Review Article

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An overview of amenorrhea and respective remedies in Traditional Persian Medicine

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Abstract

Amenorrhea is described as complete absence or cessation of menstruation. Besides conventional treatment approaches, traditional and complementary medical systems have suggested numerous natural medications for management of amenorrhea. Current study aimed to compile the pharmacological reports on amenorrhea from the standpoints of early Persian scholars. Medical and pharmaceutical manuscripts of Persian medicine from 9th to 18th centuries A.D. have been reviewed to extract the critical points and natural remedies. Based on Traditional Persian Medicine (TPM), impairment in uterus, brain and circulation are main causes of amenorrhea. Any obstruction, either anatomical or functional, in uterus and allied organs or tissues may lead the body to this disorder. Concerning herbal therapy of amenorrhea in TPM, 71 medicinal plants related to 35 families were found. The most prevalent families were Apiaceae, Asteraceae, Lamiaceae and Fabaceae, respectively. Usual routes of administration were oral, vaginal and topical. However, there was one report on a medicament, spoken to be effective nasally. Traditionally, emmenagogue medicines should possess diuretic activity to be effective for amenorrhea. All reported remedies were known as diuretic agents. However, this description is not corresponded with what is now accepted as diuretic. On the other hand, only Foeniculum vulgare showed therapeutic effects on amenorrhea in a randomized placebo-controlled trial. Despite lack of novel information on emmenagogue activity of these remedies, design and conducting evidence-based animal or human studies may be beneficial for new drug discovery from traditional knowledge.

Keywords: Amenorrhea, Emmenagogue, Herbal medicine, Traditional medicine, Persia.

1. Introduction

As absence of menstruation, amenorrhea is defined as the most prevalent manifestations of premature ovarian failure (1). The prevalence of this disorder is reported around 3-4% in conditions not related to pregnancy, lactation, or menopause (2). It is reported that amenorrhea is one of the most important causes of referring to clinical health care and medical centers (3).

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Amenorrhea which is described as complete absence or cessation of menses is divided into primary and secondary disorder (4). Etiologically, amenorrhea is caused by hormonal disorders and anatomical or functional genital tract anomalies (5). Based on the underlying conditions, treatment of amenorrhea may vary from a patient to another. In early steps, level of estrogen should be monitored. Patients with primary amenorrhea and uterine causes may be administered oral contraceptive pills or gonadotropin-releasing hormone. Hypothalamic causes should also be considered.

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However in secondary amenorrhea, the management approach is different (6).

In addition to several conventional treatment approaches, traditional and complementary medical systems of different countries have suggested numerous natural and herbal medications for the management of amenorrhea and side effects of this disorder (7, 8). Traditional Persian Medicine (TPM) is an old medical system with various management strategies for various ailments (9). Eminent Persian scholars have remained a comprehensive source of their own experiences and also beneficial medical knowledge from pioneers in previous era (10).

Amenorrhea is remarked as "*Ehtebās-e-tams*" or "*Habs-e-tams*" or "*Ehtebās-e-heiz*" (lack of menstruation) in Persian medical and pharmaceutical manuscripts. Various etiological factors and also different treatment approaches for this disorder have been extensively mentioned in TPM resources. Therefore, an evidence-based review of those findings and reports may lead to practical clinical approaches of natural medicines originated from thousands years of experiences.

The current study aimed to compile and present clinical and pharmacological reports on amenorrhea from the standpoints of early Persian scholars compared to modern medical knowledge.

2. Methods

Medical and pharmaceutical manuscripts of Persian medicine from 9th to 18th centuries A.D. have been reviewed to extract the critical points and natural remedies. These manuscripts were as *Kitāb al-ḥāwī fī al-ṭibb* (The Comprehensive Book on Medicine) written by Rhazes (9th-10th A.D.), Avicenna's Canon of Medicine (10th-11th A.D.), *Ikhtiyārāt-i Badī'ī* (Selections for Badī'ī) by *Hājjī Zayn al-'Aṭṭār* (14th A.D.), *Tuhfat al-mu'minīn* (Present for the Faithful) authored by Daylamī *Tunakābunī* (17th A.D.), and *Makhzan al-adviyah* (The Storehouse of Medicaments) by *Alavī Shīrāzī* (18th A.D.) as well as *Eksīr-e-'Azam* (The Great Elixir) by *Mohammad Azam Khān* (18th A.D.) (11-16). The exact keywords to filter the herbs with emmenagogue activity were "*Ehtebās-e-tams*" or "*Habs-e-tams*" or "*Ehtebās-e-heiz*".

