RESEARCH PAPER

Multi-Targeted Herbal Interventions in Polycystic Ovary Syndrome: from Pathophysiology to Clinical Applications

Thakare D. R.[1], Ghube D. D.[2*], Tathe P R[3]

[1]Research Scholar, Department of Pharmacology, Samarth College of Pharmacy, Deulgaon Raja, Dist. Buldhana – 443204, Maharashtra, India. ORCID ID : 0009-0000-0628-2529

[2*]Head of the Department, Department of Pharmacology, Samarth College of Pharmacy, Deulgaon Raja, Dist. Buldhana – 443204, Maharashtra, India. ORCID ID : 0009-0001-8012-0736

[3]Principal, Samarth College of Pharmacy, Deulgaon Raja, Dist. Buldhana – 443204, Maharashtra, India. ORCID ID : 0000-0003-2163-2974

ABSTRACT

Polycystic Ovary Syndrome i.e. PCOS is intricate endocrine-metabolic condition that alter women of reproductive age. It is differentiated by excess androgen, ovulatory failure, insulin resistance, and other metabolic anomalies. Despite the availability of traditional pharmaceutical medications, current treatment techniques are essentially symptomatic and are frequently limited by side effects, poor long-term adherence, and failure to address the disease's complex nature. As a result, there is increased interest in alternative and complementary therapies, notably herbal therapy, because of their multi-targeted mechanisms and favourable safety profiles.

This review integrates evidence from experimental and clinical research to assess medicinal plants' potential for managing PCOS. The overall literature search was executed using databases such as ScienceDirect, PubMed, and Google Scholar. Medicinal plants like Glycyrrhiza glabra, Vitex agnus-castus, Cinnamomum verum, and Trigonella foenum-graecum have shown promise in altering critical pathophysiological pathways. These herbs have many pharmacological effects, including regulating the hypothalamic-pituitary-ovarian axis, improving insulin responsiveness, lowering androgen levels, and reducing oxidative stress and inflammation.

Herbal remedies have been shown to enhance metabolic and reproductive parameters, although diversity in study design, formulations, and endpoints restricts their generalizability. Validating efficacy and safety requires well-designed, large-scale randomized controlled trials and standardized formulations. Herbal treatments show promise for managing PCOS holistically and should be integrated into clinical practice based on research.

Keywords: Polycystic Ovary Syndrome, herbal medicine, phytotherapy, Cinnamomum verum, hyperandrogenism, medicinal plants, endocrine diseases, and ovarian dysfunction.

How to cite this article: Thakare D. R., Ghube D. D., Tathe P R, Multi-Targeted Herbal Interventions In Polycystic Ovary Syndrome: From Pathophysiology to Clinical Applications. Int J Drug Deliv Technol. 2026;16(17s): 992-991. DOI: 10.25258/ijddt.16.17s.112

Source of support: Nil

Conflict of interest: None

INTRODUCTION

Polycystic ovary syndrome i.e., PCOS is a common metabolic and condition altering women of reproductive age worldwide. The prevalence ranges between 6% to 20.03%, based on the reference standards used, including the NIH, Androgen Excess Society criteria, and Rotterdam. It is an important public health issue as it affects reproductive health, metabolic function, and general quality of life.

Prolonged biochemical/ clinical hyperandrogenism, anovulation, and polycystic ovarian morphology are the clinical hallmarks of PCOS. Menstrual abnormalities, infertility, excessive hair growth (hirsutism), acne, hair thinning (alopecia), and psychological issues like anxiety and sadness are common among affected women.

PCOS is closely associated with metabolic disorders, viz., obesity, insulin resistance, reduced glucose tolerance, and dyslipidaemia, in addition to reproductive issues. PCOS may raise the long-term risk of type 2 diabetes, metabolic syndrome, cardiovascular disease, and endometrial hyperplasia if it is not treated [1,2].

Polycystic Ovary Syndrome is the caused by a complex combination of genetic predisposition, lifestyle factors, and environmental variables.

