

Effect of Medicinal Herbs on Primary Dysmenorrhoea- a Systematic Review

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Abstract

Conventional treatment for primary dysmenorrhoea has a failure rate of 20% to 25% and may be contraindicated or not tolerated by some women. Herbal medicine may be a suitable alternative. To determine the efficacy and safety of Iranian herbal medicine for primary dysmenorrhea when compared with placebo, no treatment, and other treatment.

Electronic searches of the Cochrane Menstrual Disorders and Dysmenorrhoea Group Register of controlled trials, Scopus, Google Scholar, Medline, Pubmed were performed to identify relevant randomized controlled trials (RCTs).

The study abstraction and quality assessment of all studies were undertaken following the detailed descriptions of these categories as described in the JADAD Criteria for Systematic Reviews of Interventions.

25 RCTs involving a total of women were included in the review. The review found promising evidence in the form of RCTs for the use of herbal medicine in the treatment of primary dysmenorrhoea compared with pharmacological treatment. However, the results were limited by methodological flaws. Further rigorous no penetrating placebo-controlled RCTs are warranted.

The review found promising evidence supporting the use of herbal medicine for primary dysmenorrhoea; however, results are limited by the poor methodological quality of the included trials.

Keywords: Primary dysmenorrhea; Herbal medicine; JADAD Criteria; Randomized controlled trials.

Introduction

There are about 8000 species of herbs in Iran, of which 1300 are endemic to Iran. Most consumers of medicinal plants are women who use them to alleviate problems such as menstrual disorders, mood disorders and menopause disorders, cyclical mastalgia and dysmenorrhea. They use these products more than chemical

drugs because of being natural and having fewer side effects (1).

The term dysmenorrhea refers to painful menstruation. Dysmenorrhea is a cramp labor-like pain in the lower abdomen that radiates to upper abdomen, waist and thighs and is sometimes accompanied by systemic symptoms like nausea, vomiting, diarrhea, headache and dizziness (2, 3).

The prevalence of dysmenorrhea has been differently reported between 30 and 85%. Loudermilk expressed prevalence of dysmenorrhea between 50 and 80% with 10 to 18% of people

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having severe dysmenorrhea (4, 5).

In dealing with dysmenorrhea, medications such as prostaglandin synthesis inhibitors, nonsteroidal anti-inflammatory drugs and contraception pills are used irregularly because of fear of their side effects. Also, some of them have not been accepted in Iranian culture. Therefore, it seems necessary to find a new and simpler treatment for dysmenorrhea (6).

Some herbal products are effective on dysmenorrhea and its associated symptoms. Some plants are anti-spasmodic and some have a prostaglandin inhibitory effect. The mechanism of action of many herbal medicines is not completely understood.

Regarding the increasing demand for herbal medicine, many studies have been conducted on the analgesic effect of herbal extracts in Iran, but this is the first systematic review article in this field. This study aimed to systematically review and summarize analysis of clinical trials in this context and to investigate safety and efficacy of various methods for relieving dysmenorrhea.

Experimental

Methods

All clinical trials of herbal products in treatment of primary dysmenorrhea were studied. Studies with inclusion criteria of women at reproductive age with moderate to severe primary dysmenorrhea and with regular menstrual periods as well as exclusion criteria of mild dysmenorrhea, irregular menstrual periods and obligation to use a particular drug entered this systematic review.

Databases such as Scopus, Google Scholar and Pubmed were searched and articles were evaluated according to Jadad Scale (7). This scale investigates articles based on probability of randomization error, patient's follow-up and blinding. In this scale, the maximum score is 5. The papers which had scores of 3 or more were examined in this study. The results are presented qualitatively.

Results

The systematic search primarily investigated clinical trials of herbal products (investigating

abstracts) in Iran. Then, according to Jadad Scale, 25 studies were investigated in the secondary study (investigating the whole article). These clinical trials included the following:

Foeniculum vulgare (8 articles) (Table 1), *Mentha piperita* extract (1 article), *Zataria multiflora* (1 article), *Valeriana officinalis* (2 articles), *Cinnamomum zeylanicum* (1 article), *Zingiber officinale* (2 articles), *Matricaria chamomilla* (1 article), *Stachys lavandulifolia* (2 articles), *Echinophora platyloba* (1 article), *Cuminum cyminum* (1 article), *Vitex agnus-castus* (1 article), Menstrogol® (2 articles), Menastil® (1 article), *Achillea willhemsii* (1 article) (Table 2).

In terms of blinding, there were 4 triple-blind studies, 8 randomized double-blind clinical trials, 5 randomized single-blind clinical trials and 7 unblinded studies.

Foeniculum vulgare

F. vulgare is from Apiaceae family whose root, leaf and fruit can be used. This plant has been used in Iranian traditional medicine for many centuries and has anti-inflammatory, analgesic and antispasmodic effects (8).

The mechanism of its analgesic effect is explained in two ways:

1. The essential oil of this product has analgesic effects in uterus by inhibiting contractions induced by oxytocin and prostaglandins.

