

Short Communication

Herbal Remedies for Mitigating Polycystic Ovary Syndrome: A Brief Review

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Background: Polycystic Ovary Syndrome (PCOS) is a common gynecological, endocrine, and metabolic disorder of unknown etiology. It is a complex endocrine illness that is marked by reduced development of follicles, hyperandrogenemia, insulin resistivity, infertility, increased luteinizing hormone, obesity, and augmented cystic ovaries.

Objective: This review aimed to assess the efficacy of herbal and bioactive components of medicinal plants for mitigating PCOS.

Materials and Methods: To conduct this review, keywords like “herbal treatment”, “ayurvedic treatment”, “bioactive components of medicinal plants”, “polycystic ovary syndrome”, and “PCOS” were used to search for various articles in search engines such as Google Scholar, PubMed/MEDLINE, Web of Science, Scopus, Elsevier from 1992 to 2023.

Results: More than 28 relevant studies were found and were briefly described in this review. According to the evidence, medicinal plant extracts containing phytoestrogens and these herbal treatments in animal models of PCOS were used to decrease hyperandrogenism, restoration of abnormalities in serum sex steroid profile, ratio of LH: FSH, steroidogenic enzymes, cardiovascular parameters, insulin resistance, ovary weight, lipid profile, and estrous cycles.

Conclusion: The results of this review revealed the variability and efficacy of phytoestrogen activity and herbal treatments associated with PCOS disorder which can be partly effective. These findings may represent an opportunity to investigate and discover new bioactive components of medicinal plants which may help future studies on the etiology, pathophysiology and treatment of PCOS disorder.

Keywords: Polycystic ovary syndrome; Hyperandrogenism; Infertility; Phytochemical; Herbal

Introduction

Polycystic Ovarian Syndrome is a common reproductive, endocrine and metabolic disorder of unknown etiology that was first described in 1935 by Stein and Lavenhel, with a preponderance ranging from 8.7% to 21% [1] in women of the reproductive age. According to the Rotterdam criteria, the prevalence of PCOS is 10%, while the prevalence of polycystic ovaries is 28% [28]. Many works of literature suggested that PCOS phenotype may vary widely and is most commonly observed in the post-pubertal period. Many studies suggested that the happening of PCOS is relatively higher among Asian women (52%) than

among Western Caucasian women (20-25%) [2]. According to World Health Organization (WHO), PCOS affects 116 million women (4%-12%) globally in 2012, and in 2020, its ratio increased abruptly to 26% [2]. Experts claim that in India 10% of women are affected by PCOS [3]. Hyperandrogenism, polycystic ovaries, and gonadotropin abnormalities are the three main phenotypic characteristics of PCOS. Classical structure of PCOS shows thickening of ovarian cortical, numerous small follicular cysts, hyperplasia, luteinized inner theca, stromal hyperplasia, and numerous immature follicles, an indication of a halting of

Table 1: Summary of the studies reported on the effect of some common herbal medicinal plants on PCOS.

