

Effects of hot temperament herbs on primary Dysmenorrhea: a systematic review

Farrin Rajabzadeh (1)
 Seyyed Mohammadbagher Fazljou (2)
 Laleh Khodaie (3)
 Shamsi Abbasalizadeh (4)
 Leila Sahebi (5)

(1) Department of Iranian Traditional Medicine, School of Traditional Medicine, Tabriz University of Medical Sciences, Tabriz, IR Iran.

(2) Department of Iranian Traditional Medicine, School of Traditional Medicine, Tabriz University of Medical Sciences, Tabriz, IR Iran.

(3) Medical Philosophy and History Research Center, Tabriz University of Medical Sciences, Tabriz, IR Iran.

(4) Department of Obstetrics and Gynecology, Alzahra Hospital, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, IR Iran.

(5) Assistant Professor of Epidemiology, Maternal, Fetal and Neonatal Research Center, Tehran University of Medical Sciences, Tehran, IR Iran.

Corresponding author:

Seyed Mohammad Bagher Fazljou,
 Department of Iranian Traditional Medicine,
 School of Iranian Traditional Medicine, Tabriz University of Medical Sciences,
 Tabriz, IR Iran.
 Tel: +98-4113379527, Fax: +98-4113379527

Received: January 30, 2018; Accepted: February 10, 2018; Published: March 1, 2018. Citation: Rajabzadeh F. et al. Effects of hot temperament herbs on primary Dysmenorrhea: a systematic review. World Family Medicine. 2018; 16(3):257-263. DOI: 10.5742/MEWFM.2018.93338

Abstract

Context: Dysmenorrhea refers to the symptom associated with painful menstruation which affects the quality of life of a large number of females who suffer from this disorder. Dysmenorrhea has two categories: primary, which occurs in the lack of pelvic pathology and secondary, from identifiable organic causes. Current treatment for primary dysmenorrhoea has a failure rate of 20% to 25% and may be contraindicated or not tolerated by some patients. Herbal medicine may be an appropriate alternative. In this article we focus on herbal medicine to identify the efficacy and safety of herbs with 'hot temperament' for primary dysmenorrhea compared with placebo and other treatments.

Evidence Acquisition: This systematic review study was designed and executed in 2017. In this review, 128 studies were evaluated, only 18 of which were randomized clinical trials of herbal medicines in Iran. These trials included hot temperament herbs. Required data was gathered using electronic databases, such as Scopus, Pub med, Web of science, EMBASE and Chinese scientific journal database, also articles were evaluated according to the JADAD scale.

Result: There is no negative result in the studies. Most of studies showed that the effects of Ginger are higher than other herbs in the treatment of primary dysmenorrhea. All of the mentioned studies showed the higher effect of herbal medicines than Ibuprofen on the treatment of dysmenorrhea.

Conclusions: The present study discusses the use of hot temperament herbs for primary dysmenorrhea. Effective herbal medicines can be used as a good alternative to treat women who do not respond well to conventional therapies or have contraindications to use of these drugs.

Key words: herbal medicine, dysmenorrhea, randomized clinical trial

Introduction

Dysmenorrhea is defined as symptoms associated with painful menstruation which can be divided into primary and secondary dysmenorrhea (1). The latter is a type of menstrual pain not a primary gynecologic disorder (2). More than 50% of women have primary dysmenorrhea. (3). For most women, menstrual pain tends to occur after pregnancy. Primary dysmenorrhea is affected by unnecessary levels of prostaglandins, hormones which make uterus indenture during menstruation and childbirth. The pain seems to result from uterus contractions, due to reduced blood supply in the inner uterine lining (endometrium) (4). Other factors which can cause the pain of primary dysmenorrhea, include a retroverted uterus (5). Non-steroidal anti-inflammatory drugs (NSAIDs) are operative in dismissing the pain of primary dysmenorrhea but which has side effects of nausea, dyspepsia, peptic ulcer, and diarrhea. (6). Hormonal birth control may progress signs of primary dysmenorrhea (7). Recent studies have shown that the birth control pill, comprising low doses of estrogen, reduces pain related with dysmenorrhea. (6,8). Norplant and Depo-Provera are also effective, since these methods often induce amenorrhea (9). Because of side effects and contraindication of these medicines, some peoples cannot use chemical or hormonal drugs. That is what makes us think of new treatments (10). Traditional medicine has enjoyed a special status among people throughout the past, most of which is related to medicinal herbs (11).

