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Review Article

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Effect of Iranian herbal medicines in Dysmenorrhea phytotherapy

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ABSTRACT

Dysmenorrhea is one of the most prevalent medical disorders of gynecologic system that affects almost 50% of women with regular menstruation. Today, for the treatment and control of pain and symptoms, various methods such as herbal therapy, local heat, thiamin, vitamin E, fish oil supplements, acupuncture and transcutaneous nerve stimulation are used. In this study, the most important medicinal plants native to Iran, which are effective on pain are reported. Iranian herbs such as mint, platyloba, anise, valerian, thyme, mountain tea, ginger, lemon balm, sage, vitakous, dill, cinnamon, chamomile, celery, saffron, anise, anise, cumin, borage, marshmallow, citron, yarrow, black beans, buttercup, cardamom, oregano, black pepper and so on are used for dysmenorrhea.

Keywords: Dysmenorrhea, herbal medicine, herbs, Iran

INTRODUCTION

Dysmenorrhea is one of the most prevalent medical disorders of gynecological system [1]. Dysmenorrhea refers to pain associated with menstrual cramping, which usually occurs in the lower abdomen. It is the most common type of cyclic pain, depending on the anatomic pathology [2,3]. Dysmenorrhea clinically is divided into two categories. Primary dysmenorrhea refers to menstrual pain without pelvic disorders and secondary dysmenorrhea refers to menstrual pain due to pelvic diseases [4,5].

Since 1970s, prostaglandins have been identified as a cause of primary dysmenorrhea and non-steroidal anti-inflammatory drugs have been introduced as the choice treatment of primary dysmenorrhea [6][7]. Menstrual pain that is associated with ovulation, cramps occur in the midline suprapubic and sometimes in the lower back and groin spread [8]. The pain usually begins with the onset of bleeding and lasts 12 to 48 hours. It seems that the cause of menstrual pain and associated symptoms such as nausea, vomiting, fatigue and headaches are related to the release of prostaglandins during menstruation [9].

Primary dysmenorrhea is due to uterine contractions and ischemia [10-12]. Another reason that researchers noted include increasing the concentrations of prostaglandins, vasopressin, increasing levels of leukotrienes and psychological factors which have been implicated in the development of primary dysmenorrhea [13].

The most prevalence of pain is in the first 20 years of life and after the age of 35 years, it begins to decline. Dysmenorrhea and pain are associated with impaired quality of life and social activities for young women,

especially if the symptoms such as headache, fatigue, nausea and vomiting, diarrhea, irritability, chills, muscle cramps and other symptoms occur [14].

The prevalence of primary dysmenorrhea in different countries is 50 to 90 percent and in Iran is 74 to 84.4 percent [15]. Published reports have estimated that approximately 15% of women suffer from severe pain during menstruation [16].

In America it has been reported that about 60 percent of teens suffer from dysmenorrhea who reveal different degrees of pain, and 14% of patients are frequently absent from school [17]. This disease is the leading cause of school absenteeism and workplace which is about 600 million hours per year and it costs about $ 2 billion annually for US economy [18][19]. The disease does not pose a problem for women, but the effect on the productivity of the national problem is known [20].

Nowadays, for the treatment and control of pain and symptoms, various methods are applied such as local heat, medicine, thiamin, vitamin E, fish oil supplements, acupuncture and transcutaneous nerve stimulation. Among the most effective of these methods, inhibitors of prostaglandin synthesis by about 80%, are impressive. The side effects of these drugs, such as mefenamic acid and ibuprofen, like all chemical medications, are numerous [21-23]. Especially in synthetic drugs that are prescribed for a long-term, the side effects are notable. Nausea, stomach irritation, ulcers, gastrointestinal, renal papillary necrosis and renal blood flow are the side effects of synthesis inhibitors of prostaglandin [24]. Due to the side effects of these drugs, the use of alternative therapies such as herbs or nutrients in the treatment of primary dysmenorrhea or other complications has received special attention [25-32].

This review paper presents the native plants which are scientifically or traditionally are used in the treatment of dysmenorrhea.

RESULTS

The present study demonstrated that people in different regions of Iran use from medicinal plants such as Peppermint extract, *Echinophora platyloba* extract, *Foeniculum vulgar* extract, *Valeriana officinalis root extract*, *Zataria multiflora*, *Stachys lvandulifolia* powder, *Vitex plant*, *Cinnamomum zeylanicum*, *Anethum graveolens* extract, *Zingiber officinale*, *Matricaria chamomilla* tea and *Apium graveolens* ,*Crocus sativus*, *Pimpinella anisume* Capsule to treat dysmenorrhea and its symptoms and complications. The results details of the study are summarized in table 1.