Sl no.	Herbal medicine/compound	Model or design used	Duration/doses	Results	Reference
1	Anise (<i>Pimpinella anisum</i>)	Rats/ estradiol valerate induced PCOS	200 mg/kg, 400 mg/kg for 15 days	improve PCOS by effects on the histomorphologies of the ovarian tissue	Mahood <i>et al.</i> , 2012 [13]
2	Sausage fruit (<i>Kigelia africana</i> [Lam] Benth)	Human trial(two PCOS patients)	1 tsp. of powder daily before food for 24 months	Size of the right ovary becomes normal due to the strong anti-inflammatory effect of the plant extract.	Oyelami <i>et al.</i> , 2012 [14]
3	Berberine, a major bioactive component of <i>Rhizoma Coptidis</i> , <i>Cortex Phellodendri</i> and <i>Cortex Berberidis</i>	Human trial (89 women)	500mg thrice daily for 3 months	Reduced level of LDL, triglycerides, cholesterol, glucose, insulin and insulin resistance, increased level of HDL and SHBG	Wei <i>et al.</i> , 2012 ; Cai <i>et al.</i> , 2012 ; Wang, 2015 [15-17]
4	Fennel(<i>Foeniculumvulgare</i>)	Rats/estradiol valerate induced PCOS	250,500,1000 mg/kg, for 4-10days	Increased serum concentration of FSH and decreased LH	Karampoor <i>et al.</i> , 2014 [18]
5	Pomegranate (<i>Punica granatum</i>)	Rats/estradiol valerate induced PCOS	100mg/kg,200 mg/kg,400 mg/kg, for 81 days	Reduced the difficulties associated with PCOS and reduced concentration of E2, free T, and and restandion hormones in PCOS	KargarJahromi <i>et al.</i> , 2015 [19]
6	Shatavari/Satamul (<i>Asparagus racemosus</i>)	human trial	10mg/day for 105 days with satapushpa and guduchi 1000 mg/day for 60 days with guduchi, jatamansi and amla	reduce PCOS symptoms, improve follicular growth, development and ovulation	Siriwardene <i>et al.</i> , 2010 [20]
7	Cinnamon (<i>Cinnamomum</i>)	Rats/DHEA Induced PCOS	10mg/100g for 20 days	Improvement in insulin resistance and insulin sensitivity, decreased IGF-1, increased IGFBP-1 and down-regulated T in PCOS rats	Dou <i>et al.</i> , 2018 [21]
8	Welsh onion (<i>Allium fistulosum</i>)	Rats/letrozole induced PCOS	500mg/kgfor 14 days	Low plasma LH:FSH ratio, high E2 levels, ovarian morphology, folliculogenesis-related gene expression	Lee <i>et al.</i> , 2018 [22]
9	<i>Vitex negundo</i>	Rats/letrozole induced PCOS	200mg/kg,400 mg/kg up to 66 days	improved the abnormality in serum sex steroid profile, LH:FSH ratio, steroidogenic enzymes, cardiovascular parameters, lipid profile and the glucose and estrous cycles	Kakadia <i>et al.</i> , 2019 [23]
10	<i>Guizhi Fuling Wan</i>	Letrozole induced PCOS rats	1.24g/kg for 35 days	improve insulin resistance in PCOS with the underlying mechanism of regulating intestinal flora to control inflammation	Zhu <i>et al.</i> , 2020 [24]
11	<i>Bryonia dioica</i> Jacq	Androgenized PCOS rats	30mg/kg for 28 days	Normalized LH, FSH and glucose level	Gravandi <i>et al.</i> , 2022 [25]
12	Bitter Melon (<i>Momordica charantia</i> L.)	Letrozole induced PCOS rats	500mg/kg for 28 days	Reduced LH surge, insulin, and testosterone levels and improvement in FSH levels	Hussain <i>et al.</i> , 2022 [26]
13	<i>Caesalpinia crista</i>	Letrozole induced PCOS rats	500mg/kg for 15 days	Increased levels of luteinizing hormone and follicle-stimulating hormone, decreased testosterone	Shende <i>et al.</i> , 2023 [27]

folliculogenesis. Ovary sizes varies from normal to very large size (volume increases >10cm). In ultrasound, histological detections appear as a peripheral ring of small follicles (610mm in diameter) [4]. Abnormalities in biochemical parameters of PCOS are characterized by elevated serum concentrations of androgenic hormones. In vivo and in vitro studies on theca cells suggested that ovarian theca cells produce androgen in response to Luteinizing Hormone (LH); therefore the blood levels of androgen increase in people with PCOS [5]. The high levels of androgens especially testosterone in PCOS, their role in lack of ovulation, and disrupted synthesis of sex hormones, which causes clinical symptoms and dysfunction of the genital tract in the patients, are the main reasons for infertility in reproductive age women [6,7]. The pathophysiological study of PCOS is distinguished by primary faults in the hypothalamic-pituitary-gonadal -axis, resulting in a variety of metabolic abnormalities such as production of excessive ovarian androgen, ovarian dysfunction, and insulin resistance. PCOS is extensively associated with gonadotropin secretion irregularities, increased steroid hormone secretion, and a high level of LH/FSH ratio, resulting into increase in androgen synthesis and prevents development

