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Review Article

Polycystic Ovary Syndrome Herbal Treatments and Medicinal Plants: A Comprehensive Review

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Abstract

Polycystic ovary syndrome (PCOS) represents one of the most common endocrine disorders affecting women of reproductive age, serving as a major contributor to infertility on a global scale, with an estimated prevalence varying from 6 to 20% worldwide. PCOS is a complex syndrome defined by hyperandrogenism, irregular ovulation, and the presence of polycystic ovarian morphology. This syndrome is often associated with metabolic complications, including obesity, dyslipidemia, and an elevated risk of insulin resistance and developing type 2 diabetes. Symptoms include menstrual irregularities, weight gain, hirsutism, acne, and infertility. The presently available conventional treatment options for PCOS include hormonal contraceptives, insulin sensitizers, anti-androgens, and ovulation-inducing agents. While these treatments may offer symptomatic relief, they often entail potential side effects and do not adequately address the underlying cause of this syndrome. Herbal remedies have been used for centuries across cultures to manage various disorders due to their cost efficiency, availability, and safe nature. Several studies have demonstrated the efficiency of herbal remedies in the treatment of female reproductive disorders, including PCOS. This review comprises an extensive survey of the latest animal and clinical studies concerning plants and phytochemicals that have demonstrated effectiveness in alleviating symptoms associated with PCOS, as well as treating the underlying mechanisms involved in their efficacy.

Keywords: herbal medicine; infertility; oxidative stress; polycystic ovary syndrome; phytochemical

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1. Introduction

Polycystic ovary syndrome (PCOS) is recognized as one of the most prevalent endocrine disorders among women of reproductive age, with an estimated global prevalence ranging from 6 to 20%, contingent upon the specific diagnostic criteria utilized [1,2]. It is a multifaceted syndrome defined by the presence of hyperandrogenism, irregular ovulation, and distinct polycystic morphology of the ovaries. This disorder frequently coexists with metabolic irregularities, including obesity, dyslipidemia, insulin resistance, and an elevated susceptibility to type 2 diabetes mellitus [3,4]. The heterogeneity of PCOS makes its management challenging, requiring a personalized and multifactorial approach that addresses both reproductive and metabolic aspects [1].

The exact etiology of PCOS remains elusive, but genetic predisposition, environmental influences, and lifestyle factors play crucial roles in its pathogenesis. Hormonal imbalances, particularly elevated androgens, disrupted gonadotropin secretion, and insulin resistance, contribute to its clinical manifestations, including menstrual irregularities, hirsutism, acne, and infertility [5,6]. Conventional treatment options, such as hormonal contraceptives, insulin sensitizers, anti-androgens, and ovulation-inducing agents, provide symptomatic relief but may have side effects and fail to address the root cause of the disorder [7,8].

Given the chronic nature of PCOS and the limitations of pharmacological treatments, there is a growing interest in alternative and complementary therapies, particularly herbal medicine. Traditional herbal and complementary remedies have been used for centuries in various cultures to manage gynecological disorders and metabolic syndrome, and recent scientific investigations have provided evidence supporting their potential efficacy in PCOS management [9–14]. This review intends to investigate the role of medicinal herbs in the management of PCOS, focusing on their mechanisms of action, clinical efficacy, and safety profiles.

2. Methods

This study reviews the relevant literature on PCOS, plants, and medicinal herbs. We conducted a thorough search of international databases, including Google Scholar, PubMed, Web of Science, Frontiers, Scopus, and ISI repositories, to pinpoint animal studies and clinical trials centered on herbal treatments for PCOS. The present search utilized medical terminology along with various keyword combinations, including: “polycystic ovary syndrome” or “PCOS” combined with “natural plant” or “herb” or “ovarian cysts” or “phytochemicals used for PCOS” or “medicinal herbs. A list of plants and phytochemicals was compiled from the complete text articles. The studies were assessed for controls, method of induction, the dosage and duration of treatment, mechanisms of action, and outcome.

3. Literature Review of Natural Products

Herbal medicine has been an integral part of traditional healthcare systems for managing reproductive health issues, including menstrual irregularities and infertility. Many herbal and complementary remedies possess bioactive compounds that exhibit anti-androgenic, insulin-sensitizing, anti-obesity, anti-inflammatory, and hormonal regulatory effects, making them promising candidates for PCOS treatment [14–16].

The growing preference for natural therapies is driven by the perception that herbal and complementary treatments are safer, more holistic, and exhibit fewer adverse effects when compared to conventional pharmaceuticals [10,15]. Nonetheless, it is essential to critically assess their efficacy and safety through scientific investigations, encompassing clinical trials involving human participants and experimental studies conducted on animal subjects (Tables **1** and **2**). Numerous herbal agents have exhibited substantial potential in the management of PCOS:

Table 1: The effective medicinal herbs against polycystic ovary syndrome (PCOS) in animals.

