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Review Article

Effective Herbal Treatments for Enhancing Female Fertility: A Comprehensive Review

Running Title: Herbal Treatments for Female Fertility: A Review

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Abstract

Background and Objective: Female fertility represents a significant global challenge, influenced by numerous factors including hormonal imbalances, environmental stressors, and lifestyle choices. These factors impact both physical and mental health and have significant social and economic implications. Consequently, there is an urgent need for effective and natural approaches to identify safe and efficacious treatments. The objective of this study was to conduct a comprehensive review and analyze the efficacy of herbal therapies in enhancing female fertility.

Methods: A thorough search of the PubMed, Scopus, and Google Scholar databases was conducted for English-language studies using MeSH terms such as women's fertility, herbal medicine, reproductive health, plant extracts, and complementary therapies. The research focused on the effects of improving fertility components in both primary and secondary studies published from 1995 to the end of the year 2024.

Results: Herbal treatments have become a natural and effective alternative for enhancing female fertility, addressing issues like hormonal imbalances and oxidative stress. Plant extracts, particularly polyphenolic compounds, help neutralize free radicals and may enhance reproductive health by regulating hormone levels. Certain herbs, such as Vitex agnus-castus, fennel, and Ashwagandha, aid in menstrual regulation and fertility enhancement. Systematic reviews suggest that these remedies can enhance pregnancy rates and improve the quality of oocytes and embryos. However, potential risks must be considered, and further research through rigorous clinical trials is needed to establish standardized guidelines

Conclusion: Herbal treatments have been introduced as a natural and effective option for enhancing women's fertility. Further research in pharmacology, phytochemistry, and toxicology could lead to the development of new and effective medications by evaluating the biological activity of compounds extracted from plant extracts. This approach aids in the identification of novel treatments for women's fertility disorders and improves their quality of life and reproductive health.

Keywords: Complementary Therapies, Herbal Medicine, Plant Extracts, Reproductive Health, Women's Fertility

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Introduction

Globally, Globally, one in six couples faces infertility, defined as the inability to conceive after one year of unprotected intercourse (1). Approximately half of the causes of infertility in couples are attributed to female-related disorders. Female infertility can arise from various conditions, including ovulatory disorders, damage to the fallopian tubes (tubal infertility), cervical disorders (such as polyps or benign tumors and cervical stenosis), and hormonal imbalances (2). These hormonal conditions include polycystic ovary syndrome, endometriosis, premature ovarian failure, hypothalamic disorders, hyperprolactinemia, uterine fibroids, and pelvic inflammatory disease (3). Major risk factors include smoking, alcohol consumption, chemotherapy or radiation therapy, prolonged use of high-dose nonsteroidal anti-inflammatory drugs, antipsychotic medications, recreational drug use such as marijuana and cocaine, obesity, advancing age, and sexually transmitted infections (3, 4).

The consequences of infertility in women can be divided into two main categories: physical and psychological disorders. The physical symptoms of this condition include menstrual irregularities (amenorrhea, irregular menstruation, abnormal menstruation, painful menstruation), skin changes, alterations in sexual desire and preferences, excessive hair growth (dark hair on the lips, chest, and chin), and weight gain. Psychological-social disorders resulting from this condition include difficulties in interpersonal relationships, decreased self-esteem, feelings of shame, social isolation, depression, anxiety, hopelessness, feelings of guilt and worthlessness, and other psychological harms (5, 6). Women today have access to various treatments for achieving pregnancy, including ovulation-inducing medications (like clomiphene and gonadotropins) and assisted reproductive technologies (ART) (7-8). Micronutrients, including antioxidants, B vitamins, vitamin D, and various fatty acids (e.g., saturated, monounsaturated, polyunsaturated, docosapentaenoic acid, eicosapentaenoic acid, and linoleic acid), demonstrate significant efficacy in treating female infertility as standalone or adjunctive therapies (11–13). Concurrently, rising concerns regarding the adverse effects of conventional pharmaceuticals on fertility and their prohibitive costs have amplified global reliance on herbal medicines. These botanicals serve as complementary agents due to their phytoestrogenic, antioxidant, and nutritional properties, with phytoestrogens offering a viable strategy for mitigating symptoms of steroid deficiency and menopausal sequelae (5, 14, 15). Herbal therapeutics, among humanity's oldest pharmacological interventions, continue to have substantial global utilization despite advancements in medicine. Notably, 90% of African populations, 70% of Indians, and 40% of Hong Kong residents prioritize herbal treatments over synthetic drugs (19, 20), while 12.8% of Americans consume daily herbal supplements (21). Economic analyses reveal that alternative therapy expenditures reached $13.7 billion in 1990, doubling within seven years. This preference intensifies when the efficacy of conventional drugs remains uncertain, particularly in conditions such as advanced malignancies (22).

Herbal medicines comprise a significant proportion

of the World Health Organization's List of Essential Medicines (479 medicines) (5), and approximately 25% of the world's prescription medicines are of plant origin (19). They are used to boost immunity, treat cancer, and manage conditions such as heart disease, depression, and infertility (23). They are available in tea, capsule, and tablet forms, and their use in the treatment of infertility dates back to the 2nd century AD (24). Herbs such as Artemisia and Ricinus have been used in traditional medicine to address women's health issues (25). However, some species, including Senna and Castor oil, may cause miscarriage or premature labor (26).

Herbal treatments are recognized as a core component of alternative medicine, and we are currently witnessing their rapid growth. These treatments are accompanied by numerous claims that have not yet been fully evaluated (27). The use of herbal remedies is consistently increasing and is gradually being accepted within the framework of modern medicine. The main reasons for many individuals' preference for herbal treatments over synthetic drugs include relatively low costs, easy accessibility, and sometimes fewer side effects compared to chemical medications (28). Many people perceive herbal treatments as natural and safe, which has historically been a major driver of their use. Therefore, there is a pressing need to expand knowledge regarding the effectiveness and safety of herbal treatments in managing women's fertility issues (29).

