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Role of herbals in the management of polycystic ovarian syndrome and its associated symptoms

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Abstract
Polycystic ovarian syndrome or (PCOS) is a complex endocrinal and metabolic disorder affecting every 1 in 10 women worldwide of reproductive age. In these women hyperinsulinemia may contribute to the pathogenesis of PCOS by promoting abnormal androgen secretion, disrupting folliculogenesis and menstrual cyclicity. PCOS is associated with an increased risk of type 2 diabetes, high blood pressure and high cholesterol level this may finally lead to stroke and cardiovascular diseases. Early diagnosis of PCOS is necessary to prevent the future health co-morbidities. Nowadays people are focusing towards allopathic medicines to get the temporary relief for many diseases, however, women with PCOS can find alternative therapy for permanent cure. Herbal medicines are the most popular alternative therapy among all. In this review, the literature was analyzed from the published manuscripts focusing on the herbal medicines used in the treatment of PCOS.

Keywords: polycystic ovarian syndrome, conventional therapy, herbal medicines

1. Introduction
Polycystic ovary syndrome (PCOS) is a common condition of infertility in females, affecting women of reproductive age with the prevalence ranging from 6 to 10% [1]. Its major hallmark features are hyperandrogenism, hyperinsulinemia, chronic anovulation and polycystic ovary. The polycystic ovarian syndrome is associated with an increased risk for metabolic conditions such as insulin independent diabetes dyslipidemia, visceral obesity, endothelial dysfunction and chronic low-grade inflammation [2]. Women with PCOS often have many small cysts on their ovaries. Multiple cysts on the ovaries diagnosed by ultra sound [3]. In addition, some women experience physical changes due to the presence of male hormones. These can include the growth of facial hair, hair loss on the scalp, facial acne and accumulation of excess fat in the abdomen. If diagnosed early and managed properly with the lifestyle modification, the onset of Type2 diabetes mellitus and its resultant risk of coronary artery disease may be delayed or prevented [4]. The causes of PCOS are not fully understood. Recently, increasing evidence has shown that insulin resistance has an important implication in the pathogenesis of PCOS by acting directly on ovarian androgen secretion andabnormal follicular development leading to the dysfunctional ovary and menstrual activity due to hyperinsulinemia [5] and the use of insulin-sensitizing drugs is an effective approach in the management of PCOS. Conventional therapy is effective in the treatment of PCOS but itmay cause some side effects after prolonged usage. Women with PCOS can approach an alternative therapy to manage such infertility problems. Hence the current scientific research focused on identifying the proven evidence from preclinical evaluation and summarizing the importance of herbal medicines in polycystic ovarian syndrome.

2. Herbal medicine in pcos treatment
2.1 Aloe Vera

Fig 1: *Aloe Barbadensis*

Aloe Barba densis Miller has been used in traditional medicine in the treatment of arthritis, burns, skin cancer, digestive problems, diabetes and high blood pressure. Radha*et al*evaluated the role of Aloe vera gel as a pre-conceptive herb for managing polycystic ovarian syndrome (PCOS) in rats. PCOS was induced in the rats using Letrozole followed by treating them for 2 months with Aloe vera gel. Pregnancy was induced and animals were sacrificed at the late gestational period. These were then evaluated for key steroid hormone status and regulatory proteins. Assays for biosynthetic and metabolizing enzymes of steroidogenesis done. Results of assays showed that Aloe vera gel altered ovarian-placental steroid status by modulating luteinizing hormone receptor, androgen receptor, aromatase and steroidogenic acute regulatory. Reproductiveperformance was improved after Aloe vera gel treatment. The study showed Aloe vera gel is a good pre-conceptive agent for PCOS phenotype [6].

2.2 Atractylodes

Fig 2: *Atractylodes macrocephalakoids*

Zhou *et al* assessed the activity of a polar extract of *Atractylodesmacrocephalakoids* (AMK) in a hyperandrogenic rat model of PCOS which had been induced by testosterone propionate.AMK is a tonic herb usually clinically used in Chinese medicinal formula of treating PCOS. Five groups of animals were used and PCOS was induced with testosterone propionate. Enzyme-linkedimmunosorbent assays were used to measure total testosterone (TT), sex hormone binding globulin, androstenedione, follicle stimulating hormone (FSH), luteinising hormone and antimullerian hormone. Real-time PCR and immunohistochemistry were used to measure the expression of FSH receptors and Aquaporin -9.Polar extract of AMK improved estrous cycle reduced plasma levels of TT and androstenedione of the PCOS in rats. It also reduced FSH receptor expression and increased aquaporin -9 in the rat's ovaries. It was concluded that polar extract of AMK relieves PCOS and regulates FSH receptor and aquaporin-9 expression [7]

