

Use of dietary supplements to alleviate vasomotor symptoms among menopausal women

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Vasomotor symptoms (VMS), such as hot flashes and night sweats, are the most commonly reported symptoms among menopausal women. Clinical guidelines recommend hormone therapy and/or nonhormonal prescription medication for VMS. However, due to personal concerns and/or beliefs, women may prefer complementary and integrative health approaches. Hence, it is important for nurse practitioners to have a good understanding of the full spectrum of treatment options and to individualize care to each woman's concerns, beliefs, and preferences.

KEY WORDS: menopausal symptoms, vasomotor, alternative, herbal, complementary medicine

Womens Healthcare. 2023;11(2):35-41. doi: 10.51256/WHC042335

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Vasomotor symptoms (VMS), including hot flashes and night sweats, are very common in women undergoing menopause.^{1,2} These symptoms typically result from the alteration of the hypothalamus-pituitary-ovarian-uterine axis as the body undergoes perimenopausal processes such as ovarian aging, hormone fluctuations, decreased estrogen levels, irregular menstrual cycles and cessation.^{3,4} As a result, 75% of women transitioning naturally and the majority of women with medically induced menopause experience VMS.^{4,5} VMS also can be accompanied by a variety of other symptoms such as changes in mood, cognition, sleep, and vaginal dryness, headaches, and decreased libido.^{6,7} These can have a compounding or clus-

tering effect, negatively impacting quality of life.^{5,6,8} Although hormone therapy (HT), selective serotonin reuptake inhibitors (SSRIs), and serotonin and norepinephrine reuptake inhibitors (SNRIs) are clinically standardized treatments, many women seek alternatives with fewer adverse side effects.⁹ Among the options are complementary and integrative health (CIH) alternatives such as acupuncture, homeopathy, mind-body techniques such as meditation, mindfulness, yoga, biofeedback, and guided imagery, and dietary supplements.⁹ This article reviews current knowledge about the efficacy and safety of available dietary supplements to alleviate VMS in menopausal women and implications for clinical practice.

Clinical treatment guidelines

In 2011, the American Association of Clinical Endocrinologists released guidelines for the diagnosis and treatment of VMS.¹⁰ Three years later, the American College of Obstetricians and Gynecologists and the North American Menopause Society (NAMS) published clinical guidelines and recommendations for clinical care of menopausal women.^{11,12} While dated, these guidelines may still be directing clinical practice. The most recent guidance comes from NAMS' 2022 hormone therapy position statement, which is endorsed by multiple international and national menopause and women's health associations. A summary of current clinical recommendations for VMS management is provided here.¹³

The first line of treatment for VMS is HT with or without progestin, depending on whether the woman has an intact uterus.¹⁰⁻¹² Due to health risks such as cancer (ie, endometrial, breast, uterine, colon), thrombotic events, and cardiovas-

cular events, HT should be given at the lowest dose and for the shortest period to alleviate symptoms.¹⁰⁻¹² Clinical guidelines for nonhormonal treatments include SSRIs, clonidine, gabapentin, and SNRIs.¹⁰⁻¹² Side effects of these nonhormonal treatments include nausea, dry mouth, shakiness, and dizziness.¹¹ Empiric data to support the use of CIH supplements (ie, phytoestrogens, herbal supplements, vitamins, and minerals) is lacking. For now, none of the guidelines support the use of CIH supplements. However, it is important to note that studies investigating CIH supplement safety and efficacy are ongoing.

CIH supplements

The National Center for Complementary and Integrative Health states that while HT is the most effective treatment for VMS, there are multiple health concerns regarding their use (eg, cancers, thrombotic events, coronary events).¹⁴ In the Woman's Health Initiative released in 2002, findings from two large, randomized HT trials showed the risks of HT outweigh the benefits.¹³ Since that time, reanalysis of these data and information from other trials have reduced many of the safety concerns. Based on this information, the 2022 NAMS guidelines state that the benefits of HT outweigh the risks for symptomatic women younger than age 60 or within 10 years of menopause who have no contraindications.¹³ These guidelines also state that although the benefit-risk ratio may be less favorable, women older than 60 or more than 10 years from menopause onset with persistent VMS affecting quality of life can continue HT based on shared decision making and careful follow-up.¹³ Due to remaining concerns about health

risks and unwanted side effects when taking HT, there are women and healthcare providers opting for a more integrative approach to individualized care and seeking alternative methods for the treatment of VMS.¹⁴ Data suggest that CIH supplements may aid in alleviating VMS among menopausal women.¹⁵⁻

⁴⁰ These CIH supplements are discussed here and in the Table.



