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HERBAL CARE FOR WOMEN: A GUIDE TO PHYTOTHERAPEUTIC AGENTS IN GYNAECOLOGY AND REPRODUCTIVE HEALTH

CHAPTER 4 : PHYTOTHERAPY IN POLYCYSTIC OVARY SYNDROME AND HORMONAL IMBALANCE

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Abstract

Polycystic Ovary Syndrome (PCOS) is one of the most common endocrine and metabolic disorders among women of reproductive age. It is manifested by hormonal imbalance, hyperandrogenism, insulin resistance, menstrual disorders, anovulation, infertility, obesity, and accompanying psychological disorders. Traditional methods of treatment, which include hormonal therapy and use of insulin sensitizers, only alleviate symptoms of the disease and can





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be accompanied by side effects and insufficient effectiveness. Therefore, considerable efforts have been made to investigate the possibility of using phytotherapy as a complementary and alternative method of PCOS and other endocrine diseases treatment. This chapter will discuss the role of medicinal plants and bioactive compounds in the treatment of PCOS and hormonal imbalance. The focus will be made on pharmacological actions of plant drugs, which include anti-inflammatory, antioxidant, antiandrogenic, insulin-sensitizing, and hormone regulation properties that promote restoration of metabolic and reproductive homeostasis. Key medicinal plants *Glycyrrhiza glabra*, *Aloe vera*, *Actaea racemosa*, *Angelica sinensis*, and *Serenoa repens*, which possess beneficial properties for PCOS treatment will be described in detail. Mechanisms of their activity and application in improving ovulation, menstrual cycle, ovarian morphology, and fertility will be examined. The chapter will describe the role of various types of phytochemicals (flavonoids, polyphenols, alkaloids, phytoestrogens) in endocrine regulation and alleviation of oxidative stress associated with the pathogenesis of PCOS. Experimental and clinical data on efficacy and safety of herbal drugs will be critically analyzed. Challenges associated with standardization of preparations, bioavailability, and dosage adjustment will also be discussed.

Keywords: Polycystic Ovary Syndrome, Phytotherapy, Herbal Medicine, Hormonal Imbalance, Medicinal Plants & Reproductive Health.

1. Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders affecting women during their reproductive years and is increasingly recognized as a major public health problem because of its reproductive, metabolic, and psychological consequences (1,2). PCOS is a multifactorial disorder with genetic and environmental influences, characterized by hormonal and metabolic disturbances that alter ovarian function and impair reproductive health (1,3). According to the Rotterdam diagnostic criteria, PCOS is diagnosed when at least two of the following three features are present after exclusion of related disorders: ovulatory





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dysfunction, clinical and/or biochemical hyperandrogenism, and polycystic ovarian morphology on ultrasonography (4). Women with PCOS commonly present with irregular menstrual cycles, infertility, hirsutism, acne, androgenic alopecia, obesity, insulin resistance, metabolic syndrome, and other reproductive abnormalities (1,2,5). In addition, PCOS is associated with an increased risk of developing type 2 diabetes mellitus, cardiovascular disease, dyslipidemia, non-alcoholic fatty liver disease (NAFLD), and endometrial hyperplasia or carcinoma(2,5,6). Psychological disorders, including anxiety, depression, reduced quality of life, and low self-esteem, are also highly prevalent among women with PCOS, (2,6).

The principal pathogenic mechanisms underlying PCOS involve complex endocrine and metabolic disturbances that interact to promote disease progression (1,2). Hyperandrogenism, resulting from excessive ovarian androgen production, disrupts normal follicular development, leading to arrested follicular maturation, chronic anovulation, and menstrual irregularities (1–3). Simultaneously, insulin resistance develops in peripheral tissues, prompting compensatory hyperinsulinemia to maintain glucose homeostasis. Elevated insulin levels further stimulate ovarian androgen synthesis and suppress hepatic production of sex hormone-binding globulin (SHBG), thereby increasing circulating free testosterone concentrations and exacerbating hyperandrogenism (2,7). In recent years, accumulating evidence has highlighted the important roles of chronic low-grade inflammation and oxidative stress in the pathophysiology of PCOS. Increased production of pro-inflammatory cytokines and reactive oxygen species (ROS) contributes to endocrine dysfunction, insulin resistance, ovarian dysfunction, and metabolic abnormalities associated with the syndrome (5,8).

Current management strategies primarily focus on symptom control through lifestyle modification, hormonal contraceptives, insulin-sensitizing agents such as metformin, and ovulation-inducing medications including letrozole and clomiphene citrate (5). Although these interventions are clinically effective, they often target only specific manifestations of the disorder, may produce adverse effects, have contraindications in certain patient populations,





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and frequently show poor long-term adherence (9). Consequently, increasing attention has been directed toward complementary and alternative therapeutic approaches capable of simultaneously targeting multiple pathogenic pathways involved in PCOS.

The use of medicinal plants and herbal remedies has a long history in the traditional medical systems of Asia, the Middle East, and Africa for managing menstrual disorders, infertility, and endocrine dysfunction (10,11). Contemporary pharmacological research has demonstrated that many medicinal plants contain biologically active constituents, including polyphenols, flavonoids, terpenoids, alkaloids, saponins, and phytoestrogens, which possess antioxidant, anti-inflammatory, insulin-sensitizing, anti-androgenic, and phytoestrogenic properties that may improve hormonal balance and metabolic dysfunction in women with PCOS (11–14). These phytochemicals have shown promising effects in experimental and clinical studies by reducing oxidative stress, improving insulin sensitivity, regulating steroidogenesis, and restoring ovulatory function. Therefore, herbal medicine has emerged as a promising adjunctive therapeutic strategy for PCOS. The following sections discuss the mechanisms of action of medicinal plants, summarize the available experimental and clinical evidence for commonly used botanicals, evaluate their therapeutic efficacy and safety, and highlight future directions for integrating herbal therapies into the management of PCOS (13,14).

