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Effects of *Rosa damascena* (Damask rose) on menstruation-related pain, headache, fatigue, anxiety, and bloating: A systematic review and meta-analysis of randomized controlled trials

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Abstract:

Recent studies have reported inconclusive results regarding the therapeutic effects of Rosa damascena on the outcomes of primary dysmenorrhea (PD) and premenstrual syndrome (PMS). Hence, this study is aimed to summarize the findings of randomized controlled trials (RCTs) regarding the effects of this treatment on menstruation-related pain as the primary outcome and menstruation-related headache, fatigue, anxiety, and bloating as the secondary outcomes. This study evaluated parallel-group and cross-over RCTs on aromatherapy, topical treatment, or oral intake of R. damascena products for the treatment groups versus placebo, nontreated, or conventional treatment groups. Seven electronic databases (Web of Science Core Collection, Scopus, Embase, CENTRAL, CINAHL, SID, and MagIran) and one search engine (PubMed) were searched from inception to January 15, 2021. Of 1468 trials found in the initial search, 983 potentially relevant articles were screened by title and abstract. After examining the full-text of 13 studies for compliance with the inclusion criteria, seven studies were considered eligible for this review. A random-effects model was used to pool the data; otherwise, a narrative summary was presented. The retrieved studies were conducted on females with PD or PMS, aged 18–35 years. The total sample size of the intervention and comparator arms was 276 and 272. The results showed that R. damascena had a nonsignificant alleviating effect on the menstruation-related pain (weighted mean difference [WMD]: −0.47; 95% confidence interval [CI]: −1.25, 0.31; P = 0.234). Such findings were also found for menstruation-related anxiety (WMD: −0.40; 95% CI: −0.91, 0.11; P = 0.125). However, the treatment significantly reduced the menstruation-related headache (WMD: −0.42; 95% CI: −0.74, −0.11; P = 0.008), fatigue (WMD: −0.48; 95% CI: −0.87, −0.09; P = 0.015), and bloating (WMD: −0.72; 95% CI: −1.21, −0.22; P = 0.005). Since R. damascena had no significant effects on menstruation-related pain and anxiety, further studies with improved methodological quality are suggested to evaluate the effects of the treatment on these symptoms, using different dosages and durations.

Keywords:

Dysmenorrhea, herbal medicine, menstruation, review, *Rosa damascena*

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Introduction

Menstruation-related symptoms (MRSs) are common gynecological complaints in female adolescents and young adults.[1] These symptoms include dysmenorrhea, heavy menstrual bleeding, headaches, premenstrual abdominal pain, and premenstrual mood disorders with different prevalence rates.[2,3] During the menstrual period, women with MRSs experience a low quality of life in psychological, physical, behavioral, and social domains.[4] Furthermore, MRSs may impose significant economic burdens on individuals, mainly due to the loss of work productivity and the costs of medical appointments, nonprescription medications, and medical treatments.[5]

Recently, some complementary and alternative medicine (CAM) approaches, including herbal remedies, have attracted the researchers' attention for the management of common MRSs worldwide, especially in Iranian traditional medicine (ITM).[6-12] *Rosa damascena* (*R. damascena*), commonly known as Damask rose, have been used in different forms of administration for the treatment of MRSs.[13,14] In ITM, the decoction of *R. damascena* flowers is used in the case of menstrual bleeding and other menstrual problems.[15,16] Moreover, *R. damascena* is recognized as an important Unani medicine for the treatment of primary dysmenorrhea (PD), due to its anti-spasmodic properties.[14] In Taiwan, women with severe menstrual symptoms use rose tea before menstruation to regulate hormonal secretion and manage painful and irregular periods.[17] Furthermore, in Indian traditional medicine, the petals of *R. damascena* are used to treat uterine hemorrhage and menstrual bleeding.[15]

Today, the effects of both oral and inhaled use of *R. damascena* on different MRSs have been investigated; however, the findings are conflicting.[18-28] Recent studies have reported that inhalation and oral intake of *R. damascena* could improve some psychological, physical, and social outcomes of premenstrual syndrome (PMS).[18,19,25] Other studies showed that supplementation with *R. damascena* extract during PD only induced alleviating effects on bloating and sweating[24] or pain and fatigue.[22] On the other hand, a study reported similar rates of menstrual pain among the students who received mefenamic acid and *R. damascena* capsules.[23] Furthermore, some studies showed that aromatherapy massage of the abdomen with *R. damascena* essential oil was more effective against menstrual pain than massage alone in the second cycle of menstruation.[20,21]

Nowadays, women's health needs significant attention because it might affect family and society's health.[29] In most low-income countries, women use self-prescribed medicinal herbs for the treatment of MRSs, and healthcare providers do not routinely prescribe these herbal remedies due to the lack of evidence-based reports.[8] However, in some developed countries, different herbs are prescribed for MRSs in the health-care setting.[6] Although *R. damascena* has been recently used as a herbal medicine in different communities,[14,15] to the best of our knowledge, no review has yet synthesized the conflicting findings of recent trials on the potential effects of this herbal medicine in treating MRSs. Therefore, this review was carried out to summarize and statistically pool the findings of recent randomized controlled trials (RCTs) regarding the effects of *R. damascena* on menstruation-related pain as the primary outcome and menstruation-related headache, fatigue, anxiety, and bloating as the secondary outcomes.

Materials and Methods

Search strategy

To retrieve relevant articles, we searched five electronic databases, including Web of Science Core Collection, Embase, Scopus, Cochrane Central Register of Controlled Trials, and Cumulative Index to Nursing and Allied Health Literature (Plus with Full Text). Furthermore, a search was conducted in the PubMed search engine and two Iranian databases including Scientific Information Database (http://www.sid.ir/) and MagIran (http://www.magiran.com). Moreover, the reference lists of relevant studies were searched.

To avoid missing any relevant studies, we performed an extensive search strategy by two investigators independently, with no limitations in language or publication date [Table 1]. First, all data sources were searched on August 22, 2020. Then, a search was conducted on January 15, 2021, to retrieve relevant new eligible studies. Screening of the retrieved studies and extracting the data of the included studies in the first search were performed by two investigators independently from September to November 2020. The same investigators screened the retrieved studies in the second search, but no eligible study was found. Any uncertainty or disagreement between the investigators was resolved by discussion. If the articles contained any unclear data, the main trial investigators were contacted via E-mail to obtain additional information.