2. This product facilitates discharge of blood in shorter time, which reduces dysmenorrhea (9).

Eight studies have examined the effect of *F. vulgare* on primary dysmenorrhea. Three of them compared the effect of *F. vulgare* with placebo (10-12), two compared the effect of *F. vulgare* with mefenamic acid (13 and 14) and one compared the effect of *F. vulgare* and placebo with mefenamic acid (15).

In one study, the effect of *F. vulgare* and *M. chamomilla* (16) and in another, the effect of *F. vulgare* and *E. platyloba* were compared (17). Khorshidi *et al.* showed that *F. vulgare* essential oil was useful in reducing pain and systemic symptoms of primary dysmenorrhea compared with placebo (11), but in the study by Zahrani *et al.*, *F. vulgare* did not affect systemic

Table 1. Clinical trials have been conducted on the impact of *Foeniculum vulgare* on primary dysmenorrheal (PD).

Ref	Authors (year)	method	Experimental group	Control group	Participants	Measure	Results	Side effects and possible reaction	Jadad score
16	Yazdani (2004)	A clinical trial (before - after)	1 st cycle as control, cycles 2 and 3 <i>Foeniculum vulgare</i> , cycles 4 and 5 <i>Matricaria Chamomilla</i>		60 students	VAS	The pain Reduced by <i>F. vulgare</i> and <i>M. chamomilla</i> .	Not mentioned	Cannot be calculated
13	Namvar-Jahromi (2003)	A clinical trial witnessed 3 cycles	1 st cycle without drug, 2 nd cycle Mefenamic Acid 250mg/QID, 3 rd cycle 25 drops <i>F. vulgare</i> from 1 st day.		30 students 15-24 years old with PD (moderate and severe)	VAS	The pain reduced by <i>F. vulgare</i> and Mefenamic acid.	Increased bleeding in 1 case	Cannot be calculated
11	Khorshidi (2002)	A double-blind, randomized clinical trial, 3 cycles	<i>F. vulgare</i> oil 1% or 2% and placebo cross over during 3 cycles	placebo	60 single female students 17-25 years old	VRS	more reduction in pain intensity with <i>F. vulgare</i> 2%	Three groups did not differ	5
10	Tork-zahrani (2007)	A blind, randomized clinical trial, 2 cycles	<i>F. vulgare</i> capsules daily for 5 days during the first 3 days	placebo	130 single female students 17-25 years old who experienced moderate to severe dysmenorrhea	VAS	Reduction pain in <i>F. vulgare</i> group compared to the placebo group. Systemic symptoms in the two groups did not differ	Uncomplicated	5
15	Nazarpoor (2007)	A blind, randomized clinical trial, 2 cycles	<i>F. vulgare</i> 20 to 30 drops every 4 to 8 hours with onset menstruation	Mefenamic acid 250 mg/QID and placebo (drop)	120 single students 17-25 years old who experienced moderate -severe dysmenorrhea	Questionnaire and VAS	The pain reduced by <i>F. vulgare</i> and Mefenamic acid than placebo group. There was no difference between the 2 drugs, reduction systemic symptoms were seen in <i>F. vulgare</i> group.	Uncomplicated	4
14	Modarres-nejad (2006)	A blind, randomized clinical trial, 1 cycle before -2 cycles after	1 st group 30 drops <i>F. vulgare</i> QID with onset pain during 3 days, 2 nd group Mefenamic Acid 250 mg/QID with onset pain during 3 days.		110 female students 13 years and older	VMSS	not difference between the 2 groups	Uncomplicated	4
12	Delaram (2001)	double-blind, randomized, placebo controlled trial	30 drops <i>F. vulgare</i> extract TID for 3 days before menstruation and in the first 3 days of menstruation.	placebo	60 single students 18-25 years old who experienced moderate-severe dysmenorrhea	VAS	The pain reduced by <i>F. vulgare</i> group than placebo	Uncomplicated	5
57	Delaram (2011)	A clinical trial before - after, 2 cycles	A group, 30 drop <i>Echinophora platyloba</i> extract TID for 3 days before menstruation and in the first 3 days of menstruation, Another group <i>F. vulgare</i> extract in same condition		60 single students 18-25 years old who experienced moderate-severe dysmenorrhea	VAS	Mean pain scores were similar between the 2 groups before the inter-vention, pain intensity decreased in 2 groups, but this reduction in <i>F. vulgare</i> was more than <i>Echinophora platyloba</i>	Uncomplicated	5

Table 2. Clinical trials have been conducted on the impact of other herbs on primary dysmenorrheal (PD).

