



## **Traditional Herbal Medicines and their Fertility Potential: A Review**

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### **Authors' contributions**

This work was carried out in collaboration between both authors. Author AK designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author NG and managed the analyses of the study and managed the literature searches. Both authors read and approved the final manuscript.

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### **ABSTRACT**

Rapid increase in population growth is causing strain on medical resources world wide. Traditional folk medicines are region-specific, local resources based indigenous herb based, village based, and in many cases, community-specific. Different systems of medicine developed accordingly, which have been termed as Ayurvedic, Japanese, Chinese, Korean, Malaysian, Yunani and more recently Homoeopathic. Aim of the present review is to study and review role of traditional herbal medicines in regulation of fertility problems including impotency and female gynaecological problems. The method used was results of our own studies, existing literature, traditional knowledge from gunis vaidyas etc. It has been found that *Chlorophytum borivilianum* Santapau & Fernandes (Liliaceae), *Asparagus adscendens* Roxb and *Mucuna pruriens* L (DC) is being used in the indigenous systems of medicine as a galactagogue and aphrodisiac. It can be concluded that traditional medicines have an important role in improving fertility potential in humans.

**Keywords:** Ayurvedic; aphrodisiac; safed musli; mucuna; male infertility.

## 1. INTRODUCTION

The plant-based medicinal agents continue to play a vital role in health care [1-4]. Several of the herbal drugs used by the traditional folk healers since long have proved to be of great biological significance and modern researches have convincingly established their medicinal property and restored their credibility which has been eroded with the coming of the modern synthetic medicines [5-8]. Antioxidants are compounds found mostly in plants and they inhibit oxidative damage to body cells by scavenging free radicals that might cause degenerative disease [9].

Medicinal plants have been used since ancient times for the treatment of various diseases. Antioxidants are found mostly in plants and they inhibit oxidative damage to body cells by scavenging free radicals. Free radicals such as reactive oxygen species (ROS) and reactive nitrogen species (RNS) are produced naturally in the body during oxidative reactions and they play an important role in many normal cellular processes [10]. However, at high concentrations, free radicals can be hazardous to the body and damage all major components of cells, including proteins, cell membranes and deoxyribonucleic acid (DNA) [11]. The damage to cells caused by free radicals may lead to diseases which include aging [12], diabetes, cancer [13] and neural disorders [14].

Recent studies on antioxidant from plants with free radical scavenging activities have reported that different parts of plants with antioxidant properties may be used as therapeutic agents for the treatment of diseases caused by free radicals [15, 16].

The World Health Organization (WHO) defines infertility as the inability of a couple to conceive after 1 year of regular, unprotected intercourse [17]. Infertility is attributed to the male factors in almost 50% of cases and in the remainder, infertility may be due to either a female factor or a combination of male and female factors [18]. In the ancient Indian Ayurvedic and Unani medicine systems, numerous plants and their products have been recommended for general resistance against infection, retardation of the aging process, endurance against stress, and eventual improvement of male sexual function, alleviating disorders like unexplained infertility and psychogenic impotence [19]. Because of its many deleterious effects on both the neuronal

and vascular supply to the penis, diabetes can be an especially challenging cause of erectile dysfunction (ED) to treat.

Recently the use of complementary and alternative medicines (CAMs) has increased in treating infertility [20]. The finding of many studies that studied the effect of different medicinal herbs on the testes, epididymis, sperm and prostate parameters, testosterone level and steroidogenesis, erection/ejaculation function and libido [21]. Prostatectomy and radiotherapy for prostate cancer both cause damage to the neurovascular structures supplying the penis, that can lead to severe and refractory ED. However, there is still a need for more studies to have certain results, as conflicting results were noted in different studies done on the effect of the same medicinal plant on spermatogenesis [20].