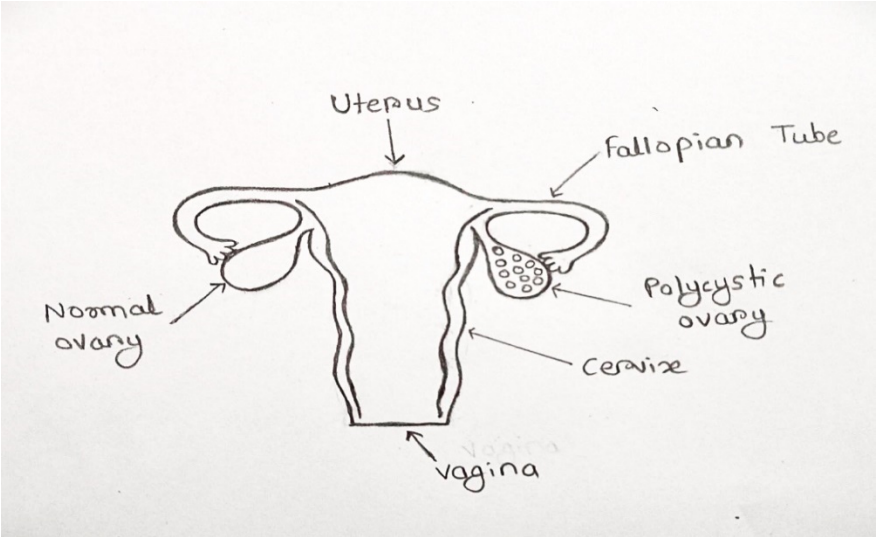


Figure 1. The female reproductive system: a normal and polycystic ovary [3].

Insulin resistance, together with counteracting excessive insulin, is a crucial pathogenic factor in disease progression. Elevated insulin levels encourage excessive production of androgen by ovarian theca cells while suppressing synthesis of sex hormone-binding globulin in liver, leading to increased circulating free androgens. This hyperandrogenic condition disturbs normal follicular maturation, resulting in follicular stoppage, persist anovulation, and the polycystic ovarian morphology seen in afflicted women [4,5].

Despite breakthroughs in understanding the underlying mechanisms of PCOS, most traditional treatments focus on symptom management rather than disease etiology. Lifestyle modification, the use of insulin-sensitizing agents like, metformin, induction of ovulation with agents viz., letrozole for infertility management, and the administration of oral contraceptives to reduce hyperandrogenic symptoms and regulate menstrual cycles are all common strategies [6,7].

Herbal remedies have been used for centuries in numerous traditional medical systems, includingTraditional Chinese Medicine, Ayurveda, and Unani medicine, to treat gynecological and metabolic diseases. Medicinal plants include a wide range of biologically active phytoconstituents, including flavonoids, alkaloids, phenolic compounds, and saponins terpenoids, each of those contribute to a variety of pharmacological actions. Evidence from experimental and clinical studies suggests that herbal medicines may benefit PCOS through a variety of mechanisms, including hormonal balance modulation, insulin sensitivity enhancement, antioxidant and anti-inflammatory actions, and lipid and glucose metabolism regulation.

Recent preclinical and clinical studies with several herbal agents, including Vitex agnus-castus, Cinnamomum verum, Trigonella foenum-graecum, Glycyrrhiza glabra, Trigonella foenum-graecum, and Caesalpinia bonduc, have yielded positive outcomes in improving both reproductive and metabolic standards associated with PCOS. Herbal medications, with their multi-targeted modes of action and relatively good safety profiles, may be excellent complementary or alternative therapy alternatives in PCOS management. However, existing evidence is fragmented throughout individual experimental and clinical investigations, emphasizing the importance of rigorous evaluation. As a result, the current systematic review attempts to critically assess and integrate the available evidence, with a focus on the therapeutic efficacy and underlying mechanisms of action of herbal drugs used to treat/ cure polycystic ovary syndrome [8,9].

Rationale of the Review:

Despite the availability of several pharmacological treatments for polycystic ovarian syndrome (PCOS), current treatment choices are mostly symptomatic and typically associated with side effects, poor long-term adherence, and inconsistent therapeutic outcomes. Furthermore, the multisystem and multifactorial nature of PCOS cannot be fully addressed with a single pharmaceutical intervention, highlighting the need for multi-targeted therapeutic alternatives [1, 2].

2. POLYCYSTIC OVARIAN SYNDROME: PATHOPHYSIOLOGY

Polycystic ovary syndrome is a multifaceted metabolic and endocrine condition distinguished by a combination

of genetic susceptibility, neuroendocrine dysfunction, metabolic abnormalities, and ovarian factors. Although the exact cause is uncertain, insulin resistance, hyperandrogenism, and hypothalamic pituitary ovarian axis malfunction are considered the key pathogenic mechanisms of PCOS [1,5].

