

The Effect of Herbal Teas on Management of Polycystic Ovary Syndrome: A Systematic Review

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ABSTRACT

Background & aim: Polycystic ovary syndrome (PCOS) is a common endocrine and metabolic disorder. Recently, the tendency towards complementary therapies such as using herbs with anti-androgenic effects has been increased. This study reviewed the documents related to the effect of four types of herbal teas on the treatment of PCOS based on the literature review.

Methods: The searched databases included ISI, PubMed, Google Scholar, Scopus, Science Direct, Cochrane library, International Clinical Trials registry, MedLib, Society for Information Display (SID), Iranian Registry of Clinical Trials (IRCT), IranMedex and Magiran,. The databases were searched for the clinical trials without any time limit and using English and Persian key terms included "polycystic ovarian syndrome", "herbal therapy", and "herbal medicine".

Results: Among 104 randomized controlled trials (RCTs) about the effects of herbal medicines on the treatment of PCOS, only four studies were conducted on diverse types of tea. The results of one study on the effects of mint tea revealed a significant reduction in the total and free testosterone levels in the intervention group ($P < 0.05$). Furthermore, the level of hirsutism measured by the patients' self-assessment significantly decreased in the intervention group ($P < 0.05$). One study on the effects of green tea demonstrated the positive effect of this herb on weight loss (2.4% reduction) and decreasing the number of amenorrhea cases ($P > 0.05$). Likewise, there was no significant alteration in the serum hormone levels in both groups ($P > 0.05$). Another clinical trial determined the same effects of using *Stachys lavandulifolia* and hormone therapy. According to another study, the level of dehydroepiandrosterone-sulphate (DHEA-S) significantly dropped after treatment with marjoram tea ($P = 0.05$).

Conclusion: The positive effects of various types of herbal teas on PCOS has been reported in different trials; however, further RCTs are recommended with larger sample size and prolonged duration.

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Introduction

Polycystic ovary syndrome (PCOS) is a common endocrine and metabolic disorder and affects 3% to 8% of reproductive-age women. This abnormality is determined by chronic anovulation, elevated androgens, or polycystic ovarian morphology (1, 2). Moreover, insulin resistance and hyperinsulinemia are common

findings in females with PCOS. Insulin has direct and indirect effects on hyperandrogenism in PCOS patients (2, 3).

The precise etiology of the PCOS remains unknown due to complex interactions among genetic, environmental, and behavioral factors. Additionally, anxiety, depression, and poor

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quality of life are frequent in the PCOS patients (4). Currently, there are multiple treatment methods acting as androgen antagonists.

Recently, due to suboptimal results of using several drugs, the tendency towards using complementary therapies and natural anti-androgens has been increased. Anti-androgen factors found in plants and foods provide an alternative for chemical and industrial drugs (5). Further, it is confirmed that these alternatives are not associated with major adverse effects.

The preference of herbal anti-androgens has been revealed inefficient therapeutic effects of several medicines in multitude patients and the necessity of changing their type or dose (5). Nevertheless, the effects of most of the herbs are not investigated and remained unknown (6). Nowadays, the traditional herbal medicine is widely used in the health sector.

Herbal therapy has reached a turning point; nonetheless, it is essential to coordinate the herbal medicine with other fields of academic medical sciences (7). Several herbal teas, as dietary supplements, are more accepted as a daily beverage; therefore, they can be widely used for therapy aims in PCOS. Herbal therapy with green and some other herbal teas such as the family Lamiaceae (mint family) might be one of the best and acceptable options for women with PCOS. This study aimed to review the studies conducted to evaluate the effects of four types of herbal teas on PCOS.

Materials and Methods

This study is a review of the latest randomized controlled trials (RCTs) performed on the effects of herbal teas on PCOS. Data collected from different sources such as Information Sciences Institute (ISI), PubMed, Google Scholar, Scopus, Science Direct, International Clinical Trials registry, MedLib, Society for Information Display (SID), Iranian Registry of Clinical Trials (IRCT), Iran Medex, Magiran, and Cochrane library. The time of retrieving the information from the databases was 6/15/2017.

