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Review article

Traditional Persian Medicine and management of metabolic dysfunction in polycystic ovary syndrome

Ayda Hosseinkhani ^{a, b}, Nasrin Asadi ^c, Mehdi Pasalar ^a, Mohammad M. Zarshenas ^{b, d, *}^a Research Center for Traditional Medicine and History of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran^b Department of Phytopharmaceuticals (Traditional Pharmacy), School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran^c Maternal-fetal Medicine Research Center, Shiraz University of Medical Sciences, Shiraz, Iran^d Medicinal Plants Processing Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

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ABSTRACT

Polycystic ovary syndrome (PCOS) is a common endocrine disorder in women of reproductive age. Its cause is unknown and it remains the most enigmatic of reproductive disorders. The extant written documents of Traditional Persian Medicine (TPM) – with holistic approaches towards human health – contain remedies used for centuries. Before further experimental research on any of these treatments, it is appropriate to study current related scientific evidence on their possible pharmacological actions. This work aims to study PCOS and its treatments in TPM. To collect data from medieval medicinal texts, six of the most famous manuscripts of Persian medicine were studied. Medicinal treatments for a problem similar to PCOS were searched for in these books. The plants were listed and their authentications were confirmed in accordance with botanical books. PubMed and ScienceDirect databases were searched for related mechanisms of action or pharmacological activities of the medicinal plants reported. From numerous articles, the current work tried to cite the latest publications with regard to each reported plant and PCOS-related mechanisms of action. We studied herbal treatments recommended by ancient Persians to treat a condition called *Habs-e-tams*, which had the same symptoms of PCOS. It could be concluded that ancient physicians not only wanted to treat the irregular menstrual cycle—which is the most obvious symptom of PCOS—but also their treatment options were aimed at ameliorating the related underlying metabolic dysfunctions. The recommended herbs, which have the most scientific proof for their related actions, can be studied further in experimental analyses.

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1. Introduction

There are many medical issues for which common treatments are suboptimal. The majority of medicines today contain single active ingredients that are active against a single biological target. Owing to the complexity of the human body, this approach might seem rather simplistic.¹ The scientific viewpoint, in many studies, still reflects reductionist logic. Although it has provided us valuable cellular information, it lacks an overall vision. This approach started to change from the early years of the second millennium. In recent years, a more comprehensive and holistic approach was applied in

health-related studies.² Traditional medicines of the world often adopt holistic approaches towards human health as well.³ Unlike conventional drugs, traditional medicine contains medications that are often multicomponent and, therefore, multi-target.¹ In medical practice, one of the areas in which physicians find difficulties in curing patients are syndromes that have a set of signs and symptoms correlated with each other and with a specific disease. One of these syndromes is the polycystic ovary syndrome (PCOS), which affects up to 17.8% of women of reproductive age. The medical management of this problem requires a multidisciplinary approach. At present, conventional therapies are not effective, and some have unwanted side effects. Women with PCOS prefer alternative therapies.⁴ The extant written documents of traditional medicinal systems contain a list of drugs that have been used for centuries. These can be good sources for finding possible new drugs for medical conditions which do not have a satisfying treatment. One

* Corresponding author. Department of Phytopharmaceuticals (Traditional Pharmacy), School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran.
E-mail address: zarm@sums.ac.ir (M.M. Zarshenas).

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of the traditional systems of medicine still practised today is Traditional Persian Medicine. This system of medicine was replaced in Iran by Western medicine in the late 19th century. Although physicians were not allowed to apply the treatments of this system of medicine, valuable information was preserved in the books of scholars. Iranian people still seek help for their health-related problems from local herbal shops, which have kept the practice of TPM alive. In the past few years, Iranian universities have changed their policies towards TPM. Today, specialists are studying this system of medicine from different aspects. Recently, traditional Persian therapies have been evaluated by modern methods.⁵ Iranian pharmaceutical companies are interested in formulations based on TPM remedies. In this work, we aim to study the polycystic ovary syndrome and its treatments in TPM. The recommended herbs, which have had the most scientific proof for their related pharmacological actions in the treatment of PCOS, have been preferred for the experimental research.