2.1 Hyperinsulinemia and Insulin Resistance:

Insulin resistance exists in a significant fraction of women with PCOS, regardless of body weight, and is regarded as a primary metabolic characteristic of the condition. Impaired insulin sensitivity leads to compensatory hyperinsulinemia, which involves a crucial role in pathophysiology of PCOS by affecting ovarian steroid metabolism and synthesis. Excess insulin promotes production of androgen in ovarian theca cells while inhibiting hepatic release of sex hormone-binding globulin, raising the amount of physiologically active circulating androgens. This endocrine imbalance disrupts normal follicular growth, resulting in follicular arrest and chronic anovulation, linking metabolic changes to reproductive dysfunction in PCOS. As a result, insulin resistance and hyperinsulinemia are important pathophysiological elements that increase the syndrome's metabolic and reproductive symptoms [4,5].

2.2 The Impact of Hyperandrogenism on Ovarian Function:

Hyperandrogenism is a distinguishing characteristic of Polycystic Ovary Syndrome & is frequently linked with clinical symptoms like, acne, hirsutism, and alopecia. Elevated androgen ranges interrupt normal follicular growth by causing follicular arrest at the antral stage, preventing ovulation. While the ovaries are responsible for leading source of excess androgens, peripheral tissues, particularly adipose tissue, contribute significantly. Insulin has been demonstrated to enhance the production and activity of aldo-keto reductase 1C3 (AKR1C3), an enzyme that converts lesser androgen precursors like androstenedione into more strong androgens like testosterone in adipose tissue.

According to experimental data, insulin-mediated upregulation of AKR1C3 in adipocytes increases local androgen production, which exacerbates metabolic dysfunction and promotes systemic androgen excess. This adipose-derived androgen accumulation may further impair insulin sensitivity, contribute to lipotoxicity, and establish a self-perpetuating cycle of metabolic and endocrine dysregulation in PCOS, ultimately exacerbates hyperandrogenism and negatively impacts folliculogenesis and insulin homeostasis [10,5].

2.3 Neuroendocrine Disorders:

substrate-1 (IRS-1), androgen receptor (AR), insulin receptor (INSR).

The main reason behind polycystic ovary syndrome is neuroendocrine dysfunction involving the (HPO) hypothalamic-pituitary-ovarian axis. The LH/FSH ratio increases because GnRH is released too frequently in these women, which preferentially increases luteinizing hormone (LH) secretion over follicle-stimulating hormone (FSH). While comparatively low FSH levels hinder proper follicular maturation and the distinctive polycystic ovarian morphology and cause chronic anovulation, excess LH increases ovarian androgen production.

This abnormal pattern of GnRH and LH secretion indicates defective negative feedback regulation by ovarian steroid hormones at the hypothalamus GnRH neuron level. This disturbance of neuroendocrine signaling is a major cause driving the imrovement and persistence of polycystic ovarian syndrome [1,11].

2.4 The role of obesity, inflammation, and oxidative stress:

Women with PCOS often have insulin resistance and hyperandrogenism are significantly exacerbated by obesity, especially central or abdominal adiposity. Reduced levels of adiponectin and higher levels of resistin, leptin, interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) are the results of dysfunctional adipose tissue's altered adipokine secretion. These alterations lead to a persistent low-grade systemic inflammatory state that disrupts insulin signaling pathways, increases oxidative stress, and adversely impacts ovarian function, egg quality, and overall reproductive outcomes.

According to clinical evidence, women with PCOS and greater central fat storage have lower adiponectin concentrations and higher circulating levels of leptin, resistin, TNF-α, and IL-6. This imbalance demonstrates a strong correlation between inflammation of adipose tissue and the problems with metabolism and reproduction seen in PCOS. By interfering with insulin receptor signaling, pro-inflammatory mediators generated from adipose tissue worsen insulin resistance and add to the disorder's intricate and multifaceted etiology [4].

