

# The Impact of Achillea Millefolium on Primary Dysmenorrhea and Menstrual bleeding: A Systematic Review

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## ABSTRACT

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**Background & aim:** This study systematically reviewed the clinical trials to assess Achillea millefolium's impact on primary dysmenorrhea and menstrual bleeding.

**Methods:** In this systematic review, the databases of Science Direct, PubMed, ProQuest, Cochrane library, Scopus, Web of Science were searched using the keywords of "Dysmenorrhea", "Pain", "Menorrhagia" and "Achilles" until Aug 2022. The study population included women with moderate to severe dysmenorrhea or menorrhagia with a score of 100 on Pictorial menstrual bleeding Assessment Chart (PBLAC). Intervention included oral administration of Achillea millefolium with other modern dosage forms. The Cochran's Risk of Bias tool was applied to evaluate the quality of articles.

**Results:** Among 80 initial articles, six studies were systematically reviewed. Among six reviewed studies, three studies examined the impact of Achillea millefolium on primary dysmenorrhea, two studies evaluated the effect of Achillea millefolium on menorrhagia and one study assessed the impact of Achillea millefolium on both primary dysmenorrhea and menorrhagia. The results showed the effect of Achillea millefolium in pain relief of dysmenorrhea and reduction of menstrual bleeding.

**Conclusion:** Achillea millefolium is an effective and safe herbal remedy for primary dysmenorrhea and reduction of menstrual bleeding.

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## Introduction

Primary dysmenorrhea usually occurs within 1-2 years after menarche (1-2). The prevalence of this problem is about 71% in Iran (3-5). Dysmenorrhea is one of the main factors affecting the quality of life and social activities (6-7). Heavy menstrual bleeding is the other common gynecological problem experienced by 30% of childbearing age women (8-9).

The common treatment methods include combined estrogen-progesterone contraceptives or progestin alone (10-11). Side effects of medical treatments include gastrointestinal disorders such as nausea and vomiting, kidney disorders, stomach ulcers, dizziness, tinnitus, allergic reactions, blood and liver complications, bleeding and spotting (12-14).

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Herbs are among the basic treatment methods and are significantly more superior to chemical drugs due to higher acceptability and less complications (15-16). Thyme, fennel, marigold, anethum graveolens, saffron, teucrium polium, bromelain, fenugreek, rosemary are effective plants for dysmenorrhea and menstrual disorders, but due to the small number of studies and poor methodology, definitive conclusions about the effect of these plants are not reported (17-23). Millefolium Achillea, commonly known as yarrow, is one of the native plants of Iran, which is used as one of the herbal remedies for dysmenorrhea (24). Achillea millefolium inhibits the cyclooxygenase enzyme and can be effective as an antiprostaglandin drug to improve primary dysmenorrhea. Achillea millefolium also inhibits smooth muscle contraction by closing calcium channels, so it can have an antispasmodic effect on uterine smooth muscle (25). Achillea millefolium is used in the treatment of blood clotting and blood coagulation (24, 28). In one study, the reduction of dysmenorrhea severity was greater in the Achillea millefolium and mefenamic acid groups compared with the placebo and mefenamic acid groups. The duration of pain was reduced in both groups, but there was no statistically significant difference between the two groups in terms of reducing the duration of pain (29). In another study with aimed to compare the impact of chamomile and Achillea millefolium capsules on the intensity of primary dysmenorrhea, both Achillea millefolium and chamomile capsules reduced pain intensity, but reduced pain intensity was greater in the group of Achillea millefolium capsules with their long-term sedative properties (30). In other study, the amount and duration of menstrual bleeding were significantly reduced before and after treatment in both Achillea millefolium and mefenamic acid groups, which was significantly higher in Achillea millefolium group compared to the control group (31). Also, another study reported that the amount and duration of menstrual bleeding were significantly reduced before and after treatment in both Achillea millefolium and mefenamic acid groups, which was more significant in the Achillea millefolium group compared to the control group. Although the amount and duration of menstrual bleeding

increased during the follow-up period after treatment in both groups, it was less than the pre-intervention period. Drowsiness and gastrointestinal complications were among the reported side effects after consumption of Achillea millefolium (32).