2.3 Guggul

Fig 3: *Commiphora wightii*

Kavitha *et al* evaluated effects of *Commiphorawightii* in polycystic ovarian syndrome (PCOS) in rats. The experiment was performed in four groups of animals. PCOS was induced by dehydroepiandrosterone (DHEA). The animals were given metformin and *Commiphora wightii*resin ethanolic extract in addition to DHEA. Serum glucose levels and steroid hormones were measured. The study confirmed that *Commiphora wightii* has a role in alleviating DHEA-induced PCOS by decreasing morphological abnormalities of ovarian follicles and also restoring hormonal levels to normal in adults rats [8].

2.4 Hazelnut

Fig 4: *Corylusavellana*

Demirel *et al* also studied the activity of *Corylusavellana* seed oil also known as hazelnut oil to assess its activity in letrozole-induced polycystic ovarian syndrome (PCOS) in rats. The parameters that were evaluated included a serum follicle stimulating hormone, luteinizing hormone, estradiol, testosterone, progesterone, serum lipid parameters, leptin, and glucose. Other parameters such as antioxidant activity and phytosterol content of the oil were determined. Results showed that high-density-lipoprotein-cholesterol were high. Leptin and glucose concentration low in the treatment group. The oil was found to contain the following tocopherol, sitosterols, squalene, campesterol and stigmasterol in the phytochemical analysis. It was found to be effective in PCOS because of its ability to regulate gonadotropins, steroids, serum lipid parameters and also its antioxidant properties [9]

2.5 Turmeric

Fig 5: *Curcuma longa* rhizomes

Curcumin is found in *Curcuma longa* rhizomes. It is used as a food additive and possesses anti-inflammatory, anti-oxidant, antihyperlipidemic and hypoglycemic properties. Reddy *et al* evaluated the benefit of Curcumin in female Wistar rats with PCOS. Five groups of animals were used. Letrozole was used to induce PCOS. The animals were given Curcumin and a

comparison made with that of clomiphene citrate which is used in the treatment of PCOS. Biochemical estimation of fasting blood glucose, glycosylated hemoglobin, lipid profile was performed. Antioxidant activity of Curcumin determined using catalase and superoxide dismutase. Results showed that Curcumin reduced fasting blood glucose levels and glycosylated hemoglobin levels in the serum. It also normalized serum lipid profiles and serum sex steroid profiles. Curcumin showed beneficial effects in PCOS induced by letrozole in female Wistar rats [10]

2.6 Mistletoe fig

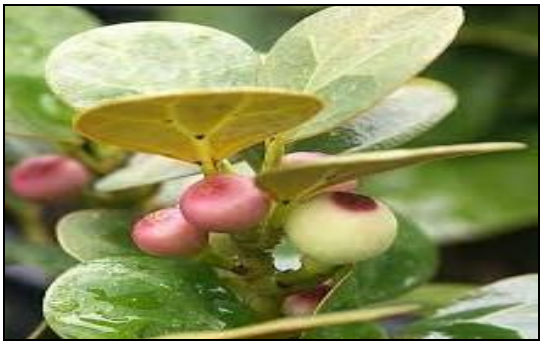

Fig 6: *Ficus deltoidea*

Suhaimi *et al* determined the effects of ethanolic extract of leaves of *Ficusdeltoidea* on reproductive organs of letrozole-induced PCOS in Sprague-Dawleyrats. Six groups of animals were used. PCOS was induced with letrozole. The rats were treated with different concentrations of and clomiphene citrate used as a standard. Ovary and uterus were collected at the end of the treatment period and weighed. Tissue of ovaries and uterus prepared for histopathological studies. Results of pathological studies showed that the groups treated with the extract had less number of cystic follicles as compared to the group which was not given any treatment. *Ficusdeltoidea* decreased the ovarian wet weight of PCOS female and increased uterine wet weight. The study concluded that ethanolic extract of *Ficusdeltoidea* leaves has protective effects against ovarian and uterine induced PCOS [11]

