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REVIEW ARTICLE

THERAPEUTIC POTENTIAL OF MEDICINAL PLANTS IN POLYCYSTIC OVARY SYNDROME: A NARRATIVE REVIEW

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Polycystic ovary syndrome (PCOS) is a complex endocrine disorder that affects the reproductive, metabolic, and psychological health of women of reproductive age. Conventional therapies for PCOS primarily focus on symptom management; however, their associated side effects have led many women to explore complementary approaches. This review aimed to evaluate the clinical efficacy and safety of herbal medicines in the management of PCOS based on data from clinical trials and preclinical models. An extensive literature search was conducted using PubMed, ScienceDirect, Scopus, and the Cochrane Library, covering studies published between 1995 and 2025. Inclusion criteria encompassed clinical trials and randomized controlled trials investigating herbal interventions for PCOS, as well as relevant in vivo and in vitro preclinical studies. The main outcomes analyzed were hormonal regulation, insulin sensitivity, ovarian function, and anti-inflammatory effects. Numerous herbs demonstrated therapeutic potential in PCOS management, including *Nigella sativa* L. (Ranunculaceae), *Vitex agnus-castus* L. (Lamiaceae), *Trigonella foenum-graecum* L. (Fabaceae), and *Cinnamomum verum* J.Presl (Lauraceae). These herbs exhibited diverse mechanisms of action, including modulation of insulin signaling pathways, reduction of oxidative stress, hormonal regulation, and anti-androgenic effects. Clinical studies reported improvements in menstrual regularity, insulin resistance, and hirsutism, with generally favorable safety profiles. Herbal medicine appears to be a promising adjunctive or alternative strategy for the management of PCOS. However, while existing evidence supports its efficacy, variability in study designs, dosage regimens, and outcome measures limits definitive conclusions. Future standardized, high-quality clinical trials are needed to confirm these therapeutic benefits and safety profiles.

Keywords: polycystic ovary syndrome, herbal medicine, insulin resistance, phytotherapy, reproductive health, complementary therapy

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INTRODUCTION

Polycystic ovary syndrome (PCOS), originally described as Stein-Leventhal syndrome (2), is an endocrine disorder widespread among women, affecting various aspects of their health (1). Research indicates that PCOS currently affects 11.9% of women globally, according to the Rotterdam diagnostic criteria (3). This common endocrine condition affects women of reproductive age and is characterized by hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology (4). Increasing evidence suggests that PCOS is a complex multisystem disorder extending beyond reproductive abnormalities and involving substantial metabolic disturbances and an increased risk of cardiovascular and psychological comorbidities. Changes in the diagnostic criteria greatly affect the reported prevalence of PCOS (5). PCOS incidence in the USA is increasing and is now estimated to approach 18% (6), whereas among Australian women, it ranges from 12% to 21% (7).

The pathophysiology of PCOS is multifactorial and involves hormonal imbalance, insulin resistance, and ovarian dysfunction (8,9). Elevated luteinizing hormone (LH) levels stimulate androgen production in ovarian theca cells, contributing to hyperandrogenism, which, in turn, disrupts normal follicular development, leading to anovulation and the characteristic polycystic ovarian morphology (10). Furthermore, insulin resistance and compensatory hyperinsulinemia play central roles in the pathogenesis of PCOS by further promoting ovarian androgen production and decreasing sex hormone-binding globulin levels, thereby exacerbating hyperandrogenism (11). In addition, chronic low-grade inflammation and oxidative stress have been increasingly implicated in the pathogenesis of PCOS, as they disrupt insulin signaling pathways, enhance ovarian steroidogenesis, and contribute to both metabolic disturbances and reproductive dysfunction (12,13). Hyperandrogenism, as a key feature of PCOS, is detected in approximately 60%–80% of affected women, while insulin resistance occurs in around 50%–70%, representing a central metabolic disturbance that contributes to the increased risk of long-term complications such as type 2 diabetes mellitus, dyslipidemia, hypertension, and cardiovascular disease (14,15).

According to the Rotterdam criteria, four PCOS phenotypes are distinguished based on different combinations of hyperandrogenism, oligo-anovulation, and polycystic ovarian morphology, as summarized in Table 1 (3,16,17).

The primary, first-line approach for all patients with PCOS is modification of lifestyle (18, 19). Clomiphene citrate (CC), letrozole, or estradiol are widely used in patients seeking fertility treatments, whereas oral contraceptives are commonly used for the chronic management of PCOS symptoms (20,21). Metformin is generally not considered for use alone, but is often combined with CC for treating women who are resistant to CC treatment alone (22). Conventional treatments for PCOS, besides lifestyle modifications, frequently involve insulin-sensitizing agents, anti-androgens, and ovulation-inducing medications (19). However, concerns about the potential side effects associated with conventional pharmacological therapies, together with growing interest in natural and complementary treatment approaches, have encouraged many women with PCOS to seek alternative therapeutic options. Among these, herbal medicine has attracted increasing scientific attention in recent years (4,23). As PCOS remains a complex and challenging disorder to manage, this study aimed to provide an overview of herbal medicines that have demonstrated potential therapeutic benefits in the treatment of this condition, with particular emphasis on clinically evaluated herbal drugs (24).

Table 1. *Classification of PCOS phenotypes according to the Rotterdam criteria*

	Phenotype A	Phenotype B	Phenotype C	Phenotype D
Hyperandrogenism	+	+	+	-
Oligo/anovulation	+	+	-	+
Polycystic ovarian morphology	+	-	+	+

Herbal medicine has been used for centuries in various traditional medical systems to treat a wide range of health conditions, including PCOS (4). Several medicinal plants have been investigated for their potential benefits in managing PCOS symptoms and associated metabolic and reproductive disturbances (25). These herbs may exert insulin-sensitizing, anti-androgenic, anti-inflammatory, and ovulation-regulating effects (25). However, the efficacy and safety of herbal medicines for PCOS management remain inconclusive due to the limited number of high-quality clinical trials and the substantial heterogeneity in study designs, interventions, and outcome measures (4).

Several review articles have previously addressed the role of medicinal plants and natural compounds in the management of PCOS (23–25). However, most available reviews focus on individual plants or on general herbal approaches, without systematically discussing underlying mechanisms of action or incorporating the most recent experimental and clinical findings. Furthermore, given the increasing number of studies published in recent years,

there is a need for an updated and comprehensive synthesis of the available evidence. Therefore, this review aimed to provide a comprehensive and up-to-date overview of medicinal plants investigated in the context of PCOS, based on a thorough analysis of recent literature, with particular emphasis on their bioactive compounds, mechanisms of action, and findings derived from experimental and clinical studies. By integrating available data, this review aimed to provide insights into the potential therapeutic benefits, limitations, and future research directions of herbal medicine as a complementary or alternative approach to PCOS treatment.

METHODS

We performed an extensive literature search of English-language studies across electronic databases, including PubMed, ScienceDirect, Scopus, and the Cochrane Library, from 1995 through 2025. Our objective was to identify clinical research on the use of herbal treatments for polycystic ovary syndrome (PCOS). The search terms included “polycystic ovary syndrome” and “PCOS” in the title or abstract, along with “plant”, “medicinal plant”, “herb”, “phytotherapy”, “botanical extract”, “root”, “fruit”, “hydroalcoholic”, “powdered”, “traditional medicine”, “integrative”, and “alternative therapy” in all fields.