Ref.	Authors (year)	method	Experimental group	Control group	Participants	Measure	results	Side effects and possible reaction	Jdad score
23	Khodakarami (2009)	double-blind, randomized, placebo controlled trial, 3 cycles	One group 500 mg/TID Menstrugol® (saffron, celery and aniseed) for first 3 days of menstruation, another group Mefenamic acid 250 mg/TID	placebo	180 students 18-27 years old	VAS	Herbal extract was more effective than mefenamic acid in pain reduction	Uncomplicated	5
24	Khodayari (2004)	double-blind, randomized, placebo controlled trial, 3 cycles	Menstrugol® (saffron, celery and aniseed)/ TID for first 3 days of menstruation, another group Mefenamic acid 250 mg/ TID	Placebo	161 students 17-30 years old	VAS	There was no difference between the two groups.	Uncomplicated	4
53	Shahhosseini (2006)	double-blind, randomized, placebo controlled trial, 3 cycles	Vitagnus® (<i>Vitex agnus-castus</i>) 40 drops daily for 3 months from the 1 st day of menstruation	placebo 40 drops daily for 3 months from the 1 st day of menstruation	60 students with moderate or severe dysmenorrhea	VAS	70% reduction in pain intensity in experimental group versus 6% in control.	Two patients were excluded due to nausea.	4
18	Ozgoli (2007)	double-blind, randomized, placebo controlled trial, 3 cycles	250 mg ginger/QID for 3 days	One group Mefenamic acid 250 mg/QID, another group Ibuprofen 400 mg/QID	150 students	VMSS	There was no difference between the 2 groups.	Uncomplicated	5
21	Kariman (2007)	double-blind, randomized, placebo controlled trial, 2 cycles	A topical lotion Menastil daily maximum of 3 doses in the first 2 days of menstrual cycles within 2	Baby oil	72 single female students 18-26 years old with moderate and sever PD	VAS	Reduction the severity of dysmenorrhea and signs and pain killer and menstrual bleeding	Uncomplicated	4
32	Mirabi (2011)	randomized clinical trial, 2 cycles	250 mg valerian root/TID for 3 days beginning at the onset of menstruation, for 2 consecutive menstrual cycles	Placebo (starch) 3 days beginning at the onset of menstruation	100 students 18-24 years	VAS and VMSS	Reduction the severity of dysmenorrhea in valerian group than placebo. The total scores of the systemic manifestations decreased after the intervention, but there was no significant difference between the groups, with the exception for syncope.	Uncomplicated	5
46	Irvani (2009)	double-blind, randomized, placebo controlled trial, 3 cycles	One group 25 drop <i>Zataria multiflora</i> 1%, another group 25 drop <i>Z. multiflora</i> 2% onset dysmenorea	Placebo	108 students 18-25 years old with dysmenorrhea (moderate or severe)	VAS and VMSS	<i>Zataria multiflora</i> 1% or 2%, compared with placebo in reducing dysmenorrhea	Not mentioned	4
51	Amoyi-rokn abaad (2012)	Randomized clinical trial, 2 cycles	1 st cycle without drug, for 2 nd cycle 40 drops <i>Mentha piperita</i> every hour in case, another group 400 mg Ibuprofen every 4 hours in first 3 days of menstruation	-	100 single female students 18-22 years old who experienced moderate-severe dysmenorrhea.	Questionnaire, VMSS and Criterion Andrish Mylsvm	There was no difference between the 2 groups.	Uncomplicated	3

Table 2. Continue.

37	Akhavan-amjadi (2009)	double-blind, randomized, placebo controlled trial, 2 cycles	5 capsules 420 mg cinnamon for first 3 days of menstruation in 2 consecutive cycles	Placebo	47 single female students 18-30 years old who experienced moderate-severe dysmenorrhoea.	Questionnaire and VMSS	Reduction in pain compared to placebo group, cinnamon Higher. Systemic symptoms were not different between the two groups	Uncomplicated	5
42	Mirabi (2012)	Clinical trial, 2 cycles	<i>Stachys hvandulifolia</i> (5 g infusion)/TID in starting bleeding		50 single female students 18-25 years old	VAS and VMSS	During the time of dysmenorea and pain Intensity after consumption <i>Stachys hvandulifolia</i> significant difference was observed. Systemic symptoms, the scores did not differ from factors other than changes in the nervous.	Uncomplicated	Cannot be calculated
27	Jenabi (2009)	Randomized clinical trial	1 st group valerian 250 mg within 2 to 3 days of menstruation cycles, and the 2 nd group 250 mg Mefenamic acid		102 students	Questionnaire and VAS	There was no difference between the 2 groups.	Uncomplicated	4
19	Rahnema (2011)	triple-blind, randomized, placebo controlled trial	500 mg ginger TID in first 3 days of menstruation	Placebo	Mean age 21 years, 78 female students with moderate to severe dysmenorrhoea	VAS and VMSS	The duration and severity of primary dysmenorrhoea in ginger. To be significantly reduced compared with placebo.	Uncomplicated	5
56	Delaram (2010)	A clinical trial before-after 2 cycles	<i>Echinophora platyloba</i> extract 30 drops TID for 3 days before the start of menstruation and in the first 3 day of menstruation	Placebo	60 students	VAS	Pain severity in <i>Echinophora platyloba</i> , to be significantly reduced compared with placebo.	Two patients were excluded due to nausea	5
28	Modaress (2011)	triple-blind randomized cross over clinical trial	<i>Matricaria chamomilla</i> (400 mg) within 1 st day or a day before the start of menstrual bleeding for 2 consecutive cycles and for 3 days 800 mg QID in each, and the 2 nd group with the same group of 500 mg Mefenamic acid in the same way before		80 single female students 20-30 years old who experienced moderate-severe dysmenorrhoea	Questionnaire and VAS	In both Mefenamic acid and <i>Matricaria chamomilla</i> (MC), menstrual pain decreased after 2 cycles of treatment, but this reduction was seen in MC.	Uncomplicated	5
22	Tavasoli (2002)	Randomized clinical trial 3 cycles	5 groups: three groups consumed <i>C. cymimum</i> (65 mg/TID, 130 mg/TID and 65 mg per 12 h), one group consumed placebo and the last group took Mefenamic acid		100 students 14-18 years old	VMSS	Among consumer groups <i>Cuminum cymimum</i> , 2 doses TID had the lowest pain. Also reduction in pain intensity between the 1 st and 2 nd cycles of treatment. Significantly differences between the intervention groups than previously reported.	Uncomplicated	Cannot be calculated

Table 2. Continue.

