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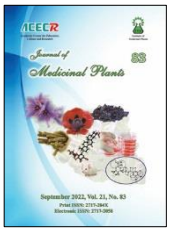

Review Article

Suggested herbal remedies effective on polycystic ovarian syndrome from the viewpoint of Persian medicine

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ABSTRACT

Background: According to the reverse pharmacological method, traditional medicine has a good source of information for discovering new drug candidates. Polycystic ovarian syndrome (PCOS) is the most common cause of endocrine disorder and infertility among women of reproductive age. This syndrome is commonly treated by oral contraceptive pills; however, it could be associated with side effects. **Objective:** The purpose of this study was to identify and prioritize medicinal plants proposed by Persian medicine (PM) for the treatment of PCOS. **Methods:** The first step was to find out the most relevant keywords to the symptoms of PCOS among five authentic PM manuscripts because there was no medical term called PCOS in PM texts. According to those keywords, all materia medicas that was described in the selected books were recorded. Each materia medica received scores based on specific criteria. The scores were used to prioritize medicaments. **Results:** *Ferula assa-foetida* L., *Tanacetum parthenium* L., *Lycium barbarum*, *Cymbopogon schoenanthus* L., *Lepidium sativum* L. *and Marrubium vulgare* were six top materia medica identified in this study. **Conclusion:** Identification of closely related terminology for PCOS in traditional medical texts and prioritization of herbal remedies could be a sound approach to discover new drugs. Accordingly, *Ferula assa-foetida* L. with the highest score was considered the best candidate for the treatment of PCOS in PM.

Abbreviations: PCOS, Polycystic ovarian syndrome; PM, Persian medicine

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1. Introduction

The discovery of new drugs is a time-consuming and costly process [1]. The pharmaceutical industry in process of discovering drugs is facing important challenges [2]. Reverse pharmacology is a rigorous approach to integrate experiential observation and documented experiences to make and formulate drugs [3], which offers platforms for new herbal formulations [2]. Also, traditional medicine is a proper source for finding novel agents to treat chronic diseases [4]. In this approach, herbs can be used for discovering new drug candidates [5].

Persian medicine (PM) is a medical culture that dates back to about 10000 years ago [6] and it has the potential for solving common medical problems such as the pain of knee osteoarthritis, allergic rhinitis symptoms, constipation, atopic dermatitis and gynecologic problems [7-11]. Moreover, PM methods of treatment is associated with very few side effects [12]. In PM references, different choices were proposed for each disease. To achieve the best choice, prioritization is important. Some methods have been introduced to rank these choices based on PM principles [13-15].

Polycystic ovarian syndrome (PCOS), with a prevalence of 6 to 15 % [16, 17], is the most common cause of endocrine disorder and infertility among childbearing-aged women [16, 18]. PCOS could be identified by the polycystic figure of ovaries in sonography, chronic anovulatory status, hyperandrogenism [16] and commonly is related to obesity [16, 19-22]. PCOS patients may face some complications like uterine dysfunctional bleeding or endometrial cancer [16]. Oral contraceptive pills are common treatment for PCOS [23, 24] which are accompanied by side effects such as decreasing insulin sensitivity or increasing the risk of cardiovascular disease [25].

PM references introduced various material medicas for managing PCOS which may open a new horizon for its treatment. This study intends to rank proposed material medicas in PM resources to find suitable candidates for PCOS treatment.

2. Methods

This study focused on five authentic PM references documented during 9-18 centuries AD including *Al-havi fi al-tebb* (Rhazes, 865-925 AD) [26], *Al-Qanon fi al-Tibb* (*Canon* of medicine; Avicenna, 980-1037 AD) [27], *Aghraz al-tebbiah va aJl-mabahes al-alaaeiah* (Jorjani, 1042-1136 AD) [28], *Tohfa al-momenin* (Tonekaboni, 1679) [29] and *Makhzan al adviyeh* (storehouse of medicaments; Aghili Shirazi, 1689-1791 AD) [30].

To find out the most suitable herbal remedies for the treatment of PCOS, the following steps were taken, based on a previous recommendation [13].