1.1. Modern description of PCOS and its treatments

This syndrome presents itself in menstrual irregularity, androgen excess and polycystic ovaries. It is the most common endocrine disorder in such women.⁶ It is associated with insulin resistance, hyperinsulinism⁷ and diabetes.⁸ Women with this syndrome often suffer from dyslipidemia and obesity as well.^{9,10} Today, the treatment of PCOS includes restoring normal menstruation cycle and ovulation, reducing hirsutism and acne, and also reducing cardiovascular risk for the patients.⁶ Oral contraceptives and metformin are commonly prescribed forms of medication for these patients. Lifestyle modification is recommended to overweight/obese patients with PCOS.¹¹ One of the main characteristics of the PCOS is obesity. It affects fertility in women suffering from PCOS through different mechanisms. Excess androgen levels, insulin resistance and increased luteinizing hormone (LH) play the main role.¹² Research has suggested that weight loss in these women can restore ovulatory cycles, which allows spontaneous pregnancy.¹³

1.2. Description of PCOS in Traditional Persian Medicine

Traditional Persian Medicine deploys a holistic approach. It is a protracted method of practice from ancient Persia. Though terminology that is the same as PCOS cannot be found in TPM textbooks, that does not mean that evidence is absent. Regarding signs and symptoms of PCOS in current literature, there is a reasonable description of this issue in Persian resources. Symptoms of PCOS have been indicated and described under the topic of 'uterus and ovary'-related disorders, such as 'female infertility', 'uterine inflammation', and 'amenorrhea'.¹⁴ Signs and symptoms of the latest disorder in TPM textbooks, titled *Ehtebās-e-Tams* (lack of menstruation), come very close to PCOS.¹⁵ The main sign that can be attributed to PCOS is prolonged intervals of menstrual bleeding (more than two months). According to TPM books, it could occur as a result of two groups of factors: intrinsic and extrinsic. Intrinsic factors are related to the genitourinary (GU) system itself and other factors focus on the entire human body and interconnected body systems. In the first category, there are: severe cold temperament of GU system, hyper-dense humor (caused by cold temperament), and plethora of phlegmatic humor. There are also general classifications of extrinsic factors. These are cold and dry dystemperament, cold dystemperament with excess of phlegm, or black bile and overt obesity.¹⁶ Some of the aforementioned terms—such as overweight—have been approved in recent literature as causes of PCOS. The TPM therapeutic approach for these ailments emphasizes the removal of the cause instead of the symptom. As regards the abovementioned pathologic categorization, a TPM practitioner

should follow the curative plan in a holistic manner. Obeying a specific diet regimen and lifestyle modifications are the first essential steps for a patient's cure. If nutritional and lifestyle instructions are not appropriately responded to, the treatment strategy would be converted to medicinal options.¹⁷ Most of the medicinal choices are herbal medicine, which have been defined in detail in ancient Persian pharmacopoeias. Some of these medications are single herbs and some are combined preparations. The present work considers these herbs. Their respective efficacies have been reviewed in multiple in vitro or in vivo surveys.

2. Current methods

To collect data from medieval medicinal texts, six main manuscripts of Persian medicine were studied. These texts are currently known as the main university reference books for research into TPM in departments of traditional medicine and pharmacy in Iranian universities. Since the end of the 19th century, when TPM was replaced in Iran by Western medicine, no written document on the practice of this system has been available. The definition and causes of *Ehtebās-e-Tams* was studied in *Exir-e-Azam* (Azam Khan, 19th century) and *Moalejat* (Aghili, 18th century). Medicinal treatments for this problem were searched in *Kitab al-hawi fi al-tibb* (Rhazes, 9th–10th centuries), Canon of Medicine (Avicenna, 10th–11th centuries), *Tuhfat al-muminin* (Daylami Tunakabuni, 17th century), and *Makhzan al-adviyah* (Aghili, 18th century).^{16,18–21} The plants used in the treatment of *Ehtebās-e-Tams*, according to Persian manuscripts, are listed in Table 1. Authentications of the plants were also confirmed by botanical books such as *Dictionary of Medicinal Plants, Matching the Old Medicinal Plant Names with Scientific Terminology, Indian Medicinal Plants, and Dictionary of Iranian Plant Names*.^{22–25} PubMed and ScienceDirect databases were searched for related mechanisms of action or pharmacological activities of the medicinal plants that were reported. The scientific name of each herb was searched along with these keywords: 'anti-hyperglycemic', 'anti-dyslipidemia', 'anti-obesity' and 'ovulation-inducing'. From numerous articles, the current work tried to cite the latest publications with regard to each reported plant and PCOS-related mechanisms of action.

