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SHORT REVIEW

A Systemic Review on Use of Medicinal Plant for Management of Male Infertility

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Abstract

A recent issue with current society is the fall in male infertility. In 50% of instances, couple infertility is caused by the failure in spermatogenesis of the male partner. The male reproductive system is impacted by a variety of factors that lead to infertility, including genitourinary tract infections, endocrine abnormalities, immunological factors, lifestyle, stress, and drug-related damage. There are medications and therapies for male infertility, but they are not very effective, have harmful side effects, and are contraindicated. Plants are among the greatest natural cures for illnesses since they have very few side effects and include a variety of phytoconstituents from different chemical classes. Depending on their concentration, plant bioactive such as flavonoids, polyphenols, glycosides, alkaloids, and terpenoids might have a variable effect on sperm quality - either positively or adversely. These compounds have been suggested as organic reactive oxygen species scavengers for the treatment of male infertility. This review makes an effort to compile the available information and offer perspectives for upcoming investigations on how plants affect male gonads. This review summarizes the most recent research on the use of phytoconstituents to increase testosterone production, support healthy spermatogenesis, and prevent age-related degenerative illnesses linked to low levels of testosterone. This review includes information on about 45 herbal plants that have been published in several papers. The articles have several headings, including plant taxonomy, bioactive components, impacts on fertility, and medical applications. This review provides information on the applications of natural sources for male fertility enhancement and their potential mechanisms of action.

Keywords: Male Infertility, Medicinal Plant, Phytochemical, Reactive Oxygen Species

1. Introduction

Male Infertility (MI) is receiving more attention as a result of its widespread occurrence worldwide and evidence of deterioration in the quality of young, healthy men's sperm. Male infertility is defined as the inability to conceive after a year or more of regular unprotected sexual intercourse by the couple or female partners of a couple[1]. Male infertility is a new problem in the present time, the rising trend of couples having children later in life, combined with unhealthy lifestyles and negative environmental factors, is lowering overall fertility rates[2]. A wide range of factors, including poor testicular development, reproductive system illnesses, high scrotal temperatures, immunological problems, endocrine abnormalities, lifestyle choices, environmental factors, nutritional considerations, and many others, have an impact on men's ability to reproduce[3]. However, 30-50% of Male infertility cases causes are unexplained and classified as idiopathic. Recently, it was suggested that idiopathic infertility could be explained by the presence of high amounts of Reactive Oxygen Species (ROS)[4]. Furthermore, Jensen *et al.* revealed men with obesity exhibited decreased sperm count, concentration, and percentages of healthy spermatozoa[5]. The present medications and treatments are ineffective, have unpleasant side effects, and are not appropriate for everyone. However, several

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natural fertility enhancers are used in the treatment of infertility[6]. Natural antioxidants derived from botanical materials have recently attracted a lot of attention as potential replacements for manufactured medicines. Phytopharmaceuticals appear to be safe and effective; however, little scientific attention has been paid to them. Herbs are one of the best remedies for the problems encountered because they contain a variety of phytoconstituents from various chemical classes. These phytoconstituents, such as tannin increase male infertility, alkaloids treat infertility, human sperm parameters are known to be improved by saponins, flavonoids enhance male sperm quality by reducing the detrimental effects of metals on sperm quality, terpenoids reduce seminal oxidative stress, and the antioxidant found in phytochemicals may be able to help prevent cellular damage to erectile tissues[7]. The goal of the current review is to provide a concise summary of the research that has been done on numerous herbs that have been investigated for their ability to increase male fertility and act as aphrodisiacs. The purpose of a systematic review on the use of medicinal plants for the management of male infertility is to systematically and comprehensively evaluate the existing body of scientific literature to provide evidence-based insights into the efficacy, safety, and potential benefits of using medicinal plants in addressing male infertility.

2. Significance of Male Infertility as a Global Health Issue

Male infertility is a significant global health issue with far-reaching implications for individuals, families, and society as a whole[8]. Understanding its significance involves considering the following aspects:

2.1 Prevalence

Male infertility is a prevalent condition worldwide. It is estimated that approximately 7-10% of men of reproductive age experience infertility. This prevalence has been increasing over the years, likely due to various environmental and lifestyle factors[8].

2.2 Reproductive Health

Infertility can cause immense emotional and psychological distress for couples who are unable to conceive naturally. It often leads to feelings of inadequacy, stress, and relationship strain. This can impact overall mental health and well-being[8].

2.3 Family Planning

Infertility can hinder family planning and the realization of desired family size. Couples may need to resort to expensive and emotionally taxing Assisted Reproductive Technologies (ARTs) like *In Vitro* Fertilization (IVF) or surrogacy to have children, which may not always be successful[9].

2.4 Economic Implications

Treating male infertility and its associated complications can be financially burdensome for individuals and healthcare systems. Costs include diagnostic tests, fertility treatments, and potential costs related to the emotional and psychological support required.

2.5 Demographic Trends

In some regions, declining sperm counts and quality have raised concerns about the long-term demographic consequences. A decline in male fertility can influence population growth and age structures[9].

2.6 Health and Lifestyle Factors

Male infertility is often associated with underlying health issues such as obesity, diabetes, hormonal imbalances, and exposure to environmental toxins. These same factors can contribute to other chronic health conditions, making male infertility a potential marker of overall health (Figure 1).

2.7 Environmental Factors

Environmental factors, including exposure to endocrine-disrupting chemicals, pesticides, and pollution, have been linked to reduced male fertility. Addressing male infertility may involve addressing these environmental issues[7].

2.8 Sexual and Reproductive Rights

The inability to conceive and have biological children can be seen as a matter of sexual and reproductive rights. Access to fertility treatments and education about infertility are important components of reproductive rights.