## 2. MATERIALS AND METHODS

Local survey and identification of plants of medicinal value growing in our locality in Jaipur was done. The plants were collected, identified and preserved. Plants were identified using floras of Herbarium of Department of Botany, University of Rajasthan, and Jaipur. Crude herbal drugs (dried specimens of plant parts – roots, stems, leaves, flowers, fruits and seeds) were also collected from the crude drug dealers (Pansarias, Attars etc.) of Jaipur located in the Johari Bazar market and deposited in herbarium. Comparative details were recorded. Meeting the Vaidyas and Hakim, folk people taking medicine for healthcare were arranged to gather firsthand information. In order to verify the efficacy of the traditional herbal medicine, the small information was collected from folk or tribal people. Besides this, many Vaidyas and Hakims practicing traditional system of medicine like Ayurveda, Siddha and Yunani were consulted. Detailed investigations were conducted on *Chlorophytum borivillianum* Santapau & Fernandes (Liliaceae), *Asparagus adscendens* Roxb and *Mucuna pruriens* L (DC) were obtained from Udaipur, Jobner, Jaipur and raised in nursery condition. Available literature, published phytochemical, ethno botanical and pharmacological data were also consulted for writing this review.

## 3. APHRODISIAC MEDICINAL HERBS

The area of natural product research is rapidly progressing from traditional medicine to modern medicine having proper scientific basis of its

usage. Erectile dysfunction and male sexual debilities are among the most explored areas in traditional medicine. A number of natural products, mostly plant based, have been claimed to cure erectile dysfunction and related male sexual debilities. These products often are aphrodisiac and have multi-fold effects on male reproductive system [22].

### 3.1 *Asparagus adscendens* Roxb

*Asparagus adscendens* Roxb. has many common names viz. Safed musli, Shatawari, Shatavar and Shatamuli in India. We conducted several studies on this plant which have been published. Several studies showed the effect of different medicinal herbs on the testes of experimental animals. *Asparagus adscendens* is usually found in all parts of India and also in forests of western Himalaya. The root of *Asparagus adscendens* is used in ayurvedic medicine as antipyretic, demulcent, nutritive tonic and for the improvement of fertility in males and females [23,24]. *Asparagus adscendens* has a promising role in modulation of various disorders such as leucorrhoea, diarrhoea, diabetes, dysentery, asthma, senile pruritus, antifungal, fatigue, antifilarial and sperm [25-27]. A study showed that *A. adscendens* root extract "200 and 300 mg/kg doses orally for 30 days" significantly increased testes weight and testicular tubular diameter [28].

Studies on the in vitro antioxidant activities of the root aqueous and methanolic extract of *Asparagus racemosus*; a plant belonging to the genus *Asparagus* have been documented [29]. *Asparagus adscendens* root ethyl acetate extract fraction have high antioxidant potentials and could be explored as a therapeutic agent for the treatment of free radical induced diseases [25]. *Asparagus adscendens* Roxb (Liliaceae) known as is claimed to be used in the treatment of seminal weakness [30], others use its stem as aphrodisiac [8].

Besides this, *Asparagus racemosus* Willd, *Asparagus filicinust* Buch-Ham- ex. D. Don., *Asparagus gonocladus* Baker and *Asparagus officinalis* Linn. have been reported to have medicinal value [8]. Musli is a suberect prickly shrub, with white tuberous roots. It is distributed in West Himalayas and Punjab to Kumaon. The underground part of *A. adscendens* and *A. racemosus* is dug out and eaten. The leaves, flowers and fruits are candied and pickled in different parts of the country [31].

### 3.2 *Withania somnifera*

*Withania somnifera* roots have many active components in the root, the most significant are alkaloids and flavonoids. It is reported to have positive effects on semen parameters [32]. The flavonoids have antioxidant activity and some alkaloids have been proved to reactivate the main free radical scavenging enzymes [33]. This was concluded to be due to the antioxidant activity of *W. somnifera* root [34]. Yet, *W. somnifera* stem presented spermicidal and antifertility activity [35].