The terms “polycystic ovarian syndrome”, “herbal therapy”, and “herbal medicine” were selected from the herbal medicine journals and were applied to setup the study search strategy and were used in MeSH term format.

Inclusion criteria of the studies

Those RCTs which assessed the effects of herbal tea extracts on the treatment of PCOS and its complications were included and those which evaluated the daily used tea were selected (in Persian or English terms) (5). The clinical trials conducted on other herbs as well as the animal and laboratory studies were excluded.

Study selection

A total of 104 RCTs were found to be about the effects of herbal compositions on the treatment of PCOS (Figure 1). Six studies were

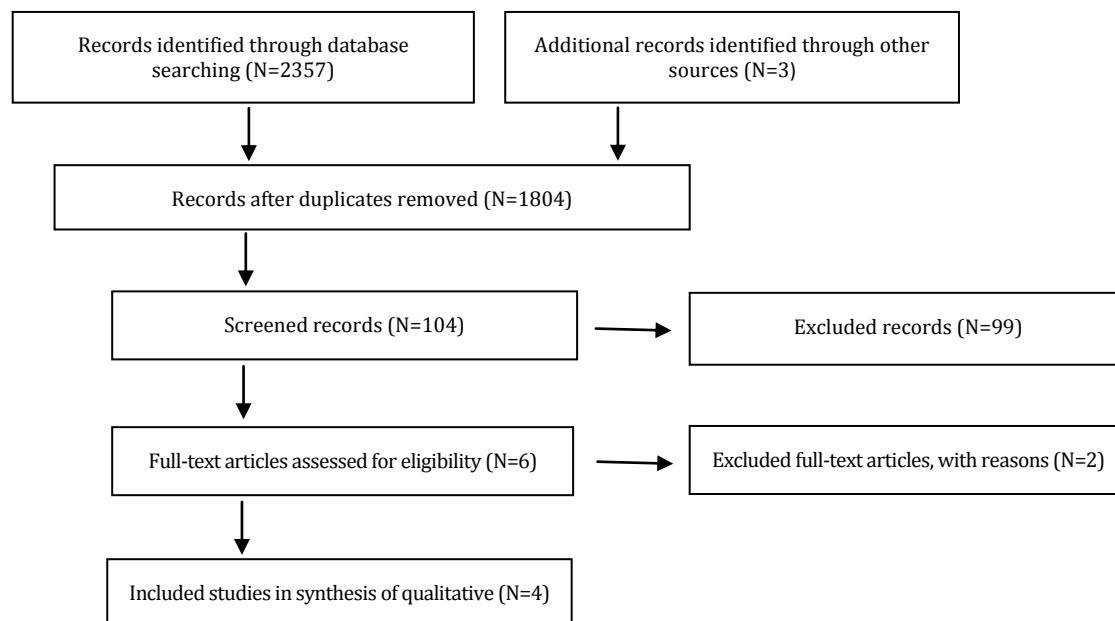


Figure 1. The PRISMA diagram of the retrieved studies**Table 1.** Characteristics of the selected studies

