extract of C. benthamiana		contains	benthamine, fatty
(Caesalpiniaceae)		showed		flavoinoids, phenols,	acids, flavonoids,
		significant increase in		anthraquinones such as gallic	& alkaloids
		mounting frequency &		acid, esveratrol; the	
		intromission frequency		chloroform & n-butanol	
		the dosage of 50 mg/kg		extract contains methyl	
		the debuge of be mg/ng		gallate, shikimic acid-3-0-	
				gallate, 1-0-methyl-D-	
				chiroinositol, (-)-epicatechin	
Cannabis sativa		In India's Ayurveda &		Narcortic resin, cannabidiol,	Cannabinoids,
(Cannabinaceae)	Marijuana,	Chinese, Unani medicine,		cannabidiol-carboxylic acid,	Phenol, alkaloid,
	bhaang	cannabis used to overcome		cannabigerol &	flavonoid, &
		impotence & raise libido &		cannabichromene,	volatile
	I	impotence & raise influo &			volatile

		as a general cure for the disease		cannabipinol & cannabidivarin, phloroglucinol β-D-glucoside, tetrahyrocannabinol,	oils
Chlorophylum borivilianum (Asparagaceae)	Safed Musli	In a study of the aqueous extract of dried roots of <i>C. borivilianum</i> in rats, there was increase in libido, sexual vigour & sexual arousal at 250 mg/kg. The study supported treatment of premature ejaculation & oligospermia	The chemical structure of stigmasterol is related to that of testosterone & mainly contributes to its aphrodisiac potentials; hecogenin produces anabolic hormone	Isolated compounds include stigmasterol & hecogenin which are responsible for its antioxidant power, anticancer & aphrodisiac activities. Chlorophytoside-1, fatty acids, eicosadienoic	glycosides, saponins, fatty acids, & hydrocarbons
Citrullus lanatus (Cucurbitaceae)	Watermel- on	The effect of red watermelon flesh extract on male sexual behaviour has been determined. In the research, the suspension of the flesh extract was administered on doses 100, 500, & 1000 mg/kg to different groups of male rats (n=5) daily for 22 days. The result showed that oral administration of water melon flesh extract caused significant increase in mounting frequency, intromission frequency. Watermelon flesh extract did not produce undesirable side effects on the male rats & thus its short-term use is apparently safe	Citrulline improves blood drive to the genital regions & plays a significant role in the relaxation of blood, a major tool in high sexual performance	Watermelon contains bioactive agents such as citrulline, β-carotene & lycopene which have been used in the management of prostate cancer	Carotenoids
Eurycoma longifolia (Simaroubaceae)	Tongkat ali, pasak bumi	Standardized extract F2 at 25 mg/kg & its quassinoids improved rat spermatogenesis, improved testosterone steroidgenesis. standardised water extract at 400 mg/day for six weeks on testosterone, epitestosterone ratio showed significant difference between supplementation & placebo. Treatment with <i>E. longifolia</i> extract at 400	Improves spermatogenesis by affecting the hypothalamic- pituitary-gonadal axis. Improves testosterone by inhibiting aromatic conversion of testosterone to estrogen & may also involve phosphodiesterase (PGs) inhibition. The extracts	Quassinoids such as eurycomanone, eurycomnol, pasakbumin-B, hydroxylklaineanones, β- carboline alkaloids, canthin-6-one alkaloids, eurycomalactone, laurycolactone, biphenyl neolignan and steroids, alkaloids such as 5,9- dimethoxycycanthin-6-one, 9,10-dimethoxy-3- methylcanthin5,6-dione have been reported	Phenols, quassinoids, alkaloids, volatile oils, & hydrocarbons

		mg/day for 5 weeks resulted to increase in free & total testosterone concentration & muscular force in men & women	of <i>E. longifolia</i> affects male infertility by suppressing α-2HS glycoprotein expression which thereby increases testosterone level and insulin sensitivity		
Ginkgo biloba (Ginkgoaceae)	Gingko	According to some researches, extracts of <i>G. biloba</i> may also help in psychological conditions by easing stress, mild depression & anxiety- major causes of poor sexual performance thereby improving the mood for sexual pleasure. <i>G. biloba</i> extract have been used in traditional Chinese medicine to improve blood circulation. <i>G. biloba</i> constituents have a thinning effect on the blood besides helping to improve the muscle tone in the walls of the blood vessels	Improved blood circulation results to an increase in the amount of oxygen in the blood & to all major organs of the body including the heart & brain thereby resulting to an increased arterial inflow to arterial tissues through arteries & veins without obstructing systemic blood pressure. This enhanced supply of blood to sex organs is crucial in maintaining strong erection	GC-MS, HPLC-MS, HPLC-RI analysis of samples have led to the characterization of ginkgolides A, B, C, J, M with cage structures involving a tertiary butyl group & six membered rings including a spirononane system, a tetrahydrofuran and three lactones groups. 33 flavonoids have been isolated from the leaves including amento flavone, quercetin, myricetin, sesquojaflavone, Ginkgetin, Isorhamnetin, etc. Ginkgolic acids have also been isolated; the albumen of the seed also contains neurotoxic 4'-Omethylpyridoxine (ginkgotoxin), etc	Steroids, flavonoid, & ginkgosides
Hibiscus sabdariffa (Malvaceae)	Roselle	Pharmacology of the testicular effects of sub chronic administration of <i>H. sabdariffa</i> calyx aqueous extract in rats has been determined. Doses of 1.15, 2.30, & 4.60g/kg for 12 weeks showed in significant change in the absolute & relative testicular weights; significant decrease in the epididymal sperm count & induced testicular toxicity	It decreases the viscosity of the blood & stimulates internal peristalsis	Several compounds have been isolated from different parts of <i>H. sabdariffa</i> including β - carotene, vitamin C, riboflavin, thiamine, and nutrients such as protein, carbohydrates & minerals like calcium and iron. <i>H. sabdariffa</i> is composed chiefly of organic acids, anthocyanins, polysaccharides & flavonoids. Spectroscopic analysis off the aqueous extract of <i>H. sabdariffa</i> have yielded citric acids, hydroxycitric acid, hibiscus acid, malic acid & tartaric acids; oxalic acid as minor compounds. Delphinidin & cyanidin based anthocyanins including delphinidin-3-	Carotenoids, vitamins, flavonoids, minerals, & amino acids