2. Pathophysiology of PCOS and Hormonal Imbalance

PCOS is a multifactorial endocrine and metabolic disorder resulting from the interaction of hormonal imbalance, insulin resistance, hyperandrogenism, chronic low-grade inflammation, oxidative stress, genetic susceptibility, and environmental influences. As illustrated in Figure 1, these mechanisms interact synergistically to disrupt normal ovarian physiology, leading to reproductive, metabolic, and endocrine abnormalities rather than acting independently (1–4). Dysregulation of the hypothalamic-pituitary-ovarian (HPO) axis results in increased pulsatile secretion of gonadotropin-releasing hormone (GnRH), which preferentially stimulates luteinizing hormone (LH) secretion over follicle-stimulating hormone (FSH), producing an elevated LH/FSH ratio (15,). Increased LH stimulates ovarian theca cells to produce excessive





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androgens, whereas relatively low FSH concentrations impair granulosa cell function and follicular maturation, resulting in arrested follicular development, chronic anovulation, menstrual irregularities, infertility, and the characteristic polycystic ovarian morphology (2,6). Insulin resistance is another fundamental feature of PCOS and is present in both obese and lean women. Impaired insulin signaling leads to compensatory hyperinsulinemia, which directly enhances ovarian androgen synthesis and suppresses hepatic production of sex hormone-binding globulin (SHBG), thereby increasing circulating free testosterone levels and aggravating clinical manifestations such as hirsutism and acne (17,18). Hyperinsulinemia also potentiates insulin-like growth factor-1 (IGF-1) activity, further stimulating ovarian steroidogenesis. Moreover, dysregulation of intracellular signaling pathways, including PI3K/Akt and AMP-activated protein kinase (AMPK), contributes to impaired glucose metabolism, dyslipidemia, obesity, and an increased risk of type 2 diabetes mellitus and cardiovascular disease (18).

Chronic low-grade inflammation and oxidative stress further exacerbate PCOS pathogenesis. Elevated circulating concentrations of inflammatory mediators such as tumor necrosis factor- α (TNF- α), interleukin-6 (IL-6), and C-reactive protein (CRP) impair insulin signaling and ovarian function, while excessive production of ROS activates the nuclear factor-kappa B (NF- κ B) pathway, promoting cellular damage, endothelial dysfunction, and abnormal follicular development (19). Genetic predisposition, together with environmental and lifestyle factors including obesity, sedentary behaviour, and dietary habits, further amplifies these endocrine and metabolic disturbances (1–3). Collectively, hyperandrogenism, insulin resistance, inflammation, and oxidative stress constitute the central pathogenic mechanisms of PCOS. A comprehensive understanding of these interconnected pathways provides the foundation for developing integrated therapeutic strategies that combine pharmacological interventions with lifestyle modification and plant-based therapeutics to improve both reproductive and metabolic outcomes in women with PCOS (20).





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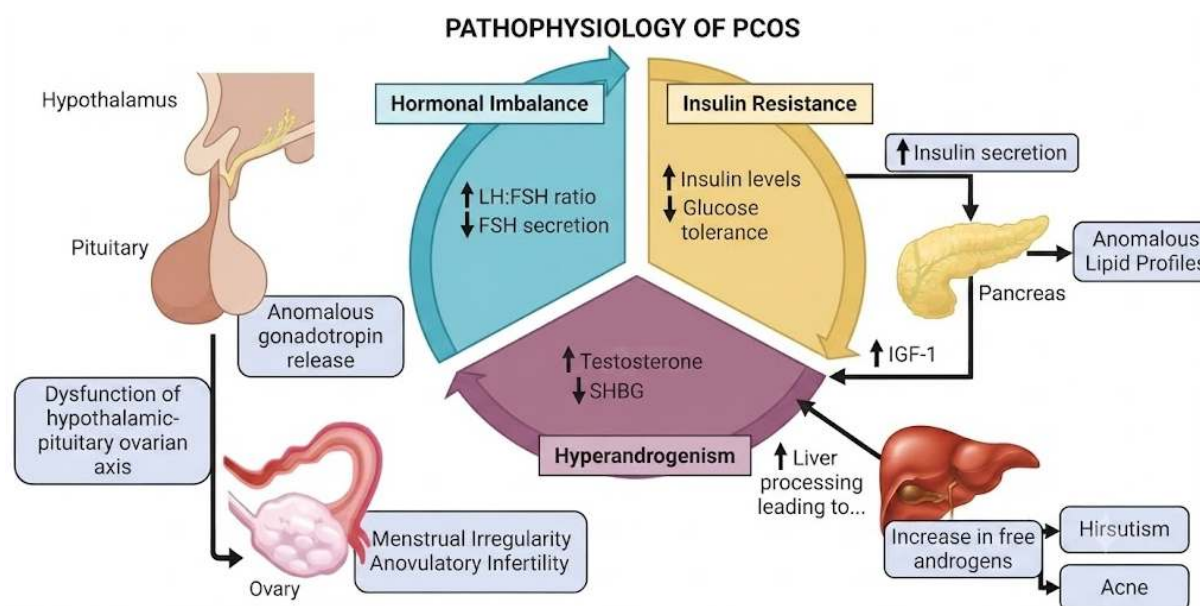


Figure 1: Pathophysiology of PCOS

3. Conventional Therapeutic Approaches for PCOS

The clinical presentation of PCOS is highly heterogeneous; therefore, treatment should be individualized according to the patient's symptoms, metabolic status, and reproductive goals (21, 22). Lifestyle modification remains the cornerstone of PCOS management and is recommended for all women regardless of body mass index. Dietary intervention, regular physical activity, and behavioral support improve insulin sensitivity, restore ovulatory function, reduce hyperandrogenism, and enhance fertility. In overweight and obese women, a modest weight loss of 5–10% is associated with significant improvements in both reproductive and metabolic outcomes (3).

