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Review

A review on role of medicinal plants in polycystic ovarian syndrome: Pathophysiology, neuroendocrine signaling, therapeutic status and future prospects

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ABSTRACT

Polycystic ovary syndrome (PCOS) is one of the most important gynecological disorders among reproductive-age women. In patients with PCOS, the secretion rate and metabolism of androgens and estrogens are disrupted. With regards to the increasing prevalence of PCOS and associated physical and mental problems as well as the effects of changes in sex hormones in development of this disease, our aim is to investigate the effects of different herbal extracts on changes in the serum levels of sex hormones and ovarian tissue. To conduct this review, an extensive literature search was conducted using, relevant publications published between 1990 and 2017, and indexed in Google Scholar, PubMed, Elsevier, Scientific Information Database, and Science Direct were studied. The search terms used to retrieve the publications were as follows: Herbal medical extract، Names of medicinal plants ، polycystic ovary syndrome, PCOS, the mechanism of hormone. According to the evidence, herbal extracts containing phytoestrogens cause decrease in hyperandrogenism, insulin resistance, and ovary weight as well as increase in ovulation. Therefore, these plants can be partly effective in this syndrome via affecting the serum levels of different hormones and ovarian weight and morphology, representing an opportunity to investigate and discovery new bioactive products.

Contents

Abbreviations: PCOS, polycystic ovary syndrome; LH, luteinizing hormone; FSH, follicle-stimulating hormone; GC, granulosa cells; GnRH, gonadotropin-releasing hormone; HPG, hypothalamic–pituitary–gonadal; β-HSD, beta hydroxysteroid dehydrogenase; NF-κB, nuclear factor kappa-light-chain-enhancer of activated B cells; SHBG, sex hormone-binding globulin.

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1. Introduction

Polycystic ovary syndrome (PCOS) is characterized by endocrine, metabolic, and genetic disorders, chronic absence of ovulation of polycystic ovary, and clinical and biochemical presentations of hyperandrogenism [1]. The symptoms of PCOS include clinical ones (menstrual disorders, hirsutism, acne, baldness, and infertility), changes in endocrine hormones (increased levels of androgen, estrogen, and prolactin and decreased level of progesterone), and metabolic disorders (insulin resistance, diabetes, dyslipidemia, and type 2 diabetes). However, in some cases, estradiol level does not change [2]. In vivo and in vitro studies on theca cells suggested that ovarian theca cells are much more active to convert androgenic precursors into testosterone in women with PCOS than in healthy women. Indeed, Theca cells produce androgen in response to luteinizing hormone (LH); therefore, the blood levels of androgens increase in people with PCOS [3]. 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 genital tract in the patients, are the main reasons for infertility in reproductive-age women [4,5]. PCOS is one of the most common gynecological disorders in reproductive-age women with the incidence likelihood of 4–12% [6,7]. The prevalence rate of this disease was reported 5.6–8% in Europe [8,9]. According to the latest studies, the prevalence of PCOS in Iran is 19.5% based on Rotterdam criteria and 6.8% based on the NIH criteria [10]. The cause of infertility is lack of ovulation in approximately 75% of the cases [11]. Currently, clomiphene citrate, metformin, and tamoxifen are the most widely used drugs to treat PCOS [12]. With regards to the side effects of such drugs and relative treatment of PCOS by them, it is essential to identify and develop alternative drugs [2], out of which plant-based drugs especially estrogen-containing ones (phytoestrogens) are considered to be comparatively more effective [13,14]. Phytoestrogens are weak antagonists of estrogen, and exhibit more potent estrogenic effects when estrogen level of the body is low [15]. With regards to the increasing prevalence of PCOS and associated physical and mental problems as well as the effects of changes in sex hormones in development of this disease, our aim is to review evidence on the pathophysiology and etiology of this disease and the effects of different herbal extracts on changes in the serum levels of sex hormones and ovarian tissue.

2. Methods

2.1. Database and search strategies

A systematic review of the literature between the periods of 1990–2017 was made based on Google Scholar, PubMed, Elsevier, Scientific Information Database, and Science Direct. The keywords used for the search were Herbal medical extract، Names of medicinal plants ، polycystic ovary syndrome, PCOS ،The mechanism of hormone.