Articles were selected based on title and abstract reviews in accordance with specific inclusion and exclusion criteria. Studies were included if they were English-language articles reporting clinical trials, randomized controlled trials (RCTs), and relevant in vivo and in vitro preclinical studies investigating the use of medicinal plants or natural compounds in PCOS. Exclusion criteria included conference abstracts without full-text availability and studies not directly related to the condition.

Ultimately, scientific papers that met the inclusion criteria were selected for in-depth analysis. The types of herbs used, the specific plant parts studied, the year of publication, study design, sample size, and the effects of these herbal treatments on reproductive and metabolic outcomes in patients with PCOS were all carefully extracted from the full-text articles.

RESULTS

Various herbs, such as *Aloe barbadensis* Mill. (Asphodelaceae), *Cinnamomum verum* J.Presl (Lauraceae), *Camellia sinensis* (L.) Kuntze (Theaceae), *Trigonella foenum-graecum L. (Fabaceae), and Mentha spicata L. (Lamiaceae),* have garnered attention for their potential therapeutic applications in the management of PCOS (26). An overview of key medicinal plants and their reported therapeutic actions is summarized in Table 2 for clinical studies and Table 3 for preclinical studies. *A. barbadensis* gel, when administered to rats with PCOS induced by the nonsteroidal aromatase inhibitor letrozole, demonstrated notable effects, including increased HDL cholesterol levels and reduced plasma triglyceride and LDL cholesterol levels (27,28). Studies investigating *C. verum* have highlighted its insulin-sensitizing and anti-inflammatory properties, suggesting a potential role in improving glucose metabolism and restoring estrous cyclicity in PCOS models (29). *C. sinensis*, known for its antioxidant and anti-inflammatory properties, has also been proposed as a beneficial herbal remedy for PCOS (30). *T. foenum-graecum*, another plant under investigation, has shown potential in regulating ovarian function in PCOS by promoting follicle-stimulating hormone (FSH) levels and decreasing luteinizing hormone (LH) levels (31). In addition, recent research has indicated that *M. spicata* may be effective in alleviating mild hirsutism in women with PCOS (32,33). Collectively, these findings suggest a promising role of herbal medicine as a complementary approach to addressing various aspects of PCOS symptoms and associated metabolic disturbances.

Camellia sinensis (L.) Kuntze (Theaceae)

Camellia sinensis has attracted considerable attention as a potential therapeutic agent for PCOS due to its antioxidant and anti-inflammatory properties. Several studies have investigated the effects of *C. sinensis* extract on metabolic parameters, hormone levels, and ovarian function in PCOS. Green tea contains a variety of catechins, among which epigallocatechin gallate (EGCG) is considered the most biologically active and influential constituent of *C. sinensis* (34).

A systematic review summarized findings from four human and four animal primary studies on *C. sinensis* extract in PCOS (35). Human studies reported reductions in body weight and, in some cases, testosterone levels. For instance, in a randomized double-blind clinical trial, overweight and obese women with PCOS aged 20–40 years received either a *C. sinensis* tablet at an unspecified dose or placebo capsules containing wheat flour daily for 12 weeks. This study found that *C. sinensis* supplementation significantly reduced body weight, fasting insulin levels, and free testosterone concentrations compared to the placebo group. These results suggest that

Table 2. *Summary of medicinal plants investigated for their therapeutic effects in polycystic ovary syndrome (PCOS) - clinical studies*

Plant/extract	Patients	Results	Active substance	Dosing	Duration of administration	Author
Camellia sinensis (L.) Kuntze, (Theaceae)	20-40 y.o.PCOS women	↓BW, FI, T	Green tea tablets	500 mg green tea capsules	12 weeks	(36)
Mentha spicata L. (Lamiaceae)	Women with PCOS	↓T, ↑LH,	Spearmint tea	250 ml freshly prepared tea, 2 x daily	30 days	(32)
Mentha spicata L. (Lamiaceae)	Women with hirsutism caused by PCOS	↓FT, ↓TT, ↑LH, ↑FSH, ↓hirsutism	Spearmint tea	tea 2 x daily	30 days	(33)
Crocus sativus L. (Iridaceae)	Obese women with DMT2		Saffron powder	200 mg, 400 mg	12 weeks	(46)
Cinnamomum verum J.Presl, (Lauraceae)	Women with PCOS	↓TC, ↓ LDL, ↑HDL	Cinnamon capsules	500 mg, 3 capsules	8 weeks	(48)
Cinnamomum verum J.Presl, (Lauraceae)	Women with PCOS	↓, WC, ↓BMI, ↓LDL	Cinnamon powder	500 mg cinnamon, 3 x daily	12 weeks	(50)
Trigonella foenum-graecum L. (Fabaceae)	Premenopausal women with PCOS	↓ LH, ↓ FSH, improved ovarian function	Fenugreek seed extract (Furocyst) enriched with ≈40% furostanolic saponins	500 mg capsule, 2 x daily	90 days	(51)
Apium graveolens L. [Apiaceae] *Pimpinella anisum* L., (Apiaceae)	Obese women with PCOS	↓T, ↓LH/FSH ratio, ↑menstrual bleeding episodes	Apigenin (celery) and anethole (anise)	750 mg capsules, 3 x daily for 15 days over 3 menstrual cycles	-	(54)
Nigella sativa L., (Ranunculaceae)	Adolescent girls with PCOS	↓LH, ↓FSH, ↓T, improve menstrual cycle regularity, ↓OV	-	1000mg capsules (*N. sativa*) daily	16 weeks	(72)

BW -body weight; FI- fasting insulin; T- testosterone (F-free, T-total); LH – luteinizing hormone; FSH – follicle-stimulating hormone; DMT2 -diabetes mellitus type 2; TC – total cholesterol; LDL – low-density lipoprotein; HDL – high-density lipoprotein; WC- waist circumference; BMI – body mass index; OV- Ovarian Volume

C. sinensis consumption may contribute to weight loss and improvements in metabolic and hormonal profiles in women with PCOS (36).

Another study examined the effect of a hydroalcoholic extract prepared from dried leaves of *C. sinensis* on reproductive improvement in estradiol valerate-induced PCOS in rats. Following the induction of PCOS, the rats were divided into four groups: a PCOS group and three experimental groups receiving 50, 100, or 200 mg/kg BW of *C. sinensis* extract intraperitoneally for 10 days. The results showed a significant reduction in serum LH levels, body and ovarian weights, and the insulin resistance index in the *C. sinensis* extract-treated groups compared with the PCOS group. Histomorphometric studies further revealed significant improvements in the number of follicles and thickness of the theca layer, indicating a marked improvement in PCOS symptoms (37).

Overall, supplementation with *C. sinensis* extract may reduce serum levels of LH, free testosterone, and 17-β-estradiol, while significantly increasing the serum levels of FSH and progesterone in PCOS. C. sinensis regulates PCOS through its polyphenol content (especially EGCG), which modulates insulin signaling, reduces oxidative stress, and helps decrease androgen production, thereby improving metabolic and reproductive outcomes (35).

Notably, while intraperitoneal administration of high-dose EGCG resulted in reduced serum 17-β-estradiol and LH levels in female rats and reduced serum testosterone levels in male rats, such reductions in female sex hormones were not consistently observed in human subjects (34).