3. Current results

Forty herbs—either as single or as a component of a compound medication to treat *Ehtebās-e-Tams*—were found in TPM books. The majority of these herbs exhibited anti-hyperglycemic (90%) and anti-dyslipidemic (77.5%) effects. Some of these herbs showed significant anti-obesity properties (37.5%). The effect of some of these were studied on ovulation induction and 27.5% had shown positive effects. Table 1 represented herbal remedies for *Ehtebās-e-Tams* from *Reports of Traditional Persian Medicine*. In this table, related pharmacological activities and citations of the current proof are also reported.^{26–99}

4. Conclusions and further suggestions

Polycystic ovary syndrome is the most common endocrine disorder in women of reproductive age.⁷ While the cause is unknown, this disorder remains the most enigmatic reproductive disorder. Therefore, there is no known cure for this problem.¹⁰⁰ Most common treatments for PCOS are oral contraceptives to suppress the secretion of gonadotropin and decrease free androgen blood levels.¹⁰¹ This can lead to regular menstruation cycles. It is remarkable that the use of oral contraceptives may have unfavorable effects on hyperglycemia and insulin resistance. Metformin is also one of the medications for the treatment of PCOS. Today, the

Table 1
Herbal Remedies for “Ehtebās-e-Tams” from reports of Traditional Persian Medicine.