Eligibility criteria of studies

Parallel-group and cross-over RCTs were included in this review if they: (1) recruited women of reproductive age, experiencing moderate to severe MRSs during the menstrual cycle (according to the reported baseline score), (2) used *R. damascena* products (i.e. dried rosebuds, dried petals, rose hips, oil, syrup, extract, juice, water,

Table 1: Search characteristics in selected data sources for the effects of *Rosa damascena* on menstruation-related symptoms

Data sources	Search strategy	Search results
PubMed	(Rosa[MH] OR Rosa[TIAB] OR Rose[TIAB] OR Rosaceae[TIAB] OR Rosewater[TIAB] OR "Rose water"[TIAB] OR "Rose oil"[TIAB] OR "*Rosa damascena*"[TW] OR "Damask rose"[TW] OR "Rose damask"[TW]) AND ("Menstruation disturbances"[MH] OR Dysmenorrhea[MH] OR Dysmenorrhea*[TIAB] OR "Menstrual pain"[TIAB] OR "Painful menstruation"[TIAB] OR "Painful period*"[TIAB] OR "Period pain"[TIAB] OR "Pelvic pain"[TIAB] OR "Menstrual cramp*"[TIAB] OR Menstrua*[TIAB] OR Amenorrhea[MH] OR Amenorrhea[TIAB] OR Menorrhagia[MH] OR Menorrhagia[TIAB] Polymenorrhea[TIAB] OR Hypomenorrhea[TIAB] OR Hypermenorrhea[TIAB] OR Oligomenorrhea[MH] OR Oligomenorrhea[TIAB] OR "Irregular periods"[TIAB] OR "Premenstrual syndrome"[MH] OR "Premenstrual syndrome"[TIAB] OR "PMS"[TIAB] OR Premenstrual[TIAB])	52
Scopus	(TITLE-ABS-KEY (Rosa*) OR TITLE-ABS-KEY (Rose) OR TITLE-ABS-KEY (Rosaceae) OR TITLE-ABS-KEY ("*Rosa damascena*") OR TITLE-ABS-KEY ("Damask rose") OR TITLE-ABS-KEY (Rosewater) OR TITLE-ABS-KEY ("Rose water") AND TITLE-ABS-KEY (Menstrua*) OR TITLE-ABS-KEY (Dysmenorrhea*) OR TITLE-ABS-KEY ("Menstrual pain") OR TITLE-ABS-KEY ("Painful menstruation") OR TITLE-ABS-KEY ("Period pain") OR TITLE-ABS-KEY ("Painful period*") OR TITLE-ABS-KEY ("Menstrual cramp*") OR TITLE-ABS-KEY (Amenorrhea) OR TITLE-ABS-KEY (Menorrhagia) OR TITLE-ABS-KEY (Polymenorrhea) OR TITLE-ABS-KEY (Hypomenorrhea) OR TITLE-ABS-KEY (Hypermenorrhea) OR TITLE-ABS-KEY (Oligomenorrhea) OR TITLE-ABS-KEY ("Premenstrual syndrome"))	846
Web of Science Core Collection	(TS=(Rosa) OR TS=(Rosaceae) OR TS=(*Rosa damascena*) OR TS=(Damask rose) OR TS=(Rose damask) OR TS=(Rose oil) OR TS=(Rosewater) OR TS=(Rose water)) AND (TS=(Menstrua*) OR TS=(Dysmenorrhea) OR TS=(Menstrual pain) OR TS=(Painful menstruation) OR TS=(Period pain) OR TS=(Painful period*) OR TS=(Menstrual cramp*) OR TS=(Amenorrhea) OR TS=(Menorrhagia) OR TS=(Polymenorrhea) OR TS=(Hypomenorrhea) OR TS=(Hypermenorrhea) OR TS=(Oligomenorrhea) OR TS=(Premenstrual syndrome))	133
Embase	('*Rosa damascena*'/exp OR '*Rosa damascena*' OR 'Damask rose' OR 'Rose damask' OR 'Rose water' OR 'Rosewater' OR 'Gole Mohammadi' OR 'Gol-E-Muhammadi' OR 'Gol-E-Mohammadi') AND ('Menstruation'/exp OR 'Menstruation' OR 'Dysmenorrhea' OR 'Menstrual pain' OR 'Painful menstruation' OR 'Painful period' OR 'Period pain' OR 'Pelvic pain' OR 'Menstrual cramp' OR 'Amenorrhea' OR 'Polymenorrhea' OR 'Hypomenorrhea' OR 'Hypermenorrhea' OR 'Oligomenorrhea' OR 'Irregular periods' OR 'Premenstrual syndrome')	16
CENTRAL	(Rosa OR Rose OR Rosewater OR "Rose water" OR "Rose oil" OR "*Rosa damascena*" OR "Damask rose" OR "Rose damask") in Title Abstract Keyword AND (Dysmenorrhea* OR "Menstrual pain*" OR "Painful menstruation*" OR "Painful period*" OR "Period pain" OR "Pelvic pain" OR "Menstrual cramp*" OR Menstrua* OR Amenorrhea OR Polymenorrhea OR Hypomenorrhea OR Hypermenorrhea OR Oligomenorrhea OR "Irregular periods" OR "Premenstrual syndrome") in Title Abstract Keyword - (Word variations have been searched)	88
CINAHL Plus with Full Text	Rosa OR Rose OR Rosewater OR "Rose water" OR "Rose oil" OR "*Rosa damascena*" OR "Damask rose" OR "Rose damask" AND Dysmenorrhea* OR Menstrua* OR "Menstrual pain*" OR "Painful menstruation*" OR "Painful period*" OR "Period pain" OR "Pelvic pain" OR "Menstrual cramp*" OR Amenorrhea OR Polymenorrhea OR Hypomenorrhea OR Hypermenorrhea OR Oligomenorrhea OR "Irregular periods" OR "Premenstrual syndrome" (All keywords have been searched based on "all felids" box)	63
MagIran	Dysmenorrhea OR Menstruation AND Rosa OR Rose OR *Rosa damascena* OR Damask rose OR Rosewater OR Gole Mohammadi OR Gol-E-Muhammadi OR Gol-E-Mohammadi (All keywords have been searched based on "all felids" box)	138
SID	Dysmenorrhea OR Menstrua* AND Rose OR Rose water OR *Rosa damascena* OR Damask rose OR Gole Mohammadi (Database have been searched in Persian and English)	132

CINAHL=Cumulative Index to Nursing and Allied Health Literature, SID=Scientific Information Database, CENTRAL: Cochrane Central Register of Controlled Trials

tea, and Gulkand) in the form of aromatherapy, topical application, or oral intake for the treatment groups versus placebo, nontreated, or conventional treatment groups, and (3) measured menstruation-related pain or menstruation-related headache, fatigue, anxiety, and bloating by using standardized questionnaires with established reliability and validity. On the other hand, studies were excluded if *R. damascena* was administered

in combination with other herbal products or species other than *R. damascena* was used.

