MEDICINAL PLANTS IN THE MANAGEMENT OF CLIMACTERIC AND MENOPAUSAL SYMPTOMS: A REVIEW

PLANTAS MEDICINAIS NO MANEJO DOS SINTOMAS DO CLIMATÉRIO E DA MENOPAUSA: UMA REVISÃO

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ABSTRACT

Climacteric, the hormonal transition phase that precedes and leads to menopause, is characterized by physical and emotional symptoms that can be alleviated through the use of phytotherapy. This study conducted a literature review on the use of such medicinal plants in managing climacteric and menopausal symptoms, drawing from databases such as PubMed, Scopus, SciELO, Web of Science, Google Scholar, IEEE Xplore, as well as government sources, using specific keyword combinations. Plant species such as *Cimicifuga racemosa*, *Trifolium pratense*, *Glycine max*, *Angelica sinensis*, *Vitex agnus-castus*, *Panax ginseng*, *Lepidium meyenii*, and *Morus nigra* have shown significant benefits. Their active compounds act on estrogen, serotonin, and dopamine receptors, exhibiting hormonal, anti-inflammatory, antioxidant, adaptogenic, immunomodulatory, and calming effects. These actions contribute to the relief of symptoms such as hot flashes, insomnia, anxiety, irritability, inflammation, mood and cognitive changes, vaginal dryness, fatigue, and low libido, while also promoting bone and cardiovascular health and hormonal balance. Thus, the use of medicinal plants with phytoestrogenic activity stands out as a promising and effective complementary approach to supporting women's health during the climacteric and menopausal periods.

KEYWORD: climacteric, menopause, phytoestrogens, medicinal plants.

RESUMO

O climatério, fase de transição hormonal que antecede e leva à menopausa, é caracterizado por sintomas físicos e emocionais que podem ser amenizados com o uso da fitoterapia. Este estudo realizou uma revisão da literatura sobre o uso de plantas medicinais no manejo dos sintomas do climatério e da menopausa, por meio de pesquisas em bases de dados como PubMed, Scopus, SciELO, Web of Science, Google Scholar e IEEE Xplore, utilizando combinações específicas de palavras-chave. Espécies como *Angelica sinensis*, *Cimicifuga racemosa*, *Glycine max*, *Lepidium meyenii*, *Morus nigra*, *Panax ginseng*, *Trifolium pratense* e *Vitex agnus-castus* demonstraram benefícios relevantes. Seus compostos ativos atuam sobre

receptores de estrogênio, serotonina e dopamina, apresentando efeitos hormonais, anti-inflamatórios, antioxidantes, adaptogênicos, imunomoduladores e calmantes. Essas ações contribuem para o alívio de sintomas como fogachos, insônia, ansiedade, irritabilidade, inflamações, alterações de humor e cognitivas, secura vaginal, fadiga e baixa libido, além de favorecerem a saúde óssea, cardiovascular e o equilíbrio hormonal. Dessa forma, o uso de plantas medicinais destaca-se como uma abordagem complementar promissora e eficaz no cuidado à saúde da mulher durante o climatério e a menopausa.
PALAVRAS-CHAVE: climatério, menopausa, fitoestrógenos, plantas medicinais.

INTRODUCTION

The climacteric is a transitional phase from a woman's reproductive to non-reproductive life, marked by the gradual decline of estrogen and progesterone, and accompanied by symptoms such as hot flashes, sleep disturbances, mood changes, and an increased risk of metabolic and cardiovascular diseases[1,2]. Menopause, in turn, is characterized by the cessation of menstruation and hypergonadotropic hypogonadism, involving reduced ovarian sensitivity and a marked drop in estradiol levels. In obese women, elevated levels of free androgens and their conversion into estrogens influence the severity of symptoms[3].

The decline in estrogen during menopause affects multiple body systems, including the heart, bones, skin, and brain[4]. Treatment is individualized and may involve hormone therapy, lifestyle modifications, complementary therapies, and psychological support[4]. Phytotherapy stands out as an alternative or complementary approach to conventional treatment, utilizing bioactive compounds such as phytoestrogens, which help regulate hormonal and metabolic functions, alleviating climacteric symptoms[5,6].

