

A comprehensive review on promisable herbal drugs for mitigation of polycystic ovarian syndrome

Sagar N. Ande¹, Komal N. Pavitrakar¹, Ravindra L. Bakal¹, Nitin I. Kochar²

¹Department of Pharmacology Toxicology, Dr. Rajendra Gode College of Pharmacy, Amravati, Maharashtra, India, ²Department of Pharmacology and Toxicology, P. Wadhvani College of Pharmacy, Yawatmal, Maharashtra, India

Correspondence:

Sagar N. Ande, Dr. Rajendra Gode Institute of Pharmacy, University-Mardi Road, Amravati - 444 602, Maharashtra, India. E-mail: sagar986ande@gmail.com

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ABSTRACT

Polycystic ovarian syndrome (PCOS) is a gynecological endocrine, metabolic, and genetic condition that affects about one in five women of reproductive age. Polycystic ovaries, chronic anovulation, and hyperandrogenism are all characteristics of this condition. Signs and symptoms of PCOS include monthly irregularity, painful menses, infertility, frequent miscarriage, acne, and hirsutism. It can also cause insulin resistance, obesity, and cardiovascular diseases. This signals the need for a multidisciplinary approach to treat PCOS. Traditional medicine, western medicine, drugs, surgery, and radiation treatment focus on a specific symptom and are frequently accompanied with risk and side effect including harmful interaction, allergic reaction, and unexpected effects as well as being inappropriate and inefficient in other cases. Complementary or alternative medicine such as herbal formulations containing herbal extracts of Ashwagandha, Shatavari, Nirgundi, Lodhra, Black cohosh, Ashoka, have been highly regarded natural sources with low side effect and additional benefits of reducing hyperandrogenism, insulin resistance, ovary weight, as well as contributing in hypoglycemic and anti-obesity effects. These plants have multiple chemical constituents with known or unknown mechanism of action, but they show significant effects on the PCOS. Many marketed formulations have these constituents in single or in combination with others. All these formulations have shown positive feedback from the patients of PCOS. These plant-based herbal formulations can be effective in this syndrome affecting serum levels of different hormones and ovarian morphology representing an opportunity to investigate and discover new bioactive products. Some of the most effective herbs and their formulations that play a critical role in the treatment of PCOS are summarized in this article.

Keywords: Herbal Formulations, Herbs, Hyperandrogenism, Infertility, Pathophysiology Of Polycystic Ovarian Syndrome, Polycystic Ovarian Syndrome

Introduction

Polycystic ovarian syndrome (PCOS) is associated with chronic oligoanovulation and polycystic ovarian morphology, as well as psychological impairments and metabolic abnormalities, primarily insulin resistance, and compensatory hyperinsulinemia, which may be responsible for altered androgen production and metabolism in reproductive age.^[1] PCOS puts women at a higher chance of having complications with their reproductive systems. This is also known as Stein–Leventhal syndrome, and it is a primary cause of infertility in women. Hormone imbalance has a variety of causes, none of which

are conclusive. For PCOS, various pharmaceutical therapies have been proposed.^[2] Due to the adverse effects of long-term allopathic and other chemical-based, radiation-based treatments, as well as their low efficacy, complementary and alternative medicines have become a valuable choice these days.^[3] Herbal formulations are currently being recommended as a part of complementary treatment, they are naturally occurring medicines that have been shown to be beneficial in treating a number of PCOS symptoms with minimal or no industrial processing. In this Review, we evaluated different herbs and herbal formulations that are widely used to treat PCOS. Traditional, conventional, and modern herbal formulations are attracting a lot of attention in the world of global health. It has become crucial to demonstrate that herbal therapy can compete in terms of scientific rigor and practical application with other professions of medicine.^[4] Herbal formulation treatment has the advantage of being safer than other pretended therapy, with less side effects and a broad choice of active compounds in herbs.^[5] Herbal drugs such as ashwagandha, shatavari, nirgundi, lodhra, ashoka, and black cohosh are effective in

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management of PCOS. All these drugs are discussed in this article with their pharmacognosy and therapeutic effects.

