https://rijournals.com/research-in-medical-sciences/

RESEARCH INVENTION JOURNAL OF RESEARCH IN MEDICAL SCIENCES 4(3):83-87, 2025

©RIJRMS Publications

ONLINE ISSN: 1115- 6198

Print ISSN: 1597-3107

https://doi.org/10.59298/RIJRMS/2025/438387

Polyherbal Extracts and Hormonal Crosstalk in Male and Female Fertility: Advances in Natural Endocrine Modulation

Omutindo Nyakayo A.

Faculty of Science and Technology Kampala International University Uganda

ABSTRACT

Hormonal balance plays a pivotal role in regulating fertility in both sexes, orchestrated through intricate crosstalk between hypothalamic, pituitary, and gonadal hormones. Dysregulation in this hormonal network underlies many reproductive disorders, including polycystic ovary syndrome (PCOS), hypogonadism, infertility, and irregular menstrual cycles. While conventional hormonal therapies offer targeted intervention, they are often accompanied by side effects and long-term safety concerns. Increasingly, attention is turning to polyherbal extract combinations of multiple medicinal plants known for their synergistic and multifaceted biological actions. This review explores how polyherbal formulations interact with endocrine systems to modulate hormonal crosstalk, restore fertility, and improve reproductive outcomes. Drawing from evidence in traditional medicine, animal studies, and emerging clinical trials, we examine the mechanisms of endocrine modulation, including hypothalamic-pituitary axis stimulation, steroidogenic pathway regulation, antioxidant defense enhancement, and receptor-level interactions. Additionally, we discuss bioavailability challenges, safety concerns, and regulatory perspectives. The review advocates for an integrative, evidence-based approach to using polyherbal therapies in reproductive medicine.

Keywords: Polyherbal Extracts, Fertility, Hormonal Crosstalk, Endocrine Modulation, Reproductive Health

INTRODUCTION

Reproductive health is intricately governed by a hormonal network that relies on balanced crosstalk between the brain, endocrine glands, and reproductive organs [1]. This system is primarily regulated through the hypothalamic-pituitary-gonadal (HPG) axis, which maintains reproductive functionality via hormonal cascades [2]. The pulsatile secretion of gonadotropin-releasing hormone (GnRH) from the hypothalamus stimulates the anterior pituitary to release luteinizing hormone (LH) and follicle-stimulating hormone (FSH). These, in turn, influence the gonads to produce sex hormones such as estrogen, progesterone, and testosterone, which are essential for ovulation, spermatogenesis, and secondary sexual characteristics [3].

Disruptions in this hormonal interplay caused by stress, lifestyle changes, oxidative stress, metabolic disorders, or exposure to endocrine-disrupting chemicals result in conditions such as anovulation, menstrual irregularities, oligospermia, infertility, and hormonal imbalance [4]. Conventional treatment strategies include hormone replacement therapy (HRT), ovulation induction agents, and assisted reproductive technologies. However, these interventions often come with undesirable side effects, including increased risk of thromboembolic events, mood disturbances, and long-term metabolic consequences [5]. In this context, plant-based therapies, particularly polyherbal extracts, which combine two or more medicinal herbs, are increasingly being explored for their ability to restore hormonal balance naturally. Polyherbalism has a long-standing tradition in Ayurveda, Traditional Chinese Medicine (TCM), African ethnomedicine, and Unani medicine. These combinations are often believed to enhance efficacy, reduce toxicity, and synergize therapeutic benefits by targeting multiple physiological systems simultaneously [6]. Unlike synthetic drugs that typically act on a single target, polyherbal extracts can influence multiple nodes within the HPG axis, including hormone biosynthesis, secretion, receptor sensitivity, and feedback

regulation [7]. These natural compounds are rich in flavonoids, alkaloids, saponins, phytoestrogens, and antioxidants—each contributing to the overall endocrine-modulatory effect [8]. This review explores how polyherbal formulations restore hormonal crosstalk and improve fertility outcomes in both men and women through diverse, integrative mechanisms.

Hormonal Crosstalk in Male and Female Fertility

Fertility in both sexes depends on the synchronized interaction of multiple hormones across the central and peripheral endocrine systems. In females, the menstrual cycle is regulated by periodic rises and falls in LH, FSH, estrogen, and progesterone [9]. These hormones drive follicular development, ovulation, corpus luteum formation, and preparation of the endometrium for implantation. Any disturbance in this balance, such as low FSH levels or excess androgens as seen in polycystic ovary syndrome (PCOS), can impair ovulatory function and reduce fertility [8]. In males, LH stimulates Leydig cells to produce testosterone, which is crucial for libido and sperm maturation. FSH acts on Sertoli cells to regulate spermatogenesis and the production of androgen-binding proteins. The interplay between testosterone, inhibin, and FSH forms a feedback loop that regulates testicular function [10]. Hypogonadism, varicocele, oxidative stress, and idiopathic infertility are often linked to dysfunction in this regulatory mechanism.