Identification of each plant's scientific name was done by searching and matching the valid name in some main botanical textbooks including "Matching the Old Medicinal Plant Names with Scientific Terminology", "Indian Medicinal Plants", "Dictionary of Iranian Plant Names" and "Dictionary of Medicinal Plants" (17-20).

In addition, related emmenagogue activities for each reported plant were checked to report via searching through databases and search

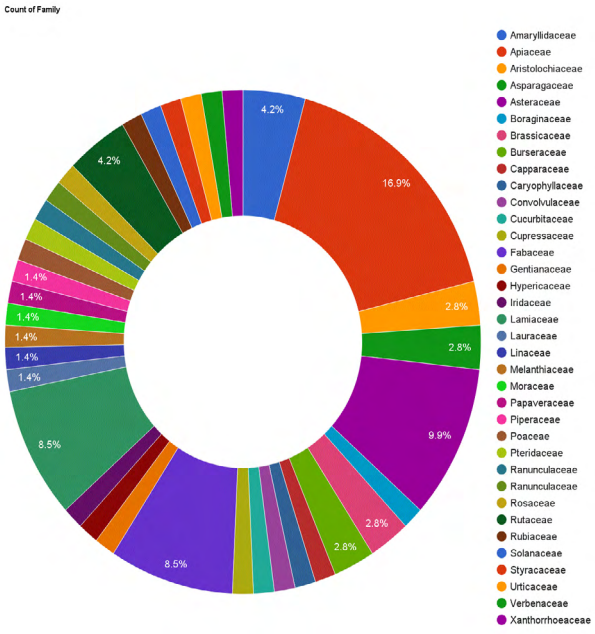

Figure 1. Prevalence of reported families.

engines such as PubMed, ScienceDirect, Scopus, and Google scholar.

3. Results and discussion

According to the descriptions in Persian manuscripts, amenorrhea is divided into two categories as primary (*Tām* or total) and secondary (*Gheir-e-tām* or non-total). The first occurs in young girls who never experienced the menstruation at the time of adolescence. Later was defined as the absence of menstruation in young girls who previously experienced the menses. Etiologically, the impairment in uterus, brain and circulation was mentioned as main causes of amenorrhea in TPM. It was also believed that any obstruction, either anatomical or functional, in uterus and allied organs or tissues may lead the body to this disorder (16). In current medicine, based on functional compartments, any obstruction in genitalia and birth canal as well as endocrine dysfunctions may result in the occurrence of this disorder (21).

Concerning the herbal therapies of amenorrhea in TPM, 71 medicinal plants related to 35 families were found in studied manuscripts. The most prevalent family was Apiaceae followed by Asteraceae, Lamiaceae and Fabaceae with 12, 7, 6 and 6 reports/plant, respectively (Figure 1). Usual routes of administration were oral, vaginal and topical. Interestingly, nasal application was also reported in some cases. Additionally, vaginal semisolids as well as bath were some considerable applications (Table 1). In all, 63.4% of remedies were only reported as oral medicines for amenorrhea. On the other side, 15% of plant were administered purely from vaginal route (Figure 2). In regard of the botanical part used, seeds were the most abundant which were followed by roots and aerial parts (Figure 3).