This study aims to investigate the effects of various plants on women's reproductive health, with a specific focus on infertility. In this narrative review, the authors critically examine different research studies that have utilized herbal treatments for women's fertility disorders to identify herbal options with therapeutic potential, side effects, and future research opportunities. This study serves as an update in the literature related to herbal interventions for fertility disorders.

Methods

In this narrative review, the authors' search was limited to research articles, case reports, reviews, and meta-analyses published in English, with only findings in English being evaluated. The databases searched included PubMed, Scopus, and Google Scholar, using the keywords "Fertility, Herbal Medicine, Reproductive Health, Plant Extracts, Complementary Therapies," which were selected based on the Medical Subject Headings (MeSH) standards. The keyword selection protocol for this study was implemented through a systematic multi-stage methodology. Initially, core research concepts—including female infertility, micronutrient interventions, botanical therapeutics, psychosocial outcomes, and assisted reproductive technologies—were identified and semantically expanded using established medical thesauri: subsequent refinement incorporated search syntax optimization and database-specific adaptation to enhance terminological precision. The finalized lexicon underwent expert consultation and iterative pilot testing to validate the comprehensiveness and accuracy of the search strings, thereby enabling the exhaustive retrieval of interdisciplinary literature relevant to the research objectives. The filters applied

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included restricting the search to articles published in English and studies conducted between 1995 and the end of 2024 to examine the most recent findings and clinical results.

For the screening of articles, the titles and abstracts were initially reviewed to eliminate unsuitable papers. The remaining articles were then assessed based on specified inclusion and exclusion criteria, including methodological quality and relevance to the topic. Screening tools included a quality assessment checklist aligned with the inclusion and exclusion criteria, as well as reference management software (Mendeley Desktop v1.19.5) for organizing the articles.

Inclusion Criteria:

- Articles published in English.
- Clinical studies examining the effects of herbal plants on women's fertility.
- Articles containing empirical or clinical data on the effects of herbal factors on fertility-related disorders in women.
- Theoretical studies or systematic reviews related to the topic.

Exclusion Criteria:

- Articles unrelated to the research topic.
- Articles with low methodological quality or significant conflicts in results.
- Articles published before 1995.

These criteria were established to ensure the accuracy and validity of the final results. The initial search and extraction of articles from the databases were conducted by three authors, with the corresponding author responsible for reviewing the titles and abstracts and deciding on their inclusion or exclusion from the study. This division of labor helped increase accuracy and reduce the likelihood of missing relevant articles. To resolve conflicts, the authors independently reviewed the articles and engaged in discussions to reach a consensus in case of disagreements. Additionally, when the inclusion and exclusion criteria were unclear, the corresponding author was consulted as an overseer for final evaluation and decision-making.

The search results were evaluated for relevance to the research question, duplication, and study quality, resulting in the selection of suitable articles for further review. Initially, 292 articles were identified, which were then narrowed down based on specific criteria to include 127 articles in the final evaluation. The data extraction process involved identifying key information such as study design, population, treatment methods, outcome measures, and results for each article. In this narrative review study, the screening method included defining inclusion and exclusion criteria, reviewing titles and abstracts, and assessing the quality of the selected articles. Additionally, conflicts among authors were transparently expressed and effectively managed, thereby maintaining the credibility of the research and ensuring that all perspectives were presented fairly and without bias.

Results

Plants and Fertility

As presented in **Figure 1**, plants can enhance fertility through various mechanisms. They contribute to the strengthening of the hypothalamic-pituitary-gonadal (HPG) axis and interact with both alpha and beta

estrogen receptors. Additionally, these plants can prevent bacterial, viral, and fungal infections that are directly transmitted through reproduction, as well as reduce inflammatory responses, sensitivities, and autoimmune disorders. Ultimately, they provide appropriate nutritional conditions that aid in the proper regulation of ovulation, implantation, embryo retention in the uterus, and fetal development (30, 31).

So far, two types of estrogen receptors have been identified: ER-alpha and ER-beta. Physiological responses to estrogen typically occur in specific tissues through the action of these two receptors. ER-alpha receptors are present in breast and uterine tissues, while ER-beta receptors are found in bone and vascular tissues. These receptors are classified as nuclear hormone receptors and function as ligand-activated transcription factors (32). Many plants produce compounds with estrogenic activity, known as phytoestrogens. Compounds such as formononetin, genistein, daidzein, and biochanin A are likely to have a greater affinity for the ER-β receptor (33). Although these compounds bind more strongly to ER-beta, the concentration required to activate both ER-alpha and ER-beta is nearly the same and significantly higher than expected based on their binding affinity (34).

These compounds reduce bone degradation associated with menopause; however, they do not impact bone formation markers such as alkaline phosphatase and osteocalcin (35). Additionally, phytoestrogens are utilized as a treatment for menopausal symptoms, including hot flashes, involuntary vaginal contractions (vaginismus), and painful intercourse (dyspareunia), due to their vasoconstrictive properties (36,37). Furthermore, compounds found in medicinal plants, such as flavonoids and isoflavonoids, can lower blood sugar levels, improve lipid profiles, and reduce triglycerides and LDL while increasing HDL, which are crucial factors in reproductive cycles (38, 39).

Additionally, various studies have demonstrated that plants containing polyphenolic compounds can inhibit breast tumor growth by blocking pathways such as the insulin-like growth factor-1 (IGF-1) and the PI3K/AKT pathway (40). Research on the effects of plant polyphenols (such as isoflavones) on the skin indicates that plant extracts containing these compounds enhance the production of hydroxyproline, a marker of collagen and elastic fiber production. Furthermore, these extracts promote vasodilation in the skin by increasing levels of vascular endothelial growth factor (VEGF) and regulating the secretion of sweat and sebaceous glands. They also influence collagen production in the hair follicle layers. These effects may help alleviate menopausal symptoms and infertility (41, 42).

