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Phytotherapy and Fertility Enhancement: Herbal Medicine Strategies for Reproductive Hormone Modulation

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ABSTRACT

Fertility challenges continue to affect millions globally, necessitating the exploration of innovative therapeutic strategies. In recent years, bioactive plant extracts have gained prominence for their ability to influence endocrine function, particularly through interactions with key reproductive hormones. This review provides a detailed analysis of current scientific evidence on the hormonal effects of selected phytochemicals and plant-based formulations, focusing on prolactin, estrogen, progesterone, luteinizing hormone (LH), and follicle-stimulating hormone (FSH). Drawing from in vivo, in vitro, and clinical studies, we discuss the mechanisms of action, dose-dependent effects, and therapeutic implications for male and female fertility enhancement. We also highlight safety considerations, herb-drug interactions, and regulatory gaps in the use of these botanicals for fertility treatment. This article calls for rigorous, standardized research to validate these natural interventions and integrate them into personalized fertility management strategies.

Keywords: Phytotherapy, Fertility Enhancement, Reproductive Hormones, Herbal Medicine, Endocrine Modulation

INTRODUCTION

Infertility remains a pressing public health issue, affecting an estimated 186 million individuals globally, according to the World Health Organization [1]. It is often defined as the inability to conceive after 12 months of regular, unprotected intercourse. While advances in assisted reproductive technologies (ARTs) such as in vitro fertilization (IVF) and intrauterine insemination (IUI) have revolutionized infertility treatment, these methods are expensive, technologically demanding, and may be inaccessible to many in low-resource settings. This has led to a growing interest in alternative and complementary approaches, particularly those grounded in traditional medicine. Among these, the use of herbal medicine for fertility enhancement has gained renewed attention. In various cultural contexts, the use of plant-based remedies to enhance reproductive capacity has been practiced for centuries [2]. Contemporary scientific research is now validating some of these traditional practices by exploring the molecular interactions between phytochemicals and the human endocrine system. Specifically, certain plant extracts have shown the ability to modulate reproductive hormones such as estrogen, progesterone, luteinizing hormone (LH), follicle-stimulating hormone (FSH), prolactin, and testosterone [3]. These hormones are intricately involved in regulating gametogenesis, sexual function, and the menstrual or estrous cycle, making them attractive targets for phytotherapeutic intervention [4].

As fertility disorders are often rooted in endocrine imbalances, the exploration of phytochemicals with hormone-modulating properties is particularly promising. This review article aims to provide a critical evaluation of scientific evidence supporting the use of hormone-modulating plant extracts for fertility enhancement. It focuses on the pharmacological mechanisms, clinical efficacy, safety, and regulatory concerns associated with these herbal therapies. By integrating findings from traditional medicine and modern endocrinology, we seek to highlight how natural products can contribute to holistic and individualized fertility treatment strategies.

Reproductive Hormones and Fertility: Targets for Modulation

The human reproductive system operates under the precise regulation of several hormones secreted by the hypothalamus, pituitary gland, and gonads [5]. These hormones not only regulate the production of gametes—sperm in males and ova in females—but also coordinate the menstrual cycle, maintain pregnancy, and influence libido [6]. The primary reproductive hormones include luteinizing hormone (LH), follicle-stimulating hormone (FSH), estrogen, progesterone, prolactin, and testosterone [7]. Their actions are interdependent, and disruption at any point in the hormonal cascade can lead to subfertility or infertility. Luteinizing hormone (LH) and follicle-stimulating hormone (FSH) are secreted by the anterior pituitary gland in response to gonadotropin-releasing hormone (GnRH) from the hypothalamus [8]. In females, FSH stimulates follicular development in the ovaries, while LH triggers ovulation and corpus luteum formation [8]. In males, LH acts on Leydig cells to promote testosterone production, whereas FSH supports spermatogenesis through its action on Sertoli cells [9]. Estrogens, primarily produced by the ovaries, play a key role in endometrial proliferation, ovulation, and maintenance of secondary sexual characteristics [10]. Progesterone, also of ovarian origin, supports the luteal phase of the menstrual cycle and prepares the endometrium for implantation [11]. Prolactin, secreted by the pituitary, has dual roles in lactation and reproductive suppression; elevated levels (hyperprolactinemia) can inhibit ovulation [12]. Testosterone, the principal male sex hormone, regulates sperm production and sexual behavior, though it also has physiological roles in females, including libido and ovarian function [13]. Given the sensitivity of these hormonal pathways, even minor imbalances can impair reproductive capacity. Conventional treatments often rely on hormone replacement or suppression, which can have adverse effects. Consequently, attention has shifted to gentler alternatives—specifically, herbal medicines with evidence-based endocrine-modulating properties. These therapies may help restore hormonal balance and support natural reproductive function with potentially fewer side effects and better cultural acceptability.