Based on the pharmacotherapy of TPM, it was mentioned that medicaments should possess diuretic activity to be administered for amenorrhea (16). The underlying mechanisms for the action of these medicaments in traditional medicine were as increasing blood circulation in uterine arteries, irritating the neighboring organs, and stimulating the uterine muscles and nerves as well as generally increasing the blood formation in order to act as emmenagogue (22). However, the activity of diuretic for amenorrhea is not corresponded with what is now accepted as this term. According to the current knowledge, there was scant new and contemporary information on the effectiveness of reported plants in amenorrhea. Except few herbs, most of the reported remedies were not accompanied by evidenced-based documents in amenorrhea. Among all reported plants, only *Foeniculum vulgare* showed therapeutic effects on depot medroxyprogesterone acetate-induced amenorrhea in a randomized placebo-controlled trial (23). Accordingly, from all reported data, only this remedy may be introduced as a lead medicament for further comprehensive researches.

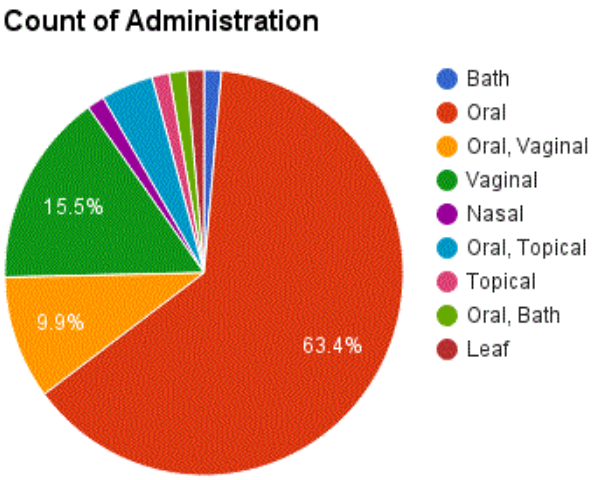

Figure 2. Different route of administrations.

Table 1. Cited medicinal plants for the management of amenorrhea disease.

Family	Scientific name	In traditional	Part(s)	Administration	Dose (up to)
Amaryllidaceae	*Allium sativum* L.	Soom	Aerial	Bath	-
	Allium cepa L.	Basal	Bulb	Oral	4.2 g
	Narcissus tazetta L.	Narjes	Root	Oral	6.3 g
Apiaceae	*Levisticum officinale* W.D.J.Koch	Anjedan-roomi	Fruit	Oral	
	Pimpinella anisum L.	Anisoon	Fruit	Oral	18 g
	Dorema ammoniacum D.Don	Oshagh	Gum	Oral	-
	Prangus ferulacea (L.) lindel.	jawshir	Gum	Oral	4.2 g
	Daucus carota L.	Jazar	Seed	Oral, Vaginal	7.2 g
	Foeniculum vulgare Mill.	Razyanaj	Seed	Oral	4.2 g
	Pastinaca sativa L.	Ra'y-ol-ebal	Leaf	Oral	7.2 g
	Anethum graveolens L.	Shebet	Seed	Oral	28.8 g
	Petroselinum crispum (Mill.) Fuss	Fetrasalioon	Seed	Oral	-
	Apium graveolens L.	Karafs	Aerial	Oral	3.6 g
	Carum carvi L.	Kommoon	Seed	Oral	7.2 g
	Trachyspermum ammi (L.) Sprague	Nankhah	Seed	Oral	10.8 g
Aristolochiaceae	*Asarum europium* L.	Asarun	Root	Oral	12.6 g
	Aristolochia fontanesii Boiss. & Reut.	Zaravand	Root	Oral	7.2 g
Asparagaceae	*Drimia maritima* (L.) Stearn	Esgheel	Root	Oral	7.2 g
	Asparagus officinalis L.	Helyoon	Root	Vaginal	-
Asteraceae	*Tanacetum parthenium* (L.) Sch.Bip.	Ogh'hovan	Aerial	Vaginal	-
	Artemisia absinthium L.	Afsantin	Aerial	Oral	3.6 g
	Lactuca sativa L.	Khas	Leaf	Oral	-
	Inula helenium L.	Rasan	Root	Nasal	-
	Matricaria chamomilla L.	Baboonaj	Flower	Oral, Topical	12.6 g
	Ferula persica Willd.	Sakbinaj	Gum	Oral	1.8 g
	Helianthus annuus L.	Azaryoon	Root	Topical	-
Boraginaceae	*Arnebia euchroma* (Royle) I.M.Johnst.	Abu khalsa	Root	Vaginal	-
Brassicaceae	*Lepidium sativum* L.	Horf	Seed	Oral	13.6 g
	Erysimum × *cheiri* (L.) Crantz	Kheyri	Flower	Oral ,Vaginal	10.8 g
Burseraceae	*Commiphora mukul* (Hook. ex Stocks) Engl.	Moghl	Gum	Vaginal	-
	Commiphora myrrha (Nees) Engl.	Morr	Gum	Oral	1.8 g
Capparaceae	*Capparis spinosa* L.	Kabar	Root	Oral	10.8 g
Caryophyllaceae	*Acanthophyllum squarrosum*	Azarbu	Root	Oral	3.6 g
Convolvulaceae	*Convolvulus arvensis* L.	Lablab	Leaf	Vaginal	-
Cucurbitaceae	*Citrullus colocynthis* (L.) Schrad.	Hanzal	Fruit	Vaginal	-
Cupressaceae	*Juniperus sabina* L.	Abhal	Fruit	Oral	10.8 g
Fabaceae	*Lupinus albus* L.	Termes	Seed	Vaginal	29.4 g
	Trigonella foenum-graecum L.	Holbeh	Leaf	Oral	-
	Cicer arietinum L.	Hammaz	Seed	Oral	56 g
	Phaseolus vulgaris L.	Loobia	Seed	Oral, Bath	8.4 g
	Glycyrrhiza glabra L.	Soos	Root	Oral	18 g
	Melilotus officinalis (L.) Pall.	Eklil-ol-malek	Fruit	Leaf	72 g

