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Review Article

Impact of flavonoid-rich herbal medicines on idiopathic heavy menstrual bleeding: A systematic review and meta-analysis of randomized controlled trials

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Abstract

Objective: Persian medicine has recommended flavonoid-rich plants for idiopathic heavy menstrual bleeding (HMB), highlighting their blood-reducing and antioxidant properties in menorrhagia. We aimed to explore the potential of flavonoid-rich plants as a safe and effective therapy for HMB.

Materials and Methods: A systematic search was conducted on 10 databases from inception to July 11, 2023. Randomized controlled trials (RCTs) reporting the use of Persian medicine-recommended plants for idiopathic HMB were included. Outcome measures included the pictorial blood assessment chart (PBAC), duration of bleeding, quality of life, and hemoglobin levels.

Results: A total of 12 RCTs involving 425 participants were included in the analysis. The results indicated the potential benefits of plants in terms of PBAC, duration of bleeding, and quality of life. Furthermore, these plants were found to cause a slight statistically significant increase in hemoglobin levels.

Conclusion: This study provides valuable insights into the use of the Persian medicine-recommended flavonoid-rich plants for idiopathic HMB. It suggests that flavonoid-rich plants based on Persian medicine may be effective and safe options for idiopathic HMB.

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Introduction

Idiopathic heavy menstrual bleeding (HMB) is a term used to describe regular heavy bleeding without any identifiable pelvic pathology or general bleeding disorder (Abu Hashim 2013). It is a significant gynecological problem that negatively impacts women's quality of life, affecting them physically, socially, and emotionally in their daily lives (Naoulou and Tsai 2012). HMB can also lead to anemia, and the treatment of this condition poses challenges even with continuous iron therapy (Oehler and Rees 2003). The management of HMB is influenced by various factors including underlying patient conditions, treatment protocols, and fertility desires. Medical treatments typically involve the use of hormonal or non-hormonal drugs such as non-steroidal anti-inflammatory drugs (NSAIDs) (Kitawaki et al. 2022). However, these medical agents are associated with side effects and may cause digestive system or kidney issues (Rindfleisch et al. 2015). As a result, many young women prefer to use alternative remedies for pain relief or to reduce bleeding (Kattuoa et al. 2020).

Persian medicine has shown promise in the treatment of menorrhagia through the use of herbal formulations that alleviate disease symptoms and improve patient compliance (Issa and Basheti 2017). Various plant polyphenols including flavonoids, have demonstrated the potential to reduce HMB and improve menorrhagia symptoms due to their intrinsic immunity, antioxidant and multiple beneficial medicinal effects (Alanwar and Abbas 2018). Flavonoids are a group of natural polyphenols found in various plant parts such as fruits, grains, tree bark, roots, stems, flowers, and dietary foods (Middleton 1996). They have been reported to possess diverse beneficial effects including antioxidant and anti-inflammatory properties (Górniak et al. 2019). Growing evidence suggests that flavonoids have therapeutic effects in abnormal uterine bleeding and blood clot formation, making them effective and safe agents due to flavonoids' inherent immunity and multiple medicinal benefits (Khan et al. 2018; Mobli et al. 2015). Pharmaceutical and health industries have also shown great interest in flavonoids,(Górniak et al. 2019) aligning with Persian medicine's recommendation of using plants containing flavonoids to reduce HMB (Goshtasebi et al. 2015; Mobli et al. 2015; Qaraaty et al. 2014).

However, the effects of herbal medicines containing flavonoids for the treatment of idiopathic HMB remain unclear. Although there have been numerous randomized controlled trials (RCTs) investigating their efficacy in HMB, a systematic and meta-analysis review is currently lacking. Therefore, this research aims to assess the effectiveness of flavonoid-rich plants in Persian medicine (Quince, Persian Golnar, Chamomile, Ginger, Purslane, Plantain, and Myrtle) for treating HMB using an evidence-based medicine approach.

Materials and Methods

The present study conforms to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for systematic reviews and was performed in accordance with best practice guidelines (Moher et al. 2009).

PICO question

This review sought to evaluate evidence addressing the PICO (population, intervention, control, outcome) question: In Idiopathic heavy menstrual bleeding patients (P), what is the role of flavonoids plants (I) on menstrual bleeding (HBM, duration of bleeding, quality of life and hemoglobin) (O), when compared to control group (C).

Search strategy

On 11 July 2023, we conducted a search in PubMed, Web of Science, Scopus, Ovid, Embase, Cochrane, ProQuest, Wiley,

ABSTRCT, and CINAHL databases. A three-step process was performed to determine the search keywords and design the search syntax. In the first stage, after PICO analysis, the concepts needed for the search were extracted according to the research topic. Also, synonyms, abbreviations, related terms, UK/US spellings, singular/plural forms of words, thesaurus terms (where available) were extracted and embedded in the search syntax to achieve maximum comprehensiveness in retrieving concepts. The thesaurus MeSH and Emtree were used to complete keywords and perform thematic searches on databases that had these tools. In the last stage, by conducting a preliminary search and analyzing the keywords of related and main articles in this field, the vocabulary was completed and enriched. Therefore, the baseline syntax was ((Heavy Menstrual Bleeding OR Hypermenorrhea OR Heavy Period* OR Menorrhagia) OR (Uterine hemorrhage* OR Uterine Bleeding* OR Vaginal Bleeding*) OR (Menstruation Disturbance* OR Menstruation Disorder* OR Polymenorrhea OR Retrograde Menstruation OR Menstrual Irregularity OR Irregular Menstruation OR Irregular Menses OR Menstrual Irregularities OR Hypomenorrhea)) AND ((Herbal Medicine* OR Herbalism) OR (Polyphenol* OR Provinol*) OR (Flavonoid* OR 2 Phenyl Chromene* OR 2 Phenyl Benzopyran* OR Bioflavonoid* OR Adiantum capillus-veneris OR Boswellia sacra Flueck OR Ceratonia siliqua L OR Cuscuta chinensis Lam OR Cydonia oblonga Mill OR Cymbopogon OR schoenanthus Spreng OR Hyoscyamus OR Juglansregia OR Lens culinaris Medik OR Myrtus communis OR Nymphaea alba OR Oleae uropaea* OR Onopordum acanthium OR Paeonia officinalis OR Paeonia emodi Wall OR Royle OR Pistacia lentiscus OR Plantago major OR Polygonum aviculare OR Portulaca oleracea OR Punica granatum OR Rhus coriaria OR Rumex acetosa OR Solanum nigrum OR Symphytum OR Tragopogon OR Valeriana dioscorides OR Valeriana celtica OR Nardostachys jatamansi OR Ziziphus spina-christi)). Complete search strategies are presented in Supplementary 1 for each database with their respective hits. Third, the manual search of reference lists of all included studies and relevant systematic reviews was done for any potentially eligible studies. Citation tracking was also performed for all the included articles. The details and search strategy in each database are provided in Supplement 1.

Data extraction

Two investigators (M. G. and M. R.) independently extracted the original data. Any disagreement was resolved by discussion. If a consensus was not reached, the results were reviewed by a third investigator (A. R.). The extracted data consisted of the following items: first author name, year of publication, country, type of study, sample size, study population, duration of treatment, type of outcome, type of intervention, and measure of effects and standard error.

Methodological quality assessment

The included studies were critically assessed using the standardized JBI critical appraisal tool for RCTs.(Tufanaru et al. 2017) This tool has 13 criteria that can be scored as being met (yes), not met (no), unclear, or not applicable (n/a). The quality of the individual studies was determined as high quality if 8 or more of criteria were scored “yes”, moderate quality if 5–7 of criteria were scored “yes”, and low quality if 4 or less of criteria were scored “yes”. Two independent reviewers were involved throughout the process and any disagreements arising between reviewers were resolved through discussion. All studies, regardless of their methodological quality, were included in the review. The exclusion criteria were uncompleted data in primary study and non-interventional study.

