International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 24s, 2025
https://theaspd.com/index.php

# Impact Of Herbal Drugs On Ovarian Function In PCOS: A Biochemical Perspective

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***Abstract***
*Polycystic ovarian syndrome (PCOS) is a female neuroendocrine and metabolic disorder that affects 1 in 10 women worldwide. This occurrence is primarily due to hormonal imbalances, including the luteinizing hormone and follicle-stimulating hormone ratio, gonadotropin-releasing hormone, insulin resistance, and elevated testosterone and androgen levels in PCOS. This leads to anovulation, diabetes, hyperandrogenism, depression, hirsutism, acne, and infertility. Regulating those conditions leads to managing and curing PCOS. There are many ways to treat PCOS, such as allopathic, ayurvedic, homoeopathic, etc. Among those, many allopathic and homoeopathic drugs have effects in practice to treat PCOS, but they are mainly used to manage PCOS and fail to focus on regulating PCOS. Patients have benefited from natural remedies containing adequate phytoconstituents and various receptors that help alleviate the symptoms of PCOS. These herbal drugs effectively manage and regulate PCOS, rather than the limitations of allopathic medicines.*
***Keywords:*** *PCOS, herbal drugs, LH: FSH ratio, Estradiol cycle, GhRH, Diabetes.*

## INTRODUCTION

Polycystic Ovary Syndrome (PCOS) is one of the most common endocrine disorders, affecting 5–20% of women of reproductive age worldwide. It is characterised by a spectrum of symptoms, including hyperandrogenism, irregular ovulation, polycystic ovarian morphology, insulin resistance, and metabolic abnormalities, such as obesity and dyslipidaemia. These symptoms not only compromise reproductive health but also increase the risk of long-term complications, including type 2 diabetes, cardiovascular diseases, and infertility. [1].

Despite the availability of conventional treatments, including hormonal therapies and insulin-sensitising agents, many women experience side effects, incomplete symptom relief, or find these interventions unsuitable for long-term use. This has led to an increasing interest in complementary and alternative medicine (CAM), particularly herbal remedies, as a more natural and holistic approach to managing PCOS [2].

Herbal medicines have been used for centuries in traditional systems of medicine, such as Ayurveda, Traditional Chinese Medicine, and Unani, to treat reproductive and metabolic disorders. Their bioactive compounds exhibit diverse pharmacological properties, including hormonal modulation, anti-inflammatory, antioxidant, and insulin-sensitising effects, particularly relevant to PCOS management [3]. In ancient times, Traditional practitioners used various plant resources to treat numerous diseases. Some plants have and haven't been supported by scientific evidence. Commonly studied herbs, such as flax seeds, Aloe vera, *Labisia Pumila, Nilambo nucifera, Cocus nucifera, Stachys lavandulifolia, Heracleum persium, Saraca Asoca, Curcuma longa*, cinnamon, spearmint, Vitex (Chaste Tree Berry), fenugreek, and Liquorice root, have demonstrated potential benefits in clinical and preclinical studies, including regulating menstrual cycles, improving ovulation, reducing androgen levels, and alleviating insulin resistance [4]. PCOS is a neuroendocrine and metabolic disorder that affects women worldwide. These diseases mainly occur due to imbalanced hormones, irregular oestrogen cycles, and frequent infertility [5]. There are many synthetic drugs in practice that only manage PCOS effectively, and the lack of specific mechanisms to cure PCOS permanently, as well as these synthetic drugs, leads to many side effects. Nowadays, patients are stepping towards herbal medication, which is a long-term treatment, but its efficacy will be long-lasting with minimal side effects. However, these growing conditions in herbal medicine have sparked investigations into their effectiveness and safety in managing PCOS [6].

This review is focused on the potential of the individual herb to fight against PCOS, with the available literature on herbal interventions for PCOS, clinicians, and patients with a comprehensive understanding of their potential role in PCOS management by critically analysing various herbal remedies' efficacy, safety, and mechanisms of action [7][8]. Additionally, it will identify gaps in the existing literature and suggest avenues for future research to clarify the therapeutic potential of herbal medicine in the management of PCOS.

This review concentrates on some of the important medicinal plants, such as aloe vera, cinnamon, curcumin, flax seeds, *Labisia pumilla, N. nucifera, Cocus nucifera, Stachy lavandulifolia*, *Heracleum persium, Saraca asoca, Curcuma longa,* spearmint, vitex, Fenugreek, Liquorice, their origin, family, chemical composition, therapeutic application, and mode of action in regulating PCOS.

**Herbal medicine in PCOS**

Herbal remedies have long been used to support hormonal balance, improve insulin resistance, and manage symptoms associated with conditions like PCOS. These effects are achieved through a combination of mechanisms that address the underlying dysfunctions and related symptoms [7]. Herbs can influence hormonal pathways by modulating the hypothalamic-pituitary-gonadal (HPG) axis or directly interacting with hormone receptors. For example, phytoestrogens found in plants like red clover and liquorice root can mimic or modulate estrogen activity by binding to estrogen receptors, helping to regulate hormonal imbalances [8]. Adaptogenic herbs such as ashwagandha and rhodiola support the stress response by balancing cortisol levels, which indirectly stabilises sex hormones. Such effects are particularly valuable in conditions where hormonal dysregulation plays a central role [9]. Some of the other factors include that the use of herbal medications to treat PCOS shows promise because of their steady efficacy and few adverse effects. Herbal medications strengthen the body's defences against disease and aid in regulating the menstrual cycle without altering hormone levels. PCOS can be managed with medication, a good diet, frequent exercise, and lifestyle modifications. Yoga has also been demonstrated to help ladies with PCOS [10].