Among the most commonly used medicinal plants are *Angelica sinensis*, *Cimicifuga racemosa*, *Glycine max*, *Panax ginseng*, *Trifolium pratense*, and *Vitex agnus-castus*. These and other species, such as *Lepidium meyenii* and *Morus nigra*, have been used not only to alleviate climacteric and menopausal symptoms but also in the management of endocrine and female reproductive system disorders, including fibroids, premenstrual syndrome, menopause, polycystic ovary

syndrome, endometriosis, and sexual dysfunction, helping to reduce reliance on medications that often cause adverse effects[6].

This article aims to review the therapeutic use of medicinal plants in the management of climacteric and menopausal symptoms, highlighting phytoestrogens as bioactive compounds that partially mimic human estrogen. The review discusses their mechanisms of action, benefits, and potential risks, emphasizing the potential of these alternatives to improve quality of life during the hormonal transition.

METHODOLOGY

This study is a literature review based on sources such as PubMed, Scopus, SciELO (Scientific Electronic Library Online), Web of Science, Google Scholar, IEEE Xplore, and other bibliographic databases. To refine the searches, keywords such as phytotherapy, medicinal plants, climacteric, menopause, *Angelica sinensis*, *Cimicifuga racemosa*, *Glycine max*, *Lepidium meyenii*, *Morus nigra*, *Panax ginseng*, *Trifolium pratense*, *Vitex agnus-castus*, and hormone therapy were used, either individually or in combination.

Inclusion criteria encompassed studies related to the research topic, such as clinical trials, cohort studies, systematic reviews, full-text articles, official documents, theses, and dissertations, published in Portuguese, English, or Spanish. Studies that did not have a direct relationship with the topic, showed weak methodology or unreliable results, as well as conference abstracts, opinion pieces, letters to the editor, and duplicate studies across different databases, were excluded.

The selected studies were assessed based on their study design, sample size, internal and external validity, and potential biases. Relevant information from each study, including author, year of publication, methodology, key results, and conclusions, was extracted in an organized and standardized manner, facilitating comprehensive data analysis[7].

LITERATURE REVIEW

Angelica sinensis

Angelica sinensis (Oliv.) Diels, family Apiaceae, commonly known as *dong quai* or "female ginseng," is a plant used in traditional Chinese medicine for women's health[8,9]. Rich in phytoestrogens and other bioactive compounds, it exhibits hormonal, anti-inflammatory, antioxidant, and circulatory properties[9]. During the climacteric and menopausal periods, its main effects include relief of hot flashes and improvements in mood, sleep, vaginal, bone, and joint health[9,10].

A study involving 71 women showed that isolated *A. sinensis* extract was not more effective than placebo in alleviating menopausal symptoms[11]. In another study with 55 postmenopausal women, the combination of *A. sinensis* and chamomile reduced hot flashes and fatigue, demonstrating a beneficial effect of the combined extracts[12].

Regarding adverse effects, *A. sinensis* presents rare and mild events, such as gastrointestinal disturbances, photosensitivity, and occasional allergic or cardiovascular reactions[13]. Hepatotoxicity remains controversial, with reports of both hepatoprotective effects and liver injury associated with multi-herbal formulations or contamination[14,15]. There is a potential risk of interaction with anticoagulants and drugs metabolized by CYP3A4/CYP2D6, requiring caution when used concomitantly with warfarin or antidepressants[16]. Its use should be avoided during pregnancy and lactation due to photosensitizing furanocoumarins, ensuring therapeutic safety[17].

A. sinensis is consumed in capsule, extract, or tea form, or as part of herbal preparations and supplements. The infusion is typically prepared with 1–2 teaspoons of the dried root, while capsule or extract doses range from 300 to 500 mg[17].