2.5 Molecular and Genetic Factors:

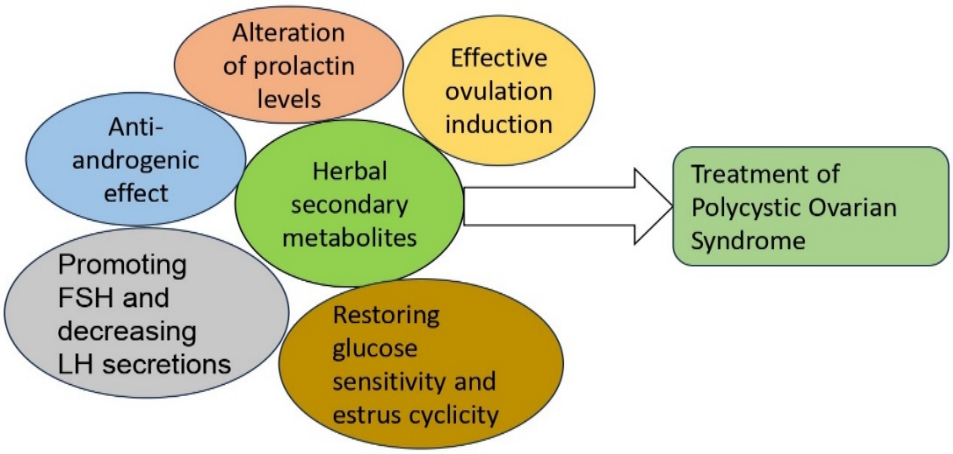
The development of Polycystic ovarian Syndrome is significantly affected by genetic susceptibility. Increased vulnerability to PCOS and associated hormonal disorders has been linked to genetic variations implicated in steroid hormone production, endocrine regulation and insulin signaling pathways. Notably, the pathophysiology of the condition has been linked to polymorphisms in genes including CYP17A1, CYP19A1, insulin receptor

Evidence from candidate gene studies and meta-analyses suggests that changes in steroidogenic enzyme genes,

such as CYP17A1, as well as genes that regulate insulin signaling, may influence the likelihood of developing PCOS. These findings highlight the syndrome's complex nature, in which inherited genetic differences combine with environmental, metabolic, and endocrine factors to determine individual vulnerability to Polycystic ovarian syndrome [1].

Overall, PCOS is caused by self-sustaining interaction of insulin resistance, androgen excess, neuroendocrine dysregulation, inflammatory processes, oxidative stress, and hereditary vulnerability. This complex pathophysiology explains the wide range of reproductive and metabolic manifestations seen in affected women and underscores the limitations of traditional therapy approaches that target individual symptoms. The intricacy of PCOS gives a compelling basis for investigating multi-targeted therapy options, such as the use of herbal medications, in its long-term care [4,5].

Figure 2: The mechanisms by which different herbal secondary metabolites treat PCOS [3].



3. HERBAL DRUGS USED IN PCOS MANAGEMENT

Herbal medicines used in the management of PCOS. work through a range of biological processes, such as insulin sensitization, anti-androgenic action, hormone regulation, and reduced oxidative stress and inflammation. These plants may be classified to the subsequent categories depends on their primary modes of action [3].

3.1 Herbs for Regulating Ovulation and Menstrual Cycle:

Several medicinal plants have been shown in clinical and experimental research to stimulate ovulation and normalize menstrual cycles in women with Polycystic Ovary Syndrome. Vitex agnus-castus, Asparagus racemosus, Caesalpinia bonduc, Saraca asoca, and Tribulus terrestris are some of the most commonly studied plants. Vitex agnus-castus, for example, modulates the HPO viz., hypothalamic-pituitary-ovarian axis by controlling prolactin ranges and restoring the luteinizing hormone (LH) to follicle-stimulating hormone (FSH) ratio, that enhance ovulatory function [7,12].

3.2 Anti-androgenic Herbal Drugs:

Polycystic Ovary Syndrome is marked by hyperandrogenism, which can present as hirsutism, acne, or alopecia. Certain medicinal herbs have strong anti-androgen effects and can help lower circulating androgen levels. Studies have revealed that Glycyrrhiza glabra, Mentha spicata, Paeonia lactiflora, and Cimicifuga racemosa can reduce androgen receptor activity or suppress testosterone production. These herbal therapies help to restore hormonal balance and relieve androgen-related symptoms [13,14].

3.3 Insulin-Sensitive Herbal Medicines:

Insulin resistance ia a main problem driving the condition hallmark of Polycystic Ovary Syndrome, involved in both metabolic and reproductive problems. Momordica charantia, Trigonella foenum-graecum, Cinnamomum verum, Gymnema sylvestre, and Syzygium cumini, are medicinal plants that are shown to enhance insulin sensitivity and glucose metabolism. These plants' effects on glycemic management can help to minimize hyperandrogenism and restore normal ovarian function [4,15,16].