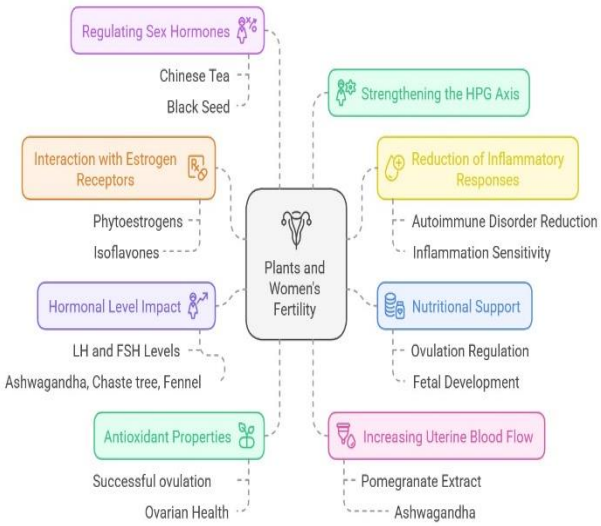

Figure. 1. Mechanisms of Plant Influence on Women's Fertility

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Pomegranate

Pomegranate (Punica granatum) is extensively cultivated in regions such as Asia, the Middle East, and the Mediterranean, known for its juice rich in vitamin C and polyphenols like anthocyanins, punicalagin, ellagic acid, and gallic acid (43). The seeds contain phytoestrogens, including genistein, daidzein, and coumestrol, as well as amino acids such as glutamate and aspartate (44). Research indicates that pomegranate consumption may reduce oxidative stress and enhance fertility in women, while its anti-inflammatory properties could be beneficial in treating fertility-related disorders (43, 44).

A study on mice with polycystic ovary syndrome (PCOS) demonstrated that pomegranate extract, due to its phytoestrogens, can regulate and reduce the symptoms of this syndrome. The extract increases blood flow to the uterus (vasodilation), enhancing mucus secretion and increasing the thickness of the uterine wall. This increase in mucus secretion improves embryo implantation rates through anti-inflammatory mechanisms (45, 46). Additionally, research by Hagag et al. demonstrated that incorporating pomegranate peel and garlic powder into the diet of female rabbits significantly enhanced reproductive efficiency and overall antioxidant status. Specifically, feeding with 3% pomegranate peel resulted in a 28.5% increase in the number of healthy offspring at birth, as well as a notable improvement in progesterone levels and protective immunoglobulins (47).

Pomegranate peel contains calcium and tannins. A controlled clinical study conducted by Mohammadzadeh et al. in 2019 on 110 healthy women found that using this peel in gel form significantly increased women's sexual satisfaction and reduced inflammatory and infectious symptoms in their reproductive tract (48). Research on various human cancer cell lines, including breast (MCF-7), endometrial (HEC-1A), cervical (SiHa and HeLa), ovarian (SKOV3), and normal breast fibroblasts (MCF-10A), indicated that pomegranate extract acts as a selective estrogen receptor modulator (SERM) by binding to estrogen receptors, inhibiting the growth of these cell lines in vitro and ovariectomized mouse models, thus preventing cell proliferation (49). In a trial involving 23 women with PCOS, it was demonstrated that pomegranate fruit extract improved serum androgen levels (specifically, reducing testosterone) and enhanced their lipid profile (50). Additionally, in a study on rats with PCOS, pomegranate fruit extract increased serum estrogen levels and reduced symptoms after 81 days (45).

Chamomile

Chamomile (Matricaria chamomilla) is a plant from the daisy family that contains flavonoids and antioxidants such as gallic acid, chamazulene, farnesene, matricin, coumarin derivatives, apigenin, and choline (51). Due to its active compounds, this plant has positive effects on the reproductive system. A study on the growth and maturation of ovarian follicles in a three-dimensional culture system revealed that chamomile extract increases the levels of progesterone, 17-beta estradiol, and dehydroepiandrosterone in the culture medium. Additionally, this extract reduces reactive oxygen

species (ROS), follicle diameter, and antrum formation, thereby prolonging oocyte survival (52). In gonadectomized mice, chamomile extract improves estrogen-dependent components of sexual function, including hair growth, body temperature regulation, and menstrual cycles (53). Furthermore, a double-blind clinical trial conducted by Gholami et al. in 2016 on 80 pregnant women at or beyond 40 weeks of gestation found that after one week of consuming capsules containing chamomile extract, labor symptoms began to appear, and compared to the control group, labor pain and contraction duration were significantly reduced (54). The use of chamomile vaginal gel has also been shown to significantly improve sexual performance in women compared to a placebo gel (55).

Phytostrogenic compounds found in chamomile contribute to increased milk production in breastfeeding women. Human studies have demonstrated that the extract of this plant can enhance the lactogenesis process (56, 57). In a controlled study involving 56 women with idiopathic hyperprolactinemia, those who consumed chamomile syrup (5 mL, twice daily) exhibited a reduction in prolactin levels compared to the placebo group after four weeks. These findings indicate the role of chamomile in regulating prolactin secretion by influencing dopamine receptors (58). Furthermore, another study involving 130 women showed that inhaling the scent of chamomile improved uterine contractions during labor (59). Additionally, the administration of chamomile extract has been proposed as a strategy to prevent postpartum hemorrhage and alleviate pain in women, showing superior effects compared to chemical agents such as mefenamic acid and other nonsteroidal anti-inflammatory drugs (NSAIDs) (60).