Phytoestrogens

Phytoestrogens are the most frequently used alternative products for VMS.¹⁵⁻¹⁸ Found in plants, fruits, or vegetables, one major class of phytoestrogens is isoflavones.¹⁵⁻¹⁸ Isoflavones can be found in soybeans and soy products.^{9,15-18} Phytoestrogens have chemical structures that resemble estradiol and have estrogenic effects.^{9,15-18} Recent studies suggest that these estrogenic qualities may have positive effects for the treatment of VMS.¹⁵⁻¹⁸ Epidemiologic studies show that women in Asian countries, such as China and Japan, have a much lower incidence of VMS compared to women in Western countries, such as the United States, possibly due to a higher soy intake.^{16,17} In a meta-analysis of 15 high-quality randomized controlled trials, hot flashes were reduced in participants taking soy isoflavones tablets or capsules ranging from 5 mg to 100 mg when compared to the use of a placebo.¹⁷ Due to their natural estrogenic effects, there are safety concerns with phytoestrogens such as higher risk for cancer (eg, breast, endometrial, uterine, ovarian, colon), thromboembolic events, and/or cardiovascular events that warrant further studies.¹⁸ Phytoestrogens have minimal side effects and can be obtained by adding soy-rich foods to a balanced diet.¹⁶⁻¹⁸

Table. Complementary and integrative health supplements^{16,17,19,21–29,33,34,36,39,42,43}

Supplement	Dosage	Action	Side effects	Contraindications
Phytoestrogens	Isoflavones 80 mg daily	<ul style="list-style-type: none"> Reduces hot flashes Reduces inflammation 	GI symptoms (nausea, bloating, diarrhea, constipation)	Strong family history of hormone-dependent cancers (breast, uterine, ovarian) or of thromboembolic or cardiovascular events
Valerian	530 mg twice daily	<ul style="list-style-type: none"> Reduces hot flashes Improves sleep quality Improves anxiolytic symptoms Improves depressive symptoms 	<ul style="list-style-type: none"> GI symptoms (nausea, abdominal cramps) Abnormal heart rhythm Headaches 	<ul style="list-style-type: none"> Abnormal heart rhythm Drug interactions: (benzodiazepines, barbiturates, antidepressants, opiates or narcotics, OTC or prescription sleep aids, dietary supplements such as St. John's Wort, kava, melatonin)
Black cohosh	20 mg twice daily	<ul style="list-style-type: none"> Reduces hot flashes Reduces joint pain 	GI symptoms (nausea, vomiting)	Liver disease
Ashwagandha	300 mg twice daily	<ul style="list-style-type: none"> Reduces hot flashes Reduces inflammation Improves anxiolytic symptoms Improves depressive symptoms 	<ul style="list-style-type: none"> GI symptoms (abdominal pain, abdominal discomfort, insomnia, nausea) Hepatotoxicity in high doses 	Liver disease
Evening primrose	500 mg–1,000 mg twice daily	<ul style="list-style-type: none"> Reduces hot flashes Reduces inflammation 	<ul style="list-style-type: none"> Mild GI symptoms (nausea, vomiting, diarrhea, bloating) Anticoagulant effect Lowers seizure threshold in patients with seizure disorders or taking antiepileptic drugs 	<ul style="list-style-type: none"> Taking anticoagulants Seizure disorders
Curcumin	500 mg daily	<ul style="list-style-type: none"> Reduces hot flashes Reduces inflammation Improves anxiolytic symptoms Improves depressive symptoms Anticancer properties Improves cognition 	<ul style="list-style-type: none"> GI symptoms (loose stools, reflux, bloating, abdominal discomfort) Hepatotoxicity rare in high doses Anticoagulant properties Elevated liver enzymes Decrease in serum iron 	<ul style="list-style-type: none"> Iron deficiency Anemia of chronic disease Liver disease
Pollen extracts	20 g–40 g daily	<ul style="list-style-type: none"> Reduces hot flashes Reduces inflammation 	<ul style="list-style-type: none"> GI symptoms (constipation, nausea) Skin rash Headaches Allergic reactions (urticaria, itching, sneezing, angioedema) Hepatitis 	<ul style="list-style-type: none"> Liver disease Allergies or hypersensitivity to bee pollen or other bee products
Omega-3 supplements	<ul style="list-style-type: none"> FDA approved for age > 18 years 425 mg/dL twice daily as adjunct to diet and exercise 	<ul style="list-style-type: none"> Reduces hot flashes Reduces inflammation Lowers triglycerides 	<ul style="list-style-type: none"> GI symptoms (fishy taste, dyspepsia, diarrhea, eructation, gas, nausea) Headache Arthralgia Altered platelet function Lipid peroxidation 	On anticoagulant, antiplatelets, or simvastatin
Vitamin E	500 mg orally twice daily	<ul style="list-style-type: none"> Reduces hot flashes Reduces inflammation 	<ul style="list-style-type: none"> GI symptoms (abdominal pain and discomfort, vomiting, diarrhea) Headache Allergic reaction Rash Increased bleeding tendencies 	On anticoagulants