In addition to hormonal effects, certain herbs help improve insulin sensitivity, a key aspect of metabolic conditions, such as PCOS and type 2 diabetes. Cinnamon (Cinnamomum cassia), for instance, enhances insulin receptor signalling, promoting glucose uptake into cells. At the same time, berberine, a bioactive compound found in herbs such as barberry, activates AMP-activated protein kinase (AMPK), improving glucose metabolism and reducing insulin resistance [11]. Fenugreek, another well-researched herb, contains compounds that delay carbohydrate digestion and improve glucose tolerance, making it a valuable addition to managing metabolic dysfunctions [12].

Herbs also exhibit potent anti-inflammatory and antioxidant effects, addressing systemic inflammation and oxidative stress commonly elevated in metabolic disorders. For example, turmeric (Curcuma longa) contains curcumin, which has been shown to reduce markers of systemic inflammation such as C-reactive protein (CRP) [13]. Similarly, green tea (Camellia sinensis) is rich in catechins, antioxidants that support metabolic and cardiovascular health by reducing oxidative stress and inflammation [14].

Beyond these systemic benefits, certain herbs specifically target PCOS symptoms such as irregular menstrual cycles, hirsutism, and acne. Spearmint has demonstrated anti-androgenic properties, potentially reducing excess hair growth and acne [15]. Vitex (Chasteberry) supports progesterone production by modulating prolactin levels, which helps regulate ovulation and menstrual cycles, thereby improving fertility in women with PCOS [15]. The usage of herbs in managing hormonal imbalances, improving insulin resistance, and addressing specific symptoms offers a holistic approach to conditions like PCOS. However, their efficacy and safety depend on proper identification, dosage, and usage. While promising, these therapies should be employed under the guidance of a healthcare professional to ensure personalised and safe treatment. Supporting evidence for these claims can be found in review articles, such as those on hormonal management [16], Dietary supplements for insulin resistance [17], and Anti-inflammatory agents [18]. These sources emphasise the importance of integrating traditional herbal knowledge with modern clinical research for optimal health outcomes.

## KEY HERBS AND THEIR BENEFITS

**Flax seeds**

Flax seeds are also termed linseed, *Linum usitatissimum*, in the family *Linaceae* [20]. Flax eeds are rich sources of macronutrients and micronutrients, such as carbohydrates, proteins, fats, vitamins, and minerals. Among the minerals, such as zinc, magnesium, potassium, sodium, manganese, copper, and iron, have been found. It also contains enough phenolic compounds, such as phenolic acids, flavonoids, and lignans [19]. Flax seeds are rich in lignans, which help to reduce the androgen level in men with prostate cancer and are also a good source for women with PCOS. Omega-3 fatty acids in flaxseed could increase adiponectin levels, which have anti-atherosclerotic, anti-diabetic [20], anti-hypertension, anti-cancer [21] and anti-inflammatory properties by improving insulin sensitivity. The consumption of flaxseeds can substantially elevate the glycaemic index [22]. It is also a good source for regulating the hormonal imbalance [23]. By raising FSH levels and lowering the LH/FSH ratio, flaxseed supplements may help women with PCOS, indicating that they could be used as a supplemental treatment for PCOS's hormonal imbalances [24].

Among the literature surveyed, the efficacy of flaxseed against PCOS has been proven. The authors stated that there is no significant difference in levels of DHEA and progesterone, which increased, along with the absence of structural abnormalities at different stages of follicle development and regression of the corpus luteum. Additionally, the PCOS group had no cystic follicles, and the numbers of preantral follicles, antral follicles, and corpus luteum decreased [25]. Their study also demonstrated that flaxseed reduced signs of PCOS in rats;

however, the estradiol valerate model of PCOS did not replicate all the phenomena of human PCOS. The sex-steroid hormonal profile and histomorphometry characteristics of the ovaries in treated rats were improved by flaxseed.

In contrast, when the flax seeds were combined with spearmint, the estrous cycle showed that the induced PCOS using estradiol valerate, the reproductive animals were arrested in their estrous stage, where the treatment of flax seeds and spearmint helps to begin with a prolonged interval. There was no impact of estradiol levels between treatment, PCOS, and control groups due to the presence of lignan in flaxseed that may lead to a rise in SHBG production, which in turn decreases the level of free estradiol. The testosterone was massively reduced in the PCOS rats treated with a combination of spearmint and flaxseed extracts due to the anti-androgenic effect of spearmint and phytoestrogen action of flaxseed, which is four times lower than when flaxseed was administered alone. The primary, preantral, and antral follicles decreased, whereas the cystic follicles increased significantly in the PCOS treatment group; the extract improved the follicle [26]**.**

**Aloe vera**

Aloe Vera, also termed *Aloe barbadensis milleri,* belongs to the family of Asphodelaceae (Liliaceae). It provides vitamins A, C, E, $B_{12}$, folic acid, and choline. It also contains some enzymes, minerals such as copper, calcium, manganese, zinc, chromium, magnesium, sodium, selenium, potassium, and phenolic compounds, hormones, fatty acids, and some amino acids [26]. It also contains Anthraquinone derivatives, flavonoids, phytosterols, polyphenols, and other secondary metabolites. Barbaloin and aloe emodin [6]. Aloe Vera is a good source for HIV infection, diabetes [30], mucositis (Puataweepong *et al*, 2009), radiation dermatitis, and lichen plague [28]. In addition to controlling PCOS and being antidiabetogenic, aloe vera has been found to possess "antimicrobial," "anti-carcinogenic," "anti-viral," "immunomodulatory," "anti-oxidant," "anti-inflammatory," "skin protecting," and "wound healing" properties [10]. The analysis of the effect of the petroleum ether extract of *Aloe barbadensis* mill. The formulation contains elevated phytoconstituents such as phenols and phytosterols [29]. Protein, cholesterol, and glucose are the functional components that maintain steroidogenesis and hyperglycemic conditions. The letrozole-induced PCOS rats show hyperglycemia and metabolic syndrome that leads to insulin resistance. Where the Aloe vera-treated PCOS rats were back to their normal glycemic condition [30]. *In-silico* study revealed that the partially purified non-polar phytoconstituents of aloe vera gel have stable adhesion and high docking scores along with steroidogenic and metabolic regulatory proteins [35]. The *in vivo* study (KGN Cell line) showed a high molecular target cohort with PCOS. They systematically observed that Aloe vera in letrozole rats restored the steroidogenesis and its marker, HOMA-IR, estrus cyclicity, body weight, glucose intolerance, gonadotropin receptors gene expression, triglyceride, hormonal profile, ovarian histopathology, hormonal imbalance, and the estrogen level would be significantly increased. In contrast, the testosterone and LH levels decreased [31]. The Aloe vera gel restored glucose metabolism and reduced lipid levels in the rats induced by PCOS. The chemical constituents, such as polyesters and polyphenols, reduced the hyperglycaemic condition [32]. The current investigation on the efficacy of aloe vera gel formulation in PCOS indicates that the formulation protects against the PCOS phenotype by restoring the ovarian steroid status and altering significant steroidogenic activity. This is because of the phyto-components in the extract. In addition to lowering the liver's cholesterol synthesis, it can also restore the estrus cycle, glycemic sensitivity, and plasma lipoprotein levels. Because aloe vera also regulates blood glucose and cholesterol, it can help treat PCOS caused by metabolic issues [38].

