RESEARCH INVENTION JOURNAL OF RESEARCH IN MEDICAL SCIENCES 4(3):43-47, 2025

ONLINE ISSN: 1115- 6198

Print ISSN: 1597-3107

https://doi.org/10.59298/RIJRMS/2025/434347

Reproductive Hormone Imbalance in Metabolic Syndrome: The Intersection of Prolactin, Fertility Hormones, and Nutraceutical Extracts

Nabirye Akello Kemigisha

Faculty of Science and Technology Kampala International University Uganda

ABSTRACT

Metabolic syndrome (MetS), a constellation of interconnected risk factors including insulin resistance, dyslipidemia, hypertension, and central obesity, exerts profound effects on reproductive hormone homeostasis. Disruptions in metabolic pathways not only lead to cardiovascular and endocrine complications but also significantly alter the regulatory axes of reproductive hormones, particularly prolactin, luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone, and estrogen. These hormonal disturbances contribute to infertility, sexual dysfunction, and menstrual irregularities. Recent evidence highlights the potential role of nutraceutical extracts in ameliorating both metabolic and reproductive dysregulations by targeting oxidative stress, inflammation, and endocrine imbalances. This review elucidates the intricate links between metabolic syndrome, prolactin dysregulation, and fertility hormones and critically explores how plant-derived bioactives may offer therapeutic interventions. Emerging trends, mechanistic insights, and future research directions for integrating nutraceutical strategies into metabolic and reproductive health management are also discussed.

Keywords: Metabolic Syndrome, Prolactin, Fertility Hormones, Nutraceutical Extracts, Reproductive Dysfunction

INTRODUCTION

Metabolic syndrome (MetS) is a multifaceted pathological condition that has garnered increasing global attention due to its alarming prevalence among adults and adolescents [1]. Defined by the coexistence of central obesity, insulin resistance, hypertension, hyperglycemia, and dyslipidemia, MetS presents not only a major risk factor for cardiovascular diseases and type 2 diabetes mellitus but also profoundly affects endocrine and reproductive health [2]. Growing evidence demonstrates that the metabolic disturbances inherent in MetS interfere with the finely tuned mechanisms of reproductive hormone regulation, leading to notable dysfunctions in fertility across both sexes. At the core of reproductive health lies the hypothalamic-pituitary-gonadal (HPG) axis, a dynamic system responsible for regulating the production and function of critical fertility hormones, including gonadotropins (LH and FSH), sex steroids (testosterone and estradiol), and prolactin [3]. In the context of MetS, hormonal disturbances become inevitable, either directly due to metabolic aberrations or indirectly via systemic inflammation, oxidative stress, and adipokine dysregulation [4]. Recent years have seen a surge in the exploration of alternative therapeutic strategies to mitigate these interconnected pathologies. Among them, nutraceutical extractslike bioactive compounds derived from foods or medicinal plants, have attracted substantial interest for their potential in restoring metabolic and hormonal homeostasis [5]. The dual targeting of metabolic abnormalities and reproductive hormone imbalances via nutraceutical interventions presents a promising integrative approach that addresses the systemic nature of MetS. This review delves into the intricate intersections between metabolic syndrome, prolactin dysregulation, fertility hormone alterations, and the role of nutraceutical extracts in therapeutic modulation.

Metabolic Syndrome and Reproductive Hormone Imbalance: An Overview

The pathophysiological underpinnings of MetS intricately link to widespread dysregulation of the endocrine system, particularly the reproductive hormonal network [1]. Chronic insulin resistance, a hallmark of MetS, plays a pivotal

role in disrupting the HPG axis [6]. In hyperinsulinemic states, insulin acts synergistically with luteinizing hormone at the ovarian theca cells to stimulate excessive androgen production, particularly in women, contributing to conditions such as polycystic ovary syndrome (PCOS) [7]. Conversely, in males, insulin resistance and associated obesity drive reductions in circulating testosterone levels, contributing to the so-called "hypogonadal-obesity cycle," wherein diminished testosterone exacerbates fat accumulation, further deepening hormonal imbalance [7]. Obesity, especially central adiposity, is another critical factor. Adipose tissue is not merely a passive storage depot but an active endocrine organ producing adipokines (e.g., leptin, adiponectin, resistin) and inflammatory cytokines (e.g., TNF-α, IL-6). In MetS, leptin resistance and hypoadiponectinemia further impair hypothalamic sensitivity to reproductive signals, disrupting GnRH pulsatility and thereby altering LH and FSH secretion patterns [8]. Additionally, aromatase activity within adipose tissue increases the peripheral conversion of testosterone to estradiol, promoting estrogen dominance in males and relative androgen excess in females, both of which contribute to reproductive dysfunction [9]. Beyond gonadotropins and sex steroids, other hormonal axes are disrupted in MetS, including thyroid and adrenal hormones, compounding the complexity of reproductive dysfunction [10]. Oxidative stress and chronic low-grade inflammation exacerbate endothelial dysfunction and microvascular impairments in gonadal tissues, further hindering gametogenesis and steroidogenesis [11]. Therefore, understanding the comprehensive hormonal and metabolic alterations in MetS is essential for identifying effective therapeutic interventions aimed at restoring not only metabolic health but also reproductive competence.