GI, gastrointestinal; OTC, over the counter.



Valerian

Valerian (*Valeriana officinalis*), also known as cat grass, is a widely used phytoestrogenic herb with sedative and/or anxiolytic effects.^{19,20} It contains components that act on the central nervous system, aiding relaxation and improved sleep quality in menopausal women.²⁰ Studies indicate that valerian may reduce VMS as well as anxiety and depressive symptoms.^{19,20} In a triple-blind randomized clinical trial, 64 menopausal women with VMS received either valerian capsules (530 mg twice daily) or placebo.²¹ After 2 months, the valerian group reported a reduction in VMS as compared to the placebo group.²¹ The results of this study suggest that valerian may be a potential approach to alleviating VMS among menopausal women.²¹ While no side effects were reported in this study, other studies have reported gastrointestinal (GI) symptoms such as nausea and abdominal cramps.^{21,22}

Black cohosh

Black cohosh (*Cimicifuga racemosa* or *Actaea racemosa*) is a perennial plant and the most widely studied botanical used to treat VMS.¹⁸ Of the 13,096 menopausal women treated with tablets of black cohosh ranging from 8 mg to 128 mg in a 35-study meta-analysis, a reduction in VMS was seen after 4 weeks.²³ Sleeping difficulties and anxiety also were reduced.²³ Black cohosh demonstrates dopaminergic, serotonergic, and GABAergic effects that aid in addressing hot flashes and assisting with thermoregulation, mood, and

sleep.^{9,20,23} Treatment with black cohosh is generally well tolerated with few to no side effects other than some reports of GI symptoms such as nausea and vomiting.²³ In rare cases, a concern with long-term use of black cohosh is hepatotoxicity.^{9,24} However, other studies report no significant changes in liver function parameters.²³ Data indicate that black cohosh is a relatively safe supplement, but caution should be taken due to the variety of different dosages on the market.^{10,23}



Ashwagandha

Ashwagandha (*Withania somnifera*) has been used in Ayurvedic medicine for thousands of years to enhance longevity, improve overall health, and to treat stress and anxiety.^{25,26} Ashwagandha, believed to raise estradiol levels through its antioxidant effects, is known for its calming and mood-enhancing abilities.^{25,26} Studies indicate that ashwagandha may improve VMS and mood in menopausal women.^{25,26} In an 8-week, randomized, double-blind, placebo-controlled study, 100 women with menopausal symptoms were placed into two groups, an ashwagandha group and a placebo group.²⁵ Results of the study showed that women given ashwagandha 300 mg capsules twice daily experienced improvements in VMS after 8 weeks.²⁵ More long-term studies are required to examine the

safety and efficacy of ashwagandha treatment for VMS.²⁵ Side effects reported were mild (ie, abdominal pain, abdominal discomfort, nausea, insomnia).^{25,26} Long-term use of ashwagandha has been linked to hepatotoxicity.²⁷