of normal follicle. A lot of findings suggest that increased oxidative stress contributes in the pathophysiology of PCOS, resulting in difficulties such as chronic inflammation, disrupted follicular development, altered steroidogenesis in the ovaries, hyperandrogenemia, infertility and insulin resistance [8]. Again the histopathological features of PCOS include the following changes in the ovarian tissues: enlarged, sclerotic, numerous cyst follicles, whole ovarian hypertrophy, and thickened capsule >100µm, multiple numbers of sub capsular follicular cysts, albicantia, hyperplasia and premature luteinization of theca cells [2]. Diagnosis of PCOS is currently based on the criteria of the ESRHE/ASRM Rotterdam Consensus meeting in 2003. This criteria suggests that ultrasound of polycystic ovaries along with an ovulation and hyperandrogenism, which widened the previous classification of NIH, 1990 i.e., PCOS should consist hyperandrogenism, an ovulation [9]. The Androgen Excess Society (AES) set up a committee of experts to review all the data published on PCOS to simplify diagnosis in 2006 [10]. The first clinical manifestation of PCOS is present in adolescence. Again, PCOS can be also associated with obesity, insulin resistance (found in 60%-80% of women with PCOS), hyperinsulinemia, and type-2

diabetes mellitus. Apart from this, PCOS can also be associated with psychological disorders including anxiety, bipolar disorder, clinical depression and other mental illness. Ayurveda suggests PCOS to be a “kapha” predominant disorder; where “kapha” is irritated by consumption of more “kapavardhak” and “sneha” consists of “Ahara” and by inactive lifestyle [11].

Herbal medicines, a popular type of Complementary Medicine (CM) are known to contain pharmacologically active components with physiological effects on female reproductive system. According to literature findings, they have been positively related with reduces cases of cardiovascular disease, breast cancer, and osteoporosis in female. Oral Contraceptive Pills (OCP) and Clomiphene Citrate are widely used in pharmaceutical treatment for menstrual irregularities and ovulation induction in females respectively. Metformin, an anti-androgen and hypoglycemic pharmaceutical which is widely used in management for hyperandrogenism. Though it has improved effectiveness on insulin sensitivity and hyperandrogenism, but it shows adverse effects including vomiting, nausea, and gastrointestinal disturbances.

Herbal medicine has the potential for synergistic and antagonistic interactions between compounds [12]. The rationale of this review was to identify herbal medicines with specific reproductive endocrinological effects in PCOS, oligo/amenorrhoea and hyperandrogenism.

Methods and Materials

A comprehensive search was conducted using literature search of English language studies in electronic databases such as Web of Science, PubMed/MEDLINE, Elsevier, SCOPUS and Google databases from 1992 to 2023 in order to regain clinical studies on herbal remedies for PCOS. Keywords like "polycystic ovary syndrome", and "PCOS", herbal treatment", "ayurvedic treatment", "bioactive components of medicinal plants" were used to conduct this review. Search was conducted for all animal studies related to PCOS, pre-clinical and clinical studies which are explaining the ameliorative effect of herbal extracts on PCOS. In addition manually searching of bibliography of review articles have been done.

Result

Numerous studies on the etiology and pathophysiology of PCOS have been done. Again, various common, traditional herbal and non-chemical treatments of PCOS have been also studied. Most of the studies reveal that they can partially improve metabolic dysfunction and abnormalities of certain hormones. So this can be considered as an effective way for prevention and treatment of PCOS by targeting the factors involved in the disorder.

Conclusion

PCOS is one of the most common gynecological disorders of reproductive age. Herbal treatment of PCOS provides a consistent impact with few adverse effects. This review comprises of the evidence for mechanisms of effect for herbal medicine in PCOS, oligo/amenorrhoea and hyperandrogenism. It includes 13 preclinical laboratory based and clinical trials. Clinical investigations found no adverse effects for the herbal medicines included in the Table 1. The evidence for *Caesalpinia crista* and *Vitex negundo* in the treatment of infertility and oligo/amenorrhoea is variable. *Asparagus racemosus* and *Cinnamon* are for improving metabolic hormones in PCOS. *Fennel*, *Welsh onions* are for

increased serum concentration of FSH in PCOS. These herbal medicines not only prevent but also help in healing of ovarian cysts. So, these herbal medicines may present an opportunity to investigate and discover new bioactive components which may help future studies on the etiology and treatment of PCOS disorders.

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