Ashwagandha

Ashwagandha (Withania somnifera), also known as Indian ginseng, belongs to the Solanaceae family and has been shown to have positive effects on women experiencing pregnancy-related issues. This wild plant naturally grows in dry and semi-arid regions, including the southern Mediterranean and the Canary Islands, as well as from North Africa to Northern India, spanning countries such as Iran, Jordan, Sudan, Palestine, Afghanistan, and Egypt (61). In traditional medicine, Ashwagandha is recommended as a treatment for various conditions, including premature ejaculation, multiple arthritis, painful swellings, lower back pain, low sperm motility, vitiligo, general weakness, wounds, sexual dysfunction, uterine infections, abnormal vaginal discharge, and orchitis (62). The compounds present in Ashwagandha extract include anaferine, anahygrin, hygrine, tropine, pseudotropine, withananine, and somniferin. Most of these compounds are recognized as polyphenols (isoflavones and flavonoids) and possess estrogenic activity (63).

Research suggests that this medicinal plant can improve reproductive health by affecting various mechanisms, including hormonal balance and antioxidant properties. Evidence suggests that Ashwagandha increases the balance of luteinizing hormone (LH) and follicle-stimulating hormone (FSH), which are crucial for successful folliculogenesis and proper ovarian function (61).

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Improved hormonal profiles can lead to better ovulation performance and increased chances of pregnancy. Additionally, this plant exhibits significant antioxidant properties that help mitigate oxidative stress, which can affect ovarian health and enhance overall reproductive function (63). In traditional medicine, Ashwagandha has been used to address various specific health issues in women, including polycystic ovary syndrome and menopausal symptoms. The adaptogenic properties of this plant, which help alleviate anxiety and fatigue, may reduce stress-related reproductive disorders and enhance fertility (64).

While evidence supporting the benefits of Ashwagandha in enhancing women's fertility appears promising, some studies indicate that its effects may vary depending on dosage and preparation methods, highlighting the need for further research to optimize its use (61). In a study conducted by Batrai and colleagues, it was found that Ashwagandha extract, with properties similar to GABA (one of the most important inhibitory neurotransmitters), increases the secretion of gonadotropin hormones, ultimately leading to improved ovulation. These effects are attributed to the strengthening of the HPG axis and improved serum estrogen balance (65). Numerous studies have shown that this plant extract possesses anticancer properties against various breast tumor cell lines (such as MCF-7 and MDA-MB-231) as well as in animal models (Balb/c mice), resulting in reduced tumor cell growth. Additionally, Ashwagandha extract has been shown to benefit breast cancer patients by improving their survival and quality of life (66, 67).

Chaste tree

Chaste tree (Vitex Agnus-castus or Desert pepper), a species from the Verbenaceae family, has been studied for its effects on women's fertility, particularly in relation to hormonal balance and reproductive health. Traditionally, this plant has been used to treat menstrual issues, including menstrual pain, premenstrual symptoms, specific menopausal problems, and low breast milk supply, as well as to treat acne. Studies have shown that chaste tree contains beneficial compounds like orientin, casticin, and biochanin, which bind to estrogen receptors and promote women's sexual health. These compounds enhance hormonal function by increasing blood flow to the uterus and reducing levels of prolactin and FSH hormones (68).

Chaste tree is primarily recognized for its potential to reduce prolactin levels, which can be beneficial for women experiencing fertility issues related to hyperprolactinemia (69). It is believed that chaste tree extract has an affinity for dopamine D2 receptors and can inhibit prolactin secretion, thereby potentially improving fertility in women with elevated prolactin levels (70). Other studies have indicated that chaste tree extract may help manage conditions such as premenstrual syndrome (PMS) and PCOS, both of which can impact fertility (69, 71).

Various animal studies have shown that administering chaste tree improves corpus luteum secretions after ovulation and progesterone production, ultimately regulating women's sexual cycles (72). In a study on rats, serum levels of estrogen and progesterone in the group receiving chaste tree extract were found to be higher than those

in the control group. In contrast, levels of LH and prolactin—hormones that disrupt sexual function—were reduced (73). Additionally, in a study involving induced PCOS in rats, the extract of this plant decreased the number of preantral and antral follicles and corpus luteum compared to the control group, while increasing the diameter of antral follicles and the thickness of the follicular capsule and tunica albuginea of the ovaries (74). A recent study by Noori et al. found that the alcoholic extract of chaste tree has a positive effect on physiological and hormonal parameters in female rats with polycystic ovary syndrome, particularly by increasing levels of estrogen and progesterone at doses of 150 and 250 mg/kg. Furthermore, the control group exhibited weight gain and changes in levels of LH, testosterone, and prolactin hormones (75).

However, the effects of chaste tree on fertility outcomes can vary based on the timing and dosage of administration. Chaste tree extract may influence pregnancy rates, live birth rates, and miscarriage rates, with effects differing depending on when consumption begins and the stage of pregnancy. Additionally, the weight of newborns can also be affected by the use of this plant, and these effects should be considered with caution in pregnant women, warranting further studies in this area (76). Caution is also advised when administering to women who are pregnant or trying to conceive, as the effects can be dual.

Red clover

Red clover (Trifolium pratense), belonging to the legume family, is widely used in the food, pharmaceutical, and cosmetic industries. It contains essential minerals such as phosphorus, magnesium, chromium, potassium, calcium, sodium, and iron, which can regulate various molecular pathways and biological processes, particularly in the immune system (77). Analytical studies of red clover extract have confirmed the presence of compounds like cinnamic acid, p-coumaroyl quinic acid, epigallocatechin, caffeic acid, and quercetin (78). The phytoestrogenic compounds in red clover mimic hormone production in women's bodies, reducing the severity and frequency of menopausal symptoms and positively affecting women's health by binding to estrogen receptors ER-beta (79, 80).

