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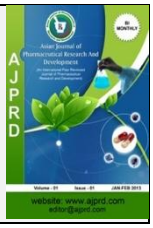

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Review Article

Therapeutic Effect of Herbal Medicinal Plants on Polycystic Ovarian Syndrome: A Review

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A B S T R A C T

Abstract:

Polycystic ovarian syndrome (PCOS) problem affects mature female in entire world. Menstrual irregularity, infertility, and hirsutism symptoms are all caused by PCOS patients' altered androgen and oestrogen metabolism and secretion rates. PCOS is associated to insulin resistance, obesity, and amplified concentration of hormones found in male. Both allopathic and natural treatments can be used to treat PCOS, which is becoming more common, as well as the physical and emotional issues it is connected with. Changes in sex hormones can also contribute to the development of this disease. *Asparagus racemosus, Bauhinia variegata, Nigella sativa, Vitex negundo, Cocus nucifera,* and other herbal plants have bioactive compounds that are safe and efficient for treating PCOS and associated complications. This review attempts to comprehend the bioactive components of natural medicinal plants that are either utilised alone or in combination to treat this condition.

Keywords: Ovary, cysts, hormone, obesity, herbs, metabolism

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is a slow occurring and assorted chaos of the endocrine system, characterized by menstrual dysfunction, infertility, hirsutism, acne and obesity[1.] It has been reported that both environmental and gentic related factors are concern with this disease, causes fatness and infertilty[2, 3]. This disease leads a remarkable loss in the quality of patients' life when diagnosed[4.] It has been reported that approximately 8-21% women of reproductive age affected with this disease globally and leads to great economical pressure which is forced by disease and is characterized by its elevated occurrence and association with release of egg during monthly cycle and menstrual abnormalities, infertility, hair loss, and metabolic issues [5,6,7.] Though Polycystic ovary syndrome can grow at any age, initially beginning of period and between the ages of 20 and 30, number of cases are recognized [8.] According to the Global Burden of Disease (GBD) project, it has been reported that occurrence of PCOS has not been significantly observed at regionally, nationally or internationally along with its association with research and socioeconomic condition[9]. Despite its great frequency, PCOS's actual aetiology is still unknown, and there is no known treatment for it [10.] Due to ovarian steroids and implants, this condition has found to be primarily afflicting mature female among the ages of 25 and 35. There is a definite connection between endometriosis and [11.] Women's social, mental, and physical wellbeing are all impacted by endometriosis. Endometriosis affects approximately 10% of females, according to statistics [12.] According to studies, the pathogenesis of endometriosis is unclear; however, the main mechanism of the diseased state is caused by the spread of the endometrium to various ectopic sites, as a result of which ectopic endometrium is deposited [13.] This review defines

the only some environmentally present natural herbs used for cure and their role in the management of PCOS-related issues.

SEARCHING METHODS

A thorough assessment of the literature was done using Google Scholar, PubMed, Elsevier, the Scientific Information Database, Pharmaceutical review articles, Scientific reports, Science Direct and various research Articles,

Essentiality to study PCOS: Studying PCOS is essential because two out of every ten Indian women have the condition, according to a PCOS Society study. Six of every ten women with PCOS are still in their teen years. A necessary side effect given that PCOS requires long-term management They may show promise in addressing the causes of PCOS, relieving symptoms, and promoting the body's natural healing processes by enhancing your immune system[15].

Organs involved in PCOS: Ovaries, adrenals, pituitary, fat cells, and the endocrine pancreas are just a few of the endocrine organs that are affected by PCOS, which is a multiorgans illness. The ovaries are producing more androgen, which inhibits the maturation of ovarian follicles. An ovulation results from an improperly formed and unreleased ovum. When sperm and ovum come into contact fertilization result. Therefore, if a woman has PCOS, she will have trouble getting pregnant because her ovum is unavailable. PCOS is linked to a number of anatomical abnormalities. The stroma increases and ovaries are get inflamed two to five times of their normal size (Fig.-1.). The capsule has grown in size and is pearly white in hue. The typically oval-shaped ovary will have a lot of cysts[16.] Poor diet, according to a poll, is the main lifestyle factor that causes PCOS. Young, anxious women with PCOS have a tendency to consume excessive amounts of fat, sugary drinks, and highly refined carbohydrates, which raises insulin levels unhealthily. Insulin causes the usual symptoms of PCOS, which also contribute to the obstruction of ovum release from follicle, by stimulating androgen receptors outside of the ovary. This kind of diet will lead to obesity, which will worsen PCOS and it will also result in the development of obesity-linked PCOS[17].