Author & year	Method	Participants	Experimental group	Control group	Measurement scales	Results	Side effects
Grant p. in 2010	RCT*	On the 42 patients with PCOS** and hirsutism	21 patients using spearmint tea	21 patients using placebo tea	-Free and total testosterone levels -LH*** and FSH**** levels -Hirsutism	-Significant decrease in total and free testosterone levels - Significant rise in LH and FSH levels - Significant decrease in hirsutism level via DLQI*****	Without any side effects
Chan C.W in 2006	RCT	On the 34 obese patients with PCOS	19 patients using green tea capsules	19 patient using placebo capsules	-BMI***** and weight -Biochemical profiles -Hormone profiles	-No significant difference in the hormonal levels (LH, FSH, and androgens) -No significant difference in the weight of the intervention group -Significant enhancement in the weight, BMI, and body fat percentage in the control group -Similar results of biochemical profiles (except for significant rise in the triglyceride level in the intervention group)	No adverse effects were reported
Jalilian N. in 2013	RCT	On the 66 patients with AUB***** due to the PCOS	-33 patients using <i>Stachys lavandulifolia</i>	-33 patients under treatment with MPA****	- Age-adjusted prevalence rate of AUB - Elevated level of testosterone -LH/FSH ratio -Abnormal ultrasonography	-decrease of AUB in both groups but with no significant difference between the groups	- Abdominal cramps and bloating, which could be better tolerated than nausea and vomiting associated with MPA
Haj-Husein in 2015	RCT	-On the 25 patients with PCOS	-14 patients receiving the marjoram tea	-11 patients receiving the placebo tea	-Anthropometric assessment including weight, height, waist-hip ratio -Biochemical analysis including FSH, LH, Oestradiol (E2), progesterone, total testosterone, DHEA-S***** , insulin, glucose levels	-Significant reduction of DHEA-S and fasting insulin levels in the intervention group -In comparison to the placebo group, the iteration was significant only for the DHEA-S level	-In the intervention group: bloating, nausea, mild sedation, urinary frequency -In the control group: bloating, urinary frequency

* Randomized clinical trial, ** Polycystic ovary syndrome, *** Luteinizing hormone, **** Follicle-stimulating hormone, ***** Dermatology life quality index, ***** Body mass index, ***** Abnormal uterine bleeding, ***** Medroxyprogesterone acetate, ***** Dehydroepiandrosterone sulphate

about the effects of green tea, mint, *Stachys lavandulifolia*, and marjoram. Two studies were excluded due to non-random allocation and using combination of green tea and coffee polyphenols, respectively (8, 9). The aforementioned four herbs were selected because of their common family source and regular use, especially about green and mint tea. The features of the selected studies are presented on Table 1.

The Jadad scale (Jadad et al., 1996) such as

Consort statement was used to determine the quality of methodology of the RCTs. This scale is based on the probability of bias in the sampling process, sample loss, and how to blind correctly. The studies which were scored at least 3 using this scale (ranged from 0 to 5) considered as satisfactory quality for including and were selected (10).

Results

Mint (*Mentha spicata* or spearmint) is a strong and stable plant used to flavor tea, which grows to the height of one meter, and can be planted in most areas of Iran. Its blooms, fresh leaves, and floral and leafy buds can be dried for using in foods. The chemical components of mint is linalool, 8-cineole, limonene, menthone carvone, menthol, and isomenthone. Mint has various usages in traditional medicine as a stomach tonic, analgesic, and anticonvulsant, as well as using for calming the nerves (11-13).

For many years it has been thought that mint can lower the testosterone level and was commonly used in Middle East for treatment of hirsutism. Given its anti-androgenic effect, this plant can reduce the level of free testosterone; however, it has no effect on the levels of total testosterone and dihydrotestosterone (DHT) (5).

Grant in 2010 conducted a study on the effect of peppermint tea on the level of androgens in women with PCOS. The patients were randomly assigned to two groups of intervention and control (21 subjects for each group). The subjects in the intervention and control groups consumed spearmint tea and placebo twice a day for one month, respectively.

Prior to the intervention, 15 and 30 cases had increased androgen levels and hirsutism using Ferriman-Galwey scale, respectively. The results revealed a significant reduction in the total and free testosterone levels in the intervention group ($P < 0.05$). Moreover, self-assessment of hirsutism in the intervention group determined a significant reduction in the level of this disorder ($P < 0.05$); nevertheless, there was no significant difference using the Ferriman-Galwey scale. Therefore, this study found a significant reduction in androgen levels, but due to short-term follow-up, a longer duration is needed to demonstrate the effectiveness of this herb on hirsutism (14).

