

Original Article



A Systematic Review of Effective Herbal Medicine in Alleviating Hot Flashes During Menopause

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Abstract

Introduction: Approximately three-quarters of menopausal women experience vasomotor symptoms, with hot flashes being one of their main complaints. Due to the side effects of hormonal treatments such as estrogen in controlling this condition, many women prefer to use herbal medicines. Therefore, this study was conducted to review clinical trials investigating the effects of herbal drug on hot flashes in menopausal women.

Methods: This systematic review used the main search terms, including “hot flashes”, “herbal medicine”, and “menopause” along with their synonyms from medical subject headings (MeSH) and Emtree. A comprehensive literature search was conducted across databases such as PubMed, EMBASE, Cochrane Library, Scopus, Web of Science, and Google Scholar, covering studies from 2014 to 2024.

Results: Thirty-one clinical trial studies, with a total sample size of 2660 menopausal women, were examined. The results indicated that herbal medicine such as *Humulus lupulus* L. (Hop), *Rheum ribes* root (Rhubarb), a combination of *Agnus Castus*, magnolia, and soy isoflavones, *Hypericum perforatum*, chlorogenic acids (CGAs), fennel, *Silybum marianum*, lavender, *Salvia officinalis*, *Vitex agnus-castus*, *Black cohosh*, *Evening primrose*, a combination of fennel-valerian, herbal tea, kudzu flower, licorice, *Nigella sativa* and *Vitex* combinations, *Schisandra chinensis*, grape seed proanthocyanidin, soy isoflavones, Fenugreek Husk, and *Capsicum frutescens* L. (Solanaceae) were effective in reducing the intensity, frequency, or duration of hot flashes through different mechanisms.

Conclusion: Overall, herbal medicines seem to have a positive impact on menopause symptoms such as hot flashes and may be used as an alternative to hormonal treatments without having adverse effects on breast and uterine tissues. However, future research should consider both the effects and side effects of these herbal medicines.

Keywords: Hot flashes, Herbal medicine, Menopause



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Introduction

As we enter the third millennium, menopause has become a focus of society and is regarded as a basic health problem (1). Menopause is a stage of a woman's life, which is accompanied by the permanent cessation of menstruation due to the loss of ovarian activity. The average age of menopause in Iran is estimated to be 48.2 years (2). Furthermore, with increasing life expectancy, women now spend almost a third of their lives in the menopause phase (3).

Menopause is a multifaceted condition affecting women's quality of life (4). The decrease in ovarian activity and estrogen levels leads to several symptoms

such as disturbances in the menstrual pattern, vasomotor instability, genital system atrophy, which causes painful intercourse, itching, inflammation of the urethra, bladder infections, and urinary incontinence occur in menopause. In the long term, major problems caused by estrogen deprivation (e.g., heart diseases and osteoporosis) further threaten postmenopausal women's health (5).

Vasomotor symptoms occur in 80% of postmenopausal women and significantly impact their quality of life (6). Hot flashes are one of the most common and problematic symptoms for women during the climacteric period, which is a mental feeling of intense heat in the upper part of the body that lasts from 30 seconds to 5 minutes, typically



about 4 minutes. Hot flashes, caused by the sudden drop in estrogen, usually end in sweating and feeling cold. It is obvious that estrogen replacement would be the treatment of choice for managing these symptoms (7).

Hormone replacement therapy (HRT) is the most effective method available for the treatment of vasomotor symptoms and is extremely effective in relieving short-term symptoms related to menopause, preventing postmenopausal osteoporosis. However, HRT increases the risk of developing endometrial, breast, ovarian, gall bladder, and bladder cancers (8). Many women look for alternatives due to the risks and side effects of long-term HRT use (9).

Among non-hormonal treatments, herbal therapy holds a special place and is recommended for the treatment of menopause symptoms (4). Some plants, particularly those containing estrogen (phytoestrogens), play a special role in treating menopause symptoms (10). Phytoestrogens are plant derivatives that can show estrogenic and antiestrogenic effects due to their structural similarity with estrogens (11). A study investigating the effects of phytoestrogens on menopause's physical, psychological, and urogenital symptoms found a significant reduction in physical and psychological symptoms due to phytoestrogens influence (12).

Systematic review is an essential tool for summarizing available evidence in an accurate, correct, and reliable manner (13). Globally, several studies have been conducted on the effect of various medicinal plants on the treatment of various menopausal complications, including hot flashes (14). Ghazanfarpour et al conducted a review study on the effect of Iranian medicinal plants on menopause symptoms, evaluating 19 double-blind controlled clinical trials. Their results showed that licorice, fennel, soy, black mountain ash, red clover, primrose, flax seed, marigold, soybean oil, shepherd's flower, and valerian can reduce hot flash side effects (15). Chen and colleagues' systematic review on phytoestrogens in menopause analyzed seven studies, finding no significant difference between phytoestrogens and placebo in improving menopausal symptoms using the Kupperman index. However, 10 other studies reported a significant reduction in hot flashes in the groups consuming phytoestrogens compared to placebo groups (16). Given the different results of these studies, the need for a systematic study that provides a clear and uniform result and serves as a comprehensive guide for policymakers and researchers seems necessary. Therefore, this study was conducted to review clinical trials on the effects of herbal medicine on hot flashes in menopausal women.