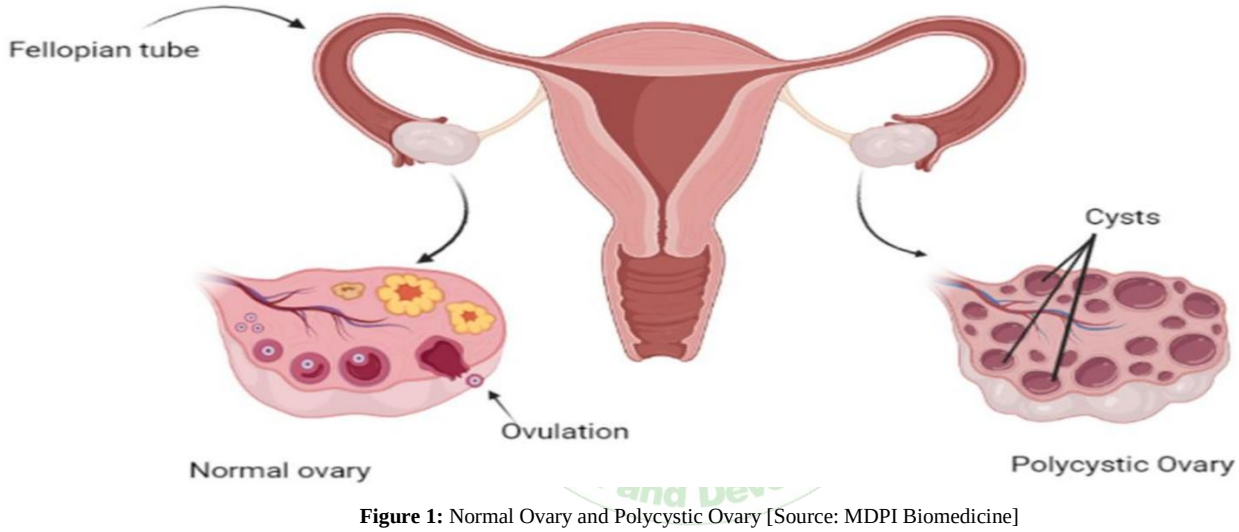

Figure 1: Normal Ovary and Polycystic Ovary [Source: MDPI Biomedicine]

Pathogenesis of PCOS

PCOS symptoms can be mild to severe, some women can't get pregnant, simply have menstrual issues, or both. PCOS common signs and symptoms include:

- No periods at all or irregular periods
- Trouble conceiving (no ovulation)
- Put on weight, hair loss
- Hirsutism
- Oily skin, acne
- Infertility
- Depression and mood swings
- High blood pressure and high cholesterol
- Type 2 diabetes
- Cancer of the lining of the womb
- Sleep apnoea
- Endometrial cancer

Reasons for PCOS

The specific basis of (PCOS) is unsure, but deviant hormone levels are considered to the main cause for this. The following factors are also responsible for the disease:

Insulin resistance

The pancreas secretes the hormone insulin, which aids in regulating blood sugar levels.Extra insulin is produced as a result of insulin resistance. High insulin levels cause the ovaries to overproduce testosterone, which interferes with follicle growth and prevents healthy ovulation. Follicles are the sacs in the ovaries where eggs form. Since the body produces more insulin as a result of the additional fat, weight gain brought on by insulin resistance may make PCOS symptoms worse [18.]

Hormone imbalance

Small amounts of luteinizing hormone (LH), which induces ovulation, may cause adverse effect on the ovaries, if concentrations are too high, are produced by PCOS patients and are discovered to have disproportion in testosterone and elevated amount of this hormone. Low levels of SHBG, a blood protein that binds to testosterone and lessens its effects, was associated with higher concentration of prolactin (only in certain women with PCOS), a hormone that increases the production of milk in the breasts

during pregnancy. It is unknown exactly why these hormonal changes take place[19].

