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Abstract



Review A review of medicinal herbs in the management of male infertility

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Received: 01-04-2022 Revised: 12-09-2022 Accepted: 02-10-2022 Online: 17-10-2022 Male infertility can result from a number of factors, such as neurohormonal imbalances, problems with the reproductive system, and semen quality and quantity degeneration. Male reproductive health is declining globally, and current therapy alternatives to address male infertility are expensive, less widely available, and have prolonged treatment durations and side effects. When it comes to male reproductive health, herbal therapies are in a much better position to provide more holistic approaches. As aphrodisiacs, a unique class of herbs defined in herbal pharmacology, nourish and stimulate the body's sexual tissues. A careful evaluation of the current information on drugs and their probable functions in treating male infertility is the purpose of this paper.

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Introduction

The inability to get pregnant after a year of sexual activity without the use of contraception is known as infertility [1]. We, as a culture, deal with a variety of infertility-related problems. According to the World Health Organization [2, 3], 40% of infertility issues are related to the male factor and affect 15-10% of couples globally. The ability to generate semen with normal spermatozoa in a sufficient number of individuals (quantity), as well as the desire and capacity for mating, are requirements for males [4]. Some of the causes of male infertility include genetic abnormalities, genital duct obstructions, Varicocele, reduced semen quality parameters, erectile dysfunction, and male impotence are all associated with decreased sperm production [2]. According to research [5,] 25 to 40% of young men have sperm parameters that fall below WHO standards. Surgery, prescription drugs, natural remedies, and laboratory techniques are all used as fertility therapies. Numerous studies [6] have found that some herbal treatments can improve some sperm parameters. It is common knowledge that people have been using medicinal plants since the dawn of humanity. A multilateral strategy for using herbal remedies in addition to traditional medical treatment has arisen in recent years [7]. Alternative therapies, such those that employ herbal plants, are more advantageous than traditional forms of medical and psychological care. Interest in complementary and hormonal therapy has developed as a result of the absence of particular treatments for many infertile men. These therapies are predicated on the hypothesis that some cases of male infertility may be brought on by vitamin or hormone deficiency, and that supplemental therapies (vitamins, herbal remedies, and hormones) may enhance male reproductive capability and semen quality [8]. Studies [3,4] demonstrating that a sizable percentage of infertile men produce appreciable levels of semen oxidants led to the development of antioxidant therapy. Although it is thought that the high amounts of oxidants in their semen are what are causing these men's infertility, the efficacy of treating them with oral antioxidant therapy has not yet been proven. Because lay books praising their benefits are published frequently, alternative medicines are growing in popularity. These lay articles are largely based on poor clinical research (uncontrolled, nonrandomized). Because of this, we think that complementary and alternative medicine are widely used. The goal of this study was to look into the types of alternative and hormonal therapies that male infertility patients used. [9] Free radical-induced oxidative damage is one of the most frequent causes of idiopathic oligospermia and leads to abnormal sperm despite having an adverse effect on sperm structure. For instance, nitric oxide free radicals, for instance, cause oxidative stress in diabetics by producing reactive oxygen species, which interfere with estrogenic and spermatogenesis pathways and cause testicular insufficiency [10-12]. Varicocele has been found in 19% to 41% of infertile men, making it a frequent cause of male infertility [13-15]. One of the potential causes of decreased spermatogenesis is thought to be increased ROS levels and oxidative stress. Vacuoles are formed in the testis tissue as a result of oxidative stress and are linked to aging [17–19]. This process may be inhibited by antioxidants. A diet lacking in antioxidants, vitamin A, flavonoids, carnitine,

folate, zinc, and selenium may increase the risk of infertility, especially in persons with oligospermia and asthenozoospermia [21–23]. Antioxidants including vitamin C, vitamin E, coenzyme Q10, glutathione, and natural polyphenols like flavonoids and phenolic acids can be used to treat male infertility because they reduce free radical damage, improve the blood-testis barrier, and protect and repair sperm DNA [24]. Many infertile couples choose not to use assisted reproductive technologies (ART) due to their expensive expense, including zygote intrafallopian transfer (ZIFT), in vitro fertilization (IVF), and intra-cytoplasmic sperm insemination (ICSI). On the other side, there are effective drugs that are more widely available and less expensive. Plant extracts are treasured for their bioactive components, which are valued for being sourced from natural sources and compatible with key systems. For a very long time, herbal medicines have been utilized to improve conditions including hormonal imbalance, oligospermia, low sperm motility, prostatitis, varicocele, Table and more. [25]. 2 Semen parameter values

According to a 2010 World Health Organization report, normal human semen has a volume of 1.5 ml or more, a pH of 7.2 or higher, 15x106 or more spermatozoa per ml, 39x106 or more spermatozoa per ejaculate, and at least 32% motility within 60 minutes. If the male's sperm count is less than 11 million sperm per milliliter of sperm, it is regarded as infertile. The most crucial functional indicator to take into account when evaluating spermatozoa's capacity to fertilize is sperm motility [27].