Table 1. Continued.

Family	Scientific name	In traditional	Part(s)	Administration	Dose (up to)
Gentianaceae	*Gentiana lutea* L.	Jentiana	Root	Oral	3.6 g
Hypericaceae	*Hypericum perforatum* L.	Hofarighoon	Seed	Vaginal	-
Iridaceae	Iris sp.	Irsa	Root	Vaginal	-
Lamiaceae	*Ajuga reptans* L.	Jo'dah	Aerial	Oral	10.8 g
	Thymus vulgaris L.	Hasha	Aerial	Oral	18 g
	Mentha pulegium L.	Foodanaj	Seed	Vaginal	-
	Origanum majorana L.	Marzanjoosh	Leaf	Oral	8.4 g
	Zataria multiflora Boiss.	Sa'atar	Aerial	Oral	8.4 g
	Melissa officinalis L.	Badranjbooyeh	Aerial	Oral	18 g
Lauraceae	*Cinnamomum verum* J.Presl	Darchin	Bark	Oral	18 g
Linaceae	*Linum usitatissimum* L.	Katan	Seed	Oral	4.2 g
Melanthiaceae	*Veratrum album* L.	Kharbagh sefid	Root	Oral, Vaginal	4.2 g
Moraceae	*Ficus carica* L.	Tin	Fruit	Oral, Vaginal	126 g
Papaveraceae	*Papaver somniferum* L.	Shaghayegh	Leaf	Oral	3.6 g
Piperaceae	*Piper longum* L.	Darfelfel	Fruit	Oral	4.2 g
Poaceae	*Cymbopogon schoenanthus* (L.) Spreng.	Ezkher	Flower	Oral, Topical	4.2 g
Pteridaceae	*Adiantum capillus-veneris* L.	Barsiavashan	Aerial	Oral	-
Ranunculaceae	*Helleborus niger* L.	Kharbagh siyah	Root	Oral, Vaginal	4.2 g
	Nigella sativa L.	Shoniz	Seed	Oral	7.2 g
Rosaceae	*Prunus domestica* L.	Ajjas	Fruit	Oral	200 g
Rotaceae	*Citrus medica* L.	Otroj	Fruit	Oral, Topical	3.6 g
Rubiaceae	*Rubia tinctorum* L.	Fowweh	Seed	Oral	4.2 g
Rutaceae	*Citrus* × *aurantium* L.	Naranj	Peel	Vaginal	-
	Ruta graveolens L.	Sodab	Seed	Oral	12.6 g
Solanaceae	*Lycium afrum* L.	Hozoz	Aerial	Oral	3.6 g
Styracaceae	*Styrax officinalis* L.	Astarak	Olive gum	Oral, Vaginal	-
Urticaceae	*Urtica dioica* L.	Anjoreh	Aerial	Oral, Vaginal	10.8 g
Verbenaceae	*Verbena officinalis* L.	Re'ay-ol-hamam	Root	Oral	7.2 g
Xanthorrhoeaceae	*Asphodelus ramosus* L.	Khonsa	Root	Oral	4.2 g