Genetics

The syndromic disorder PCOS is polygenic and multifactorial. PCOS can run in families in some cases. Although PCOS has an autosomal dominant genetic inheritance, the most recent research has shown that the condition has several gene origins. Many genetic loci and particular genes have been shown to be connected to this illness according to genome-wide association studies [21].

Diagnosis

Adolescents with PCOS may have difficulty being diagnosed. PCOS in adolescent should be diagnosed primarily on the basis of clinical and biochemical symptoms of hyperandrogenism and menstrual irregularities. Delaying the diagnosis for at least two years after menarche is advised because PCOS symptoms and normal pubertal development are comparable. Uncommon causes of the symptoms have been checked out and the patient has intermittent periods, and must focus on other symptoms managements. PCOS can be diagnosed male hormones "testosterone" in blood tests. If your ovaries contain a significant number of follicles, an ultrasound scan can reveal this (polycystic ovaries). The fluid-filled sacs called follicles are where eggs grow. A blood test checks for diabetes and excessive cholesterol as well as hormone levels.[22]

Treatment-Polycystic ovary syndrome

It is not possible to find a treatment strategy that is ideal for all PCOS women; instead, patients only get symptomatic relief [23, 24]. According to the patient's state and the complication of the disease individualized cure strategies are required [25, 26].

Non-Pharmacological Approach

Weight Loss

Due to an overabundance of androgen, PCOS women have obesity, particularly in the abdominal region. For these girls, losing weight is the first line of treatment. A 5% weight loss may help PCOS women's irregular menstrual cycles, according to the study [27]. Lowered free testosterone and decreased metabolic syndromes are the outcomes of achieving a normal BMI level [28].

Diet

Great strategy for losing weight is to eat the correct foods, particularly those that are rich in fibre, low in glycemic index, and high in unsaturated fat. In order to avoid those 29, patients need also be mindful of high glycemic index foods.

Exercise

Exercise is crucial to the process of losing weight [30]. Diet and exercise both influence how well the ovulation cycle is regulated. Hypothalamus-pituitary-gonadal (HPG) axis modulation is the mechanism responsible for ovulatory control [31].

Complementary and Alternative Medicines (CAM)

It has been reported that merely 60% of PCOS patients have been treated pharmacologically [32]. A mix of nutritional, psychological and physical, variables are all included in CAM methods[33]. A sort of adjuvant therapy, which incorporates CAM 34, has traditionally been used in the management of PCOS. In addition, 70% of PCOS female patients had used such a treatment at least once. Immunotherapy, yoga, spa, and food therapy (herbs, probiotics, and supplements) come under CAM and proved to be useful.[35-40].

Acupuncture

In China, this complementary medicine has been practiced for more than 3,000 years. For sensory stimulation, the little needles are inserted into the skin and muscles which leads to increased endorphin production and improves the clinical symptoms of PCOS [31, 33].

Diet Therapy (Health Supplementation)

In addition to the medications, several supplements, such as vitamin D, resveratrol, lipoic acid, omega 3, folic acid, myoinositol, and d-chiro inositol, have proved successful in treating PCOS in females [34-37]. Myoinositol, d-chiro inositol, and other compounds have been shown in studies to enhance the incidence of ovulation and decrease the regularity of FSH-targeted ovulation for pregnancy [38-40].

Medicinal Approach

Patients with PCOS are always advised to lead a healthy lifestyle that includes diet and exercise. The medical strategy is determined by the condition and preferences of the patient [41, 42, 43].

Intermittent or absent periods

Periods were brought on by using the pill, which also lowers the long-term risk of endometrial cancer. Other hormonal methods of contraception, such as an intrauterine device (IUS), will reduce the chance of it by keeping a thin womb lining, but they might not cause periods [44].

Fertility troubles

The drug metformin is frequently used to treat type 2 diabetes, lowering high cholesterol levels, heart disease and also for promoting regular ovulation, and lessen the possibility of miscarriage. Clomifene is occasionally substituted for letrozole when trying to promote ovulation. Breast cancer can also be treated with this medication. Gonadotrophins are a separate class of medication that may be suggested in order to become pregnant despite taking oral medications. [45].

Unwanted hair growth and hair loss

It has been found that combined oral contraceptive pill is typically utilized to treat both hair loss and excessive hair growth (hirsutism) (alopecia). The development of undesirable facial hair can also be slowed down by applying a lotion called eflornithine. For hair growth, anti-androgens such cyproterone acetate, spironolactone, flutamide, and finasteride may also be used. A minoxidil lotion applied to the scalp may be advised for hair loss on the head[46].