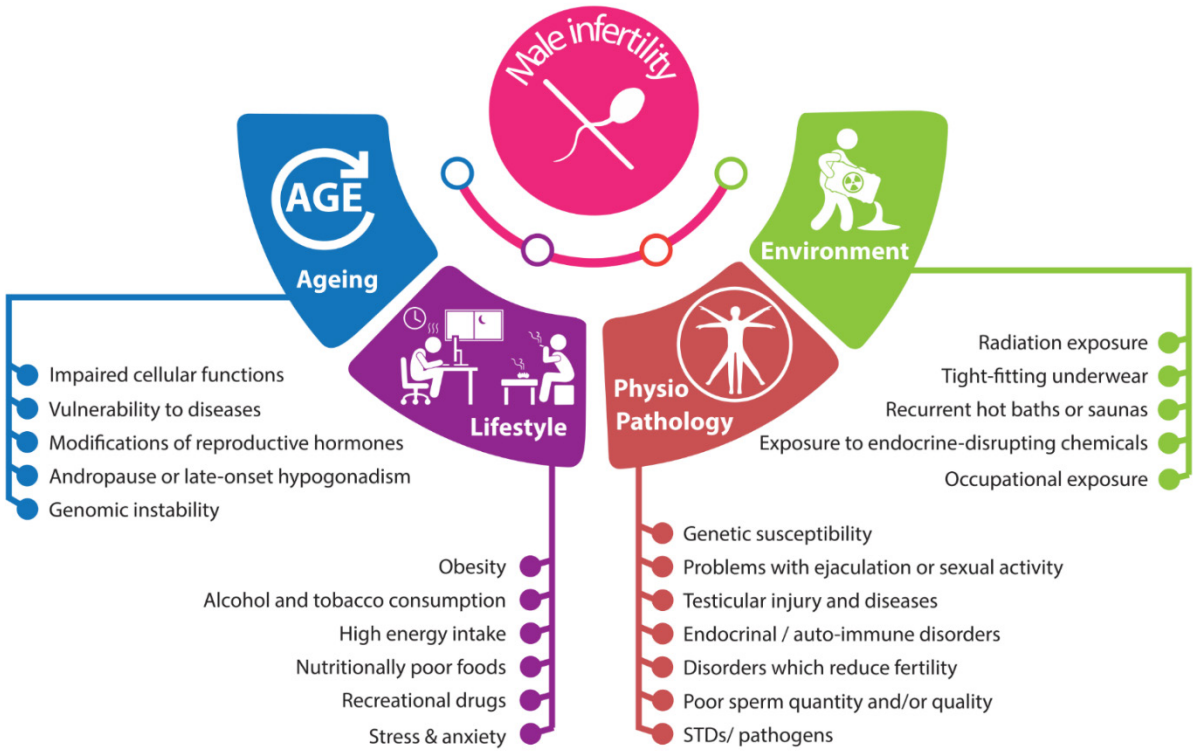

Figure 1. Cause and etiology of male infertility.

2.9 Genetic Considerations

Male infertility can also have genetic underpinnings, and understanding the genetic basis of infertility can have broader implications for genetic counselling and family planning[7].

2.10 Public Health Implications

Male infertility is not only a personal concern but also a public health issue. Addressing the root causes and promoting male reproductive health can lead to healthier future generations. Male infertility is significant as it affects not only individual reproductive health but also has broader implications for emotional well-being, family dynamics, healthcare costs, and even demographic trends[8].

3. Etiology and Pathogenesis of Male Infertility

Male infertility is a complex condition with various potential causes (etiology) and underlying mechanisms (pathogenesis). Understanding the factors that contribute to male infertility is crucial for diagnosing and effectively managing the condition. Here, we will explore the etiology and pathogenesis of male infertility[5]:

3.1 Sperm Production Disorders (Spermatogenic Failure)

3.1.1 Primary Testicular Causes

These include genetic factors (such as Klinefelter syndrome), testicular trauma, infections (e.g. mumps orchitis), radiation exposure, and chemotherapy. These factors can disrupt normal sperm production in the testes[9].

3.1.2 Varicocele

A varicocele is the enlargement of veins within the scrotum, which can increase testicular temperature and negatively impact sperm production[10].

3.1.3 Hormonal Imbalances

Conditions like hypogonadism (low testosterone production) and pituitary gland disorders can affect the hormonal signals required for spermatogenesis.

3.2 Sperm Transport Disorders

3.2.1 Obstruction

Blockages or congenital abnormalities in the reproductive tract, such as the vas deferens or ejaculatory ducts, can prevent sperm from being ejaculated[10].

3.2.2 Retrograde Ejaculation

In this condition, semen is directed backwards into the bladder instead of outward through the penis during ejaculation. This may result from neurological issues, surgery, or certain medications.

3.3 Sperm Quality and Function

3.3.1 Sperm Morphology

Abnormal sperm morphology (size and shape) can affect sperm's ability to fertilise an egg[10].

3.3.2 Sperm Motility

Poor sperm motility, or asthenozoospermia, makes it challenging for sperm to reach and penetrate the egg (Figure 2).

3.3.3 Sperm DNA Damage

High levels of DNA fragmentation in sperm can impair fertility and increase the risk of miscarriages[9].

3.4 Lifestyle and Environmental Factors

3.4.1 Smoking and Alcohol

Excessive smoking and alcohol consumption can negatively impact sperm quality[8].

3.4.2 Drug Use

Some recreational drugs, like marijuana and anabolic steroids, may reduce sperm production and motility[7].

3.4.3 Environmental Toxins

Exposure to pollutants, pesticides, and endocrine-disrupting chemicals can disrupt male reproductive function[11].