Selection of studies

The initial search identified 1468 trials. Also, nine additional citations were retrieved from the reference lists of eligible trials. After duplicate removal, 983 potentially relevant articles were screened as to the title and abstract. The full-text of 13 studies was examined for compliance with the inclusion criteria. Four studies were excluded for using other *Rosa* species (e.g., *Rosa gallica* and *Rosa centifolia*)[17,27] or administering *R. damascena* in combination with other herbal extracts.[28,30] Also, two articles were multiple publications from the same dataset and were excluded from the final analysis.[18,20] Finally, seven studies were considered eligible for this review[19,21-26] [Figure 1].

Assessment of risk of bias

The risk of bias was assessed, using the Cochrane risk-of-bias tool by two investigators independently. This tool consists of seven items, including random sequence generation (selection bias), allocation concealment (selection bias), performance bias, detection bias, attrition bias, reporting bias, and other bias. Each item is rated as "low risk of bias," "unclear risk of bias," and "high risk of bias."[31]

Data analysis and synthesis

If sufficient studies (at least three studies) reported the same outcomes, they were pooled in the meta-analysis, using a random-effects model; otherwise, a narrative synthesis was presented. The effect sizes were presented as weighted mean differences (WMDs) with 95% confidence intervals (CIs). To assess the heterogeneity among the studies, Cochran's Q test and I^2 were used. Also, subgroup analysis and sensitivity analysis were performed if needed. To assess the potential publication bias, we used the Begg test. All statistical analyses were performed using Stata version 11.2 (Stata Corp., College Station, TX, USA). $P < 0.05$ were considered to be significant.

Ethical considerations

The formal ethical assessment was not needed for this study, as collected data were anonymized and synthesized from previous RCTs in which consent had already been obtained by the trial investigators. When each main

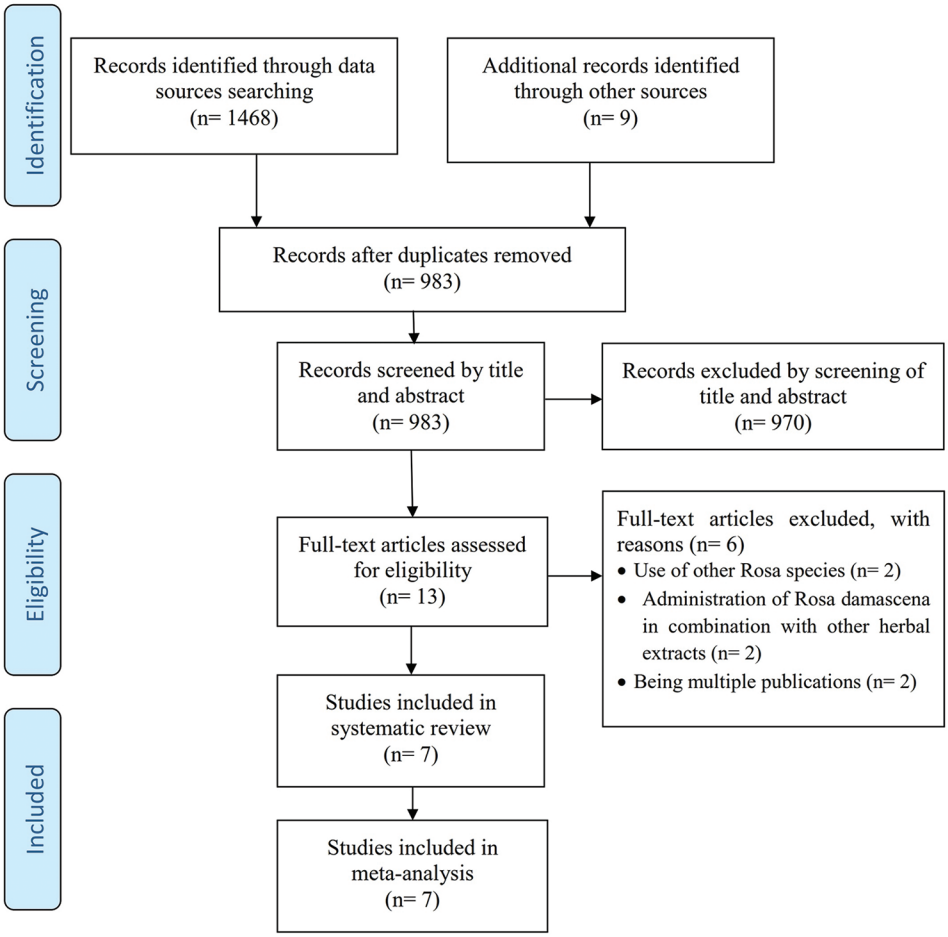

Figure 1: Flow diagram for the study identification and selection

trial investigator was contacted to obtain additional information, no raw data was received. The review was registered in the international prospective register of systematic reviews (approval No: CRD42020205062).

Results

The retrieved studies were conducted on females with PD or PMS, aged 18–35 years. Of seven included studies, one was performed in Turkey,[26] while the rest were conducted in Iran. Most studies were published in the English language, and only two were published in Farsi.[22,25] Most studies had two arms with a parallel-group design. The total sample size of the intervention and comparator arms was 276 and 272. The included trials investigated the effects of *R. damascena* oil or extract, using aromatherapy (i.e., massage, inhalation, and vapor diffusion) or oral intake (i.e., drops or capsules) on different MRSs. The comparators included conventional and placebo treatments, administered in the same method and duration as *R. damascena*. Three studies recorded the adverse effects;[19,20,23] only one of them reported headache associated with nausea and vomiting.[19] The results of trials indicated that *R. damascena* might be suitable for reducing the adverse effects of MRSs on the psychological, physical, and social aspects of life [Table 2].

Of five studies which measured menstruation-related pain, all used a 0–10 scale (visual analog scale [VAS] or McGill pain questionnaire).[21-24,26] However, there were some variations in the time of data recording. Hence, to compare the pain, the changes of mean and standard deviation in each group were calculated by considering the baseline value in the first menstrual cycle, as well as the end-of-trial value for either the first[23,26] or second[21,22,24] menstrual cycle. In one cross-over trial,[23] data were extracted from the first study period before cross-over, because carry-over of the treatment effect was thought to be a problem. In one trial with both placebo and nontreated groups,[20] data were only extracted from the placebo group for comparison. Based on the combined effect sizes of five trials,[21-24,26] *R. damascena* could nonsignificantly reduce the menstrual pain in females with PD (WMD: −0.47; 95% CI: −1.25, 0.31; $P = 0.234$) [Figure 2]. Furthermore, sensitivity analysis did not change the results of primary meta-analysis after excluding the cross-over trial from the primary meta-analysis[23] (WMD: −0.63; 95% CI: −1.60, 0.35; $P = 0.206$). The subgroup analysis suggested the administration route and dosage of *R. damascena* as sources of heterogeneity [Table 3].