A study by Farhadian et al. (2020) demonstrated that theca layer of ovarian follicles was thicker in the PCOS control group than in the normal control group. Treatment with *C. sinensis* extract significantly decreased the thickness of the theca layer in a dose-dependent manner compared to the PCOS control group. This reduction in theca layer thickness may relate to decreased androgen and steroid hormone secretion, contributing to the amelioration of PCOS symptoms. The thickness of the granulosa layer was, conversely, reduced in the treated groups, further indicating normalization of follicular structure. These changes, along with increased counts of healthy follicles

Table 3. *Summary of medicinal plants investigated for their therapeutic effects in polycystic ovary syndrome (PCOS) - experimental studies*

Plant/extract	Model - animal	Results	Active substance	Dosing	Duration of administration	Author
Camellia sinensis (L.) Kuntze, (Theaceae)	Estradiol valerate-induced PCOS in rats	↓LH, ↓BW, ↓OW, ↓IRI	Hydro-alcoholic green tea extract	50 mg/Kg BW or 100 mg/Kg BW green tea extract intraperitoneally daily	10 days	(37)
Mentha spicata L. (Lamiaceae) *Linum usitatissimum* L. (Linaceae)	Estradiol-valerate induced PCOS in rats	↑P, ↓T, ↓E	Hydro-alcoholic spearmint and flaxseed extracts	40 mg/kg hydroalcoholic extract of spearmint + 200 mg/kg flaxseed extract for 30 days by gavage	30 days (7 weeks induction)	(39)
Mentha aravensis L. (Lamiaceae)	T-enanthate-induced PCOS in rats	↓LH, ↓FSH, ↑antioxidant capacity	Mentha arvensis hydroalcoholic extract	50, 100, and 200 mg/kg of extract powder daily	4 weeks (3 weeks induction)	(42)
Crocus sativus L. (Iridaceae)	T-enanthate-induced PCOS in rats	↓inflammatory markers, ↑insulin sensitivity, ↓LH, ↓E, ↓T, ↑FSH	Saffron petal extract (SPE) and saffron petal anthocyanins (SPA)	SPE [50, 200, and 600 mg/kg/body weight] and SPA [20, 40, and 80 mg/kg/body weight] daily	-	(43)
Vitex negundo L., (Lamiaceae)	Letrozole-induced PCOS rat model	↓LH, ↑FSH, ↑ serum concentrations E & P	Aqueous and hydroalcoholic extracts	200 and 400 mg/kg daily	66 days	(76)
Vitex negundo L., (Lamiaceae)	Letrozole-induced PCOS rat model	↑hormonal profiles, ↓OSM, ↓ BW	Hydro-ethanolic extract of Vitex negundo seed (VNE) (Cinnamic acid, plumbagin, nigundin B)	250 mg/kg daily	-	(77)
Vitex agnus-castus L. (Lamiaceae)	Letrozole-induced PCOS rat model	↑FSH, ↑E, ↑P	Ethanolic extracts	365 mg/kg orally	30 days	(78)
Glycyrrhiza glabra L. (Fabaceae)	Letrozole-induced PCOS rat model	↓LH, ↓T, ↑FSH, ↑E, ↑P	Methanolic extract	3.5 g tablet per day	21 day	(81)
Zingiber officinale Roscoe (Zingiberaceae)	Letrozole-induced PCOS rat model	↓LH, ↓FSH, ↓E, ↓T, ↑P,	6-gingerol and ginger extract	100mg/kg or 200 mg/kg of ginger extract, 200 µg/kg or 400 µg/kg of 6-gingerol	28 days	(84)
Trifolium pratense L. (Fabaceae)	Letrozole-induced PCOS rat model	↓OW, ↓OV, ↓ ST, ↑E, ↓LDL, ↑HDL	Red clover extract	500 mg/kg or 750 mg/kg orally	30 days (21 days model induction)	(87)

BW -body weight; FI- fasting insulin; T- testosterone (F-free, T-total); LH – luteinizing hormone; OW-ovarian weight; IR(I) – insulin resistance (index); P – progesterone; E – estradiol; FSH – follicle-stimulating hormone; DMT2 -diabetes mellitus type 2; TC – total cholesterol; LDL – low-density lipoprotein; HDL – high-density lipoprotein; WC- waist circumference; BMI – body mass index; OV-Ovarian Volume; OSM – oxidative stress markers; STR – serum triglycerides; FBGL- fasting blood glucose level

and corpus luteum numbers, suggest a beneficial effect of C. sinensis extract on ovarian morphology and function in PCOS (38).

Mentha spicata L. and *Mentha arvensis* L. (Lamiaceae)

Mentha spicata has been investigated as a potential treatment for mild hirsutism in women with PCOS, with two studies demonstrating its potential to reduce androgen levels (32,33).

Akdoğan et al. (2007) investigated the effects of *M. spicata* tea prepared from dried leaves on androgen levels in hirsute women. Twenty-one participants (12 with PCOS and 9 with idiopathic hirsutism) consumed *M. spicata* tea twice daily for 5 days during the follicular phase. After treatment, free testosterone levels decreased significantly, whereas LH, FSH, and estradiol levels increased markedly, and total testosterone and dehydroepiandrosterone sulfate (DHEA-S) levels showed no significant change. The authors suggested M. spicata could serve as a mild natural antiandrogen for hirsutism, warranting further research (32).

In a 1-month clinical trial, Grant (33) demonstrated that *M. spicata* tea significantly reduced free and total testosterone levels in women with PCOS-induced hirsutism, while concurrently elevating LH and FSH levels. Subjective assessments of hirsutism, evaluated via the modified Dermatology Life Quality Index (DLQI), showed significant improvement in the treatment group, while objective Ferriman-Gallwey scores did not decrease significantly. Despite only partially meeting the primary clinical endpoints, the study demonstrated significant changes in hormone levels, and the herbal tea was well-tolerated with no reported side effects (33).

In a rat model of estradiol valerate-induced PCOS, treatment with hydroalcoholic extracts prepared from dried leaves of *M. spicata* and ground seeds of *Linum usitatissimum* L. (Linaceae) for 30 days, starting 7 weeks after PCOS induction, led to a significant increase in serum progesterone and significant decreases in testosterone and estradiol levels compared to the untreated PCOS group. Conversely, no significant hormonal differences were found among the treatment, treatment-control, and control groups. Histologically, the treated group showed a significant increase in primary, pre-antral, and antral follicles, a reduction in cystic follicles, increased granulosa layer thickness, and decreased theca layer thickness relative to the PCOS group. These findings suggest that the combined *M. spicata* and *L. usitatissimum* treatment improves endocrine profiles and ovarian morphology in PCOS, possibly through phytoestrogenic effects, inhibition of 5-α reductase, increased sex hormone-binding globulin (SHBG), and modulation of key enzymes such as aromatase, which collectively may help alleviate hyperandrogenic symptoms like hirsutism and acne (39).

A recent preclinical study further supports these findings, demonstrating that *M. spicata* extract and its major constituent, carvone, improved hormonal imbalances, metabolic dysfunction, and ovarian inflammation in a letrozole-induced PCOS rat model. Treatment suppressed overactivation of the sterol regulatory element-binding protein 1 (SREBP1) and Toll-like Receptor 4 (TLR4) pathways, thereby restoring key reproductive and metabolic parameters (40). This suggests an additional mechanistic basis for the potential therapeutic effects of *M. spicata* in PCOS. Sadeghi Ataabadi et al. also showed that M. spicata effectively reduces testosterone levels (41).

