Oxidative stress induced by reactive oxygen species (ROS) is a major disruptor of semen quality and quantity. Male infertility can range from hormonal or neuronal imbalances, reproductive tissue disruptions, qualitative and quantitative deterioration of semen, to sexual behavioral problems. The global deterioration of male reproductive health is a major concern, and the modern therapeutic approaches to combat male infertility are expensive, less accessible, have long-term treatment tenure and possess various side effects. Whereas, the herbal therapies are better positioned to offer more holistic approaches to improve male reproductive health. In Ayurvedic pharmacology, there exists a special group of herbs, classified as vajikarana or aphrodisiacs, which nourishes and stimulates the sexual tissues. This review concentrates on the Ayurvedic approach to ameliorate male reproductive health referring to some of the most important scientifically tested herbs which have been reported to accentuate male fertility by imposing either stimulating or nourishing effects on the male reproductive organs.

Abstract

Male infertility can range from neurohormonal imbalances, reproductive tissue disruptions, qualitative and quantitative deterioration of semen to sexual behavioral problems. The global deterioration of male reproductive health is a major concern and the modern therapeutic approaches to combat male infertility are expensive, less accessible, have long-term treatment tenure and possess various side effects. Whereas, the herbal therapies are better positioned to offer more holistic approaches to improve male reproductive health. In Ayurvedic pharmacology, there exists a special group of herbs, classified as vajikarana or aphrodisiacs, which nourishes and stimulates the sexual tissues. This review concentrates on the Ayurvedic approach to ameliorate male reproductive health referring to some of the most important scientifically tested herbs which have been reported to accentuate male fertility by imposing either stimulating or nourishing effects on the male reproductive organs.

Introduction

Organisms strive to exist and preserve own genetic characteristics through subsequent progenies owing to their reproductive potencies. In this aspect, human being is one of the most successful survivors on earth. But the present scenario is alarming, as besides female reproductive complications and dysfunctions, male reproductive health is suffering a deteriorating trend throughout the globe [1-6]. Sexual dysfunction, an earnest medical issue marring social and biological relationships, occurs in 25%-63% of women and 10%-52% in men. Sexual dysfunction in men can be explained as the failure to accomplish normal sexual intercourse, inability to respond to erectile stimuli or sustain an erection, retarded ejaculation, decreased libido, unregulated sexual behavior etc. [7]. Innumerable synthetic products are abundantly flooding in the global market with quick remedial claims. But most of them are associated with suppressing symptoms and side effects [8]. Thereby people are again oriented back to herbal and ayurvedic aphrodisiacs having the holistic approach to cure male reproductive problems from the root of the causes.

Aphrodisiacs, agents to arouse sexual desire and performance, when derived from herbs, have been observed to directly been able to excite male sexual libido, contribute to sustenance of reproductive activities, restore healthy tissue functioning and also aid the neuroendocrine regulation for exhibiting required sexual strength with content state of mind and body [9]. This review, with the aim to highlight the healthy long-term remedy of male sexual problems, concentrates on the scientifically tested herbs which have been reported to accentuate male fertility.

Overview of male reproductive disruptions

Standard clinical and laboratory evaluations are not enough to find out the causes behind most of the male infertility cases [10]. It can range from hormonal or neuronal imbalances, reproductive tissue disruptions to qualitative and quantitative deterioration of semen. Oxidative stress induced by reactive oxygen species (ROS) is a major causative factor in male infertility [11,12]. The mature spermatozoa are encased in polyunsaturated lipid membrane which is vulnerable to the oxidative damage induced by ROS, and this, in turn, can impair spermatogenesis and reduce sperm quality, motility and morphology [10,14]. The regulation of hypothalamic-pituitary-gonadal (HPG) axis is the main controller of male reproductive function where the hypothalamus produces gonadotropin-releasing hormone (GnRH) to stimulate the secretion of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) from the anterior pituitary. The secreted FSH and LH act on the Sertoli cells and Leydig cells, respectively to stimulate spermatogenesis and testosterone [11,14,15]. Spermatogenesis is regulated by well-maintained crosstalk of FSH, LH, intratesticular testosterone and other hormones. Thereby, HPG axis disruptions are detrimental to semen parameters [16,17].