Since no systematic review has been conducted to gather the information on the impact of Achillea millefolium on primary dysmenorrhea, menstrual bleeding volume and additional side effects of common drugs: uncertainty has remained regarding the efficacy of Achillea millefolium. Further studies are needed to address this uncertainly. Although, several studies have investigated the effects of Achillea millefolium on dysmenorrhea and menstrual bleeding, a conclusive decision regarding its use has not been reached. Therefore this present review systematically evaluated and summarized the results of clinical trials focusing on the impact of Achillea millefolium on primary dysmenorrhea and menstrual bleeding.

## Materials and Methods

The current study was performed based on the preferred reporting items for systematic reviews (PRISMA 2020 checklist). In this study, international databases including Pubmed, Web of Science, Scopus, Science direct, Cochrane databases, Google Scholar and Research Proposal Information System (RPIS; <https://rpis.research.ac.ir/>) were searched to access the related articles. Search strategies were developed using Medical subject headings (MeSH) and synonyms. The searches were conducted using the English keywords and Persian equivalents as followings: chilleas OR Yarrows\* OR Achillea millefolium OR Achillea millefoliums\* OR millefolium OR Achillea AND dysmenorrhea OR menstruation disturbances OR menstruation disorders OR menstrual disorder OR pelvic pain OR painful menstruation OR painful period OR period pain OR primary dysmenorrhea AND Heavy Menstrual Bleeding OR Menorrhagia OR Menstrual Bleeding OR Hypermenorrhea OR Heavy Periods OR Heavy Period AND randomized clinical trial. The search terms for specific oils were used after pilot screening the databases (lavender and rose).

The references were assessed manually to access all related articles.

**Table 1.** Descriptive summary of included studies

| Author / Year Reference number      | Type of study               | Country   | Variable             | Research sample   | Intervention group  | Control group  | Tool               | Results  |
|-------------------------------------|-----------------------------|-----------|----------------------|---|---|--|--------------------|--|
| Ebrahimi a Varzaneh et al. 2017(17) | Three-blind clinical trial  | Tehran    | Primary dysmenorrhea | 50 women year-old 18-30 with regular menstruation and moderate to severe dysmenorrhea (score 4-10 based on pain ruler)                      | 150 mg Achillea millefolium capsules every 8 hours And 250 mg mefenamic acid capsules every 6 hours for the first three days of the menstrual cycle for two consecutive months  | Placebo capsule containing starch similar to Achillea millefolium capsule every 8 hours and 250 mg mefenamic acid every 6 hours for two consecutive months | Visual scale (VAS) | Greater reduction of severity of dysmenorrhea in the Achillea millefolium group        |
| Radfer et al. 2018 (29)             | Double-blind clinical trial | Sanandaj  | Primary dysmenorrhea | 50 single female students of Kurdistan University of Medical Sciences with moderate to severe dysmenorrhea (score 4-10 based on pain ruler) | Group 1: 20 women with 250 mg of chamomile capsules every 8 hours<br>Group 2: 26 women with 150 mg of Achillea millefolium capsules every 8 hours for the first three days of menstruation for two consecutive months | The two intervention groups were compared and the absence of the control group   | Visual scale (VAS) | Both Achillea millefolium and chamomile capsules reduce the severity of menstrual pain |
| Jenabi et al. 2015 (33)             | Double-blind clinical trial | Toyserkan | Primary dysmenorrhea | 96 female students 19-23 year- old Tuyserkhan Azad University with moderate to  | Tea bags with 4 grams of dried Achillea millefolium flower powder for the first three days  | Tea bags similar to the intervention group with 4 grams of placebo   | Visual scale (VAS) | Greater reduction of severity of dysmenorrhea in the Achillea millefolium group        |

| Author / Year Reference number | Type of study                              | Country | Variable             | Research sample   | Intervention group   | Control group   | Tool               | Results  |
|--------------------------------|--|---------|----------------------|---|--|---|--------------------|--|
| Maleki Dizaji et al. 2019 (34) | Double-blind and cross-over clinical trial | Tabriz  | Primary dysmenorrhea | 70 single female students without a history of sexual intercourse Tabriz University of Medical Sciences 26± 2 with moderate to severe primary dysmenorrhea (score of 5 or more based on pain ruler) | of menstruation for two consecutive months (one tea bag in 300 ml of warm water per cup) in the morning, noon, night with each meal for 3 days each month<br><br>This group was followed up for three consecutive cycles:<br>1- In the first cycle, both groups received placebo.<br>2- In the second cycle, both groups randomly received Achillea millefolium capsules (1000 mg) or mefenamic acid capsules (250 mg).<br>3- In the third cycle of treatments, the two groups changed to cross-over. Pain intensity was then measured during periods of one, two, three and every six hours | for the first three days of menstruation for two consecutive months (one tea bag in 300 ml of warm water per cup) morning, noon, night with each meal for 3 days each month | Visual scale (VAS) | menstrual bleeding, symptoms of dysmenorrhea, duration of bleeding, and pain in the Achillea millefolium - treated group were lower than in mefenamic acid group |