Scientific name	Related Pharmacological activities/method, model or assay			
	Anti-hyperglycemic	Anti-dyslipidemic	Anti-obesity	Ovulation-inducing
<i>Adiantum capillus-veneris</i> L.	+ (Aqueous, Methanol extract)/ Streptozotocin-induced diabetic rats ²⁶	–	–	–
<i>Allium cepa</i> L.	+ (Seed ethanol extract) Improvement in FBS and HOMA-IR levels/Diabetic-prone rat ²⁷	+ Reduction in FFA and TG levels/obesity-prone diabetic fatty rat ²⁷	+ May be effective in formation of oil drop in preadipocyte cells/ indict ²⁷	+ Antioxidants level compensation to modulate apoptosis/PCO -induced rat ²⁸
<i>Allium sativum</i> L.	+ (Ethanol extract), Serum glucose level reduction and Increasing serum insulin level/ streptozotocin-induced diabetic rat ²⁹	+ (Ethanol extract), Decreasing the ALT, AST, cholesterol, urea, uric acid and creatinine ²⁹	+ Reduction in body weight, visceral fat, MDA and cholesterol levels/High-fat diet rat ³⁰	–
<i>Anethum graveolens</i> L.	+ (Leaf hydroalcoholic extract), Regulation of diabetes mellitus/ corticosteroid-induced type II in rats ³¹	+ Dill tablets versus Gemfibrozil/(Human study) Reduction of cholesterol (18%) and TG (7%) ³²	–	+ (Ethanol extract), Increase in estrous cycle duration and diestrus phase and progesterone concentration/ Rat ³³
<i>Apium graveolens</i> L.	–	+ (Ethanol extract)/Decrease in TG, LDL-Cholesterol, increase in HDL (rat) ³⁴	+ (Aqueous extract)/Based on body and organs weights as well as biochemical parameters (rat) ³⁵	–
<i>Artemisia absinthium</i> L.	+ Improvement in glucose tolerance by increasing in tyrosyl phosphorylation of insulin receptor/Shikonin treated mice ³⁶	+ Improvement in lipid profile/ Shikonin treated mice ³⁶	+ Decrease in weight, resistance to high fat diet/ Shikonin treated mice ³⁶	–
<i>Asparagus officinalis</i> L.	+ (Methanol extract), improving in insulin secretion and β-cell function/ streptozotocin-induced diabetic rats ³⁷	+ (Ethanol, aqueous extracts), decrease in cholesterol and LDL/Hyperlipidemic mice ³⁸	+ (Ethanol, aqueous extracts), decrease in body weight gain/ Hyperlipidemic mice ³⁸	+ (Aqueous extract), increase in GnRH, FSH, LH, estrogen, progestin hormones levels and number of ovarian follicles/ rats ³⁹
<i>Cappari spinosa</i> L.	+ (Aqueous extract), decrease in blood glucose level/ Streptozotocin-induced diabetic rats ⁴⁰	+ (Aqueous extract), decrease in TG and cholesterol/normal and Streptozotocin-induced diabetic rats ⁴¹	–	–
<i>Carum carvi</i> L.	+ (Aqueous extracts), decrease in blood glucose/ Streptozotocin-induced diabetic rats ⁴⁰	+ (Aqueous extract), hypotriglyceridemic, hypocholesterolemic effects/ Normal and Streptozotocin-induced diabetic rats ⁴²	+ Reduction in weight, body mass index, body fat percent, and waist-to-hip ratio/Clinical trial ⁴³	–
<i>Cicer arietinum</i> L.	+ improvement in insulin resistance, preventive effects on postprandial hyperglycemia and hyperinsulinemia/Rat ⁴⁴	+ Reduction in LDL-cholesterol and LDL/HDL levels/Rat ⁴⁴	+ Increase in lipoprotein lipase activity/Rat ⁴⁴	–
<i>Cinnamomum verum</i> J. Presl	+ (Aqueous extract), reduction in fasting blood glucose level (no hypoglycemic activity)/ Diabetic rats ⁴⁵	+ (Aqueous extract), decrease in levels of total cholesterol, HDL, LDL and TG/Diabetic rats ⁴⁵	–	–
<i>Citrulluscolocynthis</i> (L.) Schrad.	+ (Fruit capsules), decrease in HbA1c and fasting blood glucose/Clinical trial ⁴⁶	–	–	–
<i>Citrus × aurantium</i> L.	+ (Isolated neohesperidin), increase in oral glucose tolerance and insulin sensitivity, decrease in insulin resistance/KK-A ^y diabetic mice ⁴⁷	+ (Neohesperidin), decrease in TG, total cholesterol, leptin level, and liver index/KK-A ^y diabetic mice ⁴⁷	+ (Extract), increase glycogenolysis, glycolysis, oxygen uptake, perfusion pressure/Rat ⁴⁸	–
<i>Citrus medica</i> L.	–	–	–	+ (Petroleum ether extract), estrogenic effects/Immature ovariectomized rat ⁴⁹
<i>Commiphora mukul</i> (Hook. ex Stocks) Engl.	+ (Ethanol extract), preventive effects against alteration in hexokinase, phosphofructokinase, pyruvate kinase, and glucose-6-phosphatase/Streptozotocin-induced diabetic rats ⁵⁰	+ (Ethanol extract), preventive effects against alteration in fatty acid synthase, malic enzyme and lipoprotein lipase/ Streptozotocin-induced diabetic rats ⁵⁰	–	–
<i>Commiphora myrrha</i> (Nees) Engl.	+ (Aqueous extract), decrease in blood glucose level/Diabetic rats ⁵¹	+ (Guggulipid), decrease in cholesterol level, LDL, TG and cholesterol/HDL levels/Fruit- and vegetable-enriched prudent diet in hypercholesterolemic patients (Clinical trial) ⁵²	–	–

(continued on next page)

Table 1 (continued)