3. The pathophysiology and etiology of PCOS

The cause of PCOS has not yet been definitely determined; however, it is mainly characterized by hyperandrogenism, infertility, lack of ovulation [16], increased level of LH [17], increased insulin resistance, decreased sex hormone-binding globulin (SHBG) [18,19], and hirsutism [20] which visualized as well as diagnosed by ultrasonography and laboratory tests [21]. Because of disrupted secretion rate and metabolism of androgens and estrogens in women with PCOS, the serum concentrations of androgens such as testosterone, androstenedione, and dehydroepiandrosterone are most probably high in such women [20,22]. In addition, the incidence of certain complications such as environmental insulin resistance and hyperinsulinemia is very likely. Such complications lead to obesity at different degrees. Insulin resistance can occur due to impaired signaling pathway of insulin receptor. Therefore, insulin function in the cell is impaired, which causes further increase in insulin secretion to compensate for its shortage. With increase in insulin, the effect of gonadotropins on ovarian function increases, and adiponectin decreases in patients with PCOS due to insulin resistance [22]. Insulin resistance and subsequently excessive increase in insulin levels cause the frequency of GnRH to escalate, which results in increased LH/FSH. These hormone changes in the theca cells and granulosa cells (GCs) cause increase in the synthesis of androgens and decrease in the synthesis of estradiol, and stops the maturation of follicles, leading to impaired ovulation and therefore development of PCOS [23].

4. The role of the neuroendocrine system in PCOS

The reproductive system is a constituent of the endocrine system and includes an axis called reproductive axis that is located at three levels; hypothalamic, pituitary, and gonadal [24], and is therefore referred to as the hypothalamic–pituitary–gonadal (HPG) or gonadotropic axis. In this axis, hypothalamus neurons produce gonadotropin-releasing hormone (GnRH) that enters the hypophyseal portal system and then stimulates release of gonadotropins, luteinizing hormone (LH), and follicle-stimulating hormone (FSH) from the anterior lobe (adenohypophysis) of the pituitary gland (hypophysis). These hormones affect the gonads and lead to gametogenesis through producing the sex steroids estrogen, progestins, and androgens [25]. Sex steroids control secondary sexual characteristics, and contribute to regulating other parts of the HPG axis using negative and positive feedback. The HPG axis is temporarily active during embryonic development, but then it remains inactive until puberty. During puberty, a series of developments lead to increased secretion of GnRH from the hypothalamus. Release of adequate amounts of leptin from adipose tissue and genetic, environmental, and social conditions are some of the most important factors for these developments [26]. After puberty, regulatory signaling such as temperature and light, certain factors such as blood sugar levels and body metabolism, and mental states can affect the secretion of GnRH that in turn influences on gonadotropic cells of adenohypophysis and causes increase in the secretion of FSH and LH [27]. LH and FSH are both secreted in a type of cell (hypophyseal gonadotropin) and stored in separate granules but the rhythm of LH release is compatible with GnRH pulses [28]. GnRH is the main regulator of sexual maturity and reproduction in mammals [29]. To date, 20 different types of GnRH have been identified in vertebrate three main types of which are GnRH I, II, and III. In mammals, GnRH I and II are secreted. GnRH I serve as the regulator of gonadotropins and GnRH II acts as a neuromodulator and also contributes to sexual behaviors [30]. GnRH is released from the hypothalamus as pulse and surge. The pulse mode of GnRH represents the coordinated activity of over 1500 GnRH neurons that comprise a network in the hypothalamus. Each GnRH pulse is accompanied by an LH pulse. In human, the interval between LH pulses is one hour. This high coordination among the GnRH neurons is derived from a neuropulse generator referred to as the GnRH pulse generator [31]. This pulse mode of the GnRH release is essential for normal functioning of the gonadotropins in the long term and the capacity of normal reproduction [32]. Slow GnRH pulses release further FSH while rapid pulses are more compatible with increased LH [33]. In normal conditions, theca cells mainly produce androstenedione under LH influence. Androstenedione enters GCs and waits for either of these two