3.4 Anti-inflammatory and Antioxidant Herbs

The biological processes involved in PCOS and it is related consequences is mostly influenced by redox imbalance and persistent mild inflammation. Curcuma longa, Tinospora cordifolia, Nigella sativa, Withania somnifera , and Camellia sinensis are just a few of the medicinal plants that have potent anti-inflammatory and antioxidant qualities. By lowering oxidative damage, promoting normal ovarian function, and enhancing metabolic homeostasis, these botanicals help control PCOS [17,18].

The following table lists the botanical traits, phytochemical composition, mechanisms of action, and supporting experimental data of the herbal remedies used to treat PCOS in order to give a comprehensive perspective.

Table 1: 25 Herbal Drugs For Pcos

Sr. No.	Botanical Name	Part of Plant	Extract	Active Chemical Constituents	Mechanism Of Action	Effective Dose	Reference
1.	***Vitex agnus-castus***	Fruit	Ethanolic	Flavonoids, iridoids	HPO axis regulation, ↓ prolactin	20–40 mg/day	[03]
2.	***Cimicifuga racemosa***	Rhizome	Ethanolic	Triterpenes	Ovulation induction	20–40 mg/day	[03]
3.	***Moringa oleifera***	Leaves	Aqueous	Quercetin	Antioxidant	300 mg/kg	[03]
4.	***Tribulus terrestris***	Fruit	Ethanolic	Saponins	Follicular development	5–10 mg/kg	[04]
5.	***Paeonia lactiflora***	Root	Ethanolic	Paeoniflorin	Hormonal balance	50–100 mg/kg	[05]
6.	***Momordica charantia***	Fruit	Aqueous	Charantin	Insulin sensitization	150 mg/kg	[08]
7.	***Caesalpinia bonduc***	Seed	Ethanolic	Flavonoids, diterpenes	Ovulation induction, anti-androgenic	200 mg/kg	[09]
8.	***Emblica officinalis***	Fruit	Aqueous	Ascorbic acid	Metabolic regulation	250 mg/kg	[09]
9.	***Glycyrrhiza glabra***	Root	Hydroal-coholic	Glycyrrhizin	Anti-androgenic	100 mg/kg	[13]

10.	***Aloe vera***	Leaf gel	Aqueous	Polysaccharides	Ovarian steroidogenesis	1 mL/kg	[17]
11.	***Asparagus racemosus***	Root	Aqueous	Saponins (Shatavarins)	Estrogenic, ovulation support	200 mg/kg	[19]
12.	***Saraca asoca***	Bark	Aqueous	Tannins, flavonoids	Menstrual regulation	250 mg/kg	[19]
13.	***Nigella sativa***	Seeds	Oil extract	Thymoquinone	↓ Insulin resistance	2 g/day	[20]
14.	***Mentha spicata***	Leaves	Aqueous	Phenolics	↓ Testosterone	2 cups/day (tea)	[22]
15.	***Cinnamomum verum***	Bark	Aqueous	Cinnamaldehyde	Insulin sensitization	1–1.5 g/day	[23]
16.	***Trigonella foenum-graecum***	Seeds	Ethanolic	Diosgenin	Improves ovulation,	500 mg/day	[24]
17.	***Gymnema sylvestre***	Leaves	Ethanolic	Gymnemic acids	↓ Blood glucose	200 mg/kg	[25]
18.	***Bauhinia variegata***	Bark	Ethanolic	Flavonoids	Endocrine modulation	200 mg/kg	[25]
19.	***Tinospora cordifolia***	Stem	Aqueous	Alkaloids	Metabolic modulation	250 mg/kg	[26]
20.	***Syzygium cumini***	Seeds	Methanolic	Jamboline	Glucose metabolism	200 mg/kg	[26]

21.	***Curcuma longa***	Rhizome	Ethanolic	Curcumin	Anti-inflammatory, antioxidant	100 mg/kg	[27]
22.	***Camellia sinensis***	Leaves	Aqueous	Catechins	Antioxidant	3–4 cups/day	[28]
23.	***Withania somnifera***	Root	Hydroalcoholic	Withanolides	Stress & hormonal balance	300 mg/day	[29]
24.	***Foeniculum vulgare***	Seeds	Aqueous	Anethole	Estrogenic activity	100 mg/kg	[30]
25.	***Ocimum sanctum***	Leaves	Ethanolic	Eugenol	Anti-stress, hormonal balance	200 mg/kg	[31]

4. MECHANISMS OF ACTION FOR HERBAL THERAPIES IN PCOS

The herbal treatments included in the table have a diverse set of pharmacological activities that address the complicated pathophysiology of Polycystic Ovary Syndrome (PCOS). Many of these herbs have impacts on both reproductive and metabolic abnormalities caused by the disease [14].