The results of four studies regarding headache, fatigue, bloating, and anxiety were suitable for meta-analysis.[19,22,24,25] The same as pain, there were some variations in the time of data recording. Hence, we calculated the changes of mean and standard deviation for all symptoms in each group by considering the baseline value in the first menstrual cycle, as well as the end-of-trial value for either the second[19,22,24] or third[25] menstrual cycle. Of four studies, three used a 0–3 scale, while one study used a scale of 0–10 (VAS).[24] To compare the variables, we converted the data of this study to a value in the range of 0–3, using standard methods. Based on the combined effect sizes, *R. damascena* significantly reduced the menstruation-related headache (WMD: −0.42; 95% CI: −0.74, −0.11; $P = 0.008$)

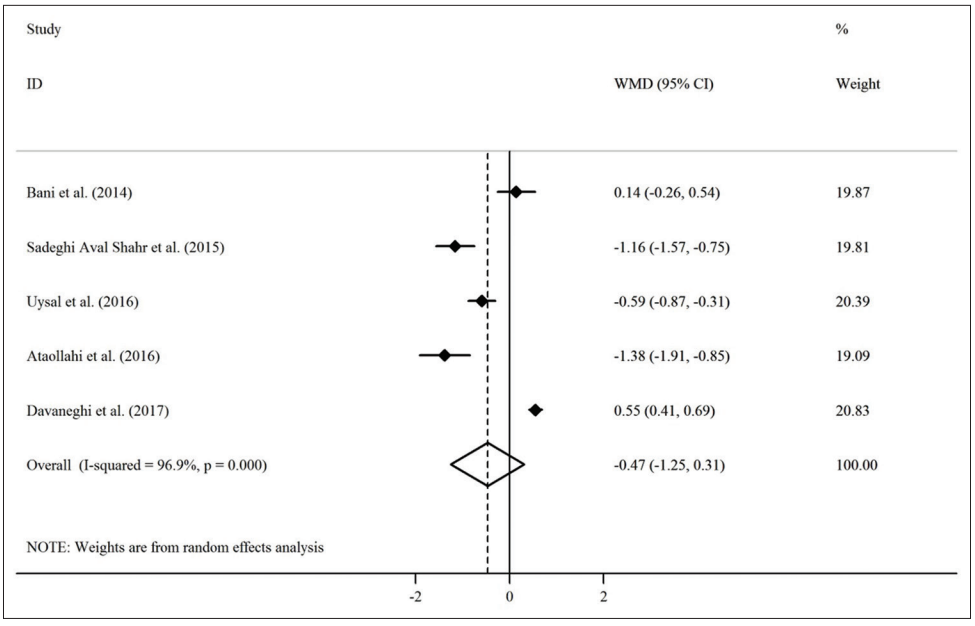

Figure 2: Forest plot for the effect of *Rosa damascena* on menstruation-related pain

Table 2: Characteristics of the studies included in the review

Authors (publication date)	Study design	Participants	Sample size/ age	Intervention		
				Method	Groups	Dosage/duration
Heydari *et al.* (2019)[19]	Double-blind, placebo-controlled, 3-arm, parallel-group, single-center	College students with moderate to severe PMS (PSST>20)	Intervention: 33/22.66±3.41 Control: 31/21.84±1.50	Self-aromatherapy (inhalation) [a]	Intervention: 4% R. D oil Control: Placebo (100% odorless sweet almond oil)	10 topical drops (BID) during 5 days of luteal phase for 2 subsequent MC, total dosage: 200 drops
Davaneghi *et al.* (2017)[24]	Double-blind, placebo-controlled, 4-arm, parallel-group, multi-center	Individual with moderate to severe PD	Intervention: 27/22.63±0.47 Control: 25/22.08±0.39	Oral intake	Intervention: RD extract (800 mg) + fish oil placebo Control: RD extract placebo+fish oil placebo	One capsule of each product daily from first day of menstruation until 60 consecutive days, total dosage: 480 g
Uysal *et al.* (2016)[26]	Nonblind, placebo-controlled, 2-arm, parallel-group, single-center	Individual with moderate to severe PD (VAS≥5)	Intervention: 50/20.74±2.41 Control: 50/20.59±2.13	Aromatherapy (vapour diffusion) [b]	Intervention: 2% RD oil+DS Control: Placebo (N/S) + DS	1 time, nr
Ataollahi *et al.* (2016)[22]	Double-blind, placebo-controlled, 2-arm, parallel-group, multi-center	College student with moderate to severe PD	Intervention: 55/21.41±1.49 Control: 55/21.38±1.72	Oral intake	Intervention: RD extract Control: Placebo (water and sugar) drop	10 oral drops (BID) during first 3 days of menstruation for 2 subsequent MC, total dosage: 120 drops
Sadeghi Aval Shahr *et al.* (2015)[21]	Single-blind, placebo-controlled, 3-arm, parallel-group, single-center	College student with moderate to severe PD (VAS≥5)	Intervention: 25/26±3.6 Control: 25/24.6±3.1	Self-aromatherapy (massage) [c]	Intervention: 4% RD oil diluted in almond oil Control: Placebo (odorless almond oil)	5 topical drops at the 1st day of menstruation for 2 subsequent MC, total dosage: 10 drops
Bani *et al.* (2014)[23]	Double-blind, placebo-controlled, 2-arm, cross-over groups, single-center	College student with moderate to severe PD (VAS≥5)	Intervention: 46/22.20±2.11 Control: 46/22.13±2.06	Oral intake	Intervention: RD extract (200 mg) Control: Mefenamic acid (250 mg)	One capsule (QID, every 6 h) during first 3 days (72 h) of menstruation for 2 subsequent MC, total dosage: 4800 mg
Jamilian *et al.* (2013)[25]	Double-blind, placebo-controlled, 3-arm, parallel-group, single-center	Women with moderate to severe PMS	Intervention: 40/25.93±4.68 Control: 40/26.56±3.53	Oral intake	Intervention: RD extract Control: Placebo (DW) drop	15 oral drops (BID) from 14 days before menstruation until end of menstruation for 3 subsequent MC, total dosage: 200 drops

Authors (publication date)	Outcome (measures)/time		Findings		Cochrane risk-of-bias assessment
Heydari *et al.* (2019)[19]	Psychological, physical, and social symptoms (PSST)	Baseline, at the end of 2nd cycle	NS	Anxiety, decreased interest in work activities, decreased interest in home activities, decreased interest in social activities, feeling overwhelmed or out of control, overeating, insomnia, work efficiency or productivity	Fair quality[†]
			Significantly*	Anger, increased sensitivity to rejection, depressed mood, difficulty concentrating, fatigue, hypersomnia, breast tenderness, headaches, joint/muscle pain, bloating, weight gain, interference with family relationship, interference with social life activities, interference with home responsibilities, interference with relationship with friends and colleagues	
		Baseline, at the end of 1st and 2nd cycles	Significantly*	Psychological, physical, and social symptoms, total score of PSST	

Contd...