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scenarios: It is converted to estrone, which is then converted to beta-estradiol under the influence of 17-beta hydroxysteroid dehydrogenase (17β-HSD), under the aromatase CYP19 influence; or it is converted to testosterone under 7βHSD influence and then testosterone converted to beta-estradiol under the influence of aromatase. The expression rate 7βHSD in the GCs is regulated by FSH effect [17,22]. In the first sexual cycle (the follicular phase), estradiol leads to formation of further receptors from FSH, increases the GCs sensitivity to FSH, and also reduces FSH secretion through exerting negative feedback on the pituitary. But, because the dominant follicle expresses a great number of the FSH receptors, it responses proportionately to the reduced amounts of the FSH and continues to produce estradiol [22,34]. When estradiol levels increase, this hormone can exert positive, rather than negative, feedback on the hypothalamus and lead to a sudden and considerable increase in GnRH secretion, which in turn results in LH surge, and therefore ovulation occurs [34,35]. Although the cause of PCOS has not yet been determined, it is obvious that excessive increase in insulin secretion, which is due to insulin resistance, can cause increase in the frequency of the GnRH pulses and therefore increase in the secretion of LH compared to that of FSH. This hormonal change at the surfaces of theca and GCs leads to increased production of the androgens and decreased production of estradiol that stops follicular maturation and therefore disrupts ovulation[34] .

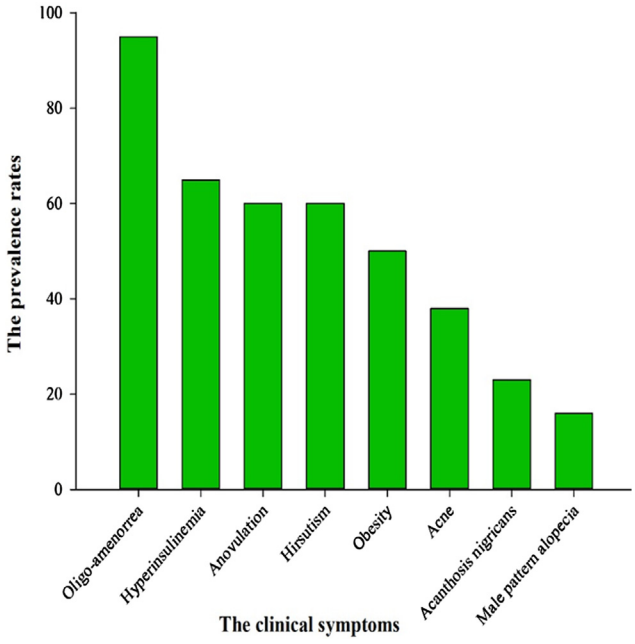

Fig. 1. The prevalence rates of clinical symptoms in women with polycystic ovary syndrome (PCOS).

5. Clinical symptoms of women with PCOS

The prevalence rates, associated clinical symptoms and pathogenesis in women with PCOS are presented in Figs. 1 and 2 [35,36].

5.1. Treatments for PCOS

Weight loss via Diet and Exercise.

Laparoscopy using different methods such as: electrocautery, laser, and biopsy.

Synthetic drugs:

- Oral contraceptive pills;
- Progestins such as medroxy progesterone acetate;
- Anti-androgens such as cyproterone acetate, spironolactone or flutamide;
- Insulin-sensitizing drugs (insulin-metformin);
- Clomiphene citrate [36–38].

5.2. Medicinal plants effective on PCOS

See Tables 1 and 2.

