



The Herbal Medicine Proposed by Iranian Traditional Medicine (Persian Medicine) for Treatment of Primary Dysmenorrhea: A Review

Saeedeh Ghafari¹, Zahra Tavakoli¹, Pantea Shirooyeh², Razieh Nabi Meybodi², Elham Behmanesh³, Roshanak Mokaberinejad², Mojgan Tansaz², Shirin Fahimi^{4*}

¹Traditional Medicine and Materia Medica Research Center (TMRC), Shahid Beheshti University of Medical Sciences, Tehran, Iran

²Department of Traditional Medicine, School of Traditional Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

³School of Traditional Medicine and History of Medical Science Research Center, School of Traditional Medicine, Babol University of Medical Sciences, Babol, Iran.

⁴Department of Traditional Pharmacy, School of Traditional Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Received: 14 Nov 2017

Revised: 15 Dec 2017

Accepted: 19 Dec 2017

Abstract

Primary dysmenorrhea (PD) is defined as painful menstrual in the absence of any pelvic pathology. Nowadays, the first line treatment is the use of NSAIDs that unfortunately has contraindication and side effects. Persian Medicine has noted menstrual pain with the defined treatments by use of herbs and herbal formulations. The aim of this study is to introduce the medicinal plants used to treat menstrual and uterine pains (M & UP) in Persian Medicine for evaluating in field of PD. For this purpose, first the medicinal plants used to treat M & UP were listed using prominent Persian Medicine references. In the next step, data were collected in relation to treat PD by searching in 'Google Scholar', 'Scopus', 'PubMed' and 'SID' databases between 2000 and 2016. Finally, the plants from identified Persian Medicine list, whose effect on PD have been revealed in modern literatures were introduced. According to this review, more than 100 medicinal plants were recommended for the treatment of M & UP in Persian Medicine. They belong to 60 plant families, the most frequent of which are Asteraceae, Apiaceae, Fabaceae, Rosaceae and Lamiaceae, respectively. Also, only about 13% of the aforementioned medicinal plants have been evaluated for the treatment of PD. It seems that many plants have been introduced in Persian Medicine for the treatment of menstrual pain, which have not yet been evaluated for their therapeutic effects and precise mechanisms of action. Thus, the introduced plants could be suitable candidates for future investigations.

Keywords: Menstrual pain, Dysmenorrhea, Iranian Traditional Medicine, Persian Medicine, Medicinal plants

Citation: Ghafari S, Tavakoli Z, Shirooyeh P, Nabi Meybodi R, Behmanesh E, Mokaberinejad R, Tansaz M, Fahimi S. **The Herbal Medicine Proposed by Iranian Traditional Medicine (Persian Medicine) for Treatment of Primary Dysmenorrhea: A Review.** Trad Integr Med 2018; 3(1): 30-42.

*Corresponding author: Shirin Fahimi
No.19, Tavaneer Alley, Vali-e-Asr Ave., postal code:1434875451, Tehran, Iran.
Email: s.fahimi@sbm.ac.ir
Tel: +982188773525
Fax: +982188776027

Introduction

Primary dysmenorrhea

Primary dysmenorrhea (PD), typically known as menstrual pain, is a common gynecological problem consisting of painful menstruation in the absence of any underlying abnormality and pelvic pathology [1-3]. PD is the most common cause of menstrual pain in women with a prevalence ranging from 60% to 93% and can cause to experience the absence from work or decrease the participation in social activities [4, 5]. The postulated etiology of PD is related to the combination of different factors, including increase of synthesis and secretion of prostaglandin F_{2α}, raised vasopressin and oxytocin that subsequently enhance the secretion of prostaglandin and stimulation of the type C pain fibers [6]. Also, PD must also be related to genetics, stress, and different body types [7]. The first line treatment of PD is the use of NSAIDs that unfortunately has contraindication, side effects, and 20- 25% failure to treatment [8, 9].

Because of the limitations of conventional treatments, herbal medicines are considered as feasible alternatives for the treatment of PD [10]. Nowadays, the most users of medicinal plants are women that use them to alleviate problems such as menstrual pain [11].

Importance of Iranian Traditional Medicine

Today, in complementary medicine medicinal plants, are recommended for treating many gynecological problems [12, 13]. Iranian Traditional Medicine (Persian Medicine) as a category of complementary medicine inherits all the

knowledge and practices of diagnosis, prevention and elimination of many diseases and illnesses in Persia from the ancient times to present. Supposedly, Persian Medicine might have offered alternative herbal medicines to treat PD [1, 14-16]. Although, the term “dysmenorrhea” was not mentioned in Persian Medicine references, menstrual pain has been noted as a type of uterine pains with defined treatments according to some recommended herbs and herbal preparations [17, 18].

In this study, at first, the herbs recommended for treatment of menstrual and uterine pains (M & UP) were listed by searching through prominent Persian Medicine references. In the next step data were collected from retrieved preclinical and clinical studies of PD appeared between 2000 and 2016. Finally, the identified plants from Persian Medicine list, whose effect on PD have been evaluated in modern literatures were introduced.

Methods

Traditional search

Persian Medicine references

Some main and available Persian medicine and pharmacy textbooks in the field of gynecological diseases and medicinal plants were selected belong to 4-14 AH. (Table1).