Types of PCOS

PCOS has types as (1) insulin resistance PCOS, (2) post pill PCOS, (3) inflammatory PCOS, and (4) adrenal PCOS.^[6]

Causes of PCOS

According to studies, the following are the causes of PCOS: Genetic susceptibility, insulin resistance and obesity, strong stimulations in adrenal glands in childhood, hormonal imbalance, accumulation of toxins, inflammation to uterus and ovaries, stress, etc.^[4-7]

Symptoms of PCOS

Around the time of their first menstruation, some women begin to experience symptoms. Others are not aware that they have PCOS until they acquire weight or have difficulty conceiving. PCOS is marked by irregular or absent menstrual cycles, heavy periods, excessive body and facial hair, acne, pelvic discomfort, infertility, and thick, darker, velvety skin in some areas. Type 2 diabetes, obesity, obstructive sleep apnea, heart disease, mental illness, and endometrial cancer are all linked to PCOS. The ovaries produce a large number of little fluid-filled sacks called follicles, which may fail to release eggs on a regular basis. This condition is caused by a rise in the number of follicles per ovary from an average of 6–8/month to double, treble, or more per month. PCOS manifests itself in a variety of ways. When you have at least two of these symptoms, you are diagnosed with PCOS. The following is the most common PCOS symptoms.^[3-8]

Menstrual Problems

PCOS is most usually associated with oligomenorrhea or amenorrhea, although it can also cause other menstrual problems.^[8]

Infertility

The most prevalent cause of infertility is prolonged anovulation (lack of ovulation).

Increased Levels of Masculinizing Hormones

The most frequent signs of hyperandrogenism are acne and hirsutism (male pattern hair growth, such as on the chin or chest), although it may also cause hypermenorrhea (heavy and extended menstrual cycles), androgenic alopecia (increased hair thinning or generalized hair loss), and other symptoms. Hyperandrogenemia affects almost three-quarters of women with PCOS.^[6-8]

Metabolic Syndrome

This is defined by a predisposition to central obesity, as well as other signs of insulin resistance and dietary aversions. Serum insulin, insulin resistance, and homocysteine levels are all higher in PCOS women.^[4-8]

Polycystic Ovaries

The ovaries may expand and follicles that enclose the eggs may form. The ovaries may become dysfunctional as a consequence of this.^[9]

Heavy Bleeding

Because the uterine lining develops up over a longer length of time, your period may be heavier than usual.^[4,5]

Organs Involved in Manifestation of PCOS

PCOS is a multiorgan disorder that affects the majority of the endocrine organs, including the testes, ovaries, and pancreas.^[1-5]

Ovary

In PCOS, the ovaries grow by 2–4 times and are surrounded by a number of fluid-filled sacs known as follicles (string of pearl morphology). Due to an excess of Androgen, these sacs stay immature and unable to release an egg, leading in anovulation.

Pituitary gland

The pituitary gland produces luteinizing hormone (LH) and follicle-stimulating hormone (FSH). In general, LH regulates the ovary's production of female hormones (estrogen and progesterone), while FSH regulates the ovary's development and release of eggs. Hypersecretion of LH which stimulates androgen production, and decreased secretion of FSH, which affects both ovarian androgen production and oocyte development, and also results in the disruption of hypothalamic-pituitary-ovarian (HPO) axis.

Adrenal gland

In PCOS, the adrenal glands are in charge of releasing excess hormones. Both at rest and in response to pituitary hormone, PCOS patients create excessive pregnenolone and DHEA in the adrenal cortex. Patients with PCOS have been found to have an enhanced peripheral cortisol metabolism as well as an excess of adrenal androgens.

Pancreas

Excess insulin production from the pancreas is noted in many cases of PCOS, leading in insulin resistance. Insulin resistance can result in hyperinsulinemia, which causes the ovaries to overproduce androgen, resulting in hyperandrogenism and hypertrophy. To maintain a normal glucose and lipid level, more insulin is required. The pancreas is in charge of regulating blood glucose and fat levels (lipids).

Pathophysiology of PCOS

PCOS develops in the early years of puberty.^[6] However, the majority of relevant data have come from clinical trials including adult women, with referral bias focusing on the more severe phenotypes. Excessive ovarian and/or adrenal androgen production are a feature of PCOS.

Excessive ovarian androgen production is caused by both intrinsic ovarian mechanisms such as altered steroidogenesis and external ovarian causes like hyperinsulinemia. In women with PCOS, there are more developing follicles compared to normal controls, and antral follicle development is prematurely stopped around 5–8 mm. Androgen exposure causes the typical ovarian phenotype of enlarged ovaries with string-of-pearl morphology and theca interstitial hyperplasia; similar morphology has also been seen in women with congenital adrenal hyperplasia and female-to-male transgender persons.^[8] Ovarian dysregulation in PCOS may be caused by distorted interactions among the endocrine, paracrine, and autocrine systems involved in follicular development. Follicular maturation phases are briefly discussed. Pregranulosa cells surround meiotically arrested oocytes in primordial follicles, which form throughout pregnancy. As a result, throughout pregnancy, a woman's ovaries have been exposed to the ambient maternal environment. Until the commencement of adolescence, the ovaries remain mostly dormant.^[10] The morphology of follicles in prepubertal and early pubertal ovaries is poorly understood. Follicle form and development potential vary between prepubertal and early pubertal females' ovarian tissue. Prepubertal ovaries, in particular, have a higher number of aberrant no-growth follicles than pubertal ovaries.^[9] The physiologic significance of this discovery is unknown.