Medicinal plants and/or phytochemicals	Study design	Dose and Duration	Outcomes	References
Licorice (*Glycyrrhiza glabra L.*)	40 mice with 0.2 mg/kg/bw of estradiol-induced PCOS, divided into 4 groups	*Glycyrrhiza glabra L.* aqueous extract at 100 mg/kg per day for 6 weeks	A drop in FSH, LH, PRL, testosterone, Estradiol, TNF-α, IL-1β, IL-4, IL-6, and IL-10 levels, slight increase in insulin and progesterone levels, decrease MDA and NO levels, increase of SOD, GPx, CAT, and GSH in the ovaries, decrease in urea, creatinine, cholesterol, TG and liver enzymes, considerable recovery in histopathological evaluation	Kandeel et al. [17]
Curcumin (*Curcuma longa*)	18 female Sprague-Dawley rats with induced PCOS using 60 mg/kg/bw of DHEA, divided into 3 groups	50 mg/kg/bw of curcumin for 21 days orally	Decrease in estradiol, LH, testosterone levels, and the LH/FSH ratio, reduced insulin resistance, recovery of ovarian morphology and the estrous cycle, decrease MDA, increase of SOD, GPx, upregulation of PPAR-γ	Zhang et al. [18]
Berberine	42 female Sprague Dawley rats with DHEA induced PCOS, divided into 6 groups	Berberine at 150 mg/kg each day for 6 weeks	Reduction in insulin resistance and testosterone levels, decrease in TLR4, LYN, PI3K, NF-κB, TNF-α, IL-1, IL-6, and caspase-3	Shen et al. [19]

Table 1: Continued.

Medicinal plants and/or phytochemicals	Study design	Dose and Duration	Outcomes	References
Peppermint (*Mentha piperita*)	40 Albino Wistar rats with 1 mg/kg letrozole-induced PCOS, divided into five groups	Peppermint at 40 g/l of peppermint once a day for 3 weeks	Body and ovarian weight decrease, drop in LH and testosterone level, increase in estrogen level, improvement of ovarian cysts and stromal mesenchymal cells necrosis, hyperplasia of luminal epithelial cells	Amoura et al. [20]
Vitex agnus-castus	50 adult female rats with 1 mg/kg letrozole-induced PCOS, divided into 5 groups	Vitex agnus-castus alcoholic extract at dose of 150 and 250 mg/kg/bw orally for 30 days	Decrease in the body weight, a drop in LH, FSH, testosterone and PLR levels, increase in estrogen, progesterone levels	A. Norii et al. [21]
Green tea (*Camellia sinensis*)	48 female Wistar rats with letrozole induced PCOS at 1 mg/kg by gavage, divided into 8 groups	50, 100, 200 mg/kg/bw green tea extract by gavage for 28 days	Increase in CAT, GPx and SOD levels and decrease in MDA levels (a statistically significant difference at the dosage of 200/kg body weight compared to PCOS-control group)	Khodarahmi et al. [22]
Coconut, (*Cocus nucifera* L.)	24 female virgin Wistar rats with 1 mg/kg letrozole-induced PCOS, divided into 4 groups	*Cocus nucifera* flower aqueous extract at 100 and 200 mg/kg orally for 4 weeks	Estrus cyclicity and increased uterus weight, decreased ovary weight, improved sugar level, recovery of histopathology evaluation	Soumya et al. [23]
Ampelopsis japonica	32 female Sprague-Dawley rats with 1 mg/kg letrozole-induced PCOS, divided into 4 groups	*Ampelopsis japonica* at 1 mg/kg per day gavage for 2 weeks	Improved estrous cycle, reduce body weight and ovarian mass, lower levels of LH and testosterone, increase in FSH and estradiol, decrease of cystic follicles and increase of the corpus luteum	Zhu et al. [24]
Aloe vera (*Aloe barbadensis* Mill.)	20 virgin female Swiss albino mice with 0.5 mg/kg/bw letrozole-induced PCOS, divided into 4 groups	1 ml of the aloe vera gel once a day for 30 days	Recovery in the glucose and cholesterol levels, increase in SOD, a drop in LH and testosterone and increase in FSH level, remarkable recovery of histopathological symptoms	Ghagane et al. [25]
Mentha spicata	48 mature Wistar albino female rats with 1 mg/kg orally letrozole induced PCOS, divided into 6 groups	*Mentha spicata* hydroalcoholic extract at dosage of 250 and 500 mg/kg for 20 days	Decrease in rat weight, decrease in testosterone and LH levels, increase in the numbers of corpus luteum	Alaee et al. [26]
Red grape (*Vitis vinifera*)	84 female Wistar rats with 2 mg estradiol valerate- induced PCOS, divided into 7 groups	Grape seed extract at the dosage of 50, 75, 100 and 200 mg/kg/bw by intraperitoneal injections for 10 days	Reduced visceral fat, drop in TG and LDL-C levels, a significant drop in IL-6 levels	Salmabadi et al. [27]

Table 1: Continued.