Reproductive endocrinologist opts for injectable medications including recombinant FSH, human menopausal gonadotropin (hMG), human chorionic gonadotropin (hCG) and gonadotropin-releasing hormone (GnRH) to treat men with abnormal semen parameters. An oral medication, Clomiphene citrate which is an estrogen receptor antagonist, is also given to the patient in order stimulate gonadotropin release from the pituitary. But these options are expensive, less accessible, having long-term treatment tenure and possess various side effects [18]. Whereas, the herbal therapies, are better positioned to offer more holistic approaches to improve male reproductive health.

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Herbal therapy and male reproductive health

According to the Ayurvedic concept, health depends upon balance between three fundamental bodily bio-elements or doshas referred to as Vata, Pitta and Kapha [19].

Vāta or Vata (airy element), characterised by dry, cold, light, minute, and movement.

Pitta (fiery element) or bile, flowing through the liver and permeating the overall heating of the body.

Kapha (watery element) is characterised by heaviness, cold, tenderness, slowness, lubrication, nutrient carrier, nourishment.

In Ayurvedic pharmacology, there exists a special group belonging to rasayana herbs, classified as vajikarana, that aid nourishment and also stimulate the sexual tissues. Moreover, they also help to promote beauty and sex appeal. Further classifications of herbs that increase spermatogenesis, are known as shukrāla. With the knowledge of the possible causes and factors leading to male infertility, the appropriate herb can be selected to meet the need [19].

In Sanskrit ‘vaj’ and ‘karana’ mean ‘horse’ and ‘power’ respectively, in order to convey the notion about the power or strength that a horse possesses. These are the herbs which can be referred to in Western term as aphrodisiacs. Vajikarana herbs can be used as stimulants or tonics to improve male reproductive vitality. Stimulants to reproductive functions are typically heating substances like fenugreek, garlic, damiana, and onion. They have an invigorating action on the male sexual organs. Tonics provide better nourishment to the reproductive tissues to rejuvenate the quality and quantity of the same. Some herbs have both stimulating as well as nourishing properties, such as garlic, fenugreek, shilajit, and ashwagandha (Withania somnifera).

The Ayurvedic herbal drugs can be classified in varied ways, and one such simplified classification according to their functions on male reproductive health is as follows [20]:

- Herbs increasing the quantity of semen or stimulating semen production, for example, Polygonatum verticillatum, Mucuna pruriens, Microstylv wallichii, Roscoea prosera, and Asparagus racemosus.

- Herbs purifying and improving semen quality, for example, Vettiveria zizanioides, Saussurea lappa, Myrica nagi, Sesamum indicum, and Anthocephalus cadamba.

- Herbs rejuvenating ejaculatory functions, for example, Strychnos nux vomica, Myristica fragrans, Cannabis sativa, and Cassia occidentalis.

- Herbs improving sustenance and ejaculatory performance, for example, Cinnamomum tamala, Anacrylus pyrethrum, Sida cordifolia, Asparagus racemosus, Mucuna pruriens, and Cannabis sativum.

- Herbs increasing libido, namely, Asparagus racemosus, Withania somnifera, Datura stramonium, Anacrylus pyrethrum, Hibiscus abelmoschus, and Opium.

Some common Ayurvedic herbs to improve male fertility

Ashwagandha (Withania somnifera)

In Sanskrit, ashwagandha refers to ‘the smell of a horse’ owing to its root’s strong odor resembling that of horse urine. Another reason for its naming for mythological comparison of the sexual vitality it may impart to men with that of a horse. Innumerable beneficial qualities to alleviate male reproductive disorders including induction of spermatogenesis, improved blood flow to the reproductive tissues and regulated endocrine functions. It relieves conditions such as spermatorrhea, nocturnal emission, premature ejaculation, and enlarged prostate.

Withania somnifera is able to combat stress-induced male infertility and protects against swimming-induced endocrine dysfunctions of male reproduction in rat [21]. The aqueous extract of this herb has been shown to improve spermatogenesis, owing to elevated interstitial cell stimulating hormone and testosterone-mimicking effects together with induction of nitric oxide synthase [22]. Yet another study showed that Ashwagandha root extract administration resulted in a significantly greater improvement in spermatogenic activity and increase in serum hormone levels in the oligospermic patients as compared to the placebo treated [23]. This herb evidently combats against oxidative stress by reducing lipid peroxidation as well as protein carbonyl content, increasing sperm count and motility, rejuvenating the seminal plasma levels of antioxidant enzymes. Withania somnifera root powder when administered to normozoospermic infertile man in a dosage of 5g/day for 3 months showed a significant reduction in stress, improved antioxidants, and enhanced semen volume and levels of vitamins A, C, and E and also corrected fructose. This herb’s action at the HPG axis level is also evident through various studies, one such showed significant increased serum testosterone and LH levels and decreased levels of FSH and prolactin (PRL) in infertile men [24-26].