DISCUSSION

Synthetic drugs, especially the ones prescribed for long-term reveal a few side effects, especially prostaglandin inhibitors [45]. Herbs have always been a source of human drugs [46-48]. Medicinal herbs are widely used by people in different regions [49-53] and possess various therapeutic effects [54-61]. Academic and industrial researches are in progress to produce natural remedies from medicinal plants [62-67].

Women especially tend to use the herbal medicines and commonly used to treat problems like frequent symptoms of dysmenorrhea, menopause, menstrual disorders, mood disorders, prevention of osteoporosis and pregnancy problems by using herbal medicines .Some plants such as Cinnamon, dill seeds and drops, *Anethum graveolens*, *Nannorrhops ritchiana*, thyme, *Pimpinella anisum*, *Ajwain*, *cumin*, ginger, chamomile, fennel, saffron, borage, marshmallow, Fenugreek, Citron, valerian, yarrow, Nigella , Buttercup, *Hypericum perforatum*, cardamom, oregano, black pepper, peppermint, Gelder, *Artemisia vulgaris* be used in different regions [68].

In traditional medicine of Iran and ethnobotany, some plants are traditionally used to reduce menstrual pain and dysmenorrhea. In the North West of Iran, in Arasbaran region, the effective plants on menstruation and dysmenorrhea include sumac (*Rhus coriaria* L.), savory (*Satureja hortensis*), pursuant to (*Juniperus commonis*), Tiger's Tail (*Leonurus cardiaca*), marjoram or oregano (*Origanum vulgare*), sage (*Salvia sclarea* L.), pennyroyal (*Mentha longifolia*), *Ballota nigra*, mountain ash (*Sorbus boissieri*) and nettle (*Urtica dioica* L.). In ethnobotany of Sīstān, located in the south east of Iran, fennel (*Foeniculum vulgare* Mill.) is used to control the menstrual cycle [77].

Table 1. Effective dysmenorrhea native medicinal plants in Iran

Number	The scientific name of the plant	Type of study, type of dysmenorrhea	Results	References
1	Peppermint extract	Human clinical trials	Primary dysmenorrhea in both groups receiving supermint oil (peppermint extract) at a dose of 40 drops and ibuprofen 400 mg dose was reduced.	[33]
2	*Echinophora platyloba* extract	Human clinical trials	The mean pain intensity in the two months prior to drug administration in the treatment group and the placebo group was 10.86 ± 34.72 and 11.16 ± 35.55 which the differences were not significant. After the treatment, the mean of group platyloba 7.33 ± 22.49 and 9.91 ± 28.93 in the control group and the difference was significant.	[34]
3	*Foeniculum vulgar* extract	Human clinical trials	Fennel extract can reduce the severity of dysmenorrhea. Based on the findings of the two groups was statistically significant difference in pain intensity. The symptoms of systemic disease with decreased compared to before treatment. (P <0/001), but this reduction was not statistically significant between the two groups. Except in the case of lethargy variable statistical difference between the groups was significant at the threshold	[35]
4	*Valeriana officinalis root extract*	Human clinical trials	Mean pain intensity before taking the drug in the treatment group and control group were not significantly different but average pain intensity after drug consumption decreased in both groups, but it's more treated groups and a reduction in the difference between the two groups was statistically significant. Also, the total systemic symptoms severity scores a total of differences between groups in terms of dysmenorrhea were significantly associated with decreased compared to before treatment, but this reduction of t (g) between the two groups in terms of statistical consumers also of valerian and placebo was not significant. Except in the case of highly variable statistical differences between the two chapters of the Group was significant.	[36]
5	*Zataria multiflora*	Primary dysmenorrhea Human clinical trials	Primary dysmenorrhea pain scores using linear-visual pain scale in the placebo group, 1% thyme, thyme 2%, respectively, 1.6 ± 7.8, 1.5 ± 7.3 and 1.7 ± 7.5 were measured.	[37]
6	*Stachys lvandulifolia* powder	Primary dysmenorrhea Human clinical trials	Pain before and after *lvandulifolia* significant difference was observed. *Lvandulifolia* using the traditional method can alleviate the pain of primary dysmenorrhea, and no side effects. In addition to effective pain patterns that can better tolerate the pain.	[38]
7	*Vitex plant*	Primary dysmenorrhea Human clinical trials	The results showed that pain intensity was reduced 60% in the first cycle of treatment and the severity of pain at the end of the third month of drug use, to 70 percent. While the reduction in the control group was 1.2% in the first months of the end of the third month up to 6 per cent. Results showed significant differences in mean pain intensity of the pain level 2 before and after treatment were observed.	[39]
8	*Cinnamomum zeylanicum*	Primary dysmenorrhea , Human clinical trials	The severity of pain in the test group, taking the cinnamon, reduced from 2.15 before treat to the 1.04 after treatment in the second cycle or a placebo of 2.14 before treatment to 1.67 after treat in the second cycle. The total scores of symptoms of systemic disease decreased compared to before treatment.	[40]
9	*Anethum graveolens* extract	Primary dysmenorrhea Human clinical trials	Dill and mefenamic acid extracts were effective on pain. Mean pain intensity in both groups before intervention was not significant. After the intervention, the three cycles and in both groups there was a decrease in pain and this reduction was higher in the group of mefenamic acid and in the second and third cycles was significant.	[41]
10	*Zingiber officinale*	‘ Primary dysmenorrhea Human clinical trials	The 64% improvement in severity of pain with ginger, 66% with ibuprofen and mefenamic 58%, which was statistically significant.	[42]
11	*Matricaria chamomilla* tea	Primary dysmenorrhea ‹Human clinical trials	In the intervention group, a week before menstruation and menstrual 5 days, 2 cups of chamomile tea every day was given for a period of 3 months of treatment was continued. Pain, anxiety, and feelings of the group, after a month of tea than in the control group was significant. The total mean score of four questionnaires in the intervention group, after 1 and 3 months after taking chamomile tea has a significant difference compared to control group.	[43]
12	*Apium graveolens +Crocus sativus +Pimpinella anisume* Capsule	Primary dysmenorrhea ‹Human clinical trials	Herbal capsule consists of several plant was better than mefenamic acid in reducing the severity of primary dysmenorrhea.	[44]