In the past, a verity of studies have been conducted for treatment of dysmenorrhea (12). There are inadequate data to commend the use of herbal supplements for the treatment of dysmenorrhea such as melatonin, vitamin E, and fennel (13). Supplementary research is recommended to follow up strong evidence of advantage of ginger, valerian, zinc sulphate, fish oil, and vitamin B1(14). Traditional Chinese herbal medicines are a method for the treatment of dysmenorrhea, some of which were not accepted in Iranian Culture (15). Traditional Iranian books are a rich source of medicinal herbs for dysmenorrhea. Some of these herbs have undergone clinical trials and have had effective results (16).

The functional mechanism of herbal medicines is still not understood but some of them have anti-inflammatory and anti-spasmodic effects (17). However, a variety of studies have focused on herbal medicines. In addition, a lot of studies have shown the effect of herbal medicines on dysmenorrhea in Iran. Because of dysmenorrheal etiology which is prostaglandin F₂ α (PG-F₂α) effects stimulate the uterine muscles and cause severe vascular contraction (18). For this reason, one of the effective treatments for primary dysmenorrhea is the administration of prostaglandin-medications. Some women cannot use herbal medicines with 'cold temperament', so the present study focused on hot temperament herbs to find the efficacy of 'hot temperament' herbs on primary dysmenorrhea.

Methods

Study design and search strategy

In this systematic review which was performed in 2017, the required data was gathered using electronic databases, such as Scopus, Pubmed, Web of Science, EMBASE and Chinese scientific journal database. The key words used in the present study were dysmenorrhea, primary dysmenorrhea, herbal medicines, medicinal plants, hot temperament. All randomized controlled trails (RCTs) had to be included in this study. Observational, cohort, qualitative, and laboratory studies were excluded. Women of reproductive age with primary dysmenorrhea and no identifiable pelvic pathology, ultrasound scan and laparoscopy examination and self reporting women were included in this study. Exclusion criteria consisted of dysmenorrhea resulting from use of intra uterine contraceptive devices and patients with a diagnosis of pregnancy, stroke, and organic disease; in addition, cold temperament herbs were excluded from the study.

Article evaluation

The selected papers extracted from the databases were assessed by two investigators using Jadad scale. Discrepancies between the two raters were referred to the third investigator. In this balance, the maximum mark is 5 and the papers with marks of 3 were examined in this study.

Results

In this review, 128 studies were identified, only 18 of which were clinical trials of herbal medicines in Iran. These trials include hot temperament herbs (Figure 1 & Table 1).

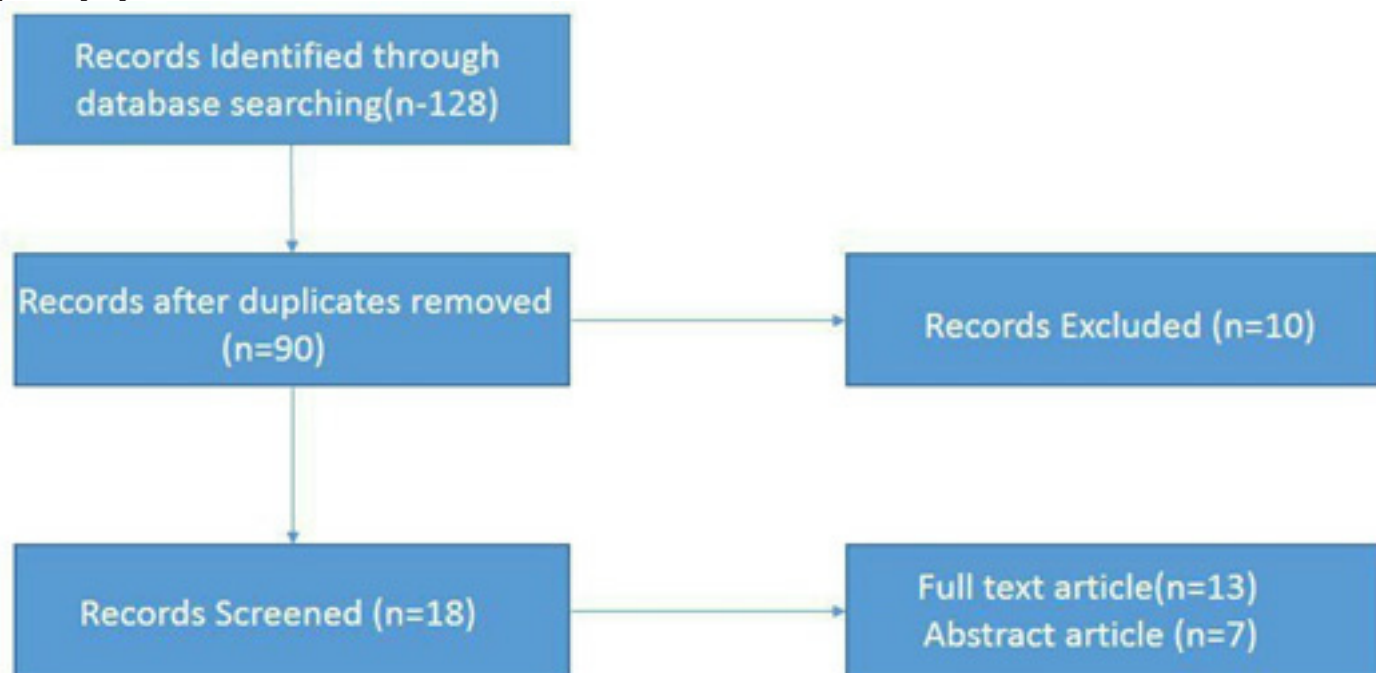
Ginger (*Zingiber officinale* Rosc)