***Stachys lavandulifolia* (Mountain tea)**

Stachys lavandulifolia is a multi-stemmed, viable, wooden, short, green or somehow gray, and fluffy plant from the family Lamiaceae with a warm nature. This plant contains components with biological activity such as phenylethanoid, terpenoid, and flavonoids. Further, its other components are myrcene (20%), α -pinene (18%), gamma muurolene (13.2%) and agnole

(7%) (15).

Stachys lavandulifolia is a native plant in Iran, which is used in traditional medicine as an herbal tea for treatment of gastrointestinal disorders and is prescribed as an antispasmodic, diuretic, antiulcer, antipyretic, and antidiarrheal. Its leaves and flowers are used as an antimicrobial agent to treat skin infections as well as hypermenorrhea.

According to the literature, this herb is an anxiolytic, antioxidant, and antimicrobial agent with anti-leishmanial activity, which can be used to treat primary dysmenorrhea (16-18). Its anti-prostaglandin and anti-inflammatory effects attract the interests of researchers to treat the PCOS complications using this herb.

The only RCT conducted on this issue is performed by Jalilian et al. in 2013. In the mentioned study, 66 patients with PCOS were randomly divided into two groups. The patients in the intervention group ($n=33$) were treated by *Stachys lavandulifolia* brewed tea three times a day (each time 5 g) for three months. The patients in the control group received medroxy-progesterone acetate (MPA) with the dose of 10 mg per night for 10 continued nights in a month for three months.

There was no significant difference in the prevalence of age-adjusted abnormal uterine bleeding (AUB) in both groups. The prevalence of adverse effects in the intervention group was lower in comparison to the control group; however, this difference was not significant. Therefore, it was concluded that *Stachys lavandulifolia* may be used as an alternative for MPA in management of AUB caused by PCOS (19).

Marjoram (*Origanum majorana* or Marzanjosh in Persian)

Marjoram (*Origanum majorana*) is a somewhat cold-sensitive perennial herb or undershrub with sweet pine and citrus flavors from family Lamiaceae. It is a longaevus plant with the height of 30 to 90 cm and a nice smell, which grows in drylands, beaches, mountain ranges, and forests. The leaves, flowers, and fresh aerial parts of the plant are used for medical purposes (20).

Marjoram is used for treatment of gastrointestinal diseases, common cold, respiratory allergies, diabetes, skin damages, nervous system disorders, disinfection, dysmenorrhea, and

menopause complications (21-24). According to the results of Vagi et al. study, the main component of marjoram was terpinen-4-ol in the marjoram essential oil and the others were c-terpinene, linalool, α -terpineol, α -terpinolene, α -terpinene, β -caryophyllene, and spathulenol.

The antibacterial and antifungal activities of marjoram essential oil are well-known; however, to the best of our knowledge, there was no evidence about more chemically complex extracts (25). Regarding the Iranian and Jordanian traditional medicine, marjoram was used to treat complications of menstruation and PCOS (19, 26).

The study of Haj-Hussein et al. in 2015 is the only scientific evidence that investigated the therapeutic effects of this herb in women with PCOS (27). To declare this effect, several pharmaceutical studies revealed that marjoram ethanol extract activated the peroxisome proliferator-activated receptors (PPAR), which improved the insulin sensitivity (28, 29). Given the results of multitude animal studies, the other possible mechanisms are anti-hyperlipidemic and anti-diabetic activities of marjoram extracts (30, 31).

Haj-Hussein et al. in 2015 conducted a study on 28 patients with PCOS, who were randomly assigned to two groups of intervention (n=14) and control (n=11). The patients in both groups received marjoram and placebo teas twice a day for one month, respectively. The hormonal and metabolic parameters were measured at the pre- and post-intervention phases.

In the intervention group the DHEA-S and fasting insulin levels significantly reduced; nevertheless, there was a significant difference between two groups only in terms of DHEA-S level. Therefore, it was confirmed that marjoram tea has a positive effect on the hormone profile of females with PCOS. It improves the insulin sensitivity and inhibits the adrenal androgen secretion (27).

