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Unveiling Nature's Secrets: A Comprehensive Review of Poly-Herbal Anti-Infertility and Aphrodisiac Powders for Reproductive Health

Renuka G. Pawar*, Vaishali N. Tidke, Akshay R. Gadhari
Dr. Y. S. Khedkar College of Pharmacy, Chattrapati, Sambhaji Nagar, India
Corresponding author*

Abstract: *This review article aims to evaluate the efficacy of a poly-herbal anti-infertility and aphrodisiac powder preparation. The preparation consists of five different plant ingredients, including Punicagranatum, Withaniasomnifera, Foeniculumvulgare, Nigella sativa, and Glycyrrhizaglabra. Each plant powder is added in varying quantities ranging from 10% to 35%. The article discusses the traditional use and scientific evidence supporting the use of each plant in the powder. In conclusion, the review highlights the potential of this poly-herbal powder as an effective natural remedy for infertility and enhancing sexual function. However, further clinical studies are necessary to establish the safety and efficacy of the preparation.*

Keywords: Poly-Herbal Anti-Infertility

I. INTRODUCTION

Around the world, one out of six couples trying to conceive has difficulties. Infertility is defined as one year of regular and unprotected intercourse without conception. On evaluation, roughly 50% of affected couples have causal or associated male factors as a cause of infertility [1]. The couples suffering from infertility use concomitantly traditional medicine from natural plants and modern medicine as possibilities of treatment [2,3]. The use of medicinal plants in the treatment of diseases and dysfunctions goes back to several millennia and has considerably contributed to the development of pharmaceuticals since about 25% of modern drugs are derived from plants. In addition, up to 60% of the world's population uses herbal products for medical purposes [4,5]. Since two decades, the evaluation of natural materials as a source of potential drugs has been of resurgent interest in developing countries as well as in the developed ones. This growing interest for phytotherapy is due to several reasons namely; conventional medicine can be inefficient (ineffective therapy), abusive and/or incorrect use of synthetic drugs results in side effects and other problems, finding of the "natural", large therapeutic spectrum of plant products and their effectiveness in the treatment of chronic diseases, need for development of new drugs. Phytomedicines are dietary supplements with nutritional and revitalizing effects on the organism [5–8]. The World Health Organization encourages the use of medicinal plants, and invites researchers to define the rational use of medicinal plants as a source of new drugs [9]. Several extracts, fractions or molecules isolated from these plants are today largely used to treat or relieve different aspects of male infertility such as: absence of libido, sexual asthenia, erectile dysfunction, ejaculatory and relaxation dysfunctions, loss of orgasm, and sperm abnormalities. Although the causes of infertility in males are diverse, psychogenic and endocrinal disorders, vascular injuries and drug abuse are found as symptoms in infertile people [10]. Many in vitro, in vivo and clinical studies proved the empirical use of plants in the improvement of male fertility parameters. In this review, we focused on the use of medicinal plants in the treatment of male infertility symptoms (libido dysfunction, erectile and ejaculatory disorders, and sperm abnormalities) as well as the effectiveness of phytomedicines as a mode of treatment. Original papers and reviews published on google, pubmed and science direct from 1990 to 2008 were found using key words as: male infertility, incidence or prevalence of infertility, use of traditional medicine, androgenic activity of plant extracts, medicinal plants and male reproductive hormones, plant extract and sexual desire, aphrodisiac activity of plant extracts, plant extracts and sperm characteristics, etc. Information from selected articles was classified according to the target

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effect of a plant extract on male reproductive function and to the subject (rodent, human) used to assess the potential activity of a plant extract.

Plants in the treatment of male infertility The inability to have a child is a personal tragedy for couples suffering from infertility [11]. These couples use both traditional medicine and modern therapies as treatment. In developing countries, traditional medicine particularly medicinal plants thanks to their accessibility, availability, and affordability are generally the first recourse of infertile couples [9]. Several plants are empirically used to treat different aspects of male infertility such as sexual asthenia, libido (sexual desire), erectile and ejaculatory disorders, and sperm abnormalities (azoospermia, oligospermia). The biological activities of many of these plants were confirmed by in vitro, and/or in vivo animal studies and in humans.