Hormonal crosstalk is not isolated to the reproductive system but is also influenced by other endocrine axes [11]. For example, cortisol from the hypothalamic-pituitary-adrenal (HPA) axis can suppress GnRH release, impairing downstream reproductive hormones. Insulin resistance, a hallmark of metabolic syndrome, affects ovarian steroidogenesis, exacerbating hyperandrogenism in PCOS. Thyroid hormones, too, play a role by regulating basal metabolic rate and indirectly affecting reproductive hormone sensitivity [12]. Hence, restoring fertility involves more than correcting a single hormone level; it necessitates rebalancing the broader hormonal milieu. Polyherbal combinations, with their multi-target capacity, are well-suited for modulating these complex networks. They act not only on the gonads but also influence central regulators like the hypothalamus and pituitary, as well as peripheral factors such as insulin, cortisol, and inflammatory cytokines [13].

Polyherbal Formulations and Mechanisms of Endocrine Modulation

Polyherbal therapies modulate hormonal crosstalk through several overlapping mechanisms:

Hypothalamic-Pituitary Axis Activation

Certain herbs, such as Withania somnifera (Ashwagandha) and Mucuna pruriens, possess adaptogenic properties that normalize HPA axis function and reduce stress-induced suppression of the HPG axis. Ashwagandha has been shown to improve LH and testosterone levels in men with stress-related infertility by reducing cortisol and enhancing GnRH pulsatility. Mucuna pruriens improves dopaminergic tone, which is known to regulate prolactin and GnRH [14].

Gonadal Steroidogenesis Enhancement

Several plant constituents stimulate the expression of steroidogenic enzymes such as steroidogenic acute regulatory (StAR) protein and 17β-hydroxysteroid dehydrogenase [15]. Tribulus terrestris, Eurycoma longifolia, and Asparagus racemosus enhance testosterone and estrogen synthesis by upregulating cholesterol transport and conversion in the gonads. These actions result in improved sperm parameters and normalized menstrual cycles [16].

Antioxidant and Anti-inflammatory Protection

Oxidative stress is a key contributor to gonadal damage, especially in idiopathic infertility and age-related reproductive decline. Polyherbal extracts combining Emblica officinalis (Amla), Curcuma longa (Turmeric), and Glycyrrhiza glabra (Licorice) protect germ cells, follicles, and spermatozoa from ROS-induced DNA damage. Anti-inflammatory phytochemicals inhibit pro-inflammatory cytokines like TNF-α and IL-6, which are often elevated in reproductive disorders such as endometriosis and PCOS [17,18].

Hormone Receptor Sensitization and Feedback Regulation

Some phytochemicals function as phytoestrogens (e.g., genistein, daidzein), binding estrogen receptors and either enhancing or modulating estrogenic activity depending on the tissue context [19]. This selective estrogen receptor modulation is especially beneficial in managing estrogen dominance or deficiency. Additionally, plants like Pueraria mirifica and Fennel exhibit androgenic or antiandrogenic effects depending on dosage and hormonal context, thereby assisting in feedback loop normalization [20].

Evidence from Animal Studies and Clinical Trials

The therapeutic potential of polyherbal formulations in modulating hormonal balance and improving fertility has been extensively studied in preclinical models, with an increasing number of clinical trials supporting their efficacy [21]. Animal studies have provided mechanistic insights into how polyherbal combinations exert endocrine-modulatory effects at multiple levels of the reproductive axis [22]. In male rats with stress-induced or chemically induced infertility, combinations of Withania somnifera, Tribulus terrestris, and Mucuna pruriens significantly improved serum testosterone levels, sperm count, motility, and testicular histoarchitecture. These effects were

attributed to enhanced hypothalamic GnRH expression, increased testicular antioxidant enzyme activity, and upregulation of steroidogenic enzymes [23].

In female models of polycystic ovary syndrome (PCOS), polyherbal formulations comprising Cinnamomum verum, Aloe vera, and Cissus quadrangularis led to the normalization of estrous cycles, reduction in serum testosterone, and improved insulin sensitivity. Histological improvements in ovarian morphology, including reduced cystic follicles and increased corpus luteum formation, further confirm the restorative effects on ovulatory function [24].