2.1. Subjects matching and finding keywords

The main observation during sonography of patients with PCOS is the enlargement of ovaries and the appearance of cysts [16]. However, during 800-1800 AD, not only such diagnostic facilities were not available but also the term PCOS was not quoted in PM texts. Therefore, the first step in searching the PM references to find the most appropriate medications for PCOS was to search the most relevant keywords that match the main symptoms of this syndrome and to select the appropriate expressions in PM resources.

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2.2. Searching in PM references

According to the keywords matching the symptoms of this syndrome found in the previous step, all remedies were searched among those five PM references.

2.3. Scoring material medicas

Regarding the description of those PM references, each material medica got a special score. This description included the following: the effect of material medica on swellings similar to the cysts of ovaries in PCOS, the tissue affinity of material medica, the author's emphasis on materia medica's efficacy and the effect of material medica on stimulation of menstruation.

2.4. Summing up and prioritizing

The scores of each materia medica in all five mentioned books were summed up and the herbal remedies with the highest score were prioritized.

3. Results

3.1. Subject matching and finding keywords

In PM references, the most relevant keywords to this syndrome were: "*oram_e tokhmdan"* (swelling of ovaries), "*oram_e rahem"* (swelling of uterus), "*oram_e bateni"* (swelling of internal organs), "*oram_e rakhv"* (loose swellings).

Also according to some menstruation cycle disorders present in PCOS including amenorrhea and oligomenorrhea, the keyword of "*moder_e tamth"* (menstruation stimulant) was chosen too.

3.2. Searching in PM references

Keywords were searched in PM references. Finally, 123 materia medicas were found to be effective on polycystic ovaries and 244 materia medicas were found to be effective on menstruation disorders of PCOS. These herbal medicines had commons.

For the next step, for each medicament all data of those 5 books which were related to keywords were collected (Table 1).

3.3. Scoring material medicas

Materia medicas were scored based on the following descriptions in PM references:

The extent of effectiveness of every medicament on polycystic ovaries according to the type of author's emphasis on that material medica, the location of tissue effect of remedy, the effect of remedy on swellings similar to the PCOS's cysts according to PM references and the level of its effect on stimulation of menstruation.

For example, Author's use of the words "excellent" or "great" got more scores than "good" or "beneficial". Also being effective on the ovarian or uterine swelling got more scores than being effective on internal swelling. Or being effective on "loose swelling" was more valuable than being effective on "swelling".

3.4. Summing up and prioritizing

Points were collected and materia medicas were prioritized (Table 2). Among those medicinal herbs that were searched, 18 of them with the highest score may be the best choices for treatment of PCOS and *Ferula assa-foetida* L. with the highest score can be used in future clinical trials as the first choice.

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Table 1. An example of scoring system for materia medicas (ex. *Commiphora mukul*) to treat PCOS according to PM references

Effect on swelling (original text)	Effect on swelling	Points	Effect on menstruation (original text)	Effect on menstruation	Points	Persian medicine reference	Sum of points
نافع للاورام الباطنه	(Useful) for (internal) swelling	(1)+(2)	یدرالطمث	Menstruation stimulant	1	*Qanon fi al-Teb*	13
مفید جهت اورام باطنی	(Beneficial) for (internal) swelling	(1)+(2)	مدر حیض	Menstruation stimulant	1	*Makhzan al adviyeh*	
-	-	0	-	Menstruation stimulant	1	*Tohfa al-momenin*	
-	-	0	-	-	0	*Aghraz al-tebia*	
محلل اورام داخلی	(Dissolvent) of (internal) swelling	(1)+(2)	خاصته انزال الحیض	Menstruation stimulant	1	*Al-havi fi al-teb*	

Table 2. Prioritization of effective remedies to treat PCOS according to PM scoring system