In Shiraz which is located in southern Iran, flax (*Linum album* Ky. Ex Boiss.), *Marrubium vulgare* L., *Nepeta persica* Boiss., Black cumin (*Nigella ciliaris* L.) and *Senecio glaucus* L. are used for treatment of menstrual cycle problems [69].

In Kazerun, in south of Iran, chameleon plant (*brevilimbe Boiss. Heliotropium*) and red clover (*Trifolium repens* L.) are used to control menstrual pain [70].

In Kerman, located in east of Iran, Achillea eriophora, Cuminum cyminum, flax (*Linumus itatissimum*), *Salvia macrosiphon* and *Teucrium polium* are used for menstrual cramps [71].

Mobarakeh is located in Isfahan in central of Iran, *Achillea santolina*, valerian (*Valeriana officinalis* L), cumin (*Cuminum cyminum* L.) and sage (*Salvia nemorosa* L) are used to reduce menstrual cramps [72]. In Urmia, North West of Iran, *Achillea millefolium* L., *Centaurea behen* L., *Grammosciadium daucoide* DC., Nettle water (*Polygonum hydropiper* L.), *Salix triandra* L ., *Stachys lavandulifolia* Vahi. and *Teucrium orientale* L are consumed for alleviating the menstrual pain [73].

Different areas of Iran, depends on the type of plants, fauna and culture of this region, a few of medical plants are used to treat the symptoms of dysmenorrhea.

Peppermint oil inhibits the contractions induced by cell depolarization and the calcium channels are blocked [74]. Peppermint has antispasmodic effect on smooth muscle [74]. Mint has muscle relaxant, anti-inflammatory and analgesic properties [75]. *Echinophora platyloba* contains flavonoids, alkaloids and saponins, Trans-B-Ocimene, 2-Furanone, Myrcene, Linalool and is Cisocimene [76]. Platyloba has antispasmodic effect and reduces muscle contraction [76]. It seems that the flavonoid, saponin and alkaloid compounds are effective and are involved in reducing uterine contractions and decreasing dysmenorrhea problems [76].