Ginger is one of the main hot temperament herbal inhibitors of prostaglandins, which has been traditionally used for the treatment of dysmenorrhea, arthritis, and colic (19). Ginger is grown in more countries such as India, China, Nigeria, and Thailand (20). The main effects of Ginger are anti-nausea, blood clotting, antibacterial, antioxidants, anti cough, anti-liver poisons, anti-inflammatory, urinating, reduced spasm, anti-flatulence. In Iranian traditional medicine ginger was used with a mix of candy and buckthorn to prevent flatulence of premature fruit (21). Also Ginger can secrete cortisol and manage kidney transplantation (22). Blood cholesterol lowering Oleoresin and essential oil are also produced from ginger (23). Ginger can be boiled in water and drinking the solution can reduce the pain. Ozgoli et al., in a double-blinded clinical trial study, showed that ginger has the same effect of mefenamic acid or ibuprofen in pain reduction. Their study had 3 groups, including Ginger (64%), ibuprofen (66%) and mefenamic acid (58%). The mechanism of Ginger is to inhibit cyclooxygenase and lipooxygenase pathways in prostaglandin, which is the main effect of ginger on menstrual pain (24).

Chamomile (*Matricaria Chamomilla*)

This flower is a traditional herbal medicine whose extract shows both anti-inflammatory and anti-spasmodic effects. It is also helpful for women with constipation, leading to

Figure 1: Flowchart showing the trial selection process for the study investigating hot temperament plants on primary dysmenorrhea



pain reduction with sedative and anti-anxiety effects (25-27). Chamomile is used for a sore stomach, bowel syndrome, and gentle sleep aid. It is also affected as a mild laxative and is anti-inflammatory and bactericidal (28). Chamomile is a little bitter herb that effects to soothe nerves, increase mental awareness, settle the stomach and promote digestion (29). Its formal use is tea to calm hyperactive children, menstrual cramps, and asthma. Chamomile is useful for the liver and lungs and helps reduce jaundice, relieve chest pain, eliminate infection, swelling, and ease withdrawal from drugs (30-34, 35). For treating the sore stomach can take a cup not accompanied by food for three months. Chamomile assists healing of wounds in animals. It also showed some benefit in an animal model of diabetes (36). Essential oil of chamomile is an important antiviral agent against herpes simplex virus type 2 (HSV-2) in vitro (37). The methanol extract of *M. recutita* showed effective anti allergic activity by reserve of histamine release from mast cells in cell-mediated allergic models (38). A variety of studies have examined the effect of Chamomile on primary dysmenorrhea. A study carried out by Bani et.al. showed that prescription of Chamomile tea to a study group was significantly different from control groups after one month's drinking (39). Another study showed that the Chamomile was more effective than mefenamic acid in pain reduction.

Mint (*Mentha Longifolia*):

This medicine is another hot temperament herb which has been used to treat stomach disorders, nausea, vomiting, and dysmenorrhea (40). Mint has a common use for alleviation of stomach pain, as a blood diluent and is effective in strengthening the stomach. Mint contains phenolic compounds such as Rosmarin Acid and Flavonoids and has antimicrobial, antiviral, antioxidant and analgesic properties. It has been shown in laboratory studies that the menthol content of mint oil acts as an antagonist of calcium channels and has the property of muscle relaxation (41).