3.5 Infections and Inflammation

3.5.1 Infections

Certain infections, such as Sexually Transmitted Infections (STIs), can lead to inflammation of the

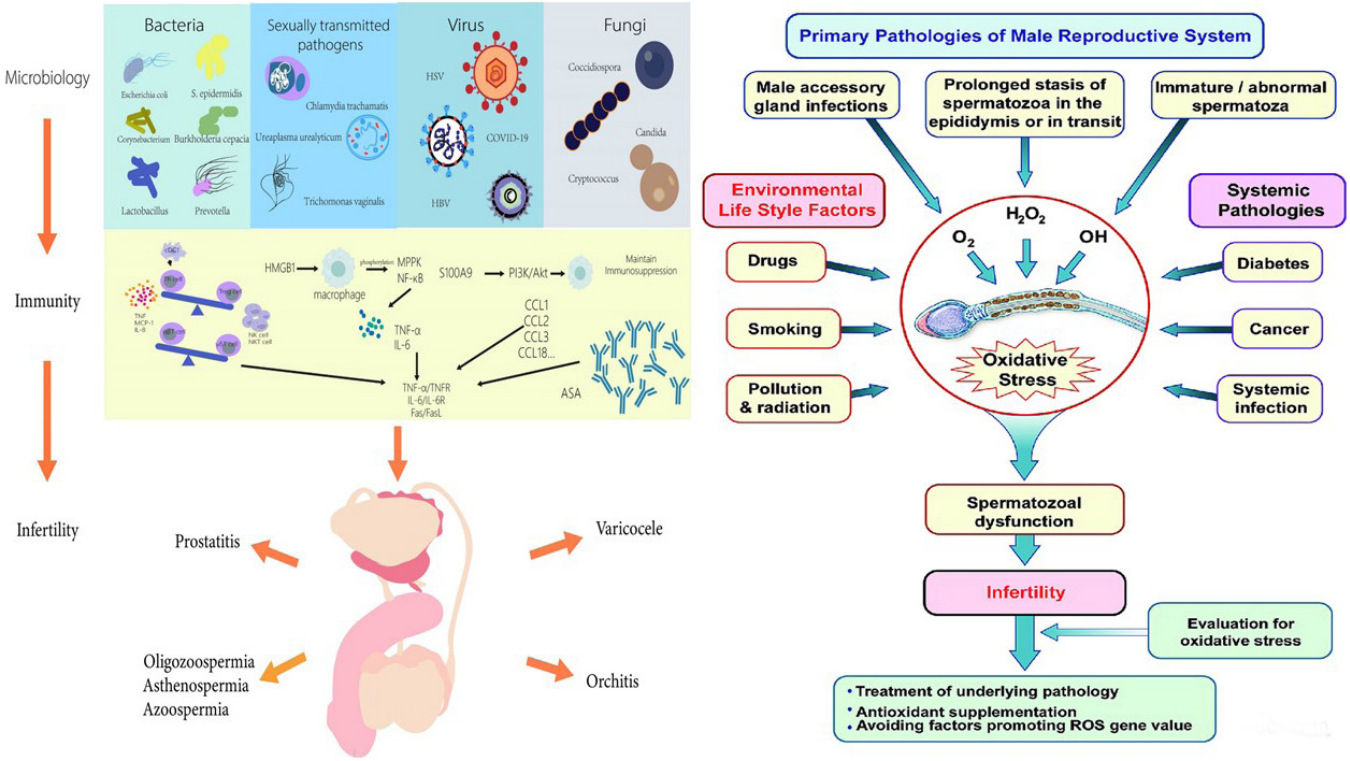

Figure 2. Etiology and pathogenesis of male infertility.

reproductive organs and affect sperm production and function[11].

3.6 Genetic Factors

3.6.1 Genetic Abnormalities

Inherited genetic mutations or chromosomal abnormalities can result in male infertility. Conditions like Y-chromosome microdeletions or genetic disorders like cystic fibrosis can impact fertility[10].

3.7 Systemic Diseases

3.7.1 Chronic Illnesses

Conditions like diabetes, kidney disease, and autoimmune disorders can affect male fertility through various mechanisms.

3.8 Medications

3.8.1 Certain Medications

Some medications, such as chemotherapy drugs, antihypertensives, and antidepressants, can interfere with sperm production and function[11].

3.9 Psychological Factors

Stress and Psychological Factors: Chronic stress, anxiety, and depression can have physiological effects that may contribute to male infertility.

3.10 Age

3.10.1 Advanced Age

While not as pronounced as in women, advanced paternal age has been associated with decreased sperm quality and an increased risk of certain genetic disorders in offspring[8].

4. Factors and Endocrine Causes in Male Infertility

Male infertility can result from various factors, including endocrine (hormonal) causes. These factors can disrupt the delicate hormonal balance necessary for normal sperm production and reproductive function. Here are some of the key factors and endocrine causes of male infertility[8]:

4.1 Hypogonadism

This condition is characterised by low testosterone levels, which can impair sperm production. Primary hypogonadism occurs when the testes do not produce sufficient testosterone, while secondary hypogonadism results from problems in the hypothalamus or pituitary gland that affect hormone signaling[11].

4.2 Hypothyroidism

An underactive thyroid gland can lead to reduced sperm production and impaired sperm motility. Thyroid hormones play a crucial role in regulating metabolism and overall health, including reproductive function.

4.3 Uncontrolled Diabetes (Type 1 or Type 2)

High blood sugar levels can damage blood vessels and nerves that are essential for the normal functioning of the male reproductive system. This can result in erectile dysfunction and reduced sperm quality[8].