				saambubioside (Hibiscin), cyanidin- 3,5-diglucoside, delphinidin, etc. have been reported	
Lepidium meyenii (Cruciferae)	Peruvian ginseng, maca	In a research, treatment of rats with maca at high altitudes prevented high altitude spermatogenic disruption. In a separate study, 1500 mg/kg or 3000 mg/kg orally showed no significant effect on serum levels of leutinizing & follicle stimulating hormone (FSH)	Maca improves stamina & endurance, mood, & libido & erectile capabilities due to the presence of arginine which boosts NO which relaxes blood vessels, the same basic effect Viagra produces	Macamides such as benzylglucosinolate, benzylisocyanate, benzyl nitrile, benzyl alcohol, benzylaldehyde, benzylamine, hexanal, linoleic acid, N- benzylhexadecanamide, alkaloids, fatty acids, amino acids	Macamides, alkaloids, amino acids, & fatty acids
Mimosa tenuiflora (Fabaceae)	Jurema preta, calumbi	A research into the spermatic characteristics of <i>M. tenuiflora</i> on ram showed no significant differences (P>0.05) for the progressive motility, spermatic strength & morphology among the sheep with or without <i>M.</i> <i>tenuiflora</i> . The result indicated that <i>M. tenuiflora</i> does not influence negatively on spermatic characteristics of the sheep		Two alkaloids have been isolated from <i>M tenuiflora</i> & includes 5-hydroxy-typtamine and N, N- dimethyltryptamine. <i>M</i> <i>tenuiflora</i> is also composed of yuremanine and two chalcones; kukulkan A (2'.4',- dihyroxy-3'-4- dihydroxychalcone), kukulkan B (2',4',4- trihydroxy-3- methoxychalcone). <i>M</i> <i>tenuiflora</i> is also composed of the steroids campesterol-3-O- β -D- glucopyranosyl, stigmasterol- 3-O- β -D-glucopyranosyl and β -sitosterol-3-O- β - Dglucopyranosyl. Saponins such as mimonoside A, mimonoside B, mimonoside C have been isolated. Five 2- phenoxychromones ("uncommon" flavonoids), the tenuiflorin A [5,7-dihydroxy- 2-(3-hydroxy-4- methoxyphenoxy)-6 methoxychromone], tenuiflorin B [5,7-dihydroxy-2-(4- hydroxy-3-methoxyphenoxy)- 6-methoxychromone] & tenuiflorin C & 6-demethoxy- 4'-O-methylcapillarisin were isolated from the leaves of <i>M</i> . <i>tenuiflora</i>	Alkaloids, steroids, & flavonoids