In a randomized, placebo-controlled study, 190 postmenopausal women were treated with red clover extract (28.6 mg/kg/day) for 90 days, which significantly reduced symptoms of depression and anxiety while improving hair and skin characteristics (81). In the study by Giurno et al., which was randomized, double-blind, and placebo-controlled, a dosage of 40 mg/kg of body weight of red clover over 12 months did not significantly improve menopausal symptoms or libido in 120 women aged 45 to 65 with menopausal symptoms (82). Another study involving 30 postmenopausal women treated for over 12 months with 80 mg/kg of isoflavones from red clover showed improvements in hormonal levels and endometrial thickness, along with a 44% reduction in hot flashes compared to the control group (83). In the study by Santel et al., red clover extract at doses of 375 and 750 micrograms per gram resulted in increased uterine weight in laboratory rats after 21 days, an effect attributed to binding to estrogen

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receptor alpha. Additionally, this extract stimulated mammary gland development and increased plasma prolactin levels by binding to estrogen receptor beta, preventing bone mass loss in "ovariectomized" mice (84). In another study, doses of 200 and 400 mg/kg of hydroalcoholic red clover extract inhibited the proliferation of triple-negative breast tumor cells and their metastasis to the lungs and brain in Balb/c mice with 4T1 tumors after 35 days. These effects were partially mediated through the activation of estrogen receptor alpha signaling pathways, a reduction in 17β-estradiol levels, and the regulation of apoptosis-related pathways (78, 85).

In an in vitro study, endometrial gland cells were isolated from the endometria of five premenopausal, non-pregnant women whose endometria were in the proliferative phase. These cells were then incubated with red clover extract. The results showed that red clover extract significantly reduced the mRNA expression of estrogen receptor alpha while increasing the mRNA expression of estrogen receptor beta, and it also suppressed the secretion of cytokines such as TNF-α and IL-1α. These findings suggest that the expression of estrogen receptors in endometrial gland cells may be regulated by phytoestrogens at both mRNA and protein levels (86). Additionally, in a study by Lian et al. on animal models, a single subcutaneous injection of genistein (1 mg/30 grams of body weight) over a short period (2 weeks) and daidzein (1 mg/30 grams of body weight) over a more extended period (30 weeks) inhibited the expression of estrogen-dependent genes (c-fos and c-jun) and suppressed cytokines IL-1α and TNF-α through cytokine-related pathways and estrogen receptors, which are important for the proliferation and differentiation of endometrial cells (87). Recently, it has been demonstrated that red clover extract can increase platelet and white blood cell counts, thereby aiding in the improvement of chemotherapy-induced thrombocytopenia and enhancing bone marrow cellularity. These effects may be considered as a supportive option in managing the side effects of chemotherapy, including infertility (88).

Cinnamomum

Among the 250 species of cinnamon found worldwide, 33 species are known to possess therapeutic and nutritional effects. The four main species include C. verum (true cinnamon, also known as Ceylon cinnamon), C. burmannii (Java or Indonesian cinnamon), C. cassia (Chinese cinnamon), and C. loureiroi (Vietnamese or Saigon cinnamon), which are recognized as significant plants in traditional medicine and the pharmaceutical industry (89). Cinnamon extracts and their active compounds have been used to treat various conditions, including asthma, bronchitis, diarrhea, headaches, inflammation, cardiovascular disorders, and polycystic ovary syndrome. Additionally, they are believed to enhance sexual potency in both men and women and increase women's libido (24).

The main compounds of this plant include polyphenols (flavonoids and isoflavonoids) such as eugenol, pyrogallol, cinnamic acid, ferulic acid, caffeic acid, and gallic acid (90). In a randomized controlled trial, it was demonstrated that a six-month treatment with cinnamon improved menstrual cycles, insulin resistance, and androgen secretion in women with PCOS (91). Additionally, studies have shown that

cinnamon regulates the hypothalamic-pituitary-gonadal axis and increases the secretion of gonadotropin hormones, partly through the induction of norepinephrine and nitric oxide production by compounds like delta-cadinene (92).

Fennel

Fennel (Foeniculum Vulgare) is a plant with yellow flowers and feathery leaves, belonging to the Umbelliferae (Apiaceae) family. It is native to the Mediterranean regions, Western Asia, and Eastern Europe. This plant has a long history of use as a traditional medicine (93). Research has shown that fennel possesses beneficial properties against various infectious disorders caused by fungal, bacterial, viral, and protozoan agents. Additionally, this plant has anti-tumor, antioxidant, cytoprotective, and liver-protective effects, and it may help reduce blood sugar levels and increase estrogen levels (94). The main compounds of this plant include polyphenols (flavonoids and isoflavonoids), with quercetin and kaempferol being notable examples. These compounds are responsible for many of fennel's therapeutic properties and can be effective in improving overall health (95).

Hirsutism with an unknown cause is linked to alterations in androgen and estrogen levels and irregularities in the ovulatory menstrual cycle (96). A double-blind, placebo-controlled study by Javidiya et al. found that a cream containing fennel extract significantly improved hirsutism in a dose-dependent manner, with average hair diameter reductions of 18.3%, 7.8%, and 0.5% in the 2%, 1%, and placebo groups, respectively (97). Fennel contains active compounds, such as anethole, which mimics catecholamines and stimulates prolactin secretion, and diosgenin, a steroid saponin that regulates dehydroepiandrosterone synthesis (98). Additionally, due to its components dianethole and photoanethole, fennel is recognized as a lactogenic herb, promoting breast gland growth and enhancing prolactin secretion by competing with dopamine for receptor binding (99).