4.4 Excess Body Fat

Obesity is associated with hormonal imbalances, including increased estrogen levels and decreased testosterone. These changes can negatively impact sperm production and function[11].

4.5 Congenital Adrenal Hyperplasia (CAH)

This genetic disorder can lead to the overproduction of androgens (male sex hormones) by the adrenal glands. Elevated androgen levels can affect the balance of hormones required for fertility[11].

4.6 Klinefelter Syndrome

This genetic condition results from an extra X chromosome (XXY) and can lead to abnormal testicular development and impaired hormone production.

4.7 Testicular Tumours

Certain tumours, including Leydig cell tumours, can disrupt normal testicular function and hormone production[10].

4.8 Medications

Some medications, such as anabolic steroids, certain antifungal drugs, and chemotherapy agents, can negatively affect hormone levels and sperm production.

4.9 Chronic Stress

Prolonged stress can lead to the release of stress hormones, which can interfere with the hormonal balance required for fertility[8].

4.10 Exposure to Endocrine-disrupting Chemicals

Some environmental toxins, such as pesticides, industrial chemicals, and plastics containing Bisphenol A (BPA), can mimic or interfere with hormonal signalling in the body, potentially affecting male fertility.

Identifying the specific endocrine causes of male infertility often requires a comprehensive evaluation by a healthcare provider, including hormone testing and a thorough medical history. Once the underlying hormonal issues are diagnosed, appropriate treatments or interventions can be recommended to address the root causes and improve fertility (Figure 3). This may include hormone replacement therapy, lifestyle changes, or other medical interventions, depending on the specific diagnosis[11]. The key findings related to the Factors and endocrine causes in male infertility highlight the diverse range of factors that can contribute to this condition. The relevance of these findings lies in the importance of accurate diagnosis, individualized treatment plans, and a holistic approach to address the specific underlying causes in each case of male infertility. A comprehensive assessment, including medical, lifestyle, and psychological factors, is essential to guide effective management and improve the chances of achieving a successful pregnancy[12].

5. Brief Overview of Medicinal Plants and their Historical use in Traditional Medicine for Male Fertility

5.1 *Tribulus terrestris*

Tribulus terrestris (TT), a widespread weed primarily found in tropical regions, is a member of the Zygophyllaceae family. Traditional Chinese medicine uses TT leaves to treat gastrointestinal issues, bladder stones, and issues with male reproduction[12]. Saponin rich in the *Tribulus* genus is protodioscin, which stimulates Sertoli cells and induces germ cell proliferation and seminiferous tubule growth by converting testosterone into dihydrotestosterone via

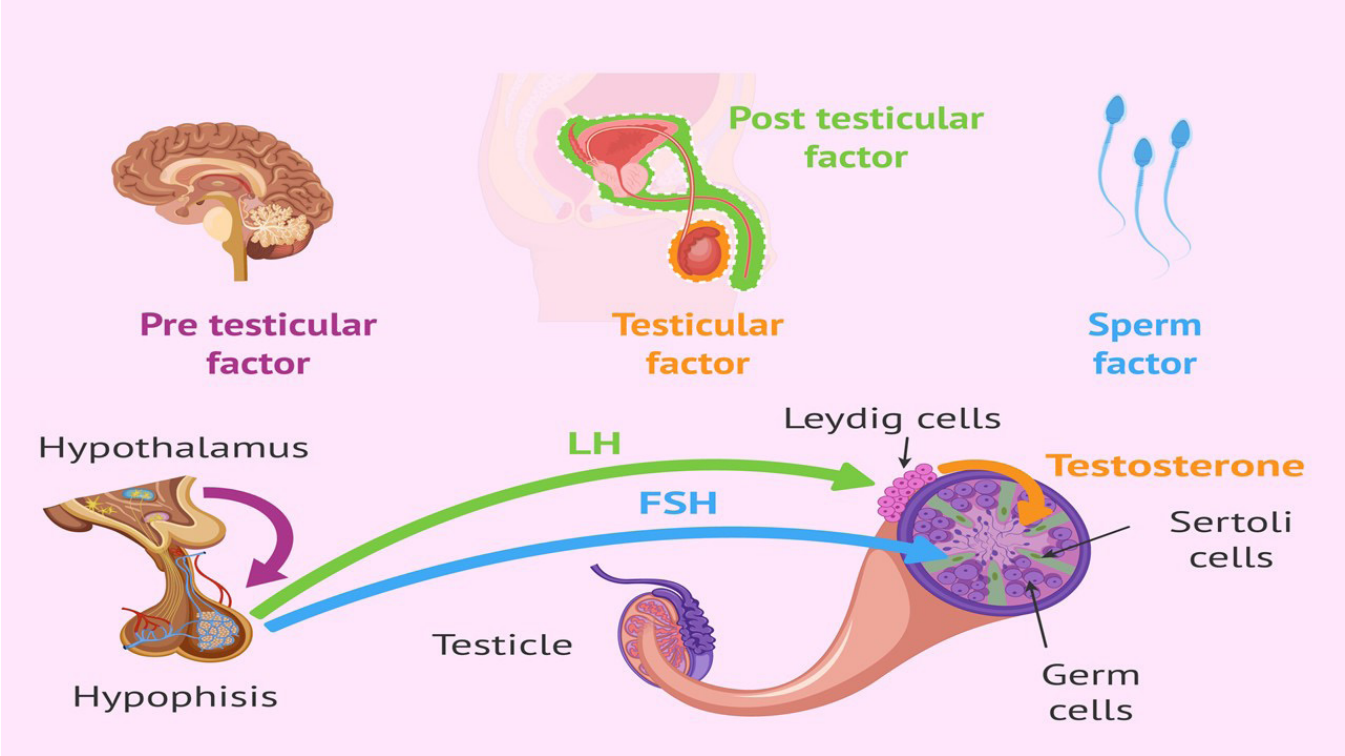

Figure 3. Factors and endocrine causes in male infertility.