2.7 Fennel

Fig 7: *Foeniculum vulgare*

Foeniculumvulgare usually known as fennel in English is an aromatic plant. It has antioxidant, diuretic, analgesic and antipyretic properties. Sadrefoza *et al* studied the renoprotective effect of *Foeniculumvulgare* extract in experimental PCOS female rats. Five groups of animals were used. PCOS was induced with estradiol in three groups and the remaining two groups remaining non-PCOS. One of the non-PCOS group served as a control and the other received treatment of *Foeniculumvulgare* extract. Two of the PCOS groups of the rats were treated with an extract of *Foeniculumvulgare*. Rats were sacrificed after four weeks and kidneys processed for light microscopy and serum biochemical parameters were also measured. Results showed that serum levels of urea had decreased in PCOS rats treated with *Foeniculumvulgare* at a dose of 150mg per body weight. Histopathological changes of kidney samples were comparable in PCOS rats with respect to groups treated with the extract. *Foeniculumvulgare*aqueous extract showed benefit effect at dose of 150mg per kg body weight on renal function of PCOS rats [12]

2.8 Flax seed

Fig 8: *Linumusitatissium*

Flax botanical name *Linumusitatissium* is used traditionally as a medicine to treat various diseases. The seeds are also incorporated in food products. Fatima *et al* did an open-label interventional study for three months. Thirty-two women with the polycystic ovarian syndrome who fitted the inclusion criteria were selected. After the study flaxseed had reduced the ovarian volume and number of follicles. Subjects did not have peripheral follicles after flaxseed therapy and the menstrual cycle had improved. Thus flaxseed can be studied further as it is promising as another possible source of new drug for PCOS [13]

2.9 Fenugreek seed

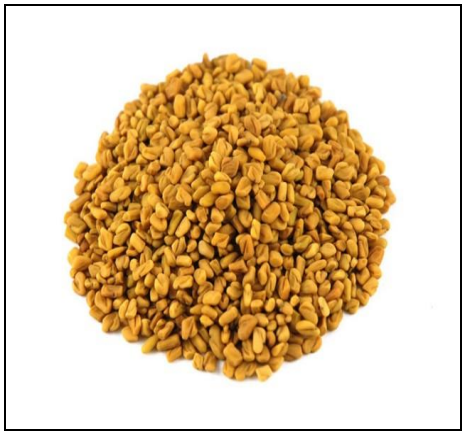

Fig 9: *Trigonellafoenum-graecum*

Swarop *et al* did an open-label, one arm, non-randomized, post-marketing surveillance study using fenugreek seed. Fenugreek botanical name is *Trigonellafoenum-graecum*. It was studied for its efficacy in PCOS. The study was

performed in 50 pre-menopausal women aged between 18-45 years with a body mass index of less than 42 who had PCOS. The study was determining the efficacy of *Trigonellafoenum-graecum* seed extract on reducing ovarian volume and ovarian cysts number. Results obtained showed that fenugreek seed extract caused a reduction in ovarian volume and number of ovarian cysts. It also increased luteinizing hormone and follicle-stimulating hormone levels. Fenugreek seed extract was found to be effective in alleviating the symptoms of PCOS in women [14]

2.10 Licorice

Fig 10: *Glycyrrhizaglabra*

Licorice is the root of *Glycyrrhizaglabra*. Armanini *et al* concluded that licorice can reduce serum testosterone and thus could be used as an alternative therapy in PCOS. In atrial performed by Armani, seven men aged between 22-27 were used. The subjects were given 7gm of licorice tablet daily for a week. The results showed that levels of testosterone had fallen by 40% within four days of licorice administration. In another in-vitro study done in 1991 to test effects of several constituents of plants from peony and licorice on rat ovary cell; it suggested that glycyrrhizic acid a metabolite of glycyrrhizin can inhibit conversion of androstenedione to testosterone [15]

2.11 Green tea

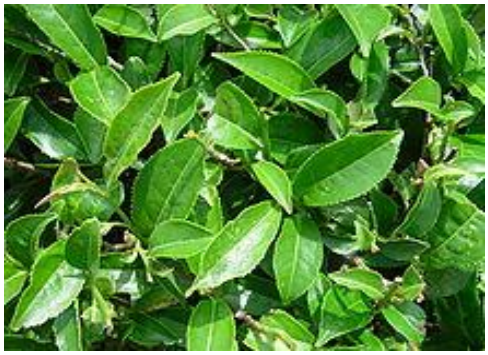

Fig 11: *Camellia Sinensis*

Green tea is obtained from the *Camellia sinensis* contains a lot of catechins, minerals, and vitamins. It has many health benefits mainly in obesity, insulin resistance and diabetics [16]. Ghafurniyan H *et al*., reported the effect of green tea extract on PCOS rats. The researchers induced the polycystic ovaries in female Wistar rats by estradiol valerate. The animals were divided into control group and experimental group. The study analyzed the serum hormonal level and ovarian histopathology. The study concluded that green tea extract is effective in improving the endocrine condition in the treatment of disturbances of ovulation in PCOS rats [17].