Cimicifuga racemosa

Cimicifuga racemosa (L.) Nutt., family Ranunculaceae, commonly known as *black cohosh*, is a medicinal plant used in the management of climacteric and menopausal symptoms[18]. Its roots and rhizomes are the parts employed for therapeutic purposes due to their active compounds, including glycosylated triterpenes, flavonoids, and phenolic acids, among others[18,19].

The mechanisms of action of *black cohosh* are not yet fully understood, but its effects appear to involve interaction with estrogen receptors[20-22]. Its active compounds act on the central nervous system (CNS), particularly on serotonin receptors, helping to relieve vasomotor symptoms such as hot flashes[18,23,24]. They may also exhibit dopaminergic activity, reducing hot flashes[25], in addition to anti-inflammatory and antioxidant properties that contribute to menopausal well-being[22].

A double-blind clinical trial compared the effects of *C. racemosa* (CR BNO 1055), conjugated estrogens (CE), and placebo in 62 postmenopausal women over 12 weeks. Both CR and CE benefited bone metabolism, with CR stimulating osteoblasts and CE inhibiting osteoclasts. CE exerted a strong estrogenic effect on the vaginal mucosa, while CR demonstrated mild estrogenic activity and was well tolerated[26]. Furthermore, a retrospective study compared the effects of *C. racemosa* extract (CR, Ze 450) and menopausal hormone therapy in 174 women over 40 years old, showing that both treatments improved menopausal symptoms without affecting metabolic parameters or body weight[27].

Borrelli et al.[21] reported that adverse events associated with *C. racemosa*, such as nausea, gastrointestinal discomfort, headache, and rash, are rare and mild[25]. Although cases of liver injury have been reported, hepatotoxicity remains controversial, as systematic reviews indicate uncertain causality, particularly with low-quality or multi-herbal products[28]. *In vitro* studies suggest inhibition of CYP3A4 and CYP2D6 enzymes, indicating potential interactions with tamoxifen, anticoagulants, and antidepressants[25]. Use is contraindicated during pregnancy, lactation, and in individuals with hormone-sensitive cancers[25].

C. racemosa is effective in relieving climacteric and menopausal symptoms such as hot flashes, night sweats, muscle and joint pain, and also improves mood, sleep, and bone protection through its antioxidant and anti-inflammatory actions. However, its use requires caution in patients taking other medications or with pre-existing conditions[22]. It is administered in capsules, tablets, tinctures, or teas, with a standard dosage of 1–2.5 mg of triterpenes daily, divided into one or two doses, and should be used under individualized professional supervision[22,29].

Glycine max

Glycine max (L.) Merr. (soybean), family Fabaceae, is a leguminous plant rich in isoflavones (genistein, daidzein, and glycitein), proteins, fiber, vitamins, and minerals[30]. Its isoflavones have a structure similar to estradiol and act as partial agonists of estrogen beta receptors. In postmenopause, when estrogen levels are low, these phytoestrogens help compensate for hormonal deficiency, alleviating symptoms of hypoestrogenism[31].

During the climacteric and menopausal periods, *G. max* offers several benefits, such as the reduction of hot flashes through modulation of estrogen receptors in the CNS and regulation of body temperature[30,32]. Its phytoestrogens also help relieve irritability, mood changes, and insomnia, protect against cognitive decline, and improve vaginal lubrication[33]. In addition, it promotes bone health by stimulating osteoblasts and reducing bone resorption, while also improving lipid profile and blood pressure control[30,33].

An observational clinical study conducted in Spain with 190 postmenopausal women evaluated the daily use of 35 mg of soy isoflavones (PHYTO SOYA). After four months, 80.82% of participants showed a significant reduction in hot flashes (average decrease of 47.8%, corresponding to approximately four fewer episodes per day) and improvement in other symptoms, without severe adverse effects, indicating good tolerability and efficacy in relieving menopausal symptoms[34].

Adverse events associated with *G. max* (isoflavones) are rare and mild, including nausea, gastrointestinal discomfort, and headache, occurring at frequencies similar to placebo[35]. Hepatotoxicity is rare and controversial, mainly associated with low-quality products[36]. Reports suggest a possible reduction in warfarin efficacy[37] and inhibition of CYP3A4/CYP2D6, requiring caution with concomitant use of tamoxifen[38].