Table 1. Persian Medicine textbooks

Book	Author	Language	Century (AH)
<i>Alhavi Al-Hawi fi tebb</i>	Rhazes	Arabic	4
<i>The Royal Book (Kamil al-sina 'a al-tibbiya)</i>	Haly Abbas	Arabic	4
<i>Attasrif leman ajeza an-e-taalif</i>	Zahravi, khalaf ebn abbas	Arabic	4
<i>The Canon of medicine (al-Qanun fi al-tibb)</i>	Avicenna	Arabic	5
<i>Zakhireh (ZaKira-ye Kharazmshahi)</i>	Sayyed Esmā'īl Jorjānī	Arabic	6
<i>Aghraz al-Tebbiya</i>	Sayyed Esmā'īl Jorjānī	Arabic	6
<i>Sharh-e-Aghsaraee (Hall ol Mujazz)</i>	Jamaleddin Aghsaraee	Arabic	8
<i>Mujaz fi al-tibb</i>	Ibn alNafis	Arabic	9
<i>Tohfāt ul- Mo'menin</i>	Momen tonekaboni	Persian	11
<i>Mojarrabat-e akbari</i>	Arzani, Mohammad Akbar	Persian	12
<i>Makhzan-ul-advia</i>	Aghili Alavi khorasani Shirazi	Persian	12
<i>Moalejat e- Aghili</i>	Aghili Alavi khorasani Shirazi	Persian	12
<i>Behjat ur-roasa fi amraze n-nesa</i>	Ahmad Alrashidi	Arabic	13
<i>Exir-e-Aazam</i>	Nazem Jahan Mohammad Azam	Persian	14
<i>Khazaen ul- moluk</i>	Shams e ddin ,Ahmad	Persian	14

Plants used to treat menstrual and uterine pains in Persian Medicine references

The above mentioned textbooks were searched with the principal traditional keywords relating to menstrual pain, uterine pain, and menstrual cramps in order to find a list of traditional names of medicinal plants. Thereafter, plants were identified using different comprehensive glossaries by matching their traditional names with scientific names [19-21].

Modern search

Some dominant scientific databases such as 'Google Scholar', 'Scopus', 'Pub Med' and 'SID' were searched using a combination of keywords such as "dysmenorrhea" OR "menstrual" OR "menstrual pain" OR "painful menstruation" OR "menstruation" OR "painful"

AND "extract" OR "herb" OR "plant" OR "herbal medicine" OR "nature". Data were collected for the years 2000- 2016. Among 200 articles retrieved, 129 articles were excluded due to: not referring to primary dysmenorrheal pain, duplicating, lack of full text, non-English or Persian language, and lack of scientific name of medicinal plants. Overall, 24 articles were included in the review based on the plants identified in Persian Medicine list. Finally, the plants, whose effect on PD have been revealed in modern literatures by preclinical (*in vitro*, *in vivo*) or clinical studies were introduced.

Results

Traditional search

Based on the Persian Medicine references men-

tioned in table 1, about 120 traditional medicinal plants were recommended to treat M & UP (Table 2). Their used dosage forms were found orally or topically as fumigation (“*bakhur*”), vaginal suppository (“*hamul, farzajeh*”), poult-

tice (“*zemaḍ*”) and sitting in the decoction of medicinal plants. Also table 2 shows scientific names, phonetic spellings, families and used parts of those medicinal plants.

Table 2. Traditional name, phonetic spellings, scientific names, family and used parts of medicinal plants used to treat M & UP in Persian Medicine

Traditional name	Phonetic spellings	Scientific name	Family	Used part
Abhol	/æbhəʊl/	<i>Juniperus sabina</i> L.	Cupressaceae	fruit
Afsantin	/æfsæntɪn/	<i>Artemisia absinthium</i> L.	Asteraceae	aerial part
Antolah	/æntəʊlə/	<i>Aconitum</i> spp.	Ranunculaceae	-
Arak	/æra:k/	<i>Salvadora</i> spp.	Salvadoraceae	fruit
Ar-ar	/ær ær/	<i>Juniperus</i> spp.	Cupressaceae	flowers
		<i>Ajuga</i> spp.	Lamiaceae	
Ass	/a:s/	<i>Myrtus communis</i> L.	Myrtaceae	-
Azad derakht	/a:zɑ:d deræχt/	<i>Azadirachta indica</i> A.Juss.	Meliaceae	leaves
Babunaj	/bɑ:bənædʒ/	<i>Matricaria</i> spp.	Asteraceae	-
Badam-e-shirin	/bɑ:dɑ:meʃɪrɪn/	<i>Prunus dulcis</i> (Mill.) D.A.Webb	Rosaceae	oil
Badam-e-talkh	/bɑ:dɑ:metæχ/			
Badian	/bɑ:dɪɑ:n/	<i>Foeniculum vulgare</i> Mill.	Apiaceae	leaves
Baghlat-ul-homgha	/bæχlætəʊlhəʊmχɑ:/	<i>Portulaca oleracea</i> L.	Portulacaceae	leaves, stem
Balasan	/bælæsɑ:n/	<i>Commiphora gileadensis</i> (L.) C.Chr.	Burseraceae	seed
Bondogh-e-Hendi	/bəʊndəʊχehendɪ/	<i>Caesalpinia bonduc</i> (L.) Roxb.	Caesalpiaceae	-
Banj	/bændʒ/	<i>Hyoscyamus</i> spp.	Solanaceae	seed
Barzad	/bɔ:rzæd/	<i>Ferula gummosa</i> Boiss.	Apiaceae	-
Basbaseh	/bæsba:se/	<i>Myristica fragrance</i> Houtt.	Myristicaceae	-
Berendasaf	/berendʒɑ:sæf/	<i>Artemisia vulgaris</i> L.	Asteraceae	-
Botm	/bəʊtm/	<i>Pistacia</i> spp.	Anacardiaceae	gum
Darcini	/dɑ:rsɪnɪ/	<i>Cinnamomum</i> spp.	Lauraceae	bark
Daroonaj	/dæru:nædʒ/	<i>Doronicum</i> spp.	Asteraceae	-
Dazi	/dɑ:zɪ/	<i>Hypericum</i> spp.	Clusiaceae	-
Eklil-ul-malek	/əkɪlɪləʊlmælek/	<i>Melilotus</i> spp.	Fabaceae	seed, leaves
		<i>Astragalus hamosus</i> L.		
Enab	/ənæb/	<i>Vitis vinifera</i> L.	Vitaceae	bud
Esghil	/əsχɪl/	<i>Urginea maritima</i> (L.) Baker	Hyacinthaceae	seed
Ezkher	/əzχer/	<i>Andropogon</i> spp.	Poaceae	bud, root
Fanjankosht	/fændʒænkəʊʃt/	<i>Vitex agnus-castus</i> L.	Lamiaceae	seed, leaves
Favania	/fɑ:vɑ:nɪɑ:/	<i>Paeonia officinalis</i> L.	Paeoniaceae	fruit
Foodanaj	/fu:dænædʒ/	<i>Mentha</i> spp.	Lamiaceae	-
Fostogh	/fəʊstəʊχ/	<i>Pistacia vera</i> L.	Anacardiaceae	bark, leaves
Ghantoorioon	/χæntu:ri:u:n/	<i>Centaurium erythraea</i> Rafn.	Asteraceae	-
Ghantarioon-e- kabir	/χæntu:ri:u:nekæbɪr/	<i>Centaurea</i> spp.	Asteraceae	-
Gharasanah	/χæræs ænæ/	<i>Eryngium</i> spp.	Apiaceae	-