| Author / Year<br>Reference number    | Type of<br>study                               | Country | Variable    | Research sample   | Intervention group  | Control group  | Tool               | Results   |
|--------------------------------------|--|---------|-------------|---|---|--|--------------------|---|
| Khademi et al. 2019 (30)             | Three-blind clinical trial                     | Arak    | Menorrhagia | 90 women 18-45 year-old with regular menstruation and menorrhagia with a score of 100 or more based on the visual chart of menstrual bleeding PBLAC                                 | Two 2.5 mg capsules of Achillea millefolium (4 capsules per day equivalent to 920 mg of Achillea millefolium extract equivalent to 10 grams of Achillea millefolium) every 12 hours and two 250 mg capsules of mefenamic acid (6 capsules per day) every 8 hours from the first day of menstruation until its completion and for a maximum of 7 days for 2 cycles | Two 250 mg capsules of mefenamic acid every 8 hours and two 2.5 mg capsules of Achillea millefolium placebo filled with cornstarch from the first day of menstruation to its end and for a maximum of 7 days | Visual scale (VAS) | The amount and duration of menstrual bleeding before and after treatment were significantly reduced in both groups, which was significantly higher in the Achillea millefolium group compared to the control group  |
| Ebrahimi a Varzaneh et al. 2020 (31) | Random, control and three-blind clinical trial | Tehran  | Menorrhagia | 120 women 18-45 year-old with menorrhagia with a score of 100 or more and equivalent to a bleeding volume greater than 80 cc based on the Pectoral Bleeding Assessment Chart (PBAC) | 150 mg capsules of Achillea millefolium extract and 500 mg capsules of mefenamic acid every 8 hours for 7 days during menstrual bleeding for two consecutive months   | 150 mg placebo capsules of Achillea millefolium starch powder and 500 mg capsules of mefenamic acid every 8 hours for 7 days during menstrual bleeding for two consecutive months                            | Visual scale (VAS) | The amount and duration of menstrual bleeding before and after treatment were significantly reduced in both groups, which was significantly higher in the Achillea millefolium group compared to the control group. |

The research question was based on Population, Intervention, Comparison and Outcomes (PICO). The study population included women with moderate to severe dysmenorrhea OR menorrhagia with a score of 100 in the Pictorial Blood Loss Assessment Chart (PBLAC). The women were non-smoker or non-alcoholic, with no cervical secretions, no stressful events, no history of uterine disorders (fibroids, duodenal ulcers, polyps, endometrial hypertrophy and endometriosis) and ovarian disorders (ovarian cysts and polycystic ovaries). Interventions of the including trials were oral administration of Achillea millefolium, with other modern dosage forms. The dosage and treatment course were not limited. The control group included placebo, blank control, and conventional medicine (such as NSAIDs). The outcomes were pain and menstrual bleeding, a reduction in menstrual pain and bleeding which occurs only during the intervention or as a result of the intervention.

Three reviewers evaluated all the articles, and the data were based on a pre-designed table (Table 1). First, one researcher read the different sections of the article separately and noted her impression in each section. Then, the second researcher assessed the articles in the same way and recorded the results in a table. If there was disagreement between the two researchers, the third researcher (first author as a project manager) reviewed each case independently.

Data which extracted from the articles included the first author's name, year of publication, place of study, type of study, variables, research sample, intervention and control group, complications, results, and tools which were cited in the results of the article (Table 1). Any discrepancies between the reviewers were resolved through discussion until consensus was achieved.

The Cochrane Risk of bias tool was applied to evaluate the articles' quality and reviewed the studies in terms of selection bias (random sequence generation and allocation concealment), implementation (blinding participants and evaluators), diagnosis (statistical analyst blinding), sample dropout (leaving the study after randomization), and reporting (selective outcome report) (32).

Procedures of study selection and the reasons for their exclusion were represented in the flowchart (Figure 1).

Method of synthesis of data was qualitative. This study was approved by Ethics Committee of Mashhad University of Medical Sciences with the code of (IR.MUMS.NURSE.REC.1400.082).