In vitro fertilization treatment

When PCOS medication and trying to conceive are unsuccessful, *in vitro* fertilization (IVF) cure is helpful which entails removing eggs from the ovaries and fertilizing them exterior of the uterus and fertilized egg after needed procedure is returned to the uterus for further developmet[47.]

Surgery

For PCOS-related reproductive issues, a laparoscopic ovarian drilling (LOD) has been shown to increase follicle-stimulating hormone (FSH) levels while decreasing testosterone and luteinizing hormone (LH) levels (FSH) and results in the correction of hormone imbalance and can return the ovaries' normal functioning [48.]

Herbal Treatment of PCOS

Medicinal plants play important role in the alleviating of polycystic ovarian syndrome symptoms by the herbal extracts' treatment. The following medicinal plants are used to treat PCOS:

***Tribulus terrestris* (Puncture vine):** Traditional medicine makes use of *Tribulus terrestris* (Zygophyllaceae), also referred to as Puncture Vine or Devil's Eyelashes. It was discovered that *Tribulus terrestris* works well for polycystic ovarian syndrome and the extract of this plant is very efficient in enhancing ovulation in rats, according to research done in animals with polycystic ovaries caused by estradiol valerate. The use of extracts stabilized ovarian follicular development, steroidal hormone levels, and estrous cyclicity. *Tribulus* is a superb option for women with polycystic ovaries since it is a potent, all-around ovarian stimulant and female fertility tonic, according to many herbalists[49.]

***Gymnema sylvestre* (Gymnema):** This palnt belongs to Asclepiadaceae family, is a plant that has historically been utilised in the Ayurvedic medical system. It has a number of pharmaceutical effects, including antidiabetic, hypoglycemic, and lipid-lowering ones. Saponins, particularly gymnemic acids, are the *Gymnema* plant's active ingredient. *Gymnema* may have hypoglycemic effects in diabetic experimental animals. It controls the level of blood glucose. It is common practise to treat PCOS with metformin. *Gymnema* can therefore be utilised to treat the underlying cause of insulin resistance. Due to its ability to modulate insulin and the additional advantages of lowering the high triglycerides linked to PCOS and *Gymnema* is well recommended for PCOS [50.]

***Aloe barbadensis* (Aloe vera):** It belong to Liliaceae family, is a renowned plant with a mixture of therapeutic benefits. Gel of this plant has been used to treat and prevent polycystic ovarian syndrome. Formulation's phytocomponents of the plant were examined for flavonoids, polyphenols, sterols, and other nutrients. The Aloe vera gel formulation was subsequently administered orally to the female rats. Aloe vera reduces ovarian ateretic cysts, according to the results of the histological study. A PCOS control group was used to compare the outcomes. According to research, aloe vera may be effective or useful in the treatment and management of PCOS8 [51].

***Symplocos racemosa* (Lodh Tree):** belongs to Symplocaceae family, is primarily used for female health issues. In a female rat model induced by letrozole, the anti-androgenic effects of *S. racemosa* showed ovarian tissues and levels of oestrogen, testosterone, and progesterone significantly improved. It enhances fertility and stops ovarian cell malfunction in PCOS [52].

***Cocus nucifera* (Coconut):** *Cocus nucifera* (Arecaceae) flowers were found to have a positive impact on lowering the main PCOD symptoms that letrozole-induced female rats experienced. The estrogenic effect of *C. nucifera* flower extract, showed increased uterine weight and estrus cyclicity in rat. The recovery from poly cystic ovaries was demonstrated by the improved optimum lipid profile, good antioxidant status, blood sugar level, and histopathological results. Extract of *C. nucifera* brings down the active levels of hormones like FSH and LH to normal levels [53.]

***Linum usitatissimum* (Flaxseed):** The plant *Linum usitatissimum* (Linaceae), from which flaxseed is derived is well known for its high concentration of omega-3 fatty acids and is also one of the great sources of dietary lignan. Studies on the usage of isolated lignan or flaxseed indicate that they may normalize lipid levels and reduce androgen levels. The excess testosterone that is a main factor in the pathophysiology of PCOS appears to be reduced by lignans. According to a case study, supplementing with flaxseed may assist women with PCOS control their androgen levels. The analysis found that the levels of androgen and hirsutism had significantly decreased [54.]