### 3.3 *Chlorophytum borivilianum* (Safed Musli)

Safed Musli has been described in ancient Indian literature such as Bhavaprakash nighantu, Rasendra Sarsangrah, Raja Ballabh Nighantu as 'Vajikaran' or aphrodisiac which is a special type of immunomodulator [36]. In Ayurveda, *Chlorophytum borivilianum* belongs to the group of "Vajikaran Rasayana". The drug safed musali belongs to the various species of two different well known liliaceous genera viz., *Asparagus* L. and *Chlorophytum* Ker-Gowl [9,37]. Safed musli (*Chlorophytum borivilianum* Santapau & Fernandes (Liliaceae) is an eminent medicinal plant of India and is used in indigenous systems of medicine as a galactagogue and aphrodisiac [38,39]. *C. borivilianum* is a rich source of over 25 alkaloids, vitamins, proteins, carbohydrates, saponins, steroids, calcium, potassium, phenol, magnesium, resins, mucilage, and polysaccharides besides high quantity of simple sugars, mainly fructose, sucrose, glucose, galactose, xylose mannose [40]. *Chlorophytum borivilianum* is used [40]. It is used to cure physical illness and weakness, as an aphrodisiac agent and revitalizer. It is also used as general sex tonic, increasing body immunity, remedy for arthritis, antimicrobial, anti-inflammatory, antitumor agent, in diarrhoea, dysentery, gonorrhoea, leucorrhoea etc. diabetes, and curative for natal and postnatal problems along with for rheumatism and joint pains. It is reportedly used for rejuvenating, aphrodisiac, natural sex tonic properties and alleviating sexual disorders. *Chlorophytum borivilianum* has spermatogenic property and is found useful in curing impotency and is considered as an alternative 'Viagra' [40]. It is considered as a 'white gold' or 'divya aushad' in Indian systems of medicine. It is largely used as ethnic medicine by local healers of indigenous communities of India [38]. *C. borivilianum* root extract is an effective

immunostimulatory principle [40]. The inference that can be drawn from the present study is that the total ethanolic extract is superior over sapogenin fraction of the plant as far as immunostimulatory activity is concerned [39].

### 3.4 *Mucuna pruriens*

*Mucuna pruriens* is reported to contain many bioactive constituents, alkaloids, coumarins, flavonoids, alkylamines, including, and which may increase the antioxidant capacity of treated men.

*M. pruriens* increases semen volume, improves sperm quality, and regresses unspecific generation of reactive oxygen species in infertile subjects [19]. Testosterone is secreted by the Leydig cells under LH stimulation and is essential for promoting spermatogenesis. *Mucuna pruriens* seeds are a rich source of L-DOPA and its metabolites, which include epinephrine and norepinephrine. Though the mode of action of DOPA and catecholamines on human infertility is not yet established, this may be linked with the activation of the b-adrenergic system by increasing the cyclic adenosine monophosphate (cAMP) levels, which in turn regulates the carbohydrate metabolism, lipolysis of fat, and functioning of genitourinary and gastrointestinal tracts. There are a few reports that the levels of cAMP in the semen of oligozoospermic and azoospermic men are significantly reduced compared with levels in fertile men [41]. Moreover, it is also reported that patients treated with clomiphene citrate exhibit significantly elevated levels of cAMP in their seminal fluid, leading to an increase in sperm motility. It is well known that spermatogenesis is controlled by the hypothalamus and anterior pituitary working together.

Lipids constitute a major component of cellular membranes, and they play an important role in maintaining the structural and functional integrity of the spermatozoa [42]. Seminal plasma contains a typical combination of proteins, lipids, and carbohydrates, with a minor quantity of a variety of biomolecules and some metals [43]. The seminal plasma is characterized by abundance of cholesterol and phospholipids, mainly phosphatidyl ethanolamines and sphingomyelins and present for the most part in the form of high-density lipoprotein lipids [44]. Seminal plasma also contains high concentration of fructose, which is essential for normal sperm metabolism and also serves as a nutrient for