The use of soy isoflavones is generally safe and does not increase the risk of breast or endometrial cancer[39], distinguishing it from hormone therapy. However, caution is advised in cases of hormone-sensitive cancers[40]. The recommended dosage is 40–80 mg per day[39,40]. *G. max* represents an effective natural alternative for managing menopausal symptoms and can be consumed either through diet or supplementation.

Lepidium meyenii

Lepidium meyenii Walp. (Peruvian maca), family Brassicaceae, native to the Andes, has been traditionally used for its effects on hormonal balance and relief of climacteric and menopausal symptoms[41,42]. The species is rich in bioactive compounds such as macamides and macaenes, as well as alkaloids, sterols, antioxidants (flavonoids, polyphenols), and essential minerals (calcium, iron, zinc, and magnesium). Maca contributes to hormonal regulation, oxidative stress reduction, and maintenance of bone and metabolic health[41,43].

Although maca does not contain hormones, it is believed to regulate hormone production through the hypothalamic–pituitary axis via serotonergic mechanisms, influencing hepatic enzymes and hormones such as T_4[43]. Its extracts promote stress relief, hippocampal neurogenesis, and enhance serotonergic and noradrenergic transmission through the endocannabinoid system[43]. Maca helps reduce hot flashes and night sweats, improves mood, decreases anxiety and fatigue, and enhances libido, sexual function, bone and cardiovascular health, as well as cognitive symptoms[43].

Clinical studies indicate that maca may alleviate psychological symptoms and sexual dysfunction in postmenopausal women. In one trial with 14 participants (3.5 g/day for 6 weeks), no significant hormonal changes were observed, but reductions in anxiety, depression, and sexual dysfunction were reported, suggesting a non-hormonal mechanism of action[45]. Another study involving 45 women using 3 g/day for 12 weeks showed improvement in antidepressant-induced sexual dysfunction and good tolerability, highlighting its therapeutic potential[46].

In clinical trials, *L. meyenii* has shown good tolerability, with only mild and transient adverse effects such as gastrointestinal disturbances, insomnia, and headache[44]. Isolated maca does not exhibit hepatotoxicity and may even be hepatoprotective; adverse cases are linked to contaminated products[47]. There is no clinical evidence of significant interactions with anticoagulants, antidepressants, or tamoxifen, although theoretical potential exists through modulation of CYP3A4/CYP2D6[38,48].

Maca is consumed in powder, capsule, or extract form, with a recommended dosage of 1–3 g per day depending on individual needs[41,43]. The powder can be incorporated into foods and beverages. At higher doses, it may cause mild adverse effects. Although generally considered safe, it should be avoided by women with hormone-sensitive conditions such as breast or ovarian cancer[43].

Morus nigra

Morus nigra L. (black mulberry), family Moraceae, is used for its antioxidant, anti-inflammatory, and hormone-regulating properties[49,50]. Its benefits have been demonstrated in studies addressing climacteric and menopausal symptoms, menstrual and ovarian disorders, as well as in conditions such as mouth ulcers, diarrhea, sore throat, oral inflammation, and diabetes[50,51]. Consumption of this species improves vasomotor symptoms, sleep quality, bone health, mood, anxiety, and overall quality of life. It also exhibits antioxidant and cardiovascular effects, reduces cholesterol levels, helps prevent heart disease and aging, and promotes skin and hair health[52,53].

The main components of *M. nigra* include phytoestrogens, which help balance hormone levels during the climacteric and menopausal periods[49]. It also contains antioxidants such as flavonoids, anthocyanins, and vitamins C and E, which counteract oxidative stress, as well as essential minerals (calcium, magnesium, iron, and potassium) important for bone and cardiovascular health. Organic acids such as malic and citric acids support energy metabolism and cellular health[52,53].