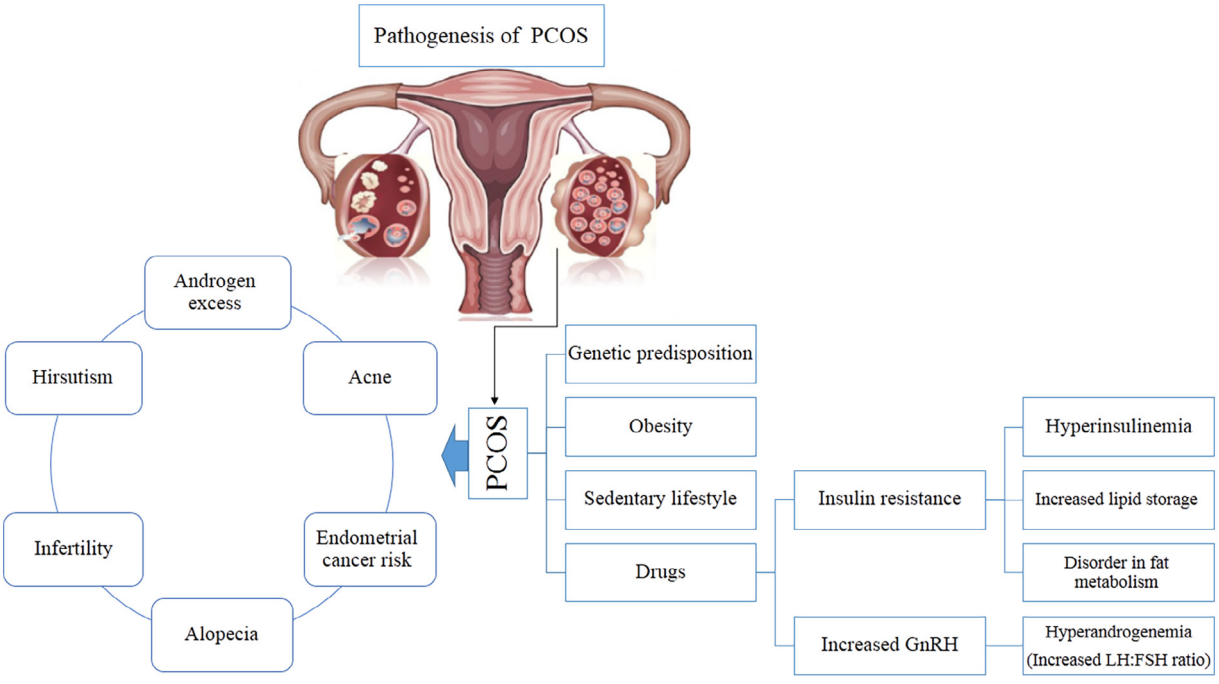

Fig. 2. The main pathogenic factors in PCOS.

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Table 1
Summarizes evidence on medicinal plants that are effective on PCOS in human (Clinical studies).

Medicalplants &scientific name	English name	Family	Study design	Study duration	Mechanism of action	Outcomes	References
Mentha spicata	Spearmint	Lamiaceae	42 women with PCOS and hirsutism treated with *M. spicata* tea twice a day compared with placebo tea.	One month	Not clear	Decreased levels of total and free testosterone in *M. spicata*-treated group after 1-month treatment, increased FSH and LH, and decreased degree of hirsutism	[41]
Cinnamomum zeylancum	Cinnamon	Lauraceae	Fifteen women with PCOS orally treated with *C. zeylanicum* and placebo.	For eight weeks	Improved insulin sensitivity	Significant decrease in insulin resistance in *C. zeylanicum*-treated group.	[48]
Grifola frondosa	Maitake or Hen-of-the-wood	Meripilaceac	72 patients randomly assigned to the group treated with the extract or clomiphene citrate alone and 18 ones who did not respond were co-treated with the extract and clomiphene citrate.	Treatment with the drug alone for 12 weeks and co-treatment with the drug and extract for 16 weeks.	Improved insulin sensitivity	Observation of ovulation in the patients of all groups	[49]
Origanum majorana	Sweet Marjoram	Lamiaceae	25 patients were treated with *O. majorana* tea (14 patients) and placebo tea (11 patients).	For one month	Improved insulin sensitivity and antiandrogen	Decreasing fasting insulin levels and DHEA-S.	[52]
Trigonella foenum-graceum L	Fenugreek	Leguminosae	58 women with PCOS assigned to two groups: One 30 + individual group treated with *T. foenum-graceum* seed capsule + metformin and the other group treated with placebo + metformin.	8 weeks	Improved insulin sensitivity	According to ultrasound scans, decrease in the polycystic ovaries and improvement of the ultrasound results and menstrual cycle in the women	[56]
Phoenix dactylifera	Date palm	Arecaceae	48 female Wistar rats assigned to 6 groups of 8 each: Control group, sham group administered with estradiol valerate solvent for 60 days and then treated with water for 21 days, PCOS1 control and PCOS2 control groups.	60-day administration with estradiol valerate and 21-day treatment with the extract.	Antiandrogen	Decreased levels of estrogen and LH, increased levels of progesterone andFSH, decreased number of cystic follicles, increased number of primary and antral follicles and Graafian such as corpus luteum.	[61]