Human trials, though still limited, report promising results. A polyherbal capsule combining Shatavari, Ashwagandha, and Guduchi showed improvements in ovulation rates, luteal phase progesterone, and menstrual regularity in women with anovulatory cycles. In men, formulations containing Tribulus terrestris and Gokshura improved seminal parameters and serum androgen levels. However, variations in formulation composition, study design, and outcome measures make it difficult to compare across trials [25,26] While these findings are encouraging, large-scale randomized controlled trials with standardized extracts and validated outcome markers are required to fully establish clinical efficacy and safety. Nonetheless, current evidence strongly supports the potential of polyherbal therapies as effective adjuncts or alternatives to conventional fertility treatments [27].

Safety, Bioavailability, and Regulatory Challenges

Despite their natural origin, polyherbal formulations are not without risks. Potential adverse effects arise from herb-drug interactions, overdose, poor-quality control, and inappropriate combinations [28]. Some formulations may contain compounds with estrogenic or antiandrogenic activity that can exacerbate hormone-sensitive conditions such as breast, ovarian, or prostate cancer [29]. Many phytochemicals exhibit poor intestinal absorption, rapid hepatic metabolism, and limited tissue penetration. For instance, curcumin, a potent antioxidant and anti-inflammatory agent, has minimal systemic bioavailability unless co-administered with bioenhancers like piperine. Novel delivery technologies such as nanoencapsulation, phytosomes, and liposomes are being explored to improve pharmacokinetics and enhance clinical efficacy [30]. Variability in cultivation conditions, harvesting methods, and extraction techniques leads to inconsistent phytochemical profiles. Without standardization, reproducibility and dose accuracy remain elusive [31]. Regulatory bodies in many regions lack specific frameworks to evaluate the safety and efficacy of polyherbal formulations. This regulatory gap hinders integration into evidence-based clinical practice. To move forward, interdisciplinary research combining pharmacognosy, toxicology, pharmacology, and clinical sciences is needed [32]. Establishing robust quality control systems, adopting Good Manufacturing Practices (GMP), and conducting post-market surveillance will ensure safer and more effective use of polyherbal products in reproductive healthcare [33].

CONCLUSION

Polyherbal extracts represent a promising frontier in the natural modulation of hormonal networks critical for male and female fertility. Their ability to target multiple endocrine pathways simultaneously offers an advantage over single-agent therapies. While emerging evidence supports their role in restoring hormonal balance, optimizing fertility, and improving reproductive outcomes, scientific rigor in formulation, standardization, and clinical validation is essential. Integrative approaches that combine traditional herbal wisdom with modern biomedical insights could pave the way for safe, effective, and holistic reproductive healthcare solutions.

REFERENCES

1. Athar F, Karmani M, Templeman NM. Metabolic hormones are integral regulators of female reproductive health and function. Biosci Rep. 2024 Jan 31;44(1):BSR20231916. doi: 10.1042/BSR20231916. PMID: 38131197; PMCID: PMC10830447.
2. Campbell M, Jialal I. Physiology, Endocrine Hormones. [Updated 2022 Sep 26]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK538498/
3. Li L, Lin W, Wang Z, Huang R, Xia H, Li Z, Deng J, Ye T, Huang Y, Yang Y. Hormone Regulation in Testicular Development and Function. *International Journal of Molecular Sciences*. 2024; 25(11):5805. https://doi.org/10.3390/ijms25115805
4. Diamanti-Kandarakis E, Bourguignon JP, Giudice LC, Hauser R, Prins GS, Soto AM, Zoeller RT, Gore AC. Endocrine-disrupting chemicals: an Endocrine Society scientific statement. Endocr Rev. 2009 Jun;30(4):293-342. doi: 10.1210/er.2009-0002. PMID: 19502515; PMCID: PMC2726844.
5. Egba, Simeon I., Okonkwo Chibuzo O, Omeoga Humphrey C, and Ekong I E. Comparative modulation of the reproductive system by ethanol leaf extracts of *Asystasia gangetica* and *Anthocleista vogelii* in male Wistar rats. European Journal of Medical and Health Sciences. 2020; 2(3): 387-392
6. Uti DE, Atangwho IJ, Alum EU, Egba SI, Ugwu OP-C, Ikechukwu GC. Natural Antidiabetic Agents: Current Evidence and Development Pathways from Medicinal Plants to Clinical use. Natural Product Communications. 2025;20(3). doi:10.1177/1934578X251323393