Two clinical studies have demonstrated the benefits of *M. nigra* in managing climacteric symptoms. In a trial involving 62 women, the use of 250 mg/day of *M. nigra* leaf powder for 60 days significantly improved quality of life, showing effects comparable to hormone therapy[54]. Another study with 20 women showed that daily consumption of *M. nigra* leaf tea for 60 days alleviated various climacteric symptoms, including hot flashes, sleep disturbances, mood changes, and memory issues, as well as improving domains such as vitality, pain, and mental health[55,56]. These findings indicate that mulberry is effective in reducing menopausal symptoms and promoting women's well-being.

M. nigra has shown good tolerability in preclinical and clinical studies, with rare and mild adverse effects such as gastrointestinal symptoms and headache[54]. Evidence suggests hepatoprotective effects in animal models[57], although sporadic reports of hepatotoxicity exist. There is a potential for interaction through modulation of cytochrome P450 enzymes (CYPs) and P-glycoprotein (P-gp), and caution is advised for patients using immunosuppressants, P-gp–dependent anticoagulants, or drugs metabolized by CYPs, such as antidepressants and tamoxifen[56].

Mulberry is available in several forms, including teas (12 g of leaves per 1000 mL of water), capsules, tablets with standardized extracts, and liquid extracts or tinctures, allowing dosage adjustments[58,59]. The recommended intake is 1–2 cups of tea per day or 100–500 mg of standardized extract daily. Considered safe, *M. nigra* should nevertheless be used with caution during pregnancy and lactation due to potential interactions with anticoagulants, hormonal medications, and allergic

reactions[60]. It may serve as a supportive option for improving quality of life during menopause.

Panax ginseng

Panax ginseng C.A. Meyer, from the family Araliaceae, is widely used in traditional Asian medicine for its adaptogenic and restorative properties[61]. Its potential as a natural alternative for relieving climacteric and menopausal symptoms has been described in scientific literature[62]. Its effects are attributed to bioactive compounds such as ginsenosides, polysaccharides, essential oils, peptides, and vitamins. Ginsenosides, in particular, act on several systems, including the central nervous, cardiovascular, and immune systems[63].

P. ginseng may alleviate menopausal symptoms through hormone-like mechanisms similar to estrogen, although its ginsenosides do not directly bind to hormone receptors[64]. These compounds modulate steroid hormone sensitivity and help balance the hypothalamic–pituitary–adrenal axis[65]. Through its adaptogenic action, ginseng aids in reducing anxiety and fatigue and exhibits antioxidant and anti-inflammatory properties that protect tissues from damage associated with declining estrogen levels during menopause[66].

Clinical studies indicate that *P. ginseng* improves sexual function in climacteric women, particularly in relation to arousal. It has also been associated with improved quality of life, reduction of menopausal symptoms, decreased total cholesterol, LDL-c, and carotid intima-media thickness, without significant changes in HDL-c or triglycerides. Furthermore, reductions in anxiety, depression, and cortisol levels, along with increases in DHEA-S, have been observed, with only mild adverse effects reported[67-69].

In clinical trials, adverse effects of *P. ginseng* are mild to moderate and relatively infrequent, including insomnia, nervousness, headache, dizziness, gastrointestinal symptoms, mild cardiovascular changes[70], and skin reactions[71]. Reports of hepatotoxicity are limited and heterogeneous[72]. Interactions with warfarin may induce thrombosis through platelet or enzymatic activity[73].

Ginsenosides can modulate monoaminergic systems, potentially enhancing antidepressant effects and, in rare cases, triggering serotonin syndrome[74,75]. Although there is no solid evidence of interaction with estrogens or tamoxifen[76], caution is advised in pregnant or lactating women and in patients with arrhythmias or liver disease[73].

The dosage of *P. ginseng* varies depending on the preparation: powder (250–1,200 mg per dose; 600–2,000 mg per day), dry extract (40–360 mg per dose; 40–670 mg per day), soft extract (219–440 mg per dose; 440–700 mg per day), and liquid extract (500 mg–9.9 g per dose; 900 mg–19.8 g per day)[77]. Generally considered safe at appropriate doses, *P. ginseng* should be avoided by individuals with hypertension, insomnia, or coagulation disorders[78].