This herbal medicine can be used as a tea. In a study conducted by Xu Huaxi et al., no significant difference was found between Mint and nonsteroidal anti-inflammatory drugs (NSAIDs)(42). *Zataria Multiflora* is a member of the mint family and its oil is thymol and carvacrol. Some studies showed that *Zataria* is useful to treat respiratory diseases and dysmenorrhea(43). Antispasmodic effects of smooth muscles are a common property of *Multiflora*. This herb can inhibit contractions caused by cell depolarization and block calcium channels. Amoueeroknabad. divided these herbs randomly into 3 groups, including placebo, 1% of the multiflora oil and 2% of the multiflora oil. The study showed that multiflora leads to pain reduction in a third group (44).

Valeriana officinalis:

This has been a sedative drug since the 11th century (45). The main effects of valeriana are strengthening the brain, reducing infections and strengthening the liver and stomach to treat icterus (jaundice). It is also useful for uterine inflammation and kidney pain (46). It can reduce chest pain (47). Valerian has a function similar to benzodiazepines; however, as a substitute of binding to the gamma subunit like a benzodiazepine, it seems to bind to the beta subunit on the GABA-A receptor instead (48). Valerian can decrease the removal or metabolism of GABA, thereby allowing GABA to stay around longer (49). Valeriana roots and rhizomes have essential oil which contain valepotriates. Three studies have been conducted on Valeriana which associated the consequence of its root with placebo, mefenamic acid and other NSAIDs, respectively. The first study showed that Valeriana was most effective in pain reduction, as compared with placebo (50). In the second and third studies, it was found that valeriana has the same effect as mefenamic acid and other NSAIDs. Recent studies have shown that systematic symptoms of dysmenorrhea were reduced after taking Valeriana (51).

Table 1.summary of included trials

References	Participants	Experiment Group	Control Group	Results	Treatment Duration	Side Effects	Jadad Score
25	60 students	Chamomile	Mefnamic A	No significant Difference	3MCs	No	Not Calculated
26	50 single F	Chamomile	placebo	Chamomile is effective in Dysmenorrhea	3MCs	No	4
27	90 students	Chamomile	placebo	Chamomile is effective in Dysmenorrhea	3MCs	No	4
30	50 students	Chamomile	placebo	Chamomile is effective in Dysmenorrhea	6MCs	No	3
31	104 single F	Chamomile	Mefnamic A	No significant Difference	3MCs	No	5
52	110 single F	Cramp Bark	placebo	Cramp is effective in Dysmenorrhea	6MCs	No	4
53	65 single F	Cramp Bark	Ibuprofen	No significant Difference	3MCs	No	5
55	105 single F	Cramp Bark	placebo	Cramp is effective in Dysmenorrhea	3MCs	No	5
56	60 single F	Cramp Bark	placebo	Cramp is effective in Dysmenorrhea	3MCs	No	3
20	150 students	Ginger	Mefnamic A	Ginger is effective in Dysmenorrhea	3MCs	No	5
22	122 students	Ginger	Mefnamic A	Ginger is effective in Dysmenorrhea	3MCs	No	Not Calculated
23	150 single F	Ginger	Mefnamic A	Cramp is effective in Dysmenorrhea	3MCs	No	Not Calculated
24	120 single F	Ginger	Mefnamic A	Ginger is effective in Dysmenorrhea	3MCs	No	5
25	47 single F	Ginger	placebo	Ginger is effective in Dysmenorrhea	3MCs	No	4
49	100 students	Valerian	placebo	valerin is effective in Dysmenorrhea	6MCs	No	3
42	102 students	Mint	Ibuprofen	No significant Difference	3MCs	No	5
43	210 single F	Mint	Ibuprofen	No significant Difference	6MCs	No	Not Calculated
44	100 single F	Mint	placebo	Mint is effective in Dysmenorrhea	3MCs	No	4

Cramp Bark and Black Haw:

Cramp Bark and Black Haw are most effective herbs to reduce uterine cramps and relieve pains and uterine muscle contractions (36, 52). The suitable dose of cramp bark depends on user's age, health, and several other conditions. There is no study to regulate a suitable range of doses for cramp bark. (32, 53-55). A study carried out by Su Zhaoilaiang et al. showed that these herbs are safe for use for several days to prevent painful cramps. In that study, the herbs were compared with ibuprofen, and their results showed that there is no significant difference between the herbs and chemical effects. However, ibuprofen exhibits more side effects as compared with Cramp (28, 33, 56-58).