Traditional name	Phonetic spellings	Scientific name	Family	Used part
Ghasab-oz-zarirah	/Gæsæbəʊzzærɪræ/	<i>Swertia</i> spp.	Asteraceae	-
Ghaysum	/Gæjsu:m/	<i>Artemisia abrotanum</i> L.	Asteraceae	aerial part
Ghennab	/Gennæb/	<i>Cannabis sativa</i> L.	Cannabaceae	leaves
Ghotlob	/Gəʊtləʊb/	<i>Arbutus</i> spp.	Ericaceae	leaves
Ghost	/Gəʊst/	<i>Alpinia</i> spp.	Zingiberaceae	root
		<i>Costus</i> spp.	Costaceae	
Ghar	/Gɑ:r/	<i>Laurus nobilis</i> L.	Lauraceae	fruit
Haeghti (Khaman)	/hɑ:egɪ/	<i>Sambucus</i> spp.	Caprifoliaceae	-
Hamama	/hæmɑ:mɑ:/	<i>Amomum compactum</i> Sol. ex Maton	Zingiberaceae	-
Handaghooghi (Handaghoogha)	/hændægu:Gɪ/ (/hændægu:Gɑ:/)	<i>Trigonella caerulea</i> (L.) Ser.	Fabaceae	seed, aerial part
		<i>Trigonella hamosa</i> Del. ex Smith <i>Trifolium pratense</i> L.		
		<i>Melilotus</i> spp. <i>Colocasia esculenta</i> (L.) Schott	Araceae	
Hasha	/hɑ:fɑ:/	<i>Thymbra capitata</i> (L.) Cav.	Lamiaceae	aerial part
Heltit	/heltɪt/	<i>Ferula assa-foetida</i> L.	Apiaceae	-
Hendebe-ye-hendi	/hendebe:jehendɪ/	<i>Cichorium intybus</i> L.	Asteraceae	-
		<i>Cichorium pumilum</i> Jacq.		
		<i>Taraxacum campyloides</i> G.E.Haglund.		
Henna	/henna:/	<i>Lawsonia inermis</i> L.	Lythraceae	leaves
Holbeh	/həʊlbe/	<i>Trigonella foenum-graecum</i> L.	Fabaceae	aerial part
Hammaz	/hæmma:z/	<i>Rumex</i> spp.	Polygonaceae	seed
		<i>Oxalis acetosella</i> L.	Oxalidaceae	
Irsa	/ɪrsɑ:/	<i>Iris</i> spp.	Iridaceae	root
Javshir	/dʒɑ:vʃɪr/	<i>Opopanax chironium</i> Koch.	Apiaceae	-
Jolnar	/dʒəʊlnɑ:r/	<i>Punica granatum</i> L.	Lythraceae	-
		<i>Balaustion pulcherrimum</i> Hook.	Myrtaceae	
Karafs	/kæræfs/	<i>Apium</i> spp.	Apiaceae	fruit
		<i>Petroselinum</i> spp.		
Katan	/kætɑ:n/	<i>Linum</i> spp.	Linaceae	seed
Khamasooghi	/χɑ:mɑ:su:Gɪ/	<i>Euphorbia chamaesyce</i> L.	Euphorbiaceae	-
Khazama	/χæzɑ:mɑ:/	<i>Hyacinthus orientalis</i> L.	Hyacinthaceae	-
Khardal	/χærdæɪ/	<i>Brassica nigra</i> (L.) K.Koch	Brassicaceae	-
		<i>Sinapis</i> spp.		
		<i>Lepidium campestre</i> (L.) R.Br.		
Khashkhash	/χæʃχɑ:ʃ/	<i>Papaver somniferum</i> L.	Papaveraceae	-
Korath	/kɔ:rɑ:θ/	<i>Allium</i> spp.	Alliaceae	-
Kornob	/kɔ:rənəʊb/	<i>Brassica oleracea</i> L.	Brassicaceae	-
Koroviya	/kɔ:rəʊvɪjɑ:/	<i>Carum carvi</i> L.	Apiaceae	fruit
Lazan	/lɑ:zæn/	<i>Cistus ladanifer</i> L.	Cistaceae	-
		<i>Cistus creticus</i> L.		
Lesan-ul-asafir	/lesɑ:nəʊl æsɑ:fɪr/	<i>Fraxinus excelsior</i> L.	Oleaceae	-