Materials and Methods

This systematic review was conducted to evaluate the effects of herbal medicine in alleviating hot flashes during menopause in 2024, following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (17).

Eligibility Criteria

Inclusion criteria involved randomized clinical trials that investigated the effects of herbal medicine on hot flashes in women with physiological menopause who were not suffering from acute and chronic diseases such as cancer or endometriosis. Studies need to measure hot flashes using valid and reliable tools, provide full-text access, and be published between 2014 and 2024. Exclusion criteria included studies with unrelated results, duplicate studies, and other types of research such as reviews, meta-analyses, case studies, letters to the editor, editorials, commentaries, opinions, and conference papers.

Information Sources

To identify articles related to the purpose of the study, a comprehensive search was conducted in international databases, including PubMed, EMBASE, Cochrane Library, Scopus, and Web of Science from 2014 to January 2024 by a medical librarian specialist (NS). In addition, manual searching was conducted to achieve maximum comprehensiveness. To further maximize the comprehensiveness, related keywords were selected based on PICO and included Medical Subject Headings (MeSH) and Emtree terms. The main search terms were "hot flashes", "herbal medicine", and "menopause", along with their synonyms. In the present study, PICO included the following:

P: Menopause women

I: Herbal medicine

C: Comparison between any of the plant and placebo or HRT, and the like

O: Alleviating the number, intensity, or duration of hot flashes

A search strategy in PubMed is as follows:

(menopause[tiab] OR ("Change of Life"[tiab] AND Female[tiab]) OR "hot flashes"[tiab] OR climacteric*[tiab]) AND ("herbal medicine"[tiab] OR (Medicine*[tiab] AND Herbal[tiab]) OR "Hawaiian Herbal Medicine"[tiab] OR ("Herbal Medicine"[tiab] AND Hawaiian[tiab]) OR (Medicine[tiab] AND "Hawaiian Herbal"[tiab]) OR "La'au Lapa'au"[tiab] OR "Lau Lapaau"[tiab] OR "La au Lapa au"[tiab] OR Herbalism[tiab] OR (Extract*[tiab] AND Plant[tiab]) OR "Plant Extract"[tiab]) AND 2014:2024[dp].

This strategy was modified and performed in other databases according to the characteristics of each database (Supplementary file 1).

Study Selection

The abstracts of all retrieved records were entered into EndNote x8. After the exclusion of duplicates, the titles and abstracts of all remaining records were reviewed, and those related to the research topic were identified. Finally, two reviewers (VGH and FD) independently assessed and studied the full text of the relevant studies. Any disagreement was resolved by a third reviewer (MB), as depicted in Figure 1. The data extraction form was