Table 2: Contd...

Authors (publication date)	Outcome (measures)	time	Findings		Cochrane risk-of-bias assessment
Davaneghi *et al*. (2017)[24]	Systemic symptoms (VAS)	Baseline, 30th day and 6th day	NS	Nausea, vomiting, diarrhea, cramp, low back pain, headache, fatigue, anxiety, weakness, dizziness, drowsiness, feeling cold	Fair quality†
			Significantly*	Bloating, sweet	
Uysal *et al*. (2016)[26]	Menstrual-related pain (VAS) + vital signs	Baseline, 10 min and 30 min after intervention	NS	Pain at 10 min after intervention, systolic arterial blood pressure; diastolic arterial blood pressure; mean arterial blood pressure; heart rate	Fair quality†
			Significantly*	Pain at 30 min after intervention, respiratory rate at 10 min and 30 min after intervention	
Ataollahi *et al*. (2016)[22]	Menstrual-related pain (McGill)	Baseline, at the end of 2nd cycle	Significantly*		Fair quality
	Systemic symptoms (VMS)	Baseline, at the end of 2nd cycle	NS	Nausea and vomiting, diarrhea, headache, emotional liability, lack of energy, syncope	
			Significantly*	Fatigue, total score	
Sadeghi Aval Shahr *et al*. (2015)[21]	Menstrual-related pain (VAS)	Before and after intervention in 1st and 2nd cycles	NS	At the 1st MC	Good quality††
			Significantly*	At the 2nd MC	
Bani *et al*. (2014)[23]	Menstrual-related pain (VAS)	Baseline and 1, 2, 3, 6, 12, 24, 48, 72 h after taking the first drug in 1st and the 2nd cycles	NS		Good quality††
Jamilian *et al*. (2013)[25]	Affective, psychological, and physical symptoms of PMS (DSRS)	Baseline, at the end of 3nd cycle	NS	Headache, forgetfulness, palpitation, edematous extremities, bloating, breast tenderness	Fair quality†
			Significantly*	Nervous tension, irritability, emotional liability, anxiety, depression, fatigue, desire to eat sweets, crying, impaired concentration, difficulty in sleeping, suicidal thoughts, overeating	

[a]The products were poured on an eye pad and then it was held at a distance of 30 cm from the participants' nose and they were asked to inhale the products for 5 min with normal breathing, [b]The products were poured on an electronic vapourizer and it was set to spray the products every 10 min in a room of the emergency ward, [c]Abdomen was massage for 15 min with clockwise circular movements using the products, *Significantly lower in the intervention group compared to the comparison group after the intervention, †One criterion not met (high risk of bias for one domain) or two criteria unclear, ††All criteria met (low for each domain). BID=Bis in die (2 times a day), DS=Diclofenac sodium, DSRS=Daily symptom rating scale, DW=Distilled water, MC=Menstrual cycle, McGill=McGill pain questionnaire, NS=Not significant, N/S=Normal saline, PD=Primary dysmenorrhea, PMS=Premenstrual syndrome, PSST=Premenstrual symptoms screening tool, RCT=Randomized controlled trial, RD=*Rosa damascene*, QID=Quarter in die (4 times a day); VAS=Visual analogue scale, VMS=Verbal multidimensional scale

Table 3: Subgroup analysis for the effects of *Rosa damascena* on menstruation-related symptoms

Variables	Effect sizes (*n*)	I^2 (%)	Cochran's Q test	WMD (95% CI)	*P*-within	*P*-between
Menstruation-related pain						
Administration route						
Aromatherapy	2	80.1	0.025	−0.86 (−1.41-−0.30)	0.003	<0.001
Oral intake using drop	1	-	-	−1.38 (−1.91-−0.85)	<0.001	
Oral intake using capsule	2	72.4	0.057	0.39 (−0.01-0.78)	0.052	
Total administration dosage						
≤120 drops	3	78.2	0.010	−1.01 (−1.50-−0.51)	<0.001	<0.001
≤480 mg	1	-	-	0.55 (0.41-0.69)	<0.001	
>481 mg	1	-	-	0.14 (−0.26-0.54)	0.491	
Administration duration						
1 menstruation cycle	2	88.3	0.003	−0.24 (−0.95-0.48)	0.512	0.197
2 menstruation cycles	3	98.0	<0.001	−0.65 (−2.06-0.76)	0.293	
Menstruation-related headache						
Patient's condition						
PD	2	85.8	0.0018	−0.19 (−0.41-0.02)	0.074	<0.001
PMS	2	41.9	0.190	−0.65 (−0.93-−0.37)	<0.001	
Administration route						
Aromatherapy	1	-	-	−0.91 (−1.41-−0.41)	<0.001	<0.001
Oral intake using drop	2	84.3	0.012	−0.45 (−0.70-−0.21)	<0.001	
Oral intake using capsule	1	-	-	−0.10 (−0.12-−0.08)	<0.001	
Total administration dosage						
≤120 drops	2	41.9	0.190	−0.65 (−0.93-−0.37)	<0.001	<0.001
>121 drops	1	-	-	−0.32 (−0.48-−0.16)	<0.001	
≤480 mg	1	-	-	−0.10 (−0.12-−0.08)	<0.001	
Administration duration						
2 menstruation cycles	3	88.4	<0.001	−0.33 (−0.61-−0.05)	0.020	<0.001
3 menstruation cycles	1	-	-	−0.57 (−0.68-−0.46)	<0.001	
Menstruation-related fatigue						
Patient's condition						
PD	2	98.9	<0.001	−0.39 (−1.15-0.36)	0.310	<0.001
PMS	2	66.3	0.085	−0.55 (−0.88-−0.23)	0.001	
Administration route						
Aromatherapy	1	-	-	−0.78 (−1.17-−0.39)	<0.001	<0.001
Oral intake using drop	2	92.7	<0.001	−0.60 (−0.94-−0.26)	0.001	
Oral intake using capsule	1	-	-	−0.01 (−0.05-0.03)	0.633	
Total administration dosage						
≤120 drops	1	-	-	−0.78 (−0.94-−0.62)	<0.001	<0.001
>121 drops	2	66.3	0.085	−0.55 (−0.88-−0.23)	0.001	
≤480 mg	1	-	-	−0.01 (−0.05-0.03)	0.633	
Administration duration						
2 menstruation cycles	3	98.0	<0.001	−0.51 (−1.13-0.11)	0.107	<0.001
3 menstruation cycles	1	-	-	−0.43 (−0.53-−0.33)	<0.001	