***Ocimum sanctum* :**The main medical applications of the sacred herbal plant Tulsi are the treatment of hypoglycemia and obesity [55]. Because of its anti-androgenic qualities, it is used to treat polycystic ovarian syndrome. It controls obesity and reduces testosterone production. The anabolic steroids are not utilised by the body since proper ovulation does not occur. Unused androgens are the cause of hir sutism and the acne issue. Tulsi's function is to maintain and utilise androgen levels appropriately. Additionally, it has antioxidant properties [56,57,58].

***Tinospora cordifolia*:** The scientific name for the family member Guduchi is *Tinospora cordifolia*. A medicinal plant called Menispermaceae has a variety of medical applications, including hypoglycemia, anti-inflammatory, anti-stress, and ovarian balance. The pant uses the stem portion. Guduchi's primary use is in the management of PCOS. The primary contributors to tissue inflammation are insulin disturbances and ovarian cysts. Guduchi is thought to have anti-inflammatory properties. It serves to naturally strengthen immunity. Women who have PCOS develop insulin resistance, aids in overcoming resistance and modulates the menstrual flow.[59] All bodily tissues are regenerated by guduchi, which also aids in increasing immunity and metabolism [60, 61].

Nigella sativa A plant of significant therapeutic value that can be found all throughout the nation is *Nigella sativa*, and

belongs to the family, Ranunculaceae. It is thought to be actively employed in the treatment and management of polycystic ovarian syndrome in female patients. Women who suffer from PCOS are thought to have a higher risk of developing cholesterol. It has a favorable impact on the lipid profile because of choleretic activity [62-63.] According to another study, black cumin has been effective in helping PCOS-affected women's oxidative stress and dyslipidemia. The levels of steroids, the decreased fasting blood glucose, and the increased gonadotropin levels were all returned to normal. It directly affects insulin regulation and has an anti-androgenic impact to lessen PCOS side effects [64 , 65].

Hypericum perforatum : It belongs to member of the Hypericaceae family. The herb was prescribed by Greek doctors to cure menstruation disturbances[66.] There are various situations in which the patient's psychological discomfort or psychology could influence the course of treatment or reduce the likelihood of successful outcomes [67.] Any trigger that worsens stress or depression has a negative effect on ovarian function and the medications used to treat it Aiming for a synergistic impact or supporting the treatment for better results, patients with ovarian dysfunctions and PCOS are now embracing alternative medicine[68]. Women typically utilize plant extracts between the ages of 25 and 35 when they are fertile since they are widely recognized as synthetic medications that modulate serotonin. Plant extract of this plant is also used to treat depression[69-70-71].

Bauhinia variegata :The Indian subcontinent's tropical and temperate regions are home to the *Bauhinia variegata*, also known as Kanchanar, a tree with numerous therapeutic applications that has been used for a very long time in Ayurveda. Kanchanar guggul is the form of kanchanar that is used to treat PCOS. It works well to cure a variety of ailments, including PCOS, uterine cysts, various joint issues, and hormone imbalances[72, 73, 74.]

Caesalpinia bonducella: It belongs to family, Caesalpiniaceae and is widely distributed throughout globally. The phytochemical components of C. bonducella seeds include bonducellin, a homoisoflavone, caesalpinianone caesalpin, and g-caesalpin, a crystalline bitter molecule and F-furanoditerpene [75.] Several portions of the plant have therapeutic potential and used in the conventional medical system [76,77,78]. This plant's seed is used in India to control female fertility and parts of *C. bonducella* and other species are employed as emmenagogues and labor aids for expectant mothers [79.]

Actaea racemosa **(Black Cohosh):** it is used to treat a variety of female reproductive system illnesses, including PCOS-related problems with hormonal balance, infertility, and an ovulation [80, 81]. *Actaea racemosa* was well-known as a menstruation and childbearing-related women's treatment. Amenorrhea, leucorrhea, dysmenorrhea, and other uterine and menstrual problems could be effectively treated with it.[82]

Lepidium meyenii **(Maca):** belong to family, Brassicaceae and traditionally used to treat menopausal symptoms and to stimulates the endocrine system to maintain the normal level of hormones. The body's progesterone and oestrogen hormones aid in promoting a regular menstrual cycle. It is a powerful superfood for fertility and an adaptogen. The men' testosterone levels are restored by *Lepidium meyenii* [83].