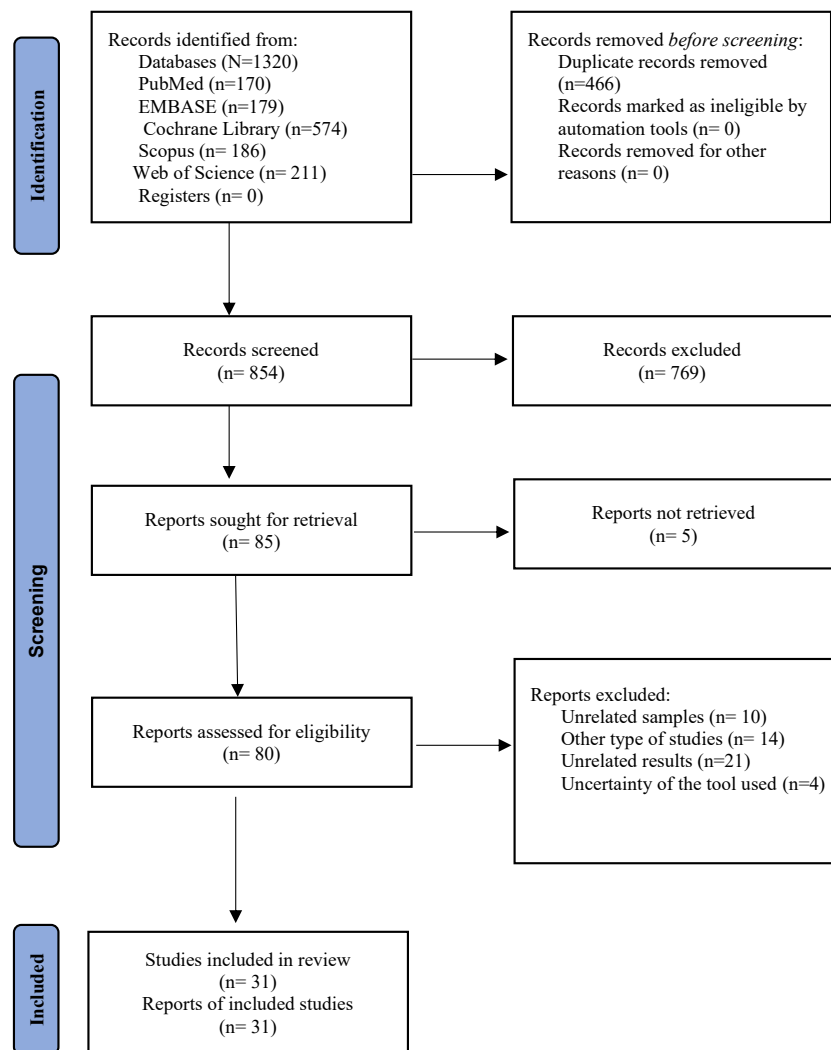


Figure 1. Process of Selecting Article

prepared by the researchers in an Excel sheet, and the bibliographic characteristics of each article, including the first author, year of the study, study method, types of plants, and the effect of herbal medicine on the severity, duration, and number of hot flashes were recorded.

Quality Evaluation

Articles underwent quality evaluation using Verhagen's checklist, originally designed by Verhagen et al, and its accuracy and precision were approved through a detailed Delphi process. This checklist contains 8 questions, including treatment allocation, the similarity of groups at baseline, specified eligibility criteria, the blindness of the outcome assessor, blindness of the care provider, blindness of the patients, point estimates, measures of variability presented for the primary outcome measures, and intention-to-treat, with a range of three options "Yes", "No", and "I don't know" (18). Quality assessment was conducted independently by two investigators (VGH and FD), with the intra-class correlation coefficient used to assess inter-rater agreement. In case of disagreement, the third author (NS) was consulted to reach a consensus.

Results

Thirty-one clinical trials with a sample size of 2660 menopausal women were fully examined and included in this systematic review. All articles met the acceptable quality standards for inclusion in the study. This review covered a variety of herbal interventions, including: Combined Herbal Capsule Menohelp (2 studies) (19, 20), *Humulus lupulus* L. (Hop) (1 study) (21), combination of *Nigella sativa*, *Melissa officinalis* extract, and fennel fruit (1 study) (22), fennel (1 study) (23), *Rheum ribes* root (Rhubarb) (1 study) (24), combination of *Labisia pumila* and *Eurycoma longifolia* (Nu-femme™) (1 study) (25), *Morus nigra* L. (black mulberry) (1 study) (26), *Salvia officinalis* (2 studies) (27, 28), combination of *Agnus castus*, magnolia, and soy isoflavones (1 study) (29), *Hypericum perforatum* (1 study) (30), chlorogenic acids (CGAs) (1 study) (31), *Silybum marianum* (1 study) (32), lavender (1 study) (33), *Vitex agnus-castus* (1 study) (34), black cohosh (2 studies) (35, 36), evening primrose (2 studies) (35, 37), fennel-valerian (1 study) (38), herbal tea (1 study) (39), kudzu flower (1 study) (40), licorice (1 study) (41), combination of *N. sativa* and *Vitex agnus-castus* with citalopram (1 study) (42), *Schisandra chinensis*

(1 study) (43), grape seed proanthocyanidin (1 study) (44), soy isoflavones (2 studies) (45, 46), Herbal Extract (EstroG-100) (1 study) (47), Fenugreek (1 study) (48), *Capsicum frutescens* L. (Solanaceae) (1 study) (49).

More than 50% of the studies were conducted in Iran. In most cases, a placebo was used for comparison. However, several studies used the following items for comparison: citalopram (22), HRT and placebo (26), isoflavones (29), and HRT (41).

To measure the effect of herbal products on hot flashes, most studies evaluated the intensity, duration, and number of hot flashes. The tools used in most of these studies were the Blatt-Kupperman Index (BKI), Menopause Rating Scale (MRS), Menopause Specific Quality of Life Questionnaire (MENQOL), and the Greene Climacteric Scale (GCS). The characteristics of the studies are described in Table S1 (Supplementary file 1).