Traditional name	Phonetic spellings	Scientific name	Family	Used part
Marmahooz	/mærmɑ:hu:z/	<i>Origanum syriacum</i> L.	Lamiaceae	aerial part
Mastaki	/mæstækɪ/	<i>Pistacia lentiscus</i> L. <i>Pistacia chia</i> Desf.	Anacardiaceae	-
Mazoo	/mɑ:zu:/	<i>Quercus infectoria</i> G.Olivier	Fagaceae	-
Meshketaramashi	/meʃketæra:mæʃɪ/	<i>Mentha</i> spp. <i>Origanum dictamnus</i> L. <i>Ballota pseudodictamnus</i> (L.) Benth.	Lamiaceae	aerial part
Mezmar-or-raee	/mezma:rɔ:rrɑ:i:/	<i>Alisma</i> spp.	Alismataceae	-
Meeah Saelah	/mi:æ sɑ:elæ/	<i>Styrax officinalis</i> L.	Styracaceae	-
Moghilan	/mɔgɪlɑ:n/	<i>Acacia nilotica</i> (L.) Delile	Fabaceae	root skin
Moo	/mu:/	<i>Meum athamanticum</i> Jacq.	Apiaceae	-
Morr	/mɔ:r/	<i>Commiphora myrrha</i> (Nees) Engl.	Burseraceae	gum
Naranj	/nɑ:rændʒ/	<i>Citrus × aurantium</i> L.	Rutaceae	skin
Narges	/nærdʒes/	<i>Narcissus</i> spp.	Amaryllidaceae	root
Nargil	/nɑ:rdʒɪl/	<i>Cocos nucifera</i> L.	Arecaceae	-
Namam	/næmɑ:m/	<i>Thymus pulegioides</i> L.	Lamiaceae	aeial part
Nastaran	/næstæræn/	<i>Rosa canina</i> L.	Rosaceae	-
Ollaygh	/ɔllæjɟ/	<i>Rubus</i> spp.	Rosaceae	-
Oghhovan	/əʊghəvɑ:n/	<i>Anthemis</i> spp. <i>Tanacetum</i> spp.	Asteraceae	aerial part
Quasab	/gæsæb/	<i>Arundo</i> spp.	Poaceae	-
Quotn	/gəʊtn/	<i>Gossypium</i> spp.	Gossypieae	leaves, root
Ray-ul-Hamam	/ræjəʊlhæmɑ:m/	<i>Verbena officinalis</i> L.	Verbenaceae	leavea
Rayhan Soleiman	/ræjhb:n sɔleɪmɔ:n/	<i>Ocimum filamentosum</i> Forssk.	Lamiaceae	flowers
Ravand	/rɔ:vænd/	<i>Rheum</i> spp.	Polygonaceae	roots
Selgh	/selɟ/	<i>Beta vulgaris</i> L.	Chenopodiaceae	fruit
Semsem	/semsem/	<i>Sesamum indicum</i> L.	Pedaliaceae	seed
Sodab	/sɔdɔ:b/	<i>Ruta graveolens</i> L.	Rutaceae	-
Sarakhs	/særæxs/	<i>Dryopteris filix-mas</i> (L.) Schott	Dryopteridaceae	-
Sakbinaj	/sækbɪnædʒ/	<i>Ferula stewartiana</i> O.E.Schulz <i>Ferula persica</i> Willd.	Apiaceae	-
Salikkeh	/sælɪχe/	<i>Cinnamomum cassia</i> (L.) J.Presl <i>Cinnamomum bejolghota</i> (Buch.-Ham.) Sweet	Lauraceae	bark
Sonbol-e-Hendi	/sɔnbɔʊlehendɪ/	<i>Nardostachys jatamansi</i> (D.Don) DC.	Valerianaceae	-
Soosan-e-Sefid	/su:sænesefɪd/	<i>Lilium candidum</i> L.	Liliaceae	root
Sisalius	/sɪsɔ:lɪu:s/	<i>Seseli tortuosum</i> L. <i>Tordylium officinale</i> L. <i>Laserpitium latifolium</i> L. <i>Levisticum officinale</i> W.D.J.Koch	Apiaceae	-
Sisanbar	/sɪsænbær/	<i>Mentha</i> spp. <i>Thymbra capitata</i> (L.) Cav	Lamiaceae	aerial part