Green tea

Globally, green tea makes up nearly 20% of tea consumption mainly used in Asia, especially China and Japan (32). According to the literature, green tea positively affect the glucose and lipid metabolism and endocrine system in mice and humans, this effect is principally associated with PCOS management (33, 34).

Moreover, those mice which were treated with this herbal tea revealed weight loss and ovulation; nonetheless, only two clinical trials were conducted to evaluate the effects of this herb on humans. The main component of green tea is epigallocatechin-3-gallate (EGCG) that causes weight loss and reduces the levels of serum testosterone, estradiol, leptin, insulin, luteinizing hormone (LH), glucose, cholesterol, and triglyceride (TG) in rats.

In vitro studies demonstrated that green tea extract and EGCG inhibited the testosterone secretion in basal and stimulated Leydig cells (4). Anti-androgenic effects are associated with EGCG and 5 α -reductase inhibitor, which prevent the conversion of testosterone to DHT (5). Chan et al. in 2006 conducted a study to evaluate the effect of green tea on the weight, and hormonal and biochemical profiles in obese women with PCOS.

In this study, 34 obese women with PCOS were randomly divided into two groups of intervention and control, who received capsules of green tea and placebo for three months, respectively. According to the results of the mentioned study, the patients' weight in the intervention group was reduced by 2.4%; however, this reduction was not significant.

In the control group, weight, body mass index (BMI), and body fat percentage (BFP) were significantly higher before and after the study. Given the results of the mentioned study, there was no significant difference between the groups in terms of the hormone profile. The biochemical profiles were similar in both groups except for a significant enhancement in TG level in the intervention group.

A Few number of the patients remained amenorrhic in the intervention group; nevertheless, this difference was not significant. According to the evidence, different effects of green tea on the weight loss might be due to different amounts of consumption, sample size, and duration of treatment. Furthermore, those studies conducted on menstrual changes in women with PCOS may have diverse results (34).

Discussion

There are few studies conducted on the effect of different teas on the PCOS; nonetheless, their positive effects on the PCOS is confirmed. Additionally, using these teas in the treatment of

PCOS is a newer modality than using the other medicinal plants, which both can open a new window towards researchers in this field.

According to the principles of clinical trials and Jadad scale, the quality of these four studies was satisfactory and the anti-androgenic effects of mint was more pronounced than the other teas. Akdogan study showed a significant decrease in the level of free testosterone; consistent with the mentioned study, Grant's study revealed a significant reduction in the total and free testosterone levels.

In Akdogan study, a significant increase in follicle-stimulating hormone (FSH), LH, and oestradiol, as well as a significant reduction in TG level were reported, which could confirm the effects of this herb on the other PCOS complications. Further, several animal studies confirmed the significant anti-androgenic effects of mint (5, 8, 11, 14). Given the results of Chan et al. study, treatment with green tea insignificantly decreased the subjects' weight (by 2.4%) and number of dysmenorrhea cases.

Moreover, no significant difference was observed between the groups in terms of hormonal and biochemical profiles, except for an increase in TG level of the patients in the intervention group. According to anti-androgenic effects of this tea, this difference might be due to low-dose, short-term intervention, including both males and females in several studies, and the gender-related effects of previous human studies (34).

Regarding the results of several animal studies which revealed the positive effects of green tea, continued attention was paid to this safe tea. In the only clinical trial study on *Stachys lavandulifolia*, AUB was studied and demonstrated the same results as hormonal therapy in the PCOS patients. The reduction in the testosterone levels was not significant in the intervention group; nevertheless, correction of clinical abnormalities in LH/FSH ratio was significant in this group (19).

The antioxidant and antimicrobial effects of marjoram is well documented; nonetheless, to the extent of our knowledge, there is not any published study about the effects of the other chemical component of this herb (21, 25). Increased attention to the antidiabetic effect of marjoram leads to the first intervention study in

women with the PCOS. In congruence with Haj-Hussein study and regarding the use of this herb as food flavoring, this herbal tea is safe for using in low-dose and is not associated with any major adverse effect (14, 19, 27, 34).