5-reductase activity, thereby supporting the use of TT as an MI-enhancing agent[13]. Haghmorad *et al.,* revealed that the biological actions of TT's active ingredients, protodioscin and protogracilin, increase libido and spermatogenesis by up-regulating testosterone and LH. Testosterone stimulates spermatogenesis and may improve spermatogenesis[13]. It is analysed by Ștefănescu *et al.*, in oxidative stress, nitric oxide and ROS react in the vasculature and form reactive nitrogen species, which plays a role in the pathogenesis of erectile dysfunction, the antioxidant effect of TT could contribute to the booster action in erectile dysfunction[14]. Further, TT strengthens the sperm cells' acrosome morphology and enhances the acrosome reaction, as measured by the acrosin reaction, resulting in a rise in fertility[4].

5.2 *Morinda officinalis*

Morinda officinalis (MO) belongs to the Rubiaceae family. Male rats exposed to 900 MHz microwaves at 218 m/cm^2 radiation levels for 10 days had dramatically better sexual performance after receiving 40 g/kg of MO root aqueous extracts for 2 weeks. The number of seminiferous cells or sperm in the testis and epididymis greatly rise, whereas the levels of LH and GnRH significantly reduced, and the protein expression of GnRH in the hypothalamus significantly decreased. Additionally, MO oligosaccharides can guard against H2O2 damage to human sperm DNA[15]. The study showed that Bajijiasu, a bioactive substance from MO, activated the cell's Nrf2-mediated signalling pathway, upregulating P-gp expression. Moreover, Bajijiasu increases P-export gp's activity, which simultaneously reduces the toxicity of doxorubicin to cell[16].

5.3 *Withania somnifera*

Withania somnifera, also known as Indian ginseng, poison gooseberry, winter cherry, or *Ashwagandha* in *Ayurvedic* medicine, has been used in traditional Indian systems of medicine for more than 2500 years. Steroid lactones containing ergostane, including withanone, withaferin, withanolides, withanolide C, sitoindosides, and around 0.2% alkaloids, are the active ingredients in *W. somnifera* root extract. The results of the experiments demonstrated that an aqueous extract of *W. somnifera* influences the seminiferous tubules, inducing folliculogenesis in young female rats, and stimulating the development of the testicles and spermatogenesis in young Wistar rats[17]. Sengupta *et al.,* 2018 reported *W. somnifera* increases antioxidant levels, improves sperm quality (concentration and motility), lowers seminal LPO levels, stress and serum cortisol levels, and reduces the generation of ROS[18]. Also, male rats were given a methanolic extract of *W. somnifera* root at a dose of 3000 mg/kg/day for seven days, which significantly improved penile erectile dysfunction, sexual performance, and libido impairment. Studies have demonstrated that ashwagandha extracts decreased morning cortisol and were linked to an increase in male testosterone levels. According to a clinical trial conducted in 2019 by Nasimi *et al.*, *W. somnifera* treatment significantly improved sperm morphology (25.56%), progressive motility (21.42%), and mean sperm count (12.5%)[14].

5.4 *Zingiber officinale*

The Zingiberaceae family includes *Z. officinale*, widely known as ginger (rhizomes). Since the 13th century, people have known about ginger's health benefits. According to a study, ginger appears to have both androgenic activity and potent antioxidant qualities (a result of the existence of active phenolic chemicals). Sperm produced by ginger have normal morphology and better-integrated chromatin as a result of the antioxidant and androgenic effects of the spice. All specialized sperm fertility markers as well as the biological characteristics of sperm (number, overall motility, survival rate, and normal morphology) are enhanced by ginger. Additionally, a testicular histological study showed progress. The authors concluded that the antiapoptotic, antioxidant, and free-radical scavenging properties of ginger may be responsible for its protective effects. Furthermore, Sharma *et al.*, found that administering methanolic or watery extracts of *Z. officinale* orally for 65 continuous days to male diabetic *rats* (rendered by alloxan) enhanced sperm count, sperm motility, and sexual blood testosterone levels[6].

5.5 *Curcuma longa*

The perennial plant *Curcuma longa* (Linn.), also known as turmeric, is a member of the Zingiberaceae family. *C. longa* extract contains phytochemicals such as flavonoids, phenolics, and saponins that can

pass through the blood-testis barrier and reestablish the seminiferous tubules' microenvironment to restore normal spermatogenesis while also protecting against the effects of cimetidine[19]. In this regard, Ara *et al.* demonstrated that turmeric protects against the harmful effects brought on by butylparaben and increases sperm count in rats exposed to the chemical. Additionally, 100 nM of curcumin dramatically enhanced spermatozoa's motility in asthenozoospermic people via enhancing mitochondrial activity[20]. According to the study, curcumin can increase sperm motility without regard to dose. The effects of a high-fat diet on blood testosterone levels and abnormal spermatogenesis and apoptosis were mitigated by curcumin. Curcumin may also prevent the apoptosis that is caused by palmitic acid in these cells and restore testosterone synthesis[21].

5.6 Cinnamon

Cinnamomum zeylanicum Blume belongs to the family Lauraceae and was administered for 4 weeks to male rats at a dose of 75mg/kg resulting in higher levels of total serum testosterone, sperm quality indicators, superoxide dismutase, catalase, and glutathione peroxidase and lowers the level of malondialdehyde (Table 1). Compared to the control group, cinnamon (75mg/kg) and ginger (100mg/kg) enhanced blood total testosterone, LH, FSH, sperm counts, sperm viability, and sperm motility in the experimental groups[22] an optimal phytotherapy remains an elusive challenge. Aim of the review: We sought to critically analyze the evidence in the phytotherapic literature beyond the effects of tribulus on testosterone (T. Additionally, cinnamon enhances testicular and epididymal weights while improving sperm quality, lowering LPO levels, and enhancing apoptotic index[23] herbal medicines are known to help in the treatment of various diseases, as rich sources of antioxidants and minerals. Objectives: To study the effect of *C. zeylanicum*.