A study on rats showed that low doses (50 mcg/100 grams of body weight) of fennel extract led to vaginal cornification and enhanced receptivity (fertility) after 10 days (100). At medium doses (250 mcg/100 grams of body weight), the extract increased the weight and volume of reproductive organs (mammary glands, fallopian tubes, endometrium, myometrium, cervix, and vagina) in female rats. Additionally, fennel extract reduced the frequency of uterine contractions. It alleviated dysmenorrhea pain by affecting the synthesis of oxytocin and prostaglandin F2, with effects even more potent than those of mefenamic acid (101). In an investigation on ovariectomized rats, doses of 500 to 1000 mg/kg of fennel extract increased bone mineral density and collagen fiber synthesis in a dose-dependent manner after 30 days, indicating the plant's role in preventing osteoporosis, particularly in postmenopausal women (102).

Furthermore, a study by Pourjafari revealed that hydroalcoholic extract and fennel seeds could improve folliculogenesis and increase total antioxidant capacity in the offspring of NMRI mice. Pregnant mice receiving 500 or 1000 mg of fennel showed significant increases in body weight, ovarian weight, and follicle count compared to the control

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group, with the 500 mg treatment having a more pronounced effect. These results suggest that fennel may serve as a natural supplement to enhance fertility during pregnancy and lactation (103).

In a clinical trial investigating the effects of fennel seed extract on fertility outcomes in women with poor ovarian response, 19 infertile women were treated with fennel extract for two months before starting IVF. The results showed significant increases in LH levels relative to FSH, endometrial thickness, and ovarian volume after treatment. Additionally, the number of days required to induce ovulation was reduced (104). Overall, the use of fennel had positive effects on improving egg quality and fertility indicators in women. However, a study examining the effects of fennel and metformin on insulin resistance in women with polycystic ovary syndrome found no significant differences in insulin resistance and related indices between the two groups post-treatment. In other words, fennel was not as effective as metformin in improving insulin resistance and other body metrics; however, it is essential to consider the limitations of these findings (105).

The date palm

The date palm (Phoenix Dactylifera), belonging to the palm family (Arecaceae), has been utilized in traditional medicine across various cultures, including Iran, Ancient Rome, Ancient Egypt, China, and Greece, for enhancing sexual potency and alleviating menopausal symptoms in women (106). Rich in essential elements such as cobalt, copper, fluorine, magnesium, manganese, selenium, and zinc, along with various vitamins, this plant is efficacious in improving women's fertility. Research indicates its anticancer and anti-inflammatory properties, as well as its ability to protect the kidneys and liver, while also preventing fertility disorders caused by toxins in animal models (107). Furthermore, the presence of polyphenolic compounds like gallic acid and isoflavones, along with saponins that increase blood flow to the female reproductive system through the release of nitric oxide and stimulation of the HPG axis, underscores the date palm's significance as a natural supplement for enhancing fertility and promoting women's health (108).

Studies on mice have shown that Phoenix extract stimulates ovulation and increases the number of antral and secondary follicles, as well as the growth and maturation of pre-antral follicles, due to the presence of bioactive compounds similar to gonadotropins, such as rutin, sterols, carotenoids, and androsterone (109). In PCOS, a high LH to FSH ratio leads to increased synthesis of androgens, insulin, and insulin-like growth factors, resulting in a rise in the number of cystic follicles. However, a study indicated that the consumption of date palm extract, due to its estrogen-like compounds, reduces the LH to FSH ratio and the number of cystic follicles while regulating estrogen and androgen synthesis, thereby increasing the number of secondary and antral follicles (110-112). The estrogenic compounds in this extract may be effective in treating uterine disorders, as they have been shown to help reduce endometrial tissue destruction, necrotic areas, and hyperplasia in endometrial glands (113).

In an animal study by Jihil, the effects of the ethanolic extract of date palm pollen on the fertility of female

mice under oxidative stress induced by sodium nitrate were examined. The groups receiving the date palm pollen extract showed significant improvements in fertility, pregnancy, and survival rates compared to those treated with sodium nitrate. The best results were observed in the group that underwent long-term treatment with the extract, indicating its potential to enhance fertility and protect against sodium nitrate-induced damage (114). The impact of raw extract and components of date palm pollen on the reproductive system of female mice was also investigated, revealing that n-butanol and petroleum ether fractions exhibited the highest fertility activity, with significant increases in FSH, estrogen, and progesterone levels (115). A double-blind, placebo-controlled clinical trial conducted in 2019 on infertile women and their partners in Iran showed that the intervention group receiving date seed capsules experienced significant improvements in overall sexual function scores and various aspects of sexual performance, including arousal, orgasm, lubrication, pain during intercourse, and satisfaction. Similarly, all aspects of male sexual performance, including erectile function, orgasm, libido, and relationship satisfaction, significantly improved in the intervention group (116). Recently, it has been demonstrated that the meristem, or heart, of the date palm enhances the oxidant-antioxidant balance and mitigates the adverse effects of PCOS on oxidative stress (117).

Chinese tea

Chinese tea (Camellia sinensis) belongs to the Theaceae family and is primarily grown in East Asia, the Indian subcontinent, and Southeast Asia. Today, this plant is cultivated in tropical and subtropical regions worldwide. Analytical studies of C. sinensis extracts have confirmed the presence of compounds such as galloylquinic acid, epigallocatechin, epicatechin, succinic acid, and gallocatechin (118). Additionally, other compounds, such as strychnine, apigenin glucosyl arabinoside, quercetin, myricetin, genistein, and daidzein, have also been identified (119). These compounds have garnered significant attention due to their antioxidant properties and potential health benefits.

The compounds found in Chinese tea, primarily isoflavones and flavonoids, exhibit a variety of therapeutic properties. These compounds possess antioxidant and phytoestrogenic properties, which can help restore the secretion and concentration of sex hormones, including LH, FSH, estradiol, and testosterone, in Wistar female rats with PCOS induced by letrozole (120). Additionally, the isoflavones in this plant reduce estradiol production in a dose-dependent manner by inhibiting the aromatase enzyme, which plays a role in estradiol synthesis in granulosa cells. These findings highlight the therapeutic potential of this plant in managing hormonal disorders (121).