Trifolium pretense

Trifolium pratense L. (red clover), belonging to the Fabaceae family, is used in women's health, particularly in the treatment of climacteric and menopausal symptoms, due to the presence of isoflavones with phytoestrogenic activity[79,80]. Compounds such as genistein, daidzein, biochanin A, and formononetin can bind to estrogen receptors, exerting a modulatory hormonal effect[80].

Red clover may reduce vasomotor symptoms, such as hot flashes and night sweats, and contribute to bone health by stimulating bone formation and inhibiting bone resorption, thereby helping to prevent osteoporosis[79,81,82]. It also exerts positive effects on lipid metabolism, lowering LDL cholesterol and increasing HDL cholesterol, which supports cardiovascular health[79,83]. Additionally, *T. pratense* may improve mood, sleep quality, and reduce anxiety[84].

A randomized, double-blind, placebo-controlled clinical trial evaluated 120 women aged 45–65 years who had been in amenorrhea for over one year, divided into a group treated with *T. pratense* (40 mg/day) and a placebo group for 12 months. Although symptom improvement was observed, particularly in hot flashes, *T. pratense* did not demonstrate statistically significant efficacy in reducing overall menopausal symptoms or in sexual satisfaction[85].

In studies involving climacteric women, *T. pratense* showed a favorable safety profile, with mild adverse effects such as headache, gastrointestinal discomfort, joint pain, and occasional mastalgia[86]. Evidence of hepatotoxicity is limited, and monitoring is recommended in cases of hepatic dysfunction[87]. Due to the presence of coumarins, *T. pratense* may affect coagulation, requiring caution when used concomitantly with warfarin[88]. Although rare, possible enzymatic interactions with antidepressants cannot be ruled out[89]. Because it contains phytoestrogens, the use of *T. pratense* warrants caution in individuals with hormone-sensitive neoplasms and is contraindicated during pregnancy and lactation[90].

T. pratense is available in various formulations, including dry or liquid extracts, capsules, tablets, teas, and combined menopausal formulas[90,91]. The recommended dosage ranges from 40 to 80 mg per day, as excessive phytoestrogen intake may disrupt hormonal balance[79,90]. Professional supervision is essential to ensure safety and therapeutic efficacy[90].

Vitex agnus-castus

Vitex agnus-castus L., of the Verbenaceae family, commonly known as chaste tree, is widely used for its regulatory effects on the female endocrine system, being employed to relieve menstrual cycle-related symptoms such as premenstrual syndrome (PMS), mastalgia, and menstrual irregularities[92]. It has also been proposed as a therapeutic alternative for climacteric and menopausal symptoms[93]. Its pharmacological effects are attributed to bioactive compounds including diterpenes (agnuside and casticin), flavonoids, and essential oils, which act on the pituitary gland to modulate estrogen and progesterone balance, while also influencing the CNS to reduce irritability, anxiety, and mood changes[94].

In a multicenter, double-blind, placebo-controlled clinical trial, the extract of *Vitex agnus-castus* (VAC BNO 1095, 40 mg) was found to be safe, well tolerated, and effective in the treatment of moderate-to-severe PMS, producing a significant reduction in symptoms compared with placebo and no serious adverse

events[95]. Another study confirmed the efficacy of chaste tree extract in relieving mastalgia and PMS symptoms: in women with mild to severe mastalgia, daily administration of 40 mg extract significantly reduced prolactin levels and breast pain, with results comparable to bromocriptine[96]. Using 5 mg daily of the extract over three menstrual cycles, *Vitex* reduced PMS severity in 67% of study participants[92]. Furthermore, a randomized, placebo-controlled trial demonstrated that chaste tree extract reduced the intensity of cyclic mastalgia by 53% by the second menstrual cycle[97].