Herbs that regulate menstrual cycles and ovulation: These plants work largely by regulating the hypothalamic-pituitary-ovarian (HPO) axis, promoting hormonal homeostasis and follicular growth. Commonly studied examples include Vitex agnus-castus, Asparagus racemosus, Caesalpinia bonduc, Saraca asoca, and Tribulus terrestris [3].

Anti-androgenic Herbs: Hirsutism, acne, and alopecia are symptoms of PCOS, a condition marked by hyperandrogenism. Glycyrrhiza glabra, Mentha spicata, Paeonia lactiflora, and Cimicifuga racemosa are some of the herbs with anti-androgenic properties that can reduce elevated androgen levels and ameliorate clinical symptoms [15, 27].

Insulin-Sensitizing Herbs: Insulin resistance, a defining feature of PCOS, is linked to metabolic and reproductive difficulties. Herbs such as Cinnamomum verum, Trigonella foenum-graecum, Gymnema sylvestre, Momordica charantia, and Syzygium cumini increase insulin sensitivity and glucose metabolism, indirectly decreasing hyperandrogenism and supporting normal ovarian function [25].

Anti-inflammatory and antioxidant herbs: Both chronic low-level inflammation and oxidative stress contribute to the development of PCOS. Curcuma longa, Nigella sativa, Tinospora cordifolia, Camellia sinensis, and Withania somnifera are herbs with potent anti-inflammatory and antioxidant properties that aid in ovarian function and metabolism [33].

5. DISCUSSION

This review emphasizes the multi-targeted potential of herbal medications in treating Polycystic Ovary Syndrome (PCOS), as they address both reproductive and metabolic problems. Their methods include endocrine modulation, increased insulin sensitivity, anti-inflammatory and antioxidant effects, and management

of menstrual cycles and ovulation. According to preclinical and clinical research, herbs such as Cimicifuga racemosa, Tribulus terrestris and Vitex agnus-castus can improve hormonal balance & metabolic phenotype in both PCOS models & affected women [3,14]. In some circumstances, Herbal extracts have demonstrated comparable efficacy as conventional therapy in recovering ovulation and balancing hormone levels [3].

A significant advantage of using herbal remedies into PCOS therapy is their ability to give holistic advantages while having less negative effects than standard drugs. These treatments have been proven to improve critical symptoms including menstrual abnormalities, insulin resistance, and hyperandrogenism [14].

However, there are a number of limitations to existing studies. Preclinical research or small clinical trials with a variety of approaches and outcome metrics provide a large portion of the current knowledge. To verify effectiveness and optimize dosage strategies for particular herbal medicines, well-designed, large-scale clinical trials are required [3]. Direct comparisons between research are also difficult due to the variety in herbal preparations, which includes variations in plant parts, extraction techniques, and phytochemical content. For herbal formulations to be included into evidence-based practice, standardization and quality control are crucial. In order to enable customized treatments for various PCOS characteristics, future research should concentrate on large randomized controlled trials to assess long-term safety and efficacy in addition to mechanistic investigations that elucidate the molecular pathways through which these herbs exert their effects [1,14].

6. FUTURE PERSPECTIVES / RECOMMENDATIONS

Future studies on herbal treatments for PCOS should prioritize the use of standardized formulations and consistent dosage schedules for repeatability. To determine the long-term safety & efficacy in human populations, extensive randomized controlled trials are required. To clarify the molecular mechanisms by which these herbs produce their therapeutic effects, mechanistic research on people is also crucial. Additionally, focusing on particular PCOS phenotypes may allow for customized herbal remedies, improving therapeutic results while reducing possible side effects [14].

7. CONCLUSION

Herbal medications have significant multi-targeted therapeutic promise in the treatment of Polycystic Ovary Syndrome (PCOS), as they address both reproductive and metabolic abnormalities. Preclinical and clinical evidence suggests that plants like Vitex agnus-castus, Cimicifuga racemosa, Caesalpinia bonduc, and Trigonella foenum-graecum can improve ovulation, restore hormonal balance, improve insulin sensitivity, and reduce hyperandrogenism, all while having fewer side effects than conventional treatments.