Medicinal plants and/or phytochemicals	Study design	Dose and Duration	Outcomes	References
Black cumin (*Nigella sativa*)	36 female Wistar rats with induced PSCO using DHEA at 60 mg/kg, divided into 6 groups	Hydroalcoholic extract of *Nigella sativa* seeds in doses of 50, 100, and 200 mg/kg for 30 days	Decreased LH, testosterone, and estrogen levels, increase in the levels of progesterone, decreased in the FBG and insulin resistance, increased in the SOD, GPx and CAT levels, decrease in MDA levels, decrease in cystic follicles and atretic follicles, increase in graafian follicles and corpus luteum numbers	Khani et al. [28]
Hypericum perforatum	42 Sprague-Dawley female rats with letrozole-induced PCOS at the dosage of 1 mg/kg, divided into 6 groups	*Hypericum perforatum* at the dosage of 50 mg/kg for 30 days	Reduce in numbers of cystic atretic follicles, increase in graafian follicles and corpus luteum, drop in the levels of testosterone, increase in sex hormone binding globulin and GSH levels, decrease in TNF-α and MDA levels	Okay et al. [29]
Cuscuta reflexa	36 female Wistar rats with induced PCOS using letrozole at 1 mg/kg, divided into six groups	Hydroalcoholic extract of *Cuscuta reflexa* at the dosage of 280 mg/kg/bw for 3 weeks	Reduced ovarian size, weight and body weight, significant improvement of lipid profile, improved estrous cycle, decrease in oxidative stress indicators, recovery of the histopathological symptoms	Kausar et al. [30]
Peucedanum grande	36 female Wistar rats with induced PCOS using letrozole at 1 mg/kg, divided into six groups	Hydroalcoholic extract of *Peucedanum grande* at the dosage of 140 mg/kg/bw for 3 weeks	Recovery of estrous cycle, decrease in body weight and ovarian size, significant decrease in LH, testosterone, significant decrease in TC, TG, LDL and significant elevation in HDL levels, reduce in oxidative stress markers, developing healthy follicles, corpus luteum and reducted cystic follicle size	Kausar et al. [30]
Centratherum anthelminticum	36 nulliparous female Wistar rats with induced PCOS using high fat diet and estradiol valerate of 4 mg/kg orally daily, divided into 6 groups	Ethanolic seed extract of *Centratherum Anthelminticum* at the dosage of 250, 500, 750 mg/kg daily orally for 28 days	Decrease in blood glucose and insulin levels, decrease in TG, cholesterol levels, significant increase in FSH and progesterone, significant decrease in LH levels, significantly drop in IL-6, MDA level, significant rise in CAT, SOD and GSH activity, improvement of histopathological changes in ovary	Shoaib et al. [31]

Table 1: Continued.

Medicinal plants and/or phytochemicals	Study design	Dose and Duration	Outcomes	References
Angelica sinensis	70 Sprague-Dawley female rats with induced PCOS using high fat diet and letrozole at the dosage of 1mg/kg, divided to 6 groups	Water extract of *Angelica sinensis* at the dosage of 2, 4 and 8g/kg intragastrically for 4 weeks	Recovery of the estrous cycle, improvement of ovarian cystic dilatation, significant rise in granulosa cell layers, significant decrease in LH, LH/FSH, testosterone, TG, TC, LDL-C, FBG, fasting serum insulin, and insulin resistance index, significant increase in estradiol, and HDL-C levels, regulation of PI3K/AKT, PPAR, MAPK, AMPK, and insulin signaling pathways, increase in *Bifidobacterium animalis*, *Lactobacillus murinus*, decrease in *Lactobacillus johnsonii*	Gao et al. [32]
Chickpea (*Cicer arietinum* L.)	35 Virgin, cyclic, adult female Wistar Albino rats with 1 mg/kg letrozole induced PCOS, divided into 5 groups	Ethanol extract of *Cicer arietinum* L. at the dosage of 250 and 500 mg/kg for 28 days	Reduction in the ovarian weight, significant decrease in ovarian cysts numbers, recovery of granulosa cell thickness, presence of corpora luteum, significant drop in LH and testosterone level, down expression for cytochrome11α, significant decrease in TG, LDL, cholesterol and glucose levels, significant drop in MDA level and significant increase in GSH activity	Ali et al. [33]
Nervilia Fordii	64 Sprague-Dawley female rats with induced PCOS using DHEA at 6 mg/100 g/d, 0.2 ml/mouse in sesame oil, divided into 8 groups	Total flavonoids extracted from *Nervilia Fordii* at 50, 100, 200 mg/kg for 28 days	Estrous cycle and insulin resistance recovery at 200 mg/kg, significant decrease in phosphorylation of JAK2 and STAT3 at the dose of 200 mg/kg, significant decrease in expression of IL-6 at 200 mg/kg, significant increase in expression of SOCS3 at 200 mg/kg, rise in the levels of FSH, drop in the level of LH, testosterone and insulin	Zhou et al. [34]
Althaea officinalis L.	70 rats with estradiol induced PCOS, divided into 7 groups	*Althaea officinalis* L. at the dosage of 250 mg/kg for 3 weeks	Drop in LH/FSH rate, increase of FSH and progesterone levels, recovery of estrus cycle duration, apoptotic effect on cystic granulosa cells by PI3K/AKT pathway activation and increase in Ki-67 positive cells	Gao et al. [35]