Akdogan study demonstrated that using mint as a beverage did not lead to any adverse effect; likewise, those patients who were treated with mint did not reported any side effect. However, in case of consuming inappropriate dose or way of administration would lead to side effects. This study evaluated the side effects that were observed in several animal studies such as decreased iron absorption and hepatonephrotoxicity (8).

It is essential to know all the components of the herb and their mechanisms before using them. Multiple animal and human studies, confirmed the weight and cholesterol reducing effects of green tea due to increasing the thermogenic effect in the patients with PCOS (35-38). Furthermore, animal studies confirmed the effects of green tea on decreasing the fasting serum glucose, insulin, total cholesterol, and testosterone levels; if the same effects are revealed in human studies, using this herb will be effective in the treatment of PCOS (14, 33, 35-38, 39, 40).

Therefore, further studies with higher doses of green tea are recommended (34). Regardless of only 20% insulin resistance patients among the Haj-Hussein study subjects, the capacity of marjoram to activate the PPAR- α and PPAR-c resulting in increasing the insulin-sensitizing effects were determined. This may improve ovulation and significantly reduce the DHEA-S level (27).

The mechanism of the effects of *Stachys lavandulifolia* on the treatment of PCOS is remained unknown. Because of using *Stachys lavandulifolia* in several studies and traditional medicine, Jalilian evaluated its influences and confirmed the antiprostaglandins, anti-inflammatory, sedative, antispasmodic, anxiolytic, analgesic, and diuretic effects and demonstrated that this herb induced menstruation in patients with PCOS (15-19).

According to Monji et al. study in 2011, *Stachys lavandulifolia* is rich in a type of flavonoid called apigenin with estrogenic effects. *In vitro* studies conducted on *Stachys lavandulifolia* demonstrated that this herb regulated the

estrogen receptors in the rat uterus (41). Given the results of Jalilian study, this regulation reduced the complications caused by increased estrogen level in the patients with PCOS.

Moreover, regulation of the hypothalamic-pituitary-ovarian axis by using flavonoids would improve the function of uterus and ovaries. Accordingly, further clinical trials are recommended to investigate the multidimensional impacts of *Stachys lavandulifolia* on the PCOS (19). Grant conducted a study for the first time to examine the antiandrogenic effect of mint.

Nevertheless, it is suggested to evaluate the unknown mechanism of mint at the molecular level (14). According to the literature and Akdogan study, probably mint has the potential of enzyme induction of microsomal cytochrome, which leads to alterations in the concentrations of endogenous androgenic hormones.

Therefore, decrease in the level of testosterone might be due to the induction of cytochrome P450 3A4 or direct effect on the synthesis of androgen hormones (8). Properties and mentioned mechanism of mint confirmed its effects on the PCOS patients, which clarify the need for more studies with clinical trial planning.

Haj-Hussein et al. mentioned the traditional use of marjoram for hormonal regulation and its positive effects on PCOS. Several effects of marjoram were investigated and documented; nonetheless, there is not any scientific document about use of this herb in the treatment of PCOS. This herb is safe in case of using in low-doses; furthermore, it is worth mentioning that marjoram ethanol extract is used to activate the PPARs resulting in the improvement of insulin sensitivity (27).

Limitations of the study

The main limitation of the study was the few number of the clinical trials that investigated the effects of these herbal teas on the patients with PCOS. This limitation might lead to unknown definite mechanism of the herbs on the PCOS. We attempted to explain their probable mechanisms by using the evidence on their chemical structure and effects, which was the strength of the current study. Due to the increasing tendency towards medicinal plants, further clinical trials are recommended on the animals with PCOS to determine the mechanism

of action and potential adverse effects of the herbs.

Conclusion

The PCOS is a common problem in females of reproductive age, which causes many complications such as infertility and metabolic disorders. Regarding the results of this study, the effects of this four herbs were confirmed; however, further clinical trials are recommended.

Conflicts of interest

There is not any conflict of interest in this study.

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