Traditional name	Phonetic spellings	Scientific name	Family	Used part
Shahasfarm	/ʃv:hæsfærm/	<i>Ocimum minimum</i> L. <i>Ocimum basilicum</i> L. <i>Ocimum americanum</i> L.	Lamiaceae	aerial part
Shah Cini	/ʃv:hsɪnɪ/	<i>Piper betle</i> L.	Piperaceae	-
Shebet	/ʃebet/	<i>Anethum graveolens</i> L.	Apiaceae	aerial part
Shokaran	/ʃəʊkærɒ:n/	<i>Conium maculatum</i> L.	Apiaceae	aerial part
Shooniz	/ʃu:nɪz/	<i>Nigella sativa</i> L.	Ranunculaceae	seed
Shih-e-Armani	/ʃɪheærmæni/	<i>Artemisia pontica</i> L.	Asteraceae	aerial part
Saatar	/sætær/	<i>Satureja</i> spp. <i>Thymus</i> spp. <i>Thymbra capitata</i> (L.) Cav. <i>Origanum vulgare</i> L. <i>Zataria multiflora</i> Boiss.	Lamiaceae	aerial part
Tivaj	/tɪvɔ:dʒ/	<i>Holarrhena pubescens</i> Wall. ex G.Don.	Apocynaceae	-
Tobagh	/təʊbɔ:g/	<i>Inula</i> spp. <i>Dittrichia viscosa</i> (L.) Greuter.	Asteraceae	flowers, leaves
Torbod	/tɔ:rbəʊd/	<i>Ipomoea</i> spp. <i>Operculina turpethum</i> (L.) Silva Manso	Convolvulaceae	-
Trifolon	/terɪfəʊlɒn/	<i>Trifolium</i> spp. <i>Bituminaria bituminosa</i> (L.) C.H.Stirt.	Fabaceae Leguminosae	seed, leavea
Vaj	/vædʒ/	<i>Acorus calamus</i> L.	Acoraceae	-
Vard	/værd/	<i>Rosa</i> spp.	Rosaceae	flowers
Yasamin	/jɔ:sæmɪn/	<i>Jasminum</i> spp.	Oleaceae	leaves
Zaravand-e- Tavil	/zærɔ:vændetævɪl/	<i>Aristolochia fontanesii</i> Boiss. & Reut.	Aristolochiaceae	-
Zoronbad	/zɔ:rɒnbɔ:d/	<i>Zingiber zerumbet</i> (L.) Roscoe ex Sm.	Zingiberaceae	-
Zaafaran	/zæfæærɒ:n/	<i>Crocus sativus</i> L.	Iridaceae	stigma
Zoofa	/zu:fo:/	<i>Hyssopus officinalis</i> L. <i>Nepeta</i> spp.	Lamiaceae	aerial part
Zireh	/zɪre/	<i>Cuminum cyminum</i> L.	Apiaceae	fruit

-.: not mentioned

Modern search

The results of clinical and preclinical studies related to the plants (table 2) in modern literatures are shown in Tables 3 and 4, respectively.

Table 3. Clinical studies evaluated the effect of medicinal plants used to treat PD in Persian Medicine based on the modern research

Scientific Name	Clinical trial			
	Method			Findings (Reference)
	Groups	Duration (day/cycle)	Sample size (No.)	
<i>Anethum graveolens</i> L.	-mefenamic acid -Dillsun®(10gtt tid)	*/3	100	effective in dysmenorrhea [22]
	-placebo -mefenamic acid -Dill® (1000 mg bd)	5/2	75	↓pain severity as mefenamic acid [23]
<i>Apium</i> spp. (seed), <i>Crocus sativus</i> L., <i>Foeniculum vulgare</i> Mill.	-placebo -mefenamic acid -herbal drug (500 mg tid)	3/3	180	↓pain severity greater than mefenamic acid [24]
<i>Cinnamomum verum</i> J.Presl (Syn: <i>Cinnamomum zeylanicum</i> Blume)	-placebo -Ibuprofen -cinnamon (420 mg tid)	3/*	114	↓pain severity and duration lower than Ibuprofen [25]
<i>Carum carvi</i> L.	- placebo -mefenamic acid - caraway (sd) - caraway (bid) - caraway (tid)	3/2	500	↓pain <i>carum carvi</i> bid is the most effective. ↓pain between group II and mefenamic acid not significant difference [26]
<i>Foeniculum vulgare</i> Mill.	-placebo -hydro alcoholic extract (30gtt tid)	6/2	60	↓pain severity [27]
	-placebo -Vit. E -finalgin®(46 mg qid)	3/2	65	↓pain severity greater than control [28]
	-ibuprofe -finalgin©+vitamin E (46 mg+ 100 U qid)	3/2	68	↓pain intensity more than ibuprofen in the first hour and second hour [29]
	-placebo -mefenamic acid -essence (20%) of fennel's fruit (25 gtt qid)	4/3	60	↓pain severity [30]
<i>Foeniculum vulgare</i> Mill. <i>Matricaria chamomilla</i> L., <i>Zingiber officinale</i> Roscoe	-Before treatment -after treatment with herbal teabag (2 cup daily)	12/2	90	↓symptoms of dysmenorrhea [31]

Scientific Name	Clinical trial			
	Method			Findings (Reference)
	Groups	Duration (day/cycle)	S a m p l e size (No.)	
<i>Matricaria chamomilla</i> L. (Syn: <i>M. recutita</i> L.)	-mefenamic acid - <i>Matricaria chamomilla</i> (250 mg tid)	3/2	90	↓pain severity ↓hemorrhage as mefenamic acid [32]
	-control -chamomile tea (2 cup daily)	2/3	80	↓pain severity ↓consequent psycho-social problems [33]
<i>Mentha spicata</i> L.	-Ibuprofen -Supermint® (40 gtt qid)	As pain began/2	100	↓pain severity as ibuprofen [34]
<i>Rosa gallica</i> L.	-placebo -rose tea (2 cup daily)	6/6	130	↓ pain, ↓distress ↓anxiety ↑psychophysiologic well-being through time [35]
<i>Rosa × damascena</i> Herrm.	-unscented Almond oil massage - massage only -Rose oil (4%) massage (daily)	* / 2	75	↓pain severity most with Rose oil (4%) massage [36]
	-Mefenamic acid - <i>Rosa damascena</i> extract (200 mg qid)	3/2	124	↓pain intensity as mefenamic acid [37]
<i>Trigonella foenum-graecum</i> L.	-placebo - powder seed (900 mg qid)	3/3	91	efficacious, safe, cost effective, and well tolerated [38]
	- powder of fenugreek seed -fenugreek seed with dry cupping therapy - mefenamic acid	3/3	60	↓ pain as mefenamic acid [39]9
<i>Vitex agnus-castus</i> L.	-ethinyl estradiol 0.03 mg/drospirenone - Agnucaston®	3 cycle	60	effective as ethinyl estradiol/drospirenone [40]
	-Placebo -Mefenamic -Vitagnus drop®	3/2	80	↓pain severity more than mefenamic acid ↓hemorrhage as mefenamic acid [41]
<i>Zataria Multiflora</i>	-placebo -essential oil	*	108	effective [42]
<i>Zataria Multiflora</i> , Thymol, Carvacrol	- Ibuprofen -Bronco TD®	* / 2	120	↓pain severity and duration [43]