Scientific name	Related Pharmacological activities/method, model or assay			
	Anti-hyperglycemic	Anti-dyslipidemic	Anti-obesity	Ovulation-inducing
<i>Ficus carica</i> L.	+ (Aqueous extract), Insulin-like peripheral effect/Diabetic rats ⁵³	+ (Aqueous ethanol extract), increasing the HDL, decreasing the LDL and cholesterol/High-fat diet-induced hyperlipidemic rats ⁵⁴	–	–
<i>Foeniculum vulgare</i> Mill.	+ (Essential oil), Correcting the hyperglycemia and activity of serum glutathione peroxidase/Diabetic rat ⁵⁵	+ Ameliorates serum glucose, AST, ALT, GGT, LDH, protein, albumin, liver total lipids/Hyperlipidemic rat ⁵⁶	–	+ (Fennel extract), Increases the serum level of estrogen, progesterone, and prolactin/female mice ⁵⁷
<i>Glycyrrhiza glabra</i> L.	–	+ (Root powder), reduction in total lipids, cholesterol, TG, LDL and VLDL, increases in HDL/Hypercholesterolemic rat ⁵⁸	+ (Ethanol extract), reduced weight gain and adipose tissue mass/Rat model of high-fat diet induced hyperlipidemia and obesity ⁵⁹	–
<i>Helianthus annuus</i> L.	+ (Ethanol extract), decreased blood glucose level, restored lipid profile/streptozotocin induced diabetic rats ⁶⁰	–	–	–
<i>Hypericum perforatum</i> L.	+ (Ethyl acetate extract), reduction in plasma glucose level and fasting blood sugar/Streptozotocin-induced diabetic rats ⁶¹	+ (Ethyl acetate extract), Reduction in total cholesterol and TG/Streptozotocin-induced diabetic rats ⁶¹	+ Lowering the total cholesterol and LDL, Inhibiting weight gain, Normalizing the dyslipidemia and improving insulin sensitivity/High-fat-diet induced obese rats ⁶²	–
<i>Lepidium sativum</i> L.	+ (Seed powder), Decreasing in fasting blood sugar, HbA _{1c} , total cholesterol, TG, lipoprotein fractions, Increase in HDL/Alloxan induced diabetic rats ⁶³	+ Reduction in total cholesterol and ALT (6 g/kg diet)/Rats fed with high cholesterol diet ⁶⁴	–	–
<i>Linum usitatissimum</i> L.	+ (Ethanol extract), Reduction in serum glucose level in acute and subacute study/Alloxan induced diabetic rat ⁶⁵	+ Reduction in total cholesterol and increasing in HDL/Sprague Dawley rats ⁶⁶	–	+ (Aqueous methanol extract), Increasing in serum estradiol, progesterone, total proteins and cholesterol, ALT and AST activity, Decreasing ovarian cholesterol levels/Immature female rats ⁶⁷
<i>Lupinus albus</i> L.	+ (Aqueous suspension), Restore the elevated levels of glucose, urea, creatinine and bilirubin/Alloxan-induced diabetic rats ⁶⁸	+ (Isolated proteins, whole seed), Reduction in total cholesterol and related parameters/Hamsters ⁶⁹	–	–
<i>Matricaria chamomilla</i> L.	+ (Ethanol extract), Reducing postprandial hyperglycemia/Streptozotocin-induced diabetic rats ⁷⁰	–	–	+ (Ethanol extract), Decreasing the signs of PCOS in ovarian tissue, helping LH secretion/Polycystic ovary-induced rats ⁷¹
<i>Melissa officinalis</i> L.	+ (Essential oil), Reducing blood glucose and TAG concentrations, improving glucose tolerance and serum insulin levels/Mice ⁷²	+ (Ethanol extract), Reducing serum total cholesterol, lipid, ALT, AST and ALP levels, and LPO level in liver tissue/Hyperlipidemic rats ⁷³	+ (In a combination), Decreasing the adipose tissue mass and body weight/High-fat diet mice ⁷⁴	–
<i>Nigella sativa</i> L.	+ (Oil), Reducing blood glucose and hepatic gluconeogenesis/Streptozotocin-induced diabetic hamsters ⁷⁵	+ (Dietary black seed), Lowering the total cholesterol, LDL and MDA, TG/Rabbits with hypercholesterolemic diet ⁷⁶	–	+ (Hydroalcoholic extract), reduction in the serum level of LH, FSH and estrogen/Female rats ⁷¹
<i>Origanum majorana</i> L.	+ (Extraction, aqueous suspension), Comparable to Glibenclamide/Streptozotocin-diabetic mice ⁷⁷	–	–	+ (Infusion, tea), Reduction in DHEA-S, insulin sensitivity improvement/Hormonal profile, PCO (Clinical trial) ⁷⁸
<i>Petroselinum crispum</i> (Mill.) Fuss	+ Reduction in blood glucose and serum alkaline phosphatase activity/Streptozotocin-induced diabetic rats ⁷⁹	+ (Aqueous extract), attenuating the hyperlipidemia/Diabetic rats ⁸⁰	+ (Hydroalcoholic extract), ketoheokinase inhibitory activity, blocking the fructose-induced ATP depletion/Animal ⁸¹	–
<i>Phaseolus vulgaris</i> L.	+ (Aqueous extract), Decline in blood glucose, serum TG, fatty acids, phospholipids, total cholesterol, LDL, and VLDL/Streptozotocin-induced diabetic rat ⁸²	+ (Aqueous extract), Decline in lipids and fatty acids, palmitic, stearic, oleic acids, increase in linolenic and arachidonic acids/Streptozotocin-induced diabetic rat ⁸³	+ (Dry bean), Weight loss and improve in plasma lipid profile/Diet-induced obesity mice model (74)	–
<i>Pimpinella anisum</i> L.	+ (Methanol extract, mostly ethyl acetate fraction), α -glucosidase and α -amylase inhibition/in vitro ⁸⁵	–	–	–