Discussion

This study was conducted to review studies examining the effects of herbal medicines on hot flashes in menopausal women. Various studies have been conducted, both in Iran and globally, to explore the role of phytoestrogens in alleviating menopausal outcomes such as hot flashes. According to these studies, non-pharmacological and plant-based interventions can manage menopausal hot flashes with fewer adverse effects compared to hormonal or chemical drugs (50, 51). The findings of all included studies in this systematic review, which assessed the impact of a specific herbal medicine on hot flashes, are discussed as follows:

Combined Herbal Capsule Menohelp

Menohelp has phytoestrogenic properties and contains extracts of black cohosh (*Actaea racemosa* L.), burdock (*Arctium lappa* L.), chaste tree (*Vitex agnus-castus*), potato (*Dioscorea villosa*), and soybean (*Glycine max*), produced by Barij Essence Pharmaceutical Company in Kashan, Iran, to reduce early menopause symptoms. The components of this herbal formula include CGA, diosgenin, and agnoside. Each herb used in this combination may help relieve menopausal symptoms (20). The results of the study by Shayan et al (19) indicated that although the frequency, duration, and intensity of hot flashes did not differ significantly between the intervention and control group after taking Menohelp, the frequency and intensity of night sweats in the Menohelp group decreased after the intervention. Mousavi et al (20) examined 100 women aged 50-59 years suffering from menopausal symptoms and randomly assigning them to either the Menohelp or placebo group. The results revealed that the average number and intensity of hot flashes are higher in the Menohelp group at 4 and 12 weeks after intervention. Overall, these studies did not demonstrate a significant positive effect of Menohelp on the improvement of menopause symptoms.

Humulus lupulus L. (Hop)

Hop is a herbaceous and perennial plant of the Cannabaceae family with a deeply branched root system, underground stems, and serrated opposite leaves covered with coarse fibers containing lupulin (21,52). Based on the results of the study by Aghamiri et al (21), hop significantly reduced the number of hot flushes compared to the control group at 4, 8, and 12 weeks after intervention. This effect is likely due to the prenylnaringenin content in the hop, which is known as a potent phytoestrogen that binds to estrogen receptors in the body (53). The phytoestrogen properties of this plant may help reduce vasomotor symptoms such as hot flashes during menopause.

Combination of *Nigella sativa*, *Melissa officinalis* Extract, and Fennel Fruit

Nigella sativa (black seed), belonging to the Ranunculaceae family, exhibits estrogen effects. *Melissa* plant extract contains compounds such as phenylpropanoid glycoside, flavonoids, polyphenols, and flavone glycoside. Fennel (*Foeniculum vulgare*), from the Umbelliferae family, contains 80% of anethole, estragole, camphene, and fenchone (54-56). The study by Amin et al (22) showed that the combination of *N. sativa*, *M. officinalis* extract, and fennel fruit is not effective in improving menopausal symptoms compared to citalopram, but it reduces feelings of anger and fatigue. This may be due to the concentrations of compounds used in this herbal compound, suggesting that the dosage and duration of the combined product or drug consumption can alleviate the symptoms. The studies by Kennedy and Scholey (57) and Awad et al (58) confirmed the mild sedative and anti-anxiety effects of the *Melissa* plant in mice. These calming and soothing effects may be due to the inhibition of the cholinesterase enzyme that binds to nicotinic and muscarinic receptors, which are related to the treatment of menopausal symptoms via acetylcholine (59-61).

Rheum ribes Root (Rhubarb)

Rheum ribes, from the Polygonaceae family, is cultivated in temperate climates and is a rich source of vitamins A, B, C, and E, as well as minerals such as calcium, potassium, iron, zinc, copper, sodium, and the like. This plant exhibits antibacterial, anti-trichomoniasis, anti-cancer, anti-ulcer, skin-protective, anti-inflammatory, antioxidant, blood-pressure reducing, and anti-Alzheimer's effects. It has also demonstrated potential in managing anti-polycystic ovary (PCO) syndrome (62,63). According to a study by Bagheriani et al (24), treatment with *R. ribes* significantly reduced the severity of hot flashes in postmenopausal women at 4 and 8 weeks after the intervention compared to a placebo (starch powder), suggesting its potential as an adjuvant treatment for hot flashes. Additionally, another study found that *R. rhaponticum* root extract alleviates vasomotor menopausal symptoms in ovariectomized rats (64). *R. ribes* may relieve hot flashes by scavenging waste products aggregated in the body during postmenopausal.

This positive effect can also be attributed to the anti-inflammatory role of *R. ribes* (65-68). Furthermore, this effect can be due to the plant's antioxidant role, especially its phytoestrogen flavonoid compounds, which bind to estrogen receptors (69-71).

Combination of *Labisia pumila* and *Eurycoma longifolia* (Nu-femme™)

Labisia pumila and *E. longifolia* have been used in traditional medicine for reproductive health, childbirth, menopausal symptoms, energy enhancement, and mental health (72). The study by Chinnappan et al (25) showed an improvement in hot flash symptoms by the 12th week in both the intervention group (400 mg *L. pumila* (SLP + °) and 100 mg *E. longifolia* (Physta®)) and the placebo group (300 mg maltodextrin); however, the improvement in the intervention group (65%) exceeded that of the control group (60%). *E. longifolia*, known as Malaysian ginseng, contains various metabolites such as eurycomanone and a 4.3 kDa peptide, which influence testosterone production (73). According to another study, *E. longifolia* constituents may help balance testosterone production in postmenopausal women (74). *L. pumila* contains compounds such as flavonoid and phenolic and exhibits phytoestrogen properties (75).