Sperm morphology:

In sperm morphology, shape and size of sperm cells are analyzed. It is called aberrant sperm morphology if the size, shape, or characteristics of a sperm are not as predicted.

As the name suggests, Teratozoospermia refers to malformed sperm. Only identifiable sperm are counted in the sperm analysis exercise.

In the beginning, a sperm was found to be aberrant in the following ways:

Assume that the sperm head is oval and free of any abnormalities. Figure 1.

The neck, mid-piece, and tail should be free of abnormalities, and the acrosomal region (40-70%) of the head area) should be clearly defined Table 1.

Causes of male infertility

Other reasons of male infertility include abnormal androgen action, adrenal insufficiency, hyperthyroidism, congenital adrenal hyperplasia, disrupted sperm transport, and systemic disease [28]. Androgen action abnormalities, such as androgen insensitivity syndrome, cause the body to not respond to testosterone, resulting in a female phenotype while having a male genome. Patients with hypothyroidism have low testosterone levels while having high quantities of the hormone, which is more typical in women because the condition is genetic Figure 3 [29].

Pathophysiology:

Infertility and hypogonadism can result from an unbalanced hypothalamic-pituitary-gonadal axis. Despite having high blood levels of LH and FSH, the gonads in primordial hypogonadism are unable to produce enough testosterone or spermatogenesis. Primary hypogonadism is caused by congenital conditions such cryptorchidism, Klinefelter syndrome, and problems with androgen production. Cirrhosis of the liver, renal failure, drugs, autoimmune disorders, radiation, viral infections, and trauma can all cause inherited liver cancer. They are consequently either damaged or less useful. Sertoli and Leydig cells that are inactive Low GnRH, LH, or FSH can cause the hypothalamic-pituitary system to malfunction, testosterone levels which lowers and impairs spermatogenesis. Figure 4. Lack of GnRH, LH, or FSH, as in Kalman's, Prader-Willi, or Lawrence-Moon syndromes, or mutations in the GnRH receptor, the beta-subunits of LH, FSH, or kisspeptin/G protein-coupled receptor 54, may be the cause of this or any combination of these. Among them are hyperprolactinemia, panhypopituitarism, drugs (including the use of steroids and opiates), systemic diseases, tumors, and infections. Figure 2. The American Psychological Association states that prolactinomas are the most common cause of hyperprolactinemia, although it can also be brought on by systemic diseases, dopamine antagonists, anomalies of the hypothalamic-pituitary stalk, and other medications. These conditions prevent the testes from receiving their essential stimulation. Without the required inputs, Leydig-and-Sertoli cells cannot exert their actions (GnRH, LH, or FSH). As a result, testosterone levels may decrease, or spermatogenesis may stop.

Conclusion:

Unable to have children is a traumatic experience for millions of couples, and many of them have a personal frustration about it. There is an equal distribution of infertility between men and women. Medicinal plants have been used in many countries to treat male infertility issues, among other methods. Sperm disorders, libido dysfunction and sexual asthenia are all treated with these herbs. Our health care system relies heavily on herbalism as a primary treatment option for infertile couples because it's costeffective and readily available.

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Table 1. Normal values of semen parameter

Semen Parameter	Reference value
pH	7.2 to 7.8
Volume	\geq 1.5 ml
Concentration	$\geq 15 \text{ X } 10^{6} / \text{ml}$
Vitality	\geq 58% live spermatozoa
Total Motile	\geq 40% (Progressive + Non-Progressive)
Total spermatozoa per ejaculate	\geq 39X 10 ⁶
Progressive Motility	\geq 32 % motile
Normal Spermatozoa	$\geq 4\%$

Table 2. Plant products in the management of male fertility and mode of action.