Data analysis

The outcome measures of interest were PBAC, duration of bleeding, quality of life and hemoglobin which were continuously measured. The standardized mean difference (SMD) for each outcome within each study was obtained by dividing the mean difference between with flavonoids and control groups by the pooled standard deviation, using the method described by Cohen (Cohen 2013) and converted effects to Hedges' g (Hedges 1984). Therefore, summary effect sizes and corresponding 95% confidence intervals (CIs) were calculated using random effects models for each outcome, using the method described by DerSimonian and Laird (DerSimonian and Laird 1986). Heterogeneity was formally assessed using a chi-square test, with the significance level set at 0.10 (Deeks et al. 2019). The I^2 index was used to indicate the percentage of total variation across studies attributable to heterogeneity rather than sampling error. We conducted a subgroup analysis based on type of intervention in control group. Statistical analyses were performed using Stata 16 (Stata Corp, College Station, Texas). A P-value of less than .05 was considered statistically significant.

Results

The database search yielded 1883 papers, of which, 1866 studies were excluded due to not meeting the inclusion criteria. A total of 17 studies were retained for further assessment. During eligibility assessment of papers, five papers were excluded. Finally, 12 studies evaluating the effect of flavonoid–rich herbal medicine on menorrhagia were included for analysis (Figure 1).

These articles were published between 2009 and 2021. Ten RCTs were conducted in Iran, and two in India. PBCA, duration of bleeding, quality of life, and hemoglobin levels were assessed in 7, 5, 4, and 4 RCTs, respectively (Table 1).

Methodological quality of the studies

Overall, the studies were assessed as being of high quality (Table 2). The total number of "yes" answers was 8 or more in 9 studies, 6 in 1 study, and 4 or less in 2 studies.

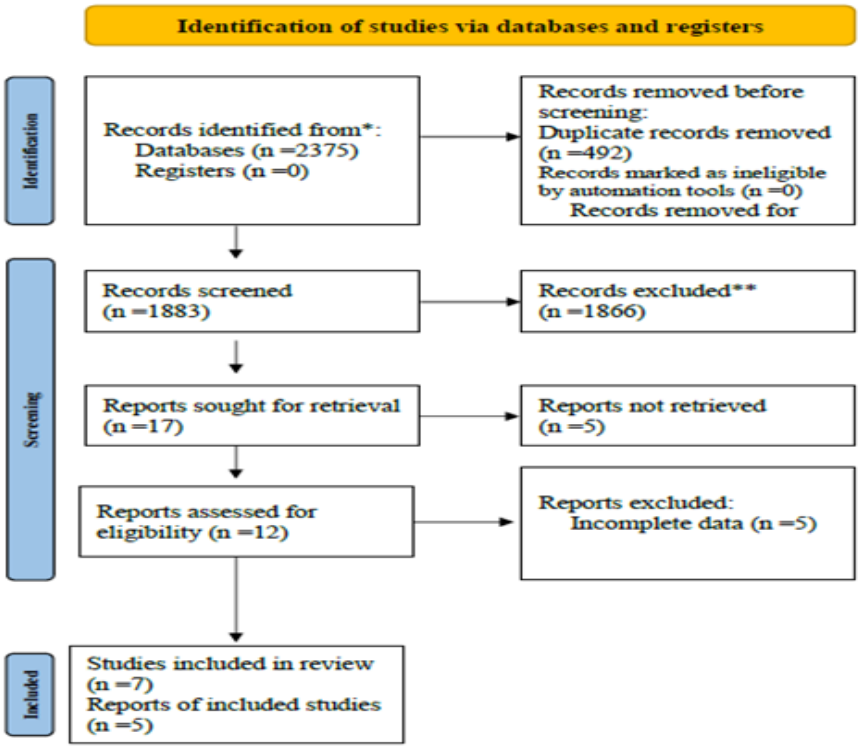

Figure 1. Flow chart of the studies reviewed

Table 1. Characteristics of the studies included in meta-analysis

First author, citation	Country	study design	Study population	Duration of treatment	Medicinal plant	Dosage	Type of treatment for control group
Bahman M. et al, 2018	Iran	Clinical trial of before-after pilot study	Premenopausal patients with menorrhagia aged 18 - 50 years	Two months	*Cydonia oblonga* (Quince)	A tea spoonful after every meal	NR
Goshtasebi A. et al, 2015	Iran	Double-blind, randomized controlled trial	Women with heavy menstrual bleeding of endometrial origin (aged 20–49 years)	From day 1 of menses for 5 days, for three consecutive menstrual cycles	*Punica granatum* L. flower (Persian Golnar)	500 mg, every 6 h	Tranexamic acid
Karimian Z. et al, 2015	Iran	Triple-blinded, randomized, clinical trial	Single female students living in dormitories of medical universities with menorrhagia (aged 21–25 years)	Two consecutive menstrual cycles	*Matricaria chamomilla* (Chamomile)	250 mg, every 8 hours	Mefenamic acid
Kashefi F. et al, 2015	Iran	Double-blind, randomized, placebo controlled clinical trial	High school girls (between 15 and 18 years old) with heavy menstrual bleeding (HMB)	From the day before menstrual bleeding until the third day (four consecutive days) for three consecutive menstrual cycles.	*Zingiber officinale* L. (Ginger)	250 mg, every 8 hours	Placebo (lactose powder)
Khanam B. et al., 2021	India	Open, observational, clinical trial	Women of 18 to 45 years, heavy irregular bleeding in amount or duration	From first day of menses till 10th day for two consecutive cycles	*Portulaca oleracea* L. (Purslane)	2 gm daily after meal	NR
Khodabakhsh M. et al, 2020	Iran	Triple blind randomized clinical trial	Women aged 36–45 years with heavy menstrual bleeding (HMB)	First 5 days of menstruation for three menstruation cycles	*Plantago major* L. (plantain)	syrup: 5 cc every 8 hr, capsule: 250 mg every 8 hours	Mefenamic acid capsule along with placebo syrup
Yousefi F. et al, 2020	Iran	Double-blind randomized clinical trial	Women age from 20 to 45 years with heavy menstrual bleeding (HMB)	Three cycles	*Punica granatum* L. and *Rosa damascene* Herrm. flowers	500 mg three times a day for the first 7 days of menstrual cycle for three cycles	Placebo
Qaraaty M. et al, 2014	Iran	Randomized double-blind, placebo-controlled pilot study	20 to 55 years old, married women	Three consecutives menstrual periods (seven days starting from the onset of bleeding)	*Myrtus communis* L. (myrtle)	15 ml (5 ml three times a day, 30 minute after each meal for seven days starting from the onset of bleeding)	Placebo
Umarami R. et al, 2021	India	Prospective patient blinded standard controlled study	Married and unmarried women between 18 and 35 years of age having regular menstrual cycle with PBAC score above 100 were included in this study	Two cycles	*Myrtus communis* L. (myrtle)	750 mg (one 500 mg and one 250 mg capsule) of drug Ter in die (TID) from first day of menses for five days	Tranexamic acid
Shobeiri S.f. et al, 2009	Iran	A Pilot Clinical Trial	Ten Iranian premenopausal women (mean age ± SD, 45.3 ± 3.7 years) with AUB comprising menorrhagia (heavy periods; blood loss >80 mL), metrorrhagia (prolonged, irregular periods), polymenorrhagia (frequent periods) and intermenstrual bleeding who had Not responded to standard medications and were candidates for hysterectomy participated in the clinical trial	One cycle (followed up for 3 months)	*Portulaca oleracea* L (purslane)	5 g of the seeds powder in a glass of hot water sweetened with sugar every 4 h by the oral route 48 h after the onset of menstruation for 3 days	NR
Mirzaei N. et al, 2018	Iran	Randomized double-blinded placebo-controlled clinical trial	Heavy menstrual bleeding with regular menstrual cycles, being 20 to 45 years old	Two menstrual cycles	*Portulaca oleracea* L (purslane)	500 mg aqueous extract of purslane seed (equivalent to 5 g seeds) every 8 hours + 500 mg mefenamic acid every 8 hours from the first to the third day of their menstruation	Placebo+ mefenamic acid
Shafiee M.et al, 2019	Iran	randomized clinical trial	women age from 18 to 50 years with heavy menstrual bleeding (HMB)	three cycles	*Lentil savigh* (roasted lentil flour)	three 10-gram sachets in the morning from the first to the seventh day of menstruation	tranexamic acid