59	Satarzadeh (2009)	Randomized clinical trial	1 capsule of <i>Achillea willhemisii</i> extract TID	70 students with moderate dysmenorrhea	Questionnaire and VAS	Pain during the first 3 days of treatment cycles compared with cycles without treatment significantly reduced.	Not mentioned	Cannot be calculated
41	Olfati (2011)	Clinical trial, 3 cycles	10 g of infused plant powder TID (2 days before and 3 days after the onset of pain)	50 single female students 18-25 years old	VAS and VMSS	After consumption <i>Stachys lvanidulifolia</i> significant difference was observed. The total scores of the systemic manifestations decreased. Decreased after the intervention, but there was no significant difference between the groups, with the exception for nervous.	Uncomplicated	Cannot be calculated

symptoms (10). Jahromi *et al.* compared *F. vulgare* and mefenamic acid for treating primary dysmenorrhea, and concluded that both drugs were significantly effective in reducing dysmenorrhea in comparison with the control group (13).

F. vulgare has been effective in reducing severity of dysmenorrhea in all studies; in comparative studies with mefenamic acid, there has been no significant difference between the two groups in terms of reducing dysmenorrheal (Table 1).

Zingiber officinale

Z. officinale has a long history in medicine and is one of the potent inhibitors of prostaglandins (via cyclooxygenase inhibition). In some sources, one of the traditional uses of *Z. officinale* is for treating dysmenorrhea. (18)

In a double-blind clinical trial, the effect of *Z. officinale* was compared with that of mefenamic acid and ibuprofen for treatment of primary dysmenorrhea and there was no significant difference in the improvement of primary dysmenorrhea in three groups of *Z. officinale* (64%), ibuprofen (66%) and mefenamic acid (58%). In other words, *Z. officinale* was effective in the treatment of primary dysmenorrhea like two conventional chemical drugs (18). In another study, rhizome powder of *Z. officinale* was effective for reducing pain intensity in

comparison with the placebo (19).

Menastil®

Menastil® containing calendula oil and mint essential oil. Menastil® prevents transmission of messages from nerve cells of uterus to brain by shortening axons of nerve cells and leads to late transfer of pain messages from brain to uterus (20).

In a clinical trial, topical use of Menastil lotions was more effective than placebo in reducing severity of dysmenorrhea and its symptoms. Furthermore, sedative consumption and menstrual bleeding decreased (21).

Cuminum cyminum

C. cyminum is useful for treatment of gastrointestinal diseases, delayed and painful menstruation. In a randomized clinical trial, patients were divided to 5 groups. Three groups consumed 65 mg of *C. cyminum* capsules (1 capsule/TID, 2 capsules/TID and, the 3rd group, 1 capsule/BID), one group consumed a placebo capsule and the last group took mefenamic acid. Finally, among consumers of *C. cyminum*, those who had 2 capsules/TID had minimal pain, which was equal to those who consumed mefenamic capsule per 8 h. Furthermore, there was a significant difference among the three groups in terms of reducing pain intensity in the first and second

periods after the treatment compared with that before intervention (22).

Menstrugol® (saffron, celery and aniseed)

In a clinical trial, an herbal capsule (Menstrugol®) containing extract of 3 plants (saffron, celery and aniseed) worked for primary dysmenorrhea and had better and more proper effects than mefenamic acid (23).

In another study, this extract was more effective than placebo on severity of dysmenorrhea (24).

Matricaria chamomilla

M. chamomilla is a traditional herbal drug whose extract has anti-inflammatory and antispasmodic effects. It also has a sedative and anti-anxiety effect (25). Many studies have shown the rate of improvement in dysmenorrhea is more for groups using *M. chamomilla* than placebo. *M. chamomilla* is more effective on relieving dysmenorrhea if it is used before pain begins (26)

Three studies examined the effect of *M. chamomilla* on primary dysmenorrhea. In the first study, after prescribing *M. chamomilla* tea, the rate of anxiety in the intervention group was significantly different from those in the control group after one month (27). In the second study, mefenamic acid was compared with *M. chamomilla* in a cross over treatment which reported that *M. chamomilla* was more effective than mefenamic acid in reducing pain (28).

Another study compared the effects of *M. chamomilla* with *F. vulgare*. Consumption of *M. chamomilla* and *F. vulgare* had a significant effect on three symptoms of premenstrual syndrome and dysmenorrhea in which *M. chamomilla* was more effective on pelvic and abdominal pain, depression and anger and *F. vulgare* was more effective on reducing fatigue and lethargy (29).