Table 1: Continued.

Medicinal plants and/or phytochemicals	Study design	Dose and Duration	Outcomes	References
Ficus religiosa	42 female albino Wistar rats with 1 mg/kg/bw letrozole induced-PCOS, divided into 7 group	100 and 300 mg/kg/bw of aqueous dry leaf extract, 10% fresh leaf extract of *Ficus religiosa* of 1.0 ml/kg/bw orally and sprayed for 30 days	Regulation of estrous cycle, increase in uterine weight and decrease in ovaries weight, drop in LH and testosterone levels, rise in progesterone and estrogen levels, decrease in TC level, reduction in 3β-HSD and 17β-HSD, increase in expression of ovarian Cyp19a1 (aromatase), significant upregulation of *PPAR-*γ in ovaries, decrease in MDA level, increase in SOD, CAT, GPX and GSH levels	Suriyakalaa et al. [36]
Guilandina bonduc L.	42 female Wistar Albino rats with rats with 1 mg/kg/bw letrozole induced-PCOS, divided into 7 groups	Aqueous seed extract of *Guilandina bonduc* L. at the dose of 100, 200 and 300 mg/kg/bw for 28 days	Recovery of the estrous cycle, significant increase in SOD and GSH levels, significant decrease in MDA activity, drop in the level of AST, ALT, ALP, urea, uric acid, and creatinine	Ayyadurai et al. [37]
Terminalia chebula Retz.	30 female Wistar rats with 1 mg/kg/ bw letrozole induced-PCOS, divided into 6 groups	Ethanolic fruit extract of *Terminalia chebula* Retz. at 100, 200, 400 mg/kg/day orally for 28 days	Recovery of estrus cyclicity, decrease in body weight, increase in uterine weight, increase in SOD, GSH, GPx and CAT levels, decrease in LPx levels, decrease in FSH, testosterone, LH, and insulin levels, rise in the progesterone and estrogen levels, development of corpus luteum and healthy follicles, decrease in expression of CYP17a1, increase in CYP19a1 and PPAR-γ expression levels	Kalimuthu et al. [38]
Cinnamon	60 female prepuberal C57BL/6 mice with induced PCOS using DHEA at 6 mg/100g/bw dissolved in 0.1 ml of sesame oil, divided into 3 groups	Cinnamon powder at the dosage of 10 mg/100g/bw mixed in 100 μL 0.5% methylcellulose via gavage for 20 days	Regulation of the disrupted estrous cycle, significant increase in numbers of corpus luteum and oocyte, decrease in testosterone and insulin levels, decrease in IGF-1 level and increase in IGFBP-1 level	Dou et al. [39]

AST: Aspartate transaminase; ALT: Alanine transaminase; ALP: Alkaline phosphatase; AMPK: AMP-activated protein kinase; Bw: Body weight; Cyp19a1: Cytochrome P450 19A1, CYP19a1: Cytochrome P450 17A1; CAT: Catalase; DHEA: Dehydroepiandrosterone; FSH: Follicle-stimulating hormone; FBG: fasting blood glucose; GPx: Glutathione peroxidase; GSH: Glutathione; HDL-C: High-density lipoprotein cholesterol; IGF-1: Insulin-like growth factor I; IGFBP-1: Insulin-like growth factor binding protein-1; IL: Interleukin; JAK2 and STAT3: Janus kinase 2/signal transducer and activator of transcription 3; LDL-C: Low-density lipoprotein cholesterol; LPx: Lipid peroxidase; LYN: Src family tyrosine kinase; LH: Luteinizing hormone; MAPK: Mitogen-activated protein kinase; MDA: Malondialdehyde; NF-κB: Nuclear factor-kappa B; NO: Nitric oxide; PI3K: Phosphatidylinositol 3-kinase; PI3K/AKT: phosphatidylinositol3-kinase/phosphorylated protein kinase B; PCOS: polycystic ovary syndrome; PPAR-γ: Peroxisome proliferator-activated receptor gamma; PPAR: Peroxisome proliferator-activated receptor; PRL: prolactin; SOD: Superoxide dismutase; SOCS3: Suppressors of cytokine signaling 3; TNF-α: Tumor necrosis factor-α**;** TG: Triglycerides**;** TLR4: Toll-like receptor 4; TC: Total cholesterol; 3β-HSD: 3β-Hydroxysteroid dehydrogenase; 17β-HSD: 17β-Hydroxysteroid dehydrogenase