In a rat model of PCOS induced by daily subcutaneous injections of testosterone enanthate (250 mg/kg) for 3 weeks, administration of *Mentha arvensis* hydroalcoholic extract resulted in a significant reduction in LH and FSH levels. This effect was most pronounced at the highest dose (200 mg/kg), where hormone levels approached those observed in healthy controls. The extract was prepared from whole, dried, and ground *M. arvensis* plants and processed into a hydroethanolic extract with 80% ethanol. After 4 weeks of treatment with the extract, blood samples were collected for hormone analysis. This highest concentration also notably decreased the number of ovarian cysts compared to the untreated PCOS group. Additionally, there was a significant increase in total antioxidant capacity in the treated PCOS rats. At the molecular level, *M. arvensis* treatment downregulated the expression of *Cyp17* and *Ptgs2* genes in ovarian tissue, which are implicated in androgen production and inflammation. These effects collectively suggest that *M. arvensis* can improve hormonal imbalances, reduce cyst formation, and enhance ovarian antioxidant defenses in PCOS (42).

Crocus sativus L. (Iridaceae)

Crocus sativus, commonly known as saffron, has been investigated for its potential therapeutic effects in PCOS and type 2 diabetes. Several studies have examined its effects on metabolic parameters, hormonal profiles, and ovarian function in women with PCOS (43–47). In a randomized, double-blind, placebo-controlled clinical trial, obese women with type 2 diabetes received either 200 mg/day of saffron powder or a placebo for 12 weeks, alongside aerobic training 3 times a week. The study demonstrated that,

compared with placebo, *C. sativus* supplementation, particularly when combined with exercise, significantly reduced body weight, BMI, body fat percentage, fasting glucose levels, and homeostatic model assessment of insulin resistance (HOMA-IR). Additionally, *C. sativus* intake led to significant decreases in inflammatory markers, including IL-6 and TNF-α, and improved hemostatic parameters, including fibrinogen and homocysteine levels. These findings suggest that *C. sativus* supplementation, particularly in combination with exercise, may improve metabolic, inflammatory, and hemostatic profiles in obese women with type 2 diabetes (46).

A recent systematic review and meta-analysis summarized findings from four human and three animal primary studies investigating the effects of *C. sativus* in PCOS (43). Across human trials, *C. sativus* supplementation was associated with reductions in body weight, BMI, waist circumference, fasting insulin levels, and insulin resistance. In animal models, studies reported improvements in ovarian morphology, reductions in cystic follicles, and decreases in testosterone levels (47).

Moshfegh et al. reported elevated levels of IL-6, TNF-α, IL-1β, IL-18, and CRP in the testosterone enanthate-induced PCOS rat group, consistent with previous findings. Treatment with *C. sativus* petal extract significantly decreased these inflammatory markers, suggesting the anti-inflammatory potential of flavonoids, tannins, and anthocyanins present in the petals. *C. sativus* exerted beneficial effects by modulating metabolic and hormonal pathways, including improving insulin sensitivity through the PI3K/Akt pathway and reducing oxidative stress and inflammation via its antioxidant properties. The study also showed that *C. sativus* extract and *C. sativus* petal anthocyanins decreased LH, estrogen, and testosterone levels, increased FSH levels, and enhanced the activities of antioxidant enzymes (GPx, SOD, CAT, GST, and GSH), collectively contributing to the amelioration of PCOS symptoms in mice (43,44).

C. sativus is widely recognized for its versatile botanical supplement properties. A network pharmacology study explored its potential in managing PCOS by identifying key targets, including AKT1, MAPK1, MAPK3, and STAT3. Subsequent molecular docking simulations suggest that *C. sativus* could potentially address PCOS-related insulin resistance and metabolic disorders (45).

C. sativus and its extracts have shown promising results in improving various aspects of PCOS, including metabolic parameters, hormonal profiles, and ovarian function. However, more research is needed to fully understand the mechanisms of action and establish the optimal dosage and duration of *C. sativus* supplementation for PCOS management (43–45).

Cinnamomum verum J.Presl (Lauraceae)

Cinnamomum verum, commonly known as cinnamon, has been extensively studied for its therapeutic effects in PCOS. Several clinical trials have evaluated its impact on metabolic parameters, hormonal profiles, insulin sensitivity, and ovarian function in women with PCOS (24).

In a clinical trial by Borzoei et al. (2017), 84 women with PCOS were evaluated over 8 weeks to determine the effects of bark powder from Cinnamomum zeylanicum Blume (Lauraceae), which is recognized as a synonym of *C. verum* J.Presl by World Flora Online. Participants who received *C. zeylanicum* capsules containing approximately 500 mg of cinnamon powder showed decreased levels of total cholesterol and low-density lipoprotein (LDL), alongside increased levels of high-density lipoprotein (HDL). Additionally, the *C. zeylanicum* group exhibited a significant increase in total antioxidant capacity, with no significant change in malondialdehyde levels. Although triglyceride levels did not significantly decrease, *C. zeylanicum* supplementation was associated with improved lipid profiles and antioxidant status (48).

Similarly, a study by Kort and Lobo (2014) investigated the effects of cinnamon supplementation on menstrual cyclicity in women with PCOS for 6 months. The results revealed a significant improvement in menstrual cycle regularity, suggesting cinnamon's role in modulating reproductive function. However, no notable changes were observed in insulin resistance markers, serum androgen levels, or body weight (49).

Hajimonfarednejad et al. (2017) found that 12 weeks of cinnamon powder supplementation reduced fasting insulin levels and improved insulin sensitivity in women with PCOS. In this double-blind trial, the treatment group received 500 mg capsules containing pure cinnamon derived from bark, while the parallel control group received capsules containing 50 mg of cinnamon powder and 450 mg of starch. The study also noted reductions in waist circumference, BMI, and LDL cholesterol, highlighting cinnamon's potential in managing both the metabolic and reproductive aspects of PCOS (50). Cinnamon improves insulin sensitivity in women with PCOS by activating the insulin receptor and increasing glucose uptake in muscle cells, while concurrently reducing systemic inflammatory markers, such as TNF-α and IL-6 (49,50).

C. verum has demonstrated promising effects in regulating

menstrual cycles, improving lipid profiles, and enhancing insulin sensitivity in women with PCOS. However, further research is required to understand its long-term effects and precise molecular mechanisms of action.

Trigonella foenum-graecum L. (Fabaceae)

Trigonella foenum-graecum, commonly known as fenugreek, has been widely investigated for its beneficial effects in the management of PCOS. Studies have explored its role in improving ovarian function, regulating menstrual cycles, and enhancing fertility in women with PCOS (24).

Swaroop et al. (2015) evaluated the effects of *T. foenum-graecum* seed extract (Furocyst) in 50 premenopausal women with PCOS over 90 days. The extract was produced using a patent-pending water-ethanol extraction process enriched with approximately 40% furostanolic saponins and administered as 500 mg capsules per day. The results showed a significant reduction in ovarian volume in all participants and a decrease in cyst size in 46% of the women, with complete cyst dissolution in 36% of cases. Additionally, regular menstrual cycles returned in 71% of the women, and 12% successfully conceived during the study. Significant increases in LH and FSH levels were observed compared to baseline. The study highlighted fenugreek's potential to improve ovarian function, regulate hormonal imbalances, and address PCOS-related infertility without significant adverse effects (51).