spermatozoa during their journey in the female genital tract [45]. The liquid component of semen providing a safe surrounding for spermatozoa, is the mixture of secretions from several male accessory glands, seminal vesicles, epididymis, including prostate, and Cowper's gland. The particular characteristic of lipid composition in seminal fluid allows a successful penetration of ovum by spermatozoa [46]. Antioxidant enzymes, namely superoxide dismutase, catalase, and glutathione peroxidase, as well as vitamins A, C, and E, continuously operate to maintain oxidant-antioxidant balance in seminal plasma [47,48]. The methanol extract of *M. pruriens* seeds has strong antioxidant activity, because it inhibits 1,1-diphenyl-2-picryl-hydrazyl and hydroxyl radical, and that it also has nitric oxide and super-oxide anion scavenging and hydrogen peroxide decomposing and reducing power [49]. *M. pruriens* helps in some central mechanism to decrease spermatorrhea, increase secretion of semen, and act as a restorative and invigorating tonic and aphrodisiac [50]. The biological basis and exact mechanism of action of *M. pruriens* on infertility is not well known. However, the beneficial effect may be attributed to its antioxidant and neurostimulatory properties [51].

## 4. DIABETES MELLITUS (DM) AND FERTILITY

Diabetes mellitus (DM), characterized by chronic hyperglycemia resulting from deficiency of insulin secretion, resistance to insulin action or both, is associated with long-term damage, dysfunction and failure of various organs [52]. Diabetic men have high percentage of sperm nuclear DNA fragmentation and apoptosis [53]. *C. borivilianum* root extract prevents impairment in sperm characteristics and morphology via preventing elevation of oxidative stress, apoptosis and free radicals levels of the sperm in diabetes [54]. This is achieved by maintaining sperm antioxidant level which could be related to free radical scavenging activity of the root extract by phenolic compounds. Further suggested that these effects could also be due to ability to maintain near normal serum FBG and HBA1c levels in diabetes [54]. Husbands of infertile couples with diabetes possess lower volume of ejaculates, sperm count and percentage of motile sperm as compared to healthy husbands of couples with proven fertility [55]. Administration of *C. borivilianum* root extract to diabetic rats alleviates oxidative stress via several mechanisms which include reduced amount of free radicals such as superoxide and nitric oxide and preservation of total antioxidant

capacity via maintaining near normal activity level of endogenous antioxidant enzymes. Additionally, a strong in-vitro free radical scavenging activity of the root extract further contribute towards the in-vivo free radical scavenging effects. The later effects may be attributed to higher amount of total phenolic content in the root extract as revealed by FTIR spectroscopic analysis. Meanwhile, ability of *C. borivillianum* root extract to lower FBG and HbA1c levels in diabetic rats could also help to reduce the risk of acquiring abnormal sperm morphology and characteristics and sperm oxidative stress [56,57]. Meanwhile, Hyperglycemia in rats diminished sperm count, seminal fluid fructose and antioxidant enzymes [58]. Husbands of infertile couples with diabetes possess lower volume of ejaculates, sperm count and percentage of motile sperm as compared to healthy husbands of couples with proven fertility.

## 5. PHARMACOLOGY

Increase in male sexual dysfunction, and its treatment with conventional aphrodisiac drugs with side effects lead to investigate the spermatogenesis and androgenesis augmentative efficacy of hydromethanolic (40:60) extract of root of *Chlorophytum borivillianum* (family - Liliaceae) against cyproterone acetate-induced subfertility in Wistar strain male albino rat [59].

*C. borivillianum* root aqueous extract prevents the decrease in sperm count, percentages of viability, forward motility, hypoosmotic swelling (HOS) and the increase in abnormal sperm percentage and caspase-3 level in diabetic rats [54]. Sperm lipid peroxidation product (LPO), nitric oxide (NO) hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) and levels, fasting blood glucose (FBG) and HbA1c were lower while total antioxidant capacity (TAC), superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and epididymal sperm density were higher in diabetic rats receiving *C. borivillianum* root extract treatment. This indicated that *C. borivillianum* root exhibited strong in-vitro free radical scavenging activity which may be due to the phenolic compound.

## 6. DISCUSSION

The drug safed-musali' belongs to the various species of two different well known liliaceous genera viz., *Asparagus* L. and *Chlorophytum* Ker-Gowl.9 *Chlorophytum tuberosum* is being used in the indigenous systems of medicine as a galactagogue and aphrodisiac [39]. *C.*

*borivillianum*, is being cultivated and marketed extensively in India and abroad for medicinal purposes [37]. The tuberous roots of other species of *Chlorophytum*, *Asparagus*, *Bombax* and *Orchids* are also sometimes called safed musali leading to confusion [39].