***Labisia pumila***

*Labisia pumila* belongs to the family Myrsinaceae. LP plants are mostly grown in tropical forests. The phytoconstituents present in *Labisia pumila* include saponins, alkenyl, ascorbic acid, flavonoids, petioles, benzoquinone, carotenoids, cinnamic acid, gallic acid, methyl gallate, and others. LP has high pharmacological activity and plays a significant role in addressing immunodeficiency and anti-estrogenic deficiency. The bioactivities of LP contribute to its phytoestrogen effects, antioxidant, anti-bacterial, anti-fungal, anti-cytotoxic, anti-inflammatory, and anti-viral properties. It is also beneficial for women's reproductive diseases, such as postmenopausal syndrome and PCOS, along with other benefits like its phytoestrogenic properties, antioxidant effects, antimicrobial activity, and potential to address osteoporosis. Elevated and some other benefits like phytoestrogenic properties, antioxidant, antimicrobial, and osteoporosis disease.

The DHT-induced PCOS rats treated with LP (orally) showed increased insulin sensitivity, circulating resisting levels, and regulated astrogenesis, decreased triglyceride and total cholesterol levels, and reduced leptin mRNA expression in adipose tissue [33]. The ERT and LP-treated OVX rats significantly affected body composition and weight development. LP is rich in bioactive phytoestrogens and heterotrophic compounds, which can influence the body weight regulated by resistin and leptin [34]. The combined reaction of LP and *E. longifolia* has improved the lipid profile and hormone states in the pre-menopausal and menopausal womb [35]. In MCF-7 cells, LP extract exhibited an estrogenic impact at low concentrations (<50 μg/mL) and an antiproliferative effect at high

concentrations (>50 μg/mL). However, there were no notable effects on the MCF-7 cell proliferation rate at low concentrations (<50 μg/mL) of LP extract [36]. The LP presented osteoporotic fractures in estrogen-deficient or postmenopausal states [37]. [44] says that the treatment with LP extract may improve insulin sensitivity, decrease osteoporosis in PCOS patients, and decrease inflammatory cytokines linked to osteoporosis and bone loss. In PCOS rats, the phytoestrogenic properties of LP have been shown to reduce osteoporosis and metabolic disorders.

***Nelumbo nucifera***

*Nelumbo nucifera*, commonly known as lotus, is an aquatic plant in the family Nelumbonaceae. This ancient traditional plant is used as an herbal medicine and serves as a functional food worldwide. Various parts of *N. nucifera* have various phytoconstituents, giving it multiple properties. A total of 8 parts of *N. nucifera* have been identified, with 171 compounds noted [38]. The embryo of *N. nucifera* contains liensinine, nuciferine, lotusine, pronuciferine, rutin, hyperin, and demethylcoclaurine. The stamen holds linalool, luteolin glucoside, dehydroanone, anone, armepavine, kaempherol-3-O-β-D-glucuronide, β-sitosterol, asimilobine, demethylcoclaurin, livinidine, dehydronuciferine, quercetin, liriodenine, dehydroemerine, isoquercitrin, nornuciferine, N-methylasimilobine, N-norarmepavine, roemerin, and kaempherol. The flower of *N. nucifera* contains quercetin, luteolin, luteolin glucoside, kaempherol, kaempherol-3-O-glucoside, and isoquercitrin. The leaf contains roemerine, nuciferine, nornuciferine, anonaine, litriodenine, quercetin, tartaric acid, gluconic acid, acetic acid, malic acid, ginnol, nonadecane, succinic acid, rutin, isoquercitrin, and hyperin. The seeds of N. nucifera have dauricine, nuciferine, roemerine, lotusine, armepavine, liensinine, neferine, and isoliensinine. Additionally, several nutrient compounds are included. The rhizomes contain protein (1.7%), fat (0.1%), carbohydrates (9.7%), and ash (1.1%). The stem includes calcium, iron, and zinc. The leaves of *N. nucifera* are utilised as a home remedy and treatment for obesity. The seeds yield 348.45% energy, 10.6 – 15.9% protein, 1.93 – 2.8% fat, 2.7% fibre, 3.9 – 4.5% ash, 70 – 72.17% carbohydrates, and 10% moisture, and also supply minerals like copper, magnesium, calcium, sodium, potassium, chromium, and iron. *N. nucifera* exhibits various pharmacological properties, such as anticancer [39], antiobesity [40], treatment for pulmonary fibrosis [41], hepatoprotective effects [42], antiaging, antioxidant, and anti-inflammatory properties [43], atherosclerosis effects [44], antipyretic properties [45], and effects on diabetes and its complications [46], along with antiviral activity [47]. *Nelumbo nucifera* inhibits estrogenesis, reduces ovary weight, and displays antiestrogen effects that tend to decrease uterine weight and play an effective role in antifertility by regulating the estrous cycle. The elevated cholesterol level aids in sex steroidogenesis [48].