Table 1 (continued)

Scientific name	Related Pharmacological activities/method, model or assay			
	Anti-hyperglycemic	Anti-dyslipidemic	Anti-obesity	Ovulation-inducing
<i>Piper longum</i> L.	–	+ (Piperine derivative), Decline in TG, increase in HDL levels, and upregulation of HMG-CoA reductase level/High-fat diet-fed rats ⁸⁶	–	–
<i>Prangos ferulacea</i> (L.) lindel.	+ (Hydroalcoholic extract), Glucose and lipid profile reduction/Alloxan-induced diabetic rat ⁸⁷	–	–	–
<i>Prunus domestica</i> L.	–	–	+ (carbohydrate-free peach and plum), Potentiality to modify the fecal microbial ecology in obese model/Obese Zucker rats ⁸⁸	–
<i>Ruta graveolens</i> L.	+ (Infusion), Amelioration of hyperglycemia, hyperlipidemia, insulin and C-peptide concentrations/streptozotocin-nicotinamide-induced diabetic rat ⁸⁹	+ (Hydroalcoholic extract), Decrease in cholesterol, LDL, VLDL and TG/Diabetic rats ⁹⁰	–	–
<i>Thymus vulgaris</i> L.	+ (Aqueous extract), Decrease in FBS, LDL, VLDL, TG and cholesterol/Alloxan-induced diabetic rats ⁹¹	+ (Aqueous extract), Decrease in FBS, LDL, VLDL, TG and cholesterol/Alloxan-induced diabetic rats ⁹¹	–	–
<i>Trachyspermum ammi</i> (L.) Sprague	–	+ (Seed powder), Reduction in lipids, cholesterol, LDL, TG and HMG-COA reductase, Increase in HDL/Hyperlipidemia-induced rabbits ⁹²	–	–
<i>Trigonella foenum-graecum</i> L.	+ (Soluble dietary fiber fraction), Lowering the serum fructosamine/Type II model of diabetic rats ⁹³	+ (Seed powder), Reduction in total cholesterol, LDL, and the atherogenic index, Increase in HDL/Hyperlipidemia-induced rabbits ⁹⁴	+ (Seed extract), Reduction in fat energy intake-total energy expenditure ratio, Decrease in insulin-glucose ratio/Overweight male participants (Clinical trial) ⁹⁵	+ (Seed powder), Increase in circulating plasma progesterone concentrations at 10 and 20 days of gestation/Female white New Zealand rabbits ⁹⁶
<i>Urtica dioica</i> L.	+ (Aqueous extract), Strong glucose lowering effect (Pretreatment)/Alloxan-induced diabetic rats ⁹⁷	+ (Aqueous extract), Decrease in the body weight, TG, Cholesterol, and LDL/Type II diabetic model rats ⁹⁸	–	+ (Dry), Decrease in testosterone and DHEA level/Woman with hyperandrogenism (Clinical trial) ⁹⁸
<i>Zataria multiflora</i> Boiss.	+ (Extract), insulin, adiponectin, glucose and TG levels improved, PPAR γ protein level increased/High fructose diet for rats ⁹⁹	+ (Extract), insulin, adiponectin, glucose and TG levels improved, PPAR γ protein level increased/High fructose diet for rats ⁹⁹	–	–

