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## Review article

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

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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.<sup>1</sup> 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.<sup>2</sup> Traditional medicines of the world often adopt holistic approaches towards human health as well.<sup>3</sup> Unlike conventional drugs, traditional medicine contains medications that are often multicomponent and, therefore, multi-target.<sup>1</sup> 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.<sup>4</sup> 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

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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.<sup>5</sup> 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.<sup>6</sup> It is associated with insulin resistance, hyperinsulinism<sup>7</sup> and diabetes.<sup>8</sup> Women with this syndrome often suffer from dyslipidemia and obesity as well.<sup>9,10</sup> Today, the treatment of PCOS includes restoring normal menstruation cycle and ovulation, reducing hirsutism and acne, and also reducing cardiovascular risk for the patients.<sup>6</sup> Oral contraceptives and metformin are commonly prescribed forms of medication for these patients. Lifestyle modification is recommended to overweight/obese patients with PCOS.<sup>11</sup> 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.<sup>12</sup> Research has suggested that weight loss in these women can restore ovulatory cycles, which allows spontaneous pregnancy.<sup>13</sup>

### 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'.<sup>14</sup> Signs and symptoms of the latest disorder in TPM textbooks, titled *Ehtebās-e-Tams* (lack of menstruation), come very close to PCOS.<sup>15</sup> 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.<sup>16</sup> 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.<sup>17</sup> 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).<sup>16,18–21</sup> 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*.<sup>22–25</sup> 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.<sup>26–99</sup>

## 4. Conclusions and further suggestions

Polycystic ovary syndrome is the most common endocrine disorder in women of reproductive age.<sup>7</sup> While the cause is unknown, this disorder remains the most enigmatic reproductive disorder. Therefore, there is no known cure for this problem.<sup>100</sup> Most common treatments for PCOS are oral contraceptives to suppress the secretion of gonadotropin and decrease free androgen blood levels.<sup>101</sup> 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

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