5.7 *Phoenix dactylifera*

Azubuike *et al.,* discovered that date fruit extracts have a protective effect against the pathophysiologic effects of cypermethrin exposure. Besides this, date fruit extracts contain estrogenic materials like gonad-stimulating compounds, which boost MI. Ahmed *et al.*, recommended Ajwa dates to treat MI because it has beneficial ingredients called ferulic acid. Ferulic acid has recently been demonstrated to reduce intracellular cAMP and cGMP levels, scavenge oxygen free radicals, and enhance sperm motility. Pretreatment with Ajwa dates significantly decreased necrosis and restored normal spermatogenic cell layer counts. This may be due to several antioxidant bioactive components in date extract that can prevent LPO from occurring[24].

5.8 *Panax ginseng*

Ginsenoside isolated from *P. ginseng* stems and leaves significantly improved Heat stress-induced morphology patterns, increased spermatocytes and decreased oxidative stress. These findings suggest that the protective effects of ginsenoside might be due to the suppression of the over-activated MAPK signalling pathway[25]. Previous research has found that ginseng increases spermatogenesis by increasing the expression of a glial cell-derived neurotrophic factor in sertoli cells and testicular cAMP-responsive element modulators. In light of this, it was proposed that ginsenosides' effects on sperm production are caused by the activation of steroid hormone receptors It's important to note that while these medicinal plants have a history of use in traditional medicine for male fertility, their effectiveness is not universally established, and scientific research on their efficacy is ongoing[26]. Furthermore, the use of medicinal plants should be approached with caution, as not all plants are safe or suitable for everyone, and interactions with medications or underlying health conditions may occur. Modern research aims to provide a more evidence-based understanding of the potential benefits and risks associated with the use of these medicinal plants for male fertility. It is advisable for individuals seeking to use medicinal plants for fertility concerns to consult with a qualified healthcare professional for guidance and to ensure their safety and efficacy[27] restore balance in the body, help the body to heal itself, reduce stress, boost energy, and enhance the immune system. The aim of this review was to assess current evidence that ginseng improves sperm quality. Materials and Methods: We searched twelve databases (PubMed, EMBASE, AMED, the Cochrane Library, five Korean medical databases, and three Chinese medical databases.

Table 1. Phytoconstituents in plants beneficial for male infertility improvement

S. No.	Plant	Family	Plant part	Bioactive compound	Type of metabolite	Activity	Reference
1	*Acacia senegal*	Leguminosae	Bark	Gum Arabica	Polysaccharide	Aphrodisiac activity	28
2	*Alpinia galanga*	Zingiberaceae	Rhizomes	Galangin, alpinin, kampferide	Flavonoid	Improve spermatogenesis	
3	*Allium cepa* L.	Liliaceae	Outer scale	Spiraeoside	Flavonoid	Promote spermatogenes-is	29
4	*Anacyclus pyrethrum*	Asteraceae	Root	anacyclin, pellitorine, hydrocarolin,	Alkaloid, flavonoids	Increase sperm count, sperm viability and motility.	30
5	*Ananas comosus*	Bromeliaceae	Stem	Bromelain	Enzyme	Inhibit testis dysfunction	6
6	*Argyreia nervosa*	Convolvulaceae	Root, flower, leaf,	Ergine	Ergoline Alkaloids	Aphrodisiac activity	31
7	*Berberis vulgaris*	Berberidaceae	Root	Berberine	Isoquinoline alkaloid	Protecting the cell against ROS destructive damage, improves sperm count, motility and morphology.	6
8	*Boesenbergia rotunda*	Zingiberaceae	Plant	1, 5-cineole, Boesenbergin A, dl-Pinostrobin corphor, Chromene	Flavonoid,	Increase sperm viability, motility and count.	32
9	*Boswellia sacra*	Cordycipitaceae	Plant	Boswellic acid	Terpenoid	Increases spermatogenesis and sperm motility	33
10	*Carduus crispus*	Asteraceae	Flower bud	Apigenin	Flavonoids	Apigenin improves spermatogenesis via its effect on testicular epigenetics.	4
11	*Castanea sativa Miller*	Fagaceae	Leaves	Rutin, hesperidin, quercetin, apigenin	Flavonol, glycoside	Scavenging activity	23
12	*Cinnamomum zeylanicum Blume*	Lauraceae	Bark	Cinnamaldehyde	Flavonoid	Increase the sperm population, motility and viability	34
13	*Citrullus vulgaris*	Cucurbitaceae	Seed	Lycopene, beta caroteen	Antioxidant	Protect sperm DNA from free radicals and increase blood testis barrier stability.	34
14	*Corchorus depressus*	Tiliaceae	Plant	Diosgenin, apigenin, luteolin, depressonol A	Saponin, Flavonoids	Aphrodisiac activity	35

Table 1. Continued...