**Cinnamon**

Cinnamon is also called *Cinnamomum cassia*, belonging to the family of Lauraceae [49]. The native true cinnamon was found in Sri Lanka [50]. Cinnamomum cassia has been found to contain a variety of polyphenolic compounds, such as benzaldehyde, linalool, eugenol, eugenol acetate, methyl eugenol, and cinnamonyl alcohol, as well as procyanidins like aldehyde, acetate, caryophyllene, monoterpene, pinene, hydrocarbon, benzyl benzoate, phellandrene, safrole, cymene, and cineol [6]. It is a reliable source to act against cancer [50], diabetes, inflammation, and antioxidants [51], neurological disorders [52], cardiovascular disease [53], lowers the lipid profile [54], and it also helps with tissue regeneration and improves blood flow in the uterus [49]. Cinnamon supplementation improves insulin resistance, restores the cyclicity and ovary morphology, and may be a potential therapeutic agent for treating PCOS in mice models induced by DHEA. Significant differences exist in serum levels of total testosterone [20].

In contrast, the supplementation of cinnamon reduces testosterone and increases insulin sensitivity, and at the same time, ginger extract reduces steroidogenesis, LH, and FSH [55]. The cinnamon is more effective for insulin resistance in non-diabetic patients with PCOS [57]. The cinnamon supplement had no significant effect on their body weight due to a reduction in the serum levels of LDL-C and triacylglycerol. In contrast, it increased the serum concentration of HDL-C [56].

***Cocos nucifera***

*Cocos nucifera*, commonly called the coconut palm, comes under the Arecaceae family. *Cocos nucifera* originates from Indo-Malaya. Now it's grown all over the world, especially in coastal areas. It is the most important palm species and the predominant crop in tropical regions. The products produced from the coconut palm include construction materials, toddy, and palm cabbage [57]. *Cocos nucifera* contains various phytochemicals such as alkaloids, condensed tannins, epicatechins, catechins, flavonoids, leucoanthocyanidins, phenols, saponins, steroids, and triterpenes [58]. *Cocos nucifera* contains antioxidant properties such as stimulating the oxidative stress on sperm function, and scavengers for ROS (reactive oxygen species), where the phenolic compounds such as salicylic, caffeic, p-coumaric, and gallic acids play a significant role. It also contains various activities such as anti-diabetes [22], anti-inflammatory, antioxidant, antimicrobial [59], analgesia [60], antineoplastic [61],

antimalarial [62], antifungal [63], anthelminthic [64], bactericidal [65]. Alpha-tocopherol and lauric acid make up the majority of the oil's composition, but roots also contain a wealth of phenolic chemicals, including flavonoids and saponins [53]. Additionally, it contains skimmiwallin, isoskimmiwallin, and lupeol methyl ether. [6]

The oral supplement increases the hormonal imbalance and neurotoxic manifestation in PCOS by altering the acetylcholinesterase and Nrf2 gene expression, whereas behaviour and memory impairment occur through chronic low-grade inflammation, as well as ROS imbalance, enhanced acetylcholinesterase gene expression in the brain, and there is no synergistic effect of VCO and CLO, and CLO+VCO was deducted. This is mainly due to the single doses, where it lowered mRNA exposure in AchE than in CLO + VCO-treated rats [66]. The PCOS-induced rats (letrozole) had decreased FSH and increased LH, estrogen, and GnRH compared to the control group. The Nrf2, CAT, HO-1, and GSR were noticeably reduced, whereas the TNF-α, AR, LHr, caspase-3, and IL-1β were markedly elevated compared to the control. When the CLO and VCO are individually fought against, they are endocrine-balanced and anti-inflammatory. Hence, VCO may symbioses with CLO to reduce oxidative inflammation and hyperandrogenism in PCOS [68].

***St*achys *lavandulifolia***

*Genus Stachys* is botanically termed as *Stachys lavandulifolia*, which is generally termed as mountain tea, belonging to the family of Lamiaceae [69]. It was widely distributed in Iraq, America, Turkey, Turkmenistan, Iran, and Azerbaijan. *S. lavandulifol*s has more than 27 compounds, among which α-thujone (0.3%-32.3%), α-pinene (trace to 37.3%), myrcene (0.5%-15.9%), β-phellandrene (1.1%-37.9%), germacrene D (0.4%-11.3%), Δ-cadinene (trace to 11.6%), and 1,4-methanol-1 H-indene (trace to 10.1%). These are the major compounds estimated through GC-MS analysis [67]. *S. lavandulifolia* is an ancient ayurvedic medicine that focuses on various properties, such as anxiolytic properties [68], analgesic, and also reduces dysmenorrhea [73], anticancer, enzyme inhibition, anti-inflammation [72], anti-microbial, and antioxidant [74]. The treatment of *Stachys lavandulifolia* and clomiphene increased the height of the surface epithelium and granular epithelium and also increased the number of glands, which is more equal to the control group, while there is no significant difference. The treatment of clomiphene and *S. lvandulifolia* (900mg/kg) reduced hyperplasia in PCOS-induced rats [75].

