

In Search of Spermatogenetic and Virility Potential Drugs of Ayurvedic Leads: A Review

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Abstract

Description about drugs of natural origin is available in different texts of Ayurveda for their spermatogenetic and virility potential activities which are being clinically practiced for a long time in India. Ayurvedic aphrodisiac therapeutics is categorized in major two groups as pharmacological and non-pharmacological. Drugs of plants, minerals and animal sources are explained in different classical texts of Ayurveda for such activities. Potentiality of pharmaco-therapeutic agents commonly used like *Mucuna pruriens*, *Chlorophytum borivilianum*, *Withania somnifera*, *Tribulus terrestris* and *Shilajit* are scientifically reported which exhibit such activities. Beside description of single natural products, there is description of use of many formulations of either polyherbal or herbo-minerals in composition for such activities.

Keywords: Aphrodisiac; Vajikarana; Ayurvedic plants; Shilajit

Introduction

Ayurveda, the ancient Indian traditional system of medicine, aimed with prevention and cure of diseases as well as promotion of quality of life. Much therapeutics are described in various classical texts of Ayurveda for the management of different diseases. *Vajikarana* is such a category of drugs that are described in Ayurveda for the management of sexual inadequacies. The sexual inadequacies discussed in Ayurveda are of six types as (1) a cessation of the sexual desire owing to the rising of bitter thoughts of recollection in the mind of a man, or fails to sufficiently rouse up the sexual desire, (2) excessive use of articles of pungent, acid, or saline taste, or of heat making articles of fare leads to the loss of the Saumya Dhatu (watery principle) of the organism, (3) virile impotency resulting from the loss of semen in persons addicted to excessive sexual pleasure without using any aphrodisiac remedy is the merit form of the virile impotency, (4) a long-standing disease, like syphilis, of the male generative organ or the destruction of a vital parts of the body injuring at which may cause death such as the spermatic cord destroys the power of coition altogether, (5) sexual incapacity from the very birth is called the congenital (Sahaja) impotency and (6) voluntary suppression of the sexual desire by a strongman observing perfect continence or through utter apathy produces a hardness of the spermatic fluid and is the cause of the sixth form of virile impotence [1]. *Rasayana*, on the other hand, is category of drugs described in Ayurveda for promotion of health and virility. Aphrodisiac group of drugs comes under both the *Vajikarana* and *Rasayana* categories.

The term "Aphrodisiac" has been derived from Aphrodite, symbol of love and beauty in Greek mythology. Since ancient times a large number of natural (plant and animal) remedies have been used as aphrodisiacs in different cultures and civilizations. Ancient literature and records show the deep interest of human beings for substances to increase libido, potency and sexual pleasure as it takes care of the disorders of sexual desire, ejaculation, orgasm and erectile dysfunction [2]. Substances which are used to treat sexual dysfunction or to improve sexual behavior and satisfaction in humans and animals are called 'aphrodisiac' [3]. Libido is clearly linked to levels of sex hormones, particularly testosterone [4]. When a reduced sex drive occurs in individuals with relatively low levels of testosterone [5], supplements of it will often increase libido. It is reported that a number of precursors intended to raise testosterone levels have been effective in older males [6]. Aphrodisiac drugs are responsible to mitigate libido by

stimulating testosterone or its precursor.

Aphrodisiac drugs in Ayurveda are classified in five categories like (i) drugs which increase the quantity of semen or stimulate the production of semen for example, *Microstylis wallichii*, *Roscoea procera*, *Polygonatum verticillatum*, *Mucuna pruriens* and *Asparagus racemosus*, (ii) drugs which purify and improve the quality of semen for example, *Saussurea lappa*, *Myrica nagi*, *Sesamum indicum*, *Vetiveria zizanioides* and *Anthocephalus cadamba*, (iii) drugs which improve ejaculatory functions for example, *Strychnos nuxvomica*, *Cannabis sativa*, *Myristica fragrans* and *Cassia occidentalis*, (iv) drugs delaying the time of ejaculation or improving ejaculatory performance for example, *Sida cordifolia*, *Asparagus racemosus*, *Cinnamomum tamala*, *Anacyclus pyrethrum*, *Mucuna pruriens* and *Cannabis sativum* and (v) drugs arousing sexual desire, namely *Withania somnifera*, *Asparagus racemosus*, *Datura stramonium*, *Anacyclus pyrethrum*, *Hibiscus abelmoschus* and *Opium* [7].