Table 2: The effective medicinal herbs against polycystic ovary syndrome (PCOS) in humans.

Medicinal plant and/or Phytochemical	Study design	Dose and Duration	Outcomes	References
Spearmint (*Mentha spicata*)	Randomized Control Trial 42 patients in two groups of spearmint tea and placebo (camomile tea)	Spearmint tea twice daily, evaluated in day 0, 15 and 30 of trial Does: two cups with standardized teabags	Free and total testosterone levels were significantly reduced. No significant reduction in the objective Ferriman-Galwey ratings of hirsutism. LH and FSH also increased	Grant et al. [40,41]
Licorice (*Glycyrrhiza glabra violacea*)	Double Blind RCT, Low-calorie diet with placebo or licorice extract 66 overweight/obese women with PCOS	three capsules of licorice extract (each containing 500 mg of licorice) extract per day 8-week RCT	Weight, BMI and body fat improved Improved FBS and insulin levels Improved lipid profile	Hooshmandi et al. [42]
Quercetin	RCT 84 PCOS	Quercetin at the dosage of 1g (two 500 mg capsules) per day 12 weeks	the expression of ADIPOR1 and ADIPOR2	Rezvan et al .[43]
Cinnamon	RCT Double-blind 66 patients with confirmed PCOS	cinnamon capsules 1.5 g/day in 3 doses 12 weeks	Homeostatic model assessment for insulin resistance , Fasting insulin and LDL were reduced in intervention group	Hajimonfarednejad [44]
Curcumin	RCT Double Blind 72 patients with PCOS , 67 completed the trial	500 mg three times daily 12 weeks	Decrease in fasting plasma glucose and dehydroepiandrosterone levels Sex hormone levels, and hirsutism remained unchanged	Heshmati et al.[45]
Trigonella foenum (Fenugreek)	RCT Triple blind study 110 patients divided into two goups: Metformin vs Fenugreek	fenugreek capsules of 333 mg three times a day 8 weeks	Improved glycemic status, lipid profile Reduced temporal baldness	Mirgaloybayat et al. [46]
Vitex agnus-castus extract (Chasteberry)	Double-blind RCT 120 women with PCOS	3.2-4.8 mg of chasteberry dry extract per day 3 months	The intervention resulted in no differences between the two groups (Chasteberry and Metformin) in terms of menstruation length, menstrual cycle intervals, or the number of pads used	Shayan et al.[47]
Berberine	60 women with PCOS divided into two groups After follow up 26 in treatment group 29 in control group	300 mg Berberine three times a day Control: 500 mg metformin twice daily 3 Months	Berberine can improve HOMA-IR, reduce serum sexual hormone levels, and regulate blood metabolism in women with PCOS-IR, exhibiting effects comparable to those of metformin.	Li et al. [48]

Table 2: Continued.