Prolactin Dysregulation in Metabolic Syndrome

Prolactin, classically known for its role in lactation, has emerged as a multifaceted hormone implicated in metabolic regulation, immune modulation, and reproductive function [12]. Produced primarily by lactotroph cells of the anterior pituitary gland, prolactin secretion is tightly regulated by hypothalamic dopamine, which exerts an inhibitory effect, and by various stimuli such as stress, sleep, and estrogen levels [12]. In MetS, prolactin regulation becomes aberrant, though its exact role appears context-dependent and somewhat paradoxical. Some studies report hyperprolactinemia associated with insulin resistance, obesity, and increased cardiovascular risk factors, suggesting a maladaptive response to metabolic stress [13]. Elevated prolactin levels can suppress hypothalamic GnRH secretion, thereby reducing LH and FSH secretion, resulting in secondary hypogonadism [14]. This hormonal suppression manifests clinically as menstrual irregularities, anovulation, infertility in women, and reduced libido, erectile dysfunction, and infertility in men.

Conversely, emerging data also indicate that relative prolactin deficiency may occur in certain MetS contexts, leading to impaired pancreatic β-cell function, diminished adipocyte proliferation control, and exacerbated insulin resistance [15]. This dichotomy suggests that prolactin operates within a narrow physiological window for maintaining metabolic and reproductive health, where both excess and deficiency are pathological [16]. Mechanistically, prolactin influences metabolic tissues by modulating adipose tissue metabolism, β-cell proliferation, hepatic gluconeogenesis, and systemic inflammatory responses [17]. In reproductive tissues, prolactin receptors mediate effects on ovarian folliculogenesis, luteal function, and spermatogenesis [18]. Hence, prolactin dysregulation not only reflects the metabolic derangements of MetS but also actively contributes to the hormonal and reproductive dysfunctions observed [18] Targeting prolactin pathways through pharmacological agents (e.g., dopamine agonists) or emerging nutraceutical strategies offers a promising therapeutic avenue for managing reproductive and metabolic abnormalities in MetS patients [19].

Fertility Hormones and Metabolic Perturbations

The intricate relationship between metabolic syndrome (MetS) and fertility hormone imbalance is increasingly recognized as a critical area of concern. Metabolic dysfunction significantly alters the homeostasis of key reproductive hormones, namely testosterone, estradiol, luteinizing hormone (LH), follicle-stimulating hormone (FSH), and progesterone, undermining reproductive capacity across genders [20] In females, hyperinsulinemia and insulin resistance is a defining hallmark of MetS stimulate androgen overproduction by ovarian theca cells, predominantly via the upregulation of the insulin-like growth factor-1 (IGF-1) receptor pathways [21]. This androgen excess disrupts follicular maturation, leading to chronic anovulation, menstrual irregularities, and conditions such as polycystic ovary syndrome (PCOS), a leading cause of infertility [22]. Furthermore, insulin resistance impairs hepatic production of sex hormone-binding globulin (SHBG), increasing the bioavailability of free androgens and exacerbating endocrine disturbances [23].

In males, MetS induces a progressive decline in total and free testosterone levels, a phenomenon frequently termed metabolic hypogonadism. Adiposity, particularly visceral fat accumulation, promotes aromatization of testosterone to estradiol via increased aromatase enzyme activity, resulting in estrogen dominance that negatively feeds back on the hypothalamic-pituitary axis [24]. The resultant decline in GnRH pulsatility reduces LH and FSH secretion, diminishing Leydig cell stimulation, spermatogenesis, and overall fertility potential [25]. Clinical manifestations include decreased libido, erectile dysfunction, reduced sperm quality, and infertility [26]. Moreover, dysregulated

secretion patterns of LH and FSH impair the normal gonadal steroidogenic response, while altered progesterone and estradiol dynamics affect uterine receptivity and endometrial maturation in women [27]. Chronic low-grade inflammation and oxidative stress inherent in MetS further damage gonadal microenvironments, contributing to impaired gametogenesis and embryonic development [28]. These multifactorial disruptions underscore the importance of addressing metabolic perturbations as part of fertility management strategies.