Combined oral contraceptive pills (COCPs) are considered the first-line pharmacological therapy for women with PCOS who are not seeking pregnancy. COCPs regulate menstrual cycles, suppress ovarian androgen production, increase hepatic synthesis of sex hormone-binding globulin (SHBG), and consequently reduce circulating free testosterone levels, thereby improving clinical manifestations such as hirsutism and acne (5,24). Insulin resistance





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represents a central metabolic abnormality in PCOS; therefore, insulin-sensitizing agents are widely used. Metformin is the most extensively studied medication and improves insulin sensitivity by reducing hepatic glucose production and enhancing peripheral glucose uptake. It also contributes to menstrual cycle regulation, ovulation, weight management, and glycaemic control, particularly in women with obesity, impaired glucose tolerance, or type 2 diabetes mellitus (21, 25,26).

For women wishing to conceive, ovulation induction is the primary therapeutic approach. Current international guidelines recommend letrozole, an aromatase inhibitor, as the preferred first-line pharmacological treatment because it achieves higher ovulation, pregnancy, and live birth rates than clomiphene citrate in an ovulatory women with PCOS. Women who fail first-line treatment may require gonadotropin therapy, laparoscopic ovarian surgery in selected cases, or assisted reproductive technologies such as in vitro fertilization (27).

Although conventional therapies are effective, they are associated with certain limitations. Combined oral contraceptives may increase the risk of venous thromboembolism in susceptible women, metformin commonly causes gastrointestinal adverse effects, and anti-androgenic drugs such as spironolactone require reliable contraception because of potential fatal teratogenicity. Moreover, many pharmacological agents primarily address individual symptoms rather than the multifactorial pathophysiology of PCOS involving endocrine dysfunction, insulin resistance, chronic inflammation, and oxidative stress. Consequently, growing attention has focused on complementary approaches, including evidence-based herbal medicines and phytochemicals, which may simultaneously target multiple pathogenic pathways and improve both reproductive and metabolic outcomes (28-30).

4. Phytotherapy and Herbal Medicine in Women's Health

4.1 Historical Perspective of Herbal Medicine

The utilization of medicinal plants for the treatment of conditions affecting women date back many thousands of years and are an integral part of the world's traditional medicine systems including China, India, Egypt, Greece as well as Middle Eastern countries (31–34). Records of





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these countries reveal that they used plant remedies mostly for treating menstrual problems, infertility, pregnancy disorders, and other health problems connected with menopause (32, 33). These medical systems like Ayurveda, Traditional Chinese Medicine (TCM), and Unani, have for a long time, recognized the importance of naturally growing medicinal plants for reproduction-related health and hormonal equilibrium. A number of the plants now under research for possible endocrine disturbances have roots in these ancient systems since their use over the years has yielded therapeutic effects (35, 36).

Initially, herbal medicine was practiced through observing and experimenting which is unlike how science is done today. But, many of the traditional treatments that were in use have produced reliable results in clinic practice which served as the basis for the investigation of their pharmacological properties (36). Discovery of the compounds which cause the medical effects and the elucidation of the mechanism by which they bring about changes in endocrine systems, metabolism and reproduction are some of the fruits of development and advancement in the fields of phytochemistry and molecular biology (37). Phytotherapy has So evolved to the point where its practice is not only guided by tradition but also by evidence, and women's healthcare today is seeing the benefit of phytotherapy more than ever before(37,38).

4.2 Role of Medicinal Plants in Gynecological Disorders

Herbal remedies, or the use of plants in the form of herbal medicine to treat diseases and maintain health, has long been a major alternative therapy for various gynecological issues mainly dysmenorrhea, amenorrhea, menorrhagia, infertility, menopausal symptoms, and hormonal imbalances (39). These days, the use of medicinal plants and herbs to deal with polycystic ovary syndrome is being given much attention because polycystic ovary syndrome is one of the most difficult diseases to treat and the side effects of the conventional treatments are quite limited (40). In fact, a number of medicinal plants are known to have chemical substances that work the same way as pharmaceutical drugs to alleviate the symptoms of certain pathologies, e.g. in PCOS, the major disease pathophysiological mechanisms contributing to the disease. We review papers showing that either of the herbal compounds or





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the extracts from herbs can: aid ovarian steroidogenesis; improve insulin sensitivity; modulate the pituitary gland's hormonal output; inhibit inflammatory pathways; reduce ROS whose role in initiating and perpetuating various cell injuries is of pivotal importance. These effects will probably translate into a decrease in dysregulated uterine bleeding and the return of fertility, a reduction in the symptoms of androgen excess, which are characterized by skin lesions and excessive growth of hair, and an improvement in the metabolic profile of patients. Also, there are reports in which herbal medicines have been used alongside drugs. This fact implies that patients are showing a growing trust in complementary treatment of disorders related to reproductive health (1).

4.3 Advantages of Herbal Therapy in Hormonal Disorders

An attractive and one of the main advantages of phytotherapy is that it exerts its effects via multiple channels of human biology at the same time. Unlike pharmaceutical drugs that often act on a single receptor or even a particular protein molecule, medicinal herb medicines, most of the time, have various different plant chemical substances and these can work in harmony with each other to enhance the curative effects (10). It is probably true that, for PCOS, which usually has a combination of different disorders: such as reproductive, metabolic, inflammatory and endocrine ones that interact with each other, multiple mechanisms of actions of drugs can be beneficial (12). A number of plants used in traditional medicine were reported to contain various compounds like flavonoids, alkaloids, polyphenols, phytoestrogens, terpenoids, saponins etc. that possess anti-oxidative, anti-inflammatory, insulin-sensitizing, and hormone-modulating properties. Because of these substances, such characteristics may assist not simply in the metabolic control of blood sugar level but also in reduction of male hormone, regulation of menstrual cycle and besides that, protection of reproductive organs from damage caused by an excessive amount of oxygen radicals (38). Patients wanting long-term therapy, or at least wishing to reduce dependence on hormone treatments, might accept the alternative herbal treatment offer more readily since herbal remedies are commonly perceived as a type of 'gentler' or 'less penetrating' intervention. Obviously it is also true that despite its numerous





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possible benefits, phytotherapy shouldn't be looked upon either as automatically more effective or safer than regular drugs. A lot of issues like the differences in phytochemical content of herbs, non-uniform production of herbal preparations, non-standardized prescription, and absence of good quality experimental studies, need to be addressed for the herb-based therapeutics to gain popularity among clinic.