No.	Scientific Name (main part)	Common Name	Traditional Name	Family	Part	Score
1	*Ferula assa-foetida* L.	Asafetida	Anghūzeh	*Apiaceae*	latex (oleo-gum resin)	25
2	*Tanacetum parthenium* (L.) Sch.Bip.	Feverfew	Oghhovān	*Asteraceae*	flower	18
2	*Lycium barbarum* L.	Chinese wolfberry	Hozoz	*Solanaceae*	leaf and seed	18
3	*Cymbopogon schoenanthus* (L.) Spreng.	Lemongrass	Ezkher	*Poaceae*	root and pollen	17
3	*Lepidium sativum* L.	Garden cress	Horf	*Brassicaceae*	seed	17
3	*Marrubium vulgare* L.	Marrubium	Farāsion	*Lamiaceae*	leaf	17
4	*Neolitsea cassia* (L.) Kosterm.	Chinese cinnamon	Salikheh	*Lauraceae*	bark	16
5	*Asphodelus ramosus* L.	Asphodelus	Khonnasā	*Asphodelaceae*	root	14

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Table 2. Prioritization of effective remedies to treat PCOS according to PM scoring system (Continued)

No.	Scientific Name (main part)	Common Name	Traditional Name	Family	Part	Score
5	*Calystegia sepium* (L.) R.Br.	Hedge bindweed	Leblāb	*Convolvulaceae*	leaf	14
6	*Allium sativum* L.	Garlic	Soom	*Amaryllidaceae*	bulb	13
6	*Levisticum officinale* W.D.J.Koch	Lovage	Anjedān	*Apiaceae*	seed	13
6	*Commiphora mukul* (Hook. ex Stocks) Engl.	Indian bdellium-tree	Moghl	*Burseraceae*	gum	13
7	*Phyla nodiflora* (L.) Greene	Turkey tangle frogfruit	Eslanj	*Verbenaceae*	leaf	12
7	*Cornus mas* L.	Cornelian cherry	Zoghāl	*Cornaceae*	fruit	12
8	*Acorus calamus* L.	sweet flag	Ghasab. Alzarirah	*Acoraceae*	seed	11
8	*Lupinus angustifolius* L.	Lupine	Tormes	*Leguminosae*	seed	11
8	*Zygophyllum fabago* L.	Syrian bean-caper	Amdoriān	*Zygophyllaceae*	leaf	11
8	*Allium ampeloprasum* L.	Wild leek	Korrās	*Amarylliadaceae*	leaf	11

4. Discussion

Ferula assa-foetida L. is an endemic plant of Iran from which an oleoresin gum is obtained [31]. Its main active component is ferulic acid [32] and has anti-inflammatory and antioxidant effects [33]. A closer look at *Ferula assa-foetida* L. reveals a variety of health benefits that are important in the management and treatment of PCOS. Controlling obesity [34], anti-hyperglycemic effect [35], being anti-oxidant, anti-cancer and lowering blood pressure are some properties that may assist to treat PCOS [36]. Importantly, it does not have side effects in therapeutic doses [37].

According to PM references, *Ferula assa-foetida* L. is useful to treat swellings [30]. In PM references "swelling" is the most appropriate term for "cyst". Accordingly, *Ferula assa-foetida* L. can be considered as the treatment for internal and external swellings [27]. *Ferula assa-foetida* L. can stimulate the menstruation cycle [38] and reduce menstrual pains [38, 39]. It has been shown that *Ferula assa-foetida* L. can decrease the number of ovarian follicles in young girls with PCOS [40].

A review study revealed that Apiace is one of the families in which the components affecting PCOS have the highest frequency [41]. The selection of *Ferula assa-foetida* L. in our study

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is in line with those effects reported for Apiace. The second material medica of choice to treat PCOS was *Tanacetum parthenium* L. It can reduce the plasma concentrations of testosterone [42] and has anti-inflammatory [43] and antioxidant properties [44]. The essential oil of remedy *Cymbopogon schoenanthus* L., that have the third rank in the prioritization of our study, has an anti-inflammatory effect [45]. As there are some documents on the relationship between PCOS and chronic inflammation [46], *Cymbopogon schoenanthus* L. like *Ferula assa-foetida* L. and *Tanacetum parthenium* L. can be effective in treating PCOS. In PCOS, increased oxidative stress is closely linked with inflammation which in turn could stimulate ovarian androgen production [47]. So *Cymbopogon schoenanthus* L. with antioxidant activity, [48] like the other two mentioned herbal remedies, can be a good candidate for the treatment of PCOS.