S. No.	Plant	Family	Plant part	Bioactive compound	Type of metabolite	Activity	Reference
15	*Crataegus aronia*	Rosaceae	Plant	Hydroxycinnamic acids, flavonol-O-glycoside 2, acetylvitexin-200-O-rhamnoside	Flavonoid, Proanthocyanidins	Increases epididymis weight, sperm count, and motility.	36
16	*Crataegus monogyna*	Rosaceae	Fruit, leaves	Chlorogenic acid, hyperoside and rutin	Phenol	Improve sperm quality by preserving the sex organs' functions.	36
17	*Curcuma longa*	Zingiberaceae	Rhizomes	Curcumin	Phenol	Inhibiting reactive oxygen species reproduction through nuclear factor erythroid 2-related factor 2 activation.	20
18	*Cuscuta chinensis* Lamark	Convolvulaceae	Seed	Astragalin	Flavonoid	Significantly improve overall sperm quality, thereby enhancing fertility.	14
19	*Aucuba japonica*	Garryaceae	Seed	Aucubin	Iridoid glycoside	Mitigated the sperm abnormalities (head/midpiece/tail), the number of dead sperms, and proapoptotic proteins.	37
20	*Eruca sativa*	Brassicaceae	Seed	Erucin, Kaempferol	Glucosinolate, flavonoids	Improve testicular steroidogenesis, keeping Leydig cells, and improving oxidative stress status.	38
21	*Eurycoma longifolia*	Simaroubaceae	Root	Quassinoids and canthin-6-one	Alkaloid	Improves erectile function	38
22	*Ginkgo biloba*	Ginkgoaceae	Leaves	Quercetin, kaempferol	Flavonoid	Improve sperm production	39
23	*Hygrophila auriculata*	Acanthaceae	Seed	Uronic, linoleic acids	Polyunsaturated fatty acid	Increases testosterone level and stimulates Leydig cells	40
24	*Lycium barbarum*	Solanaceae		Sitosterol	Phytosterol	Improve sperm production	41
25	*Morinda officinalis*	Rubiaceae	Root	Monotropein deacetyl asperulosidic acid	Monoterpenoid	Increase in testosterone level and improve sperm quality	14

Table 1. Continued...

S. No.	Plant	Family	Plant part	Bioactive compound	Type of metabolite	Activity	Reference
26	*Mucuna pruriens*	Fabaceae	Seed	Ursolic acid, β-sitosterol, prurienidine	Saponin,	Increases in mounting frequency, erections intromission frequency and ejaculation latntromission latency, postejaculatory interval and inter-intromission inter valency, and decreases in mounting latency.	34
27	*Myristica fragrans*	Myristicaceae	Seed	Eugenol	Volatile oil	An increase in sexual activity, mounting and intromission rates, intromission latency, frequency of erections, rapid flips, long flips, and the sum of the penile reaction with penile stimulation.	42
28	*Nelumbo nucifera* Gaertn	Nelumbonaceae	Petals	Quercetin	Flavonoid	Enhance sperm viability.	39
29	*Nigella sativa*	Ranunculaceae	Seed	Thymoquinone	Essential oil	Improve semen quality[9].	40
30	*Ocimum tenuiflorum*	Lamiaceae	Leaves	Eugenol, ursolic acid, rosmarinic acid	Volatile oil, Terpenoid	Increases sperm quality and prevents testicular degeneration.	43
31	*Panax ginseng*	Araliaceae	Leaves, stem	Ginsenosides	Saponin	Improve sperm concentration, morphology, viability, and motility.	44
32	*Peltophorum africanum*	Fabaceae	Leaves	Quercetin, kaempferol	Flavonoids	Increases testosterone level	44
33	*Phoenix dactylifera*	Arecaceae	Fruit	Ferulic acid	Phenol	Improves spermatogenesis	45
34	*Prosopis cineraria*	Fabaceae	Unripe fruit	Apigein, Quercitin	Flavonoid	Increases the sperm volume and count.	46
35	*Punica granatum*	Punicaceae	Fruit	Anthocyanins	Phenol	Increases daily sperm production and epididymal sperm number and spermatogenesis.	17

Table 1. Continued...

S. No.	Plant	Family	Plant part	Bioactive compound	Type of metabolite	Activity	Reference
36	*Rumex cyprius Murb.*	Polygonaceae	Leaves	Hexadecanoic acid, quercetin-3-O-alpha-L-rhamnopyranoside	Flavonoids	Improve spermatogenesis	42
37	*Serenoa repens*	Arecaceae	Plant	B-sitosterol	Sterol	Aphrodisiac activity	
38	*Terminalia chebula*	Combretaceae	Fruit	Arjungenin, Chebuloside, Gallagic acid,	Triterpenoid Ellagitannin	Aphrodisiac activity	47
39	*Solanum nigrum*	Solanaceae	Leaves	Solasonine, coumarins, carpesterol	Saponin, alkaloids,	Improve sperm quality, hormonal levels, testis and epididymis weights, and haematology parameters.	48
40	*Tribulus terrestris*	Zygophyllaceae	Leaves, Fruit, Flower	Protodioscin	Saponin	Stimulates Sertoli cells and induces germ cell proliferation and seminiferous tubule growth by converting testosterone into dihydrotestosterone.	14
41	*Trigonella foenum-graecum*	Fabaceae	Seed	Vitexin	Phenolic flavonoid	Improved sperm quality and sexual function.	48
42	*Turnera diffusa* Willd.	Turneraceae	Leaves	Beta-sitosterol, arbutin, gonzalitosin,	Sterol, Flavonoid, glycoside	Increases in proportion of ejaculation.	37
43	*Withania somnifera*	Solanaceae	Root, plant	Withaferin-A, Withanolide-D and Withanone	Terpene	Improve metabolic pathway and energy metabolism in semen, improve reproductive hormone and semen quality.	38
44	*Zingiber officinale*	Zingiberaceae	Rhizome	Gingerol, beta-caroten, quercetin, lutein, lycopene,	Flavonoid, tannin, volatile oil	Increase in volume of seminiferous tubules, enhance sperm count and testosterone level.	44
45	Grapes	Vitaceae	Seed	Proanthocyan-idins	Phenol	The antioxidant effect improves the gonado-somatic index and boosts testosterone levels.	39