In *Charaka Samhita*, an oldest text of Ayurveda which was written approximately during 3000 B.C., a group of drugs are described which exhibit spermatogenic and virility activities. Drugs which helps for providing nutrition to sperm and accelerates the process of spermatogenesis is known in Ayurveda as *Shukrajanana*. This group comprises medicinal plants like *Jivaka* (*Microstylis wallichii*), *Rishabhaka* (*Microstylis muscifera*), *Kakoli* (*Roscoea procera*), *Kshirakakoli* (*Roscoe aprocera* other variety), *Mudgaparni* (*Phaseolus trilobus*), *Masaparni* (*Teramus labialis*), *Meda* (*Polygonatum verticillatum*), *Vridhdharuha* (*Asparagus racemosus*), *Jatila* (*Nardostachys jatamansi*) and *Kulinga* (*Alpinia galanga*). Another group of drugs is described which helps to detoxicate the impure sperm is known in Ayurveda as *Shukrasodhana*.

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This group comprises natural products like *Kustha* (*Saussurea lappa*), *Elavaluka* (*Brunus cerasus*), *Katphala* (*Myrica nagi*), *Samudraphena* (internal shell of *Sepia officinalis*), latex of *Kadamba* (*Anthocephalus indicus*), *Iksu* (*Saccharum officinarum*), *Kandeksu* (*Saccharum spontaneum*), *Iksuraka* (*Asteracantha longifolia*), *Vasuka* (*Indigofera enneaphylla*) and *Usira* (*Vetiveria zizanioides*). *Prajasthapaka* is a special group of drugs which are used as fertility promoter, that comprises with *Aindri* (*Citrallus colocynthis*), *Bramhi* (*Bacopa monnieri*), *Satavirya* (*Cynodon dactylon*), *Sahasravirya* (a variety of *Cynodon dactylon*), *Amogha* (*Phyllanthus emblica*), *Avyatha* (*Tinospora cordifolia*), *Asiva* (*Terminalia chebula*), *Arista* (*Picrorhiza kurroa*), *Vatyapuspi* (*Sida rhombifolia*) and *Visvaksenakanta* (*Callicarpa macrophylla*) [8].

Besides, medicinal plants, several drugs of metals and minerals origin are also described in Ayurveda for their spermatogenic and virility activities. These include *Varatika* (calcium), gold, etc. Several animal products are also reported in Ayurveda for aphrodisiac activity like meat soup of cock, peacock, swan or sparrow; semen of crocodile, etc. However, apart from all prescriptions described in Ayurvedic text, it is clearly mentioned that aphrodisiac therapies should be administered only to a person who is self-controlled, otherwise if a person of licentious habits is administered this therapy, he, with additional potentiality gained through the therapy will prove to be nuisance to the society through his illegitimate sex acts [9].

Reported Aphrodisiac Medicinal Plants

There are a numbers of medicinal plants which are reported for their aphrodisiac properties available throughout the world. According to recent scientific literature several medicinal plants have been identified or evaluated for their aphrodisiac potential. A total 220 medicinal plants [10] have so far been scientifically screened and some of which are being described here that are commonly used for therapeutic purpose in general.

Scientific appraisal of some Ayurvedic aphrodisiac leads *Kapikacchu* (*Mucuna pruriens* Linn.) It is the most common medicinal plants used in many aphrodisiac formulations of Ayurveda like *Apatyakara svarasa*, *Vrisya mahisa rasa*, *Apatyakara ghrita*, *Vrisya gutika*, *Vanari vatika*, etc. The plant is commonly known as *Kapikacchu* or *Atmagupta* or *Alkushi*. It is reported that 130 varieties of *Mucuna* are distributed through the world and in India 14 varieties of the *Mucuna* species are available [11]. *Mucuna* genus belongs to the family Fabaceae (Figure 1) and its taxonomy is described in Supplementary Table 1. This is the second largest family of flowering plants. The seeds are traditionally used as nerve tonic, emmenagogue, astringent, aphrodisiac, and leucorrhoea and paralysis [12]. The seed of the plant is used therapeutically after purifying through boiling in cow's milk. The seed contains active chemical constituent 12.5% L-dihydroxyphenylalanine (L-dopa), as compared to the equivalent doses of L-dopa, having anti-Parkinson's effect [13].