*: not mentioned ↓: decrease, ↑: increase

Table 4. Preclinical studies evaluated the effect of medicinal plants used to treat PD in Persian Medicine based on the modern research

Scientific Name	Study design	Model	Animal	Findings (References)
<i>Boswellia sacra</i> Flueck. (Syn.: <i>Boswellia carterii</i>)	<i>in vivo</i>	-paw edema mice induced by formalin and carrageenan -dysmenorrhea test	mice	-antiinflammatory and analgesic activities [44]
<i>Commiphora myrrha</i> (Nees) Engl.	<i>in vivo</i>	-paw edema mice induced by formalin and carrageena	mice	-anti-inflammatory and analgesic activities -inhibited the number of writhing in comparison [44]
<i>Boswellia sacra</i> Flueck. + <i>Commiphora myrrha</i> (Nees) Engl.	<i>in vivo</i>	paw edema mice induced by formalin and carrageenan - dysmenorrhea test	mice	-more useful for mitigating inflammatory pain than individual herbal extract -inhibited the number of writhing in comparison than individual herbal extract [44]
<i>Foeniculum vulgare</i> Mill.	<i>in vitro</i>	uterine contraction	rat	-reduced the frequency of contractions induced by PGE2 but not with oxytocin [45]

Discussion

As mentioned, primary dysmenorrhea, a category of dysmenorrhea, is the most common cause of menstrual pain in women. Conventional treatment for PD such as use of NSAIDs has a failure rate of 20% to 25% and may be contraindicated or not tolerated.

Since the current world-wide interest in traditional medicine has led to rapid development of herbal medicine initially introduced by traditional and complementary medicine [22].

Many studies have reviewed the use of Iranian herbal medicine in treatment of PD. Mirabi et al. systematically reviewed and summarized clinical trials analysis of Iranian herbal medicine in the context of PD and quality of various methods for treating dysmenorrhea. Their review claimed promising evidence supporting the use of Iranian medicinal plants for PD [14]. Bahmani et al. introduced the most important herbal medicines native to Iran on the base of some Iranian provinces ethnobotany, which are

efficient on dysmenorrheal pain.

In another review article, Dadkhah et al. introduced 18 herbal plants and plant-based products used by Iranian women as effective treatments for dysmenorrhea.

In this study, for the first time, fifteen famous references of Persian Medicine were investigated in terms of herbal medicines effective for M & UP (Table 1).

Based on the results (Table 2), more than 100 plants belonging to 60 plant families were introduced. Among them, the most frequent families were Asteraceae, Apiaceae, Fabaceae, Rosaceae and Lamiaceae respectively. Asteraceae, Fabaceae, Lamiaceae and Apiaceae are among the principal families whose central analgesic effect has been reported [46].

Basically, plants belong to Asteraceae family biosynthesize polyacetylenes, flavonoids and terpenes which comprise large and diverse classes of organic compounds. Several studies have shown analgesic effect of different types

of terpenes derived from plants such as sesquiterpene lactones and furanosesquiterpene [44, 47-49].

According to different mechanisms for relieving or decreasing dysmenorrheal pain by medicinal plants, most of the introduced plants in Tables 3 and 4 have analgesic and antispasmodic effects which led to a decrease in pain severity and even in some cases appeared more effective than *Foeniculum vulgare*, *Vitex agnus-castus*, and the combination of *Apium* spp., *Crocus sativus* and *F. vulgare*. In addition to the effect on menstrual pain severity, some of these plants can also reduce the duration of pain such as *Cinnamomum verum* or the combination of *Zataria Multiflora*, thymol and carvacrol.

Also stress can probably lead to progesterone release by affecting the synthesis of prostaglandins [50]. Thus, the analgesic effect of *Matricaria chamomilla*, *Rosa gallica* and *Rosa damascena* could be indirectly strengthened by reducing psycho-social problems such as stress. Surprisingly, *M. chamomilla* and *Vitex agnus-castus* could decrease hemorrhage as well as mefenamic acid.

According to this review, generally about 13% of the herbs in table 2 have been evaluated for treatment of PD in modern studies through clinical trials, *in vivo* or *in vitro* tests (tables 3 and 4).

Conclusion

With regards to this review, more than 80% of the medicinal plants recommended in Persian Medicine for treatment of menstrual pain have not yet been evaluated for their therapeutic or side effects. Therefore, there are many worthy

candidates for future research such as laboratory or clinical studies, for investigating of precise mechanisms and identification of active compounds from herbs in the field of PD. In addition, Persian Medicine has referred to some other different herbal formulations which were not addressed in this research. This is a space for future investigations.

Conflict of Interest

None

Acknowledgments

The authors wish to thank the School of Traditional Medicine, Shahid Beheshti University of Medical Sciences for library support.