## Results

### Literature search and study characteristics

A total of 80 articles found in the initial search; 7 were reviewed that one study was omitted due to poor methodology (method was pre-test and post-test and not stating the method of sampling and randomization) (32). Finally, 6 studies (number of participants= 476) were systematically reviewed (Figure 1).

The characteristics of the studies included in the systematic review study were given in Table 1. Among 6 reviewed studies, 3 studies evaluated the impact of Achillea millefolium on primary dysmenorrhea (17,29,33), 2 studies evaluated the effect of Achillea millefolium on menorrhagia (30-31) and one study assessed the effect of Achillea millefolium on both primary dysmenorrhea and menorrhagia (34). The minimum and maximum sample sizes were 50 and 120, respectively. Subjects in the control group received mefenamic acid capsules and starch-containing capsules in three studies (17, 30-31), and in one study received tea bags similar to the intervention group containing 4 grams of placebo (33). The intervention group consumed Achillea millefolium capsules (17,29-34) in 5 studies and tea bags containing Achillea millefolium (33) in one study. In 5 studies, individuals were studied for 2 cycles (17,29-33) and in one study, for three menstrual cycles (34). In the studies, daily dose of Achillea millefolium was 150 mg to 10 g, which was mostly consumed every 8 hours by research units.

In all articles which evaluated the impact of Achillea millefolium on primary dysmenorrhea, the Visual Scale (VAS) tool was used to measure pain (17,29, 34).

Jenabi et al(2015) (33) reported moderate to severe dysmenorrhea (score greater than 3 based on pain scale) and Maliki et al. (2009) (34) reported moderate to severe dysmenorrhea (score greater than 5 based on



pain scale). The results of all these studies show that the reduction in the severity of dysmenorrhea was greater in the Achillea

millefolium group compared to the control group.