Galega officinalis **(Goats Rue):** More clinical research is needed to determine *Galega officinalis's* (Fabaceae) therapeutic effects on women with polycystic ovarian syndrome and diabetes mellitus. However, it is the natural source of guanidine, a biguanide medication used to treat diabetes. The biguanide medication class includes Metformin, which is frequently prescribed for PCOS [84-85].

Areca catechu **(Betal Palm):** belongs to Arecaceae family and gently supports healthy female hormone synthesis and calms clogged blood vessels in the abdomen. *Areca catechu* helps to support a healthy libido, eases the transition into menopause, and supports a healthy female reproductive system. It aids in boosting the uterus's capacity for retention and is employed to treat postpartum debility [86].

Grifola frondosa **(Maitake Mushroom):** A perennial fungus known as *Grifola frondosa* (Meripilaceae) has a well-known for lowering diabetes [87.] In animal trials, *Grifola frondosa* extract was able to rouse ovulation in women affected with PCOS [88.] *Grifola frondosa* is thought to work by modulating blood glucose levels and improving insulin sensitivity [89].

Taraxacum officinale **(Dandelion Root):** An efficient liver detoxifier and stimulator of bile flow is *Taraxacum officinale* (Asteraceae). It is utilized to eliminate any hormone accumulation and cleanse the liver due to menstruation irregularities are frequently caused by the liver, which is backed up with too many hormones and boost the creation of SHGB, lowers the free testosterone in the blood and is utilized in PCOS treatment. Additionally, it aids in toxin clearance from the body, which benefits women who have menstrual and reproductive problems [90.]

Asparagus racemosus **(Shatavari):** Traditional uses for *Asparagus racemosus* (Asparagaceae) in Indian medicine (Ayurveda). Due to its phytoestrogen, it aids in maintaining the healthy growth of ovarian follicles, regulates the menstrual cycle, and revitalizes the female reproductive system (natural plant based estrogen). Additionally, it aids in the treatment of hyperinsulinemia [91.] In addition to the aforementioned effect, A. Racemosus has a number of other pharmacological effects and leads to the improvement of mental function [92].

Future prospective of PCOS

The disorder known as polycystic ovarian syndrome has a number of long-term, chronic health issues. On the long-term impact of PCOS on a woman's health, little research has been done to date. According to numerous studies, PCOS can cause women to have a variety of side effects, including mood fluctuations, weight gain, diabetes, heart disease, and miscarriage. Choosing the best treatments for women going through the postmenopausal stage is still a challenge. Numerous studies indicate that women with

PCOS had higher bone mineral density. To understand the health hazards associated with women's ageing, more research is needed. Identifying the relevant risk factors and genetic alterations are both essential. Long-term usage of synthetic medications is linked to a number of negative effects; as a result, it is advisable to treat PCOS over time to reduce these unwanted effects. It is advised to utilize natural products over the long term. In order to improve the prognosis, untimely recognition and cure are necessary for females who may experience infertility during their reproductive years. Important gene polymorphisms are useful for early PCOS subtype detection and screening. The discovery of vulnerable loci can be greatly increased through PCOS gene mapping, which can also help in the search for new disease pathways and therapeutic targets. It's an interesting idea that genetic risk markers can be used as diagnostic aids in precision medicine. Currently, the primary line of PCOS treatment is oral contraceptives. Menstrual abnormalities are treated with the use of these medications. There are also other more medications mentioned that could improve the likelihood of pregnancy. In order to boost chances of getting pregnant, PCOS women use more artificial methods.. The development of untimely diagnostic methods that take genetic diversity into account also contributes to a better PCOS prognosis. Early disease detection offers patients a improved course of treatment.

CONCLUSIONS

Pathophysiologically, PCOS is a complex disease. Patients may benefit from its early detection and treatment because it can postpone or prevent long-term effects. With advances in genetics, PCOS testing methods have gradually improved. Many of these herbal remedies have been defined by the Ayurvedic system in order to better understand their active principles and modes of action. The medicinal herbs we studied have a variety of possible health benefits for polycystic ovarian disease. Therefore, more pre-medical and experimental research is needed to examine the efficacy of herbal treatments for PCOD.

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