***Heracleum persicum***

*Heracleum persicum* is a flowering plant belonging to the family of Apiaceae. The origin of the *Heracleum persicum* is Iran, and it is spread all over northern Europe. It is also termed as Persian Hogweed, and it is locally termed as Golpar in Iran. The chemical constituents present in the Golpar include alkaloids, flavonoids, furanocoumarins, terpenoids, and triterpenes. The oil extracted from the seeds of the Golpar contains some of the constituents such as hexyl butyrate, hexyl isobutyrate, and octyl acetate, and the compounds extracted from the fruit oils are isobutyrate, Hexyl butyrate, octyl acetate, and hexyl-2-methyl butanoate. The leaves of the Golpar contain β-springene, α-bergamotene, α-farnesene, cis-anethole, 2,5-dimethyl styrene, stragole, terpinolene, and spathulenol. The roots of the Golpar contain chemical constituents such as pimpinellin, isoberapten, isopimpinellin, bergapten, sphondin, and furanocoumarins. Yoghurt using HEO nanoparticles may be a viable method for creating functional food items like yoghurt with improved antioxidant qualities[69]. This plant has various properties such as anticonvulsant, antifungal, antibacterial, cytotoxic effects, and immune-modulatory, and also it has a therapeutic impact on PCOS patients since it decreased the levels of LH, estrogen, and testosterone while increasing the levels of FSH in PCOS rats [77]. Demonstrated that the impact of *Heracleum persium* has decreased in serum LH and testosterone, whereas the FSH was significantly increased at the dosage of 800mg/kg. The hydroalcoholic extract of golper significantly increased the primary follicles and primordial count, where the preantral and antral follicles were decreased, the atretic follicles also decreased, but not significantly, and FSH remained the same [70].

***Saraca asoca***

*Saraca asoca*, commonly termed Asoka, belongs to the family of Fabaceae. The origin of the *S. asoca* is South Asia and is widely distributed in India [79]. The *S.asoca* bark has various phytoconstituents such as 24-Ethyl-24-methyl-cholesta-5, 24-Ethylcholesta-5ccss, 24-dien-3beta-ol, leucopelargonidin-3-O-p-Dglucoside, epicatechin, catechin, procyanidin, deoxyprocyanidine-B, leucopelargonidin, and leucocyanidin. The flowers of *S.asoca* have Oleic, linoleic, palmitic, and stearic acids, p-sitosterol, quercetin, kaempherool-3-0-P-D glucoside, apigenin-7-0-P-D-glucoside, quercetin-3-0-P-D-glucoside, Pelargonidin-3,5-diglucoside, cyanidin-3, 5-diglucoside, palmitic, stearic, linoleic, linoleic, P & Y sitosterol, leucocyanidin and gallic acid and seeds of the plant contain oleic, linoleic, palmitic, and stearic acids, catechol, epicatechin, and leucocyanidin [80] [81]. *S. asoca* has various properties, such as antibacterial [82]antitumor, uterogenic, anticancer, and oxytocic [73]. The *S.asoca is* involved in antiestrogenic and anti-progestational activities to fight against menorrhagia [74]. [75] demonstrated that the ethanolic extract

of *S. asoca* has extremely restored the ovarian physiology related to a dose-dependent manner. The antioxidant activity of *S. asoca* was hypothesised due to the presence of kaempferol, rutin, and epicatechin. *S. asoca* contains flavonoid compounds such as kaempferol and rutin, which act as a barrier to the androgenesis effect compared to metformin. The phenolic compounds, such as gallic acid and salicylic acid, act as antioxidants. The rutin also decreased the action of the chemerin gene, increased insulin sensitivity, and lowered the serum insulin level. The ethanolic extract of *S. asoca* with a higher dosage (400mg/kg) contains various markers such as quercetin, luteolin, kaempferol, and β-sitosterol, ranging from 1.543mg/g, 0.924mg/g, 481mg/g, and 2.349mg/g. *S. asoca* flowers containing phytoestrogens exhibit estrogen-like activity attributed to uterine parameters such as physical, biochemical, and histological parameters [77].

***Curcuma longa***

Turmeric is also known as *Curcuma longa,* which belongs to the family of Zingiberaceae (ginger family). It originates from South Asia, which has around 133 species. The phytoconstituents present in the *C. longa* contain more than 720 compounds in 32 *Curcuma* species. Most of the compounds were identified in the rhizome, and the rest of them were isolated from the aerial parts of the plant, where these compounds are subdivided into diphenyl alkaloids, flavonoids, steroids, phenylpropene, and others [2]. The bioactivities of *C. longa* are antimicrobial [76], antioxidant [77], hepatoprotective [78], cardioprotective [79], antirheumatic [80], neuroprotective [81], endocrine-metabolic dysfunction [84], and anticancer [82]. The main components of it are terpenoids like turmerone, α-turmerone, camphene, β-sesquiphellandrene, γ-terpinene, and carotene, as well as phenolic compounds like curcumins, curcuminoids, ferulic acid, eugenol, ascorbic acid, vanillic acid, caffeic acid, syringic acid, protocatechuic acid, and p-coumaric acid [6]. *C. longa* enhances the circulating LH and reduces adiponectin. It also helps to induce ovulation and improve lipid profile, antioxidant, glycemic index, ovarian morphology, and hormonal levels in induced rats. Thus, the adiponectin circulated androgen-adiponectin values [83]. They act as endocrine and metabolic abnormalities in PCOS-induced rats. The clinical study revealed that Curcumin acts as an effective marker for lipid metabolism, weight loss, glucose level, and inflammation in PCOS. The nanoparticles of *C. longa,* which have reverted the estrous cycle to normal, decreased the LH, prolactin, insulin levels, and testosterone levels. The curcumin also increases the progesterone and FSH levels in the PCOS-induced rats. These curcumin nanoparticles also stabilised the GH, corpus luteum formation, and follicle growth in PCOS-induced rats [84].