Table 2. Critical appraisal of the studies included in meta-analysis

First Author	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Total
Bahman M. et al, 2018	N	N	NA	NA	NA	N	NA	NA	Y	NA	Y	Y	Y	4
Goshtasebi A. et al, 2015	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	12
Karimian Z. et al, 2015	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	12
Kashefi F. et al, 2015	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	U	Y	Y	12
Khanam B. et al., 2021	N	N	NA	NA	NA	N	NA	NA	Y	NA	U	Y	Y	3
Khodabakhsh M. et al, 2020	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	13
Yousefi F. et al, 2020	Y	Y	Y	Y	U	U	Y	Y	Y	Y	Y	Y	Y	11
Qaraaty M. et al, 2014	Y	Y	Y	Y	Y	U	Y	Y	Y	Y	Y	Y	Y	12
Umarami R. et al, 2021	Y	Y	Y	Y	N	U	Y	Y	Y	Y	Y	Y	Y	11
Shobeiri S.f. et al, 2009	N	N	Y	N	N	U	Y	Y	Y	Y	Y	N	N	6
Mirzaei N. et al, 2018	Y	Y	Y	Y	Y	U	Y	Y	Y	Y	Y	Y	Y	12
Shafiee M.et al, 2019	Y	Y	Y	N	N	N	Y	Y	Y	Y	Y	Y	Y	10

This tool uses a series of criteria that can be scored as being met (yes), not met (no), unclear or not applicable (n/a).Y=yes; N=no; U=unclear; NA=not applicable. JBI critical appraisal checklist for randomized controlled trials: Q1. Was true randomization used for assignment of participants to treatment groups? Q2. Was allocation to treatment groups concealed? Q3. Were treatment groups similar at baseline? Q4. Were participants blind to treatment assignment? Q5. Were those delivering treatment blind to treatment assignment? Q6. Were outcomes assessors blind to treatment assignment? Q7. Were treatment groups treated identically other than the intervention of interest? Q8. Was follow-up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed? Q9. Were participants analyzed in the groups to which they were randomized? Q10. Were outcomes measured in the same way for treatment groups? Q11. Were outcomes measured in a reliable way? Q12. Was appropriate statistical analysis used? Q13. Was the trial design appropriate, and any deviations from the standard RCT design (individual randomization, parallel groups) accounted for in the conduct and analysis of the trial?

Meta-analysis for PBAC

The overall effect on menorrhagia favored flavonoid–rich herbal medicines compared to comparators (Hedges' g= -0.02; 95% CI −0.49, 0.45) (Figures 2, and Table 3). However, the analysis of subgroups based on the type of intervention in the control group, for the control group with placebo, flavonoid–rich herbal medicines had a large and significant effect in reducing menorrhagia (Hedges' g= -0.64; 95% CI: -0.94, -0.34), but for the control group of other treatments, this effect was not observed (Hedges' g= 0.31; 95% CI: -0.02, 0.65). Of the studies included in the meta-analysis, in Mirzaei et al, and Yousefi et al studies, interventions were effective in reducing PBAC.

Meta-analysis for duration of bleeding

The overall effect on menorrhagia favored flavonoid-containing herbal medicines compared to comparators (Hedges' g= -0.25; 95% CI −0.76, 0.26; z=-0.95, p=0.34) (Figures 3, and Table 3). However, the subgroup analysis based on the type of intervention in the control group, for the control group with placebo, flavonoid–rich herbal medicines had a large and significant effect in reducing the duration of bleeding (Hedges' g=-0.63; 95% CI: -0.99, -0.27), but for the control group of other treatments, this effect was not observed (Hedges' g= 0.23, 95% CI: -0.47, 0.93). Of the studies included in the meta-analysis, in Mirzaei et al, and Yousefi et al studies, interventions were effective in reducing the duration of bleeding.

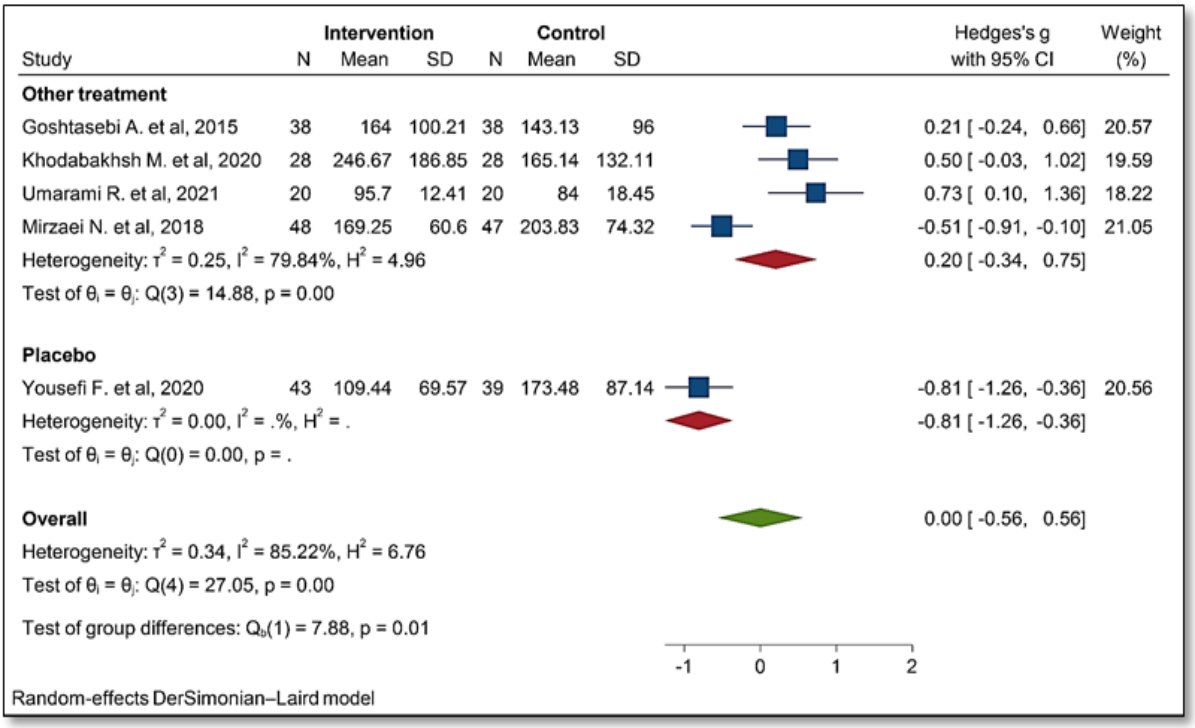

Figure 2. Forest plots of meta-analyses of the effects of flavonoid-rich herbal medicines intervention on the volume of bleeding (PBAC).

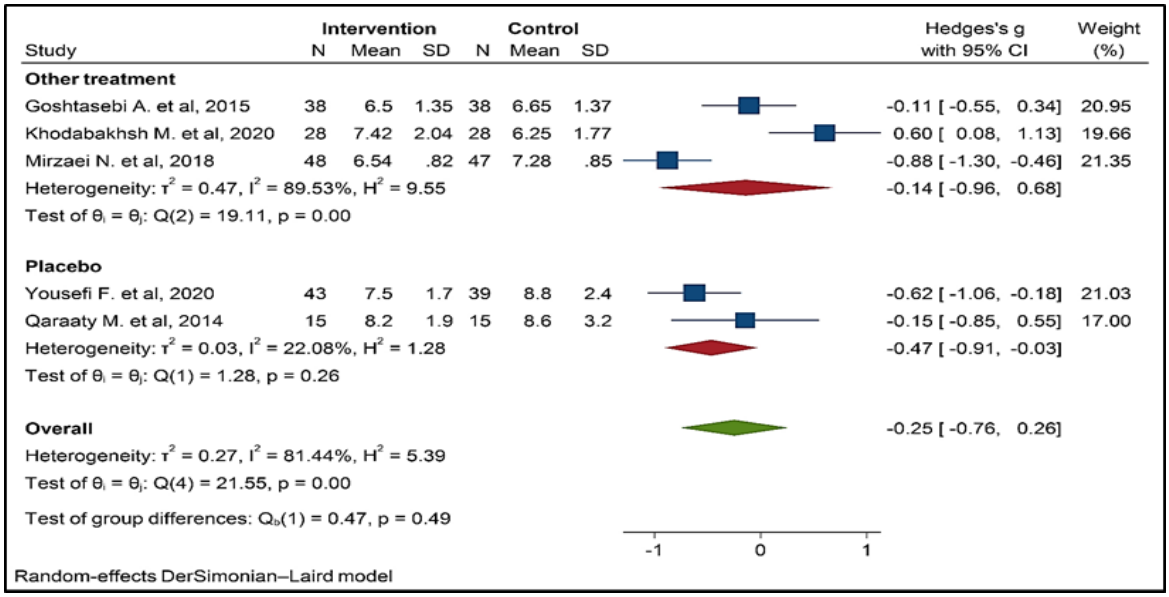

Figure 3. Forest plots of meta-analyses of the effects of flavonoid-rich herbal medicines intervention on the duration of bleeding.