Foeniculum vulgare

Fennel is a herb that has been used for many years in traditional Iranian medicine as an anti-inflammatory and analgesic pain in cats. The herb has a warm and dry effect and is used to strengthen the stomach and remove its inflammation. In addition, it is a diuretic and leads to an increase in menstrual blood and assists in breastfeeding. According to Iranian medical documents, due to its warm and dry nature, it is useful in removing biliary obstruction (59). This herbal medicine has numbing effects in uterus by constraining reductions induced by oxytocin and prostaglandins. (59). Khorshidi et al. showed that *F. vulgare* essential oil was beneficial in reducing pain and systemic symptoms of primary dysmenorrhea compared with placebo (60), but the study of Zahrani et al., showed no effect on systemic symptoms (61). Jahromi et al. compared *F. vulgare* and mefenamic acid in their study. (62). In the study of Zeraati et al *F. vulgare* and *Vitex* are more effective than mefenamic acid in reducing dysmenorrhea. (63) *F. vulgare* has been active in reducing of dysmenorrhea in all studies which compare with placebo.(64,65).

Cuminum cyminum

In a randomized clinical trial, the effect of *C. cyminum* on primary dysmenorrhea compared to placebo and mefenamic acid, demonstrated that treatment with *C. cyminum* was equal to treatment with mefenamic acid (66). Cumin has a warm and dry nature and is useful in the treatment of epistaxis and is useful for embroidery, anti-flaking and sweating, it causes weight loss. Due to its nature, it makes it easy to reduce blood pressure and reduce menstrual pain.

Cinnamomum zeylanicum

Cinnamon is warm and dry, it is mentioned in Iranian medical texts and has been used as an antibiotic, for anesthetizing, diuretic and regulating, enhancing the libido, strengthening the stomach and liver. It is also used to treat 'cough Prodotti'. Cinnamon oil has been used to relieve uterine pains. Some studies reported that *C. zeylanicum* has an antispasmodic effect. Eugenol can also prevent biosynthesis of prostaglandins and affect inflammation (67). A study where *C. zeylanicum* capsule was compared with placebo showed the effect of *C. zeylanicum* on severity of dysmenorrhea was more than effect of placebo(68). *C. zeylanicum* has anti-microbial, anti-parasitic, anti-oxidant and free radical scavenging properties. In addition *C. zeylanicum* reduced blood glucose, serum cholesterol

and blood pressure, so it can be useful in treatment of cardiovascular diseases. (69)

Melissa officinalis (Lemon Balm)

It is warm and dry, and it is a central nervous system augmentator. It is useful in the treatment of neurological diseases. It is used in the treatment of sleep disorders and also has a sedative effect. It is also helpful in relieving pain. *Melissa officinalis* can be used for pain relief and treatment of some diseases. One study showed that *Melissa* was more operative than mefenamic acid in release of pain on primary dysmenorrhea (70).

Discussion

This study was conducted to evaluate the effect of medicinal plants on the treatment of primary dysmenorrhea in Iran. The aforementioned articles had a great deal of variation in the type of plant studied, which requires more studies with more stringent methodology to apply to many of these plants. It also examined hot temperament herbal medicine on the intensity of primary dysmenorrhea. Studies conducted on Ginger found it to be more useful than those conducted on other herbs. Eight trials received score 4 from Jadad. (29). There is no negative result in the studies. Most of the studies showed that the effects of Ginger are higher than other herbs in the treatment of primary dysmenorrhea. However, only one study presented that the effect of Mint herbs is higher than Ginger (30). Collectively, all of the above-mentioned studies showed the higher effect of herbal medicines than Ibuprofen on the treatment of dysmenorrhea (41). In addition, some publications discussed 'cold temperament' herbal medicine such as Coriander to reduce dysmenorrhea. Some studies focused on Cramp and multiflora, showing positive results and on their ability to reduce dysmenorrhea. The present study demonstrated the higher effect of herbal medicines as compared with NSAIDs; in addition, Ginger may be a real and safe therapy for pain relief in women with primary dysmenorrhea if administered during the days prior to menstruation. Conclusion of this study is focus on those hot temperament herbs which passed the clinical trials studies and are common in Iranian traditional medicine. Effective herbal medicines can be used as a good alternative to treat patients who do not respond well to conventional therapies or have contraindications to use these drugs.

Acknowledgements

The authors gratefully acknowledge the financial support for this work that was provided by Tabriz University of Medical Sciences. This research presented as a PhD thesis at School of Iranian Traditional Medicine, Tabriz University of Medical Sciences.