4.4 Mechanisms of Phytotherapeutic Action

Medicinal plants' various actions in the treatment of PCOS mainly aim at different facets of the disease like hormonal and metabolic changes, inflammation as well as oxidative stress. Insulin sensitivity regulation via several phytochemicals with special reference to berberine and certain polyphenols remains the most extensively explored mechanism. These compounds stimulate AMP-activated protein kinase (AMPK) and enhance insulin receptor signaling pathways that result in better glucose uptake, hyperinsulinemia reduction, and an overall improved insulin sensitivity. As insulin hyper production results in insulin resistance, the latter, in turn, can cause excessive ovarian androgen production so it would be apparent that increased insulin sensitivity not only lowers blood insulin levels but would also lead to a reduction in androgens and the restoration of ovulation. The ability of plants to change steroid hormone levels is mainly explained by their direct effects but they can also interact with enzymes that are responsible for androgen biosynthesis (19). Some phytoconstituents have the property to lower testosterone, while others interfere with androgen's mode, because of this, reducing effects or even causing an increase in the production of liver SHBG. As a result, the number of free circulating androgens is greatly reduced. That means, the manifestations like hirsutism, acne, and other symptoms that are characteristic of an excess of testosterone will be quite a bit alleviated. Alongside the suppression of inflammation, which is another key role performed by certain herbal remedies, one can consider that a decrease in low-level inflammation is also an important action of these plants. There are some natural substances that can block the activity of NF- κ B factor as well as reduce the formation of pro-inflammatory mediators such as TNF- α and IL-6. Considering that inflammation is an established promoter of insulin resistance and





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can impair ovarian function, these anti-inflammatory properties would be of great benefit in the treatment of PCOS. The decrease of oxidative stress is another aspect of the plants' helpfulness. Phytochemicals, including flavonoids, polyphenols, and other antioxidant substances, have the capability to neutralize reactive oxygen species, both through their complete removal and through the elevation of endogenous antioxidant substances like SOD, catalase and glutathione peroxidase (10, 19, 38). This means that through the protection of ovarian cells from the detrimental effects of oxidative stress, this will not only result in more effective follicular development but also produce higher quality eggs and therefore better reproductive outcomes. In all, these multiple mechanisms that the botanical treatments have reveal their richness, variety as well as great potential. Thus, a basis of scientific evidence is formed for taking medicinal plants as alternative and complementary medicines that may be helpful not only for controlling PCOS but also for hormonal balance disturbances in general. However, the clinical use of these mechanistic findings is only possible if supported by well-designed, large-scale, adequately documented randomized controlled clinical trials with standardized herbal formulations and fixed dosages.

5. Bioactive Phytochemicals in PCOS Management

Medicinal plants have long been acknowledged as a reliable and safe resource for drugs that are beneficial to human health (10). One way such herbal medicines might help is by using a large array of plant compounds to treat a condition like PCOS. Plant-derived compounds are quite different from standard pharmaceutical drugs, which usually interact mainly at one site. Phytochemicals have been found to be involved in many different biochemical processes in the body, and this is one of the main reasons why plant-based chemicals are still considered different from the ones made in labs. As a result, plant-derived chemicals have become highly sought after for the treatment of conditions like PCOS which arise from a number of factors like hormonal imbalances, insulin resistance, oxidative stress, and chronic inflammation, as well as the reproduction system not functioning properly. Studies show that the constituents of herbs besides affecting hormone signaling are also able to increase glucose metabolism, inhibit





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the pathway for inflammation, and guard ovarian tissue against oxidative stress, which is the justification for recommending phytotherapeutic agents as a means of dealing with endocrine disorders. Flavonoids, polyphenols, phytoestrogens, alkaloids, terpenoids, and saponins are some of the phytochemical classes which have been the target of investigations mainly for PCOS. Different phytochemicals affect the key molecular processes like AMP-activated protein kinase (AMPK), phosphatidylinositol 3-kinase (PI3K)/Akt signaling, nuclear factor-kappa B (NF- κ B), as well as peroxisome proliferator-activated receptor gamma (PPAR- γ), steroidogenic enzymes, and estrogen receptors. As a result, these substances have an impact on the improvement of insulin sensitivity through reduced androgen levels in blood and the normalization of ovulation function. On top of that, they help to improve the overall reproductive health of the body (10,12,22).

5.1 Flavonoids

Flavonoids are polyphenolic compounds, the most numerous and widely distributed groups of compounds in plant kingdom (41) In their structure, flavonoids contain two fused benzene rings connected to a heterocyclic pyranone ring and are grouped by their differences in structure in several subclasses. Examples include flavonols, flavones, flavanones, flavanols, anthocyanidins, and isoflavones. PCOS research works mostly focus on quercetin, kaempferol, apigenin, luteolin, and rutin as typical flavonoids. Flavonoid's antioxidant and anti-inflammatory properties are used to counter the effects of oxidative stress, which induces insulin resistance and ovarian dysfunction. Flavonoids' main biological property with treatment of PCOS lies in this. They are good ROS scavengers and lipid peroxidation inhibitors besides activating endogenous enzyme systems like catalase, glutathione peroxidase, and SOD. One of the most popular studies for this compound is quercetin's ability to increase insulin sensitivity in animal studies via the activation of the AMPK signaling pathways and the modulation of the expression of glucose transporters. Beyond that, quercetin can prevent secretion of inflammatory cytokines including TNF- α and IL-6, which could help patients suffering from PCOS experience a lower level of chronic low-grade inflammation. On top of that, it may also





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decrease the levels of free testosterone and testosterone in PCOS patients by reducing androgen production through affecting steroidogenic enzymes in the ovary and improving ovarian morphology in PCOS animal models. A very similar set of mechanisms was reported for kaempferol and apigenin. These have antioxidant, anti-inflammatory, and anti-apoptotic properties which may preserve ovarian follicles from the negative effects of ROS (10, 12,41).