***Morus nigra* L. (Black Mulberry)**

Morus nigra L. (MN), or black mulberry, belongs to the genus *Morus* of the Moraceae family which contain various phenolic compounds such as flavonoids, flavones, isoflavones, isoprenylates, xanthenes, among others (76). The study by Costa et al (26) indicated that the administration of 250 mg of MN leaf powder for 60 days significantly improved hot flashes among climacteric women similar to the effects of HRT with 1 mg of estradiol.

Salvia officinalis

Salvia officinalis is one of the phytoestrogen plants from the Lamiaceae family which is native to Mediterranean Europe and used as a medicinal plant in Iranian medicine. According to the literature some of the properties of this plant were antibiotic anti-anxiety, anti-fungal, and anti-toxic and estrogenic properties (77,78). According to the study by Dadfar et al (27), there was a significant difference in the severity of hot flashes and night sweats following the consumption of *S. officinalis* extract. Similarly, the results of Kiani Rad et al (28) demonstrated a significant decrease in the duration, severity, and frequency of hot flashes, as well as night sweats after 8 weeks in groups treated daily with saliva compared to the control group. Rahte et al also suggested that *S. officinalis* is a safe herb for reducing menopausal hot flashes, attributed to estrogenic flavonoids (79).

Combination of *Agnus Castus*, *Magnolia*, and Soy Isoflavones

Magnolia has sedative and neurotrophic properties,

though there is limited literature on its effects on hot flashes (80). Additionally, *A. castus* has been found to increase melatonin secretion, interact with opioid receptors, and may help alleviate vasomotor symptoms and insomnia. Regarding soy isoflavones, research documents that they stimulate beta-estrogen receptors and promote the synthesis of sex hormone-binding globulin (81). In their study, De Franciscis et al (29) observed a significant reduction in hot flashes and the intensity of menopausal symptoms in individuals consuming a combination of *A. castus*, *Magnolia*, and soy isoflavones over 12 months, compared to those who consumed isoflavones 60 mg of isoflavones alone. As a result, the combination of *A. castus* and *magnolia* could be considered an effective and safe treatment for menopausal vasomotor symptoms.

Hypericum perforatum

Hypericum perforatum is an herbal plant with antidepressant and analgesic properties. Its components include flavonols, biflavones (natural estrogens), proanthocyanidins, xanthenes, and phloroglucinols. The antidepressant effect of this plant is attributed to its ability to block the uptake of serotonin (5-HT), dopamine, and norepinephrine in the synaptic clefts of interconnected neurons (82). According to the study by Eatemadnia et al (30), the frequency and severity of hot flashes significantly decreased in the *H. perforatum* group compared to the control group. Therefore, it can be inferred that the consumption of *H. perforatum* may be effective in reducing hot flashes, menopausal symptoms, and depression in postmenopausal women through its estrogenic compounds (83).

Chlorogenic Acids

CGAs are phenolic compounds found in plants such as coffee beans. However, their effects on women's menopausal symptoms remain unknown. CGAs have anti-tumor (84) antioxidant properties (85). A study conducted by Enokuchi et al (31) showed that CGAs significantly decrease the number and severity of hot flashes during sleep and the intensity of daytime sweats, compared to the placebo group, without any reported adverse effects due to CGAs. The results indicated that continuous consumption of CGA may improve menopausal symptoms, especially hot flashes, in healthy women. This effect can be partially attributed to the role of CGA in improving sleep disorders, which in turn can be effective in relieving vasomotor symptoms (86).

Fennel

Fennel, with the scientific name *F. vulgare*, is a flowering plant from the umbrella family and is widely known as fennel. The main compounds of fennel include anethole, fenchone, and phenolic compounds. In traditional medicine, different parts of the plant such as the fruit, leaves, and flowers are used for medical purposes (87). Fennel's flavonoid compounds have antioxidant and anti-

aging properties, while its phenolic compounds exhibit anti-inflammatory, anti-cancer, and cardiovascular protective effects. Golzareh and colleagues' study (23) found that the physical symptoms of menopause such as hot flashes, night sweats, muscle pains, sleep disorders, and heart discomfort significantly reduced in people who consumed fennel compared to placebo without any serious complications. Due to phytoestrogenic properties, fennel stimulates estrogen secretion and increases blood estrogen levels, which can reduce vasomotor symptoms such as hot flashes caused by estrogen deficiency during menopause (88).

Silybum marianum

Silybum marianum (L.), from the Asteraceae family, is a standardized extract derived from milk thistle fruits, containing a mixture of flavonolignans (89). Saberi et al (32), in their study, showed that *S. marianum* can significantly reduce the frequency and severity of hot flashes compared to a placebo. This plant was found to reduce menopausal symptoms, including hot flashes due to its phytoestrogen compounds (16). Additionally, it has been suggested that *S. marianum* exhibits an agonistic effect on the β -estrogen receptor (90). Silibinin, as an ingredient of *Silybum marianum*, was found effective in the expression of the estrogen receptor β in cancerous breast cells (91). Moreover, clinical evidence supports its galactagogue activity (92) and its role in inducing ovulation in PCO cases, highlighting its impact on women's sex hormones. Considering its common use and its safety as an herbal medicine, *S. marianum* can be beneficial for women experiencing menopausal symptoms.