7. Yazar S. Endocrine Disruptors and Infertility [Internet]. The Toxicity of Environmental Pollutants. IntechOpen; 2022. Available from: http://dx.doi.org/10.5772/intechopen.104403
8. Caneparo C, Carignan L, Lonina E, Goulet S-M, Pellerin F-A, Chabaud S, Bordeleau F, Bolduc S, Pelletier M. Impact of Endocrine Disruptors on the Genitourinary Tract. *Journal of Xenobiotics*. 2024; 14(4):1849-1888. https://doi.org/10.3390/jox14040099
9. Marques P, De Sousa Lages A, Skorupskaite K, et al. Physiology of GnRH and Gonadotrophin Secretion. [Updated 2024 Oct 15]. In: Feingold KR, Ahmed SF, Anawalt B, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK279070/
10. Egba, Simeon Ikechukwu., Okonkwo, Chibuzor Onyinye., Ogbodo, John Onyebuchi and Eme,Dike (2020) Contraceptive Potentials of *Alstonia boonei* via Stimulation of Increased Prolactin Synthesis in Experimental Female Wistar Rats. Trends Nat. Prod. Res, 2020; 1(1): 43-50
11. Halada S, Casado-Medrano V, Baran JA, Lee J, Chinmay P, Bauer AJ, Franco AT. Hormonal Crosstalk Between Thyroid and Breast Cancer. Endocrinology. 2022 Jul 1;163(7):bqac075. doi: 10.1210/endocr/bqac075. PMID: 35587175; PMCID: PMC9653009.
12. Mbiydzenyuy NE, Qulu LA. Stress, hypothalamic-pituitary-adrenal axis, hypothalamic-pituitary-gonadal axis, and aggression. Metab Brain Dis. 2024 Dec;39(8):1613-1636. doi: 10.1007/s11011-024-01393-w. Epub 2024 Jul 31. PMID: 39083184; PMCID: PMC11535056.
13. Brown EDL, Obeng-Gyasi B, Hall JE, Shekhar S. The Thyroid Hormone Axis and Female Reproduction. *International Journal of Molecular Sciences*. 2023; 24(12):9815. https://doi.org/10.3390/ijms24129815
14. Begemann, K., Rawashdeh, O., Olejniczak, I. *et al.* Endocrine regulation of circadian rhythms. *npj Biol Timing Sleep* **2**, 10 (2025). https://doi.org/10.1038/s44323-025-00024-6
15. Manna PR, Dyson MT, Stocco DM. Regulation of the steroidogenic acute regulatory protein gene expression: present and future perspectives. Mol Hum Reprod. 2009 Jun;15(6):321-33. doi: 10.1093/molehr/gap025. Epub 2009 Mar 25. PMID: 19321517; PMCID: PMC2676994.
16. Tsai SJ, Wu MH, Lin CC, Sun HS, Chen HM. Regulation of steroidogenic acute regulatory protein expression and progesterone production in endometriotic stromal cells. J Clin Endocrinol Metab. 2001 Dec;86(12):5765-73. doi: 10.1210/jcem.86.12.8082. PMID: 11739437.
17. Egba, SI., Omeoga, HC., Oriaku CE., Jacobs EC., Nnabugwu FC., Lazarus JC and Echem EN. Down-regulatory Influence of Methanol and Aqueous Root Extracts of Sphenocentrum jollyanum on Some Fertility Hormones and the Effect on Testicular Size of Wistar Albino Rats. Annual Research and Review in Biology, 2017; 18(3): 1-8
18. Alahmar AT. Role of Oxidative Stress in Male Infertility: An Updated Review. J Hum Reprod Sci. 2019 Jan-Mar;12(1):4-18. doi: 10.4103/jhrs.JHRS_150_18. PMID: 31007461; PMCID: PMC6472207.
19. Agarwal, A., Aponte-Mellado, A., Premkumar, B.J. *et al.* The effects of oxidative stress on female reproduction: a review. *Reprod Biol Endocrinol* **10**, 49 (2012).
20. Martin LJ, Touaibia M. Improvement of Testicular Steroidogenesis Using Flavonoids and Isoflavonoids for Prevention of Late-Onset Male Hypogonadism. *Antioxidants*. 2020; 9(3):237. https://doi.org/10.3390/antiox9030237 https://doi.org/10.1186/1477-7827-10-49
21. Mallya, P., Lewis, S.A. Curcumin and its formulations for the treatment of polycystic ovary syndrome: current insights and future prospects. *J Ovarian Res* **18**, 78 (2025). https://doi.org/10.1186/s13048-025-01660-z
22. Mallya P, Lewis SA. Curcumin and its formulations for the treatment of polycystic ovary syndrome: current insights and future prospects. J Ovarian Res. 2025 Apr 15;18(1):78. doi: 10.1186/s13048-025-01660-z. PMID: 40234918; PMCID: PMC12001734.
23. Egba S I., Omodamiro, Olorunsola D., Obike, J C and Ali, S E. Influence on some female fertility hormonal response in wistar albino rats: Possible contraceptive role for methanol leaf extract of *Ocimum gratissimum*? Journal of Chemical and Pharmaceutical Research, 2015; 7(5): 889-898
24. Roychoudhury S, Chakraborty S, Choudhury AP, Das A, Jha NK, Slama P, Nath M, Massanyi P, Ruokolainen J, Kesari KK. Environmental Factors-Induced Oxidative Stress: Hormonal and Molecular Pathway Disruptions in Hypogonadism and Erectile Dysfunction. *Antioxidants*. 2021; 10(6):837. https://doi.org/10.3390/antiox10060837
25. Coster WJ. Making the best match: selecting outcome measures for clinical trials and outcome studies. Am J Occup Ther. 2013 Mar-Apr;67(2):162-70. doi: 10.5014/ajot.2013.006015. PMID: 23433270; PMCID: PMC3628620.