References

- [1] Shirooye P, Hashem-Dabaghian F, Hamzeloo-Moghadam M, Afrakhteh M, Bioos S, Mokaberinejad R. A clinical comparative study of oral and topical ginger on severity and duration of primary dysmenorrhea. *Res J Pharmacogn* 2017;4:23-32.
- [2] Dawood M. Dysmenorrhea. *J Reprod Med* 1985;30:154-167.
- [3] Pedron-Nuevo N, Gonzalez-Unzaga L, De Celis-Carrillo R, Reynoso-Isla M, De la Torre-Romeral L. Incidence of dysmenorrhea and associated symptoms in women aged 12-24 years. *Ginecol Obstet Mex* 1998;66:492-494.
- [4] Habibi N, Huang MSL, Gan WY, Zulida R, Safavi SM. Prevalence of Primary Dysmenorrhea and Factors Associated with Its Intensity Among Undergraduate Students: A Cross-Sectional Study. *Pain Management Nursing* 2015;16:855-861.
- [5] Kannan P, Chapple CM, Miller D, Claydon LS, Baxter GD. Menstrual pain and quality of life in women with primary dysmenorrhea: Rationale, design, and interventions of a randomized controlled trial of effects of a treadmill-based exercise intervention. *Contemp Clin Trials* 2015;42(Supplement C):81-89.
- [6] Lewis RJ, Wasserman E, Denney NW, Gerrard M. The etiology and treatment of primary dysmenorrhea: A review. *Clin Psychol Rev* 1983;3:371-389.

- [7] Kashani L, Mohammadi M, Heidari M, Akhondzadeh S. Herbal Medicine in the Treatment of Primary Dysmenorrhea. *J Med Plants Res* 2015;1:1-5.
- [8] Marjoribanks J, Proctor M, Farquhar C, Derks RS. Nonsteroidal anti-inflammatory drugs for dysmenorrhoea. *Cochrane Database Syst Rev* 2010;1:1-164.
- [9] Antman EM, Bennett JS, Daugherty A, Furberg C, Roberts H, Taubert KA. Use of nonsteroidal antiinflammatory drugs. *Circulation* 2007;115:1634-1642.
- [10] Park KS, Park KI, Hwang DS, Lee JM, Jang JB, Lee CH. A review of in vitro and in vivo studies on the efficacy of herbal medicines for primary dysmenorrhea. *J Evid Based Complement Altern Med* 2014;2014:1-11.
- [11] Dmitrovic R, Kunselman AR, Legro RS. Continuous compared with cyclic oral contraceptives for the treatment of primary dysmenorrhea: a randomized controlled trial. *Obstet Gynecol* 2012;119: 1143-1150.
- [12] Jia W, Wang X, Xu D, Zhao A, Zhang Y. Common traditional Chinese medicinal herbs for dysmenorrhea. *Phytother Res* 2006;20:819-824.
- [13] Moghadam ZB, Rezaei E, Gholami RS, Kheirkhah M, Haghani H. The effect of Valerian root extract on the severity of pre menstrual syndrome symptoms. *J Tradit Complement Med* 2016;6: 309-315.
- [14] Rezaeizadeh H, Alizadeh M, Naseri M, Ardakani MS. The Traditional Iranian Medicine Point of View on Health and. *Iran J Publ Health* 2009;38:169-172.
- [15] Mirabi P, Alamolhoda SH, Esmaeilzadeh S, Mojab F. Effect of medicinal herbs on primary dysmenorrhoea-a systematic review. *Iran J Pharm Res* 2014;13:757-767.
- [16] Bahmani M, Eftekhari Z, Jelodari M, Saki K, Abdollahi R, Majlesi M. Effect of Iranian herbal medicines in dysmenorrhea phytotherapy. *J Chem Pharm Res* 2015;2:519-526.
- [17] Shirooye P, Afrakhteh M, Bioos S, Mokaberinejad R. Uterine pain explanation from Iranian traditional medicine point of view and comparison with pelvic pain from contemporary medicine. *Iran J Obstet Gynecol Infertil (IJOGI)* 2016;19:9-25.
- [18] Behmanesh E, Nabi Meybodi R, Mokaberinejad R, Tansaz M, Mozaffarpour SA, Shirooye P. Menstrual pain explanation from Iranian traditional medicine point of view compared to contemporary medicine: A review article. *Iran J Obstet Gynecol Infertil (IJOGI)* 2016;19:22-31.
- [19] Soltani A. *Encyclopedia of Traditional Medicine, Medicinal Plants*. Arjmand. Tehran 2005.
- [20] Ghahreman A, Okhovvat A. *Matching the old medicinal plant names with scientific terminology*. Tehran University publication. Tehran 2009.
- [21] Dini M. Investigation of various common names of plants used in traditional medicine. Institute of forests and ranges. Tehran 2005.
- [22] Dadkhah N, Eskandarian R, Rahimi-Madiseh M. The medicinal plants and plant-based products of Iran effective on dysmenorrheal. *Int J PharmTech Res* 2016;9:392-406.
- [23] Heidarifar R, Mehran N, Heidari A, Koohbor M, Mansourabad MK. Effect of Dill (*Anethum graveolens*) on the severity of primary dysmenorrhea in compared with mefenamic acid: A randomized, double-blind trial. *J Res Med Sci* 2014;19:326-330.
- [24] Khodakrami N, Moatar F, Ghahiri A. The effect of an Iranian herbal drug on primary dysmenorrhoea-A clinical control trial. *The Horizon of Medical Sciences* 2008;14:11-19.
- [25] Jaafarpour M, Hatefi M, Khani A, Khajavikhan J. Comparative effect of cinnamon and Ibuprofen for treatment of primary dysmenorrhea: a randomized double-blind clinical trial. *J Clin Diagn Res* 2015;9:QC04-QC07.
- [26] Tavasoli F, Sharifian J, Mazlom R. Comparison of the effect of Mefenamic acid and Carum carvi on the severity of primary dysmenorrhea in Mashhad high-school students. *J Sabzevar Uni Med Sci* 2002;8:4-9.
- [27] Delaram M, Forouzandeh N. The effect of Fennel on the primary dysmenorrhea in students of Shahrekord University of Medical Sciences. *Jundishapur Sci Med J* 2011;10:81-88.
- [28] Moslemi L, Bekhradi R, Moghaddam G. Comparative effect of fennel extract on the intensity of primary dysmenorrhea. *Afr J Pharm* 2012;6:1770-1773.
- [29] Nasehi M, Sehhatie F, Zamanzadeh V, Delazar A, Javadzadeh Y, Chongheralu BM. Comparison of the effectiveness of combination of fennel extract/vitamin E with ibuprofen on the pain intensity in students with primary dysmenorrhea. *Iran J Nurs Midwifery* 2013;18:355-359.
- [30] Namavar Jahromi B, Tartifzadeh A, Khabnadideh S. Comparison of fennel and mefenamic acid for the treatment of primary dysmenorrhea. *Int J Gynaecol Obstet* 2003;80:153-157
- [31] Samadi N, Amani F, Naghizadeh M, Alahiari I, Ghezelbash S, Kazemzadeh R. Effect of Using Combination of Fennel, Chamomile and Ginger on Relieving Symptoms of Primary Dysmenorrheal among Students in Ardabil University of Medical Sciences in 2012. *J Ilam Uni Med Sci* 2015;22: 159-164.
- [32] Karimian Z, Sadat Z, Abedzadeh M, Sarafraz N, Kafaei Atrian M, Bahrami N. Comparison the effect of mefenamic acid and *Matricaria chamomilla* on primary dysmenorrhea in Kashan Medical University Students. *J Ardabil Uni Med Sci* 2013;13:413-420.
- [33] Jenabi E, Ebrahimzadeh S. Chamomile tea for relief of primary dysmenorrhea. *Iran J Obstet Gynecol Inferti (IJOGI)* 2010;13:39-42.