II. EFFECTS OF MEDICINAL PLANTS ON MALE REPRODUCTIVE FUNCTIONS IN ANIMALS:

Punicagranatum (Pomegranate) :

Punicagranatum (pomegranate) has spread to most parts of the world, including Asia, the Middle East, and the Mediterranean countries [12]. Pomegranate contains a large percentage of water and is rich in vitamin C and polyphenols such as anthocyanins, punicalagin, ellagic, and gallic acids. Pomegranate seeds contain phytoestrogens likes genistein, daidzein, coumestrol, glutamic amino acids, and aspartic acids [13] . An animal study on rats with PCOS shows that pomegranate extract due to the presence of phytoestrogens can regulate and reduce PCOS symptoms. The extract of this plant increases mucus secretion by increasing uterine blood flow (vasodilatation) and also increases the thickness of the uterine wall. This increase in mucosal secretions through anti-inflammatory mechanisms enhance the implantation rate [14] . Pomegranate peel contains calcium and tannins, which [15] in a triple-blind randomized controlled clinical trial on 110 normal women showed increase of sexual satisfaction of women after using them as a gel, and also reduction of inflammatory and infectious symptoms in their reproductive canal. Study of different cell lines of human breast (MCF-7, MDA MB-231) endometrial (HEC-1A), cervical (SiHa, HeLa), ovarian (SKOV3) carcinoma, and normal breast fibroblast (MCF-10A) cells showed that pomegranate extract estrogen receptor modulators (SERMs) by binding to ERs inhibit the growth of these cell lines in vitro and in vivo (in ovariectomized mice) models and prevent the proliferation of these cells [16] . In a randomized controlled triple-blind parallel trial study on 23 women with PCOS, it was found that pomegranate fruit extract improved the serum levels of sex hormones (testosterone reduction) and their lipid profile (Esmaeilinezhad et al.,2019). A study on PCOS-induced rats, pomegranate fruit extract was found to increase serum estrogen levels and reduce symptoms after 81 days [14].

Withaniasomnifera (Ashwagandha)

Withaniasomnifera (Ashwagandha), also called Indian ginseng, belongs to the Solanaceae family, showing beneficial effects in women with problems in conceiving. This wild plant grows in dry and hotsemiarid climate, such as in the southern Mediterranean region, Canary Islands, and northern Africa to northern India (Iran, Jordan, Sudan, Palestine, Afghanistan, and Egypt)[17]. In traditional medicine, the plant has been recommended for the management of premature ejaculation, polyarthritis, painful swellings, lumbago, oligospermia, vitiligo, general debility, ulcers, impotency, uterine infections, leucorrhoea, and orchitis.[18] The LCESI/MS analysis of Ashwagandha extract confirmed the presence of compounds such as anaferin, anahygrine, hygrine, cuscohygrinetropine, pseudotropine, withananine, pseudowithanine, somnin, and somniferine-3-tropyltigloate .[19] Most of the plant's compounds are polyphenols (isoflavones and flavonoids) that can play an estrogenic role. In a study by Saiyed et al. (2016) on letrozole-induced polycystic ovarian syndrome in rats, it was found that the serum level of LH decreased; FSH level increased, and preantral and antral follicles and corpus luteum reduced in comparison with the control group in 22 days [20]. In the study of Bhattarai et al.[21], it was found that Ashwagandha extract via GABA mimetic properties increased the secretion of gonadotropin hormones and finally improved oogenesis, which was proposed to be due to boosting the HPG axis and improving serum estrogen balance [21].

FoeniculumVulgare (Fennel) :

FoeniculumVulgare (fennel) with yellow flowers and feather-like leaves belongs to the Umbelliferae (Apiaceae) family and is native to the Mediterranean region, western Asia, and eastern Europe. It is a popular herb with a long history of

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usage as a traditional medicine .[22] A series of studies have shown that fennel has beneficial effects against numerous infectious disorders of fungal, bacterial, mycobacterial, viral, and protozoal origin, as well as antitumor, antioxidant, cytoprotective, chemopreventive, hypoglycemic, hepatoprotective, and estrogenic properties .[23] The major constituents of this plant are polyphenols (flavonoids and isoflavones) such as quercetin-3-glucuronide, isoquercitrin, quercetin-3-arabinoside, 3-O-caffeoylquinic acid, 4-O-caffeoylquinic acid, 5-O-caffeoylquinic acid, 1,3-O-di-caffeoylquinic acid, 1,4-O-di-caffeoylquinic acid, kaempferol-3-glucuronide, kaempferol-3-arabinoside, isorhamnetinglucoside, rosmarinic acid, chlorogenic acids, Quercetin-3-Ogalactoside, kaempferol-3-O-rutinoside, kaempferol-3-O-glucoside, isorhamnetin 3-O-rhamnoside, quercetin, and kaempferol [24]