Diagnosis of PCOS

The recognition of historical and physical signs of the illness process is frequently the first step in the diagnosis of any disorder. These clues could be brought to the medical provider's attention by the patient or discovered during a regular history and physical examination.^[4-8] Whatever method is used to bring these difficulties to light, the next step is to investigate the results further with a more complete history and examination aimed at determining the diagnosis and differential diagnosis. This is critical in the examination of PCOS because, once again, there is no "single test" that can diagnose the condition. Following diagnosis can be used for PCOS detection.^[10]

A Pelvic Examination

The doctor looks for lumps, growths, or other abnormalities in your reproductive organs visually and physically.

Blood Tests are Performed

Blood tests may be used to evaluate hormone levels. This test can rule out PCOS-like menstrual abnormalities as well as androgen excess. Additional blood tests are carried out as well.

Ultrasound Device

This test uses sound waves to create images of blood vessels, tissues, and organs to find cysts. This examination also includes a measurement of the thickness of the uterine lining (endometrium). A wand-like equipment (transducer) is introduced into your vaginal canal (transvaginal ultrasound). The transducer emits sound waves, which are converted into graphics on a computer screen.^[11]

Blood pressure, glucose tolerance, cholesterol, and triglyceride levels should all be checked on a regular basis.

Treatment of PCOS with Herbal Drugs^[12-15]

We are using many herbs for human body maintenance since decades, for example, ashwagandha, shatavari, nirgundi, lodhra, ashoka, and many more. These herbs have alkaloid, cardiac glycosides, anthraquinones, flavonoids, mucilages and enzymes which have multiple pharmacological actions.^[16] These herbs can be used solely or in combination for treatment of PCOS. Some of the herbs and marketed formulations are discussed here.

Ashwagandha (Ginseng)

Botanical name: *Withania somnifera*, Family: *Solanaceae*.

The adaptogenic herb Ashwagandha is recommended in PCOS by Ayurvedic traditional texts, clinical experiences, and scientific data. Ayurveda recognizes the herb particularly for its building, strengthening, and nourishing nature. Ashwagandha's adaptogenic (anti-stress) characteristics help to balance hormone levels and thyroid function, enhance adrenal function, normalize cortisol levels, and keep insulin levels in control in the body.^[17] Ashwagandha can help with anxiety and depression symptoms associated with PCOS. Ashwagandha produces calming, anti-stress, and extremely stabilizing effects by binding to GABA receptors. Furthermore, tryptophan, a component of serotonin, the mood-lifting hormone, is found in ashwagandha root. It also relieves menstrual pain and corrects irregular menstrual cycles. Ashwagandha root extract lowers serum cortisol levels, which are elevated under stressful situations. It corrects the imbalance between the immune and neuroendocrine systems by targeting the hypothalamic-pituitary-adrenal gland axis, restoring bodily processes under stressful conditions. Ashwagandha helps reduce apoptosis and also prevents the growth of new cancer cells.^[18] *W. somnifera* root extract and leaves contain flavonoids that have hypoglycemic and hypolipidemic effects. Ashwagandha raises urine volume and salt content while reducing cholesterol levels. Some of its marketed products are enlisted in following Table 1 with brand and key benefits.

Shatavari (Sataver white)

Botanical name: *Asparagus racemosus*, Family: *Asparagus*.

Shatavari is the Sanskrit name for a medicinal plant identified with *Asparagus racemosus*. Due to their phytoestrogen content, the dried roots of the plant are used as a medication. It stimulates the formation of ovarian follicles, regulates the menstrual cycle, and revitalizes the female reproductive system.^[19] The roots have a tonic, diuretic effect, and therapeutic impact that boosts mucosal resistance and cytoprotection. It also aids in the treatment of hyperinsulinemia, the dissolution of cysts, and the prevention of new cysts from forming. Dyspepsia, tumors, inflammation, and neuropathy are all treated by shatavari. It serves to maintain hormone levels and the HPO axis in check.^[20] The *Asparagus racemosus*'s roots are boiled and the resulting liquid is used as an external wash for improving immunity, and increasing longevity. Some of its marketed products are enlisted in following Table 2 with brand and key benefits.