Table 3. Effect of flavonoid-rich herbal medicines on PBAC, duration of bleeding, menorrhagia questionnaire and hemoglobin.

Type of outcome	Number of studies	Hedges' g	95% CI	Heterogeneity test (I2) %
PBAC	6	-0.02	−0.49, 0.45	81.52%
PBAC in Flavonoid vs other treatment	4	0.31	-0.02, 0.65	34.37%
PBAC in Flavonoid vs other treatment	2	-0.64	-0.94, -0.34	0.00%
Duration of bleeding (DB)	5	-0.25	-0.76, 0.26	81.44%
DB in Flavonoid vs other treatment	2	0.23	-0.47, 0.93	75.56%
DB in Flavonoid vs other treatment	3	-0.63	-0.99, -0.27	36.54%
Menorrhagia questionnaire (MQ)	4	-0.45	-0.76, -0.15	26.17%
MQ in Flavonoid vs other treatment	2	-0.57	-1.11, -0.04	51.48%
MQ in Flavonoid vs other treatment	2	-0.33	-0.84, 0.18	39.51%
Hemoglobin (Hb)	4	0.31	0.01, 0.60	21.85%
Hb in Flavonoid vs other treatment	2	0.34	-0.02, 0.7	0.00%
Hb in Flavonoid vs other treatment	2	0.17	-0.63, 0.97	73.81%

Meta-analysis for quality of life

The overall effect on quality of life of menorrhagia cases favored flavonoid-containing herbal medicines compared to comparators (Hedges' g= -0.45; 95% CI −0.76, -0.15; z=-2.46, p=0.01) (Figures 4, and Table 3). Flavonoid-containing herbal medicines were more effective in reducing the quality of life score compared to control group. The overall effect was without heterogeneous (I^2=0.00%). When the analysis was done based on the intervention type in the control group subgroup, there was a significant effect of flavonoid–rich herbal medicines on the quality of life of the patients (Hedges' g= -0.57; 95% CI −1.11, -0.04). But there was no significant difference between the intervention and control groups for the quality-of-life score in studies where the type of intervention is placebo in the control group (Figure 4).

Meta-analysis for Hemoglobin

Flavonoid–rich herbal medicines resulted in a statistically significant small increase in hemoglobin in menorrhagia cases (Hedges' g=0.31, 95%CI: 0.01, 0.6; z=2.02, p=0.04). The overall effect was low heterogeneous (I^2=21.85%). However,

when the analysis was done based on the intervention type subgroup in the control group, there was no significant effect of flavonoid–rich herbal medicines on the hemoglobin of the patients in any of the subgroups (Figure 5, and Table 3).

Trend analysis

A point-by-point analysis of the effect of flavonoid-rich herbal medicines on PBAC, duration of bleeding, quality of life and hemoglobin in menorrhagia people is shown in Figure 6. The results of this analysis showed that PBAC in the first cycle and the third cycle was significantly different between the intervention and control groups. However, there was no significant difference in PBAC of the baseline and the second cycle. The quality-of-life score also showed that a significant difference between the intervention and control groups in the third cycle, which showed a significant decrease compared to the baseline. No significant difference was observed for other outcomes (Figure 6).

Publication bias

Funnel plot and Egger's regression test were not used to assess publication bias for each of the outcomes since the number of the included studies was less than 10 (Sterne et al. 2011).

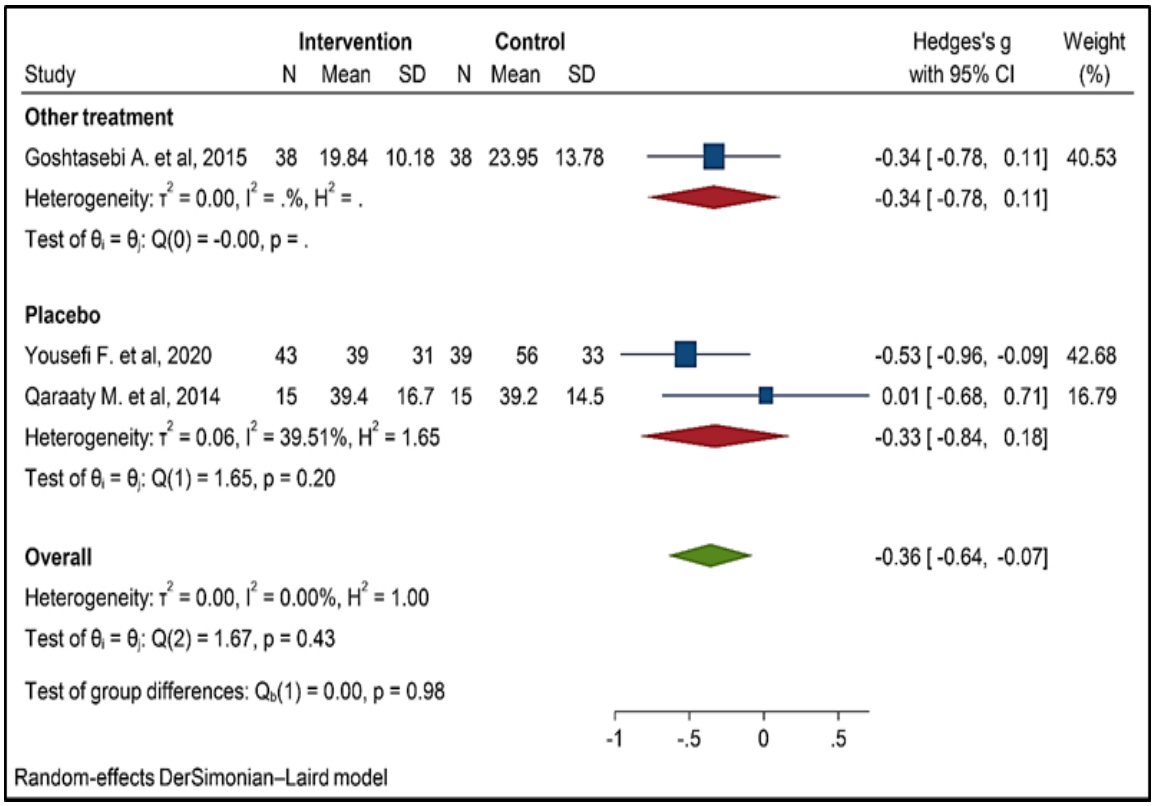

Figure 4. Forest plots of meta-analyses of the effects of flavonoid-rich herbal medicines intervention on the menorrhagia questionnaire.