Lavender

Lavender, an herb widely used in aromatherapy, belongs to the Labiales (Lamiaceae) family and contains linalool, flavonoids, linalyl acetate, geraniol, tannin, and cineole, which are commonly used to reduce stress (93,94). Based on the results of a study by Kazemzadeh et al (33), the number of hot flashes significantly decreased in the intervention group compared to the control group, indicating that lavender aromatherapy may effectively reduce menopausal hot flashes. Considering the effect of stress on hot flashes and the adverse effects of these menopausal symptoms on women's quality of life, lavender appears as a safe and effective treatment that can provide substantial benefits for menopausal women (33,95). In addition, it has been demonstrated that lavender reduces the activity of cyclic adenosine monophosphate (cAMP), consequently exerting a sedative effect and alleviating stress, which is regarded as a trigger for hot flashes in menopausal women (96).

Vitex agnus-castus

The fruit of the *Vitex agnus-castus* plant, known as a phytoestrogen drug, has been shown to reduce menopausal symptoms in women. Chemically, this plant

contains flavonoids, dopaminergic compounds, and iridoid glycosides (97). According to the findings of a study by Naseri et al (34), the mean scores of menopausal disorder and vasomotor dysfunction in the Vitex group were significantly lower than those in the placebo group ($P < 0.05$). Evidence suggests that the flavonoid components and weak estrogenic properties of such plants could be effective in relieving menopausal symptoms (98,99).

Black Cohosh and Evening Primrose Oil

Cimicifuga racemosa, also known as black cohosh, is a selective estrogen receptor modulator that affects the central nervous system. Its rhizome extract contains various active substances, including triterpene glycosides, cytosine, and phenolic acids (100,101). These substances might potentially act as agonists of serotonin 5-HT_{1A} and 5-HT₇ receptors in the hypothalamus's thermoregulatory center (102). Evening primrose oil, derived from the seeds of *Oenothera biennis*, is a rich source of gamma-linolenic acid, which is a precursor to prostaglandin E. It is widely believed to have the potential to suppress menopausal hot flashes (103). Based on the study by Mehrpooya et al (35), the implementation of an intervention using black cohosh and primrose oil significantly improved the severity of hot flashes and menopause-specific quality of life scores (MENQOL) in both groups ($P < 0.001$). Additionally, the number of hot flashes in the black cohosh group significantly reduced by the eighth week compared to the first week, but this reduction was not observed in the primrose oil group. Tanmahasamut et al (36) observed a significant improvement in the frequency of hot flashes in both black cohosh and placebo groups, but no significant difference was found between the two groups. The potential mechanisms for the effectiveness of black cohosh effectiveness in alleviating menopausal symptoms are believed to result from its ability to modulate selective estrogen receptors and exert anti-inflammatory and anti-oxidant effects (104). In the study by Motaghi Dastenaie et al (37), the daily consumption of two pearls (1 g) of evening primrose for 30 days caused a significant decrease in the intensity, duration, and frequency of hot flashes in the intervention group compared to the control group. The mechanism of action of evening primrose is unknown, but it is believed that this plant acts as an estrogen agonist and antagonist, exerting its effects through interaction with estrogen receptors. This difference between studies can be caused by differences in the dosage of black cohosh and evening primrose and the tools used to measure hot flashes.

Combination of Fennel and Valerian

The *Valeriana officinalis* plant has been studied for its potential benefits in reducing symptoms of depression, anxiety, stress, nerve pain, and menopause symptoms. In addition, studies have demonstrated that valerian contains phytoestrogen compounds and may be effective

in reducing the severity of hot flashes in postmenopausal women (105). The main compounds of fennel (*F. vulgare*) are anethole, fenchone, and phenolic compounds. Fennel has phytoestrogenic properties due to anethole and its polymers such as di-anethol and photo-anethol, which can bind to α and β estrogens receptors to exert estrogenic effects (54). The results of Jenabi and colleagues' (38) study suggested that valerian and fennel extract capsules can be a viable alternative for managing hot flashes ($P < 0.001$). The study reported that the frequency and severity of hot flashes are significantly lower in the intervention group compared to the control group after the intervention period ($P < 0.050$), but the mean duration of hot flashes increased in both groups over time. Likewise, an earlier study conducted by Kazemian et al reported a reduction in the severity, frequency, and duration of postmenopausal hot flashes after eight weeks of Valerian consumption in the intervention group compared to the control group (106).