In terms of ayurvedic explanations, the grounding and deeply nourishing qualities of Withania somnifera contribute for its being one of the best vata appeasing medicines. Its warming energy provokes pitta if used in excess and so it is recommended to combine it with cooling vajikarana herbs such as licorice, vidari, shatavari, bala, while using as a drug. Owing to its stress relieving, relaxing effect on the body and mind, as well as fortifying of all the dhatus, it is considered as the best herb to target many of the contributing factors that are associated with reduced sexual energy.

Kapikacchu (Mucuna pruriens)

This sweet yet sometimes bitter tasted herb is quite heavy and oily. Mucuna pruriens is mainly used to balance vata and pitta, as both kapha and ama are increased in excess by this herb. Typical doses of the powdered Mucuna pruriens range from 1.5 to 6 grams [27]. Alkaloids derived from M. pruriens seeds were found to stimulate spermatogenesis and overall weight of the testicles and accessory glands in the male albino rat [28]. M. pruriens is capable of stimulating sexual activities in male rats as inferred by increased mounting frequency, ejaculation latency and also enhanced intromission frequency [29,30]. In a study, M. pruriens has been shown to efficiently recover the spermatogenic loss which was induced in male rats by ethinyl estradiol administration and the herb’s beneficial effects were mediated by mitigation of ROS, apoptosis regulation, and increase in the number of germ cells. The major constituent of M. pruriens, L-DOPA, largely contributes to its pro-spermatogenic properties [31]. The seed extract of M. pruriens showed marked improvement in sexual potency and behavior, libido, sperm parameters, and endocrine levels [32]. M. pruriens has been able to ameliorate the levels lipids, triglycerides, cholesterol, phospholipids, vitamin A, C, and E and corrected fructose nullifying oxidative stress induced lipid peroxidation in seminal vesicles and restored the levels of SOD, catalase, GSH, and ascorbic acid in seminal plasma [33, 34]. From the neuroendocrine perspective, M. pruriens elevates testosterone, LH, dopamine, adrenaline, as well as noradrenaline levels and decreased...
levels of FSH and PRL in infertile men. *M. pruriens* treatment to infertile men indeed improves steroidogenesis and semen quality [35].

**Shatavari (Asparagus racemosus)**

Shatavari can serve as a powerful male tonic. With a bittersweet taste, this herb renders cooling and purifying effect to the liver and blood, and targets *pitta* at its main site in the small intestine. Its cooling properties balance the heating herbs which are used to improve sperm count, such as, garlic, onion, ashwagandha, etc. Thus, Shatavari prevents depletion of sperm caused by burning via excess *pitta*. Owing to its heavy and nourishing properties, it is useful for *vata*, especially when combined with heating *vajika* or ashwagandha or bala. As a drug, it can be prepared as a milk decoction with 3 to 6 grams of the herb, or can be taken alone or in combination with other herbs [19]. Sexual desires are associated with emotional aspects and in such conditions, this herb in combination with cooling nervine herbs like *brahmi* (gotu kola) may enhance libido and help to overcome agonizing emotions like anger and irritability. Shatavari is thus one of best *pitta* pratyanika herbs which can be associated in several Ayurvedic formulas to balance *pitta* and *vata* in mediating male reproductive functions. General fatigue, low sexual energy, anger, stress, irritability, inflammation, hyperacidity, urogenital infections, burning sensations etc. are the conditions when this herb can be used as drug in standardized dosage of 2 to 6 grams of the powdered herb, 2 to 3 times daily. This herb is avoided in cases of respiratory or sinus congestion [19].

**Bala (Sida cordifolia)**

Bala refers to ‘strength’ in Sanskrit, and being a rejuvenative tonic herb for *vata* and *pitta*, this herb finds application in nourishment and strengthening of all the bodily tissues, especially the muscle, plasma, muscle, bone marrow and reproductive tissue. It is sweet, heavy and oily and increase *kapha* when used in excess, and also is mildly cooling. Bala is one of the best anti-*vata* herbs in Ayurveda which mitigates disorders related to both body and mind. It plays a leading role as an Ayurvedic herb in the treatment of balakshaya or chronic fatigue, to rejuvenate overall health in exhaustion of physical or mental strength. It serves as a tonic to restore sexual strength, promote spermatogenesis and enhance male fertility [19,20].