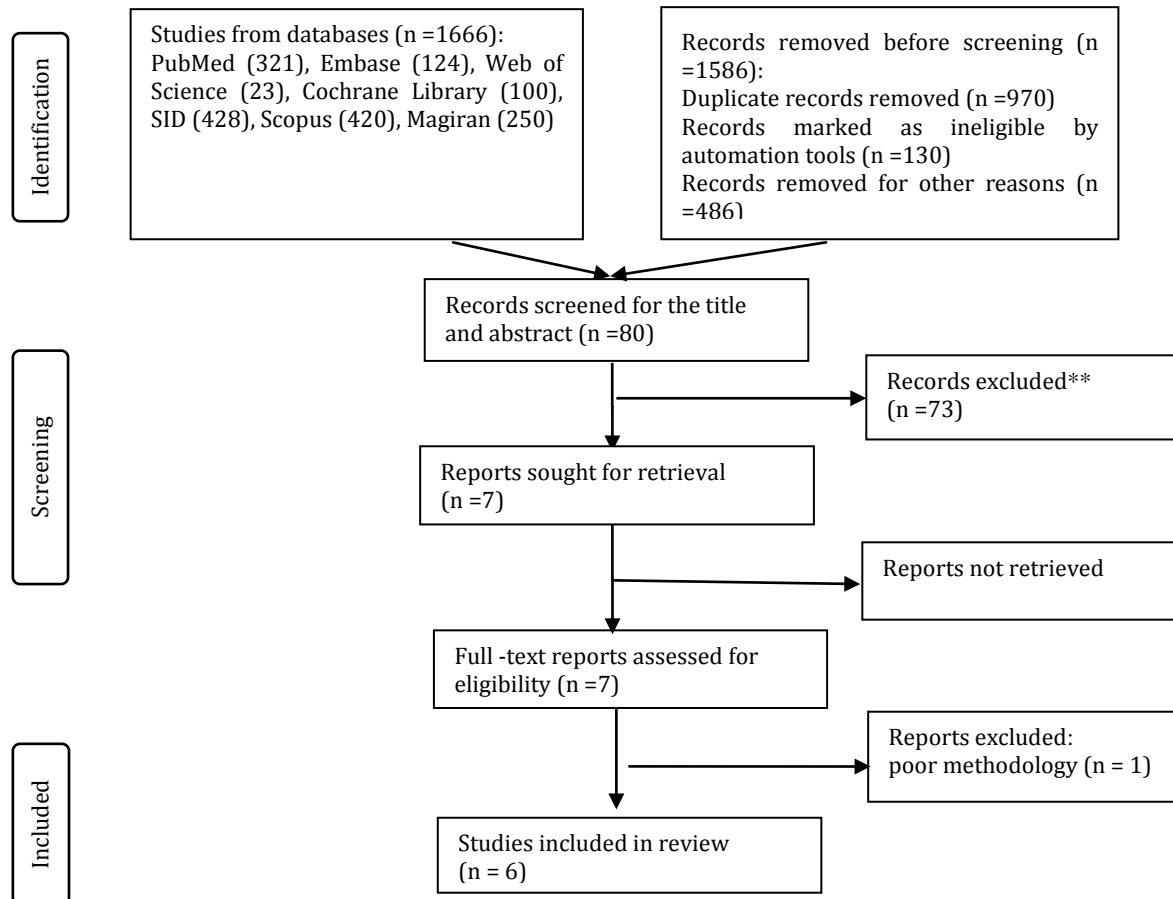


Figure 1. Study selection steps based on the PRISMA 2020 flow diagram

**Characteristics of the Included Studies**

Ebrahimi et al. (2017) (17) and Radfar et al. (2018) (29) reported moderate to severe dysmenorrhea (score 4-10 based on pain scale). Khademi et al. (2019) (30) used the Pictorial menstrual bleeding Assessment Chart (PBLAC) visual tool to assess menstrual bleeding. Ebrahimi et al. (2020) (31) used the PBLAC visual chart to assess menstrual bleeding and the participants were women with regular menstrual and those with menorrhagia with a score of 100 or more determined based on a visual chart. According to the results, the amount and duration of menstrual bleeding were significantly reduced before and after treatment in both groups, which was

significantly higher in the Achillea millefolium group compared to the control group.

Complications reported by participants in the two study groups after receiving the intervention included gastrointestinal intolerance (17-31), gastric irritation (30), and headache, insomnia, and drowsiness (31).

**Risk of bias analysis**

The risk of bias was systematically evaluated by the Cochrane Risk of bias tool. In terms of random sequence bias, 5 studies were considered less bias due to the use of a random number table (17,29-33) and one study was considered to be vague due to not explaining the randomization method (34). Five studies were

considered to have low bias due to the use of random sequence generation software to assign individuals to the control and intervention

groups. In terms of allocation concealment bias, 3 studies had low bias due to the use of computer software (17, 29-31, 33).

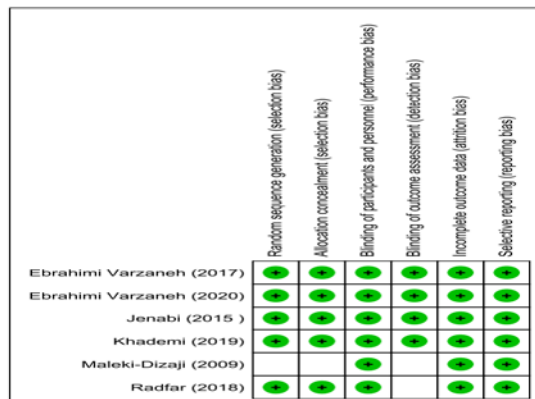


Figure 2. Risk of Bias Summary; authors' assessments of risk of bias item for each included study

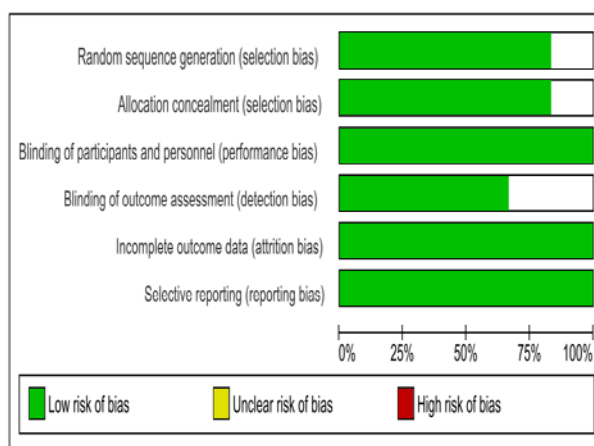


Figure 3. Risk of Bias Graph; authors' assessments of risk of bias items presented as percentages across all included studies

In terms of performance bias, 3 studies were performed by double blind method (29, 33-34) and 3 studies were performed by triple blind method (17, 30,31) which had low bias in terms of performance bias. In terms of sample dropout bias, in 3 studies participants were present from the time of randomization to the time of analysis of the results (29, 33-34) and in 3 studies the number and cause of dropout of research units were reported (30,31, 17). Therefore, these studies were evaluated to have low bias in terms of the dropout bias. Review of reporting bias indicated that all 6 published articles apparently contained all the expected consequences, so

they were considered to have no bias. A summary of the risk of bias for each study was provided in Figures 2 and 3.