Herbal Tea Capsule

Herbal tea capsules containing flavonoids and phytoestrogen compounds were found to be effective in treating mild to moderate depression, wounds, muscle pain, burns, mental disorders, anxiety, and inflammation (39,107). The study by Kheirkhah et al (39) displayed a significant difference in the intensity and duration of hot flashes between the intervention group (receiving 450 mg herbal tea capsules) and the placebo group at 4 and 8 weeks after the intervention ($P \leq 0.001$).

Kudzu Flower–Mandarin Peel

The kudzu plant (*Pueraria thomsonii* Benth), from the Fabaceae/Leguminosae family, contains tectorigenin, tectoridin, and tectorigenin (108). A study by Kim et al (40) found that the kudzu plant significantly reduces the severity and frequency of hot flashes compared to the placebo. Additionally, no serious side effects or hormonal changes were observed in either group. Therefore, based on these findings, the consumption of the kudzu plant may improve the quality of life for menopausal women. The effects of the kudzu flower–mandarin peel combination on managing hot flashes could be attributed to its isoflavones, particularly tectorigenin derivatives, which significantly decrease elevated tail skin temperature in ovariectomized mice (109,110).

Licorice

Licorice species are perennial plants native to different regions, including the Mediterranean, central and southern Russia, and Asia Minor such as Iran (111). Although its effectiveness is unknown, licorice is used to relieve menopausal symptoms. The study by Menati et al (41) although found no significant difference in reducing the duration and number of hot flashes between licorice (1140 mg/d) and HRT (conjugated estrogen 0.312 mg/d and medroxyprogesterone 2.5 mg/d). However,

licorice was more effective than HRT in improving the duration of hot flashes ($P = 0.018$ vs $P = 0.62$), and HRT was more effective than licorice in reducing the number of hot flashes ($P = 0.08$ vs $P = 0.157$) in postmenopausal women. Additionally, HRT was more effective than licorice in reducing the severity and number of hot flashes ($P = 0.019$). Given the scarcity of evidence and ongoing controversies regarding licorice and its phytoestrogenic effects compared to HRT, further investigations are warranted. Moreover, it would be valuable to measure changes in blood estrogen levels parallel with hot flash responses to licorice intervention (112).

Combination of *Nigella sativa* and *Vitex agnus-castus* With Citalopram

N. sativa, known for its beneficial effects on various body organs, has traditionally been used in the treatment of breastfeeding and menstrual disorders. The effectiveness of herbal medicines, including *N. sativa*, has been well demonstrated in the treatment of menopausal symptoms such as hot flashes (113). The ingredients of *V. agnus-castus* include flavonoids, iridoid glycosides, and dopaminergic compounds. This plant extract acts as an agonist of D2 receptors, helping to treat latent hyperprolactinemia, which is associated with reduced levels of estrogen and progesterone (98,114,115). Based on the study by Molaie et al (42), the combination of *N. sativa* and *V. agnus-castus* with citalopram significantly decreased the mean MENQOL, including vasomotor symptoms among women who received this herbal combination. Additionally, a systematic review (116), revealed that *V. agnus-castus*, as part of a menopausal herbal formula, is significantly more effective in reducing the incidence of menopausal hot flashes and night sweats compared to placebo. These findings suggest that black seed and *V. agnus-castus* may have positive effects on menopausal symptoms and quality of life in women. Furthermore, there is evidence supporting the beneficial effects of *N. sativa* in relieving menopausal complications such as metabolic syndrome and osteoporosis (117–119). Moreover, animal studies have confirmed the estrogen-like activities of this plant (55).

Schisandra chinensis

Schisandra chinensis, commonly known as “five-flavor berry”, has been traditionally used as a tea in Chinese medicine to treat different diseases such as kidney disease, colds, and memory impairments (120). According to the study by Park et al (43), *S. chinensis* has been demonstrated to be an effective complementary medicine for menopausal symptoms, particularly in alleviating hot flashes and sweating. In this study, the effect of *S. chinensis* on hot flashes and sweating was significantly greater over time in the intervention group compared to the control group. Additionally, another study displayed that the consumption of *S. chinensis* increases the expression of estrogen receptors (121). It is also assumed that *S. chinensis*

through its antioxidant and anti-inflammatory capacity mediated by components such as gamma-Schisandrin, schisandrin, gomisin A, and deoxyschizandrin, can potentially exert positive effects on vascular diseases, vasomotor symptoms, and perimenopausal complications in menopausal women (122-126).

Grape Seed Proanthocyanidin

Proanthocyanidins are a group of polyphenol antioxidants commonly found in the fruits, skins, leaves, and seeds of various plants (127). According to the study by Terauchi et al (44), the hot flash score decreased after 8 weeks of treatment with grape seed proanthocyanidin extract. Additionally, this extract was found to be effective in improving the physical and psychological symptoms of menopause, increasing muscle mass, and lowering blood pressure in middle-aged women. It is suggested that the observed positive effects on menopausal physical and psychological symptoms may be partly related to the antioxidant properties of plant polyphenols. However, the exact mechanism underlying these effects has not been revealed yet (128,129).