Mucuna pruriens improves male fertility by its action on the hypothalamus-pituitary-gonadal axis. A study on treatment with *M. pruriens* significantly improved serum testosterone, luteinizing hormone, dopamine, adrenaline, and nor-adrenaline levels in infertile men and reduce the levels of Follicle Stimulating Hormone (FSH) and Prolactin Hormone (PRL). Sperm count and motility were significantly recovered in infertile men [14]. Treatment with *M. pruriens* significantly ameliorated psychological stress and seminal plasma lipid peroxide levels along with improved sperm count and motility. Treatment also restored the levels of SOD, catalase, GSH and ascorbic acid in seminal

plasma of infertile men. *M. pruriens* not only reactivates the antioxidant defence system of infertile men but also helps in the management of stress and improves semen quality [15]. The effects of *M. urens*, another variety of *Mucuna*, on the gonads of male Guinea pigs were investigated and found to be the potential male anti-fertility agent even at a lower dosage of 70 mg/kg [16].

Safed Musli (*Chlorophytum borivilianum*)

Safed musli (*Chlorophytumborivilianum*) is a herb, belongs to family Liliaceae (Figure 2). It is originally grown in thick forests of India, but now-a-days it is cultivated in dry area. About 300 species are distributed throughout the tropical and subtropical parts of the world. Tropical and subtropical zones of Africa are the probable centres of origin of the genus. Seventeen species of *Chlorophytum* had been reported in India [17]. In Ayurveda, the plant is used for its aphrodisiac properties in lack of libido, male impotency and oligospermia and more than 100 preparation of Ayurvedic formulation is composed with the tubers of the plant [18] for the purpose of aphrodisiac property. Major biochemical constituents of *C. borivilianum* are carbohydrates 42%,



Figure 1: Kapikacchu (*Mucuna pruriens*).



Figure 2: Safed musli (*Chlorophytum borivilianum*).

protein 10%, fibres 20-30%, saponins 2-17% and alkaloids 15-25%. Primarily saponins and alkaloids impart medicinal value. Stigmasterol and saponin named as furostanol and Chlorophytoside-I are important component which are recently isolated [19].

The aqueous extract of dried roots of *C. borivilianum* is reported to have a potent aphrodisiac and spermatogenic potential. In an animal study it was observed on male Wistar albino rats treated with aqueous extract of *C. borivilianum* (cb) at the dose of 125 and 250 mg/kg/day, sexual behaviour by pairing with a pro-oestrous female rat were stimulated, indicating its marked aphrodisiac action, increased libido, sexual vigor and sexual arousal as compared with control groups. In another study, the effects of Cb on sexual dysfunction, loss of body weight, and lack of libido in hyperglycaemic rats induced with streptozotocin or alloxan was investigated. It was found that Cb extract treatment ameliorated the diabetes-induced dysfunction at 200 mg/kg dose [16].

Aswagandha (*Withania somnifera*)

This medicinal plant is popularly known as Indian ginseng, categorized under the family Solanaceae (Figure 3). *Withania somnifera* is a medicinal plant extends over a large area, from the Atlantic ocean to South East Asia and from the Mediterranean region to South Africa. The medicinal plants are widely used by the traditional medical practitioners for curing various diseases in their day to day practice. In traditional systems of medicine, different parts (leaves, stem, flower, root, seeds, bark and even whole plant) of *Withania somnifera* (known as Ashwagandha in Hindi), a small herb seen throughout India, have been recommended for the treatment of aphrodisiac, liver tonic, anti-inflammatory agent, astringent, and more recently to treat bronchitis, asthma, ulcers, emaciation, insomnia, and senile dementia etc. Clinical trials and animal research support the therapeutic use of ashwaganda for anxiety, cognitive and neurological disorders, inflammation, and Parkinson's disease. Ashwaganda's chemopreventive properties make it a potentially useful adjunct for the patients undergoing radiation and chemotherapy. Ashwaganda is also used therapeutically as an adaptogen for patients with nervous exhaustion, insomnia, and debility due to stress, and as an immune stimulant in patients with low white blood cell counts in blood. The major biochemical constituents of



Figure 3: Ashwagandha (*Withania somnifera*).

ashwaganda root are steroidal alkaloids and steroidal lactones in a class of constituents called withanolides [20].

Spermatogenic effect of the plant is reported on the basis of the clinical trial on selected 46 infertile male subjects having oligospermia and compared with 22 normal male volunteer. Significant ($p < 0.05$) improvement was observed in Aswagandha (675 mg/d) treated group in comparison with placebo on the basis of the seminal volume, sperm concentration and sperm motility after 90 days of treatment [21].

Gokshura (*Tribulus terrestris*)

Tribulus terrestris (family Zygophyllaceae, Figure 4) has been used in traditional system of medicine for treatment of various diseases particularly sexual dysfunctions in men. Efficacy of its extract, Protodioscin (PTN), in the sexual behaviour study on normal and castrated adult SD rats claimed it to be a potent aphrodisiac. The study suggested that it works probably through androgen enhancement and nitric oxide release from nerve endings of corpus cavernous tissue. Another study on male rats reported increased androgen receptor and NADPH-d positive neurons which were probably due to its androgen enhancing properties. In contrast to the above, another study on human subjects reported that *T. Terrestris* is not involved in either direct or indirect androgen enhancing properties. This plant therefore needs to be further explored further for its aphrodisiac properties and possible mechanism of action [2].