A study on rats showed that low doses (50 µg/100 g body weight) of fennel extract after 10 days caused vaginal cornification and induced the estrus cycle while at moderate doses (250 µg/100 g body weight), and it increased the weight and volume of genital organs (mammary glands, oviduct, endometrium, myometrium, cervix, and vagina) in female rats [25] Fennel extract reduced the frequency of uterine contractions by affecting the synthesis of oxytocin and PGF2 and alleviated dysmenorrhea pain at different doses. These effects were even more potent than those of mefenamic acid [26] A study on ovariectomized rats showed that 500–1000 mg/kg doses of fennel extract after 30 days increased mineral density and the synthesis of collagen fibers in bones in a dose-dependent manner through alkaline phosphatase-related pathways, suggesting a role for this plant in preventing osteoporosis, especially in postmenopausal women [27]

Nigella sativa (Black seed- Ranunculaceae) :

This plant belongs to the Ranunculaceae family and has a height of 30–60 cm and two to three pinnatisect leaves. The plant grows in many parts of the world, including Eastern Europe, West Asia, and Southeast Asia [28]Extracts of its various parts such as seeds, leaves, flowers, and stem are used to treat various diseases such as gastrointestinal disorders, headache and migraine, PCOS, male infertility, diabetes, renal injury, hyperlipidemia, stress and depression, neurological disorders, respiratory diseases, liver disorders, and cancers, as well as to mitigate menopausal symptoms [29,30.31] Most of the active ingredients of this plant are polyphenols, especially flavonoids such as kaempferol 3-glucosyl, quercetin 3-(6-feruloylglucosyl), apigenin, catechin, epicatechin, p-coumaric acid, syringic acid, and chlorogenic acid.[32,33] Various studies have shown that Nigella sativa extract due to the presence of phytoestrogenic and flavonoid compounds reduces the number of ovary cysts induced by exposure to estradiolvalerate, letrozole, and dehydroepiandrosterone in different animal models (rats and mice) of PCOS. The extract of this plant has been suggested to improve PCOS by upregulating the mRNA expression of epigenetic-related (Dnmt1 and Hdac1) and maternally derived genes (Mapk and Cdk1), reducing ROS, and affecting the HPG axis (i.e., suppressing LH and estrogen secretion and also boosting FSH levels).[34] Long-term use of the extract of N. sativa due to the presence of phytoestrogens can reduce testosterone levels, exerting a negative feedback on LH. On the other hand, LH is probably produced to a lesser extent following a decrease in androgens, reducing the dominant effect of LH on FSH. In addition, Nigella sativa extract may reduce LH dominance over FSH by inhibiting nitric oxide and leptin-releasing neurons that are directly involved in the synthesis of LH from the anterior pituitary gland, thereby increasing ovulation in women with PCOS .[35] A study by Parhizkar et al. (2016) on the ovariectomized rats treated with N. sativa extract showed that the extract of this plant, in a dose-dependent manner (300 to 1200 mg/kg), reduced menopausal symptoms including uterine weight/edema loss and decreased serum estradiol level and the number of inflammatory cells in the vagina compared with the control group [36]

Glycyrrhizaglabra (Licorice- Liquorice)

Glycyrrhizaglabra (Licorice- Liquorice) is an herbaceous perennial plant belonging to the Fabaceae family. The plant is about 50–100 cm high and has 7–12 pinnate leaves containing 9–17 leaflets with purple to pale whitish blue flowers (1-cm-long), as well as 3-cm-long pod fruits containing several seeds. This plant grows in most parts of the world but is native to western Asia and southern Europe (especially France, Uzbekistan, China, and Iran) [37] The plant contains a variety of phytoestrogens and issues potent antidiabetic, spasmolytic, antidepressive, laxative, antiulcer, and anti-inflammatory effects.[38] A dose higher than 2 mg kg−1 day−1 of pure glycyrrhizic acid (i.e., the main constituent of liquorice) may result in side effects such as hypokalemia, hypertension, apparent mineralocorticoid excess (AME)

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syndrome (via inducing sodium retention and suppressing the renin-angiotensin-aldosterone system), muscle weakness, and even death .[38,40].Due to high amounts of phytoestrogenic compounds, this plant can be beneficial in treating estrogen-dependent diseases such as breast cancer, endometriosis, PCOS, and POF . [41] Due to the presence of phytoestrogens with aromatase-inducing and 17HSDinhibiting activities, licorice can reduce testosterone synthesis and therefore can be used to treat women with PCOS. [42] In addition, according to a study on PCOS-induced mice, licorice extract was shown to improve ovarian morphology, oocyte maturation, and embryonic development in a dose-dependent manner (100 to 150 mg kg−1 day−1 for 21 days) compared to the control group [43]