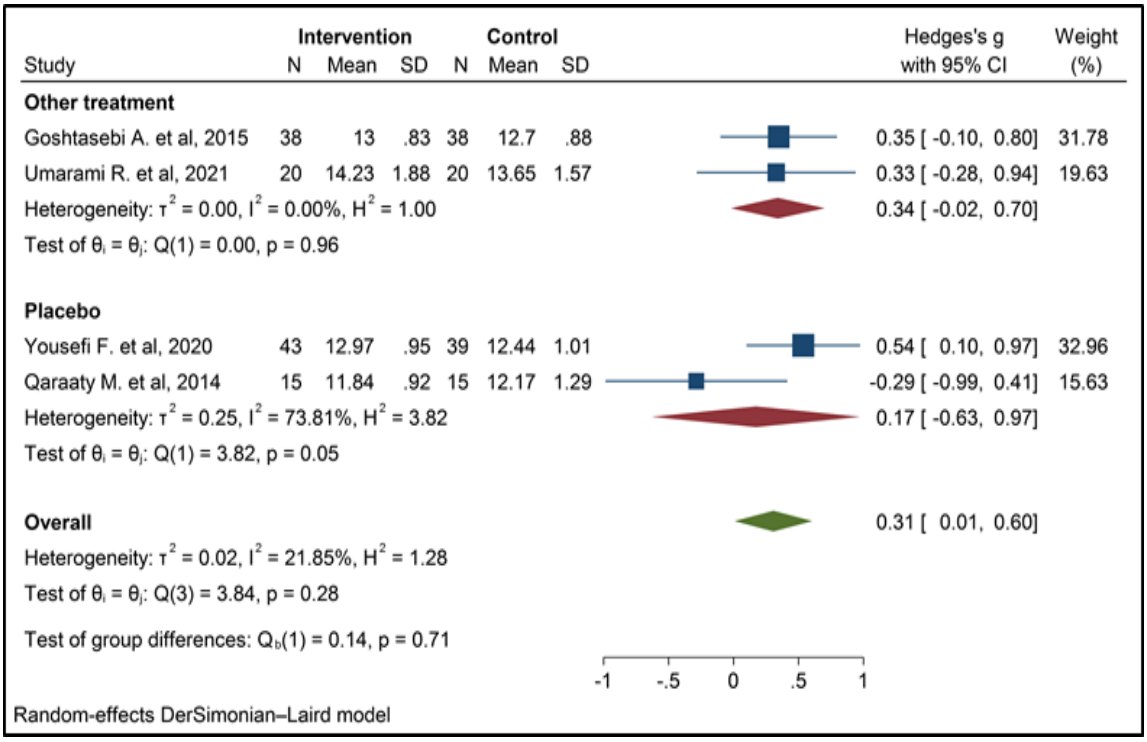

Figure 5. Forest plots of meta-analyses of the effects of flavonoid-rich herbal medicines intervention on hemoglobin.

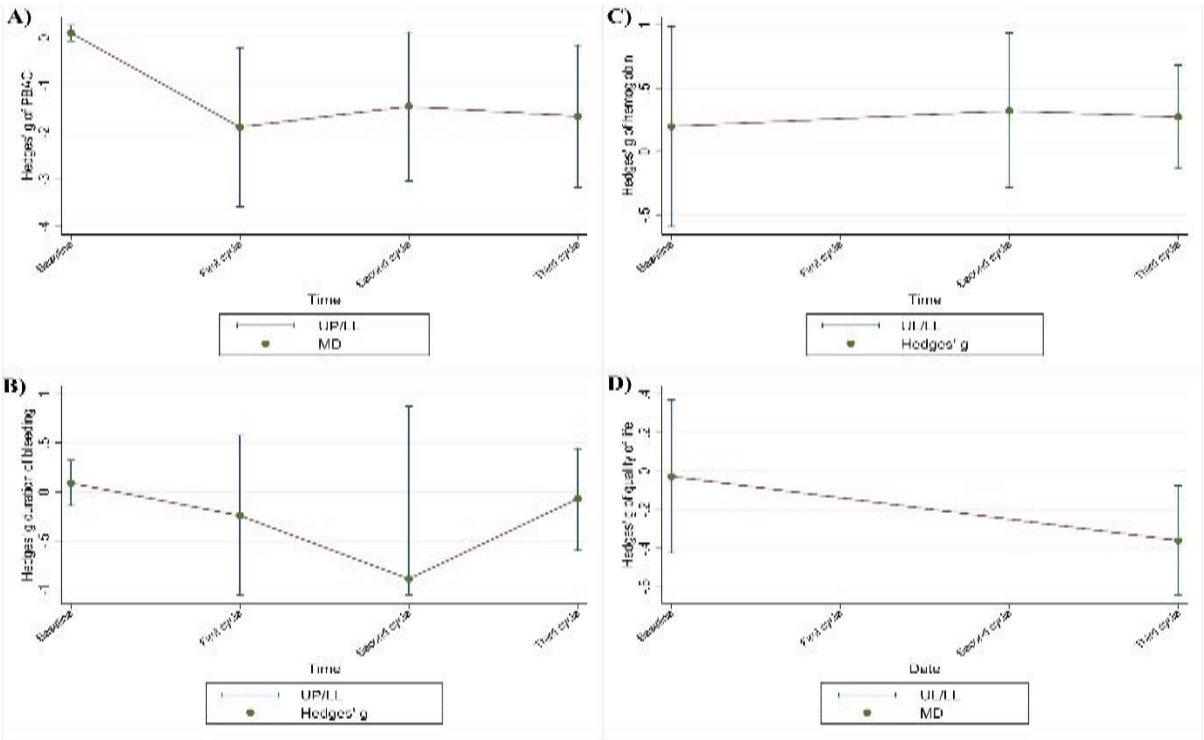

Figure 6. Changes trend of PBAC, number of bleeding days, quality of life and hemoglobin in menorrhagia women. A: PBAC, B: number of bleeding days, C: Hemoglobin, D: quality of life.

Discussion

The present systematic review and meta-analysis aimed to examine the available evidence from RCTs regarding the effectiveness of specific medicinal plants (*Lens culinaris* Medik., *Myrtus communis* L., *Plantago major* L., *Portulaca oleracea* L., and *Punica granatum* L.) in Persian medicine for the treatment of HMB.

Previous RCTs comparing these herbal medications with either standard treatment or placebo have yielded conflicting findings regarding the association between menorrhagia and the pictorial blood assessment chart (PBAC). In a randomized, double-blind, placebo-controlled study involving 43 participants, Yousefi et al (Yousefi et al. 2020) demonstrated that the Golnar capsule was significantly more effective than the control group, leading to an 8-fold reduction in PBAC score among individuals with HMB. However, in a placebo-controlled study by Mirzaei et al. with 48 participants, the purslane capsule reduced PBAC by 145.29 units (from 314.54 ± 105.03 to 169.25 ± 60.60), while the control group experienced a reduction of 115.91 units (from 319.74 ± 105.56 to 203.83 ± 74.32) after two months of intervention (Mirzaei et al. 2018). On the other hand, the clinical study by Umarami et al. found no significant association between the myrtle capsule and tranexamic acid (used as a control group) in terms of PBAC score (Umarami et al. 2021). Interestingly, other controlled studies have reported similar findings regarding PBAC in individuals with menorrhagia,(Goshtasebi et al. 2015; Khodabakhsh et al. 2020) but the heterogeneity of these studies makes their overall conclusions less conclusive.

The duration or number of bleeding episodes is another outcome measure assessed in patients with menorrhagia. Mirzaei et al.'s study demonstrated that *Portulaca oleracea* as an adjunctive therapy shortened the duration of bleeding compared to the control group (Mirzaei et al. 2018) and increased the likelihood of a reduction in bleeding duration in menorrhagic cases. However, the meta-analysis conducted on hemoglobin levels, another outcome measure assessed in the included studies, did not show a significant effect.

Despite the variations in the studies conducted, the current evidence suggests that flavonoid-rich plants commonly used in Persian medicine have a positive therapeutic effect on abnormal uterine bleeding (AUB) or heavy menstrual bleeding (HMB). These medicinal plants have been recognized as natural and traditional remedies for menorrhagia, and their effectiveness and safety have been scientifically described in the literature (Javan et al. 2016). Numerous studies have indicated that prostaglandins (PGF2, PGE2, and PGI2), which possess vasodilator and anti-aggregation properties, play a crucial role in the etiology of HMB (Mirzaei et al. 2018; Mobli et al. 2015). It appears that prostaglandin-based anti-fibrinolytic agents may be a safe option for patients with menorrhagia. The five herbal medicines mentioned in the previous section contain polyphenolic compounds such as flavonoids and tannins which contribute to their antioxidant, anti-inflammatory, and anti-proliferative effects (Goshtasebi et al. 2015; Khodabakhsh et al. 2020; Mirzaei et al. 2018; Qaraaty et al. 2014; Umarami et al. 2021; Yousefi et al. 2020). Several studies have demonstrated the anti-hemorrhagic effects of flavonoids and tannin-rich plants through their vasoconstrictor properties (Alanwar et al. 2018; Fayazmanesh et al. 2021).

Moreover, previous animal studies have shown that *Punica granatum* possesses anti-inflammatory and antispasmodic effects by inhibiting the production of PGE2 and nitric oxide (NO) while reducing the activity of cyclooxygenase-2 (COX2) (Ahangarpour et al. 2012; Rasheed et al. 2009). A clinical study has demonstrated that the purified flavonoid fraction can

suppress endometrial prostaglandins, thereby reducing or resolving AUB in women with idiopathic heavy menstrual bleeding (Alanwar et al. 2018). In line with Persian medicine principles, pharmacological studies have indicated the positive effect of lentils (*Lens culinaris* Medik.) on AUB due to their high content of flavonoids and tannins which inhibit COX2 and PGE2, leading to a reduction in menstrual bleeding (Muhammad et al. 2013; Shafiee et al. 2019).