association between PCOS, hyperglycemia, dyslipidemia and obesity is known.^{9,10,102} The metabolic consequences need to be ameliorated in these patients as well. But the pathogenesis of PCOS is not fully understood and there is no single effective treatment for this disorder.¹⁰⁰ Traditional systems of medicine often contain information on treatments which have been used for centuries. These can be sources of new drug discoveries.¹⁰³ One of the difficulties in this area is that the paradigm of medicine was different and so the terminology used in ancient manuscripts is different from what we understand today. Ancient practitioners often had a holistic approach towards the human body as regards health and sickness. But if the medicines used by ancient healers were effective, it should be explicable by a rational mechanism of action as well. The absence of the menstruation cycle was explained in TPM books under the titles *Ehtebās-e-Tams* or *Habs-e-tams* or *Ehtebās-e-heiz*.¹⁰⁴ Medicinal treatment options were also explained in detail in these books. Going through ancient Persian books, we can find that they mentioned obesity as one of the extrinsic causes of *Habs-e-Tams*. In a research, the emmenagogue activity of the herbal treatments used for amenorrhea by the ancient Persians was studied. In that study, of 71 reported plants, only *Foeniculum vulgare* had an approved emmenagogue activity.¹⁰⁴ This could mean that no direct

emmenagogue effect was expected from these drugs. In the present work, we reviewed the possible anti-hyperglycemic, anti-dyslipidemic, anti-obesity and ovulation-inducing effects of these remedies. In TPM books, *Habs-e-Tams* was defined as a condition of prolonged intervals of menstrual bleeding (more than two months).

The majority of drugs used by ancient Iranians to treat this problem showed to have proven effects on lowering blood glucose and lipids (Table 1). Also, many of these herbs had shown anti-obesity effects. But the main point of this data was that one-third of those remedies showed positive effects on ovulation induction through different underlying mechanisms. It is accepted that one of the main problems in patients with PCOS is infertility, which is related to the lack of ovulation. The same as the points and symptoms denoted in current medicine, this condition is also highly remarked upon by Persian scholars. Effects on ovulation induction, however, were studied mainly in animal models and there is a gap in human-related trials (Table 1). According to the table, only *Origanum majorana* and *Urtica dioica* had clinical trials on ovulation induction. In this respect, it may be important to evaluate the aforementioned activity on other reported plants. On the other hands, of those medicinal plants, only *Allium cepa*,

Asparagus officinalis and *Trigonella foenum-graecum* possessed all the related pharmacological activities. These remedies might show effective results in related clinical trials on patients with PCOS or ovary-related amenorrhea.

Going through the medieval and traditional treatments for *Habs-e-Tams*, as recommended by ancient Persians, one can conclude that they not only wanted to treat the irregular menstrual cycle—which is the most obvious symptom of PCOS—but their treatment options were also aimed to ameliorate the related underlying metabolic dysfunctions. In future work, traditional herbal combinations could be studied and the theoretical role of each ingredient of the formulation could be defined. Furthermore, the effectiveness of these treatments could be investigated in clinical trials after confirmation of their safety.

Conflict of interest

The authors have no conflict of interest.

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