Shilajit

Among all categories of natural products of Ayurvedic origin, Shilajit is found to be most potent component which is used as aphrodisiac and spermatogenic agent. Purified Shilajit (PS) is used in Ayurveda as a remedy for several diseases, particularly chronic diseases. Shilajit is a pale-brown to blackish-brown exudate that oozes from sedimentary rocks worldwide, largely in the Himalayas. Common people describe it from their knowledge as pahar-ki-pasina (sweat of mountains), pahar-ki-khooon (mountain blood), shilaras (rock juice), asphalt, bitumen, etc. Shilajit is said to carry the healing power of these great mountains owing to its main chemical constituent di-benzo-alpha-pyrone (dbp). It is an important drug of the ancient Ayurvedic material medica and it is to this day used extensively by Ayurvedic physicians for a variety of diseases. In Charaka Samhita Shilajit is described as an agent to cure for all diseases as well as a Rasayana (rejuvenator) that promises to increase longevity. It is composed of rock humus, rock minerals



Figure 4: Gokshura (*Tribulus terrestris*).

and organic substances that have been compressed by layers of rock mixed with marine organisms and microbial metabolites. Traditional uses of Shilajit primarily focus not only on diabetes and diseases of the urinary tract, but also on oedema, tumours, muscle wasting, epilepsy and even insanity. Modern indications extend to all systems of the human body with a significant number of additions in the reproductive and nervous system. Clinical research confirms many of the properties for which Shilajit has been used. In Ayurveda, Shilajit is employed for the management of male reproductive disorders, and in particular, under the parlance of *Vrisya* (an aphrodisiac with special reference to spermatogenesis) [22].

Safety and spermatogenic activity of Processed Shilajit (PS) was evaluated in selected 35 oligospermic patients and compared with control placebo. Significant result ($p < 0.001$) was observed on the basis of total semenogram and serum testosterone, LH and FSH and Malondialdehyde (MDA), the marker for oxidative stress [23]. A further clinical study of Shilajit on 35 healthy male volunteer was performed to observe the role of this natural product of testosterone stimulation, as a marker for spermatogenesis. It was observed that treatment with Shilajit for consecutive 90 days revealed that it significantly ($P < 0.05$) increased total testosterone, free testosterone and dehydroepiandrosterone (DHEAS) compared with placebo. Gonadotropic hormones (LH and FSH) levels were also well maintained and it was predicted that it acts via hypothalamus–pituitary–testicular axis [22].

Discussion

The free radical Nitric Oxide (NO) is one of the important biochemical marker that release from axons of parasympathetic nerve on sexual stimulation and maintain aphrodisiac activity. NO diffuses into smooth muscle cells that line those arteries of the corpus carvenosum (spongy erectile tissue) and activates the enzyme Guanylate-cyclase (GC). The later converts the nucleotide Guanosine Triphosphate (GTP) into cyclic Guanosine Monophosphate (cGMP). The cGMP in turn causes the smooth muscle cells around the penis to relax, leading to dilation and increased flux of blood into the penile tissue. This blood is essentially trapped in the penis and results in an erection. Aphrodisiac potentials inhibit the hydrolyzing action of PDE-5 with the result that active cGMP can accumulate [10]. Natural product of unknown origin may act on the basis of above hypothesis but needs its validation. The review reveals that Ayurvedic medicinal plants such as *Mucuna pruriens*, *Chlorophytum borivilianum*, *Withania somnifera*, *Tribulus terrestris* and *Shilajit* are common examples that act by means of the above mechanism. These may be used in single or in combined form. In most of the Ayurvedic literature, drugs are used either as polyherbal or herbo-mineral in nature. Besides, above descriptions, several other formulations of Ayurvedic origin are also found to be potent in clinical practice. These are *Vrihani Gutika*, *Vrishya Gutika*, *Vrishyam Yoga*, *Upatyakaram Ghrita*, *Vrishya Pippali Yoga*, *Medadi Yoga*, *Vrishya Payas Yoga*, *Vrishya Mashadi Pooplika*, etc. [24]. However, a detail scientific study is needed in the way as done for evaluation of such activity with Shilajit [22,23] to explore their activity as potent spermatogenic and virility agent.

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