Similarly, another study by Bashtian et al. (2013) found that hydroalcoholic extracts of *T. foenum-graecum* seeds normalized menstrual cycles in women with oligomenorrhea caused by PCOS. Participants treated with *T. foenum-graecum* showed a significant decrease in polycystic ovaries on ultrasound scans, indicating improved ovarian health. Although the study reported no significant changes in BMI, insulin resistance, or testosterone levels, the positive effects on menstrual regularity and ovarian function were notable (52).

Apium graveolens L. (Apiaceae)

Apium graveolens, commonly known as celery, has been investigated for its regulatory effects on hormonal balance and menstrual cycles, particularly in women with PCOS. In an evaluation using a letrozole-induced PCOS rat model, Khosrowpour et al. (2022) utilized the dried fruits of *A. graveolens* as part of a multi-herbal formulation (53). This plant contains several bioactive compounds, including flavonoids (such as apigenin), essential oils, coumarins, and phenolic acids, which are believed to contribute to its therapeutic potential in reproductive health (53). Among these, apigenin, a flavonoid found abundantly in *A. graveolens*, has attracted attention for its potential to modulate hormone-related pathways. Studies suggest that apigenin may influence estrogen receptor activity, contributing to hormonal balance and improving menstrual regularity. Furthermore, apigenin has also been noted for its anti-inflammatory, antioxidant, and anti-androgenic properties, which can help mitigate symptoms of PCOS, such as hyperandrogenism and menstrual irregularities (53).

In a triple-blind randomized clinical trial, treatment with a combination of *A. graveolens* and *Pimpinella anisum* L. (Apiaceae) demonstrated superior clinical outcomes compared to metformin in obese patients with PCOS. Specifically, the combination of *A. graveolens* and *P. anisum*, administered as 750 mg capsules 3 times daily for 15 days per cycle over three consecutive cycles, achieved a 58.3% improvement in oligomenorrhea, compared to 25.0% in the metformin cohort ($p < 0.01$). The intervention also significantly increased menstrual bleeding episodes ($p = 0.003$) and induced marked reductions in both serum testosterone levels (mean difference: 0.16 vs. −0.02 ng/mL, $p = 0.005$) and the LH/FSH ratio (mean difference: 0.75 vs. −0.08, $p = 0.002$). Furthermore, the herbal therapy exhibited a favorable safety profile with no major adverse events reported. Phytochemical analysis suggests that the synergistic interaction between apigenin from *A. graveolens* and anethole from *P. anisum* may contribute to hormonal regulation by exerting anti-androgenic activity and modulating gonadotropin secretion (54).

Another study by Khodaeifar et al. (2019) explored the hydroalcoholic extract of *A. graveolens* and *C. zeylanicum*, particularly apigenin, in a rat model of PCOS induced with estradiol valerate. The findings indicated that in the therapy groups, blood sugar, insulin, and lipid profiles in plasma decreased significantly, while serum HDL levels were enhanced, and oxidative stress was reduced in treated groups (55).

In addition to apigenin, *A. graveolens* essential oils, such as limonene and selinene, have been identified as contributors to its anti-inflammatory and antispasmodic properties, which could help alleviate menstrual discomfort and improve reproductive health in women with PCOS (53).

Lepidium meyenii Walp. (Brassicaceae)

Lepidium meyenii, commonly referred to as maca, has attracted interest for its potential benefits in managing PCOS. *L. meyenii*, a member of the Brassicaceae family, is traditionally consumed for its purported effects on fertility, energy levels, and hormonal balance (56–58).

Recent studies have highlighted the antioxidant properties of the dried hypocotyl of *L. meyenii* as a key factor in its therapeutic potential for PCOS. According to Alarcón-Yaquetto et al. (2021), oxidative stress is a significant component of PCOS pathology, characterized by an imbalance between ROS and antioxidant defenses. *L. meyenii* has been shown to enhance total antioxidant capacity, which may mitigate the oxidative stress associated with this condition (56).

Recent analyses of *L. meyenii* extracts indicate that its antioxidant activity is primarily attributed to alkaloids and phenolic compounds, with alkaloids showing a somewhat stronger contribution. These findings help clarify the basis of the antioxidant effect of *L. meyenii*, although they are derived from laboratory analyses and do not represent clinical evidence in PCOS (57).

Furthermore, specific phenotypes of *L. meyenii*, particularly red *L. meyenii*, have been associated with anti-inflammatory and reproductive benefits. Research indicates that red *L. meyenii* can enhance ovarian function and improve overall reproductive health in women with PCOS (56). The active plant part of *L. meyenii* is its hypocotyl-root axis. This is particularly relevant as PCOS is often accompanied by chronic low-grade inflammation, which can exacerbate metabolic and hormonal imbalances (58).

Tribulus terrestris L. (Zygophyllaceae)

Tribulus terrestris, commonly known as puncture vine, has been traditionally used in various cultures for its purported benefits on reproductive health, including the management of female infertility and menstrual disorders (59). In an animal study with the observation periods divided into 7 and 14 days, administration of pure *T. terrestris* extract to immature female rats significantly increased the number and diameter of the corpus luteum, thickness of the theca-interna layer, and the number of secondary and Graafian follicles, indicating a stimulatory effect on folliculogenesis and corpus luteum formation through an LH-like activity (60). These findings suggest that *T. terrestris* may support the initiation of puberty and ovulatory cycles by mimicking or enhancing endogenous gonadotropin activity (60). Recent comprehensive reviews have highlighted that the secondary metabolites of *T. terrestris*, particularly steroidal saponins like protodioscin, are responsible for its positive effects on the female reproductive system, including improvements in ovarian histology, modulation of sex hormone levels, and enhancement of ovulation (61). Additionally, clinical and preclinical studies have demonstrated that *T. terrestris* supplementation can promote regular ovulation, reduce ovarian cysts, and restore hormonal balance in PCOS models, with evidence of improved menstrual regularity and reduced hyperandrogenic symptoms (59,61). The herb also exhibits antioxidant properties, which may help mitigate oxidative stress associated with PCOS and further support ovarian function (62). Overall, while more robust clinical trials are needed, current evidence supports the potential of an ethanolic fruit extract of *T. terrestris* as a complementary approach for improving ovarian health and managing PCOS-related symptoms in women (62).

The therapeutic effects of *T. terrestris* in PCOS are attributed to several mechanisms (59). One proposed mechanism is the normalization of hormonal balance and induction of ovulation through antiestrogenic action, which helps restore regular estrous cycles and ovulatory function in PCOS models (59). Studies in animal models have shown that *T. terrestris* extract can reverse letrozole-induced hormonal disturbances by increasing FSH levels and decreasing LH, estradiol, and testosterone levels, thereby promoting follicular development and reducing ovarian cysts (60,61). Additionally, *T. terrestris* has demonstrated significant effects on metabolic parameters associated with PCOS (62). It enhances insulin sensitivity by modulating metabolic factors, including p-Akt, GLUT8, and insulin receptor expression, in ovarian tissue. This leads to lower serum glucose and insulin levels, thereby improving insulin resistance. The herb also exerts antioxidant effects, reducing oxidative stress in ovarian tissue, which is crucial for normal folliculogenesis and ovulation (60,62).