Valeriana officinalis

V. officinalis has been traditionally used as a menstruating and sedative drug since 11th century (30). Its root and rhizome have valerian essential oil which contains valepotriates. Root of *V. officinalis* is used as a diuretic, sedative and muscular antispasmodic and valerianic acid of its root has antispasmodic properties (31). Also, the

effect of anti-spasmodic valterate, isovalterate on ileum smooth muscle has been confirmed (32). *V. officinalis* inhibits contractions of cell depolarization well and blocks calcium channels (33).

Two studies have been conducted on *V. officinalis*, one of which compared the effect of its root with placebo (34) and another compared the effects of *V. officinalis* with mefenamic acid (35). In the first study, *V. officinalis* was effective on reducing pain compared to placebo, and in the second study, it had a similar effect to that of mefenamic acid. In one research, systemic symptoms of dysmenorrhea reduced after taking *V. officinalis* capsules compared to pre-intervention, but the difference was the same as placebo group, except for severity of fainting variable which was significantly different between *V. officinalis* and placebo groups (32).

In traditional medicine, *V. officinalis* is known as a menstruating herb, but in a clinical trial, *V. officinalis* had no effect on duration and severity of bleeding (6).

Cinnamomum zeylanicum

C. zeylanicum is from Lauraceae family. *C. zeylanicum* contains mucilage, tannin, a pigment, calcium oxalate, sugar, essential oil and resin. Its physiological effect is attributed to its essential oil and tannin. The main component of cinnamon essential oil is cinnamaldehyde and the essential oil from its bark contains 55 to 57% of cinnamaldehyde and 5 to 18% of eugenol. It has been reported that *C. zeylanicum* has an antispasmodic effect. Eugenol can also inhibit biosynthesis of prostaglandins and affect inflammation (36).

In a triple-blind study, *C. zeylanicum* capsule was compared with placebo. In this study, the effect of *C. zeylanicum* on severity of dysmenorrhea was more than that of placebo. The difference was statistically significant (37).

Stachys lavandulifolia

S. lavandulifolia grows in the mountains of Iran and can be abundantly found in Alvand Mountain. This plant is effective in spasm treatment, is a menstruating agent in women, increases sexuality and causes abortion and is a

pain killer (38).

According to previous studies, *S. lavandulifolia* can inhibit production of prostaglandins (mediators of pain). *S. lavandulifolia* extract is also used for stomach pain and painful menstruation (38-40). In a study, 10 g of infused plant powder was prescribed three times (in Iranian traditional medicine) and no significant difference was observed in duration of pain and severity of pain before and after using *S. lavandulifolia* (41).

In another study, *S. lavandulifolia* affected duration and severity of menstrual pain, but it did not affect systemic symptoms; only reduced diarrhea (42).

Zataria multiflora

Z. multiflora is from mint family and its essential oil is thymol and carvacrol. Investigation on ancient physicians' studies has shown that *Z. multiflora* was used to treat seizures, respiratory diseases, smooth muscular spasm and bloating (43). The most common effect of *Z. multiflora* is its antispasmodic effect on smooth muscles and its antimicrobial property (44).

Van den Broeke stated that flavonoid of *Z. multiflora* can inhibit contractions induced by cell depolarization and blocks calcium channel (45).

In a study, the participants were randomly divided to three groups. The first group was treated by placebo, the second by 1% of *Z. multiflora* essential oil and the third by 2% of *Z. multiflora* essential oil. The maximum pain reduction was reported in the group with 2% of essential oil (46).

In another study, *Z. multiflora* leaves had a similar effect to that of mefenamic acid on pain reduction (47).

Mentha piperita

M. piperita is used in traditional medicine. The essential oil of this herb is colorless or pale yellow or greenish yellow with odor and pungent taste, obtained from distillation of flowers and fresh twigs.

Experimental studies have shown that *M. piperita* oil inhibits contractions induced by cell depolarization and blocks calcium channels and has antispasmodic properties for smooth muscles

(48-50).

In a study, the effect of Supermint® (mint extract) was compared with that of ibuprofen, both of which reduced pain (51).

Vitex agnus-castus

One of the herbal medicines used for treating menstrual disorders is an herbal drop called Vitagnous® and a combination which is derived from *V. agnus-cactus* plants. This plant has a dopaminergic effect. Important combinations of *V. agnus-castus*, especially its essential oil, affect hypothalamus-pituitary axis and decrease secretion of FSH, release of LH and increase progesterone. Indeed, physiological and pharmacological effects of this drug cause human body to naturally balance hormonal reduction or increase (52)

In one study, the effects of Vitagnous® were compared with those of placebo and it was reported that Vitagnous® was more effective than placebo in terms of reducing pain intensity (53).

Echinophora platyloba

E. platyloba is from Apiaceae family and is one of the endemic plants in Iran. The growth of this plant is mostly distributed in Mediterranean region. Results have shown that the extract of this plant can reduce muscle contraction. Antispasmodic effects of this plant can completely inhibit intestinal irritability (54-55).

Two studies have been conducted in this field, one of which compared the effects of *E. platyloba* extract with those of placebo (56) and another compared the effects of *E. platyloba* and fennel on decreasing severity of dysmenorrhea (57). In the first study, *E. platyloba* extract had a significant difference with placebo in terms of reducing pain intensity, and in the second study, extracts of *E. platyloba* and *F. vulgare* could reduce severity of dysmenorrhea during the treatment. The effect of *F. vulgare* in this case was more than that of *E. platyloba*.