References

1. Joshi T, Kural MR, Agrawal DP, Noor NN, Patil A. Primary dysmenorrhea and its effect on quality of life in young girls. *Int J M Sci Pub Health* 2015; 4(3):381-5.
2. Weissman AM, Hartz AJ, Hansen MD, Johnson SR. The natural history of primary dysmenorrhoea: a longitudinal study. *BJOG* 2004; 111(4):345-52.

3. Jonathan S, Berek J. *Novak's Gynecology*. 14th ed. New York: Lippincott Williams and Wilkins Publishers; 2012.
4. Sultan C, Gaspari L, Paris F. Adolescent dysmenorrhea. *Endocr Dev* 2012; 22:171-80.
5. Ju H, Jones M, Mishra G. The prevalence and risk factors of dysmenorrhea. *Epidemiol Rev* 2014; 36:104-13.
6. Rehman H, Begum W, Tabasum H, Anjum F. Primary Dysmenorrhea: A Review with Special Reference to Unani Concepts. *J Unani Siddha Homeopat* 2014; 1(1):29-37.
7. Kalvandi R, Alimohammadi S, Pashmakian Z, Rajabi M. The effects of medicinal plants of melissa officinalis and salvia officinalis on primary dysmenorrhea. *J Hamadan Univ Med Sci* 2014; 21(4):105-11.
8. Charu S, Amita R, Sujoy R, Thomas GA. Dysmenorrhea on quality of life of medical students. *Int J Collaborat Res Med* 2012; 4(4):275-93.
9. Wang L, Wang X, Wang W, Chen C, Ronnennberg AG, Guang W, et al. Stress and dysmenorrhoea: a population based prospective study. *Occup Environ Med* 2004; 61(12):1021-6.
10. Faramarzi M, Salmalian H. Association of psychologic and nonpsychologic factors with primary dysmenorrhea. *Iran Red Crescent Med J* 2014; 16(8):e16307.
11. Tavallaee M, Joffres MR, Corber SJ, Bayanzadeh M, Rad MM. The prevalence of menstrual pain and associated risk factors among Iranian women. *J Obstet Gynaecol Res* 2011; 37(5):442-51.
12. Bettendorf B, Shay S, Tu F. Dysmenorrhea: contemporary perspectives. *Obstet Gynecol Surv* 2008; 63(9):597-603.
13. Grandi G, Ferrari S, Xholli A, Cannoletta M, Palma F, Romani C, et al. Prevalence of menstrual pain in young women: what is dysmenorrhea? *J Pain Res* 2012; 5:169-74.
14. Zangene M, Veisi F, Nankali A, Rezaei M, Ataee A. Evaluation of the effects of oral vitamin-D for pelvic pain reduction in primary dysmenorrhea. *Iran J Obstet Gynecol Infertil* 2014; 16(88):14-20.
15. Reyhani T, Jafarnejad F, Behnam HR, Ajam M, Baghaei M. The effect of brisk walking on primary dysmenorrhea in girl students. *Iran J Obstet Gynecol Infertil* 2013; 16(46):14-9.
16. Ameri F, Vahabi MR, Khatoonabadi SA, Andalibi L. On the relevance of medicinal plants consumers in Iran: investigating statistics for consumers, states of consumption, informative and source area. *Teb Tazkiyeh* 2013; 22(3):37-42.
17. Johnston L. Menstrual pain (dysmenorrhoea). *Profession Nurs Today* 2014; 18(1):4-13.
18. French L. Dysmenorrhea. *Am Fam Physician* 2005; 71(2):285-91.
19. Proctor M, Farquhar C. Diagnosis and management of dysmenorrhoea. *Br Med J* 2006; 332(7550):1134-8.
20. Ortiz MI. Primary dysmenorrhea among Mexican university students: prevalence, impact and treatment. *Eur J Obstet Gynecol Reprod Biol* 2010; 152(1):73-7.