Curcuma longa L. (Zingiberaceae) and *Phyllanthus emblica* L. (Phyllanthaceae)

The combination of *Curcuma longa* and *Phyllanthus emblica* has been investigated for its potential benefits in managing PCOS as a common endocrinopathy associated with insulin resistance, hyperandrogenism, and ovarian dysfunction (63,64). These plants, known for their antioxidant, anti-inflammatory, and insulin-sensitizing properties, have been traditionally used in Ayurvedic medicine to manage conditions such as diabetes, and their combination has shown promise in addressing the metabolic and hormonal disturbances associated with PCOS (65,66). In an open-label, randomized, active-controlled exploratory clinical study, Gupte et al. (2023) evaluated the effects of a combination of *C. longa* (rhizome) and *P. emblica* (fruit) prepared with either a traditional method (TF—Traditional Formulation) or a standardized extraction method (PNAE—Pharmanza Nisha Amalaki Extract) on glucose metabolism, inflammatory markers, and

reproductive hormones in women with PCOS. Participants were randomized into groups and received either traditional formulations or standardized extracts of *C. longa* and *P. emblica*, both with or without metformin, for 90 days. The study results indicated improvements in several key markers associated with PCOS (63).

The molecular mechanisms underlying the effects of *C. longa* and *P. emblica* in PCOS involve the modulation of key pathways related to insulin sensitivity, inflammation, and hormone regulation. Curcumin, the active compound in *C. longa*, activates PPAR-γ, a nuclear receptor that enhances insulin sensitivity and suppresses pro-inflammatory cytokines such as IL-6 and TNF-α, which are elevated in PCOS. Additionally, *P. emblica* has been shown to influence the AMPK pathway, improving glucose uptake and metabolic homeostasis, while reducing oxidative stress, a contributor to PCOS-related inflammation and metabolic dysfunction (63).

Taraxacum officinale F.H.Wigg. (Asteraceae)

Taraxacum officinale, commonly known as dandelion, is recognized for its diverse bioactive compounds, including polysaccharides, phenolic acids, and phytosterols, which contribute to its antihyperglycemic and anti-inflammatory properties (67). *T. officinale* root extracts showed no glucose-lowering effect in normoglycemic mice, but the aqueous extract exhibited clear antidiabetic activity in alloxan-induced mice, although weaker than metformin (68).

Beyond metabolic effects, *T. officinale* has been studied for its influence on ovarian cell biology. *In vitro* research using human ovarian granulosa cells found that *T. officinale* leaf extract promotes cell proliferation, upregulates the expression of hormone receptors, including *FSH, LH*, and *IGF-1* receptors, and enhances estradiol and progesterone secretion (69). These findings suggest that *T. officinale* may support ovarian steroidogenesis and endocrine function, which are often impaired in PCOS (69).

Although direct clinical evidence in women with PCOS is currently lacking, the demonstrated antidiabetic, antioxidant, and ovarian-supportive effects of *T. officinale* highlight its promise as a complementary agent for addressing insulin resistance, hormonal imbalance, and reproductive dysfunction associated with PCOS (69).

Nigella sativa L. (Ranunculaceae)

Nigella sativa (black seed, medicinal part: seed (70)) has been traditionally used in Middle Eastern and South Asian medicine for its various therapeutic properties. Its bioactive components, especially thymoquinone, possess potent antioxidant, anti-inflammatory, and insulin-sensitizing effects, making it a promising candidate for managing PCOS (71). *N. sativa* is also effective in improving gonadotropins and sex hormones, which are commonly disrupted in women with PCOS.

A randomized controlled trial involving 103 adolescent girls with PCOS demonstrated that daily supplementation with 1000 mg of *N. sativa* extract (plant part not specified) for 16 weeks resulted in significant clinical and hormonal improvements compared to a control group receiving medroxyprogesterone (72). The intervention group exhibited a significant modulation of serum reproductive hormones, including notable reductions in LH and testosterone levels, as well as a decrease in bilateral ovarian volume (72). Additionally, participants experienced an alleviation of clinical symptoms, characterized by reduced hirsutism severity and improvements in menstrual cycle irregularities such as oligomenorrhea and amenorrhea (72). These findings suggest that short-term *N. sativa* supplementation may effectively modulate hormonal imbalances and alleviate menstrual disturbances in adolescents with PCOS, likely due to the phytoestrogen compounds present in the extract (72).

Mahmoudian et al. conducted a randomized controlled trial assessing the effects of *N. sativa* supplementation on glycemic control in adolescent girls with PCOS. The study found that 16 weeks of *N. sativa* supplementation resulted in significant reductions in fasting plasma glucose and 2-hour postprandial glucose levels compared to the control group. These findings suggest that *N. sativa* may improve glycemic parameters in adolescents with PCOS (73).

Beyond hormonal and metabolic regulation, *N. sativa* has demonstrated benefits in improving reproductive cell quality. An experimental study using a PCOS-induced mouse model revealed that administration of *N. sativa* hydroalcoholic extract significantly enhanced oocyte maturation, fertilization, and blastocyst formation rates (74). These improvements were associated with elevated glutathione levels, increased glutathione peroxidase expression, and reduced reactive oxygen species in oocytes. Additionally, the extract upregulated genes involved in oocyte development and epigenetic regulation, including *Dnmt1, Hdac1, Mapk*, and *Cdk1*, while downregulating pro-inflammatory markers like *Cox2* (74). These findings support the potential of *N. sativa* to enhance reproductive competence in PCOS beyond systemic effects. Furthermore, recent evidence suggests that *N. sativa* may influence gene expression involved in oocyte maturation and epigenetic regulation, contributing to improved reproductive outcomes in PCOS (74).

Further insights come from an experimental letrozole-induced PCOS rat model, where thymoquinone, as a key bioactive component of *N. sativa*, was administered after PCOS induction (75). Rats received letrozole for 28 days, followed by intraperitoneal thymoquinone at 5 mg/kg or 10 mg/kg every 3 days for 30 days. The treatment restored disrupted folliculogenesis, reduced oxidative stress and apoptosis, and normalized hormone levels. These findings suggest that thymoquinone may improve ovarian function primarily through antioxidant and anti-apoptotic mechanisms, positioning N. sativa as a promising natural adjunct in PCOS management (75).

Vitex negundo L. (Lamiaceae)

Vitex negundo, commonly known as the five-leaved chaste tree, has been traditionally used to treat gynecological disorders, with recent preclinical research supporting its potential for managing PCOS. In a letrozole-induced PCOS rat model, both aqueous and hydroalcoholic extracts of *V. negundo* seeds (200–400 mg/kg) were administered over a total study period of 66 days, including PCOS induction and treatment phases. The extracts significantly restored regular estrous cyclicity, normalized the LH/FSH ratio by reducing elevated LH levels and increasing reduced FSH levels, and improved serum concentrations of estrogen and progesterone. Histological analysis showed decreased ovarian cysts and improved follicular development after treatment. In addition, treatment ameliorated hyperglycemia and dyslipidemia, suggesting beneficial metabolic effects, with aqueous extracts showing greater efficacy. Importantly, toxicity markers (SGPT, SGOT, creatinine) remained within the normal range even after prolonged administration, indicating a favorable safety profile (76).