This herb can be taken internally or even used as massaging oil in combination with Ashwagandha onto penis to improve its tone and also to prevent premature ejaculation. Its combination with herbs such as gokshura, ashwagandha, vidarikandha, saw palmetto, and kapikacchu, proved to be beneficial for prostate health. A typical dose of Bala ranges from 2 to 6 grams, to be taken 2 to 3 times daily [19].

**Vidarikandha (Ipomoea digitata)**

Vidarikandha is a starchy tuber, effective in promoting spermatogenesis with faster action when taken as a milk decoction. It is lighter for *kapha* types than shatavari and bala. Its combination with kapikacchu is effective in the treatment of enlarged prostate. This sweet and cool herb promotes ojas, muscle tone, motor coordination and nullifies sexual debility associated with nervousness and adrenal stress when used in formulation with ginseng, licorice, gokshura, and ashwagandha. It falls right between too warming and too cooling herbs with *vata* depriving action. Its oily nature prevents it from drying making it suitable for *vata* and its pleasant post digestive effect makes it more calming to *pitta* than other hot spices and herbs. It aids blood flow to the reproductive tissues when taken in combination with Ashwagandha [19,20].

According to the Ayurveda, Pippali enhances life energy and expels impurities via respiration. It also improves digestion, absorption, assimilation, respiration and reduces arthritic agonies. The typical dosage of this herb is 1 to 3 parts in complex formulas, or ranges from 250 mg to 1.5 grams. Pippali should be avoided in high *pitta* or inflammatory conditions [19].

**Butea superba**

*Buteas superba* Roxb (Leguminosae) or the ‘Red KwaoKrua’, has long been consumed as a stimulant of male sexual vigor. Its alcoholic extract (0.01, 0.1 or 1.0 mg/kg BW/day) for 6 months significantly elevated the sperm concentration and enhanced sperm motility with no disruptive signs to sperm or testis [36]. Powdered crude extract of this herb at the doses of 2, 25, 250, and 1250 mg/kg body weight in male rats for 8 weeks increased tests weight and sperm counts [37]. Moreover, the ethanol extract of *B. superba* has been shown to increase penile erection acting through cAMP/cGMP pathways [38].

**Curculigo orchioides**

*Curculigo orchioides* Gaertn (Amaryllidaceae), or Kali Musli or *Syah* (black) *Musli*, is an aphrodisiac or rejuvenator ameliorating sexual arousal and performance by inducing penile erection, mating sustenance, orientation behavior, etc. This herb also promotes anabolic and spermatogenic effect by pronounced increased weight of reproductive organs. Rats that received Curculigo orchioides treatment displayed reduced in mount latency, increment in penile erection index, and increased in mount frequency and affinity towards female [39,40].

Its lyophilized aqueous extracts are shown to improve the pendiculatory activity in male rats after as well as preserve the *in vitro* sperm after 30 min. of incubation [41]. The aqueous extract of the herb is effective at a dose of 200 mg/kg. In case of physically induced or heat induced sexual dysfunction, this herb is useful in ameliorating the decreased spermatogenesis and mitigated disruptionsowing to the heat shock protein [42].

**Cynomorium coccineum**

*Cynomorium coccineum* Linn. (Cynomoraceae) is a black leafless parasitic plant without chlorophyll. Aqueous extract of this herb has been shown to induce significant elevation in the sperm count, the percentage of viable sperm and sperm motility, reduced the number of abnormal sperm, increased spermatogenesis [43].

**Chlorophytm borivilianum**

*Safed Musli* (*Chlorophytm borivilianum*) of family Liliaceae is claimed to be an effective aphrodisiac and sexual stimulant. Ethanolic
roots extract of this herb or sapogenins extracted from the roots showed anabolic and spermatogenic effect in treated male rats evidenced by total body weight increase and also increment in weight of reproductive organs. The herb could also affect sexual behavior of animals by reducing mount ejaculation, post-ejaculatory latency, and intromission latency, increasing mount frequency and affinity towards female [44]. Moreover, the aqueous extract of dried roots of this herb enhanced sexual arousal, strength, and libido as well as sperm count in Wistar male rats [45]. This herb also reportedly improves male reproductive functions in diabetic scenario [46,47].