Therapeutic Potential of Nutraceutical Extracts in Modulating Reproductive Hormones

The limitations of conventional pharmacotherapy in fully addressing the endocrine and reproductive disturbances associated with MetS have prompted a surge of interest in nutraceutical interventions. Nutraceuticals, bioactive compounds derived from natural sources, offer multifaceted benefits by targeting the metabolic, oxidative, and hormonal derangements central to MetS-associated reproductive dysfunction [29]. One notable class includes polyphenols, such as resveratrol and curcumin, which possess potent antioxidant and anti-inflammatory properties. Resveratrol, for example, improves insulin sensitivity, reduces ovarian oxidative stress, and restores estrous cyclicity in PCOS models [30]. Flavonoids like quercetin and kaempferol have demonstrated abilities to modulate steroidogenesis, reduce androgen excess, and enhance ovarian folliculogenesis [31]. Saponins, abundant in plants like Tribulus terrestris and Fenugreek (Trigonella foenum-graecum), stimulate testosterone production and improve spermatogenic parameters in males [32]. Clinical studies on Maca (Lepidium meyenii) reveal enhancements in libido, semen quality, and fertility outcomes without significantly altering systemic hormone levels, suggesting a modulatory effect rather than overt endocrine disruption [33] Additionally, ashwagandha (Withania somnifera), classified as an adaptogen, exerts stress-reducing effects that lower cortisol and indirectly benefit reproductive hormone profiles by restoring HPG axis function [34]. Emerging botanical agents such as Nigella sativa and Panax ginseng also show promising benefits in restoring hormonal balance and improving fertility metrics in MetS-affected individuals [35] Mechanistically, nutraceuticals act via multiple pathways, including modulation of AMP-activated protein kinase (AMPK) signaling, suppression of nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB)-mediated inflammation, and enhancement of mitochondrial function, thereby restoring both metabolic and reproductive health [36]. Integration of these natural compounds offers a safe, accessible, and often synergistic adjunct to conventional therapies in managing MetS-related hormonal and reproductive dysfunctions.

Emerging Mechanisms and Future Directions

The therapeutic landscape of nutraceuticals in reproductive endocrinology is rapidly evolving, fueled by advances in molecular biology, nanotechnology, and systems medicine. Emerging mechanisms suggest that, beyond simple antioxidant effects, many nutraceuticals exert epigenetic modifications, influencing gene expression patterns critical for metabolic and reproductive function. For instance, resveratrol and curcumin have been shown to modulate histone acetylation and DNA methylation, thereby affecting pathways regulating insulin sensitivity, steroidogenesis, and inflammation [37]. Another frontier is the modulation of the gut microbiome, an increasingly recognized player in the regulation of metabolic and hormonal health. Polyphenol-rich extracts enhance microbial diversity, increase short-chain fatty acid production, and reduce endotoxemia, all of which positively influence systemic inflammation, insulin sensitivity, and ultimately reproductive hormone balance [38]. Moreover, innovative delivery systems such as nano-formulated nutraceuticals (e.g., nano-curcumin, nano-resveratrol) are being developed to overcome bioavailability limitations, ensuring higher systemic absorption and targeted action at reproductive organs [39]. Future directions should prioritize well-designed randomized controlled trials to establish standardized dosing regimens, identify specific bioactive components responsible for clinical effects, and elucidate potential long-term safety profiles. Personalized nutraceutical approaches, integrating individual metabolic and hormonal profiling, microbiome status, and genetic predispositions, represent an exciting new horizon in managing MetS-associated reproductive dysfunction. Thus, combining nutraceutical therapies with lifestyle interventions and conventional medical treatments holds promise for a comprehensive, patient-centered approach to restoring metabolic and reproductive health in MetS populations.

CONCLUSION

Metabolic syndrome profoundly disrupts reproductive hormone homeostasis, with significant consequences for fertility and sexual health. Prolactin and fertility hormones are critically implicated in this interplay. Nutraceutical extracts offer promising avenues for modulating metabolic and reproductive axes, restoring hormonal balance, and improving reproductive outcomes. However, more rigorous research is needed to integrate nutraceutical strategies into mainstream reproductive medicine for MetS patients. A holistic approach combining nutraceuticals, lifestyle modification, and medical therapy holds the key to optimizing reproductive and metabolic health.