6. Discussion

We conducted this review to present evidences on the etiology of PCOS and introduce plants that have been recently investigated for their effects on this disease in studies with human subjects and animal models. Most studies investigated the serum levels of sex hormones, hyperandrogenism, insulin resistance, ovarian weight and histopathology, ovulation, and the symptoms of PCOS before and after the treatment. By inducing polycystic ovary syndrome and then, treatment with different extracts the blood testosterone and LH levels were reduced and the blood progesterone and FSH levels increased. Also, histopathological changes indicated that there were many types of follicles in different stages of growth in the treatment groups, including primary follicles, antral, periantral, graafian, corpus luteum, and large oocytes. Most of these studies reported that the studied herbal extracts were effective in treating PCOS and improved the levels of sex hormones, insulin resistance, hyperandrogenism, ovulation, and PCOS symptoms. In these studies, testosterone propionate, estradiol valerate, and letrozole were used to induce PCOS. In estradiol valerate-induced PCOS, widely used in studies, LH and testosterone increase and FSH decreases [45]. Besides that, letrozole, an aromatase inhibitor, has been used to induce PCOS. Aromatase is a small member of the cytochrome p450 family that converts androsetenedione to estrogen and testosterone to estradiol. Hormone changes in such models are associated with increased levels of testosterone and LH, and decreased levels of estrogen, progesterone, and FSH that are in agreement with PCOS-induced changes in different species [62]. In women with PCOS, secretion rate and metabolism of androgens and estrogens are impaired and androgens levels increase. With development of insulin resistance and subsequently excessive increase in insulin, the frequencies of GnRH pulses may be escalated. As a result, insulin resistance causes increase in LH/FSH, and such hormone changes at theca cell surface and granulosa cause increase in the synthesis of androgens and decrease in the synthesis of estradiol. Finally, the maturation of follicles is stopped and therefore ovulation is impaired [63]. Currently, because there is no definite and ideal treatment for hormonal disorders and associated clinical manifestations, and also chemical drugs have several side effects, thereby alternative treatment, especially phytotherapy, can be considered instead of commercially available drugs. Because medicinal plants contain active compounds as well as has no major adverse effects, therefore, they have attracted much attention within recent years. For example *licorice, raspberry,* and *soybean* are some of these plants and contains large amounts of certain phytoestrogens such as biochanin A, daidzein, genistein, and formononetin. The anti-androgenic property of this plant causes decrease in androgens levels in patients with PCOS [39,44,50]. A study demonstrated that raspberry fruit extract caused decrease in testosterone through inhibiting NF-kB pathway, and improved ovarian tissue symptoms including the number of developing follicles, granulosa layer thickness, and the number of corpus luteum through antioxidant and anti-inflammatory properties [44]. Jelodar et al. reported that the consumption of *V. agnus-castus* fruit extract could cause increase in aromatase activity, and decrease in testosterone through aromatizing testosterone

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Table 2
Summarizes evidence on medicinal plants that are effective on PCOS in animals (Experimental studies).