CI=Confidence interval, PD=Primary dysmenorrhea, PMS=Premenstrual syndrome, WMD=Weighted mean difference

[Figure 3], fatigue (WMD: −0.48; 95% CI: −0.87, −0.09; $P = 0.015$) [Figure 4], and bloating (WMD: −0.72; 95% CI: −1.21, −0.22; $P = 0.005$) [Figure 5]. However, the treatment had nonsignificant alleviating effects on menstruation-related anxiety (WMD: −0.40; 95% CI: −0.91, 0.11; $P = 0.125$) [Figure 6]. After excluding one study,[24] which used different points scale, the same results were found for menstruation-related headache (WMD: −0.52; 95% CI: −0.76, −0.28; $P < 0.001$), fatigue (WMD: −0.64; 95% CI: −0.92, −0.36; $P < 0.001$), and bloating (WMD: −0.95; 95% CI: −1.08, −0.81; $P < 0.001$). Also, a significant reducing effect of treatment was found on menstruation-related anxiety (WMD: −0.60; 95% CI: −0.96, −0.24; $P = 0.001$). All predefined variables were potential sources of heterogeneity for headache and fatigue [Table 3].

Overall, three studies had a low risk of bias for all criteria.[19,23,24] Other studies showed fair quality, mostly due to the high risk in reporting bias or other bias [Figures 7 and 8]. Based on the results of Begg test, no evidence of publication bias was found for menstrual-related pain ($P = 0.221$), headache ($P = 0.734$), fatigue ($P = 0.734$), bloating ($P = 1.000$), and anxiety ($P = 1.000$).

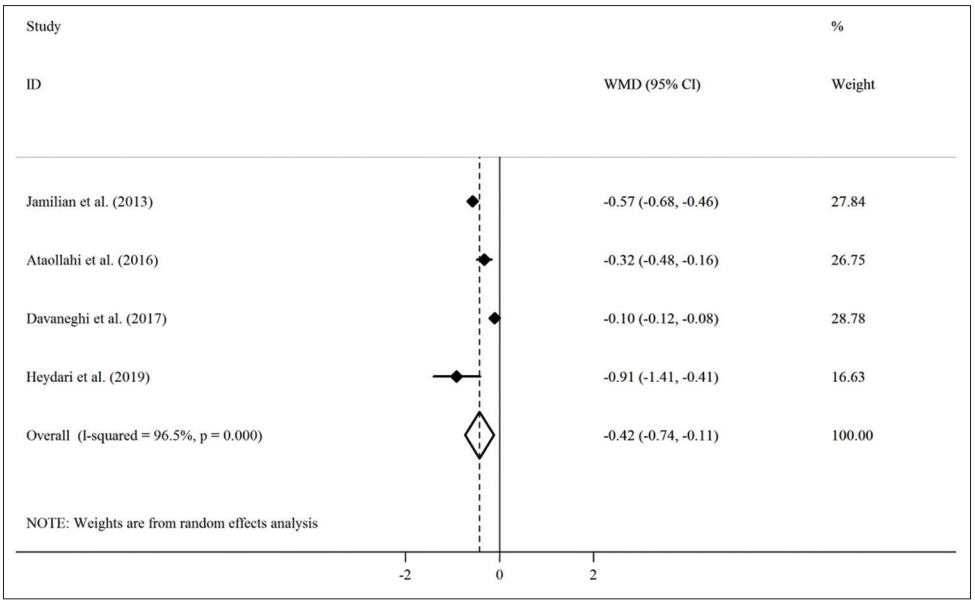

Figure 3: Forest plot for the effect of *Rosa damascena* on menstruation-related headache

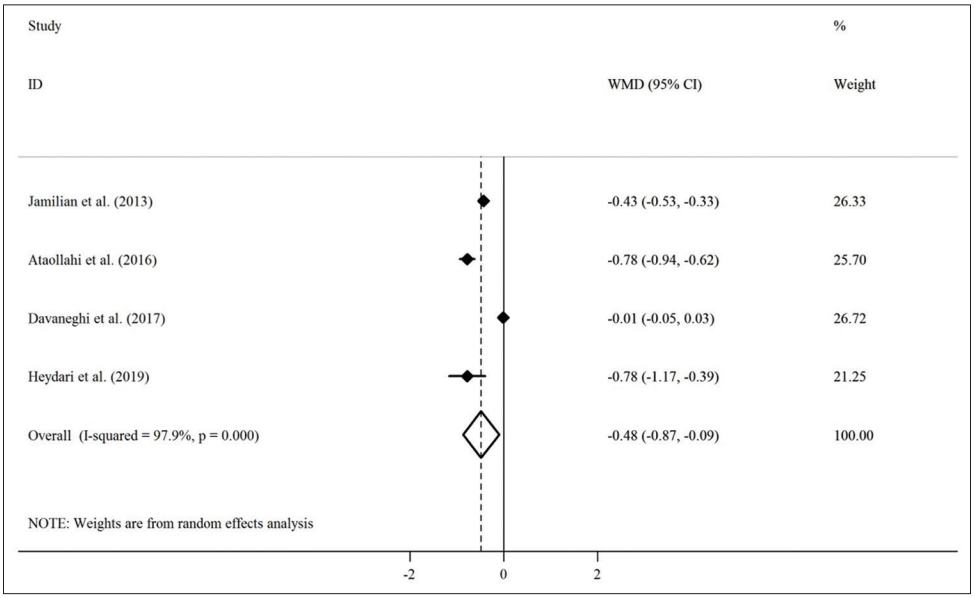

Figure 4: Forest plot for the effect of *Rosa damascena* on menstruation-related fatigue

Discussion

The systematic review indicated that the administration of *R. damascena* had potentially positive effects on different psychological, physical, and social symptoms. On the other hand, the results of the meta-analysis indicated that *R. damascena* caused a significant reduction in menstruation-related headache, fatigue, and bloating, while it had nonsignificant alleviating effects on pain and anxiety. These findings can significantly contribute to the existing literature on the potential of *R. damascena* as a traditional agent for the treatment of MRSs.