REFERENCES

1. Kassi E, Pervanidou P, Kaltsas G, Chrousos G. Metabolic syndrome: definitions and controversies. BMC Medicine. 2011;9(1). doi:10.1186/1741-7015-9-48
2. Swarup S, Ahmed I, Grigorova Y, Zeltser R. Metabolic syndrome. StatPearls – NCBI Bookshelf. 2024.

3. Klein CE. The hypothalamic–pituitary–gonadal axis. Holland-Frei Cancer Medicine – NCBI Bookshelf. 2003.
4. Heindel JJ, Blumberg B, Cave M, Machtinger R, Mantovani A, Mendez MA, et al. Metabolism disrupting chemicals and metabolic disorders. Reproductive Toxicology. 2016;68:3–33. doi:10.1016/j.reprotox.2016.10.001
5. Samtiya M, Aluko RE, Dhewa T, Moreno-Rojas JM. Potential health benefits of plant food–derived bioactive components: an overview. Foods. 2021;10(4):839. doi:10.3390/foods10040839
6. Freeman AM, Acevedo LA, Pennings N. Insulin resistance. StatPearls – NCBI Bookshelf. 2023.
7. Rosenfield RL, Ehrmann DA. The pathogenesis of polycystic ovary syndrome (PCOS): the hypothesis of PCOS as functional ovarian hyperandrogenism revisited. Endocrine Reviews. 2016;37(5):467–520. doi:10.1210/er.2015-1104
8. Clemente-Suárez VJ, Redondo-Flórez L, Beltrán-Velasco AI, Martín-Rodríguez A, Martínez-Guardado I, Navarro-Jiménez E, et al. The role of adipokines in health and disease. Biomedicines. 2023;11(5):1290. doi:10.3390/biomedicines11051290
9. Egba, Simeon I., Okonkwo Chibuzo O, Omeoga Humphrey C and Ekong I E. Comparativemodulation 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
10. Kho KH, Sukhan ZP, Yang SW, Hwang NY, Lee WK. Gonadotropins and sex steroid hormones in captive-reared small yellow croaker (Larimichthys polyactis) and their role in female reproductive dysfunction. International Journal of Molecular Sciences. 2023;24(10):8919. doi:10.3390/ijms24108919
11. Higashi Y. Roles of oxidative stress and inflammation in vascular endothelial dysfunction–related disease. Antioxidants. 2022;11(10):1958. doi:10.3390/antiox11101958
12. 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
13. Kirsch P, Kunadia J, Shah S, Agrawal N. Metabolic effects of prolactin and the role of dopamine agonists: a review. Frontiers in Endocrinology. 2022;13. doi:10.3389/fendo.2022.1002320
14. Thapa S, Bhusal K. Hyperprolactinemia. StatPearls – NCBI Bookshelf. 2023.
15. Auriemma RS, De Alcubierre D, Pirchio R, Pivonello R, Colao A. Glucose abnormalities associated to prolactin-secreting pituitary adenomas. Frontiers in Endocrinology. 2019;10. doi:10.3389/fendo.2019.00327
16. Pirchio R, Graziadio C, Colao A, Pivonello R, Auriemma RS. Metabolic effects of prolactin. Frontiers in Endocrinology. 2022;13. doi:10.3389/fendo.2022.1015520
17. Zaidalkilani AT, Al-Kuraishy HM, Al-Gareeb AI, Alexiou A, Papadakis M, Al-Farga A, et al. The beneficial and detrimental effects of prolactin hormone on metabolic syndrome: a double-edge sword. Journal of Cellular and Molecular Medicine. 2024;28(23). doi:10.1111/jcmm.70067
18. Szukiewicz D. Current insights in prolactin signaling and ovulatory function. International Journal of Molecular Sciences. 2024;25(4):1976. doi:10.3390/ijms25041976
19. Drummond JB, Molitch ME, Korbonits M. Prolactinoma management. Endotext – NCBI Bookshelf. 2025.
20. 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
21. 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
22. Wang K, Li Y, Chen Y. Androgen excess: a hallmark of polycystic ovary syndrome. Frontiers in Endocrinology. 2023;14. doi:10.3389/fendo.2023.1273542
23. Qu X, Donnelly R. Sex hormone-binding globulin (SHBG) as an early biomarker and therapeutic target in polycystic ovary syndrome. International Journal of Molecular Sciences. 2020;21(21):8191. doi:10.3390/ijms21218191
24. Cohen PG. Aromatase, adiposity, aging and disease: the hypogonadal–metabolic–atherogenic-disease and aging connection. Medical Hypotheses. 2001;56(6):702–8. doi:10.1054/mehy.2000.1169
25. Marques P, De Sousa Lages A, Skorupskaite K, Rozario KS, Anderson RA, George JT. Physiology of GnRH and gonadotrophin secretion. Endotext – NCBI Bookshelf. 2024.