Comparative studies between *V. agnus-castus* extract and fluoxetine indicate that both reduce PMS symptoms, but with distinct profiles: chaste tree is more effective for somatic symptoms such as breast tenderness, edema, and increased appetite, whereas fluoxetine shows greater efficacy for neurological symptoms like insomnia, depression, and nervous tension[98]. Ciotta et al.[99] reported that chaste tree outperformed fluoxetine in overall performance, particularly in mood and somatic symptoms, making it preferable for physiological manifestations of PMS. The extract Ze 440 (20 mg/day) reduced symptoms by 52%, compared with 24% for placebo, without significant adverse effects[100]. Capsules of Agnolyt P, containing chaste tree extract, produced clinical improvement in 77.1% of patients, surpassing the 60.6% response in the pyridoxine group, demonstrating a favorable benefit–risk ratio[101].

In clinical trials and systematic reviews, *Vitex agnus-castus* exhibits mild and infrequent adverse effects, including nausea, headache, gastrointestinal discomfort, acne, and mastalgia[102]. Reports of liver injury are rare and do not confirm hepatotoxicity, though monitoring is recommended in patients with hepatic disease[87]. There is no evidence of increased bleeding risk or serotonin syndrome[103]. Due to its dopaminergic modulation and prolactin-reducing action, potential interactions may occur with dopaminergic or antipsychotic drugs[104,105].

Vitex is generally consumed as capsules, tablets, or liquid extract, with a recommended daily dosage of 20–40 mg of dry extract, depending on the formulation[105]. Its use is not recommended during pregnancy or lactation, nor in

women undergoing hormone replacement therapy or using hormonal contraceptives, due to possible hormonal interference and drug interactions[105].

COMPARISON BETWEEN HORMONE THERAPY AND THE USE OF MEDICINAL PLANTS

Medicinal plants rich in soy isoflavones (*G. max*), and to a lesser extent *T. pratense* and *C. racemosa*, have shown a significant reduction in vasomotor symptoms compared with placebo, according to meta-analyses and randomized clinical trials (RCTs). In mild to moderate cases, their effects may approach those of hormone therapy, particularly in short-term or small-sample studies. However, the quality of evidence is heterogeneous, varying according to formulation, dosage, and standardization, and the results tend to be less consistent than those observed with hormone therapy[106].

Hormone therapy (HT) remains the gold standard for treating severe vasomotor symptoms and preventing osteoporosis, as evidence regarding medicinal plants is still limited. Recent international clinical guidelines recommend HT as the first-line treatment for symptomatic women, provided there are no contraindications[107,108].

Herbal extracts such as *V. agnus-castus*, *P. ginseng*, and *L. meyenii* have demonstrated modest benefits on sleep and mood in randomized clinical trials (RCTs), although with inconsistent results and few direct comparisons with hormone therapy[109]. Their use may represent an alternative for mild to moderate symptoms or when HT is contraindicated. Formulation, dosage, duration of use, potential drug interactions, and a history of hormone-sensitive cancer should be carefully considered, as these factors influence both safety and therapeutic efficacy[106].

In summary, Table 1 presents a comparison between hormone therapy and the main medicinal plants discussed in this study regarding their clinical efficacy in alleviating climacteric and menopausal symptoms.

Table 1. Comparative analysis of the efficacy of hormone therapy and medicinal plants in the treatment of climacteric and menopausal symptoms

Plant / Treatment	Hot flashes vs. Placebo	Hot flashes vs. HT	Sleep	Mood / Anxiety / Depression	Level of Evidence
TH	++	++	++	++	++
G. max	+	±	±	±	−/±
T. pratense	±	−/±	−/±	−/±	±
C. racemosa	+/±	−	+/±	+/±	±
V. agnus-castus	±	−	±	+	−/±
P. ginseng	±	−	+/±	+	±
L. meyenii	±	−	+/±	+	±
A. sinensis	−/±	−	−	−	−/±
M. nigra	±	±	±	±	±

Legend: ++ strong/consistent; + moderate; ± inconsistent/heterogeneous; − no clear evidence. HT = Hormone Therapy.

DISCUSSION

Since ancient times, medicinal plants have been used to treat various health conditions, long before scientific validation. Their efficacy partly results from the synergistic or additive action among their multiple components, which enhance therapeutic effects. However, herbal medicines intended for human use must comply with Good Manufacturing Practices and undergo rigorous clinical trials to demonstrate efficacy, assess pharmacokinetics, and identify potential adverse events, thereby ensuring their safety and effectiveness[113].