**SPEARMINT**

Due to its exceptional scent and economic importance, spearmint, or *Mentha spicata L.* (Lamiaceae), is widely grown worldwide. Apart from being used as a flavouring component in traditional cuisines, *M. spicata* is also well-known for its traditional medicinal applications, which include treating colds, coughs, asthma, fevers, obesity, jaundice, and digestive issues [87]. The raw spearmint contains more moisture, ash, protein, fat, fibre, carbohydrates, and minerals such as sodium, potassium, and iron. Spearmint oil contains acid values of Mg KOH, iodine, peroxide, and free fatty acid. Spearmint and spearmint oil have antifungal, antiseptic, and antibacterial properties, which are food preservatives [88]. Spearmint's antiandrogen properties do not translate well into therapeutic practice due to the relationship between testosterone and cell division time and follicular hair development [85]. Spearmint tea administration to luteinizing hormone, follicle-stimulating hormone, and estradiol levels, while free testosterone levels significantly decreased. DHE sulphate and total testosterone levels did not drop substantially [95]. For mild cases of hirsutism, spearmint may be used as an alternative to antiandrogenic medications. When administered to PCOS rats, a combination of spearmint and flaxseed extract improved ovarian histology and endocrine secretion, including levels of testosterone, progesterone, and estradiol. When administered to PCOS rats, a combination of spearmint and flaxseed extract improved ovarian histology and endocrine secretion, including levels of testosterone, progesterone, and estradiol [26]. The spearmint tea enhances anti-androgen effects in hirsutism patients during clinical research. For female patients experiencing hirsutism and other symptoms linked to increased androgens, spearmint tea may help reduce androgenic hormones [95]. Improvements in hirsute patients, longer treatment durations, and prolonged patient follow-up periods are probably required to track symptomatic improvement [86]. It helps to inhibit testosterone and restore the development of follicles in the ovary [87]. Compared to PCOS rats who did not receive spearmint, these rats showed a decrease in body weight and testosterone levels, an increase in corpus luteum, and a decrease in ovarian cysts and atretic follicles. Accordingly, issues like ovarian cysts and elevated testosterone levels linked to polycystic ovarian syndrome can be mitigated by spearmint [88].

## VITEX

*Vitex Agnus-castus* is also termed a chaste tree fruit, which contains higher secondary metabolites such as 20 flavonoids like Apigenin, 3-Methyl kaempferol, luteolin, and Casticin, 10 iridoids, 11 phenolic acids, 3 diterpene alkaloids, and 12 terpenoidal lactones, us viteagnusin [6]. These compounds possess various Pharmacological properties such as immunomodulatory, estrogenic, opioid, antineoplastic, antioxidant activity, and dopaminergic activities. This *Vitex Agnus-cactus* is more effective for the regulation of the female reproductive system [89].
The alcoholic extract of *Vitex agus-castus* fruit is slowly beneficial for suppressing the reduction of the KISS-1 gene in the hypothalamus by controlling kisspeptin gene expression in PCOS patients [90]. The effect of *Vitex negundo L.* seeds has improved the ovary and also impacted glucose tolerance, LH: FSH ratio, disruption in the estrous cycle, cardiovascular indicators, steroidogenic enzymes, and enhanced features of polycystic ovarian syndrome. The combination of various allopathic drugs and Vitex enhances further [91]. The underlying hormonal imbalance in PCOS is strongly reflected in the hormonal levels, and the current study's findings also demonstrated that *Vitex agnus-castus* is more effective in reversing the negative effects of the hormonal PCOS imbalance [102]. Through the modification of lipid and hormonal profiles and oxidative stress, VAC and VPS may have beneficial effects on PCOS. Furthermore, these substances have beneficial effects that are similar to those of metformin [92]. The correlation between lower kisspeptin serum levels, decreased mean right and left ovarian volume, and improved quality of life suggests that myo-inositol unquestionably benefits PCOS and infertile patients [104]. By reducing cystic follicles and increasing the number of different follicles and corpora lutea, subcutaneous treatment of Vitex nanofibers at a dose of 4 weight per cent can alleviate polycystic ovarian syndrome [93].

## FENUGREEK

Throughout human history, *Trigonella foenum-graecum* seeds and green leaves have been employed for both culinary and medical purposes. *T. foenum-graecum's* fresh green leaves are eaten as vegetables, its dried seeds are used as spices in cooking, and both the leaves and the seeds are used to flavour food in many countries, including India. The seed is a crucial component of the Bengali five-spice mixture panch foron, which adds flavour and appeal to food while it's being prepared. The whole seeds of *T. foenum-graecum* are used as an antacid and to treat gastrointestinal disorders and diarrhoea. The seeds can be roasted, sprouted, or even eaten raw [94]. Fenugreek's antioxidant activity protects organs and inhibits the entry of diseases into the body. It also reduces body fat and is helpful against obesity. The plant is effective against blood lipids, sugar, and certain bacterial strains. The plant is known as fenugreek (*Trigonella foenum-graecum L.*), a member of the Fabaceae family, and is found worldwide. With proper cultivation, irrigation, and harvesting management, yields can significantly increase in quantity and quality [95]. Active ingredients found in the plant include alkaloids, flavonoids, steroids, saponins, and more. This plant has long been used as a medicine. It has long been utilised as a traditional meal and remedy. It is well known that fenugreek has anti-inflammatory, hypoglycemic, and hypocholesterolemic properties [1]. Fenugreek is not only an herbal supplement; in addition to being a food supplement, it has possible medicinal components that could be used to treat several illnesses [94]. It functions well as an antioxidant and an anti-inflammatory because of its chemical components and active ingredients, which include flavonoids, alkaloids, and amino acids. Furthermore, the clinical uses of fenugreek are ascribed to its varied chemical makeup, which makes this plant an effective way to reduce reliance on different synthetic medications for illness treatment [96]. Using fenugreek will prevent illness and enhance health, with a focus on cellular and molecular mechanisms [109]. Rich in fibre and protein, fenugreek has considerable medicinal and application potential because of its valuable bioactive components. As shown in several studies, the main therapeutic benefits of fenugreek include antidiabetic, antioxidant, anticarcinogenic, hypoglycemic, and hypocholesterolemic effects. Given these numerous health advantages, fenugreek can be suggested as a component of our regular diet and added to recipes to create functional dishes [97]. In women with PCOS, the long-term use of raw fenugreek seeds was especially beneficial. Three months of fenugreek seed consumption improved ovarian volume, infertility, egg maturation, and menstrual cycle regularity [98]. For PCOS-related hyperglycemia, fenugreek cannot be used in place of metformin. However, it can be used as an adjuvant treatment for PCOS, particularly in patients with moderate to severe hair loss or hyperlipidemia, due to its lipid-lowering properties and low incidence of side effects [99].