Medicinal plant and/or Phytochemical	Study design	Dose and Duration	Outcomes	References
Green tea (*Camellia sinensis*)	Double Blind RCT 45 women with Confirmed PCOS between ages 18-45	4 tablets of 500 mg green tea extract per day (2,000 mg/day) Control group: Metformin 500 mg three times a day 3 months	No effects on inflammation markers. However Green tea consumption showed possible effects on weight control in these women. (Weight, BMI, and waist and hip circumference showed significant results)	Farhadian et al.[49]
Grape seed extract from red grape (*Vitis vinifera*)	Double-blind, randomized, controlled clinical trial with 50 PCOS patients, aged 20 to 38 years	400 mg per day 8 weeks	Serum HOMA-IR, BMI and FBS decreased significantly	Sedighi et al.[50]
Black cumin (*Nigella sativa*)	Double-Blind RCT, started with 84 patients with PCOS, after follow up, 32 in intervention, 23 in placebo	Two 500 mg capsules of *Nigella sativa* per day 16 weeks	No significant differences were observed between the two groups regarding the duration of menstruation, anthropometric measurements, or laboratory indexes. However, notable decrease in menstrual interval and a considerable increase in menstrual cycle frequency was seen.	Naeimi et al. [51]
Resveratrol	Double Blind RCT- 78 women with PCOS randomly divided to two equal groups of resveratrol and control.	2 groups receiving 1,000 mg resveratrol or 1,000 mg placebo each day 3 months	Women who got resveratrol demonstrated a higher rate of regular menstruation in comparison to the placebo group, along with reduced hair loss. However, there were no notable differences between the groups in glycoinsulinemic metabolism, lipid profile, ovarian and adrenal androgens, sex hormone-binding globulin, free androgen index.	Mansour et al.[52]
Trigonella foenum (Fenugreek)	Open-label, non-randomized, clinical study, 50 overweight girls with PCOS	1 g/day (2 capsules of 500 mg each/day) 3 months	Increased LH and FSH, reduced ovarian volume and cyst size, with complete cyst resolution in some patients.	Swaroop et al.[53]
Zingiber officinale Roscoe (Ginger)	Randomized, double-blinded, placebo-controlled trial 83 women with PCOS	1,500 mg/day ginger extract (three 500 mg capsules) Three other groups:Cinnamon, placebo, and metformin, each at 500 mg, were administered three times daily. 8 weeks	Ginger supplementation in women with PCOS showed a significant reduction in FSH and LH levels No significant impact on insulin resistance or lipid profiles, suggesting its primary benefits are in hormonal regulation.	Dastgheib et al. [54]

ADIPOR1 and 2: Adiponectin receptor 1and 2; BMI: Body mass index; FSH: Follicle-stimulating hormone; FBS: Fasting blood sugar; HOMA-IR: Homeostatic model assessment for insulin resistance; LDL: Low-density lipoprotein; LH: Luteinizing hormone; PCOS: Polycystic ovary syndrome; RCT: randomized controlled trials

3.1. Cinnamomum verum (Cinnamon)

Cinnamon, which is obtained from the inner bark of trees belonging to the *Cinnamomum* genus, part of the *Lauraceae* family, has served as a cornerstone of traditional medicine across various cultures [55]. Over the years, around 306 chemical compounds have been recognized and extracted from the *Cinnamomum* genus [56]. There have been previous studies investigating its alleviating effects on type 2 diabetes [55], blood pressure [57], lipid, and metabolic profile [58] , as well as cognitive function [59]. Cinnamon has also shown potential in managing symptoms of PCOS, particularly due to its effects on insulin resistance and its antioxidant/anti-inflammatory properties[60]. Studies suggest that the anti-inflammatory effects can be due to inhibition of the expression of inducible nitric oxide synthase (iNOS), cyclooxygenase-2 (COX-2), interleukin-1-beta (IL-1β), IL-6, and tumor necrosis factor-alpha (TNF-α) [61]. Given these effects that can potentially improve hormonal health, cinnamon has been extensively studied as a possible PCOS remedy. Research suggests that it improves menstrual cyclicity, enhances ovulatory function, and reduces insulin resistance in women with PCOS. Furthermore, there is evidence supporting the restoration of estrous cyclicity and ovarian morphology, along with the regulation of testosterone and insulin levels, decreasing insulin-like growth factor I levels while concurrently increasing levels of insulin-like growth factor binding protein-1 in animal models [39,54,62].

3.2. Vitex agnus-castus (Chasteberry)

Vitex agnus-castus, commonly known as chasteberry or monk's pepper, possesses a longstanding historical significance in the management of menstrual disorders and premenstrual syndrome [63]. In vitro studies of *Vitex agnus-castus* exhibit binding activity with several receptors, notably dopamine D2 receptors, and opioid receptors, specifically targeting the mu (μ), kappa (κ), and delta (δ) subtypes [64]. This receptor activity suggests the potential of this substance through both dopaminergic and opioid pathways. Additionally, *Vitex agnus-castus* has been shown to modulate prolactin secretion and improve luteal phase defects, thereby restoring hormonal balance in PCOS patients [65]. Consequently, It has been proposed as a possible therapeutic option for PCOS and has been studied for this purpose, showing great promise through weight loss and a decrease in luteinizing hormone (LH), follicle-stimulating hormone (FSH), and testosterone levels [21,66]. Notably, Vitex agnus-castus has demonstrated effects on rat models of PCOS by inhibiting the downregulation of kisspeptin (KISS-1 gene) in the hypothalamus [67]. Further studies are warranted to establish this herbal remedy as a viable treatment for PCO.