**Epimedium koreanum**

Epimedium L. (Berberidaceae), is a popular Chinese herb and botanical supplement used as health tonic. Most important species of this herb used for medicinal purposes are E. pubescensMaxim., E. brevicornum Maxim., E. koreanum Nakai, E. sagittatum (Sieg. EtZucc.) Maxim, and E. wushanense T.S. Ying [48]. Hydroalcoholic extract of the herb shown to display aphrodisiac effects and are commonly used to enhance erectile function [49]. The primary active component of Epimedium extracts, Icariin, is a type of flavonoid and selectively inhibits phosphodiesterase-5 (PDE5) improving erectile function [50]. Icariin also can mimic the effects of testosterone inducing spermatogenesis [51].

**Eurycoma longifolia**

*Eurycoma longifolia*Jack (Simaroubaceae) or Tongkat Ali, is one of the major aphrodisiac herb from Malaysia [52]. *E. longifolia* extract treatment showed successful induction of sexual motivation in naive male rats [53]. Ethanol extract of this herb increased the sexual libido and performance of the treated male rats by increasing the duration of coitus and copulation frequency [54].

**Tribulus terrestris**

*Tribulus terrestris* Linn. (Zygophyllaceae) or puncture vine, a perennial creeping herb, has worldwide distribution and is regarded as an aphrodisiac since ancient times besides being used for various ailments such as inflammations, leucorrhoea, urinary infections, edema, and ascites [55]. Administration of *T. terrestris* to animals showed to improve plasma testosterone level and induced spermatogenesis [56]. It also increases the levels of testosterone as well as luteinizing hormone [57] and the activities of dehydroepiandrosterone, dihydrotestosterone, and dehydroepiandrosteronesulphate [58]. The corpus cavernosal tissues of New Zealand white rabbits following treatment with this herb were tested *in vitro* with various pharmacological agents as well as electrical field stimulation and the herb was shown to have proerectile effect [59]. It increases sexual behavior evident through increase in mount frequency and intromission frequency, reduction in mount latency, intromission latency, and penile erection index as well as increase in prostate weight and intracavernosal pressure [60,61]. This herb also possesses androgen, testosterone, dihydrotestosterone (DHT), and D-dehydroepiandrosterone (DHEA) increasing property having stimulating effects on reproductive functions and thus used in mild to moderate cases of endocrine disruptions [62,63]. The ability of to induce nitric oxide release may also account for its claims as an aphrodisiac [64].

**Mechanism of action**

Male reproductive functions are restored and controlled by induction or inhibition of neurochemicals, regulation of neuroendocrine axis and their cross talks as well as by local mediators acting within the reproductive tissues [65-67]. The herbal therapies may ameliorate male reproductive functions possibly at three levels. (1) Herbs may act on the central or peripheral nervous system improving the responsiveness of male reproductive tissues. The neuronal control over the male reproductive organs is mediated by an orchestra of neurochemicals/neurotransmitters, among which the serotonin and dopamine are the prime controllers of sexual behavior with serotonin mediating inhibitory functions and dopamine playing an excitatory role [68]. (2) The effects of herbal therapies to regulate the level of the nitric oxide support their contribution towards treating erectile dysfunctions. Nitric oxide (NO) is an established endogenous mediator of penile erection [64] and its synthesis via NO synthase is mainly concentrated in structures of the brain that are involved in sexual behavior (olfactory bulb, amygdala, septal structures, supraoptic and paraventricular nuclei, etc.) [69,70]. NO is a known vasodilator which can increase blood flow to the penis inducing penile erection and to other male reproductive organs facilitating better hormonal accessibility in the same to promote robust reproductive functioning [71]. (3) Herbs can favourably interfere in the HPG axis in the regulation of sex hormones importantly testosterone, LH, FSH and interstitial hormones as well as their cross-talks which synchronise male reproductive functioning, such as, the development of secondary male sexual organs, accentuate pubertal changes and increase overall male fertility [72].

**Conclusion**

Vajikarana or aphrodisiac herbs can be used as stimulants or tonics to improve male reproductive vitality. Stimulants to reproductive functions are typically heating herbs having an invigorating action on the male sexual organs. Herbal tonics provide better nourishment to the reproductive tissues to rejuvenate the quality and quantity of the same. Some herbs have both stimulating as well as nourishing properties. Owing to the health complications, partial impact and high cost of modern therapies for male infertility, the herbal aphrodisiacs are regaining popularity and laying their long-term impact on male reproductive health by improving sexual behavior, vigor, neuroendocrine control as well as structural and functional aspects of reproductive tissues, qualitative and quantitative improvement in semen and also sperm morphology and motility. Biomedical research should pierce deeper to emerge with more hidden mechanisms by which innumerable herbs may act to eradicate male infertility which is becoming a major threat to upcoming progenies.

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