5.2 Polyphenols

Polyphilic plant compounds which are also known as polyphenols are plant phytochemicals having many phenolic groups in molecular system (42). These compounds are found in various plants readily like fruits, vegetables, medicinal plants, spices, and herbal tea. There are numerous health benefits of polyphenols, mainly endocrine and metabolic effects (10). The three polyphenols studied in PCOS, namely resveratrol, catechins, and curcumin, have attracted a great deal of research (12). Resveratrol is a natural stilbene compound found predominantly in grapes and also in peanuts. Resveratrol is a potent antioxidant. Studies show that resveratrol has a direct influence on cellular energy metabolism through activating SIRT1, an important regulator of mitochondrial function and metabolic balance. Studies on animal models have established the advantages of resveratrol on the ovary. It decreases androgen levels, enhances insulin sensitivity, and suppresses inflammatory mediators. It has also been shown to reduce serum testosterone concentrations and improve metabolic variables such as body fat mass and lipid profile. However, large-scale clinical investigations are still needed to confirm these findings. Curcumin, extracted from turmeric rhizomes, is one of the most extensively studied phytochemicals in metabolic and inflammatory diseases. It exerts its effects through multiple molecular targets including NF- κ B, PPAR- γ , AMPK, and cytokine signalling pathways (10, 12, 42). Numerous clinical studies in PCOS have demonstrated that curcumin improves insulin resistance, oxidative stress, and inflammatory markers. Catechins, particularly epicatechin found in green tea, possess antioxidant, hypolipidemic, insulin-sensitizing, and free radical scavenging activities. Overall, these polyphenols protect cells from oxidative damage, improve insulin resistance, and regulate metabolic homeostasis.





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5.3 Alkaloids

Organic compounds that have nitrogen are known as alkaloids, and they are well known for the range of medical effects they offer (43). Alkaloids, *berberines* among them, have been studied extensively and are considered the best for handling PCOS and having the highest level of studies related to themselves (44). Berberines are most prevalent in medicinal plants such as *Berberis aristata*, *Berberis vulgaris*, *Coptis chinensis* aside from which they have shown very good metabolic and endocrine properties. The major mechanism through which berberines exert their action involves AMP Kinase (AMPK), a cell's master regulator involved mainly in energy metabolism. Activators of AMPK boost the uptake of sugar, lower liver sugar release, speed-up lipolysis, and increase insulin activity. So, a decrease in hyperinsulinemia brought about by berberine should, at least in part, reduce the excessive level of androgen hormones from the ovaries, that is a characteristic of PCOS (12,43,44). Based on some clinical trials, following berberine treatment, there was a decrease in fasting blood glucose concentrations, insulin resistance indicators, lipid profiles, and reproductive hormones. Comparative experimental studies have also been conducted where berberine has been compared with metformin, some of which state that berberine might have metabolic effects similar to metformin; however, such studies are limited because there are few direct head-to-head comparison trials and many involved small sample sizes. An increasing body of research showing strong evidence for the use of berberine has led to its recognition as another potential ingredient that researchers may want to investigate when exploring natural approaches for PCOS management. *Berberine* is a phytochemical that tends to have promising therapeutic potential for the future translation of PCOS management strategies from the laboratory into clinical practice (12, 44).

5.4 Phytoestrogens

Phytoestrogens are plant derived compounds that resemble the human hormone estrogen in their shape. Since they are similar to estradiol, the principal estrogen in the human body, phytoestrogens are able to attach themselves to the estrogen receptors in the body. There are





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several kinds of phytoestrogens, such as isoflavones, lignans, and coumestans. They can be found mainly in soy, legumes, and flax, with various herbs. The actions of phytoestrogens is limited to some extent about the affinity for estrogen receptors. Given the location in the body and the hormone state surrounding them, phytoestrogens can either be the source of very weak estrogen-like activity or have a pure anti-estrogenic effect (45). Phytoestrogens may contribute to the understanding of PCOS since they are known to interfere with hormones and balance them which is an important factor in PCOS pathogenesis. The phytoestrogens' binding to estrogen receptors may have the ability to regulate gonadotropin secretion, ovarian function, and menstrual cycle. Also, genistein and daidzein, two of the main isoflavonoids, possess some antioxidant and anti-inflammatory actions, which altogether indicate a complex underlying pattern. There are still limited data for the phytoestrogens effects on PCOS patients. That's why, the role in balancing hormones has not been verified yet. (12, 46).

5.5 Terpenoids and Saponins

Terpenoids and saponins represent some of the main phytochemical constituents that may help managing PCOS (12, 47, 48). Apart from being effective as anti-inflammatory agents, these agents also act as antioxidants and inhibit the over-production of male hormones as well as metabolic regulation. Glycyrrhizin is a triterpenoidal saponin mainly isolated from the *liquorice* (*Glycyrrhiza glabra*) root, being the compound most intensively studied in this category. Both glycyrrhizin and its active metabolite glycyrrhetic acid can modify hormone metabolism and reduce testosterone levels. Changes in testosterone levels have been attributed to variations in steroidogenic enzymes and inhibition of androgen synthesis pathways by glycyrrhizin. Clinical evidence indicates that *liquorice* is effective in reducing circulating testosterone concentrations and has therefore been considered a complementary treatment for hyperandrogenic manifestations such as hirsutism and acne. Steroidal and triterpenoidal saponins present in *fenugreek* (*Trigonella foenum-graecum*) have also shown encouraging results and, apart from enhancing ovarian function, are known for their ability to improve





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insulin regulation (48). These modes of action include enhancing insulin secretion, restoring reproductive steroid levels, and normalizing ovarian architecture. Because of this, medicinal plants containing these phytoconstituents as bioactive principles provide a scientific basis for targeting oxidative stress, inflammation, insulin resistance, and hormonal imbalance, thereby explaining many of the therapeutic effects reported for herbal remedies. Further research to identify molecular targets, understand pharmacokinetics, bioavailability, and evaluate long-term clinical outcomes remains essential for translating phytochemical research into evidence-based female reproductive healthcare (49).