21. Serajadini M. Herbal medicine in ancient Iran. *J Med History* 2010; 2(2):11-33.
22. Zhu X, Proctor M, Bensoussan A, Wu E, Smith CA. Chinese herbal medicine for primary dysmenorrhoea. *Cochrane Database Syst Rev* 2008; 2:CD005288.
23. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015; 4(1):1.
24. Ozgoli G, Goli M, Moattar F. Comparison of effects of ginger, mefenamic acid, and ibuprofen on pain in women with primary dysmenorrhea. *J Altern Complement Med*. 2009 Feb;15(2):129-32.
25. Salamon I. Chamomile: a medicinal plant. *The Herb, spice and medicinal plant. Digest* 1992; 10:1-4.
26. Singh O, Khanam Z, Misra N, Srivastava MK. Chamomile (*Matricaria chamomilla* L.): an overview. *Pharmacogn Rev* 2011; 5(9):82-95.
27. Birdane FM, Cemek M, Birdane YO, Gülçin I, Büyükkuroğlu ME. Beneficial effects of chamomile on ethanol-induced acute gastric mucosal injury in rats. *World J Gastroenterol* 2007; 13(4):607-11.
28. Zeraati F, Shobeiri F, Nazari M, Araghchian M, Bekhradi R. Comparative evaluation of the efficacy of herbal drugs (fennelin and vitagnus) and mefenamic acid in the treatment of primary dysmenorrhea. *Iran J Nurs Midwifery Res* 2014; 19(6):581-4.
29. Bokaie M, Farajkhoda T, Enjezab B, Khoshbin A, Mojgan KZ. Oral fennel (*Foeniculum vulgare*) drop effect on primary dysmenorrhea: effectiveness of herbal drug. *Iran J Nurs Midwifery Res* 2013; 18(2):128-32.
30. Villa-Rodriguez JA1, Aydin E1, Gauer JS1, Pyner A1, Williamson G1, Kerimi A1. Green and Chamomile Teas, but not Acarbose, Attenuate Glucose and Fructose Transport via Inhibition of GLUT2 and GLUT5.: *Mol Nutr Food Res*. 2017 Sep 3 311-3.
31. Moslemi L, Bekheradi R, Hasani S, Khaleginejad K. Effect of chamomile on primary dysmenorrhea. *J Family Health* 2013; 1(4):15-20.
32. Moslemi L, Bekhradi R, Galini Moghaddam T, Gholamitabar Tabari M. Comparative effect of chamomile extract on the intensity of primary dysmenorrhea. *African J Pharm Pharmacol* 2012; 6:1770-3.
33. Delaram M, Forouzandeh N. The effect of chamomile on the primary dysmenorrhea in students of Shahrekord university of medical sciences. *Sci Med J* 2011; 10(2):81-8.
34. Tork Zahrani SH, Akhavan Amjadi M, Mojab F, Alavi Majd H. Clinical effect of *Foeniculum vulgare* extract on primary dysmenorrhea. *J Reproduct Infertil*. 2007; 8:45-51.
35. Nazarpour S, Azimi H. The comparison chamomile and Mefenamic acid on primary dysmenorrhea. *J Mazandaran Univ Med Sci* 2007; 17(61):54-61.
36. Modaress Nejad V, Motamedi B. Comparison between the pain-relief effect of Chamomile and mefenamic acid on primary dysmenorrhea. *J Rafsanjan Univ Med Sci* 2006; 5(1):1-6.
37. Saxena M, Shakya A, Sharma N, Shrivastava S, Shukla S. Therapeutic efficacy of Chamomile and *Rosa damascena* Mill. on acetaminophen-induced oxidative stress in albino rats. *J Environ Pathol Toxicol Oncol* 2012; 31(3):193-201.
38. *M. recutita*. Anti-allergic activity of German chamomile (*Matricaria recutita* L.) in mast cell mediated allergy model. *J Ethnopharmacol*. 2011 Sep 1;137(1):336-40