3.3. Glycyrrhiza glabra (Licorice)

Licorice is another widely utilized plant in herbal medicine since ancient times, dating back to at least 500 BC [68,69]. Different parts of this plant have been used to treat a myriad of diseases and disorders with

varying success. It has been shown to be effective in bacterial infections such as Staphylococcus aureus (specifically methicillin-resistant Staphylococcus aureus) [70] and has anti-viral activities [71,72]. Research suggests that it possesses anti-inflammatory properties [73], anti-tumor activities [74], and noteworthy cardiovascular benefits [75]. This wide-ranging application reflects licorice's rich phytochemical profile, which includes flavonoids, isoflavones, stilbenoids, and several other compounds [76]. Flavonoids are the predominant components of licorice, with nearly 300 types identified so far [77]. Glycyrrhizin, a key compound of the saponin family in licorice, has been shown to exhibit anti-androgenic properties, potentially reducing elevated testosterone levels commonly associated with PCOS [78,79]. Additionally, flavonoids like isoliquiritigenin may help regulate hormonal imbalances and reduce inflammation, which are critical factors in PCOS management [80]. Multiple studies have demonstrated its effectiveness in managing PCOS in both animals and humans [17,81].

3.4. Mentha spicata (Spearmint)

The pharmacological benefits of *Mentha spicata* have been explored for its various medicinal properties, such as antioxidant, antimicrobial, and anti-inflammatory effects [82]. Spearmint contains phytochemicals such as carvone, limonene, pulegone, menthol, and cineole [83]. Carvone, the major phytochemical component of spearmint, has been shown to inhibit the activity of enzymes involved in androgen synthesis, leading to a decline in testosterone levels [84,85]. This androgen synthesis inhibition might be able to assist in managing PCOS symptoms such as hirsutism [86], acne, and irregular menstrual cycles [87]. Another study showed that spearmint tea consumption may reduce free testosterone levels in women with androgen imbalance. This decrease could be linked to spearmint's potential as a cytochrome P450 3A4 enzyme inducer or its direct effect on androgen synthesis [88]. Additionally, spearmint's antioxidant properties may help reduce oxidative stress, which is often elevated in women with PCOS [89]. Some studies have also shown spearmint's potential for PCOS treatment through its effect on follicular restoration and reduction of ovarian cyst formation [90,91]. Numerous studies have validated its efficacy in managing PCOS in both animal and human subjects [26,92,93].

3.5. Curcuma longa (Curcumin)

Curcumin is a significant polyphenol extracted from the rhizome of *Curcuma longa*, commonly referred to as turmeric. It has been demonstrated to exhibit anti-inflammatory, antioxidant, anti-diabetic, and anti-obesity effects [94–96]. Furthermore, it has been demonstrated to be effective in addressing female reproductive disorders, including ovarian diseases, PCOS, and endometriosis [97,98]. The anti-inflammatory properties of curcumin have been substantiated through its influence on diminishing levels of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GSx), and lipid peroxides, as well as tumor TNF-α, IL-1, IL-2, IL-6 [99,100]. Curcumin has exhibited efficacy in reducing insulin resistance, lowering

fasting blood glucose levels, and enhancing the quantitative insulin sensitivity check index [101,102]. Numerous studies have illustrated the efficacy of curcumin in the management of PCOS [45,94,97,103].

3.6. Aloe barbadensis Mill (Aloe vera)

Aloe barbadensis Mill, a medicinal plant classified within the Liliaceae (Asphodelaceae) family, commonly referred to as Kumari, has demonstrated considerable evidence substantiating its efficacy in the management of the female reproductive system and related disorders, including PCOS [104,105]. It has been demonstrated that it possesses properties that are anti-diabetogenic, anti-oxidant, anti-inflammatory, anti-microbial, anti-viral, immunomodulatory, and protective of the skin [106]. Various phytochemicals were identified in aloe vera, including flavonoids, glycosides, sapogenins, tannins, anthraquinones, phytosterols, pyrones, enzymes, and numerous vitamins and minerals [104,105]. The phytosterols present in aloe vera have been demonstrated to exhibit efficacy in the treatment of PCOS by restoring ovarian steroid levels and modulating steroidogenic activity. A significant enzyme involved in the pathogenesis of PCO is 3β-Hydroxysteroid Dehydrogenase (3β-HSD), and aloe vera was proven to effectively reduce the activity of this enzyme, thereby contributing to the regulation of estradiol formation [9]. Numerous studies have substantiated the efficacy of aloe vera in the management of PCOS [25,104,105].

3.7. Camellia sinensis (Green tea)

Camellia sinensis, also known as green tea, is recognized as one of the most widely consumed beverages worldwide and has demonstrated significant efficacy in addressing various female reproductive disorders, including PCOS, endometriosis, and dysmenorrhea [107]. Many studies have proven its antioxidant, anti-diabetic, anti-cancer, anti-obesity, and anti-hyperlipidemia effects [108–111]. Catechins, identified as key phenolic compounds in green tea, exhibit remarkable antioxidant properties that exceed those of glutathione, vitamin C, and a range of flavonoids [112]. Furthermore, catechins play a crucial role in enhancing detoxification processes supported by enzymes like glutathione reductase, GPx, and CAT [107]. Numerous human studies have demonstrated that green tea is effective in promoting weight loss, decreasing testosterone levels, and enhancing glycemic status. Conversely, its effects on reducing LH levels and the rise in FSH and progesterone levels have predominantly been established through animal models [113]. Moreover, the impact of green tea on inflammatory markers, including TNF-α, IL-6, CAT, GPx, SOD, and malondialdehyde (MDA) levels, has been confined to animal studies [22,113,114].