However, present research is constrained by small sample sizes, diversity in herbal formulations, and insufficient long-term safety information. Well-designed, large-scale clinical trials and mechanistic research are required to prove efficacy, standardize dose, and enable personalized herbal therapies for women with PCOS. Combining evidence-based herbal remedies with conventional care options may provide a more comprehensive approach to improve both reproductive and metabolic outcomes in affected patients.

REFERENCE

1. Azziz, R., Carmina, E., Chen, Z., et al. (2016). Polycystic ovary syndrome. Nature Reviews Disease Primers, 2, 16057.

2. Teede, H. J., Misso, M. L., Costello, M. F., Dokras, A., Laven, J., Moran, L., Piltonen, T., & Norman, R. J. (2018). Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. Human Reproduction, 33(9), 1602–1618.

3. Lakshmi, J. N., Babu, A. N., Kiran, S. S. M., Nori, L. P., Hassan, N., Ashames, A., Bhandare, R. R., & Shaik, A. B. (2023). Herbs as a Source for the Treatment of Polycystic Ovarian Syndrome: A Systematic Review. BioTech, 12(1), 4.

4. Diamanti-Kandarakis, E., & Dunaif, A. (2012). Insulin resistance and the polycystic ovary syndrome revisited: An update on mechanisms and implications. Endocrine Reviews, 33(6), 981–1030.

5. Rosenfield, R. L., & Ehrmann, D. A. (2016). The pathogenesis of polycystic ovary syndrome (PCOS): The hypothesis of PCOS as functional ovarian hyperandrogenism revisited. Endocrine Reviews, 37(5), 467–520.

6. Teede, H. J., Misso, M. L., Costello, M. F., Dokras, A., Laven, J., Moran, L., Piltonen, T., & Norman, R. J. (2018). Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. Human Reproduction, 33(9), 1602–1618.

7. Unfer, V., & Porcaro, G. (2020). Updates on the myo-inositol plus D-chiro-inositol combined therapy in polycystic ovary syndrome. European Review for Medical and Pharmacological Sciences, 24, 102–109.

8. Fauser, B. C., & Tarlatzis, B. C. (2018). Neuroendocrine abnormalities in polycystic ovary

syndrome: Pathophysiology and clinical implications. Human Reproduction Update, 24(3), 241–257.

9. Manouchehri, A., Abbaszadeh, S., Ahmadi, M., Nejad, F. K., Bahmani, M., & Dastyar, N. (2023). Polycystic ovaries and herbal remedies: A systematic review. JBRA assisted reproduction, 27(1), 85–91.

10. O'Reilly, M. W., Kempegowda, P., Walsh, M., Taylor, A. E., Manolopoulos, K. N., Allwood, J. W., Semple, R. K., Hebenstreit, D., Dunn, W. B., Tomlinson, J. W., & Arlt, W. (2017). AKR1C3-Mediated Adipose Androgen Generation Drives Lipotoxicity in Women With Polycystic Ovary Syndrome. The Journal of clinical endocrinology and metabolism, 102(9), 3327–3339.

11. Fauser, B. C., & Tarlatzis, B. C. (2018). Neuroendocrine abnormalities in polycystic ovary syndrome: Pathophysiology and clinical implications. Human Reproduction Update, 24(3), 241–257.

12. van Die, M. D., & Burger, H. G. (2013). Vitex agnus-castus extracts for female reproductive disorders. Journal of Alternative and Complementary Medicine, 19(8), 680–689.

13. Armanini, D., Mattarello, M. J., Fiore, C., Sartorato, P., & Palermo, M. (2004). Licorice reduces serum testosterone in healthy women. Steroids, 69, 763–766.

14. Manouchehri, A., Abbaszadeh, S., Ahmadi, M., Nejad, F. K., Bahmani, M., & Dastyar, N. (2023). Polycystic ovaries and herbal remedies: A systematic review. JBRA assisted reproduction, 27(1), 85–91.

15. Zhai, Y., & Pang, Y. (2022). Turmeric extract alleviates endocrine metabolic disturbances in letrozole induced PCOS by modulating inflammation and oxidative stress. Journal of Reproductive Immunology, 103628.

16. Zhao, L., Zhu, Z., Lou, H., Zhu, G., Huang, W., Zhang, S., & Liu, F. (2021). Curcumin improves insulin resistance and ovarian function in a rat model of polycystic ovary syndrome.s Gynecological Endocrinology, 37(3), 201–206.