6. Discussion

Studies indicate that the prevalence of MI is rising, and it has grown to be an important healthcare issue. Pre-clinical and clinical studies have examined inappropriate eating habits like eating a high-fat diet, leading a sedentary lifestyle, and hereditary and environmental variables affecting fertility in males[48]. Sperm characteristics are a major factor in this problem. However, the underlying cause is still unknown in 40%-50% of cases. There is evidence that one of the most important aspects in the etiology of MI is the quantity and quality of spermatogenesis. The active process of spermatogenesis requires a healthy intake of nutrients, minerals, and antioxidants. One of the potential causes of MI is considered to be a disruption in the balance between these nutrients[8] couple infertility is attributable to the male partner, mainly due to a failure in spermatogenesis. In recent times, the crucial role that modifiable lifestyle factors play in the development of infertility have generated a growing interest in this field of study, i.e. aging, psychological stress, nutrition, physical activity, caffeine, high scrotal temperature, hot water, mobile telephone use. Several studies have investigated associations between semen quality and the presence of lifestyle stressors i.e. occupational, life events (war, earthquake, etc. The majority of plant extracts are wealthy sources of bioactive substances including phenolic components like phenols, sterols, lignans, flavonoids volatile oils, polyphenols, and saponins as well as folic acid, bio-trace elements like calcium, magnesium, potassium, zinc, phosphorus, copper, and iron. Numerous phytomedicines have been demonstrated to enhance spermatogenesis, sperm parameters (such as motility, count, and viability), Leydig cell counts, seminiferous tubule diameters, sperm abnormality reduction, histopathological recovery enhancement, sexual stimulation (such as erection, intromission, and ejaculatory latency enhancement), and sperm concentration and motility in ejaculation volume[49]. Medicinal plants' effective mechanisms for improving reproductive system performance include antioxidant activities: they can increase antioxidant enzymes such as superoxide dismutase, catalase, glutathione peroxidase, peroxidase activity, and alkaline phosphatase activity, which act as a defence system against ROS and can effectively scavenge free radical[50]. Effect of plant extracts on the relaxation of the cavernous muscle: plant compounds may aid in erection by relaxing the cavernous muscle and phosphodiesterases, boosting the production and release of Nitric Oxide (NO), or stimulating nitric oxide synthase[51] Australia, Europe, and India. Reduce the amounts of LPO byproducts: ROS are produced by an established mechanism called iron-induced LPO. Several plant extracts can prevent LPO brought on by Fe^{2+} while being non-toxic. Increase the expression of cAMP-responsive element modulator mRNA and protein. This may improve sperm motility and total sperm count. Effect of plant extracts on LH, FSH, and GnRH levels: Medicinal plants influence the levels of FSH and LH which play an important role in the regulation of male reproductive function[4]. Androgenic activity: Phytochemicals have androgenic activity, which means they can increase male sexual ability by increasing free testosterone levels. It has been demonstrated that testosterone, particularly its active converted product, dihydrotestosterone, promotes erections by maintaining nitric oxide levels[44]. Numerous studies have confirmed antioxidants' beneficial effect in reversing oxidative stress-induced sperm dysfunction, particularly in patients with idiopathic MI. In addition to enhanced sperm morphology, increased sperm motility and count phytochemicals have been proven to carry a favourable prognosis in this regard. Botanicals may be advantageous or harmful to human health. Here, we offer a comprehensive one-stop repository of clinical data on the effects of plants on MI[42]. Despite ongoing debates about the precise effects of medicinal plants on male infertility, in vitro and animal studies have confirmed the efficacy of a variety of herbal medicines in promoting MI. However, more in-depth research is needed to fully understand such effects[43]. People from various cultures have used various herbs to treat MI conditions or to treat reproductive disorders. Validation studies on herbs will be extremely beneficial for the treatment of infertility. The interaction of the many pathways involved must be taken into account while building a molecular pathway to identify a lead molecule of herbal origin for the treatment of various types of sexual dysfunction. In addition, more studies on intracellular signalling pathways and at the cellular level should be done to clarify how plant extracts improve MI[44].

7. Conclusion

Our review indicates that several medicinal plants, such as *ashwagandha*, *ginseng*, *Tribulus terrestris*, and maca, have shown promising results in improving various aspects of male reproductive health, including sperm quality, sperm count, and hormonal balance. These plants contain bioactive compounds that may positively impact male fertility. The mechanisms underlying the observed effects of medicinal plants on male infertility are multifaceted. They may include antioxidant properties, hormone regulation, reduction of oxidative stress, and enhancement of sperm motility. Further research is needed to elucidate these mechanisms fully. While many studies have reported beneficial effects, it is essential to acknowledge that the safety and potential side effects of using medicinal plants for male infertility require further investigation. Standardized dosages and rigorous monitoring are necessary to ensure patient safety. The response to medicinal plant treatments may vary among individuals due to genetic, environmental, and lifestyle factors. Tailoring treatments to each patient's specific needs and conducting personalized assessments are recommended. This systematic review underscores the need for more high-quality, randomized controlled trials to provide robust evidence regarding the efficacy and safety of medicinal plants in managing male infertility. Additionally, research should focus on long-term effects, optimal dosages, and potential interactions with other medications. In summary, while the use of medicinal plants in managing male infertility shows promise, it is imperative to approach these treatments with caution and under the guidance of healthcare professionals. The field is evolving, and more rigorous research is required to establish its role as a viable therapeutic option. Patients considering such treatments should consult with qualified healthcare providers to make informed decisions about their reproductive health.

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