2.12 Sausage fruit

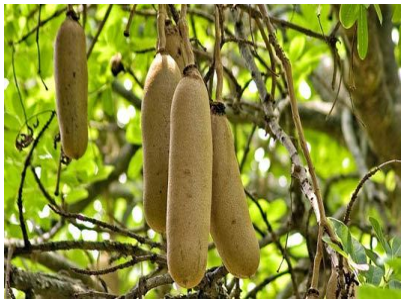

Fig 12: *Kigelia africana*

Kigelia Africana (Lam) Benth fruit widely used to treat gynecological disorders. Literature confirms that the reported pharmacological actions are due to the presence of iridoids, flavonoids, fatty acids, sterols, glycoside and napthoquinones [18]. A study conducted in two patients to evaluate the effectiveness of Kigelia africana fruit powder in the management of PCOS. The study has come with the outcome that *Kigelia africana* fruit powder restores the menstrual flow and significant reduction in the acne. Hence, it is effective in the treatment of PCOS [19].

2.13 Majoram tea

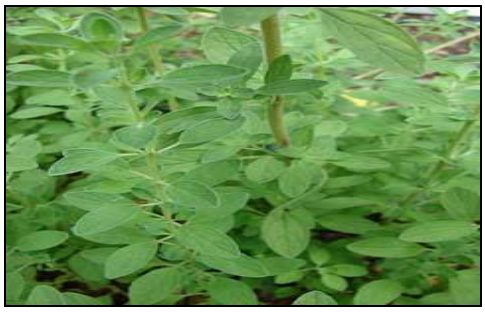

Fig 13: *Origanum majorana*

Origanum majorana is traditionally used to restore hormonal balance and to regulate the menstrual cycle. A randomized double blinded controlled placebo study was conducted in 25 women with PCOS. The Majorana tea extract significantly reduced DHEA and found to improve insulin sensitivity and reduced the level of adrenal androgens. The results obtained in the present study was showed a beneficial effecton the hormonal profile of women with PCOS [20].

2.14 Palm pollen

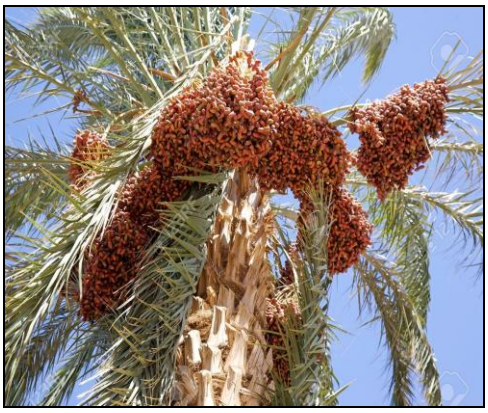

Fig 14: *Phoenix dactylifera*

Phoenix dactylifera L. is a traditional Egyptian herbal medicine for improving male and female fertility. It contains carbohydrates, alkaloids, steroids, flavonoids, glycosides and phenolic compounds. The effect of palm pollen extract in the treatment of PCOS was performed in estradiol valerate induced PCOS in the rat model. The concentration of serum levels of FSH, LH, estrogen and progesterone levels in the control and experimental group was monitored. The palm pollen extract treatment exhibited significant recovery in the hormonal profile and decreased the number of cystic follicles in the ovary. Thus the study concluded that the antioxidant property of the extract have the positive effect in reducing the number of cystic follicles and increases the number of corpus luteum represents the restarting process of ovulation [21].

2.15 Pomegranate

Fig 15: *Punica granatum L.*

Punica granatum L. is used in the treatment and prevention of cancer, cardiovascular disease, diabetes, dental conditions, erectile dysfunction, male infertility and obesity [22]. Polyphenols are the major phytoconstituents present in the fruits [23]. Hossein *et al*. reported the effect of pomegranate juice extract on PCOS induced rats and the study suggested that phenolic compounds present in the pomegranate extract lead to reduced effect of testosterone hormone. This study recommends the consumption of pomegranate extract reduces the complications associated with polycystic ovary syndrome [24].

2.16 Pergularia

Fig 16: *Pergularia daemia*

Pergularia daemia contains cardenolides, alkaloid, saponins, triterpenes and steroidal compounds. Traditionally it has been used for the treatment of various diseases. Recent research has shown that it also has hepatoprotective, antifertility and antidiabetic [25]. The combined activity of *Pergularia daemia* and metformin in testosterone propionate induced PCOS in a rat model was studied. The plasma level of LH, FSH, estradiol, progesterone and testosterone were measured and significantly regained the hormone levels. The studies concluded that the combined treatment of *Pergularia daemia* extract and metformin is an effective medicine in treating PCOS than metformin alone [25]. Another study was performed to know about the management of obesity pattern in the testosterone induced PCOS rat models through lipid profile. The study also reported that the early treatment of obesity and coronary heart disease in PCOS condition can prevent atherosclerosis. Therefore this study has come with the outcome that reduces the cholesterol level in the serum and it is an effective medication for PCOS [26].