Phytochemicals with Documented Hormonal Effects

Plant-derived bioactive compounds, commonly known as phytochemicals, can exert significant biological effects on the human endocrine system [14]. These compounds include flavonoids, alkaloids, terpenoids, lignans, and saponins, among others [14]. They are often capable of binding to hormone receptors, mimicking endogenous hormones, or altering hormone synthesis and metabolism [15]. Numerous botanicals have demonstrated such properties, with several gaining scientific recognition for their potential in fertility enhancement.

Vitex agnus-castus, commonly known as chasteberry, is one of the most extensively studied herbs for female reproductive health [16]. Its active constituents are believed to exert dopaminergic effects, reducing prolactin secretion and thereby promoting ovulatory cycles in women with hyperprolactinemia [17]. Randomized controlled trials have demonstrated improved menstrual regularity and increased pregnancy rates among users.

Trifolium pratense (red clover) contains isoflavones that are structurally similar to estrogen [18]. These phytoestrogens can bind to estrogen receptors, particularly ER-β, and exhibit selective estrogen receptor modulator (SERM)-like activity [18]. In premenopausal women, red clover is believed to support ovulatory function, though its use must be carefully titrated to avoid estrogen excess.

Withania somnifera, or ashwagandha, has shown significant promise in enhancing male fertility. It increases serum testosterone and luteinizing hormone levels, improves semen quality, and reduces oxidative stress in the testes [19]. Clinical trials involving infertile men have reported improved sperm concentration and motility following supplementation with ashwagandha extract [20].

Glycyrrhiza glabra (licorice root) contains glycyrrhizin, which inhibits 17β-hydroxysteroid dehydrogenase, an enzyme involved in androgen synthesis [21]. This anti-androgenic effect has made it a potential candidate for managing hyperandrogenic states such as polycystic ovary syndrome (PCOS), although long-term use may disrupt cortisol metabolism.

Panax ginseng is traditionally used to improve male sexual performance and vitality. Its ginsenosides are thought to enhance nitric oxide synthesis and modulate the hypothalamic-pituitary-gonadal (HPG) axis [22]. Evidence from animal studies and clinical trials supports its role in boosting testosterone levels and improving sperm morphology and motility [22].

These findings suggest that plant-based therapies offer a multifaceted approach to hormone regulation, with implications for both male and female fertility. However, variations in plant species, extraction methods, dosages, and patient responses highlight the need for standardization and individualized therapy protocols. Further research into the pharmacokinetics and long-term effects of these extracts is critical for safe clinical integration.

Mechanisms of Hormonal Modulation by Plant Extracts

The therapeutic value of medicinal plants in fertility enhancement is largely attributed to their diverse phytoconstituents capable of modulating hormonal pathways through well-defined molecular mechanisms. These mechanisms encompass receptor binding, enzyme inhibition, modulation of gene expression, and neuroendocrine

regulation. The most well-documented route involves the ability of phytoestrogens and other bioactives to interact with hormone receptors, influencing downstream signaling cascades and altering endocrine outputs [23].
One of the most explored mechanisms is receptor interaction, where phytochemicals mimic or block the action of endogenous hormones. Isoflavones such as genistein and daidzein, found in soy and red clover, can bind to estrogen receptors (ERα and ERβ) [24]. These compounds act as selective estrogen receptor modulators (SERMs), exhibiting agonistic or antagonistic activity depending on the target tissue [25]. In the reproductive axis, this can result in the normalization of estrogen levels, endometrial proliferation, and regulation of the menstrual cycle.