Based on the present findings, the administration of *R. damascena* reduced menstrual pain and headache; however, the effect was significant only for headache. The findings substantiated the available information regarding the analgesic effects of *R. damascena* on menstruation. In a systematic review of RCTs which evaluated the effects of aromatherapy on the management of PD, the oil extract of *R. damascena* was one of the main methods of aromatherapy for reducing the menstrual cramps.[32] In another systematic review on the efficacy and safety of *R. damascena*, the analgesic and antinociceptive effects of the oral intake of this medicinal herb were reported against menstruation-related pain.[13] Moreover, in another systematic review of 13 RCTs, five

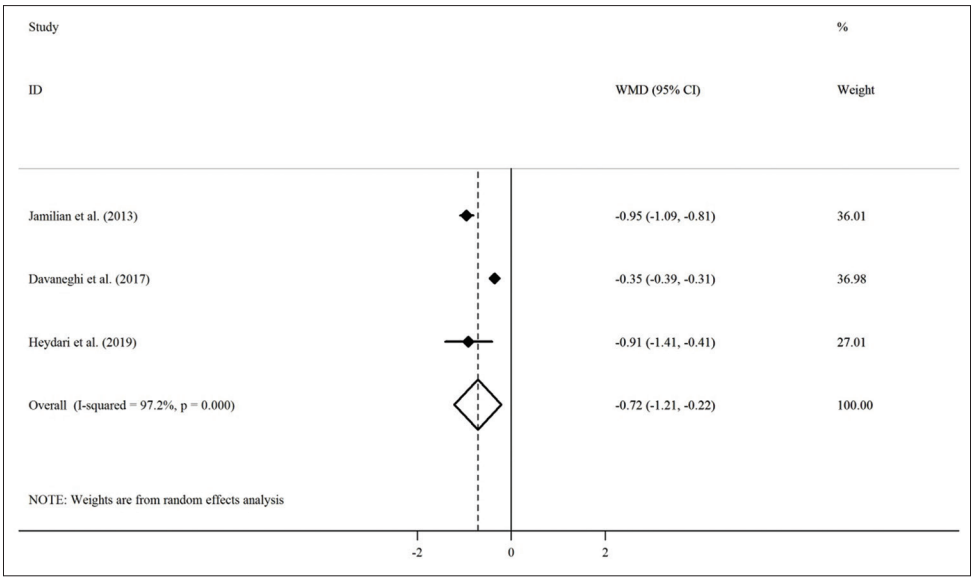

Figure 5: Forest plot for the effect of *Rosa damascena* on menstruation-related bloating

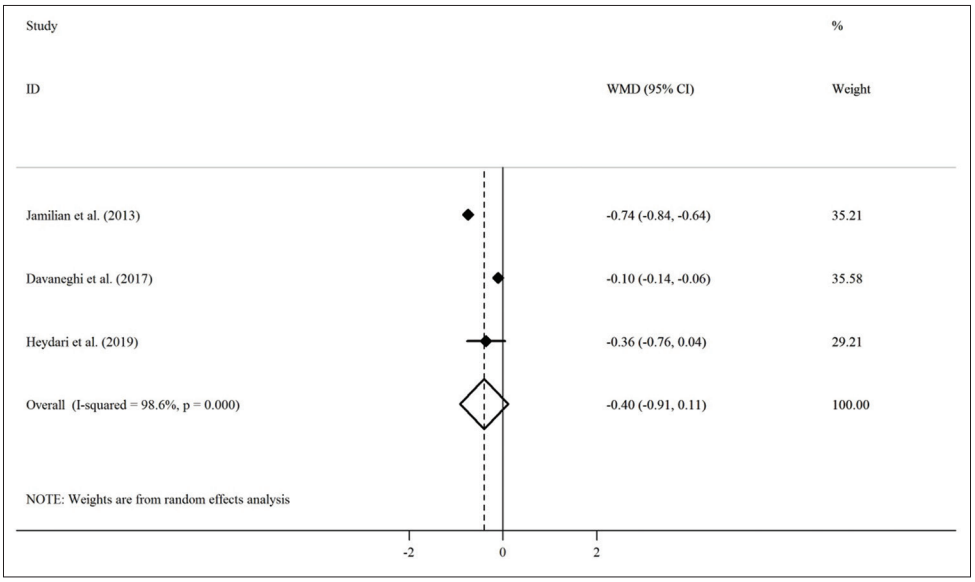

Figure 6: Forest plot for the effect of *Rosa damascena* on menstruation-related anxiety

trials evaluated the analgesic effects of aromatherapy with *R. damascena* oil and reported that treatment could be effective in reducing different painful conditions, such as menstruation-related pain.[33]

Inconsistent with our findings, a meta-analysis indicated a significant difference between menstrual pain 48 h after receiving mefenamic acid and *R. damascena* (WMD: −0.23; 95% CI: −0.24, −0.22).[34] In the current review, the effect sizes of five RCTs that addressed administration of *R. damascena* in the form of aromatherapy, topical treatment, or oral intake were pooled comparing the baseline and final posttreatment values of the outcomes, while the previously mentioned review considered the oral administration of any supplements and reported data of a single cross-over trial of 92 women in a subgroup analysis 48 h after receiving the treatments. Based on the subgroup findings in the current review, oral intake of *R. damascena* using capsule caused a nonsignificant reduction in menstruation-related pain (two RCTs), while the oral drop of the treatment had a significant pain-alleviating effect (one RCT). On the other, a meta-analysis of 16 RCTs over the effect of aromatherapy with *R. damascena* on alleviating the adults' acute pain reported the potential effects of treatment on menstruation-related pain using subgroup analysis (three RCTs, WMD: −1.18; 95% CI: −1.92, −0.43).[35] Similarly, the subgroup findings in this review indicated a significant effect of *R. damascena* in the form of aromatherapy on menstruation-related pain (two RCTs).

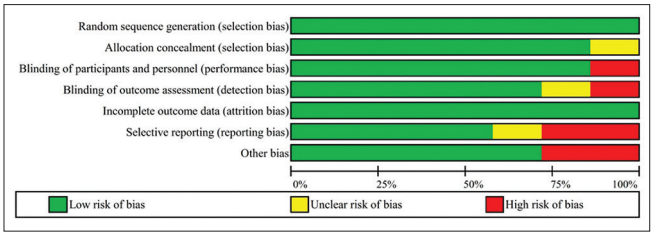

Figure 7: Risk of bias graph (review of the authors' judgments about each risk of bias item presented as percentages across all included studies)

These discrepancies could be attributed to different study objectives and the number of included RCTs.