2.17 Anise

Fig 17: *Pimpinella anisum*

Pimpinella anisum has been used in Iranian traditional medicine. The active constituents of *Pimpinella anisum* oil contain anothol, eugenol, methyl chavicol, anisaldehyde and estragole [28]. It has been used has anti-parasitic anti-bacterial anti-fungal, antipyretic, stimulating effect of digestion and used for a treatment of seizures and epilepsy. The *Pimpinella anisum* leaf oil extract at the dose of 200mg/kg, 400mg/kg resulted from a significant decrease in the signs of PCOS in the ovarian tissue and changes in the hormonal profile of female model PCOS of mice [27].

2.18 Soy isoflavone

Fig 18: *Glycine max*

Soybean (*Glycine max*) contains isoflavones which are responsible for pharmacological actions [31]. Isoflavones are classified as phytoestrogens have been postulated to be natural alternatives to hormonal therapy for menopausal women. R.K. Rajan *et al*. reported the effect of soy isoflavone on letrozole-induced PCOS rat model. Physical, metabolic and endocrinological parameters were investigated. The steroidogenic enzyme assay and the characteristics of changes in ovary were evaluated by histopathology studies. Soy

isoflavone treatment exhibited significant recovery in the biochemical and clinical parameters. Histopathology evidence shows that soy isoflavones may be beneficial in PCOS [28].

2.19 Wild indigo

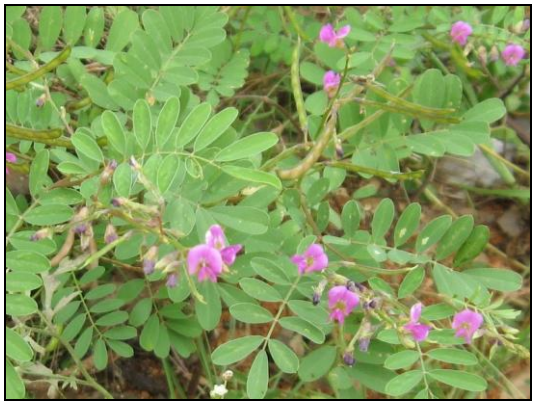

Fig 19: *Tephrosia Purpurea*

Tephrosia purpurea used as a traditional medicine for treating the female reproductive disorder and various inflammatory disorder. In an investigation done in rats with PCOS induced with letrozole found that *Tephrosia purpurea* extract has potential effect efficacy in the improvement of ovulation in rats. This herbal treatment normalized estrous cycle and steroidal hormonal levels. The hormone LH and FSH did not show any changes after plant drug treatment because these hormones are secreted from a pituitary gland at *Tephrosia purpurea* was targeted on ovarian hormones. To check ovulation and fertility female rats were mated and pregnancy was confirmed [29].

2.20 Nettle

Fig 20: *Urtica dioica*

Urtica dioica contains Flavanoids, tannins, volatile compounds, and sterols. Samad Z *et al*., reported the protective effects of *Urtica dioica* extract on the rat liver tissue which can be damaged by metabolic symptoms of PCOS. In this study, estradiol valerate is used for inducing PCOS. The animals were divided into control group and experimental group. Blood samples were collected for serological evaluation. Characteristic changes of the liver were evaluated by histopathology studies. The researchers have reported that *Urtica dioica* by increasing insulin sensitivity, reducing hepatic necrosis may reduce inflammation and improve metabolic symptoms in PCOS [31].

3. Conclusion

Polycystic ovary syndrome (PCOS) is a common endocrine and metabolic disorder in premenopausal women. Clinical manifestations of PCOS include infertility, menstrual disorders, obesity, acne, and hirsutism. Conventional therapies are effective in the prevention and treatment of PCO Sbut it might be a lifelong treatment. Prolonged usage of allopathic drugs causes severe adverse effects. These unusual effects have led to a search for alternative remedies in the management of PCOS. Naturopathic medicines return the body to a state of natural balance compared to synthetic drugs. Preclinical and clinical evidence of various herbal extracts used in the management of PCOS are promising but can be an important source of new therapies for human disease and to discover new drugs. Further investigation is required to understand the complete mechanism of action of these herbals in the reproductive disorders.

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