There are various studies about the effects of different medicinal plants on this syndrome [49-51], but the selected plants in these studies have mostly been conducted as a random screening method. Therefore, we conducted this study to achieve a novel method. Also in some studies, just being effective on one symptom of this syndrome such as menstruation problems have been considered [52] and as we know PCOS classically is accompanied with other symptoms such as ovarian cysts too. So in this study, it was considered as well.

It seems that the prioritization of drugs according to PM references can be an important step in the discovery of new drugs. A clear example of such methodology is the prioritization of effective materia medicas for the treatment of epilepsy and palpitation [14, 53]. Meanwhile, in some research like this study, herbal remedy prioritization is facing more challenges because of the lack of equivalent terms for diseases like PCOS in PM references [15]. Therefore, it is necessary to match those symptoms with reports in PM references to find the most relevant keywords. As a recommendation, it is suggested to design a standard method for these kinds of research to find the best drugs according to traditional medicine.

5. Conclusion

It seems that the proposed prioritizing method for finding materia medicas according to PM, can be a good way to discover novel effective medicines. Also according to evidence of studies that show the effectiveness of selected remedies of this study for treatment of the symptoms of PCOS, it seems that these medicinal plants may be good candidates for further studies in this field.

Limitation

The hyperandrogenism manifestations such as hirsutism were ignored in this study due to the lack of appropriate oral drugs for those manifestations in PM.

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Author contributions

M.N. designed the study; N.D. collected and interpreted the data; F.A. edited the initial version of the manuscript; S.A.M. edited the second version of the manuscript; A.N.N. edited the final version of the manuscript; Z.B. contributed in the preparation of the initial draft of the manuscript, F.GH., A.G. and M.GH.F. contributed in the preparation of the manuscript; all authors approved the final version of the manuscript.

Conflicts of interest

Authors state no conflict of interest.

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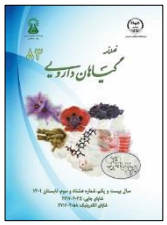

مقاله مروری

داروهای گیاهی پیشنهادی موثر بر سندرم تخمدان پلی کیستیک از دیدگاه طب ایرانی

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اطلاعات مقاله

گل‌واژگان:
تخمدان پلی کیستیک
داروشناسی معکوس
طب ایرانی
طب سنتی
کشف دارو

چکیده

مقدمه: بر اساس روش داروشناسی معکوس، طب سنتی منبع اطلاعاتی خوبی برای کشف کاندیداهای دارویی جدید است. سندرم تخمدان پلی کیستیک (PCOS)، شایع ترین علت اختلال غدد درون ریز و ناباروری در بین زنان سنین باروری است. این سندرم معمولاً با قرص های ضد بارداری خوراکی درمان می شود که با این حال، خود می توانند با عوارض جانبی همراه باشند. **هدف:** هدف از این مطالعه شناسایی و اولویت بندی گیاهان دارویی پیشنهادی طب سنتی ایرانی برای درمان PCOS است. **روش بررسی:** اولین قدم، یافتن مرتبط‌ترین کلمات کلیدی با علائم PCOS در بین پنج نسخه خطی معتبر طب ایرانی بود. زیرا هیچ اصطلاح پزشکی با عنوان سندرم تخمدان پلی‌کیستیک در متون طب ایرانی وجود نداشت. با توجه به این کلیدواژه‌ها، تمام مواردی که در کتاب‌های منتخب شرح داده شده بودند، ثبت شد. هر گیاه دارویی بر اساس معیارهای خاصی امتیاز گرفت. از مجموع امتیازات برای اولویت‌بندی داروها استفاده شد. **نتایج:** آنغوزه، اقحوان، حضض، اذخر،حُرف، فراسیون، شش ماده دارویی برتر شناسایی شده در این مطالعه بودند. **نتیجه‌گیری:** شناسایی اصطلاحات مرتبط نزدیک برای PCOS در متون پزشکی سنتی و اولویت‌بندی داروهای گیاهی می‌تواند رویکردی مناسب برای کشف داروهای جدید باشد. بر این اساس آنغوزه با بالاترین امتیاز، به عنوان بهترین کاندیدا برای درمان PCOS در طب ایرانی در نظر گرفته شد.

مخففها: PCOS، تخمدان پلی کیستیک؛ PM، طب ایرانی

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