Mucuna pruriens (Fabaceae)	Velvet beans, lyon bean	In different texts of Ayurveda, <i>M. pruriens</i> is most commonly used in aphrodisiac formulations. At 70 mg/kg, treatments significantly improved testosterone quality, ameliorated Psychological stress & improved sperm count	Producing a dose dependent increase in FSH & leutenizing hormone which increases the number of eggs released at ovulation by the action of L-DOPA & dopamine	L-DOPA, serotonin, mucunain, arachidic acid, behenic acid, genistein, glutamic acids, betacarboline, β-sitosterol, cysteine, dopamine, lysine, tryptamine, riboflavin	Alkaloids, amino acids, saponins, & vitamins
Musa (Musa paradisiacal/ sapientum) (Musaceae)	Banana, plantain	Aqueous extract of <i>M.</i> <i>paradisiaca</i> root on testicular function parameters on male rats at 25, 50 and 100 mg/kg enhanced the testosterone dependent normal functioning of the testes. <i>M.</i> <i>sapientum</i> contain bromine, norepinephrine, dopamine & serotonin in the peel & pulp. Norepinephrine & dopamine elevate blood pressure while serotonin stimulates the blood vessels of the intestine	Increase in blood Circulation	Bromine, rubidium, strontium, saponins, norepinephrine, dopamine, serotonin, vitamin B ₆ , vitamin a, c and D and natural glucose, fructose. Several compounds such as acyl steryl glycoside such a sitoindoside-I, sitoindoside-II, sitoindoside-II, sitoindoside-IV and steryl glycosides such as sitosterol, <i>myo-inosityl-ß</i> -D-glucoside have been isolated from fruits of <i>M. paradisiaca</i> , A bicyclic diarylheptanoid, <i>rel-(3S</i> , 4a <i>R</i> ,10b <i>R)-8-hydroxy-3-(4- hydroxyphenyl)-9-methoxy- 4a,5,6,10b-tetrahydro- 3<i>H</i>-naphthol[2,1-<i>b</i>] pyran, and 1,2-dihydro-1,2,3trihydroxy-9- (4-hydroxyphenyl) naphthalic anhydride, 1,7-bis(4- hydroxyphenyl) hepta-4(<i>E</i>), 6(<i>E</i>)-dien-3-one have also been isolated, cyclomusalenol, cyclomusalenone</i>	Saponins, alkaloids, vitamins, glycosides, triterpenes, & sterols
Myristica fragrans (Myristiaceae)	Nutmeg, mace	50% ethanolic extract showed significant increase in aphrodisiac properties in mice such as increase in mating frequency, libido & potency. It has also been used in Unani medicine for the treatment of sexual disorders	Stimulation of the nervous system by myristicin	A-pinene, camphene, ρ - cymene, sabinene, β phillandiene, γ -terpinene, limonene, myrcene, linalool, 3- methyl-4-decan-1-ol, fixed oils like mysristic, stearic, palmitic, oleic and olenolic acids, Licarin B & malabaricone C	Essential oils, fixed oils, & unsaturated aliphatic hydrocarbon
Ocimum gratissimum (Lamiaceae)	Ocimum, wild basil	Oral administration of extracts of <i>O. gratissimum</i> at 100, 250 & 500 mg/kg to 6 groups of male rats once a day for seven days showed significant		<i>O. gratissimum</i> consist of several essential oils such as thymol, eugenol, methyl charvical, gratissimol, pentoses, hexoses, uronic acid, alkaloids, tannins,	Volatile oils, alkaloids, & tannins

		increase in mounting frequency, intromission frequency, erection & aggregate penile reflexes		flavonoids, methyl eugenol, cis-ocimene, trans-ocimene, pinene, camphor, germacrene- D, transcarypophyllene, farnesene, l-bisaboline, p- cymene, γ-terpene, α-trans sabiene hydrate, 1,8- cineole, linalool, β-salinene, & geraniol	
Panax ginseng (Araliaceae)	Ginseng berry	Panax extract standardized with gensenoside Rg3 significantly produced significant & sustains increase in sexual activity of normal male rats. Improvement in all forms of sexual dysfunction including erectile dysfunction & premature ejaculation	Ginsenosides enhances acetylcholine- induced & transmural nerve stimulation- activated relaxation associated with increasing tissue cGMP mediated by the release of NO	Triterpene glycosides called ginsenosides. Alkanes, alkenes, sterols, fatty acids, carbohydrates, flavonoids, organic acids & vitamin	Saponins, hydrocarbons, flavonoids & vitamin
Passiflora incarnata (Passifloraceae)	Passionflo- wer, wild passion vine	The aphrodisiac effect of the methanolic extract of <i>P.</i> <i>incarnate</i> has been determined in mice. The result showed significant aphrodisiac properties in male mice at all doses- 75, 100 & 150 mg/kg with 100 mg/kg having the highest activity		Several compounds such as flavonoids and other phenolics have been isolated from <i>P.</i> <i>incarnate</i> such as apigenin and luteolin, isovitexin, vitexin, isoorientin, orientin & saponarin. Also isolated from <i>P. incarnate</i> includes schaftoside, isoschaftoside, isovitexin-2'-O- β-glucoside & isoorientin-2-O- β-glucoside	Phenolics, alkaloids, & sugars

Table 2: Medicinal Plants used for the improvement of sexual performance and virility.

Conclusion

Herbals medicinal plants have a possible to treat the assorted varieties of body ailments. The demand of herbal medicine is increasing day by day in developed yet as developing countries as a result of they are safer and well tolerated as compared to those of allopathic drugs. These plants must be subjected to animal and human studies to figure out their effectiveness in whole organism systems. Many plants have tried helpful within the management of sexual disorders throughout history, even herbs and spices are accustomed increased sexual activities in varied components of the world. There's great would like for substances that are accustomed treat sexual dysfunction in humans. The utilization of aphrodisiacs is outstanding in several countries of the world as well as Asian country like India, China, Sri Lanka, and Pakistan.

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Acknowledgement

The authors are thankful to the Mr. Jivan Kumar; Production officer of Kusum Healthcare Pvt. Ltd. Chopanki, Bhiwadi (Rajasthan) India, for her support and helpful in cooperation in the review and data collection process.

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper

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