Medical plants & scientific name	English name	Family	Study design	Study duration	Mechanism of action	Outcomes	References
Glycyrrhiza glabra L	Licorice	Fabaceae	84 mice assigned to six groups: Control group, hyperandrogenism group, and *G. glabra* extract (150, 300, and 450 mg/kg) groups	Inducing PCOS using letrozole for 21 days	Antiandrogen and phytoestrogen	Improvement of the adverse effects of hyperandrogenism due to PCOS in female mice's fertility.	[39]
Mentha piperita	Peppermint	Lamiaceae	40 Wistar rats with letrozole-induced PCOS.	Daily administration with letrozole for three weeks and treatment with the extract for three weeks	Antioxidant property	*M. piperita* supplementation caused improvement of ovarian cysts, necrosis of stromal mesenchymal cells, and hyperplasia of luminal epithelial cells.	[40]
Vitex agnus-castus	Monk,s pepper tree	Verbenaceae	32 Sprague Dawley rats with letrozole-induced PCOS and the treatment group treated with 365 mg/kg of the extract.	28-day administration with letrozole and 30-day treatment with the extract	Antiandrogen and phytoestrogen	Decreased serum level of testosterone and increased serum level of progesterone	[2]
Marrubium Vulgare	White Horehound	Lamiaceae	48 Wistar rats with letrozole-induced PCOS and the treatment group treated with 500 and 1000 mg/kg of the extract.	28-day administration with letrozole and 21-day treatment with the extract	Antiandrogen and phytoestrogen	Significant decrease in LH and testosterone (in 1000 mg/kg) and in estradiol and progesterone (at both doses).	[42]
Camellia sinensis	Green Tea	Theaceae	96 Wistar rats with estradiol valerate-induced PCOS assigned to 4 groups and the treatment groups treated with 50, 100, and 200 mg/kg of the extract.	60-day administration with estradiol valerate and 10-day treatment with the extract	Antioxidant property	Significant decrease in serum LH levels, decrease in the body's and ovarian weight and insulin resistance; changes in the number of follicles and the thickness of theca layer in histomorphometric studies	[43]
Rubus idaeus × strigosus	Raspberry	Rosaceae	120 Wistar rats with estradiol valerate-induced PCOS and the treatment groups treated with 100, 150, and 200 mg/kg of the extract.	60-day administration with estradiol valerate and 10-day treatment with the extract	Antioxidant property	Decrease in testosterone, estradiol, LH, and CRP and increase in progesterone and FSH	[44]
Chamaemelum nobile Or Anthemis nobilis L.	Chamomile	Asteraceae	30 rats with estradiol valerate-induced PCOS and treated with 25, 50, and 75 mg/kg of the extract.	60-day administration with estradiol valerate and 10-day treatment with the extract	Antiandrogen and phytoestrogen	Decrease in the symptoms of PCOS and the secretion of LH, FSH, and estradiol.	[45]
Pergularia Daemia	Trellis – vine	Apocynaceae	Inducing PCOS using testosterone propionate in Albino Wistar rats and treating them with the extract.	One-week induction and then one-week treatment with the extract	Management of obesity	Normalization of irregular estrous cycle in patients with PCOS after treatment with the extract	[46]
Foeniculum vulgare	Fennel	Apiaceae	30 rats with estradiol valerate-induced PCOS and 6 normal rats; the treatment groups were treated with 250, 500, and 1000 mg/kg of the extract.	60-day administration with estradiol valerate and 10-day treatment with the extract	Antiandrogen and phytoestrogen	Increased concentration of FSH after treatment with 500 and 1000 mg/kg of the extract and decreased LH and testosterone after treatment with 1000 mg/kg of the extract.	[47]
Glycine max	Soybean	Fabaceae	Inducing PCOS in Sprague Dawley rats using letrozole and treating them with soybean isoflavones (in 50&100 mg/kg).	21-day administration with letrozole and 14-day treatment with the extract	Antiandrogen and phytoestrogen and antioxidant	100 mg/kg of soybean significantly changed PCOS symptoms through the body's weight loss, and reducing diestrus phase, testosterone, the activities of 3 beta-hydroxysteroid dehydrogenase and 17beta-hydroxysteroid dehydrogenase, and oxidative stress.	[50]
Atractylodes macrocephala Koidz	Atractylodes	Asteraceae	60 rats assigned to 5 groups of 12 each: Healthy control,	Inducing PCOS for 12 days and	Antiandrogen	Improving estrous cycle, decreasing the plasma	[51]

(*continued on next page*)

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Table 2 (*continued*)