26. 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
27. Bosch E, Alviggi C, Lispi M, Conforti A, Hanyaloglu AC, Chuderland D, et al. Reduced FSH and LH action: implications for medically assisted reproduction. Human Reproduction. 2021;36(6):1469–80. doi:10.1093/humrep/deab065
28. Fernandez-García J, Cardona F, Tinahones F. Inflammation, oxidative stress and metabolic syndrome: dietary modulation. Current Vascular Pharmacology. 2014;11(6):906–19. doi:10.2174/15701611113116660175
29. S I Egba., I D Udom and C O Okonkwo. Comparative Effect of Oral Administration of Some Dietary Lipids on Fertillity hormones of Female Wistar Albino Rats. Global Journal of Biotechnology and Biochemistry, 2014; 9(1): 24-29
30. Huo P, Li M, Le J, Zhu C, Yao J, Zhang S. Resveratrol improves follicular development of PCOS rats via regulating glycolysis pathway and targeting SIRT1. Systems Biology in Reproductive Medicine. 2022;69(2):153–65. doi:10.1080/19396368.2022.2125855
31. Shah MZUH, Shrivastva VK, Mir MA, Sheikh WM, Ganie MA, Rather GA, et al. Effect of quercetin on steroidogenesis and folliculogenesis in ovary of mice with experimentally induced polycystic ovarian syndrome. Frontiers in Endocrinology. 2023;14. doi:10.3389/fendo.2023.1153289
32. Shehab NG, Omolaoye TS, Du Plessis SS, Rawat SS, Naidoo N, Abushawish KY, et al. Phytochemical evaluation of Lepidium meyenii, Trigonella foenum-graecum, Spirulina platensis, and Tribulus arabica, and their potential effect on monosodium glutamate induced male reproductive dysfunction in adult Wistar rats. Antioxidants. 2024;13(8):939. doi:10.3390/antiox13080939
33. Del Carpio NU, Alvarado-Corella D, Quiñones-Laveriano DM, Araya-Sibaja A, Vega-Baudrit J, Monagas-Juan M, et al. Exploring the chemical and pharmacological variability of Lepidium meyenii: a comprehensive review of the effects of maca. Frontiers in Pharmacology. 2024;15. doi:10.3389/fphar.2024.1360422
34. Wiciński M, Fajkiel-Madajczyk A, Kurant Z, Kurant D, Gryczka K, Falkowski M, et al. Can ashwagandha benefit the endocrine system?—a review. International Journal of Molecular Sciences. 2023;24(22):16513. doi:10.3390/ijms242216513
35. 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 Jornal of Pharmacy and Biological Sciences, 2014; 9(3): 61-64
36. Medoro A, Davinelli S, Colletti A, Di Micoli V, Grandi E, Fogacci F, et al. Nutraceuticals as modulators of immune function: a review of potential therapeutic effects. Preventive Nutrition and Food Science. 2023;28(2):89–107. doi:10.3746/pnf.2023.28.2.89
37. Banaszak M, Górna I, Woźniak D, Przysławski J, Drzymała-Czyż S. The impact of curcumin, resveratrol, and cinnamon on modulating oxidative stress and antioxidant activity in type 2 diabetes: moving beyond an anti-hyperglycaemic evaluation. Antioxidants. 2024;13(5):510. doi:10.3390/antiox13050510
38. Pheiffer C, Riedel S, Dias S, Adam S. Gestational diabetes and the gut microbiota: fibre and polyphenol supplementation as a therapeutic strategy. Microorganisms. 2024;12(4):633. doi:10.3390/microorganisms12040633
39. Yakubu J, Pandey AV. Innovative delivery systems for curcumin: exploring nanosized and conventional formulations. Pharmaceutics. 2024;16(5):637. doi:10.3390/pharmaceutics16050637

CITE AS: Nabirye Akello Kemigisha. (2025). Reproductive Hormone Imbalance in Metabolic Syndrome: The Intersection of Prolactin, Fertility Hormones, and Nutraceutical Extracts. RESEARCH INVENTION JOURNAL OF RESEARCH IN MEDICAL SCIENCES 4(3):43-47. https://doi.org/10.59298/RIJRMS/2025/434347