6. Medicinal Plants Used in the Management of PCOS

Herbal remedies as complementary treatments for PCOS have been the focus of research due to their capacity to address multiple PCOS pathogenic mechanisms at the same time, which are hyperandrogenism, insulin resistance, persistent inflammation, oxidative stress, and ovulatory dysfunction. Rather than modern medicines that usually address just one medical problem, botanical extracts typically consist of countless compounds with the potential to affect different hormonal and metabolic pathways (**Table 1**). The medicinal herbs featured here have been studied for their effects on the endocrine system, metabolic functions, and the reproductive cycle (10, 12). For more detail on their chemical compositions, potential medical use, safety issues, and the strength of the scientific evidence.

Table 1. Medicinal Plants Used in PCOS Management

Plant	Major Phytochemicals	Clinical Applications	Reference s
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 <i>Glycyrrhiza glabra (Licorice)</i>	Glycyrrhizin, glycyrrhetic acid, glabridin, liquiritigenin	Hirsutism, acne, hyperandrogenism	(12,47)
 <i>Aloe vera</i>	Acemannan, glucomannan, aloin, phytosterols	Insulin resistance, metabolic dysfunction	(49,50)
 <i>Actaea racemosa</i>	Actein, cimicifugoside, triterpene glycosides	Menstrual irregularities, ovulatory dysfunction	(51)
 <i>Angelica sinensis</i>	Ferulic acid, ligustilide, polysaccharides	Menstrual disorders, reproductive dysfunction	(52)





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 <i>Serenoa repens</i>	β-Sitosterol, fatty acids, phytosterols	Hirsutism, acne, androgenic alopecia	(53)
 <i>Mentha spicata</i>	Rosmarinic acid, luteolin, apigenin	Hirsutism, elevated testosterone	(54,55)
 <i>Cinnamomum verum</i>	Cinnamaldehyde, procyanidins, eugenol	Insulin resistance, menstrual irregularity	(56,57)
 <i>Trigonella foenum-graecum</i>	Diosgenin, trigonelline, 4-hydroxyisoleucine	Oligomenorrhea, metabolic dysfunction	(58,59)





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 <i>Berberis spp.</i>	Berberine	Insulin resistance, metabolic syndrome, ovulatory dysfunction	(43,60)
 <i>Curcuma longa</i>	Curcumin, demethoxycurcumin	Chronic inflammation, metabolic dysfunction	(61)

6.1 Emerging Botanicals with Stronger Clinical Evidence

Botanicals that affect the metabolic and endocrine irregularities seen in PCOS have gotten a lot of attention lately. *Berberis* species, a source of the alkaloid berberine currently have the most robust evidence that these herbs really work, with clinical studies showing they reduce insulin resistance, improve lipids, increase fertility rates, and enhance metabolic functions. *Cinnamon* also appears helpful in sugar control and restoring regular menstruation, whereas fenugreek likely helps metabolic and reproductive functions mainly by improving the body's responsiveness to insulin and production of certain hormones. Spearmint proved to be effective in managing hyperandrogenism features, probably through lowering free testosterone. *C. longa* has been a source of curcumin which exhibits anti-inflammatory and antioxidant properties that could be beneficial in PCOS patients. Even though there have been positive reports about these herbs, nowadays they must be regarded as aids rather than replacements for the standard lifestyle and medication treatments. Medicinal plants produce various active molecules that can modulate hormonal metabolic inflammation, and oxidative pathways, which are all part of





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PCOS pathogenesis. At the same time, the level of supporting evidence among different medicinal plants is very different too. Among them the best studied ones appear to be *liquorice*, *cinnamon*, *fenugreek*, *berberine*, and *spearment*, while for many others there is mainly the evidence of traditional use and some small studies. It is expected that the next studies will be mainly directed toward well-defined formulations, randomized controlled trials, and long-term safety evaluations so that these medicines would be included in the evidence-based guidelines for PCOS (12, 44).

7. Mechanisms of Herbal Drugs in PCOS Management

The use of herbal remedies as treatments for PCOS is mainly credited to the capacity of these plants to simultaneously attack several disease pathways. Then again of modern therapies that tend to attack just one mechanism, phytochemicals offer a range of biological activities which affect, in particular, hormonal activity, insulin response, inflammation, oxidative stress, and ovary function. With this diversity, plants and other herbal products might be able to help in the restoration of normal reproductive and metabolic functions of the patients with polycystic ovary syndrome (10, 12).

7.1 Anti-inflammatory Mechanisms

Chronic low-grade inflammation has been gaining ground as one of the top factors in the development of PCOS. Insulin resistance, hyperandrogenism, and ovarian dysfunction have all been linked to high levels of pro-inflammatory cytokines like tumour necrosis factor-alpha (TNF- α), interleukin-6 (IL-6), and C-reactive protein (CRP) in affected women. There is growing evidence that several medicinal plants house compounds that can dampen inflammatory pathways. These compounds like polyphenols, flavonoids, and curcuminoids effectively block the activation of nuclear factor-kappa B (NF- κ B), which is an important player in the regulation of cytokine synthesis and inflammatory reactions. The anti-inflammatory effects of curcumin from *Curcuma longa*, glycyrrhizin from *Glycyrrhiza glabra*, and rosmarinic acid from *Mentha spicata* have been reported in several in vitro and in vivo experiments. These plant extracts could reduce the production of inflammatory mediators and





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because of this aid PCOS women with metabolic disturbances and support ovarian function closer to normal.