A recent study by Kar et al. (2024) further supports the therapeutic potential of *V. negundo* seeds in PCOS management. Administration of the hydroethanolic extract of *V. negundo* seeds in a letrozole-induced PCOS rat model not only improved hormonal profiles but also reduced oxidative stress markers such as superoxide dismutase and catalase, and lowered inflammatory cytokines including TNF-α and IL-6. Treatment with *V. negundo* seeds resulted in a significant reduction in body weight compared to untreated PCOS rats, which exhibited marked weight gain after letrozole induction ($p < 0.001$). *V. negundo* seeds also modulated gonadotropin levels and corrected the LH/FSH ratio by regulating steroidogenic enzymes, ER-α signaling, and downregulating *NR3C4* expression, contributing to restored hormonal balance. Molecular docking analyses confirmed interactions between active phytochemicals—cinnamic acid, plumbagin, and nigundin B—and hormone/inflammatory signaling pathways. In addition to improvements in follicular morphology and reduced theca-layer thickness, histomorphological evaluation of the ovaries evidenced pronounced amelioration of PCOS pathology. These findings highlight *V. negundo* seed extract as a multifaceted, holistic therapeutic candidate for PCOS, owing to its antiandrogenic, antioxidant, and anti-inflammatory actions driven by key phytocompounds (77).

The pharmacological activity of *V. negundo* appears to be mediated through multiple mechanisms. Phytochemical screening revealed the presence of flavonoids and triterpenoids, known for their antioxidant and anti-inflammatory effects (76,77). The flavonoid-rich extracts are believed to exert antiandrogenic effects and modulate steroidogenic enzymes, potentially lowering intra-ovarian androgen levels (76). Additionally, improvements in insulin sensitivity and glucose tolerance were observed, suggesting an insulin-sensitizing effect which may be key in mitigating metabolic complications of PCOS (76,77). Collectively, these effects contribute to the normalization of endocrine function and ovarian morphology, making *V. negundo* a promising natural alternative in PCOS therapy.

Vitex agnus-castus L. (Lamiaceae)

Vitex agnus-castus, or chaste tree, has been traditionally used to regulate female reproductive hormones. Findings of both preclinical and clinical studies support its application in PCOS treatment. In a letrozole-induced PCOS rat model, administration of 365 mg/kg of *V. agnus-castus* ethanolic fruit extract for 30 days led to normalization of serum LH and testosterone, while increasing FSH, estradiol, and progesterone levels. Ovarian histology confirmed reduced cystic follicles, the reappearance of corpora lutea, and normalized theca and granulosa layers. Importantly, the extract significantly downregulated hypothalamic *KISS1* gene expression, which was previously elevated in the PCOS model, suggesting neuroendocrine modulation via the hypothalamic-pituitary-gonadal axis (78).

In addition to these findings in animals, a systematic review of randomized controlled trials showed that *V. agnus-castus* significantly improved premenstrual syndrome (PMS) symptoms, outperforming a placebo, vitamin B6, and magnesium in multiple trials (79).

V. agnus-castus contains dopaminergic diterpenes, such as casticin, that act as D2 receptor agonists in the anterior pituitary, thereby reducing prolactin secretion. This action supports luteal phase function and regulates the hypothalamic-pituitary-gonadal axis. Additional flavonoids

and iridoid glycosides possess anti-inflammatory and hormone-modulating properties (78,79).

Glycyrrhiza glabra L. (Fabaceae)

Glycyrrhiza glabra, commonly known as licorice (medicinal part: root/radix (80)), has demonstrated significant therapeutic potential in PCOS management due to its antiandrogenic, antioxidant, and hormonal regulatory properties. In a letrozole-induced PCOS rat model, oral administration of the methanolic extract of *G. glabra* (300 mg/kg/day for 21 days) significantly reduced LH and testosterone levels while increasing FSH, estradiol, and progesterone levels. Histopathological evaluation revealed a reduction in cystic follicles and a greater presence of corpora lutea and developing follicles, suggesting the restoration of ovulation. Additionally, *G. glabra* improved uterine and ovarian weights and normalized estrous cyclicity, confirming its broad reproductive benefits in experimental models (81).

The clinical efficacy of *G. glabra* has also been supported by human trials. In a randomized, double-blind, placebo-controlled study, *G. glabra* root extract administered alongside spironolactone for 8 weeks in women with PCOS enhanced the antiandrogenic effect of spironolactone, leading to a greater reduction in serum testosterone levels and improvements in hirsutism and acne. Importantly, this combination did not cause significant side effects, suggesting *G. glabra* may be a safe and effective adjunct therapy in the clinical management of hyperandrogenism (82).

Furthermore, *G. glabra* in combination with *Paeonia spp*. L. (Paeoniaceae) has been traditionally used in Eastern medicine for hormonal regulation. In a DHEA-induced PCOS mouse model, treatment with the *G. glabra–Paeonia* combination (50 mg/kg and 100 mg/kg) significantly reduced testosterone and fasting insulin levels and improved ovarian morphology by increasing the number of healthy primary and Graafian follicles. Animals treated with the higher dose also showed signs of ovulation, such as the presence of corpora lutea and normalized estrous cycles. These effects were associated with fewer cysts and better overall ovarian health. The beneficial outcomes are thought to be due to the combined action of bioactive compounds in both plants, which helps balance hormones and support healthy follicular development (83).

The bioactivity of *G. glabra* is primarily attributed to its active compounds, including glycyrrhizin, liquiritigenin, and flavonoids, which exhibit potent antioxidant and anti-inflammatory effects. These constituents support hormone balance by modulating the hypothalamic-pituitary-gonadal (HPG) axis and regulating ovarian steroidogenesis. *G. glabra* also reduces androgen levels by inhibiting key enzymes involved in testosterone synthesis, such as 17-β-hydroxysteroid dehydrogenase and 17,20-lyase. When used alongside pharmacologic agents such as spironolactone or combined with other herbs such as *Paeonia* L., it may further enhance therapeutic outcomes, particularly in managing both hormonal and metabolic disturbances associated with PCOS (81,82,83).

Zingiber officinale Roscoe (Zingiberaceae)

Zingiber officinale rhizome extract and its major active constituent, 6-gingerol, exhibit significant therapeutic potential in managing PCOS through their antioxidant and anti-inflammatory properties. In a rat model of induced PCOS, administration of *Z. officinale* extract at doses of 100 mg/kg and 200 mg/kg and 6-gingerol at 200 µg/kg and 400 µg/kg for 28 days produced marked improvements in reproductive hormone balance compared with untreated PCOS controls. Treatment significantly reduced LH levels across all experimental groups and decreased FSH concentration, with the most pronounced effect observed at 400 µg/kg of 6-gingerol. Both *Z. officinale* extract and 6-gingerol significantly decreased serum estradiol and testosterone levels ($p < 0.001$), while increasing progesterone concentrations ($p < 0.05$). These hormonal modulations were accompanied by improved ovarian follicular development, suggesting restoration of ovulatory function. Collectively, the findings support the potential of *Z. officinale* and 6-gingerol as natural therapeutic agents for ameliorating PCOS through endocrine regulation and ovarian recovery (84).

Clinical evidence also supports the utility of *Z. officinale*. In a randomized controlled trial, a multi-herbal formulation containing *Z. officinale* (rhizome) significantly reduced LH, the LH/FSH ratio, total and free testosterone, and HOMA-IR, compared to clomiphene citrate alone. Improvements were also seen in lipid parameters, with reductions in total cholesterol, triglycerides, LDL, and VLDL, and an increase in HDL (85). Furthermore, another study using 6-gingerol, derived from *Z. officinale* rhizome, at 50 mg/kg and 100 mg/kg in rats showed normalization of estrous cyclicity, restoration of ovarian and uterine weights, decreased cystic follicles, and increased corpus luteum formation, along with improved levels of FSH, estrogen, and progesterone (86).