The fennel essential oil, due to anethol, can reduce spasms of the gastrointestinal tract [78][77]. *Foeniculum vulgare* contains palmitic acid, oleic acid, linoleic acid, petrocilinic acid, comphen, fencho and anethol [80][81]. *Valeriana officinalis* has sedatives, analgesics, and the regulation of menorrhea properties [82][83]. Valerian root is used as a sedative and antispasmodic. Antispasmodic and anti-spasmodic and analgesic effects are ultimately it is because of valerinic acid composition [84-87].

Thyme, traditionally used as medical herbal, has anti-smooth muscle spasm properties [88]. Thymol and carvacrol are the active ingredients of thyme [89]. Antispasmodic properties of plant are because of phenolic compounds that thymol is the major part [90]. The flavonoid compounds of Thyme inhibit contraction of cell depolarization and block the calcium channels [91-92]. Studies on mouse models showed anti-inflammatory and analgesic properties of thyme [93]. Bioactive compounds of plant extract and essential oil with specific mechanism is known to improve the symptoms of dysmenorrhea.

Probably, the extract has inhibitory effect by blocking voltage-dependent calcium channels and inhibition of calcium release from intracellular sources revealing its therapeutic effect [94].

Studies have shown that plants *lvandulifolia* and *Hypericum perforatum* may inhibit the production of prostaglandins that mediate pain [95] and expose anti-inflammatory effects [96] and analgesic activity [97]. Cinnamon has amidoun, mucilage, tannins, a dye, calcium oxalate, sugar, cinamomin, essential oils and resins. The physiological effects of essential oils and tannins of cinnamon in folk medicine induce the energy sector, sedative, antispasmodic, anti-inflammatory and is used to reduce menstrual pain [98][99].

Its antispasmodic effect is due to cinnamaldehyde in cinnamon. The eugenol can also prevent the biosynthesis of prostaglandins and reduce inflammation. Pharmacology and toxicology studies in humans did not show any particular risk to Cinnamon [100].

Anethum graveolens has a volatile oil that reveals anti-spasmodic effect [101], regulates the irregular menstrual [102] and is effective on amenorrhea [103].

The researches on antispasmodic effect of *Anethum graveolens* extract on rat uterine contractions showed that the extract induced its contractile effect by blocking voltage-dependent calcium channels and the dysfunction in actions of oxytocin [94]. *Anethum graveolens* essence has volatile oil containing limonene and Karun that more than 90% of the essence oil has antispasmodic effects [101].

Gingerols and liabilities of Ginger (Zingiber forming compounds) are potent inhibitors of prostaglandin by inhibiting cyclooxygenase (] Facts and Comparisons Publishing Group. In clinical trials in patients with knee pain due to osteoarthritis analgesic effect of ginger has been reported [105]. In some of the traditional resources, ginger is consumed in the treatment of dysmenorrhea [106]. Chamomile plant possesses anti-inflammatory effect, antispasmodic, sedative and anti-agitation activies [107].

Saffron plant has sedative and regulation of menorrhea effect. Chemical compounds in saffron contain glycoside crocin, crocetin, picrocrocin and volatile essential oil [108]. Celery has chemical compounds including apigraveann, apiometin, Celenin,bergaptene and ambliophrone which have different properties including sedative, diuretic, promiscuous binding, anti-inflammatory and anti-depression activities [109].

Native medicinal plants in Iran, presented in this study due to their quality ingredients and proven mechanism of action can be effective in the treatment of pain and dysmenorrhea and can be produced effective natural remedies from them.

Although inhibition of cyclooxygenase is considered to be the main factor for the effect of these plants in alleviation of dysmenorrhea, however, the exact mechanism is not clear. Oxidative stress is involved in pain and dysmenorrhea and most of these plants have been shown to possess antioxidant activity [110-129] . Therefore, the antioxidant activity of

CONCLUSION

Because of the known side effects of synthetic drugs and the long history of herbal medicine and public confidence in the therapeutic effects of medicinal plants, they can be a good alternative to treat disorders such as dysmenorrhea. It should be noted that different plants contain very bioactive compounds that some of them have properties effective on dysmenorrhra. In fact, plants are complex chemical cocktails with different properties. It means that just one mechanism of a plant action on cancer in dysmenorrhra and it may act by several mechanisms. The rationale for using a combination of medications to control pain is based on two important principles, single drug is often accompanied by low effect, and over time causes unwanted effects, but using a combination of drugs and reducing the dosage, the side effects might be reduced more effective. The best solution is to use multi-herbal treatment for dysmenorrhea which has multiple and stronger effect, for instance anti-inflammatory, sedative and analgesic effects.

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