17. Jelodar, G., Masoomi, S., & Rahmanifar, F. (2018). Effect of Aloe vera on ovarian morphology in PCOS rats. Iranian Journal of Reproductive Medicine, 16, 701–708.

18. Moini Jazani, A., Nasimi Doost Azgomi, H., Nasimi Doost Azgomi, A., & Nasimi Doost Azgomi, R. (2020). A comprehensive review of clinical studies with herbal medicine on polycystic ovary syndrome (PCOS). Daru: Journal of Pharmaceutical Sciences, 27(2), 863–877.

31. Sharma, P. V., & Dash, B. (2014). Dravyaguna Vijnana (Materia Medica–Vegetable Drugs). Chaukhambha Bharati Academy.

19. Kandasamy, S., & Balasundaram, U. (2021). Pharmacological evaluation of Caesalpinia bonduc in female reproductive disorders. Journal of Herbal Medicine, 25, 100389.

20. Azgomi, R. N., Zomorrodi, A., Nazemyieh, H., Fazljou, S. M. B., Sadeghi Bazargani, H., & Nejatbakhsh, F. (2020). Effects of herbal medicines on polycystic ovary syndrome: A systematic review. Archives of Gynecology and Obstetrics, 301, 1–16.

21. Armanini, D., Castello, R., Scaroni, C., Bonanni, G., Faccini, G., Pellati, D., & Fiore, C. (2004). Treatment of polycystic ovary syndrome with licorice. Gynecological Endocrinology, 19(6), 341–346.

22. Grant, P. (2010). Spearmint herbal tea has significant anti-androgen effects in polycystic ovarian syndrome: A randomized controlled trial. Phytotherapy Research, 24(2), 186–188.

23. Mannerås, L., Cajander, S., Lönn, M., Stener-Victorin, E., & Holmäng, A. (2010). Cinnamon improves insulin resistance in a rat model of polycystic ovary syndrome. Journal of Endocrinology, 207(3), 385–392.

24. Rotterdam ESHRE/ASRM-Sponsored PCOS consensus workshop group (2004). Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Human reproduction (Oxford, England), 19(1), 41–47

25. Azhar, M. F., Hussain, S. A., & Khan, M. A. (2019). Medicinal plants with antidiabetic and endocrine activities. Evidence-Based Complementary and Alternative Medicine, 2019, 1–10.

26. Panda, S., & Kar, A. (2005). Syzygium cumini seed extract in glucose regulation. Journal of Ethnopharmacology, 102, 196–201.

27. Zhao, L., Wang, Y., Liu, J., Wang, K., Guo, X., & Ji, B. (2021). Curcumin improves ovarian function in PCOS rats. Journal of Ovarian Research, 14, 1–12.

28. Williamson, G. (2001). Protective effects of tea flavonoids. Journal of Nutrition, 131, 2242–2246.

29. Lakshmi, T., Rajendran, R., & Krishnan, V. (2015). Withania somnifera and female reproductive health. Pharmacognosy Reviews, 9, 57–61.

30. Kooti, W., Darvishi, M., Asadi-Samani, M., & Ashtary-Larky, D. (2016). A review of medicinal plants with potential effects on polycystic ovary syndrome. Journal of Chemical and Pharmaceutical Sciences, 9, 323–332.

32. Kwon, C. Y., Cho, I. H., & Park, K. S. (2020). Therapeutic Effects and Mechanisms of Herbal Medicines for Treating Polycystic Ovary Syndrome: A Review. Frontiers in pharmacology, 11, 1192.

33. Asgary, S., & Sahebkar, A. (2015). Herbal medicine for the management of polycystic ovary syndrome (PCOS) and associated oligo/amenorrhoea and hyperandrogenism: A review of laboratory evidence with corroborative clinical findings. BMC Complementary Medicine and Therapies, 14, Article 511.

34. Smith, J. A., & Lee, H. Y. (2024). Herbs as a source for the treatment of polycystic ovarian syndrome: A systematic review. Biomolecules, 12(1), Article 4.

35. Sadeghi, M., Ghaderi, A., & Jafarabadi, M. A. (2024). Role of medicinal herbs in improving insulin resistance and metabolic parameters in polycystic ovary syndrome: A literature review. Journal of Herbal Medicine, 30, 100678.

36. Wuttke, W., Jarry, H., Christoffel, V., Spengler, B., & Seidlová-Wuttke, D. (2003). Chaste tree (Vitex agnus-castus)—Pharmacology and clinical indications. Phytomedicine, 10(4), 348–357.