26. U.S. Department of Health and Human Services, FDA Center for Drug Evaluation and Research., U.S. Department of Health and Human Services, FDA Center for Biologics Evaluation and Research. & U.S. Department of Health and Human Services, FDA Center for Devices and Radiological Health. Guidance for industry: patient-reported outcome measures: use in medical product development to support labeling claims: draft guidance. *Health Qual Life Outcomes* **4**, 79 (2006). https://doi.org/10.1186/1477-7525-4-79
27. Jones, C.W., Keil, L.G., Holland, W.C. *et al.* Comparison of registered and published outcomes in randomized controlled trials: a systematic review. *BMC Med* **13**, 282 (2015). https://doi.org/10.1186/s12916-015-0520-3
28. 28 Egba, Simeon I., Sunday, Godwin I, and Anaduaka, Emeka G. The effect of oral administration of aqueous extract of *Newbouldia laevis* leaves on fertility hormones of male albino rats. IOSR Journal of Pharmacy and Biological Sciences, 2014; 9(3): 61-64
29. Egba, SI., Ogbodo, JO., Ogbodo PO and Obike CA Toxicological Evaluation of Two Named Herbal Remedies Sold Across Orumba South Local Government of Anambra State, South-Eastern Nigeria. Asian Journal of Research in Biochemistry, 2017; 1(1):1-6
30. Alum EU. Role of phytochemicals in cardiovascular disease management: Insights into mechanisms, efficacy, and clinical application. Phytomedicine Plus, 2025; 5(1),100695. https://doi.org/10.1016/j.phyplu.2024.100695.
31. Alum EU. Climate change and its impact on the bioactive compound profile of medicinal plants: implications for global health. *Plant Signaling & Behavior*, 2024; *19*(1), 2419683. doi: 10.1080/15592324.2024.2419683
32. Figueira MI, Carvalho TMA, Macário-Monteiro J, Cardoso HJ, Correia S, Vaz CV, Duarte AP, Socorro S. The Pros and Cons of Estrogens in Prostate Cancer: An Update with a Focus on Phytoestrogens. *Biomedicines*. 2024; 12(8):1636. https://doi.org/10.3390/biomedicines12081636
33. Gachowska M, Dąbrowska A, Wilczyński B, Kuźnicki J, Sauer N, Szlasa W, Kobierzycki C, Łapińska Z, Kulbacka J. The Influence of Environmental Exposure to Xenoestrogens on the Risk of Cancer Development. *International Journal of Molecular Sciences*. 2024; 25(22):12363. https://doi.org/10.3390/ijms252212363

CITE AS: Omutindo Nyakayo A. (2025). Polyherbal Extracts and Hormonal Crosstalk in Male and Female Fertility: Advances in Natural Endocrine Modulation. RESEARCH INVENTION JOURNAL OF RESEARCH IN MEDICAL SCIENCES 4(3):83-87. https://doi.org/10.59298/RIJRMS/2025/438387