Similarly, previous clinical studies have shown that *Myrtus communis* controls HMB through its anti-inflammatory effects and by inhibiting leukotrienes, peroxides, prostaglandins, prostaglandin E synthase (PGEs), and 5-lipoxygenase. Avicenna's book, particularly the Canon of Medicine, highlights the reduction of HMB through the use of *M. communis* (Javan et al. 2016; Qaraaty et al. 2014; Umarami et al. 2021; Wiechmann et al. 2015). Another study demonstrated the anti-inflammatory and anti-nociceptive properties of active phytochemicals derived from *M. communis* in animal models (Hosseinzadeh et al. 2011; Rossi et al. 2009).

P. oleracea has attracted significant interest in the treatment of AUB due to its diverse biological effects, including its antihemorrhagic properties through the inhibition of interferon-gamma (IFN-γ) and nitric oxide (NO) in menorrhagia (Mirzaei et al. 2018). A pilot clinical study found that *P. oleracea,* which contains flavonoids, resulted in a reduction in bleeding duration and volume in patients with AUB (Shobeiri et al. 2009). Animal models have also shown the anti-inflammatory and anti-prostaglandin properties of *P. oleracea* (Chan et al. 2000).

According to Persian medicine and several studies, *Plantago major* L. (*P. major*) has been found to have an antihemorrhagic effect, particularly in menstrual bleeding (Khodabakhsh et al. 2020; Khojastehfard et al. 2019; Najafian et al. 2018). Additionally, *P. major* has shown a positive effect on inflammation by reducing uterine bleeding in patients with leiomyomas or fibroids (NAVAEI et al. 2020). The presence of flavonoids and active phenolic compounds in *P. major* is believed to contribute to its anti-inflammatory and antihemorrhagic effects (Najafian et al. 2018; Samuelsen 2000).

In summary, the use of flavonoid-rich herbal medicine as adjunctive therapy has shown potential for improving the quality of life and reducing PBAC scores. However, to minimize result variations, it is crucial to conduct customized studies considering participant characteristics, methodology, and standardized measurement scales. It is also important to conduct better-designed clinical studies to provide more definitive evidence on the effect of herbal medicines on menorrhagia while addressing potential biases.

Limitations should be acknowledged in this systematic review and meta-analysis. Firstly, most of the included studies were conducted in Iran, limiting the generalizability of the results due to potential interactions between race, genetics, and medications. Secondly, some subgroup analyses did not significantly reduce heterogeneity. Thirdly, the number of studies was limited, and variations in formulations and study duration were observed among the included studies. Fourthly, only articles in English and Persian languages were considered, and gray literature was not included. Another limitation is the small sample size of the included RCT studies, which may affect the internal validity of the results and necessitates caution in interpreting the findings. Importantly, outcomes such as PBAC score, bleeding time, hemoglobin levels, and quality of life were not consistently reported or assessed using the same standards and methods across all included studies.

The findings of this meta-analysis indicate that flavonoid-rich herbal medicines show promise in the treatment of heavy menstrual bleeding (HMB). However, it is important to note that there

are limitations and biases in the studies included in this analysis. Therefore, further confirmation of the positive effects of these herbal medicines is necessary through large-scale randomized controlled trials (RCTs) with robust methodologies and well-documented studies.

Moreover, considering the high heterogeneity and limited number of studies on certain parameters, additional high-quality clinical studies are needed to validate the effectiveness of the mentioned herbal medicines in treating HMB. These studies should have a well-designed study protocol, including a large sample size, a double-blind placebo-controlled design, and adherence to CONSORT (Consolidated Standards for Reporting Trials) guidelines for reporting. It is also recommended to consider follow-up time in future trials. To provide conclusive evidence and have an impact on clinical practice, future studies should prioritize clinically relevant outcomes such as the PBAC score and other patient-reported outcomes.

Conflicts of interest

The authors declare none

Ethics approval and consent to participate

This systematic review was ethical approved by Golestan University of Medical Sciences (Ethical code: IR.GOUMS.REC.1401.021).

Authorship

Marzieh Qaraaty: Conceptualization, Supervision, Writing- Original draft preparation. Ayesheh Enayati: Methodology, Writing- Original draft preparation. Abdolhalim Rajabi: Analyzing data, Validation. Maedeh Rezghi: Data curation, Writing – review & editing. Mojgan Tansaz Writing- Original draft preparation. Masoud Mohammadi: Conceptualization, Methodology, Searching and gatehreing data, Writing- Reviewing and Editing. Amirhossein Sahebkar: Conceptualization, Methodology, Writing- Reviewing and Editing.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Supplementary