Nirgundi (Chasteberry)

Botanical name: *Vitex agnus-castus*. Family: *Lamiaceae*.

Nirgundi is a medicinal herb that has been extensively studied and used. It contains a certain amount of essential oil, alkaloids, and other phytoconstituents that aid in the treatment of menstruation irregularities, PCOS, and infertility. This herb can be used to control ovulatory cycles and alleviate hot flashes caused by low progesterone levels during menopause.^[21] Vitagnus has been demonstrated in clinical trials to reduce testosterone and LH levels, while raising FSH, estrogen, and progesterone levels, which can aid with premenstrual and hyperprolactinemia. *Vitex anus castus* is thought to aid in the treatment of PCOS by modulating kisspeptin gene expression. Nirgundi relieves pain, inflammation, and appetite loss. About 70 common and complicated disorders can be treated with the essential oil from fresh leaves. It is also commonly used in the treatment of oxidative stress, inflammation, CNS activity, and hepatocellular carcinoma.^[22] Some of its marketed products are enlisted in following Table 3 with brand and key benefits.

Table 1: Marketed preparations of Ashwagandha and its key benefits (tablet/capsule)

S.No.	Brand name and manufacturer	Key benefits
1	Himalaya (Himalaya global holdings Ltd.)	Stabilizes endocrine gland and nervous system
2	Rooted (Clearprisetec. Ltd.)	Regulates insulin and inflammation
3	Nutri Rise (NutriRise)	Control diabetes and balances cortisol
4	Jiva (Jivaayurvedicpharma)	Effective in Menopausal osteoporosis

Table 2: Marketed preparations of shatavari and its key benefits (powder/caplet)

S.No.	Brand name and Manufacturer	Key benefits
1	Vedaone (Atrey pharmaceutical Pvt. Ltd.)	Promotes, fertility and decrease inflammation
2	Royal bee (Royal bee Natural products Pvt. Ltd.)	Body detoxifier, acidity regulator
3	Shatavari (join lifesiences Pvt. Ltd.)	Deal with small cysts in ovaries and In prolactin production
4	Himalaya (Himalaya global holdings Ltd.)	Regulates and eases menstrual cycle

Table 3: Marketed preparations of Nirgundi and its key benefits (syrup oil capsules)

S.No.	Brand name and Manufacturer	Key Benefits
1	Krishna's herbal and ayurveda (Rajputana Agrico)	Reduces inflammation, improves blood Circulation
2	Salvia (Salvia Cosmeceuticals)	Muscle relaxant, calm menstrual pain and relives stress
3	Herbo natural (Herbo natural Pvt. Ltd.)	Reduces cramps and fluid retention
4	Ayurveda 24 (Trade India)	Increase fertility, reduces testosterone

Lodhra (Lodh)

Botanical name: *Symplocos racemosa*, Family: *Symplocaceae*.

Lodhra tree belongs to *S. racemosa* species. Is a *Symplocaceae* family plant that is commonly utilized in Ayurvedic treatment for feminine disorders? It is also known as Lodhra and is used as a single drug or in multi-component formulations and preparations in the Indian System of Medicine. In a Letrozole-induced female rat model, the anti-androgenic effects of *S. racemosa* in the treatment of PCOS were studied. Estrogen, testosterone, progesterone, and ovarian tissue levels all improved significantly after treatment with *S. racemosa*. In PCOS, it promotes fertility and prevents ovarian cell failure.^[23] The impact creates a contrast between these characteristics. Lodhra reduces testosterone while raising estrogen and progesterone levels. As a result of this action, it can help with conditions like PCOS. The herb's light and drying qualities appear to be at conflict with this effect. Hemorrhoid-related bleeding has been proven to be reduced by Lodhra.^[24] Some of its marketed products are enlisted in following Table 4 with brand and key benefits.