[1]Texts: 1; (MS A 17- NLM, NLM Microfilm Reel: FILM 48-115 no. 3) *Kitāb al-Hāwī fī al-Tibb* (Liber Continens) by Abū Bakr Muhammad ibn *Zakarīyā' al-Rāzī* (865-925), the 20th and 21st books of this encyclopedia are on materia medica containing 898 simple medicine; 2: *Kitāb al-Qānūn fī al-Tibb* (The Canon of Medicine), by Ibn Sīnā (Avicenna- 1024 A.D.) with 800 natural medicine and their application and effectiveness; 3: (MS P 9- NLM, Microfilm Reel: FILM 48-132 no. 4) *Ikhtiyārāt-i Badī'ī* (Selections for Badī'ī) by *Hājjī Zayn al-'Aṭṭār*, A Persian pharmacopoeia with simple and compound natural remedies written in 1368 A.D. 4: (MS P 21, 22- NLM, NLM Microfilm Reel: FILM 48-136 no. 2) the book of *Tuhfat al-mu'minīn* (The Present for the Faithful), a Persian comprehensive pharmacopoeia of remedies (2nd half of 17th century) by M*uhammad Mu'min Daylamī Tunakābunī* with 763 simple natural medicine; 5: (MS P 12- NLM, NLM Microfilm Reel: FILM 48-133 no. 2) *Makhzan al-adviya*h (The Storehouse of Medicaments), the largest and one of the latest Persian pharmacopoeias written by *Muhammad Hāshim Hādī Alavī Shīrāzī* (18th A.D) containing 28 chapters and 1698 monographs on natural medicine.

In regard of the effectiveness of a medicament or related metabolites, essential oils are a most important phytochemical composition in two abundant families, Apiaceae and Lamiaceae in current report. It is not well clear that essential oils may act as emmenagogue agents. But evidences re-

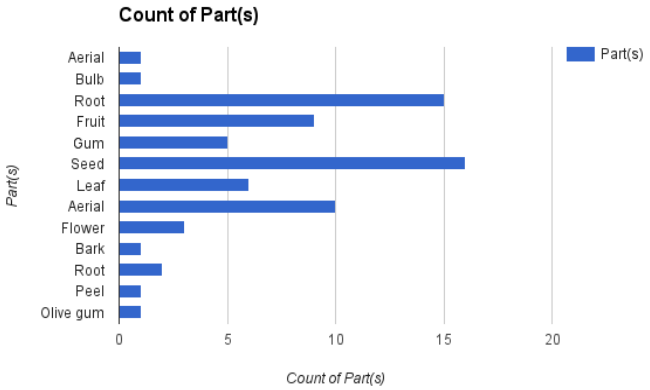

Figure 3. Prevalence of different part used of reported remedies.

vealed that these compounds may improve the procedure of menstruation (24, 25). Accordingly, remedies from these two families in the current study may be good selections for such investigations.

4. Conclusion

From the standpoints of early Persian scholars, amenorrhea (total and non-total) is occurred from impairment in uterus, brain and circulation as well as any obstruction, either anatomical or functional, in uterus and allied organs or tissues. Various natural remedies for amenorrhea have been traditionally reported in this study. According to TPM concepts, medicaments should have diuretic activities to be applied for amenorrhea. However, in current medicine this activity is not much related to emmenagogue effect. Despite lack of novel information on emmenagogue activity of these remedies, design and conducting evidence-based animal or human studies may be beneficial for new drug discovery from traditional knowledge.

Conflict of Interest

None declared.

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