Supplementary Box 1. Search strategy and terms used to identify studies

Database	Formula	Results
PubMed	((Heavy Menstrual Bleeding[Title/Abstract] OR Hypermenorrhea[Title/Abstract] OR Heavy Period*[Title/Abstract] OR Menorrhagia[Title/Abstract] OR Uterine hemorrhage*[Title/Abstract] OR Uterine Bleeding*[Title/Abstract] OR Vaginal Bleeding*[Title/Abstract] OR Menstruation Disturbance*[Title/Abstract] OR Menstruation Disorder*[Title/Abstract] OR Polymenorrhea[Title/Abstract] OR Retrograde Menstruation[Title/Abstract] OR Menstrual Irregularity[Title/Abstract] OR Irregular Menstruation[Title/Abstract] OR Irregular Menses[Title/Abstract] OR Menstrual Irregularities[Title/Abstract] OR Hypomenorrhea[Title/Abstract]) AND (Herbal Medicine*[Title/Abstract] OR Herbalism[Title/Abstract] OR Polyphenol*[Title/Abstract] OR Provinol*[Title/Abstract] OR Flavonoid*[Title/Abstract] OR 2 Phenyl Chromene*[Title/Abstract] OR Phenyl Benzopyran*[Title/Abstract] OR Bioflavonoid*[Title/Abstract] OR Adiantum capillus-veneris[Title/Abstract] OR Boswellia sacra Flueck[Title/Abstract] OR Ceratonia siliqua L[Title/Abstract] OR Cuscuta chinensis Lam[Title/Abstract] OR Cydonia oblonga Mill[Title/Abstract] OR Cymbopogon[Title/Abstract] OR schoenanthus Spreng[Title/Abstract] OR Hyoscyamus[Title/Abstract] OR Juglansregia[Title/Abstract] OR Lens culinaris Medik[Title/Abstract] OR Myrtus communis[Title/Abstract] OR Nymphaea alba[Title/Abstract] OR Oleae uropaea*[Title/Abstract] OR Onopordum acanthium[Title/Abstract] OR Paeonia officinalis[Title/Abstract] OR Paeonia emodi Wall[Title/Abstract] OR Royle[Title/Abstract] OR Pistacia lentiscus[Title/Abstract] OR Plantago major[Title/Abstract] OR Polygonum aviculare[Title/Abstract] OR Portulaca oleracea[Title/Abstract] OR Punica granatum[Title/Abstract] OR Rhus coriaria[Title/Abstract] OR Rumex acetosa[Title/Abstract] OR Solanum nigrum[Title/Abstract] OR Symphytum[Title/Abstract] OR Tragopogon[Title/Abstract] OR Valeriana dioscorides[Title/Abstract] OR Valeriana celtica[Title/Abstract] OR Nardostachys jatamansi[Title/Abstract] OR Ziziphus spina-christi[Title/Abstract])) OR ((((("Polyphenols"[Mesh]) OR "Herbal Medicine"[Mesh]) OR "Flavonoids"[Mesh]) AND ((("Menorrhagia"[Mesh]) OR "Uterine Hemorrhage"[Mesh]) OR "Menstruation Disturbances"[Mesh]))	166
Web of Science	Heavy Menstrual Bleeding OR Hypermenorrhea OR Heavy Period* OR Menorrhagia OR Uterine hemorrhage* OR Uterine Bleeding* OR Vaginal Bleeding* OR Menstruation Disturbance* OR Menstruation Disorder* OR polymenorrhoea OR Retrograde Menstruation OR Menstrual Irregularity OR Irregular Menstruation OR Irregular Menses OR Menstrual Irregularities OR Hypomenorrhea (Topic) and Herbal Medicine* OR Herbalism OR Polyphenol* OR Provinol* OR Flavonoid* OR 2 Phenyl Chromene* OR Phenyl Benzopyran* OR Bioflavonoid* OR Adiantum capillus-veneris OR Boswellia sacra fleck OR Ceratonia siliqua L OR Cuscuta chinensis Lam OR Cydonia oblonga Mill OR Cymbopogon OR schoenanthus Spreng OR Hyoscyamus OR juglansregiae OR Lens culinaris Medik OR Myrtus communis OR Nymphaea alba OR Oleae uropaea* OR Onopordum acanthium OR Paeonia officinalis OR Paeonia emodi Wall OR Royle OR Pistacia lentiscus OR Plantago major OR Polygonum aviculare OR Portulaca oleracea OR Punica granatum OR Rhus coriaria OR Rumex acetosa OR Solanum nigrum OR Symphytum OR Tragopogon OR Valeriana dioscorides OR Valeriana celtic OR Nardostachys jatamansi OR Ziziphus spina-christi (Topic)	324
Scopus	(TITLE-ABS-KEY ((heavy AND menstrual AND bleeding) OR hypermenorrhea OR (heavy AND period*) OR menorrhagia OR (uterine AND hemorrhage*) OR (uterine AND bleeding*) OR (vaginal AND bleeding*) OR (menstruation AND disturbance*) OR (menstruation AND disorder*) OR polymenorrhea OR (retrograde AND menstruation) OR (menstrual AND irregularity) OR (irregular AND menstruation) OR (irregular AND menses) OR (menstrual AND irregularities) OR hypomenorrhea)) AND (TITLE-ABS-KEY ((herbal AND medicine*) OR herbalism OR polyphenol* OR provinol* OR flavonoid* OR (phenyl AND chromene*) OR (phenyl AND benzopyran*) OR bioflavonoid* OR (adiantum AND capillus-veneris) OR (boswellia AND sacra AND flueck) OR (ceratonia AND siliqua) OR (cuscuta AND chinensis AND lam) OR (cydonia AND oblonga AND mill) OR cymbopogon OR (schoenanthus AND spreng) OR hyoscyamus OR juglansregia OR (lens AND culinaris AND medik) OR (myrtus AND communis) OR (nymphaea AND alba) OR (oleae AND uropaea*) OR (onopordum AND acanthium) OR (paeonia AND officinalis) OR (paeonia AND emodi AND wall) OR royle OR (pistacia AND lentiscus) OR (plantago AND major) OR (polygonum AND aviculare) OR (portulaca AND oleracea) OR (punica AND granatum) OR (rhus AND coriaria) OR (rumex AND acetosa) OR (solanum AND nigrum) OR symphytum OR tragopogon OR (valeriana AND dioscorides) OR (valeriana AND celtica) OR (nardostachys AND jatamansi) OR (ziziphus AND spina-christi)))	874
Embase	(('heavy menstrual bleeding':ti,ab,kw OR hypermenorrhea:ti,ab,kw OR 'heavy period*':ti,ab,kw OR menorrhagia:ti,ab,kw OR 'uterine hemorrhage*':ti,ab,kw OR 'uterine bleeding*':ti,ab,kw OR 'vaginal bleeding*':ti,ab,kw OR 'menstruation disturbance*':ti,ab,kw OR 'menstruation disorder*':ti,ab,kw OR polymenorrhea:ti,ab,kw OR 'retrograde menstruation':ti,ab,kw OR 'menstrual irregularity':ti,ab,kw OR 'irregular menstruation':ti,ab,kw OR 'irregular menses':ti,ab,kw OR 'menstrual irregularities':ti,ab,kw OR hypomenorrhea:ti,ab,kw) AND ('herbal medicine*':ti,ab,kw OR herbalism:ti,ab,kw OR polyphenol*:ti,ab,kw OR provinol*:ti,ab,kw OR flavonoid*:ti,ab,kw OR '2 phenyl chromene*':ti,ab,kw OR 'phenyl benzopyran*':ti,ab,kw OR bioflavonoid*:ti,ab,kw OR 'adiantum capillus-veneris':ti,ab,kw OR 'boswellia sacra flueck':ti,ab,kw OR 'ceratonia siliqua l':ti,ab,kw OR 'cuscuta chinensis lam':ti,ab,kw OR 'cydonia oblonga mill':ti,ab,kw OR cymbopogon:ti,ab,kw OR 'schoenanthus spreng':ti,ab,kw OR hyoscyamus:ti,ab,kw OR juglansregia:ti,ab,kw OR 'lens culinaris medik':ti,ab,kw OR 'myrtus communis':ti,ab,kw OR 'nymphaea alba':ti,ab,kw OR 'oleae uropaea*':ti,ab,kw OR 'onopordum acanthium':ti,ab,kw OR 'paeonia officinalis':ti,ab,kw OR 'paeonia emodi wall':ti,ab,kw OR royle:ti,ab,kw OR 'pistacia lentiscus':ti,ab,kw OR 'plantago major':ti,ab,kw OR 'polygonum aviculare':ti,ab,kw OR 'portulaca oleracea':ti,ab,kw OR 'punica granatum':ti,ab,kw OR 'rhus coriaria':ti,ab,kw OR 'rumex acetosa':ti,ab,kw OR 'solanum nigrum':ti,ab,kw OR symphytum:ti,ab,kw OR tragopogon:ti,ab,kw OR 'valeriana dioscorides':ti,ab,kw OR 'valeriana	996