Table 4: Marketed preparations of Lodhra and its key benefits (syrup powder)

S.No.	Brand name and Manufacturer	Key benefits
1	Baidhyanath (Shree baidyanath Ayurved)	Treats gynac ailments, and balance Hormones
2	Dabur Lodhrasav (Dabur India Ltd.)	Repairs endometrium cures menorrhagia
3	Pavaman (Pavaman pharmaceuticals)	Prevents heavy and prolongmenses
4	lodhra (Kesari)	Provide uterus strength, relives pain and discomfort

Table 5: Marketed preparations of Ashoka and its key benefits (syrup, powder, and capsule)

S.No.	Brand and Manufacturer	Key benefits
1	Deep Ayurveda (Deep Ayurveda healthcare Pvt. Ltd.)	Treat hemorrhagia and menstrual disorders, prevents anemia
2	Ashoka (Herbs forever ltd)	Treats PMS, Including hormonal balance
3	Dr. Wakde's (Natural health care)	Boosts fertility, treats irregular menses
4	Xovak pharma (Xovac pharma)	Removes cysts, control heavy bleeding, Tones uterine muscles

Table 6: Marketed preparations of black cohosh and its key benefits (Tea, capsule)

S.No.	Brand and Manufacturer	Key benefits
1	Alvita (Alvita pharma Pvt. Ltd.)	Boost immunity, strengthen uterus lining
2	Livstamin (Livstamin healthcare)	Body, mind hormone balancer during menopause
3	Sudance (Piping rock health products)	Reduces imbalances of estrogen, supports fertility
4	Higher tea (Higher tea Ltd.)	Settles hormones, body temperature and calms mind

Table 7: Marketed products with multiple herbs used for PCOS

S. No.	Brand and Manufacturer	Polyherbs used	Key benefits
1	Gynoveda (Gynoveda) capsules	Methi Neem Manjistha Shatavari	Controls cysts reduce insulin resistance
2	Body-wise (Mosaic wellness Pvt. Ltd.) capsules	Ashwagandha Red chandan Gokshur Lodhra	Balance hormones and regularize delayed periods
3	Dr. Vaidya's (Herbolab India Pvt. Ltd.) capsules	Ashoka Kumari Kanchar guggul Satapushpa	Helps restore hormonal balance controls hirsutism
4	Herbalife (herbalife nutrition) tablets	Nirgundi Soya	Regulates menstrual cycle manages obesity
5	Nuskhe (Paras) capsules	Amla Ashwagandha Flex seeds	Reduce free testosterone Controls acne

Ashoka (Ashoka tree)

Botanical name: *Saraca asoca*, Family: *Leguminosae*.

The word "Ashoka" means "no suffering," and the tree's multiple parts are used in a variety of medical applications.^[25] The Ashoka tree is renowned for its many health benefits. Women's menstrual diseases, including as dysmenorrhea, stomach ache, and uterine spasms, are commonly treated with the bark and leaves of the Ashoka tree. The Ashoka tree's bark contains a lot of tannins, flavonoids, and glycosides, which are all uterine tonics. The Ashoka tree's roots and seeds are used to treat skin conditions such as acne in PCOS, psoriasis, and dermatitis. The herb of the Ashoka tree relieves abdominal pain and spasms by acting on the uterine muscles and endometrium. It also helps with irregular menstrual cycles, amenorrhea, leucorrhea, fibroids, cysts, and other related issues. As a result, the Ashoka tree is frequently used to treat gynecological and menstrual illnesses in women.^[26] Some of its marketed products are enlisted in following Table 5 with brand and key benefits.

Black cohosh (Snake root)

Botanical name: *Cimicifuga racemosa*, Family: *Buttercup*s.

Black cohosh can be found growing wild in North America's verdant woodlands.^[27] The most prized portion of the black cohosh is the rhizomes (underground roots), which contain the majority of the active chemicals.^[28] Because it contains phytochemicals that can inhibit LH secretion, this herb has a significant impact on the endocrine system. PCOS, severe menstrual cramps, and hormone-related problems can all benefit from black cohosh. Black cohosh relieves pain by attaching to opioid receptors in the body.^[29] On a limited basis, it is now used to treat muscle aches and pains associated with menopause, perimenopause, and postmenopause. Fukinolic acid, a significant plant component in black cohosh, works as a phytoestrogen to assist women maintain hormonal balance and improve fertility by mimicking the effect of the hormone estrogen. Hot flashes, vaginal dryness, palpitations, and insomnia are all symptoms of menopause.^[30] Agitation, restlessness, and irritation black cohosh are currently commonly utilized as a tonic to help women's health. Some of its marketed products are enlisted in following Table 6 with brand and key benefits.

Some other herbal marketed products which include more than one herbs are enlisted in following Table 7.

Conclusion

PCOS is one of the most prevalent female reproductive illnesses. The management of this syndrome is possible with herbal drugs such as ashwagandha, shatawari, nirgundi, lodhra, ashoka, and black cohosh with a single herb or in combination.

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