4. Conclusions and Future Prospective

PCOS represents a prevalent endocrine disorder that impacts females during their reproductive years of age. Recent trends indicate a rising prevalence attributed to a combination of genetic, environmental, and

intrinsic individual factors. The condition is linked to multiple complications, including infertility, metabolic disorders, as well as cardiovascular problems, which can last a lifetime and diminish an individual's quality of life [1,115]. Currently, available pharmaceutical interventions focus on regulating the menstrual cycle, managing obesity and hyperlipidemia, and reducing insulin resistance. Nevertheless, conventional treatments mainly provide symptomatic relief, often with side effects, and do not effectively address the underlying cause [7,8,116]. Herbal and complementary medicine have gained significant popularity in recent times for managing various diseases, including PCOS, primarily due to their safe nature and efficacy [11,14,15,117]. In this review, we comprehensibly evaluated several medicinal herbs and their isolated phytochemicals, including curcumin, berberine, resveratrol, licorice, quercetin, catechins, *Vitex agnus-castus*, cinnamon, and spearmint, which have demonstrated efficacy in the treatment of PCOS by restoring ovarian histology, normalizing blood glucose levels, serum hormone concentrations, and lipid profiles, as well as regulating inflammatory markers and the modulation of gene expression linked to the pathology of PCOS (Tables 1 and 2). Hence, these medicinal herbs and their isolated phytochemicals have the potential to be used as alternatives to conventional treatments or in combination with them for treating PCOS. They can also serve as inspiration for developing novel, promising, effective medications for the management of this syndrome. However, extensive clinical studies are required to further evaluate the dosage and duration of these phytochemicals and herbal drugs for treating PCOS, both individually and in combination with existing medications, as well as to assess their toxicity and potential side effects.

Abbreviations

ADIPOR1 and 2: Adiponectin receptor 1and 2; AST: Aspartate transaminase; ALT: Alanine transaminase; ALP: Alkaline phosphatase; AMPK: AMP-activated protein kinase; Bw: Body weight; BMI: Body mass index; COX-2: cyclooxygenase-2; Cyp19a1: Cytochrome P450 19A1, CYP19a1: Cytochrome P450 17A1; CAT: Catalase; DHEA: Dehydroepiandrosterone; FSH: Follicle-stimulating hormone; FBG: Fasting blood glucose; FBS: Fasting blood sugar; GPx: Glutathione peroxidase; GSH: Glutathione; HDL-C: High-density lipoprotein cholesterol; HOMA-IR: Homeostatic model assessment for insulin resistance; iNOS: inducible nitric oxide synthase; IGF-1**:** Insulin-like growth factor I**;** IGFBP-1**:** Insulin-like growth factor binding protein-1**;** IL: Interleukin; JAK2 and STAT3: Janus kinase 2/signal transducer and activator of transcription 3; LDL-C: Low-density lipoprotein cholesterol; LPx: Lipid peroxidase; LYN: Src family tyrosine kinase; LH: Luteinizing hormone; MAPK: Mitogen-activated protein kinase; MDA: Malondialdehyde; NF-κB: Nuclear factor-kappa B; NO: Nitric oxide; PI3K: Phosphatidylinositol 3-kinase; PI3K/AKT: phosphatidylinositol3-kinase/phosphorylated protein kinase B; PCOS: Polycystic ovary syndrome; PPAR-γ: Peroxisome proliferator-activated receptor gamma; PPAR: Peroxisome proliferator-activated receptor; PRL: prolactin; RCT: randomized controlled trials; SOD: Superoxide dismutase; SOCS3: Suppressors of cytokine signaling

3; TNF-α: Tumor necrosis factor-α; TG: Triglycerides; TLR4: Toll-like receptor 4; TC: Total cholesterol; 3β-HSD: 3β-Hydroxysteroid dehydrogenase; 17β-HSD: 17β-Hydroxysteroid dehydrogenase

Declarations

Consent for publication

Not applicable.

Availability of data and materials

All data regarding this study have been reported in the manuscript. Please contact the corresponding author if you are interested in any further information.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

N.T. designed the study. K.G. and J.K. drafted the first draft of the manuscript and created the tables. N.T., K.G., and S.Z. contributed to reviewing and editing the manuscript. All authors approved the final version of the manuscript.

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