Herbs	Identity	Part used	Mode of action	References
Withania somnifera		Seeds	Psychiatric illness. Sexual organ dysfunction is a condition in which the sexual organs do not operate properly. The number of sperms has grown. Infertile men had higher testosterone and LH levels and lower FSH and prolactin (PRL) levels.	31 32
Eurycoma longifolia Jack	- The	Roots	Androgen production is stimulated by this substance. By lengthening coitus and boosting copulation frequency, the ethanol extract of this plant improved the male rats' performance and sexual drive.	33
Mucuna pruriens		seeds	It boosts spermatogenesis and raises the total weight of the testicles and accessory glands. By boosting mounting frequency, ejaculation latency, and intromission frequency, it can improve sexual behavior in male rats	34 35 36
Psidium guineense		Aqueous extract	This supplement improves function of the testes and seminal vesicles.	37
Tribulus terrestris		Herb	Spermatogenesis and sexual drive are aided by this supplement.	38
		Alcoholic extract	It does not induce infertility or reluctance in women, but it does help to prevent menopausal symptoms. The levels of estrogen, progesterone, and pregnenolone are all affected by testosterone levels.	
Camellia sinensis(tea)		Leaves	The activity of SOD has risen. Peroxidation of lipids is slowed. Heat-treated rats have less and significantly degraded	39
			sperm, although GTE can counteract these negative effects by increasing the amount and motility of spermatozoa, particularly after 28 days of therapy.	40
Daucus carota(carrot)		Seeds	Antioxidant qualities help to increase sperm count. Increases the synthesis of testosterone. The rate of spermatogenesis has increased.	41
Allium sativum		Extract	The number of empty seminiferous tubules in the testes significantly increased in rats fed a diet containing 10%, 15%, or 30% Allium sativum (AS), while testosterone levels significantly decreased. Male rats fed raw garlic had impaired spermatogenesis and testicular function. Citric acid levels were shown to be inversely correlated with prostate weight in rats given 30 percent garlic.	42
Zingiber officinale		Oil	DNA damage is prevented by reducing oxygen radicals. Increases spermatogenesis and testosterone levels without increasing testosterone or sperm counts.	43
Rose flowers		Oil	The diameter of the seminiferous tubules, sperm motility, Leydig cell numbers, histological flaws in the testes, and testosterone levels have all improved.	44
Capsicum		Capsaicin	When given intraperitoneally, capsaicin suppresses DNA synthesis in the testes of mice. In vitro, CAP can also induce apoptosis in two spermatogonia stem cell lines.	45
Cinnamomum		Bark	Increases caudae epididymidies and testis weight but not sperm count or motility. Male mice given Cinnamomum extract had heavier testicles, caudae epididymidies, and seminal vesicles, suggesting that their hormone levels may have risen. Additionally, the treated animals' sperm count and motility were much higher than those of the control group.	46

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Trigonella foenum- graecum	A	Seeds	Improves histological flaws in the testes. Free radical production is inhibited.	47
Flaxseed		Oil	Increases the number of sperms in the cauda epididymal sperm pool and serum LH levels.	48
Ginseng		Root	The hardness and circumference of the penile organ are both improved. Patients are more satisfied and erections stay longer. Has a protective effect against chromosomal and sperm abnormalities? A rise in testosterone concentration causes sperm counts and motility to increase.	49
Petroselinum crispum		Oil	Superoxide dismutase (SOD) and glutathione reductase (GR) activity are increased.	50
Lepidium meyenii		Hypocotyl	Improvements are made in spermatogenesis, sperm quantity and motility, as well as levels of testosterone, LH, and FSH.	51
Cucurbita pepo L.		Seed and seed oil	Testis histology and libido are improved.	52
Allium cepa			Allows the spermatogenesis cycle to take place. Inhibits the formation of aberrant sperm. The number of sperms, motility, and testosterone levels in the blood are all up.	53
Sesamum indicum		Seeds	In the epididymis, sperms are retained. FSH is inhibited, and testosterone levels are increased. Sperm count and motility are improved testicular metrics.	54
Apium graveolens	NAN YAYA	Seeds	Histopathological, it improves sperm count, motility, and healing.	55
Artemisia annual		Essential oil	increases the amount of Leydig cells, seminiferous tubule diameter, and spermatogenic cell proliferation.	56
Urtica dioica		Hydroalcoholic extract	Seminiferous tubule activity and seminiferous epithelial height are preserved.	57
Nigella sativa		Seeds	Fertility and the weight of reproductive organs are increased; however, sperm motility and testosterone levels are not increased.	58
Crocus sativus L.		Stigma	Stiffness and tumescence of the Rigiscan, as well as erectile function and sexual functions like orgasm and sexual desire, are all improved.	59
Dactylorhiza maculata		Dried root and tubers	Increases sperm count, testosterone, sperm volume, and spermatogenesis, as well as enhancing desire, erection, and spermatogenesis.	60 61



Figure 1. Normal spermatozoa



Figure 3. Causes of male infertility



Figure 4. Mechanism of sex stimulant herbs: [30]