The pleiotropic effects of ginger in PCOS are mediated through several mechanisms. Gingerols, shogaols, and zingerone, its principal phenolic compounds, exert potent antioxidant effects by increasing GSH and SOD, while

reducing MDA levels, thus protecting ovarian tissues from oxidative damage (84,86). *Z. officinale* also downregulates pro-inflammatory markers such as COX-2 and likely TNF-α and IL-6, reducing ovarian inflammation (86). These actions help improve insulin sensitivity. Metabolically, ginger has antidiabetic properties, enhancing insulin secretion (partly through serotonin receptor stimulation on pancreatic β-cells), lowering blood glucose levels, and improving lipid metabolism (85,86). Additionally, it regulates the hypothalamic-pituitary-ovarian axis, leading to balanced gonadotropin secretion (lower LH/FSH ratio), normalized steroidogenesis, and restoration of ovulation (84,85,86).

Trifolium pratense L. (Fabaceae)

Trifolium pratense, commonly known as red clover, is a leguminous plant rich in isoflavones—phytoestrogens structurally similar to endogenous estrogens—which have demonstrated therapeutic potential in the management of PCOS due to their antioxidant, anti-inflammatory, and hormone-modulating effects. In a letrozole-induced PCOS rat model, administration of *T. pratense* extract (70% ethanolic macerate; plant part not specified in the article) at doses of 500 mg/kg and 750 mg/kg for 30 days significantly improved key reproductive parameters compared to untreated PCOS rats. The treatment led to decreases in ovarian weight, ovarian volume, and number of cysts, while increasing the number of healthy oocytes. Biochemically, *T. pratense* extract decreased serum testosterone and increased estradiol levels, indicating both anti-androgenic and estrogenic activity. Ovarian histopathology revealed restoration of normal follicular architecture and a reduction in cystic follicles, with improved granulosa and theca cell layers (87).

T. pratense also exerts potent antioxidant effects in PCOS models, as evidenced by increased levels of GSH, SOD, and CAT, and reduced levels of MDA and NO, which are markers of oxidative stress (87). *T. pratense* has been widely investigated in animals and in clinical trials, most notably for menopausal symptoms, but direct evidence in PCOS is limited. Beyond a single letrozole-induced rat study showing histological, hormonal, and antioxidative improvements with *T. pratense* extract, robust clinical trials in women with PCOS are still lacking. Well-designed randomized trials are therefore needed to define the efficacy, dosing, and safety of *T. pratense* specifically in PCOS.

The evidence summarized in this narrative review suggests that a variety of medicinal plants, including *C. sinensis, M. spicata, M. arvensis, C. sativus, C. verum, T. foenum-graecum, A. graveolens, L. meyenii, T. terrestris, C. longa, P. emblica, N. sativa, V. negundo, V. agnus-castus, G. glabra, Z. officinale*, and *T. pratense*, may offer potential benefits for women with PCOS. Findings from preclinical and clinical studies indicate that these plants may influence several key pathophysiological mechanisms involved in PCOS, including insulin resistance, hyperandrogenism, chronic inflammation, and oxidative stress, thereby contributing to improvements in metabolic, hormonal, and reproductive parameters.

From a clinical perspective, these findings highlight the potential role of medicinal plants as complementary therapeutic approaches in PCOS management, particularly for women seeking alternative or adjunct options alongside conventional pharmacological treatments. Many plant-derived compounds appear to target multiple biological pathways simultaneously, which may be particularly relevant given the complex and multifactorial nature of PCOS.

However, despite these promising findings, the currently available evidence remains limited and heterogeneous. Many studies involve small sample sizes, short intervention durations, and variability in plant preparations, dosages, and study designs. Furthermore, for several plants, the available data are primarily derived from preclinical or experimental models, while well-designed randomized controlled trials in humans remain relatively scarce.

Future research should therefore focus on conducting rigorously designed clinical trials, standardizing herbal preparations and dosages, and further elucidating the molecular mechanisms underlying the observed therapeutic effects. Such efforts are essential to better define the safety, efficacy, and clinical applicability of medicinal plants and to support their potential integration into evidence-based strategies for PCOS management.

Abbreviations

AKT1: AKT serine/threonine kinase 1
AMPK: AMP-activated protein kinase
CAT: Catalase
CC: Clomiphene citrate
COX-2 : Cyclooxygenase-2
CRP: C-reactive protein
EGCG: Epigallocatechin gallate
ER-α: Estrogen receptor alpha
FSH: Follicle-stimulating hormone
FSHR: Follicle-stimulating hormone receptor
GLUT8: Glucose transporter type 8
GPx: Glutathione peroxidase
GSH: Glutathione
GST: Glutathione S-transferase
HDL: High-density lipoprotein
HOMA-IR: Homeostatic Model Assessment of Insulin Resistance
HPG: Hypothalamic-pituitary-gonadal
IGF-1: Insulin-like growth factor 1 receptor
IL-1β: Interleukin-1 beta
IL-6: Interleukin-6
KISS1: Kisspeptin-1
LDL: Low-density lipoprotein
LH: Luteinizing hormone
LH/FSH: Luteinizing hormone to follicle-stimulating hormone ratio
LHR: Luteinizing hormone receptor
MAPK: Mitogen-activated protein kinase
MAPK1: Mitogen-activated protein kinase 1
MAPK3: Mitogen-activated protein kinase 3
MDA: Malondialdehyde
NO: Nitric oxide
NR3C4: Nuclear receptor subfamily 3 group C member 4 (androgen receptor gene)
p-Akt: phosphorylated Akt
PCOS: Polycystic ovary syndrome
PI3K: Phosphoinositide 3-kinase
PPAR-γ: Peroxisome proliferator-activated receptor gamma
RCT: Randomized controlled trial
ROS: Reactive oxygen species
SGOT: Serum glutamic-oxaloacetic transaminase (AST)
SGPT: Serum glutamic-pyruvic transaminase (ALT)
SOD: Superoxide dismutase
SREBP1: Sterol regulatory element-binding protein 1
STAT3: Signal transducer and activator of transcription 3
TNF-α: Tumor necrosis factor alpha
VLDL: Very-low-density lipoprotein

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Author Contributions

Conceptualization: G.Ž. and J.J.J.; Methodology: J.J.J., N.J., and S.R.; Formal analysis: S.R., N.J., J.J.J., and V.J.; Investigation: G.Ž., A.Ć., and R.Č.Ć.; Data curation: G.Ž., A.Ć., and R.Č.Ć.; Writing – Original Draft Preparation: G.Ž., A.Ć., and R.Č.Ć.; Writing – Review and Editing: V.J., S.R., N.J., and J.J.J.; Supervision: J.J.J. All authors have read and approved the published version of the manuscript.

Statement of Ethics

Not applicable. This study is an original review based exclusively on previously published literature and did not involve any direct interventions with human participants or animals.

Statement of Competing Interest

The authors declare no relevant conflicts of interest.

Statement of Data Availability

All data analyzed during this study were retrieved from previously published, publicly available, peer-reviewed articles and databases and are included in the cited literature.

Statement of Generative AI Technologies Use

No generative AI was used.

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