Moreover, the findings of the meta-analysis indicated that the administration of *R. damascena* had a nonsignificant alleviating effect on menstruation-related anxiety, but it had significant alleviating effects on menstruation-related bloating and fatigue. In the literature review, no similar review regarding the effects of *R. damascena* on these menstruation outcomes was found. Nevertheless, the present review adds information to previous systematic and narrative reviews on the anxiolytic effects of *R. damascena*.[17,36,37]

Although this review showed that *R. damascena* might be an effective treatment for some MRSs, the mechanism of its effectiveness remains unclear. Previously, it was suggested that aromatherapy with *R. damascena* stimulated the olfactory system, increased the parasympathetic activity, reduced the sympathetic activity, and released neurotransmitters (i.e., enkephalin and endorphin), all of which might be effective in reducing pain and anxiety.[33] It is known that one cause of PMS is the reduction of parasympathetic activity. Pink roses (*Rosa Dekora*) seem to enhance the activity of the parasympathetic nervous system, but reduce the activity of the sympathetic nervous system.[38] It has been shown that aromatherapy with *R. damascena* reduces some physiological indicators of the sympathetic nervous system, such as blood pressure, heart rate, and respiratory rate in women with PD, which may be effective in reducing anxiety and pain.[26] Moreover, the beneficial effects of *R. damascena* have been attributed to the high levels of flavonoid components,[39] which seem to have pain-alleviating effects on dysmenorrhea.[40] Furthermore, the effect of *R. damascena* on the gamma-aminobutyric acid-ergic (GABAergic) system may underpin its beneficial effects on MRSs, as progesterone metabolites binding to GABA receptors contribute to MRSs, especially in females with PMS.[19] Furthermore, *R. damascena* induces anti-inflammatory effects and may have positive effects on the reduction of menstruation-related pain and the severity of other MRSs by decreasing prostaglandins in the blood flow.[24]

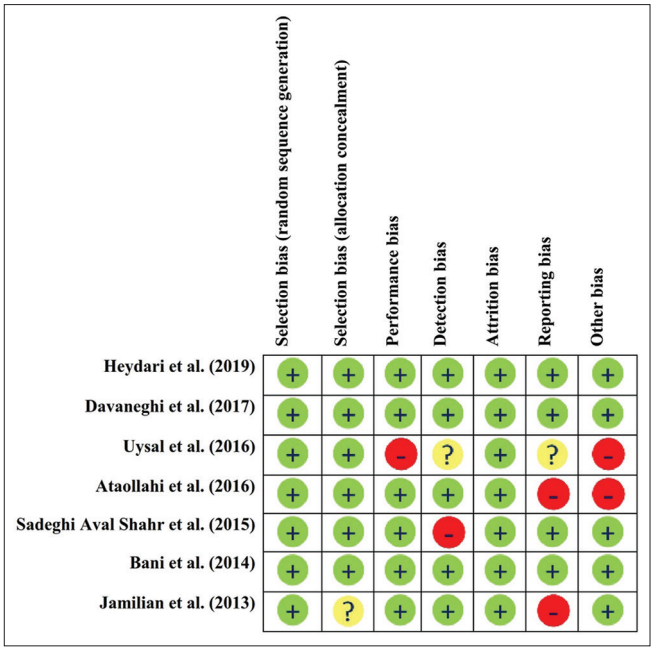

Figure 8: Risk of bias summary (review of the authors' judgments about each risk of bias item for each included study)

Implications for future research and clinical practice

Based on the findings of the present review, further research is suggested to evaluate different applications of *R. damascena* and design new effective interventions. The included studies used different dosages and durations of *R. damascena* administration, using aromatherapy or oral intake on individuals with PD or PMS. Based on the subgroup analysis, the condition and administration route as well as treatment dosage and duration were potential sources of heterogeneity for menstruation-related pain, headache, and fatigue. Accordingly, further studies are suggested to compare the effects of aromatherapy and oral intake of *R. damascena* on different MRSs, especially pain and anxiety. Further research is also recommended to determine the exact dosage of *R. damascena* that must be administered to bring positive effects. Moreover, to reach evidence-based conclusions, it is of merit to specify the administration durations and intervals of *R. damascena*.

Overall, the findings of the present review can increase our understanding of the value of *R. damascena* as a noninvasive and nonpharmacological option. Of three trials reporting the adverse effects of *R. damascena* administration, one reported minor side effects (headache, nausea, and vomiting).[19] Treatment was reported to be safe and free of side effects in most included RCTs. Considering the low cost and simple application of *R. damascena*, the use of this herbal plant can be considered as a CAM method, along with other routine treatments for MRSs. Furthermore, the use of

this method can help us concentrate on the individual as a whole, not merely the disease; therefore, we can apply a holistic care approach, as described by Martha Rogers' theory in 1970.[41] Nevertheless, the safety data are too scarce to confirm the use of *R. damascena* during menstruation as an evidence-based approach. It is also recommended to evaluate the adverse effects of treatment, especially by measuring safety laboratory parameters, to reach reliable conclusions about the possible adverse effects of *R. damascena*.

Strengths and limitations

To the best of our knowledge, this is the first review on the effect of *R. damascena* on menstruation-related pain, headache, fatigue, anxiety, and bloating. We pooled data using a meta-analysis, while most previous reviews reported the findings using systematic design. Also, previous meta-analyses have either restricted the administration route of *R. damascena* or focused on the properties of *R. damascena* in alleviating different painful conditions. Likewise, they missed some relevant studies. Accordingly, we summarized and statistically pooled the findings of studies that used aromatherapy, topical treatment, or oral intake of *Rosa damascena* on menstruation-related pain as the primary outcome and menstruation-related headache, fatigue, anxiety, and bloating as the secondary outcomes, using a comprehensive search. To investigate any possible differences regarding the effect of the administration route on the outcome, we used subgroup analysis.

Despite the aforesaid strengths, the findings should be cautiously interpreted due to some limitations. First, although we applied a random-effects model to take between-study variation into account, evidence of between-study heterogeneity was found in the main analysis. Subgroup analysis showed that some predefined variables were potential sources of heterogeneity. Moreover, we compared the baseline and final post-treatment values of the outcomes. Hence, different choices of endpoint may lead to heterogeneities; therefore, caution is necessary when interpreting the findings. Second, only three studies recorded the adverse effects; therefore, the available data are too limited to reach any definite conclusions about the safety of *R. damascena*. Third, dosages and durations of *R. damascena* administration were unknown in some studies; therefore, estimations were made based on consensus. Finally, the present findings cannot be generalized to all conditions because most trials were conducted in Iran, where the culture is relatively different from other countries.

Conclusion

This meta-analysis indicated that administration of *R. damascena* could nonsignificantly reduce the menstruation-related pain and anxiety, but it might have a significant reducing effect on menstruation-related headache, fatigue, and bloating. Therefore, further robust studies are suggested to compare the effects of aromatherapy and oral intake of *R. damascena* on different MRSs (especially pain and anxiety), using different dosages and durations and also safety laboratory parameters. Likewise, further studies are recommended to precisely determine the biochemical mechanisms responsible for the activity of *R. damascena* against MRSs.

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Conflicts of interest

There are no conflicts of interest.

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