## LICORICE

Liquorice is the common name of *Glycyrrhiza glabra*, a flowering plant of the bean family Fabaceae, from the root of which a sweet, aromatic flavouring is extracted. L. *Glycyrrhiza brachycarpa* (Boiss.). In PCOS mice, liquorice at two doses (100 mg and 150 mg) may reduce ovarian cysts and enhance egg fertilisation and embryo development [100]. Liquorice, along with the hypocaloric diet, helps upregulation in the obesity index, glucose homeostasis,

and lipid profiles more than the placebo [101]. By regulating blood FSH levels, the LH/FSH ratio, irregular follicular phase, and aberrant historical alterations in the ovaries of PCOS rats, GRR extract may be a powerful therapy for the treatment of PCOS [102]. Since the two substances have opposing effects on the mineralocorticoid effector system and a potentially synergistic detrimental effect on the androgen effector mechanism, adding liquorice may have potential therapeutic uses in hyperandrogenic women [103]. Administering suitable dosages of liquorice root extract impacted the histological structure of the reproductive system in females with hyperandrogenism, and antioxidant components were enhanced [104]. Compared to a placebo, liquorice ingestion improves lipid profiles, glucose homeostasis, and obesity markers [101]. By regulating serum FSH levels, the LH/FSH ratio, irregular follicular phase, and abnormal past alterations in PCOS ovaries, GRR extract may be a powerful therapy for the treatment of PCOS [102].
Besides the plants discussed, many herbs have been found to have therapeutic potential against PCOS (Table 1).

**Table 1: Plants with therapeutic potential against PCOS**

| S. No | Scientific name | Family | Parts of the plant | Extract | Mode of action | Inducing agent | Proposed activity | Ref |
|---|---|---|---|---|---|---|---|---|
| 1 | *Nigella sativa* | Ranunculaceae | Seeds | Hydroalcoholic extract | Estrogen receptor | DHEA | Hypoglycemic, anti-oxidant effect and modulate hormones. | [119] |
| 2 | *Genus Panax* | Araliaceae | Roots | Aqueous extract | Enhance growth factor and inhibit NF-Kb pathway | DHEA | Anti-inflammation and anti-oxidant activity in the ovary | [120] |
| 3 | *Punica granatum* | Lythraceae | Seeds | Hydroalcoholic extract | Hormonal changes | Letrozole | Normal to the hormonal level and reduces the androgen receptor expression, fibrosis, endometrial oxidative stress, and proliferation use of polyphenols. | [121] |
| 4 | *Vitex agnus – castus* | Lamiaceae | Fruits | Ethanolic extract | Kiss–1 gene expression | Letrozole | Regulating the kisspeptin expression | [90] |
| 5 | *Euphorbiaceae* | Spurges | Roots | Methanolic extract | GhRH, LH &FSH | Letrozole | Restored the estrus cycle, decreased the glucose level, and oxidation stress, and improved the hormones, lipid profile and prevent damage of the ovary | [122] |
| 6 | *Glycyrrhiza glabra* | Fabaceae | Whole Plant | Hydroalcoholic extract | Reduced testosterone and estrogen levels | Estradiol valerate | Enhanced the oocyte maturation, fertility, and embryo developmental rats. | [100] |
| 7 | *Foeniculum vulgar* | Apiaceae | Seeds | Aqueous extract | Phytoestrogen activates estrogen receptors | Estradiol valerate | Improves renal injury, and increases kidney activity, and decreases urea rate. | [123] |
| 8 | *Fagonia indica* | Zygophyllaceae | Plant | Ethanolic extract | Hypothalamic–pituitary–ovarian axis (HPO), cytochrome P450C17 (CYP17A1), Aromatase inhibition. | Letrozole | The higher dosage of 500mg/kg enhances the anti-oxidant activity, liver enzymes, lipid profile, and hormonal enzymes | [124] |
| 9 | *Matricaria chamomilla* | Asteraceae | Flower | Hydroalcoholic | GABAergic | Estradiol valerate | LH Surge secretion, increased dominant follicles, and well endometrial tissue arrangements | [125] |
| 10 | *Pimpinella anisum* | Umbelliferae | Fruits | Hydroalcoholic | Inhibit PCOS-associated | Estradiol valerate | SOD, GPX, decreased follicular cysts, altered | [126] |

| S. No | Scientific name | Family | Parts of the plant | Extract | Mode of action | Inducing agent | Proposed activity | Ref |
|---|---|---|---|---|---|---|---|---|
| | | | | | production of TNF-α, IL-6 and MDA | | gene expression, inflammation and oxidative stress markers in ovarian tissues. | |

## MECHANISM OF ACTION

Cinnamon, ginseng, liquorice, and *Heracleum persicum* reduce blood glucose and lipid levels, which lessens the negative effects of diabetes brought on by PCOS. Furthermore, by lowering estrogen and hyperplasia, fennel and Stachys lavandulifolia can effectively alter endometrial tissue characteristics in PCOS [105]. Herbal drugs facilitate symptom resolution, regulate menstrual cycles, and correct the hormonal imbalances that contribute to anovulation [106]. Antioxidant qualities effectively treat PCOS by lowering oxidative stress and raising sex hormone levels in the blood. Various phytoestrogens and antioxidant chemicals included in medicinal plants have been shown to alleviate PCOS symptoms, making them an effective treatment option [107]. Increased amounts of antioxidants like retinol and α-tocopherol indicate that changes in the LPO processes in PCOS are compensatory mechanisms. Furthermore, the activity of the SOD enzyme has somewhat decreased [108].

The ability of herbal treatments to target several pathways, including hormone regulation, insulin sensitivity, and inflammation, typically with fewer adverse effects than synthetic drugs, makes them particularly effective in treating chronic disorders like PCOS [109]. Berberine helps with insulin resistance, Vitex agnus-cestus (chasteberry) promotes hormonal balance, and Cinnamomum cassia helps with glucose metabolism. Herbs frequently operate in concert with synthetic medicines to address underlying causes as well as symptoms, providing a more comprehensive therapeutic approach. They are also more successful because of their lengthy history of usage in conventional medical systems and cultural acceptance, which increases patient adherence and confidence [110].