Achillea willhemsii

A. willhemsii is a plant with anti-prostaglandin effect. It is from Asteraceae (Compositae) family and its anti-inflammatory property of flavonoids in *A. willhemsii* is due to its inhibitory effect on

metabolism of arachidonic acid (58).

In an experimental study, a capsule containing extract of *A. willhemsii* was prescribed to 70 college students with dysmenorrhea every 6 h. They could reduce the frequency of consumption or dose of drug by 50%, but total daily consumption of capsule should not exceed 4. The results showed that duration of pain in the first three days with treatment reduced significantly compared with the cycles without treatment (59).

Discussion

The aim of this study was to evaluate the efficacy of different herbal remedies on the intensity of primary dysmenorrhea. Most acceptable studies have examined herbal and nutritional treatments. Among them, the number of studies on the use of *F. vulgare* was more than others. Nineteen trials took 3 to 5 scores of Jadad. In five studies, Jadad score could not be calculated due to the trial type.

In these studies, randomization methods, blinding, follow-up, concealment allocation and intention of treatment have been used according to Jadad Scale. However, there is not a detailed description of randomization, blinding and follow-up in most studies. Furthermore, there is the possibility of biased publication because of positive results of all the studies and there is not even one publication with negative results.

Different types of *F. vulgare* including essence, extract and capsule have been compared with placebo or sedative drugs such as mefenamic acid or other herbs (*M. chamomilla* and *E. platyloba*) in order to control pain and in none of these studies, side effects of using the plant have been reported. So, considering numerous studies on *F. vulgare*, it is suggested as a safe and efficacious plant. It seems that it can be used in the treatment of dysmenorrhea. In a study by Jahromi *et al.*, one patient had increased bleeding (13), but a study by Akhavan *et al.* showed that *F. vulgare* did not increase intensity of bleeding and duration of menstruation (60).

There is only one study on the plants such as *C. cyminum*, *C. zeylanicum*, *Menastil*, *E. platyloba*, *V. agnus-castus*, *Z. multiflora*, *M.*

piperita and *A. willhemsii*. Although the results of these studies are positive and these plants are effective on reducing dysmenorrhea, there are not enough studies in this area. Considering their safety, more powerful studies are needed to examine their side effects. It is also suggested to compare different routes of administration for these plants to determine the best route.

Although herbs such as *Z. officinale*, *S. lvanulifolia*, *M. chamomilla* and *V. officinalis* have proved effective, further clinical trials are necessary with the same scale for measuring pain, investigating possible side effects, observing blinding rules and randomization so as to provide a definitive conclusion about their effective use and dose.

References

- (1) Dennehy CE. The use of herbs and dietary supplements in gynecology, an evidence-based review. *J. Midwifery Women's Health* (2006) 51: 402-409.
- (2) Beckman CR. *Obstetrics and Gynecology*. 4th ed. Lippincott Williams and Wilkins, Philadelphia (2004) 234.
- (3) Drife J and Magowan B. *Clinical Obstetrics and Gynecology*. 4th ed. Edinburgh Sounder, London (2004) 203-215.
- (4) Loudermilk DL and Shannon E. *Maternity Nursing*. 3rd ed. Mosbey, London (2003) 138.
- (5) Schulling KD. *Women's Gynecologic Health*. 2nd ed. Amazon, London (2006) 231-234.
- (6) Mirabi P, Doulatian M, Mojab F and Namdari M. Effects of valerian on bleeding and systemic manifestations of menstruation. *J. Med. Plants* (2012) 4: 125-134.
- (7) Miguel MG, Cruz C, Faleiro L, Simoes MT, Figueiredo AC and Barroso JG. *Foeniculum vulgare* essential oils: chemical composition, antioxidant and antimicrobial activities. *Nat. Prod. Commun.* (2010) 5: 319-328.
- (8) Shams Ardakani MR, Haji-akhoundi A, Jamshidi AH and Abdi Kh. The study of volatile oil of *Foeniculum vulgare* Miller, in their tissue culture and comparison with the whole plant. *J. Med. Plants* (2005) 4: 73-80.
- (9) Shibata T, Morimoto T and Suzuki A. The effect of Shakuyukokenzo-to on prostaglandin in human uterine myometrium. *Nippon Sanka Fujinka Zasshi* (1996) 48: 321-327.
- (10) Torkzahrani SH, Akhavan AM, Mojab F and Alavi-majd H. Clinical effects of *Foeniculum vulgare* extract on primary dysmenorrhea. *J. Reproduct. Infertil.* (2007) 1: 45-51.
- (11) Khourshidi N, Ostad SN, Mosaddegh M and Sooudi M. Clinical effects of fennel essential oil on primary dysmenorrhea. *Iran. J. Pharm. Res.* (2003) 2: 89-93.
- (12) Delaram M and Forozandeh N. Effects of *Foeniculum*