III. MATERIALS AND METHOD

To make the poly-herbal anti-infertility and aphrodisiac powder, the following steps can be followed:
Collect the required plant materials, including Punicagranatum, Withaniasomnifera, Foeniculumvulgare, Nigella sativa, and Glycyrrhizaglabra.
Ensure that all the plant materials are of high quality, free from any impurities, and have been properly dried.
Grind each plant material separately using a mortar and pestle until a fine powder is obtained.
Measure out the required quantity of each plant material based on the specified percentages (Punicagranatum 10%, Withaniasomnifera 35%, Foeniculumvulgare 20%, Nigella sativa 15%, and Glycyrrhizaglabra 10%).
Mix all the powdered plant materials together in a bowl until well blended.
Transfer the mixture to an airtight container for storage.
Store the container in a cool, dry place away from direct sunlight.
Use the poly-herbal powder as directed by a healthcare practitioner or as per traditional use.

Sr no	Plant name	Scientific name	Quantity %
1	Pomegranate powder	Punicagranatum	10%
2	Ashwagandha powder	Withaniasomnifera	35%
3	Fennel powder	FoeniculumVulgare	20%
4	Black seed/kalongi seed powder	Nigella sativa	15%
5	Licorice- Liquorice	Glycyrrhizaglabra	10%

PHYSICAL EVALUATION

The physical evaluation of the poly-herbal anti-infertility and aphrodisiac powder can be conducted to assess the quality of the final product.
The powder can be evaluated for its color, odor, taste, and texture. The color of the powder should be uniform and consistent with the natural color of the plant materials used. The odor should be characteristic of the plant materials and free from any foul smell. The taste should be palatable, and the texture should be fine and free-flowing.
The moisture content of the powder can be evaluated to ensure that it is within acceptable limits. The powder should not have any clumps or lumps, and it should be easily soluble in water.
Other physical evaluations can include particle size analysis to ensure that the powder has a consistent particle size distribution, which can affect the efficacy and quality of the final product.
Microscopic evaluation of the powder can also be conducted to assess the quality of the plant materials used in the powder. This evaluation can help identify any impurities, adulterants, or foreign matter in the powder.
Overall, a comprehensive physical evaluation of the poly-herbal anti-infertility and aphrodisiac powder can help ensure that the final product is of high quality, safe, and effective.

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To evaluate the efficacy of the poly-herbal anti-infertility and aphrodisiac powder, clinical studies can be conducted to assess its safety and effectiveness in treating infertility and improving sexual function.

The clinical studies can include randomized controlled trials involving a group of individuals with infertility or sexual dysfunction who are administered the powder or a placebo for a specific duration. The study can include regular monitoring of hormone levels, sperm count, motility, and other relevant parameters to evaluate the efficacy of the powder.

In addition to clinical trials, other evaluation methods can include surveys and patient feedback to assess the efficacy of the powder in improving sexual function and treating infertility.

It is also important to evaluate the safety of the powder by conducting toxicity studies to ensure that the powder does not cause any adverse effects.

Overall, a comprehensive evaluation of the poly-herbal anti-infertility and aphrodisiac powder can help establish its efficacy and safety, and provide a basis for recommending its use as a natural remedy for infertility and improving sexual function.

IV. CONCLUSION

In conclusion, the poly-herbal anti-infertility and aphrodisiac powder reviewed in this article has shown promising results in both traditional use and scientific research for its potential to treat infertility and improve sexual function. The five plant ingredients used in this powder, Punicagranatum, Withaniasomnifera, Foeniculumvulgare, Nigella sativa, and Glycyrrhizaglabra, have a long history of use in traditional medicine for these purposes.However, more clinical studies are needed to establish the safety and efficacy of this preparation. Future research should focus on determining the optimal dosage and duration of treatment, as well as investigating potential interactions with other medications and the safety of the powder in specific populations.Further studies on the mechanisms of action and the bioavailability and pharmacokinetics of the active ingredients could lead to the development of standardized formulations for the poly-herbal powder.Overall, the poly-herbal anti-infertility and aphrodisiac powder has the potential to offer a safe and effective natural remedy for infertility and improving sexual function. Further research and clinical studies are necessary to fully explore this potential and establish its place in modern healthcare.

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