7.2 Antioxidant Activity and Oxidative Stress Reduction

Oxidative stress is essential in PCOS development and progression. Over production of reactive oxygen species causes lipid peroxidation, mitochondrial defects, poor folliculogenesis, and insulin resistance. PCOS women often have low antioxidant capabilities and high levels of oxidative stress markers compared with healthy controls. Medicinal plants are potent providers of antioxidant compounds like flavonoids, phenolic acids, curcuminoids, and saponins, which act on free radicals and strengthen endogenous antioxidant protective mechanisms. These plant compounds can enhance the activity of antioxidant enzymes, including superoxide dismutase (SOD), catalase, and glutathione peroxidase, while lessening oxidative harm to ovarian tissues. Herbs with high antioxidant capacity might therefore help restore ovarian function, follicular growth, and metabolic regulation (11).

7.3 Regulation of Insulin Sensitivity

Insulin resistance is the primary pathological characteristic related to PCOS and is strongly linked to hyperandrogenism and metabolic syndrome. Several phytochemicals have shown the ability to improve insulin sensitivity through changes in major metabolic regulators. *Berberine* activates AMP-activated protein kinase (AMPK), cinnamon polyphenols improve insulin signalling through the PI3K/Akt pathway, and fenugreek-derived compounds enhance glucose metabolism and insulin sensitivity. These botanical remedies may reduce hyperinsulinemia, decrease androgen production, and improve reproductive health (12).

7.4 Modulation of Steroid Hormones

Hyperandrogenism is a defining endocrine abnormality in PCOS. Different medicinal plants are known to modulate steroid hormone synthesis and metabolism. *Liquorice* has been reported to reduce circulating testosterone, saw palmetto inhibits 5 α -reductase activity, and spearmint may reduce free testosterone while increasing sex hormone-binding globulin (SHBG). Together, these mechanisms may contribute to reducing androgen-related symptoms.





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7.5 Improvement of Ovulation and Fertility

Herbal medicines may improve reproductive function by addressing insulin resistance, inflammation, and hormonal imbalance. *Berberine* has shown beneficial effects on ovulation and reproductive outcomes, while black cohosh and *fenugreek* have demonstrated potential supportive roles in improving ovulatory function and menstrual regularity (**Figure 2**). Although the available evidence is encouraging, additional well-designed experimental and clinical studies are needed to establish their long-term efficacy and safety. Therefore, the following section critically examines the available preclinical and clinical evidence supporting phytotherapeutic interventions in PCOS (10, 12)

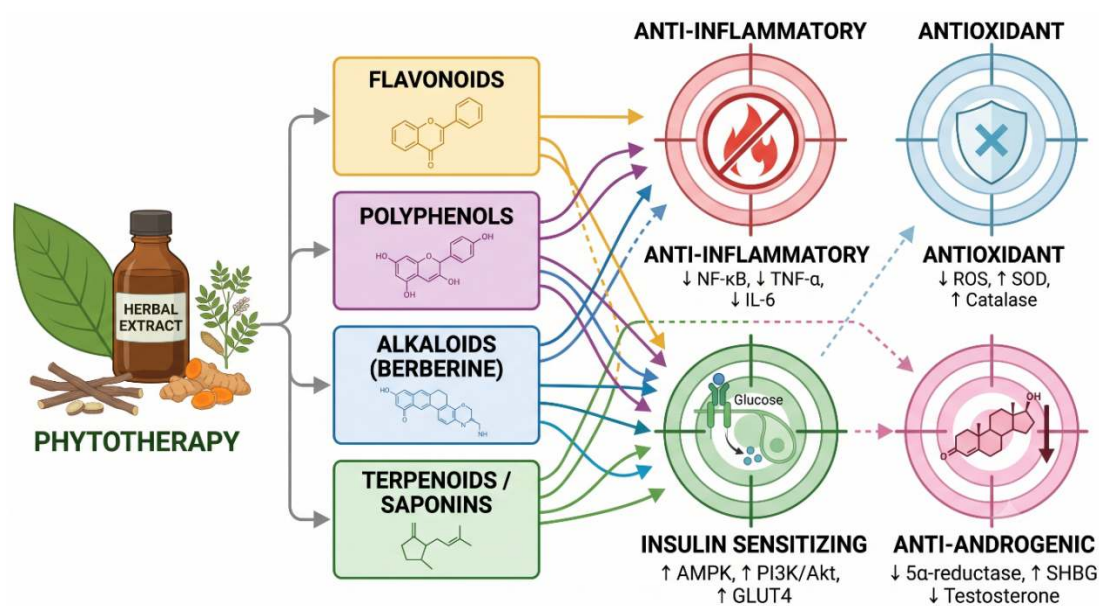


Figure 2: Mechanisms of Herbal Drugs in PCOS Management

8. Experimental and Clinical Studies

Diverse investigations including experiments on plants and their effects on patients have yielded substantial data demonstrating that herbs can have a beneficial effect in the treatment