### Discussion

The present review was systematically evaluated and summarized the findings of clinical trials on the effect of Achillea millefolium on primary dysmenorrhea. The results of this review showed the effectiveness of Achillea millefolium in reduction of menstrual bleeding volume and dysmenorrhea. Achillea millefolium has analgesic properties with derivatives of salicylic acid, orgenol, and



menthol (38-39). In two studies, the same dose and duration of treatment were used to reduce menstrual pain (17,29), but in another study (33), the research

units received tea bags with 4g of dried *Achillea millefolium* powder (one tea bag in 300 ml warm water per cup) in the first three days of menstruation for two consecutive months for 3 days per month, and its dose and consumption was different in the two studies (17,29), but the results of the three studies were the same (17,29,33). In the study by Maleki-Dizaji et al. (2019), both groups randomly received *Achillea millefolium* capsule (1000 mg) or mefenamic acid capsule (250 mg) and in the third cycle of treatments. Pain intensity was then measured every one, two, three, and six hours. Compared with placebo, mefenamic acid and *Achillea millefolium* significantly reduced pain scores, but pain relief was greater in *Achillea millefolium* group (34). In their study, the severity of menstrual pain was investigated during three cycles (34), which is in line with the findings reported by previous studies (17,29,33). The measurement tool in all 4 studies was VAS (17,29,33-34).

The flavonoids in *Achillea millefolium* regulated arachidonic acid metabolism. This plant can be used as an antiprostaglandin drug in the treatment of primary dysmenorrhea by inhibiting the enzyme cyclooxygenase (40-41).

The results of the present study showed the effectiveness of *Achillea millefolium* in reduction of menstrual bleeding. This plant affects the smooth muscles of the uterus and increases its contraction and reduces bleeding, and is used orally in the treatment of heavy menstrual bleeding or uterine bleeding (42). In the study by Ebrahimi Varzaneh et al., *Achillea millefolium* had no significant effect on reducing the duration of menstrual bleeding but was effective in reducing menstrual bleeding volume, although the amount and duration of menstrual bleeding in the first period after treatment increased compared to the two intervention periods, but it was significantly less than the pre-treatment period. In their study, 150 mg capsules of *Achillea millefolium* extract and 500 mg capsules of mefenamic acid were taken every 8 hours for 7 days during menstrual bleeding for two consecutive months by the

intervention group (31). In another study, there was no significant difference between the two groups in the mean bleeding volume before treatment and the first period after treatment, but there was a significant difference between the two groups in terms of the mean bleeding volume in the second period after treatment. The rate of bleeding was less than the control group. In their study, 2 capsules of 2.5 mg *Achillea millefolium* (4 capsules per day as 920 mg of *Achillea millefolium* extract or 10 grams of *Achillea millefolium*) were used every 12 hours and 2 capsules of 250 mg mefenamic acid (6 capsules per day) were used every 8 hours from the first day to the last day of menstruation for a maximum of 7 days and 2 cycles (30). In the other study, menstrual bleeding, symptoms of dysmenorrhea, duration of bleeding, and pain in the *Achillea millefolium* -treated group were lower than in mefenamic acid group. Despite the difference in dose and method of herbal medicine, *Achillea millefolium* was effective on menstrual bleeding (34).

The quality of the studies in this systematic review was assessed using Cochrane Risk of bias tool and the results showed that most studies had a suitable methodology. Since there are differences in the type and amount of essential oils, differences in the method of using *Achillea millefolium*, differences in the time of intervention and pain measurement time and also the limited studies and low sample size, further studies are needed to better identify the effect of *Achillea millefolium* on dysmenorrhea and menorrhagia.

## Conclusion

The present systematic review of six studies suggests that *Achillea millefolium* can be considered an effective and safe treatment for primary dysmenorrhea and reduction of menstrual bleeding. However, It is advised that additional studies be conducted to provide robust scientific evidence for identifying the impact of *Achillea millefolium* on dysmenorrhea and menorrhagia.

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Mashhad University of Medical Sciences, mashhad, Iran.

### Conflicts of interest

The authors declared no conflicts of interest.

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