Diabetes induces oxidative-stress has been reported to cause peroxidation of sperm membrane lipid which might interfere with membrane fluidity and transport processes [60]. In view of this, appearance of various abnormal sperm shapes could be due to abnormal membrane or cellular and nuclear changes induced by diabetes [57]. The percentage of sperm viability was also reduced in diabetic rats consistent with reports in both rodents [61,62] and humans [63] In rats, diabetes could induce sperm apoptosis which resulted in reduced sperm viability [56].

*M. pruriens* helps in some central mechanism to decrease spermatorrhea, increase secretion of semen, and act as a restorative and invigorating tonic and aphrodisiac [64,50]. *Mucuna pruriens* is reported to contain many bioactive constituents, alkaloids, coumarins, flavonoids, alkylamines, including, and which may increase the antioxidant capacity of treated men. The methanol extract of *M. pruriens* seeds has strong antioxidant activity, because it inhibits 1,1-diphenyl-2-picryl-hydrazyl and hydroxyl radical, and that it also has nitric oxide and super-oxide anion scavenging and hydrogen peroxide decomposing and reducing power [49]. Recently the use of complementary and alternative medicines (CAMs) has increased in treating infertility [20]. Sexual function greatly affects individual's quality of life, the normal male sexual response cycle consists of five phases: libido, erection, ejaculation, orgasm and detumescence subsequently [21]. Oxidative stress-induced sperm damage has been suggested as an important pathological mechanism underlying male infertility [65]. The sperm could be protected from oxidative damage by endogenous antioxidant enzymes which are found both in sperm [66] and seminal fluid [67]. The sperm plasma membrane is susceptible to oxidation due to high content of polyunsaturated fatty acids (PUFA) [68]. Lipid peroxidation in sperm membrane can cause various impairments including decreased sperm motility [69]. Meanwhile, the decrease in seminal fluid antioxidant level was reported to contribute to male infertility in humans [70]. The biological basis and exact mechanism of action of *M. pruriens* on infertility is not well known. However,

the beneficial effect may be attributed to its antioxidant and neurostimulatory properties [51]. *Mucuna pruriens* seeds are a rich source of L-DOPA and its metabolites, which include epinephrine and norepinephrine. The mode of action of DOPA and catecholamines on human infertility is not yet established, it may be linked with the activation of the b-adrenergic system by increasing the cyclic adenosine monophosphate (cAMP) levels, which in turn regulates the lipolysis of fat, carbohydrate metabolism and functioning of gastrointestinal and genitourinary tracts. The levels of cAMP in the semen of azoospermic and oligozoospermic men are significantly reduced compared with levels in fertile men [41].

## 7. CONCLUSION

Traditional herbal medicines have a great potential and that has been established by our experiments as well as from literature. *C. borivillianum* root extract prevents impairment in sperm characteristics and morphology via preventing elevation of oxidative stress, apoptosis and free radicals levels of the sperm in diabetes through maintaining sperm antioxidant level which could be related to free radical scavenging activity of the root extract by phenolic compounds. The increased commercial exploitation of *Chlorophytum borivillianum* and low productivity of this endangered plant has raised the concern over its conservation. It has been envisaged that efforts should be made to standardize, encourage and popularize the cultivation of *Chlorophytum borivillianum* as a commercial crop. The studies available on toxicity, safety and quality of *Chlorophytum borivillianum* are inadequate for providing information on commercial utilization. More studies are needed to elucidate mechanisms underlying abnormal sperm appearances in diabetes. Treatment with *C. borivillianum* root extract prevents the increase in the amount of sperm lipid. These studies can help in developing future cures for very important diseases like diabetes and infertility and stopping or slowing the ageing process in mankind and will help the society for healthier life.

## DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for

any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

## CONSENT

It is not applicable.

## ETHICAL APPROVAL

It is not applicable.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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