Studies have shown that extracts of Chinese tea can reduce estrogen-dependent menopausal symptoms and prevent osteoporosis. In one study involving female rats with both ovaries removed, daily consumption of 1 milliliter of the extract for 28 days resulted in a dose-dependent increase in bone mineral reserves (122). Additionally, another study demonstrated that this extract, administered at doses

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of 100, 200, and 400 mg/kg for 15 days, enhanced the secretory activity of mammary glands by regulating prolactin secretion (123). Furthermore, other research has indicated that consuming the extract during various stages of pregnancy improves implantation indices, pregnancy duration, and pregnancy rates in rats compared to the control group. These findings highlight the therapeutic potential of this plant in enhancing women's health and pregnancy outcomes (124). A study on aged female mice showed that black seed and green tea (one of the varieties of Chinese tea) could improve fertility and increase litter size. These substances significantly prolonged the fertility period and increased the weight of pups at birth and during infancy. Additionally, ovarian health and viability in treated mice were improved (125).

Black seed

Black seed (Nigella sativa), belonging to the Ranunculaceae family, grows to a height of 30 to 60 centimeters and features pinnate leaves. It is found in various regions, including Eastern Europe and Asia. This plant is used as a remedy for a variety of ailments, including digestive disorders, headaches, male infertility, diabetes, and menopausal symptoms (126). Its main active compounds include polyphenols and flavonoids such as kaempferol and quercetin. Studies have shown that black seed extract, due to its phytoestrogenic and flavonoid compounds, can reduce the number of hormone-induced ovarian cysts and improve PCOS by enhancing the expression of genes related to epigenetics and regulating the HPG axis (127, 128).

Long-term use of black seed extract, due to its phytoestrogens, can lower testosterone levels, thereby creating negative feedback on LH (129). This reduction in androgens likely decreases LH production and diminishes LH's dominant effect on FSH. Additionally, the extract may influence LH dominance over FSH by inhibiting nitric oxide-producing neurons and leptin, which are involved in LH synthesis from the anterior pituitary gland, potentially aiding ovulation in women with PCOS (129). Studies have shown that black seed extract reduces menopausal symptoms in ovariectomized rats in a dose-dependent manner, decreasing serum estradiol levels and inflammatory cell counts in the vagina (130). Furthermore, specific doses of this extract in pregnant rats with hypothyroidism have been found to lower serum estradiol levels while increasing prolactin, likely due to the stimulatory effects of phytoestrogens on dopaminergic neurons (131).

Licorice

The licorice plant (Glycyrrhiza glabra) is a perennial herb from the Fabaceae family that grows in many parts of the world but is native to Western Asia and Southern Europe, particularly in France, Uzbekistan, China, and Iran. This plant contains various phytoestrogens and has anti-diabetic, anti-spasmodic, anti-depressant, laxative, anti-ulcer, and anti-inflammatory effects (132). A high dose of more than 2 mg/kg of body weight per day of glycyrrhizic acid (the main component of licorice) may cause side effects such as hypokalemia, hypertension, and muscle weakness. Chemical analyses have shown

that licorice extract contains compounds such as matrine, oxymatrine, ferulic acid, and glycyrrhizin (133). Due to its high levels of phytoestrogens, this plant may be effective in treating estrogen-dependent diseases such as breast cancer, endometriosis, PCOS, and primary ovarian insufficiency (134). Studies indicate that licorice stimulates aromatase enzyme activity (135). Additionally, due to the presence of phytoestrogens, it may reduce testosterone synthesis, aiding in the treatment of women with PCOS (134). Furthermore, a study on mice with PCOS demonstrated that licorice extract improved ovarian morphology, oocyte maturation, and embryonic development in a dose-dependent manner (136).

Glycyrrhiza glabra has demonstrated significant therapeutic potential in various reproductive health conditions. In animal models of endometriosis, a dosage of 3000 mg /kg/day over six weeks effectively inhibited cyclooxygenase-2 and interleukin-6, enhanced the HPG axis, and reduced VEGF expression, thereby decreasing endometrial implants (137). Conversely, high, medium, and low doses of licorice during pregnancy have been linked to increased cortisol levels in newborns' saliva, suggesting potential adverse effects on neurodevelopment and psychological functioning (138). Clinical studies further support its efficacy; for instance, a randomized double-blind trial involving 60 menopausal women revealed that licorice extract significantly reduced the frequency and severity of hot flashes in a dose-dependent manner, comparable to hormone replacement therapy (139). Additionally, a cream containing 2% licorice extract was found to prevent vaginal atrophy and alleviate associated symptoms such as dryness and pain (140). Furthermore, the presence of flavonoids with anticancer properties in licorice may contribute to reduced incidence of endometrial adenocarcinoma by modulating apoptotic and inflammatory pathways, underscoring its potential role in enhancing women's reproductive health (24).

Potential Risks of Using Herbs During Pregnancy

The use of herbal medications during pregnancy is a common practice, as many believe that natural products are inherently safe. However, research indicates that the consumption of certain herbs during this period can pose risks and lead to adverse outcomes such as miscarriage and preterm labor (26). These risks are primarily due to the presence of active compounds in the plants that can cross the placental barrier and affect fetal development. Some herbs may cause fetal toxicity or congenital abnormalities; for instance, plants like aloe vera and senna (Senna alata) are recognized as having a high risk of miscarriage (141). Additionally, certain herbs can stimulate uterine contractions or disrupt hormonal balance, which further increases the risk of miscarriage. For example, castor oil and night-blooming jasmine (Cestrum nocturnum) are among the plants that have such effects. Moreover, some active compounds in herbs can lead to severe growth abnormalities or even fetal death, particularly in the first trimester of pregnancy. Specific plants, such as pennyroyal (Mentha pulegium) and blue cohosh (Caulophyllum thalictroides), are known to be highly toxic abortifacients (142, 143). However, it is important to note that not all herbs are harmful; for example,

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ginger (Zingiber officinale) is often recognized as a low-risk remedy for treating nausea during pregnancy. Therefore, pregnant women should consult with medical professionals before using any herbal medications to ensure their safety and efficacy (144, 145).