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of PCOS. Laboratory experiments have identified bioavailable substances that show multiple biological effects like *berberine*, *curcumin*, *quercetin*, and *glycyrrhizin*, exhibiting properties like being antioxidants, anti-inflammatory and insulin-sensitizing which may work through the regulation of the key molecular signaling mechanisms involved in insulin resistance, inflammation, and the function of the ovary, including those of AMPK, PI3K/Akt, NF-B etc, making it the most likely mechanism for their therapeutic application. Evidence from the animal studies also adds to the weight of the case that is being made. For the letrozole- and testosterone-induced PCOS models, herbal interventions like Aloe vera, fenugreek, berberine, and curcumin can improve ovarian histology, re-establish estrous cycle, decrease the levels of plasma androgen, and increase the ability of the body to react to insulin. Despite these results, It helps to remember that differences between the physiology of the models and the humans mean that we should not jump to clinical conclusions. Studies performed in the clinical setting also show encouraging findings, even if the results are somewhat variable. Herbs considered as potential treatments have yielded the best results with *berberine* that has consistently been found in the treatment of conditions like insulin resistance, lipid metabolism, and reproductive functions. *Cinnamon* and *fenugreek* are both effective in managing glycemic control, metabolic parameters, and regularity of menstrual cycles. *Spearmint* is known to reduce levels of free testosterone and alleviate symptoms of the disorder. But, studies involving such herbs as *Aloe vera*, *Dong Quai*, *Black Cohosh*, and *Saw Palmetto* are not only limited but also the findings are inconclusive. Because of this, large high-quality human studies are necessary for the establishment of their therapeutic potential beyond a doubt. In general, most these herbal treatments seem to be safe when used with the due care. Still, the variability for concentration of active ingredients in the herbal extract, the dosage administered, period of treatment, and the nature of study makes the interpretation of clinical trial results problematic and comparing different trials a quite challenging task. In addition, possible undesirable effects and interactions of herbs with drugs should also be considered carefully, In particular since many women who are being treated for PCOS may also be using other medicines. The standard





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treatments metformin, OCs, and drugs that bring about the resumption of ovulation remain the most frequently used means of treating PCOS. Still, the present level of evidence shows that a careful choice of herbs may be combined with these as supplements rather than as alternatives to them. In order, a large properly constructed RCTs will help identify the safety profile and effectiveness of these supplements over the long term, and their exact place among therapeutic options per the clinical evidence will be clarified (12,62)

9. Challenges and Limitations

One of the biggest things in the way of using phytotherapy on a mass scale for PCOS is that there isn't a reliable source of standardized herbal products. Plant type, growing conditions, harvest methods and techniques of extraction are all factors that may modify the phytochemical profile and this way the therapeutic outcome. Besides, phytochemicals like curcumin that enter the stomach have very low bioavailability and we don't really know what the best dose is. All these facts diminish their effectiveness in the clinics. In particular, herb-drug interactions can be a real danger that takes very careful monitoring. Licorice for instance, may increase the risk of hypokalemia and hypertension, whereas berberine, cinnamon and fenugreek can intensify the action of diabetic drugs. Medical supervision of the therapy is Because of this a must. Quality issues are a big hindrance to their utilization for treatment purposes. Contamination adulteration inconsistent quality and changing regulatory standards are all factors that make it hard for patients to trust the product. In fact, most of what is known about these treatments comes from little trials done mostly in one area of practice, with no or a very quick aftercare, so there's not one agreed on approach. That means, a few good, large and double-blind, randomized controlled trials on human subjects should help to determine long term safety and efficacy profile of using herbs for PCOS (12, 62).

10. Future Perspectives

In order for phytotherapy to become a recognized part of PCOS treatment, much more solid scientific research has to back up its use. While lots of herbs have revealed encouraging results,





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we need big, proper controlled studies that use well-established herbal formulations and clinically reliable assessments, to prove the safety and effectiveness of those herbs. This kind of supporting evidence will be essential in promoting herbal treatments as part of PCOS care that is based on solid evidence. Recently, new methods of delivering drugs open the possibility for better herbal therapy benefits. New techniques like using herbs in tiny particles (nanoformulations), in small capsules (liposomes), attached to special molecules called phytosome, and in little particles made from plastics (polymeric nanoparticles) can improve the effectiveness of herbal remedies as well as target exactly where in the body they will deliver the benefit (pharmacokinetic targeted delivery). As PCOS varies widely among affected women, new ways of treating these people will likely get to the point of being able to customize care to the individual. Thanks to progress in pharmacogenomics, metabolomics, and precision medicine, doctors of the near future may be empowered to use specific herbal remedies as medicine that suits the metabolic, hormonal and reproductive profile of an individual patient and so leads to more efficient and effective treatment (62). A strategy that incorporates all aspects: diet and lifestyle changes, traditional treatments and herbal therapy with proven effectiveness, might offer the best way to treat PCOS. This way, we will be doing more than dealing with metabolic and reproductive problems. In fact, it will be enhancing the overall physical health of the patients and their life quality. And, Besides this topics, the study of herbal medicine should also cover other issues such as how safe they actually are for extended periods, the fact of interacting with other medication, their fertility-enhancing effect and pregnancy outcome, and identifying the new active substances that control the endocrine system. The continued research into these lines, in fact, will make known what the actual properties and uses of plants are, thereby allowing them to be integrated into women's healthcare properly, responsibly, and safely.

11. Conclusion

PCOS is a complex condition that can influence diverse areas of a health, such as fertility, metabolic issues, and general well-being. Given that the reasons and signs of the disease differ





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so much, controlling the symptoms and the disease is often beyond the scope of one-treatment-only. Plant based remedies are getting more consideration as potential adjuncts therapies for their multifaceted mode of affecting various biochemical pathways of the condition. Several plant derived medicines have got the phytochemicals which have therapeutic potential such as increasing insulin sensitivity, modulating anti-inflammatory cytokines, alleviating oxidative stress, normalizing hormonal imbalances, and supporting the ovary's healthy functioning. Even though the results are quite exciting, the data is limited due several variations in research set up, small populations and inconsistent herbal products. Only when a good clinical support is available, such treatment can become a common option for PCOS management. In this view, phytotherapy could constitute a great addition to a comprehensive medical care plan of a woman with PCOS. If properly designed clinical trial and standardized herbal composition and a custom treatment strategy are put together then such a treatment could be a good addition to the regular care and eventually help women with PCOS get a much better long-term health and quality of life.

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