Another critical mechanism is neuroendocrine modulation, especially of the hypothalamic-pituitary-gonadal (HPG) axis. Some plant extracts, such as Vitex agnus-castus, act by stimulating dopamine D2 receptors, which suppress the secretion of prolactin from the anterior pituitary [17]. Elevated prolactin levels inhibit gonadotropin-releasing hormone (GnRH) secretion, thereby suppressing LH and FSH release [26]. By reducing prolactin levels, Vitex indirectly restores ovulation and menstrual regularity.
Enzyme inhibition also plays a significant role in hormonal modulation. For instance, compounds like glycyrrhizin in licorice inhibit 17β-hydroxysteroid dehydrogenase and aromatase, enzymes that convert androgens to estrogens [21]. This mechanism has implications for conditions like PCOS, where hyperandrogenism disrupts ovulatory function [21]. Similarly, the inhibition of phosphodiesterase or modulation of nitric oxide synthase by compounds in Panax ginseng can influence cyclic nucleotide levels, affecting testosterone production and vascular function in the male reproductive system [27].In addition, modulation of gene expression and intracellular signaling pathways, such as MAPK, PI3K/Akt, and NF-κB, allows phytochemicals to regulate the transcription of hormone-responsive genes [28]. This mechanism underlies the adaptogenic and pleiotropic effects of plants like Withania somnifera and Tribulus terrestris, which not only enhance endocrine function but also mitigate oxidative stress and inflammation, both of which are implicated in infertility. Overall, the ability of plant extracts to engage multiple molecular targets presents both therapeutic advantages and challenges. While polypharmacology can enhance efficacy, it also increases the risk of off-target effects and herb-drug interactions [29]. Thus, mechanistic studies are essential for elucidating safe and effective dosing strategies.

Clinical Evidence and Therapeutic Applications

A growing body of clinical research supports the efficacy of specific plant extracts in modulating reproductive hormones and enhancing fertility outcomes. These studies span various methodologies, including observational studies, pilot trials, and randomized controlled trials (RCTs), though heterogeneity in sample size, extract formulation, and outcome measures often complicates data interpretation.
Vitex agnus-castus has the most robust clinical support, particularly for women with luteal phase defects and hyperprolactinemia. Multiple studies have shown that treatment with Vitex significantly reduces prolactin levels, shortens follicular phases, and improves ovulation rates. A 2001 randomized controlled trial published in the British Journal of Obstetrics and Gynaecology demonstrated a higher pregnancy rate in women treated with Vitex compared to placebo [30].
Withania somnifera has demonstrated fertility-enhancing effects in men with oligospermia [31]. Clinical trials have shown that supplementation significantly improves sperm count, motility, and testosterone levels, likely through antioxidant and adaptogenic effects on the testes and adrenal glands. One randomized trial involving 75 men with infertility found a significant increase in seminal parameters and hormone levels following 90 days of ashwagandha supplementation [31].
In women with PCOS, Glycyrrhiza glabra combined with other herbs such as Paeonia lactiflora has shown potential in reducing free testosterone levels and improving menstrual regularity [32]. However, long-term use must be approached with caution due to risks of pseudoaldosteronism, which may lead to hypertension and hypokalemia [33]. Clinical applications of Panax ginseng have shown improvements in erectile function, testosterone levels, and sperm morphology in men with subfertility [22]. Its benefits are thought to be mediated by nitric oxide-dependent vasodilation and hypothalamic-pituitary stimulation. Nonetheless, several limitations persist in the current clinical evidence base. Many studies have small sample sizes, lack placebo controls, or fail to standardize the phytochemical composition of the extracts. Moreover, outcomes are often self-reported or based on surrogate hormonal markers rather than live birth rates or time to conception. This calls for large-scale, rigorously designed trials with standardized dosing and long-term follow-up to evaluate true clinical efficacy.