- [34] Roknabad M, Sarafraz N. Comparison between the effect of supermint and ibuprofen on primary dysmenorrhea: a randomized clinical trial. *Qom Uni Med Sci J* 2011;1:37-41.
- [35] Tseng YF, Chen CH, Yang YH. Rose tea for relief of primary dysmenorrhea in adolescents: a randomized controlled trial in Taiwan. *J Midwifery Womens Health* 2005;50:e51-e57.
- [36] Saadat E. The effect of aromatherapy with rose oil on primary dysmenorrhea. *Complementary Medicine Journal of faculty of Nursing & Midwifery (CMJ)* 2014;4:787-797.
- [37] Bani S, Hasanpour S, Mousavi Z, Garehbaghi PM, Gojzadeh M. The effect of rosa damascena extract on primary dysmenorrhea: a double-blind cross-over clinical trial. *Red Crescent Med J* 2014; 16:e14643.
- [38] Younesy S, Amiraliakbari S, Esmaili S, Alavimajd H, Nouraei S. Effects of fenugreek seed on the severity and systemic symptoms of dysmenorrhea. *J Reprod Infertil* 2014;15:41-48.
- [39] Inanmdar W, Sultana A, Mubeen U, Rahman K. Clinical efficacy of *Trigonella foenum graecum* (Fenugreek) and dry cupping therapy on intensity of pain in patients with primary dysmenorrhea. *Chin J Integr Med* 2016:1-8.
- [40] Aksoy AN, Gözükarı I, Kabil Kucur S. Evaluation of the efficacy of *Fructus agni casti* in women with severe primary dysmenorrhea: A prospective comparative Doppler study. *J Obstet Gynaecol Res* 2014;40:779-784.
- [41] Shobeiri F, Zeraati F, Mansouri Z, Araghchian M, Nazari M. The comparative effect of herbal extract of vitagnus and mefenamic acid on primary dysmenorrhea. *Zahedan J Res Med Sci* 2012;14: 30-33.
- [42] Iravani M. Clinical effects of *Zataria multiflora* essential oil on primary dysmenorrhea. *J Med Plants* 2009;2:54-60.
- [43] Direkvand-Moghadam A, Khosravi A. The impact of a novel herbal Shirazi *Thymus Vulgaris* on primary dysmenorrhea in comparison to the classical chemical Ibuprofen. *J Res Med Sci* 2012; 17:668-670.
- [44] Su S, Hua Y, Wang Y, Gu W, Zhou W, Duan J-a, et al. Evaluation of the anti-inflammatory and analgesic properties of individual and combined extracts from *Commiphora myrrha*, and *Boswellia carterii*. *J Ethnopharmacol* 2012;139:649-656.
- [45] Ostad S, Soodi M, Shariffzadeh M, Khorshidi N, Marzban H. The effect of fennel essential oil on uterine contraction as a model for dysmenorrhea, pharmacology and toxicology study. *J Ethnopharmacol* 2001;76:299-304.
- [46] Almeida RN, Navarro DS, Barbosa-Filho JM. Plants with central analgesic activity. *Phytomedicine* 2001;8:310-322.
- [47] Valério DA, Cunha TM, Arakawa NS, Lemos HP, Da Costa FB, Parada CA, et al. Anti-inflammatory and analgesic effects of the sesquiterpene lactone budlein A in mice: inhibition of cytokine production-dependent mechanism. *Eur J Pharmacol* 2007;562:155-163.
- [48] Nkeh BC-A, Njamen D, Wandji J, Fomum ZT, Dongmo A, Nguelefack TB, et al. Anti-inflammatory and Analgesic Effects of *Drypemolundein A*, a Sesquiterpene Lactone from *Drypetes molunduana*. *Pharm Biol* 2003;41:26-30.
- [49] Ahmed M, Rahman M, Alimuzzaman M, Shilpi J. Analgesic sesquiterpene dilactone from *Mikania cordata*. *Fitoterapia* 2001;72:919-921.
- [50] Casey M, MacDonald P, Mitchell M. Despite a massive increase in cortisol secretion in women during parturition, there is an equally massive increase in prostaglandin synthesis. A paradox?. *J Clin Invest* 1985;75:1852-57.