- vulgare* extract on primary dysmenorrhea. *J. Med. Sci.* (2001) 10: 81-88.
- (13) Namavar Jahromi B, Tartifzadeh A and Khabnadideh S. Comparison of fennel and mefenamic acid for the treatment of primary dysmenorrhea. *Int. J. Gynaecol. Obstet.* (2003) 80: 153-157.
- (14) Modares Nejad V, Motamedi B and Asadi-pour M. Comparison between the pain-relief effect of fennel and mefenamic acid on primary dysmenorrhea. *J. Rafsanjan Uni. Med. Sci.* (2006) 5: 1-6.
- (15) Nazarpour S and Azimi H. Comparison of therapeutic effects of fennelin and mefenamic acid on primary dysmenorrhea. *J. Mazandaran Uni. Med. Sci.* (2007) 17: 54-61.
- (16) Yazdani M, Shahriari M and Hamed B. Comparison of fennel and chamomile extract and placebo in treatment of premenstrual syndrome and dysmenorrheal. *Med. J. Hormozgan Uni.* (2004) 8: 57-61.
- (17) Delaram M and Sadeghiyan Z. Comparison of fennel and *Echinophora platyloba* extract on primary of dysmenorrhea. *Med. J. Hamedan Uni.* (2012) 18: 42-7.
- (18) Ozgoli G, Goli M and Moatar F. Comparison of effects of ginger, mefenamic acid, and ibuprofen on pain in women with primary dysmenorrhea. *J. Alter. Compl. Med.* (2009) 15: 129-132.
- (19) Rahnama P, Falah-Hosseini H, Mohamadi K, Modares M, Khajavi Shojaei K, Askari M Shahriari AR and Mozayeni P. Effects of *Zingiber officinale* on primary dysmenorrhea. *J. Med. Plants* (2011) 9: 81-6.
- (20) Blum M. *Clinical Trial effective Menastil on Primary Dysmenorrhea*. Toronto (2002) 1-10.
- (21) Kariman NAS, Zareei F, Mojab F, Alavimajd H, Ahmadi M and Gachkar L. The effects of Menastil on primary dysmenorrhea. *Pejouhandeh* (2007) 3: 177-184.
- (22) Tavasoli F, Sharifian J and 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.
- (23) Khodakarami N, Moatar F, Ghahiri A and Shahdan S. The effect of an Iranian herbal drug on primary dysmenorrhea: a clinical controlled trial. *J. Midwifery Women's Health* (2009) 54: 401-404.
- (24) Khodayari N and Moatar F. Efficacy of traditional medicine for the treatment of primary dysmenorrhea. *Iran. J. Pharm. Res.* (2004) 3: 37.
- (25) Barene I, Daberte I, Zvirgzdina L and Iriste V. The complex technology on products of German chamomile. *Medicina (Kaunas)*. (2003) 39: 127-31.
- (26) Jahanian M, Rakhshandeh H and Teimuri M. The effect of chamomile extract on dysmenorrhea. *Med. J. Mashad Uni. Med. Sci.* (1999) 42: 33-40
- (27) Jenabi E and Ebrahimzadeh S. The effect of *Matricaria chamomilla* tea on primary dysmenorrheal. *J. Med. Plants* (2009) 8: 39-42.
- (28) Modaress M, Mirmohammad M, Oshireh Z and Mehran A. Comparison of the effect of mefenamic acid and *Matricaria chamomilla* capsules on primary dysmenorrhea. *J. Babol Uni. Med. Sci.* (2011) 13: 50-8.
- (29) Yazdani M, Shahriari M and Hamed B. Comparison of fennel and chamomile drops versus control in the treatment of primary dysmenorrhea. *J. Hormozgan Uni. Med. Sci.* (2005) 8: 57-61.
- (30) Der Mardersian A. *The Review of Natural Products. Facts and Comparisons*, Philadelphia (2001) 28.
- (31) Bos R, Woerdenbag HJ, De Smet PAGM and Scheffer JJC. *Valeriana* species. In: De Smet PAGM, Keller K, Hansel R and Chandler RF. *Adverse Effects of Herbal Drugs*. Springer-Verlag. Berlin (1997) 3: 105-114.
- (32) Mirabi P, Dolatian M, Mojab F and Alavimajd H. Effects of valerian on the systemic manifestations of dysmenorrhea. *Int. J. Gynecol. Obstet.* (2011) 115: 285-288.
- (33) Gilani AH, Khan AU, Jabeen Q, Subhan F and Ghafar R. Antispasmodic and blood pressure lowering effects of *Valeriana wallichii* are mediated through K⁺ channel activation. *J. Ethnopharmacol.* (2005) 100: 347-352.
- (34) Mirabi P, Doulatian M, Mojab F and Alavimajd H. effects of *Valeriana officinalis* on the severity of dysmenorrhea. *J. Reproduct. Infertil.* (2010) 10: 253-259.
- (35) Jenabi E, Asle Toghiri M and Hejrati P. The comparison of the effects of antiplatin of *Valeriana officinalis* risom and mefenamic acid in relief of primary dismenorrhea. *Iran. J. Obstetrics, Gynecol. Infertil.* (2012) 15: 44-48.
- (36) Keller K. *Cinamomum* species. In: De Smet PAGM, Keller K, Hansel R and Chandler RF. *Adverse Effects of Herbal Drugs*. Vol. 1, Springer-Verlag. Berlin (1992) 105-114.
- (37) Akhavan Amjadi M, Mojab F and Shahbaz-Zadegan S. Effects of *Cinnamomum zeylanicum* on the severity and systemic manifestations of dysmenorrhea. *Med. J. Arak Uni.* (2009) 9: 204-209.
- (38) Zargari A. *Medicinal Plants*. Vol. 1, 4th ed., Tehran Univ. Pub., Tehran (1982) 651-652.
- (39) Khanavi M, Sharifzadeh M, Hadjiakhoondi Z and Shafiee A. Anti- inflammatory activity of aerial part of *Stachys byzanthina* C. Koch from Iran. *J. Essent. Oil Res.* (2005) 97: 475-479.
- (40) Couladis M, Tzakou O and Verykokidou E. Screening of some Greek aromatic plants for antioxidant activity. *Phytother. Res.* (2003) 17: 194-5.
- (41) Olfati F, Azarbajehani S, Hadizadeh M, Sadeghi T and Seyed Javadi E. Effect of *Stachys lavandulifolia* on primary dysmenorrhea. *J. Med. Plants* (2011) 9: 84-9.
- (42) Mirabi P and Mojab F. Effects of *Stachys lavandulifolia* on the severity and systemic manifestations of dysmenorrhea. *Int. J. Gynecol. Obstet.* (2012) 119: 598.
- (43) Akhondzadeh S. *Encyclopedia of Iranian Medical Plants*. Arjmand, Tehran (2000) 137-138.
- (44) Braun L and Cohen M. *Herbs and Natural Supplements: an Evidence-based Guide*. Elsevier, Sydney (2005) 373.
- (45) Van Den Broucke CO and Lemli JA. Spasmolytic activity of the flavonoids from *Thymus vulgaris*. *Pharm. Weekbl. Sci.* (1983) 5: 9-14.