Safety, Herb-Drug Interactions, and Regulatory Considerations

Although plant-based therapies are often perceived as safe due to their natural origin, the potential for adverse effects, toxicity, and interactions with conventional drugs should not be overlooked. Safety concerns are particularly relevant when herbal products are used in combination with fertility drugs, hormonal contraceptives, or other endocrine modulators. One of the primary risks associated with phytotherapy is hormonal overstimulation. For instance, high doses of phytoestrogens from red clover or soy may exacerbate conditions such as endometriosis, uterine fibroids, or estrogen-sensitive cancers [34]. Similarly, excessive consumption of licorice root has been linked to pseudoaldosteronism due to mineralocorticoid receptor activation, leading to water retention and hypokalemia [33]. Another important consideration is herb-drug interactions, especially involving cytochrome P450 enzymes. St. John's wort, commonly used for mood regulation, can induce CYP3A4 and alter the metabolism of oral contraceptives and fertility medications like clomiphene [35]. While not always directly estrogenic or androgenic, such interactions can significantly alter therapeutic outcomes and patient safety. Moreover, regulatory oversight of herbal products remains inconsistent across countries, with wide variation in standards for quality, safety, and efficacy. In many regions, herbal supplements are classified as dietary aids rather than pharmaceutical agents, leading to limited pre-market testing and post-market surveillance [36]. This results in variability in active ingredient concentration, presence of contaminants, and batch-to-batch inconsistency. To ensure safe clinical use, it is critical that practitioners obtain detailed patient histories, including all herbal supplements, and monitor for potential interactions. Standardization of extracts, transparent labeling, and adherence to good manufacturing practices (GMP) are essential to minimize risk. Furthermore, regulatory bodies must adopt stricter quality control measures and integrate herbal pharmacovigilance systems into national drug monitoring programs. In conclusion, while phytotherapeutics offer valuable fertility-enhancing options, their use must be grounded in scientific rigor, safety monitoring, and regulatory oversight to ensure optimal outcomes and patient protection.

Future Directions and Research Priorities

The therapeutic potential of hormone-modulating plant extracts in fertility management is vast but underexplored. Future research should prioritize the standardization of active phytoconstituents, ensuring reproducibility and efficacy across populations. Advanced techniques such as metabolomics, transcriptomics, and network pharmacology should be employed to unravel complex interactions between phytochemicals and endocrine pathways. There is also a pressing need for large-scale, multicenter randomized controlled trials (RCTs) that evaluate not just hormonal changes but also clinical endpoints such as conception rates, live births, and pregnancy outcomes. The development of personalized phytotherapy based on genetic, hormonal, and metabolic profiles represents a promising frontier. Moreover, regulatory harmonization across countries is necessary to ensure the safe integration of herbal products into mainstream fertility care. Building collaborative frameworks between traditional healers, clinicians, and researchers will enhance data sharing and innovation. Ultimately, bridging traditional knowledge with rigorous scientific validation can lead to holistic, affordable, and effective fertility interventions.

CONCLUSION

Plant-derived extracts offer a compelling adjunct to conventional fertility treatments through their ability to modulate reproductive hormones via multiple mechanisms. Compounds such as phytoestrogens, dopaminergic agents, and enzyme inhibitors have shown promise in regulating estrogen, progesterone, prolactin, and gonadotropin levels, thereby enhancing both male and female fertility outcomes. While existing clinical studies are encouraging, more robust and standardized trials are required to establish efficacy and safety profiles. Equally important is the need for stringent regulation, proper patient education, and vigilant monitoring of herb-drug interactions. Integrating phytotherapy into reproductive medicine should be evidence-based, personalized, and guided by mechanistic insights. As scientific interest in hormone-extract interactions grows, the convergence of traditional medicinal knowledge and modern biomedical research holds the key to expanding fertility care, particularly in low-resource settings where conventional options are limited. The future of fertility enhancement may well lie in the synergistic potential of nature and science.