39. Bani S, Hasanpour S, Mousavi Z, Mostafa Garehbaghi P, Gojazadeh M. The effect of chamomile extract on primary dysmenorrhea: A double-blind cross-over clinical trial. *Iran Red Crescent Med J* 2014; 16(1):e14643.
40. Flores KE and Quinlan MB. Ethnomedicine of menstruation in rural Dominica, West Indies. *Journal of Ethnopharmacol.* 2014; 153 (3): 624 - 34.
41. McKay DL, Blumberg JB. A review of the bioactivity and potential health benefits of mint. *Phytother Res* 2006; 20(8):619-33.
42. Xu Huaxi, Wei X, Triggler D. The actions of peppermint oil and menthol on calcium channel dependent processes in intestinal, neuronal and cardiac preparations. *Aliment Pharmacol Ther* 1988; 2(2):101-18.
43. Nasri S. A review of the use of analgesic drugs in Iran. *J Tradition Med Islam Iran.* 2012; 3(3):293-310.
44. Amoueeroknabad M, Sarafraz N. Effect peppermint extract on primary dysmenorrhea compared with ibuprofen: a randomized clinical trial. *Qom Univ Med Sci* 2011; 5(3):37-41.
45. Khayat S, Kheirkhah M, Behboodi Moghadam Z, Fanaei H, Kasaeian A, Javadimehr M. Effect of treatment with ginger on the severity of premenstrual syndrome symptoms. *ISRN Obstet Gynecol* 2014; 2014(4):792708.
46. Stevinson C, Ernst E. Valerian for insomnia: a systematic review of randomized clinical trials. *Sleep Med* 2000; 1:91-9.
47. Ziegler G, Ploch M, Miettinen-Baumann A et al. Efficacy and tolerability of valerian extract LI 156 compared with oxazepam in the treatment of non-organic insomnia - a randomized, double-blind, comparative clinical study. *Eur J Med Res* 2002; 7:480-6.
48. Benke D, Barberis A, Kopp S et al. GABA(A) receptors as in vivo substrate for the anxiolytic action of valerianic acid, a major constituent of valerian root extracts. *Neuropharmacology* 2009; 56:174-81.
49. Ebadi M. Valerian. In: *Pharmacodynamic basis of herbal medicine.* 2nd Ed. Taylor & Francis Group. Boca Raton, FL. 2007:599-609.
50. Mennini T, Bernasconi P, Bombardelli E et al. In vitro study on the interaction of extracts and pure compounds from Valeriana officinalis roots with GABA, benzodiazepine and barbiturate receptors. *Fitoterapia* 1993; 64:291.
51. Jenabi E, Asltugiri M, Hejrati P. Compare Valeriana Officinalis and mephenamic acid on primary dysmenorrhea. *Iran J Obstet Gynecol Infertil* 2012; 15(2):44-8
52. Ataollahi M, Akbari SA, Mojab F, Alavi Majd H. The effect of cramp Bark extract on premenstrual syndrome symptoms. *Iran J Pharm Res* 2015; 14(1):159-66.
53. Atallahi M, Akbari SA, Mojab F, Alavi Majd H. Effects of cramp bark extract on the severity and systemic symptoms of primary dysmenorrhea: a randomized controlled clinical trial. *Iran Red Crescent Med J* 2014; 16(8):e19503.
54. Zaidi SA, Khatoun K, Aslam KM. Role of herbal medicine in Ussurutams (Dysmenorrhoea). *J Acad Indus Res.* 2012; 1(3):113-7.
55. Aghajani Delavar M, Naseri Amiri F, Hoseini H. The effect of cramp barks on premenstrual syndrome. *J Herbal drug* 2001; 1(2):15-21.
56. Golian Tehrani S, Bazzazian S, Bakhtiarian A, Ghobadzadeh M. Effects of calci soya balance and cramp bark on menopausal symptoms. *Iran Red Crescent Med J* 2014; 16(10):e13551.
57. Valadi A, Nasri S, Abbasi N, Amin G. Antinociceptive and anti-inflammatory effects of hydroalcoholic extract of anethum graveolens L. seed. *J Med Plant* 2010; 2(34):124-30.
58. Alcaraz M, Hoult JR. Actions of flavonoids and the novel anti-inflammatory flavone, hypolaetin-8-glucoside, on prostaglandin biosynthesis and inactivation. *Biochem Pharmacol* 1985; 34(14):2477-82.
59. 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.
60. 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.
61. 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.
62. 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.
63. Zeraati F, Shobeiri F, Nazari M, Araghchian M, Bekhradi R. Comparative evaluation of the efficacy of herbal drugs (fennelin and vitagnus) and mefenamic acid in the treatment of primary dysmenorrhea. *Iran J Nurs Midwifery Res* 2014; 19(6):581-4.
64. Omidvar S, Esmailzadeh S, Baradaran M, Basirat Z. Effect of fennel on pain intensity in dysmenorrhoea: A placebo-controlled trial. *Ayu* 2012; 33(2):311-3.
65. Moslemi L, Bekheradi R, Hasani S, Khaleginejad K. Effect of fennel on primary dysmenorrhea. *J Family Health* 2013; 1(4):15-20.
66. 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.
67. 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.
68. 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.
69. Ranasinghe et al.: Medicinal properties of 'true' cinnamon (Cinnamomum zeylanicum): a systematic review. *BMC Complementary and Alternative Medicine* 2013 13:275.
70. Safdari Dehcheshmeh F, Parvin N. The Effect of Mefenamic Acid and Melissa officinalis on Primary Dysmenorrhea: A Randomized Clinical Trial Study. *International Journal of Pharmacognosy and Phytochemical Research* 2016; 8(8); 1286-1292. Available online on www.ijppr.com