- (46) Irvani M. The effect of *Zataria multiflora* on primary dysmenorrhea. *J. Med. Plants* (2009) 2: 54-60.
- (47) Rozbahani N, Jabari Z and Yazdi S. The comparison of Shirazi *Thymus vulgaris* and Mefenamic acid effects on primary dysmenorrhea. *Arak Med. Uni. J.* (2006) 8: 1-6.
- (48) Fennerty M. NSAID-related gastrointestinal injury: evidence-based approach to preventable complication. *Postgrad. Med.* (2001) 110: 87-92.
- (49) Zeng J, Zhao DS and Wu B. A study on chemical constituents in the herb of *Mentha spicata*. *J. Zhongguo Zhong. Yaozhi* (2002) 27: 749-751.
- (50) Hamthorn M, Ferranti J and Luchowski E. The action of peppermint oil and menthol on calcium channel dependent processes intestinal, neuronal and cardiac preparation. *J. Aliment. Pharmacol. Ther.* (1988) 2: 101-111.
- (51) Amoyi Rokn-Abaad M and Sarafraz N. Comparison effect of of supermint and Ibuprofen on dysmenorrhea. *J. Ghom. Uni. Med. Sci.* (2012) 5: 37-41.
- (52) Barbara Chopin Lucks RA. *Vitex agnus-castus* essential oil and menopausal balance: a research update. *Compl. Ther. Nurs. Midwif.* (2003) 9: 157-160.
- (53) Shahhosseini Z, Amin GH, Salehi Sormaghi MH, Danesh M and Abedian K. The effect of vitex drop on dysmenorrhea. *J. Mazandaran Uni. Med. Sci.* (2006) 15: 15-21.
- (54) Sadraei H, Asghari G and Yaghobei Kh. Study of the effect of hydro-alcoholic and essential oil of *Echinophora platyloba* on rat isolated ileum contractions *in-vitro*. *J. Res. Med. Sci.* (2003) 7: 150-155.
- (55) Avizhgan M, Saadat M, Nilfrooshzadeh MA and Hafizi M. Antifungal effect of *Echinophora platyloba* extract on some common dermathophytes. *J. Med. Plants* (2006) 5: 10-16.
- (56) Delaram M and Sadeghiyan Z. The effect of *Echinophora platyloba* extract on primary dysmenorrhea. *J. Arak Med. Uni.* (2010) 13: 61-67.
- (57) Delaram M and Sadeghiyan Z. Comparison effect of *Echinophora platyloba* and on primary dysmenorrhea. *J. Hamedan Med. Uni.* (2011) 18: 42-47.
- (58) Gerzanna R, Lindmark L and Fronzoza CG. Ginger-an herbal medicinal product with broad anti-inflammatory actions. *J. Med. Food* (2005) 8: 125-132.
- (59) Satarzadeh N, Nazemie H, Maleki N and Hashemi M. Effect of *Achillea willhemsii* on menstrual bleeding and dysmenorrhea. *Tabriz Nurs. Midwif. J.* (2009) 12: 4-10.
- (60) Akhavan Amjadi M, Zahrani SH, Mojab F and Alavi Majd H. Effect of *Foeniculum vulgare* on amount and duration of menstrual bleeding. *J. Med. Plants* (2011) 9: 117-123.

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