REFERENCES

1. World Health Organization: WHO. Infertility. 2024. Available from: https://www.who.int/news-room/fact-sheets/detail/infertility
2. Akbaribazm M, Goodarzi N, Rahimi M. Female infertility and herbal medicine: An overview of the new findings. Food Science & Nutrition. 2021;9(10):5869–82. doi:10.1002/fsn3.2523
3. Tiwari P, Sahu PKPK. Plants altering hormonal milieu: A review. Asian Pacific Journal of Reproduction. 2017;6(2):49–53. doi:10.12980/apjr.6.20170201
4. Athar F, Karmani M, Templeman NM. Metabolic hormones are integral regulators of female reproductive health and function. Bioscience Reports. 2023;44(1). doi:10.1042/BSR20231916
5. Acevedo-Rodriguez A, Kauffman AS, Cherrington BD, Borges CS, Roepke TA, Laconi M. Emerging insights into hypothalamic-pituitary-gonadal axis regulation and interaction with stress signalling. Journal of Neuroendocrinology. 2018;30(10). doi:10.1111/jne.12590
6. Ramya S, Poornima P, Jananisri A, Geofferina IP, Bavyataa V, Divya M, et al. Role of hormones and the potential impact of multiple stresses on infertility. Stresses. 2023;3(2):454–74. doi:10.3390/stresses3020033
7. Endocrine Society. Reproductive hormones. 2022. Available from: https://www.endocrine.org/patient-engagement/endocrine-library/hormones-and-endocrine-function/reproductive-hormones

8. Orlowski M, Sarao MS. Physiology, follicle stimulating hormone. StatPearls – NCBI Bookshelf. 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK535442/
9. Santi D, Crépieux P, Reiter E, Spaggiari G, Brigante G, Casarini L, et al. Follicle-Stimulating Hormone (FSH) action on spermatogenesis: A focus on physiological and therapeutic roles. Journal of Clinical Medicine. 2020;9(4):1014. doi:10.3390/jcm9041014
10. Delgado BJ, Lopez-Ojeda W. Estrogen. StatPearls – NCBI Bookshelf. 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK538260/
11. Cable JK, Grider MH. Physiology, progesterone. StatPearls – NCBI Bookshelf. 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK558960/
12. Al-Chalabi M, Bass AN, Alsalman I. Physiology, prolactin. StatPearls – NCBI Bookshelf. 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK507829/
13. Nassar GN, Leslie SW. Physiology, testosterone. StatPearls – NCBI Bookshelf. 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK526128/
14. Kumar A, PN P, Kumar M, Jose A, Tomer V, Oz E, et al. Major Phytochemicals: Recent advances in health benefits and extraction method. Molecules. 2023;28(2):887. doi:10.3390/molecules28020887
15. Alum, E. U. (2025). Role of phytochemicals in cardiovascular disease management: Insights into mechanisms, efficacy, and clinical application. Phytomedicine Plus, 5(1),100695. https://doi.org/10.1016/j.phyplu.2024.100695.
16. Alum, E. U. (2024). Climate change and its impact on the bioactive compound profile of medicinal plants: implications for global health. *Plant Signaling & Behavior*, *19*(1), 2419683. doi: 10.1080/15592324.2024.2419683. Epub 2024 Oct 26. PMID: 39460932; PMCID: PMC11520564.
17. Puglia LT, Lowry J, Tamagno G. Vitex agnus-castus effects on hyperprolactinaemia. Frontiers in Endocrinology. 2023;14. doi:10.3389/fendo.2023.1269781
18. Beck V, Rohr U, Jungbauer A. Phytoestrogens derived from red clover: An alternative to estrogen replacement therapy? The Journal of Steroid Biochemistry and Molecular Biology. 2005;94(5):499–518. doi:10.1016/j.jsbmb.2004.12.038
19. Ahmad MK, Mahdi AA, Shukla KK, Islam N, Rajender S, Madhukar D, et al. Withania somnifera improves semen quality by regulating reproductive hormone levels and oxidative stress in seminal plasma of infertile males. Fertility and Sterility. 2009;94(3):989–96. doi:10.1016/j.fertnstert.2009.04.046
20. Chavda VP, Sonak SS, Balar PC, Vyas K, Palandurkar P, Mule K, et al. Reviving fertility: Phytochemicals as natural allies in the fight against non-genetic male infertility. Clinical Complementary Medicine and Pharmacology. 2024;4(1):100128. doi:10.1016/j.ccmp.2024.100128
21. Josephs RA, Guinn JS, Harper ML, Askari F. Liquorice consumption and salivary testosterone concentrations. The Lancet. 2001;358(9293):1613–4. doi:10.1016/S0140-6736(01)06664-8
22. Leung KW, St Wong A. Ginseng and male reproductive function. Spermatogenesis. 2013;3(3):e26391. doi:10.4161/spmg.26391
23. Mauvais-Jarvis F, Clegg DJ, Hevener AL. The role of estrogens in control of energy balance and glucose homeostasis. Endocrine Reviews. 2013;34(3):309–38. doi:10.1210/er.2012-1055
24. Albuquerque TG, Nunes MA, Bessada SMF, Costa HS, Oliveira MBPP. Biologically active and health promoting food components of nuts, oilseeds, fruits, vegetables, cereals, and legumes. In: Elsevier eBooks. 2020. p. 609–56. doi:10.1016/B978-0-12-813266-1.00014-0
25. Mangalath DL, Sadasivan C. Selective estrogen receptor modulators (SERMs) from plants. In: Bioactive Natural Products: Chemistry and Biology. 2014. p. 375–86. doi:10.1002/9783527684403.ch13
26. Garcia A, Herbon L, Barkan A, Papavasiliou S, Marshall JC. Hyperprolactinemia inhibits gonadotropin-releasing hormone (GNRH) stimulation of the number of pituitary GNRH receptors. Endocrinology. 1985;117(3):954–9. doi:10.1210/endo-117-3-954
27. Kaltsas A, Dimitriadis F, Zachariou A, Sofikitis N, Chrisofos M. Phosphodiesterase type 5 inhibitors in male reproduction: Molecular mechanisms and clinical implications for fertility management. Cells. 2025;14(2):120. doi:10.3390/cells14020120
28. Paul JK, Azmal M, Haque ASNB, Talukder OF, Meem M, Ghosh A. Phytochemical-mediated modulation of signaling pathways: A promising avenue for drug discovery. Advances in Redox Research. 2024;13:100113. doi:10.1016/j.arres.2024.100113
29. Varghese D, Ishida C, Patel P, Koya HH. Polypharmacy. StatPearls – NCBI Bookshelf. 2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK532953/
30. Schellenberg R. Treatment for the premenstrual syndrome with agnus castus fruit extract: Prospective, randomised, placebo-controlled study. BMJ. 2001;322(7279):134–7. doi:10.1136/bmj.322.7279.134