Soy Isoflavones

Phytoestrogens, such as soy isoflavones, are plant-derived compounds structurally similar to 17-beta-estradiol, the primary female sex hormone. These compounds can bind to the estrogen receptor and exhibit a range of estrogenic or antiestrogenic effects (130-132). According to the study by Lee et al (45), the score of hot flashes significantly reduced in both the isoflavones and placebo groups, indicating that isoflavones did not show a positive effect on climacteric symptoms compared to the placebo. However, Imhof et al (46) demonstrated a 43% reduction in hot flashes in postmenopausal women who received soybean sprout extract containing 100 mg of isoflavone glycosides, compared to a 30.4% reduction in the placebo group. The difference between these studies may be attributed to the difference in isoflavone dosage (70 mg/d isoflavones in Lee's study versus 100 mg/d in Imhof and colleagues' study) and the tools used to measure hot flashes. A meta-analysis study found that isoflavone exposure results in a significant reduction in hot flashes compared to placebo (16). Another study reported that receiving a plant supplement with 72 mg of isoflavones from soybeans can be effective in reducing hot flashes after 6 months (133).

Herbal Extract (EstroG-100)

EstroG-100® is a concentrated mixture made from the dried and powdered forms of *Cynanchum wilfordii* Hemsley, *Phlomis umbrosa* Turczaninow, and *Angelica gigas* Nakai. Based on the findings of Kim and colleagues' study (47), the total score of the modified Kupperman's menopause index and the severity of hot flashes showed improvement after 12 weeks of treatment with EstroG-100® compared to a placebo. This study confirmed EstroG-100 as a safe and effective herbal treatment for managing

menopausal symptoms and enhancing the quality of life of menopausal women. Another study conducted in South Korea demonstrated that a three-month administration of EstroG-100® leads to a significant improvement in various menopausal symptoms such as hot flashes, sleep disturbances, and joint pain (134). Moreover, the safety and effectiveness of EstroG-100® in improving the quality of life in postmenopausal women were confirmed by another study (135).

Fenugreek Husk (FenuSMART)

Fenugreek is a medicinal plant known for its rich source of steroidal saponins, the alkaloid "trigonelline" and the non-proteinogenic amino acid '4-hydroxyisoleucine' (136). These components can bind to estrogen receptors, mediating estrogenic and androgenic effects. Fenugreek seeds have been clinically evaluated for premenopausal and postmenopausal discomforts (137,138). In addition, fenugreek contains diosgenin, a type of phytoestrogen that can be effective in improving hot flashes (83). The study conducted by Begum et al (48) demonstrated a significant increase ($P < 0.01$) in plasma estradiol levels, along with improvements in various post-menopausal discomforts and quality of life among participants treated with fenugreek bark extract. In addition, 32% of participants reported no hot flashes after the intervention, while the remaining participants reported a reduction of one or two episodes per day compared to baseline.

Capsicum frutescens L. (Solanaceae)

Capsicum, also known as red and hot peppers, belongs to the Solanaceae family, specifically the *Capsicum annuum* var. *frutescens* (L.) Kuntze species. This group includes a variety of red and hot peppers that are native to the Americas. In Brazil, one type of red pepper is known as Malagueta (139). A study by Andrade et al (49) indicated that a homeopathic medicine derived from malagueta pepper exhibits potential effectiveness in reducing the intensity of hot flashes after 4 weeks. The study also suggested that Solanaceae, the plant family to which malagueta pepper belongs, effectively reduces hot flashes.

One limitation of the present study was the inability to conduct a meta-analysis or estimate the pooled effect of these herbal medicines on hot flashes due to the heterogeneity of the data. Moreover, the small sample size and the publication bias in some included studies were other limitations of this study. In addition, most studies used a placebo for the control group. Therefore, it is recommended that more studies be conducted with larger sample sizes and that other treatment methods such as HRT or other palliative methods be used as a comparison group.

Conclusion

Generally, herbal drugs seem to have positive impacts on menopause symptoms such as hot flashes due to their phytoestrogenic properties and can be used as an

alternative to HRT without adverse effects on breast and uterine tissues. Given the alleviative properties of herbal medicines, women's tendency to use them to manage their menopausal symptoms, and the scarcity of such studies, further investigations with different product composition percentages and larger sample sizes are warranted to determine the safety, optimal type, and dosage of these plants. Therefore, future research should also take into consideration the complications and long-term side effects of these herbal medicines. This highlights the necessity of conducting more studies with larger sample sizes to accurately determine the effect of these medicinal plants.

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Competing Interests

The authors declare that they have no conflict of interests.

Ethical Approval

This study was approved by the Ethics Committee of the Asadabad School of Medical Sciences with the ethics code IR.ASAUMS.REC.1403.010. All procedures were approved by the above-mentioned committee.

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Supplementary Files

Supplementary file 1 contains search strategy and Table S1.

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