Medical plants & scientific name	English name	Family	Study design	Study duration	Mechanism of action	Outcomes	References
(AMK)			PCOS, and three PCOS groups treated with low, moderate, and high concentrations of the extract; inducing PCOS using testosterone propionate.	treating with the extract for 8 consecutive weeks.		levels of total testosterone, androsetenedione, and FAI, higher levels of FSH and lower LH/FSH and anti-Mullerian hormone in ovary, and decreasing the expression levels of FSH receptor and increasing the expression levels of aquaporin 9.	
Corylus avellana	Hazelnut or cobnut	Betulaceae Or Corylaceae	18 Sprague Dawley rats with letrozole-induced PCOS assigned to 3 groups of 6 each: Control, busereline acetate-treated, and treatment	21-day administration with letrozole and 45-day testing of the groups	Antiandrogen	Effective in treating PCOS through regulating serum lipid profile, steroids, and gonadotropins.	[53]
Bmbusa Vulgaria	Bamboo	Poaceae	4 groups of 6 each administered with letrozole, group 2 considered negative control, and groups 3 and 4 treated with 0.5 and 1 ml/kg of the extract.	21-day administration with letrozole and 3-week treatment with the extract	Antioxidant and antidiabetic	Improving estrous cycle and exerting hypolipidemic and hypoglycemic effects. Decreasing blood glucose and the levels of cholesterol, LDL, and triglyceride, improving cystic ovaries and ovulation.	[54]
Aloe vera	Aloe, Barbados aloe	Aloaceae	Two groups: Control group daily treated with carboxymethyl cellulose 1% and the other group administered with letrozole to induce PCOS and then treated with nonpolar *A. vera* extract for 60 days.	21-day administration with letrozole and 60-day treatment with the extract.	Antiandrogen	Decreasing the levels of testosterone and insulin through improving the levels of progesterone and estradiol; decreasing the transcription levels of steroid receptors; increasing aromatase expression.	[55]
Labisia pumila var. alata	Labisia	Primulaceae	Mice with PCOS assigned to two groups: The extract-treated and control groups; the extract-treated group orally treated with 50 mg/kg of the extract each day and the control group treated with 1 ml of deionized water.	4–5 weeks	Antiandrogen and phytoestrogen	Increasing uterus weight and insulin resistance; increasing resistin and improving lipid profile; in adipose tissue, decreasing the expression of leptin mRNA but ineffective on the expression of resistin and adiponectin.	[57]
Heracleum persicum	Desf	Apiaceae	In 30 rats, PCOS was induced by estradiol valerate and then treated with doses of 200 mg/kg, 400 and 800 Desf extracts.	Induction of PCOS in 60 days and 10 days treatment with extract.	Antiandrogen	Serum levels of estradiol, testosterone and LH increased, and FSH increased.	[58]
Cocos nucifera	Coconut palm	Arecaceae	Wistar rats with letrozole-induced PCOS were left untreated for 21 days and then treated with 100 and 200 mg/kg of *C. nucifera* aqueous extract. A positive control group, a negative control group, and two treatment groups were studied.	21-day administration with letrozole and 4-week treatment with the extract.	Antiandrogen and phytoestrogen	Regulating estrous cycle and increasing uterus weight.	[59]
Punica granatum L.	Pomegranate Juice	Lythraceae	56 Wistar rats were assigned to 6 groups of 8 each and PCOS was induced by estradiol valerate. The rats were treated with different doses of *P. granatum* extract.	81 days	Antioxidant property	Improving the levels of testosterone, androsetenedione, and estrogen in the treated groups.	[60]

and converting it into estradiol. This extract contains a number of phytoestrogens. Certain flavonoids such as apigenin, vitexin, and penduletin that can bind to estrogen receptors were isolated from this plant [2]. Isoflavones exert their inhibitory effects on many key enzymes of steroid metabolism and therefore decrease the levels of active hormones in the tissues in question. Many cancers of reproductive organs are dependent on hormones, and cell growth is prevented by decrease in the levels of active hormones. This can be an explanation for isoflavones' having potential to exhibit phytoestrogen activities through steroid pathway. As a result, an

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isoflavone-rich diet can be the biochemical basis of preventive effects against cancer [64]. Other studies indicated that genistein could inhibit 3β-HSD and 17β-HSD in the testicular microsomes of both human and mouse. It has been reported that isoflavonoids due to having phenolic ring preferably inhibit the activities of 3β-HSD and 17β-HSD. In addition to inhibiting steroid-synthesizing enzymes, genistein can be involved in LH receptor's binding to G-protein, and affect adenylatecyclase activity if LH receptor does not bind to the G-protein and block steroidogenesis-stimulated production of LH [50]. Oxidative stress is considered a pathological characteristic of PCOS, and in women with PCOS, total antioxidant status declines. Evidence indicates that the levels of ROS in ovarian tissue increase in PCOS, causing imbalance between oxidant and antioxidant systems. Soybean isoflavonoids exert antioxidant effect because of containing aromatic ring and genistein [50]. *P. dactylifera* pollen contains antioxidant compounds such as different vitamins and minerals, e.g. zinc and selenium, that cause regulation of the body's antioxidant balance in people with PCOS (62). Many of the studied plants including *Soybean*, *Raspberry*, *A. vera*, *L. pumila, C. nucifera, G.* max, and *G. glabra* have anti-androgenic property and certain plants such as: *P dactylifera*, *G.* max, *C. sinensis*, *M. piperita* and *T. vulgaris* have antioxidant property that are effective in treating PCOS through improving the serum levels of sex hormones and decreasing oxidative stress. In the light of the evidence, different types of phytoestrogens and antioxidant compounds found in medicinal plants can improve PCOS symptoms and therefore be effectively used to treat this syndrome.

Conflict of interest

We declare no conflict of interest.

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