Additionally, herbal remedies are cost-effective, particularly in environments with limited resources. Low-priced, locally accessible raw materials are used in their creation, which lowers the cost of production and delivery. As a result, they are available to a wider range of people, including those who cannot afford pricey synthetic medications [111]. Herbal therapies can avoid problems and lessen the long-term cost strain on healthcare systems by addressing the underlying causes of diseases like PCOS, such as insulin resistance and chronic inflammation. In addition, their ability to decrease adverse effects and lessen dependency on numerous synthetic drugs adds to overall cost savings [112].

However, these benefits, resolving major hurdles, are necessary to optimise the advantages of herbal remedies. Regulations ought to guarantee the uniformity, purity, and quality of its products. For medical professionals to offer evidence-based recommendations, more thorough clinical trials must confirm their safety and effectiveness [113]. Optimising therapeutic outcomes can be achieved by an integrated approach that incorporates herbal medicines, lifestyle modifications, and traditional treatments. Herbal remedies, when used properly, are a strong, secure, and cost-effective way to manage long-term illnesses like PCOS and provide a long-term route to better health [7].

## CHALLENGES AND CONSIDERATIONS

There are several issues and concerns when using herbal formulations to treat PCOS. The standardisation of herbal formulations is a significant problem since variations in active ingredient concentrations brought about by variations in plant species, growing practices, and extraction procedures might impact consistency and efficacy [114]. Furthermore, there is a chance that some herbs will interfere with the way that some prescriptions work, such as oral contraceptives, antidiabetic medications, or medications that are metabolised by the liver, which could have negative consequences. Because PCOS is complicated and heterogeneous, each patient needs a customised treatment plan that takes into account their unique symptoms, hormone profiles, and general health. To overcome these obstacles, strict quality control, close observation of medication interactions, and individualised treatment plans are required to guarantee both safety and effectiveness [58].

### Integration of Herbal Formulations into Modern Healthcare

Healthcare practitioners must actively participate to ensure the safe and efficient use of herbal formulations in contemporary healthcare. Informing patients on herbal treatments' advantages, restrictions, and possible hazards is a critical responsibility of healthcare professionals, such as doctors and pharmacists. Their advice aids in controlling appropriate dosage, keeping an eye out for side effects, and avoiding combinations with prescription drugs. Moreover, a patient-centred approach encourages cooperation between conventional and modern

medicine within clinical and regulatory frameworks. This type of integration preserves the safety and effectiveness of herbal preparations while enhancing their therapeutic potential, including understanding herbal formulations, the benefits of integration, and the challenges associated with it [115].
Products made from plant-based ingredients, known as herbal formulations, are frequently utilised in traditional medical systems such as Ayurveda, TCM, and Unani [116]. Complementary strategies, such as filling gaps in conventional treatment, particularly in chronic and lifestyle-related illnesses, are among the advantages of integration. Treats patients holistically by focusing on several paths. When prepared and dosed appropriately, natural origins are thought to be safer and have fewer negative effects. economical solutions for groups with little access to traditional medical care [117]. Variability in Bioactive Substances provides an abundant supply of novel medicinal substances (e.g., artemisinin for malaria). The difficulties in integrating quality control variability and standardisation in active compound concentration. Strict Good Manufacturing Practices (GMP) are required [118].

## CONCLUSION

Herbal medicine has great promise for treating PCOS since it provides a natural and comprehensive strategy for resolving its many symptoms, such as infertility, metabolic abnormalities, and hormonal imbalances. Many herbs show promise in their therapeutic benefits, such as insulin sensitisation, androgen regulation, and anti-inflammatory qualities, which make them useful adjuncts to traditional therapies. Polycystic ovarian syndrome is a complex endocrine and metabolic disorder that is interlinked with other diseases. The herbs such as Aloe vera, cinnamon, curcumin, flax seeds, *Labisia pumilla, N. nucifera, Cocus nucifera, Stachy lavandulifolia*, *Heracleum persium, Saraca asoca* can potentially improve osteogenesis, the immune system, insulin sensitivity, and decrease hyperandrogenism, testosterone level, and regulate the hormonal level and estrous cycle. This systematic review contributes to the growing body of evidence supporting the integration of herbal remedies into mainstream PCOS management protocols. By providing evidence-based insights, it seeks to empower healthcare providers and patients to make informed decisions about incorporating herbal therapies into their treatment regimens. More thorough clinical research is necessary before incorporating herbal medicine into mainstream healthcare to confirm its effectiveness, guarantee safety, and provide standardised formulations. Effective research and trials are required to address current issues, such as variations in herbal compositions and possible conflicts with prescription drugs. While preserving safety and scientific credibility, herbal therapy has the potential to significantly improve the quality of life for people with PCOS with more research and interdisciplinary cooperation.

## ABBREVIATION:

PCOS: Polycystic ovarian syndrome
LH: Luteinizing Hormone
FSH: Follicle-stimulating hormone
Gh-RH: Gonadotropin-releasing hormone
CAM: Complementary and alternative medicine
HPG: Hypothalamic- pituitary- gonadal
AMPK: AMP-activated protein kinase
CRP: C- Reactive protein
HIV: Human Immunodeficiency Virus
HOMA-IR: Homeostasis model assessment of Insulin Resistance
DHT- Dihydrotestosterone
DHEA- Dehydroepiandrosterone
ERT- Estrogen Replacement Therapy
LDL-C – Low-density lipoprotein- Cholesterol
HDL-C – High-density lipoprotein cholesterol
ACHE- Acetylcholinesterase
ROS- Reduces oxidative state
CAT- Catalase
MDA- Mass drug administration
SOD- Sodium oxide dismutase
LPO- Lipid peroxidase
GMP- Good Manufacturing Practices

**REFFERENCE**

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