	celtica':ti,ab,kw OR 'nardostachys jatamansi':ti,ab,kw OR 'ziziphus spina-christi':ti,ab,kw)) OR (('menorrhagia'/exp OR 'uterus bleeding'/exp OR 'menstruation disorder'/exp) AND ('herbal medicine'/exp OR 'polyphenol'/exp OR 'flavonoid'/exp))	
Cochrane	((Heavy Menstrual Bleeding OR Hypermenorrhea OR Heavy Period* OR Menorrhagia OR Uterine hemorrhage* OR Uterine Bleeding* OR Vaginal Bleeding* OR Menstruation Disturbance* OR Menstruation Disorder* OR Polymenorrhea OR Retrograde Menstruation OR Menstrual Irregularity OR Irregular Menstruation OR Irregular Menses OR Menstrual Irregularities OR Hypomenorrhea):ti,ab,kw AND (Herbal Medicine* OR Herbalism OR Polyphenol* OR Provinol* OR Flavonoid* OR 2 Phenyl Chromene* OR Phenyl Benzopyran* OR Bioflavonoid* OR Adiantum capillus-veneris OR Boswellia sacra Flueck OR Ceratonia siliqua L OR Cuscuta chinensis Lam OR Cydonia oblonga Mill OR Cymbopogon OR schoenanthus Spreng OR Hyoscyamus OR Juglansregia OR Lens culinaris Medik OR Myrtus communis OR Nymphaea alba OR Oleae uropaea* OR Onopordum acanthium OR Paeonia officinalis OR Paeonia emodi Wall OR Royle OR Pistacia lentiscus OR Plantago major OR Polygonum aviculare OR Portulaca oleracea OR Punica granatum OR Rhus coriaria OR Rumex acetosa OR Solanum nigrum OR Symphytum OR Tragopogon OR Valeriana dioscorides OR Valeriana celtica OR Nardostachys jatamansi OR Ziziphus spina-christi):ti,ab,kw) OR ((MeSH descriptor: [Uterine Hemorrhage] explode all trees OR MeSH descriptor: [Menstruation Disturbances] explode all trees OR MeSH descriptor: [Menorrhagia] explode all trees) AND (MeSH descriptor: [Herbal Medicine] explode all trees OR MeSH descriptor: [Polyphenols] explode all trees OR MeSH descriptor: [Flavonoids] explode all trees))	243 (9)
ProQuest	(ab(Heavy Menstrual Bleeding OR Hypermenorrhea OR Heavy Period* OR Menorrhagia OR Uterine hemorrhage* OR Uterine Bleeding* OR Vaginal Bleeding* OR Menstruation Disturbance* OR Menstruation Disorder* OR Polymenorrhea OR Retrograde Menstruation OR Menstrual Irregularity OR Irregular Menstruation OR Irregular Menses OR Menstrual Irregularities OR Hypomenorrhea) OR mainsubject(Heavy Menstrual Bleeding OR Hypermenorrhea OR Heavy Period* OR Menorrhagia OR Uterine hemorrhage* OR Uterine Bleeding* OR Vaginal Bleeding* OR Menstruation Disturbance* OR Menstruation Disorder* OR Polymenorrhea OR Retrograde Menstruation OR Menstrual Irregularity OR Irregular Menstruation OR Irregular Menses OR Menstrual Irregularities OR Hypomenorrhea) OR ti(Heavy Menstrual Bleeding OR Hypermenorrhea OR Heavy Period* OR Menorrhagia OR Uterine hemorrhage* OR Uterine Bleeding* OR Vaginal Bleeding* OR Menstruation Disturbance* OR Menstruation Disorder* OR Polymenorrhea OR Retrograde Menstruation OR Menstrual Irregularity OR Irregular Menstruation OR Irregular Menses OR Menstrual Irregularities OR Hypomenorrhea)) AND (ab(Herbal Medicine* OR Herbalism OR Polyphenol* OR Provinol* OR Flavonoid* OR 2 Phenyl Chromene* OR Phenyl Benzopyran* OR Bioflavonoid* OR Adiantum capillus-veneris OR Boswellia sacra Flueck OR Ceratonia siliqua L OR Cuscuta chinensis Lam OR Cydonia oblonga Mill OR Cymbopogon OR schoenanthus Spreng OR Hyoscyamus OR Juglansregia OR Lens culinaris Medik OR Myrtus communis OR Nymphaea alba OR Oleae uropaea* OR Onopordum acanthium OR Paeonia officinalis OR Paeonia emodi Wall OR Royle OR Pistacia lentiscus OR Plantago major OR Polygonum aviculare OR Portulaca oleracea OR Punica granatum OR Rhus coriaria OR Rumex acetosa OR Solanum nigrum OR Symphytum OR Tragopogon OR Valeriana dioscorides OR Valeriana celtica OR Nardostachys jatamansi OR Ziziphus spina-christi) OR mainsubject(Herbal Medicine* OR Herbalism OR Polyphenol* OR Provinol* OR Flavonoid* OR 2 Phenyl Chromene* OR Phenyl Benzopyran* OR Bioflavonoid* OR Adiantum capillus-veneris OR Boswellia sacra Flueck OR Ceratonia siliqua L OR Cuscuta chinensis Lam OR Cydonia oblonga Mill OR Cymbopogon OR schoenanthus Spreng OR Hyoscyamus OR Juglansregia OR Lens culinaris Medik OR Myrtus communis OR Nymphaea alba OR Oleae uropaea* OR Onopordum acanthium OR Paeonia officinalis OR Paeonia emodi Wall OR Royle OR Pistacia lentiscus OR Plantago major OR Polygonum aviculare OR Portulaca oleracea OR Punica granatum OR Rhus coriaria OR Rumex acetosa OR Solanum nigrum OR Symphytum OR Tragopogon OR Valeriana dioscorides OR Valeriana celtica OR Nardostachys jatamansi OR Ziziphus spina-christi) OR ti(Herbal Medicine* OR Herbalism OR Polyphenol* OR Provinol* OR Flavonoid* OR 2 Phenyl Chromene* OR Phenyl Benzopyran* OR Bioflavonoid* OR Adiantum capillus-veneris OR Boswellia sacra Flueck OR Ceratonia siliqua L OR Cuscuta chinensis Lam OR Cydonia oblonga Mill OR Cymbopogon OR schoenanthus Spreng OR Hyoscyamus OR Juglansregia OR Lens culinaris Medik OR Myrtus communis OR Nymphaea alba OR Oleae uropaea* OR Onopordum acanthium OR Paeonia officinalis OR Paeonia emodi Wall OR Royle OR Pistacia lentiscus OR Plantago major OR Polygonum aviculare OR Portulaca oleracea OR Punica granatum OR Rhus coriaria OR Rumex acetosa OR Solanum nigrum OR Symphytum OR Tragopogon OR Valeriana dioscorides OR Valeriana celtica OR Nardostachys jatamansi OR Ziziphus spina-christi))	72
Wiley	"Herbal Medicine* OR Herbalism OR Polyphenol* OR Provinol* OR Flavonoid* OR 2 Phenyl Chromene* OR Phenyl Benzopyran* OR Bioflavonoid* OR Adiantum capillus-veneris OR Boswellia sacra Flueck OR Ceratonia siliqua L OR Cuscuta chinensis Lam OR Cydonia oblonga Mill OR Cymbopogon OR schoenanthus Spreng OR Hyoscyamus OR Juglansregia OR Lens culinaris Medik OR Myrtus communis OR Nymphaea alba OR Oleae uropaea* OR Onopordum acanthium OR Paeonia officinalis OR Paeonia emodi Wall OR Royle OR Pistacia lentiscus OR Plantago major OR Polygonum aviculare OR Portulaca oleracea OR Punica granatum OR Rhus coriaria OR Rumex acetosa OR Solanum nigrum OR Symphytum OR Tragopogon OR Valeriana dioscorides OR Valeriana celtica OR Nardostachys jatamansi OR Ziziphus spina-christi" anywhere and "Heavy Menstrual Bleeding OR Hypermenorrhea OR Heavy Period* OR Menorrhagia OR Uterine hemorrhage* OR Uterine Bleeding* OR Vaginal Bleeding* OR Menstruation Disturbance* OR Menstruation Disorder* OR Polymenorrhea OR Retrograde Menstruation OR Menstrual Irregularity OR Irregular Menstruation OR Irregular Menses OR Menstrual Irregularities OR Hypomenorrhea" anywhere	0
Ovid	((Herbal Medicine or Herbalism or Polyphenol or Provinol or Flavonoid or 2 Phenyl Chromene or Phenyl Benzopyran or Bioflavonoid or Adiantum capillus-veneris or Boswellia sacra Flueck or Ceratonia siliqua L or Cuscuta chinensis Lam or Cydonia oblonga Mill or Cymbopogon or schoenanthus Spreng or Hyoscyamus or Juglansregia or Lens culinaris Medik or Myrtus communis or Nymphaea alba or Oleae uropaea or Onopordum acanthium or Paeonia officinalis or Paeonia emodi Wall or Royle or Pistacia lentiscus or Plantago major or Polygonum aviculare or Portulaca oleracea or Punica granatum or Rhus coriaria or Rumex acetosa or Solanum nigrum or Symphytum or Tragopogon or Valeriana dioscorides or Valeriana celtica or Nardostachys jatamansi or Ziziphus spina-christi) and (Heavy Menstrual	11

	Bleeding or Hypermenorrhea or Heavy Period or Menorrhagia or Uterine hemorrhage or Uterine Bleeding or Vaginal Bleeding or Menstruation Disturbance or Menstruation Disorder or Polymenorrhea or Retrograde Menstruation or Menstrual Irregularity or Irregular Menstruation or Irregular Menses or Menstrual Irregularities or Hypomenorrhea)).ab.	
CINAHL	AB (Heavy Menstrual Bleeding OR Hypermenorrhea OR Heavy Period* OR Menorrhagia OR Uterine hemorrhage* OR Uterine Bleeding* OR Vaginal Bleeding* OR Menstruation Disturbance* OR Menstruation Disorder* OR Polymenorrhea OR Retrograde Menstruation OR Menstrual Irregularity OR Irregular Menstruation OR Irregular Menses OR Menstrual Irregularities OR Hypomenorrhea) AND AB (Herbal Medicine* OR Herbalism OR Polyphenol* OR Provinol* OR Flavonoid* OR 2 Phenyl Chromene* OR Phenyl Benzopyran* OR Bioflavonoid* OR Adiantum capillus-veneris OR Boswellia sacra Flueck OR Ceratonia siliqua L OR Cuscuta chinensis Lam OR Cydonia oblonga Mill OR Cymbopogon OR schoenanthus Spreng OR Hyoscyamus OR Juglansregia OR Lens culinaris Medik OR Myrtus communis OR Nymphaea alba OR Oleae uropaea* OR Onopordum acanthium OR Paeonia officinalis OR Paeonia emodi Wall OR Royle OR Pistacia lentiscus OR Plantago major OR Polygonum aviculare OR Portulaca oleracea OR Punica granatum OR Rhus coriaria OR Rumex acetosa OR Solanum nigrum OR Symphytum OR Tragopogon OR Valeriana dioscorides OR Valeriana celtica OR Nardostachys jatamansi OR Ziziphus spina-christi)	54
Total= 2374 Duplicated files=492 After deleting duplicated files= 1882		