Limitations of clinical trials on the therapeutic effects of herbal medicines on reproductive health

The effects of herbal medicines on women's reproductive health show great promise; however, clinical trials in this field encounter significant challenges that impede the establishment of robust evidence for their efficacy and safety. One major limitation is the low methodological quality of many studies, which often lack appropriate standards in design and reporting (146). Additionally, small sample sizes and a lack of diversity among participants make it difficult to generalize findings to larger populations (147, 148). Variability in the preparation and dosage of herbal remedies further complicates comparisons between studies, and the absence of standardized protocols can lead to inconsistent results. Despite these challenges, the potential of herbal medicines to address reproductive health issues remains noteworthy, underscoring the need for further research to improve the quality and reliability of clinical evidence.

This review has a few key limitations: it focused only on English studies, potentially missing valuable research in other languages; the original studies varied widely in methods (like doses and treatment lengths), making comparisons difficult; there were not enough large clinical trials tracking long-term effects; and findings might be skewed because unpublished negative results were not included.

Table 1 summarizes the major clinical trials conducted on the therapeutic effects of medicinal plants on reproductive health and related symptoms in women.

Table 1. Therapeutic effects of medicinal plants on women's reproductive health and related symptoms.

Herb	Study Title	Year of Publication	Number of Participants	Key Results	Source
Pomegranate	Effects of Pomegranate Extract on Women with PCOS	2020	23	Reduction in androgen (testosterone) levels, improvement in lipid profile, increased estrogen levels, and decreased PCOS symptoms	(50)
Pomegranate	Effects of Pomegranate Topical Gel on Women's Sexual Satisfaction	2019	110	Increased sexual satisfaction and reduced inflammatory and infectious symptoms in the reproductive tract	(48)
Chamomile	Effects of Oral Chamomile Extract Capsules on Labor	2016	80	Reduction in labor pain and duration of contractions, and onset of labor after one week of consumption	(54)
Chamomile	Effects of Chamomile Syrup on Hyperprolactinemia	2020	56	Reduction in prolactin levels and improvement in hyperprolactinemia symptoms	(58)
Ashwagandha	Effects of Ashwagandha Extract on Women's Fertility Components	2021	40	Improvement in hormonal balance and increased chances of pregnancy, as evidenced by elevated LH and FSH levels.	(64)
Chaste tree	Effects of Vitex Extract on Women's Fertility Components	2020	50	Improvement in corpus luteum secretions and progesterone production, regulation of the menstrual cycle	(72)
Red Clover	Effects of Red Clover Extract on Symptoms of Low Plasma Estrogen and Progesterone Levels	2020	190	Reduction in depression and anxiety symptoms, improvement in hair and skin characteristics	(81)

Red Clover	Effects of Red Clover Extract on Hot Flashes	2019	30	Improvement in hormonal levels and a 44% reduction in hot flashes compared to the control group	(83)
Cinnamon	Effects of Cinnamon on Menstrual Cycle in Women with PCOS	2021	60	Improvement in menstrual cycle and insulin resistance, reduction in androgen secretion	(91)
Fennel	Effects of Fennel Extract Cream on Hirsutism and Other PCOS Symptoms	2018	40	Reduction in average hair diameter in a dose-dependent manner	(97)
Licorice	Effects of Licorice Extract on Hot Flashes in Women with Low Estrogen and Progesterone Levels	2020	60	Reduction in frequency and severity of hot flashes in a dose-dependent manner	(139)
Licorice	Effects of Licorice Extract on Vaginal Atrophy	2019	70	Prevention of vaginal atrophy and reduction in dryness, pain, and itching	(140)
Date Palm	Effects of Date Seed Extract on Fertility Components in Women and Men	2019	80	Increased overall sexual performance scores in women and men, improved sleep quality, and reduced stress	(116

Conclusion

This study combined pharmacological mechanisms, clinical trial evaluations, and safety guidelines for herbal fertility treatments. We described how more than 10 key herbs (including pomegranate, Ashwagandha, and licorice) improve female fertility through hormone regulation, antioxidant effects, and receptor interactions (like SERMs). Using data from 32 clinical trials (1995–2024), we created a decision-making framework for safe usage. We identified dose-related risks (e.g., low potassium from licorice) and developed a classification system for herbs to avoid during pregnancy. Finally, we propose a research plan that combines plant chemistry, pharmacology, and safety studies to support the development of future herbal medicines.

Among the plants effective in treating various female reproductive disorders, several factors that have positive effects on fertility have been comprehensively investigated. These plants are effective in preventing and treating various reproductive disorders due to their diverse compounds, including polyphenols, which exhibit numerous biological activities. These disorders include polycystic ovary syndrome, endometriosis, primary ovarian insufficiency, hypothalamic disorders, hyperprolactinemia, pelvic inflammatory disease, menopausal symptoms, osteoporosis, and cancers related to the female reproductive system (cervical, ovarian, uterine/endometrial, vaginal, and other adnexa cancers). Through further research in the fields of pharmacology, phytochemistry, and toxicology, new and effective drugs can be developed by comprehensively studying and evaluating the biological activity of various compounds extracted from these plant extracts. This approach can lead to the identification and introduction of new treatments for women's reproductive disorders and help improve their quality of life and reproductive health.

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