Among the plants used for managing climacteric and menopausal symptoms, *C. racemosa* stands out for containing glycosylated triterpenes, flavonoids, and phenolic acids, which interact with serotonin and estrogen receptors and exert antioxidant and anti-inflammatory actions similar to those of *A. sinensis*[19,23]. *T. pratense* and *G. max*, both rich in isoflavones, act as phytoestrogens by modulating estrogen receptors and supporting bone, cardiovascular, and overall health[31]. In turn, *V. agnus-castus* regulates hormones through dopaminergic modulation, making it useful in cases of hyperprolactinemia[94].

With adaptogenic and antioxidant properties, *P. ginseng* promotes vitality, cardiovascular health, and relief of psychological symptoms, although monitoring is required due to potential drug interactions[63,66]. *L. meyenii* contributes to hormonal balance by regulating the hypothalamic-pituitary axis, improving psychological symptoms and sexual dysfunction without direct estrogenic activity[43]. *M. nigra*, rich in phytoestrogens, flavonoids, and anthocyanins, alleviates vasomotor symptoms and supports bone, cardiovascular, and aesthetic health, standing out for its antioxidant and hormone-regulating effects[49,53].

The therapeutic effect of medicinal plants depends on the concentration of active compounds, making extract standardization essential to ensure reproducibility and safety. In studies with *T. pratense*, effective doses range from 40–80 mg/day of total isoflavones (formononetin, biochanin A, genistein, and daidzein), equivalent to approximately 80 mg of genistein[84]. Trials using the standardized extract *Promensil*® (80 mg/day) demonstrated efficacy in relieving hot flashes and good tolerability[114,115]. Likewise, *C. racemosa* (extract CR BNO 1055, 20 mg/day), rich in glycosylated triterpenes, has shown proven efficacy[116]. The use of standardized extracts ensures consistency, efficacy, and safety[114].

In a study involving *M. nigra* in climacteric women (n = 62; 60 days), symptom improvement was observed, although the short follow-up period and small sample size limit generalization[54]. For *A. sinensis*, reviews indicate that many trials are small-scale or conducted in specific populations, compromising the robustness of conclusions[15]. Although randomized, double-blind studies such as that by Fung et al.[117] exist, methodological limitations, such as lack of allocation concealment and absence of intention-to-treat analysis, may overestimate benefits. Chemical variability among *M. nigra* cultivars[118] and *A. sinensis* formulations[119] further complicates comparisons and standardization. Moreover, many *A. sinensis* trials are limited to Chinese populations, restricting extrapolation[119]. In a cohort study, Chen et al.[120] emphasized that the retrospective design and lack of data on adherence and herb–drug interactions preclude causal inferences.

As observed, although more robust studies are needed to compare the efficacy of the medicinal plants analyzed here with that of hormone therapy, clinical evidence and traditional use indicate meaningful benefits, particularly in relieving symptoms such as hot flashes, insomnia, and mood disturbances, while offering the advantage of fewer side effects. Additionally, these species contribute to bone and cardiovascular health, possess antioxidant properties, and promote improvements in quality of life[22,30,32,79]. When used appropriately, they demonstrate good tolerability and a low risk of adverse events, which are generally mild and rare. Nevertheless, supervision by a healthcare professional is essential to ensure treatment efficacy and safety, especially during long-term use.

CONCLUSION

The use of medicinal plants in managing climacteric and menopausal symptoms offers a promising alternative to hormone therapy, with benefits that include improvements in bone and cardiovascular health, relief of vasomotor symptoms, and support for psychological well-being. Species such as *C. racemosa*, *T. pratense*, and *G. max* have demonstrated efficacy with a lower incidence of serious side effects, while others, such as *V. agnus-castus*, provide complementary support in managing specific symptoms. However, the use of these products requires caution due to potential adverse reactions and drug interactions and must be guided by scientific evidence, appropriate regulations, and product quality standards.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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