31. Ambiye VR, Langade D, Dongre S, Aptikar P, Kulkarni M, Dongre A. Clinical evaluation of the spermatogenic activity of the root extract of Ashwagandha (Withania somnifera) in oligospermic males: A pilot study. Evidence-Based Complementary and Alternative Medicine. 2013;2013:571420. doi:10.1155/2013/571420
32. Jung W, Choi H, Kim J, Kim J, Kim W, Nurkolis F, et al. Effects of natural products on polycystic ovary syndrome: From traditional medicine to modern drug discovery. Heliyon. 2023;9(10):e20889. doi:10.1016/j.heliyon.2023.e20889
33. Sontia B, Mooney J, Gaudet L, Touyz RM. Pseudohyperaldosteronism, liquorice, and hypertension. Journal of Clinical Hypertension. 2008;10(2):153–7. doi:10.1111/j.1751-7176.2008.07470.x
34. Fritz H, Seely D, Flower G, Skidmore B, Fernandes R, Vadeboncoeur S, et al. Soy, red clover, and isoflavones and breast cancer: A systematic review. PLoS ONE. 2013;8(11):e81968. doi:10.1371/journal.pone.0081968
35. Berry-Bibee EN, Kim MJ, Tepper NK, Riley HEM, Curtis KM. Co-administration of St John's wort and hormonal contraceptives: A systematic review. Contraception. 2016;94(6):668–77. doi:10.1016/j.contraception.2016.07.010
36. Liu SH, Chuang WC, Lam W, Jiang Z, Cheng YC. Safety surveillance of traditional Chinese medicine: Current and future. Drug Safety. 2015;38(2):117–28. doi:10.1007/s40264-014-0250-z

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