Curcumin

Curcumin (*Curcuma longa*) is a polyphenolic component of the turmeric spice used for centuries for its anticancer, anti-inflammatory, and antioxidant properties.^{28,29} Curcumin is recognized worldwide for multiple potential health benefits, and recent studies show positive outcomes for its use in alleviating VMS in menopausal women.²⁸ In an 8-week, triple-blind randomized controlled trial among 81 menopausal women, reduction in hot flashes was seen in the curcumin group (taking 500 mg capsules twice daily) after 4 weeks compared to the placebo group.²⁸ The setbacks with taking a curcumin supplement are poor absorption, rapid metabolism, and rapid elimination.³⁰ Piperine, a known bioavailability enhancer, is associated with an increase in the bioavailability of curcumin and has been added to various oral curcumin supplements.³⁰ Curcumin has been approved by the US Food and Drug Administration and is available in many forms (eg, capsules, tablets, ointments, powders).³⁰ Minimal side effects have been reported such as GI symptoms (ie, nausea, diarrhea, yellow stool), headache, and rash.³¹ Recent concerns of hepatotoxicity have been linked to curcumin.³¹ Anemia and iron deficiency have been linked to curcumin intake.³² Overall, this appears to be a relatively safe supplement, although no long-term safety studies have been done.³²



Evening primrose

Evening primrose (*Oenothera biennis*) is a botanical with anti-inflammatory properties.^{33,34} It contains high levels of essential fatty acids such as omega-6 fatty acids and gamma-linolenic acid.^{33,34} For many years, Native Americans utilized the anti-inflammatory effects of evening primrose for dermal treatments, GI issues, and sore throats.^{33,34} In an 8-week randomized controlled trial of evening primrose among 170 menopausal women, improvements in night sweats were reported in the evening primrose group (taking 1,000 mg capsules daily) compared to the placebo group. Hot flashes remained unchanged.³³ However, other investigators have found menopausal women taking 1,000 mg capsules of evening primrose daily experience less severe VMS and improved quality of life.^{18,33,34} Side effects of evening primrose include mild GI symptoms (ie, nausea, vomiting, diarrhea, bloating) and lowering the seizure threshold in patients with seizure disorders or taking antiepileptic drugs.³⁰ Evening primrose is contraindicated in women taking blood thinners due to its anticoagulant effect.^{20,30}

Pollen extracts

Pollen extracts from the grass (*Poaceae*) family including rye (*Secale cereale*) have been shown to alleviate the symptoms of menopause.³⁶ In a randomized controlled trial among 54 menopausal women, intervention participants were given two tablets every morning with 40 mg of pure pollen extract (GC Fem), and 120 mg of a combined pollen and pistil extract (PI 82) per tablet.³⁶ The intervention group reported a decrease in hot flashes over a 3-month period.³⁶ At follow-up, participants who received a sec-

ond course of pollen extracts had additional positive effects over and above the original study.³⁶ Although the mechanism of action of pollen extracts is yet to be elucidated, the effects are believed to be due to their strong antioxidant power.³⁶ For safety reasons, more long-term studies are warranted.³⁶

Omega-3 fatty acids

Omega-3 fatty acids are polyunsaturated fatty acids (PUFAs) containing alpha-linolenic acid, eicosatetraenoic acid, and docosahexaenoic acid.^{37,38} Omega-3 fatty acids are found in fish (eg, sardines, tuna, salmon, halibut, other fish), some plants (ie, green leafy vegetables), seeds, nuts, and beans.^{37,38} PUFAs are known for their anti-inflammatory and triglycerides-decreasing effects as well as lowering risk for chronic diseases such as heart disease, cancer, and arthritis when ingested.^{37,38} There has been speculation that omega-3 supplements can aid alleviating VMS.³⁹ In a 16-week randomized controlled trial, a group of 86 healthy postmenopausal women were separated into two groups, with one group given two 425 mg omega-3 capsules and one group given two isoflavone capsules containing 54.4 mg of isoflavones per tablet.³⁹ The results showed a reduction in hot flashes in both groups.³⁹ It suggests that omega-3 supplements may aid in reducing hot flashes in menopausal women, but more studies are required to test for efficacy.³⁹ FDA-approved fatty acid supplements (eg, icosapent ethyl, omega-3-acid ethyl esters, omega-3-carboxylic acids, omega-3-acid ethyl esters) are generally safe with mild side effects such as GI symptoms (eg, fishy taste, dyspepsia, diarrhea, eructation, gas, nausea) and arthralgia.³⁷ Omega-3 fatty acids may affect platelet activation, so patients taking antico-

agulants and antiplatelets should not use omega-3 supplements.^{37,38} There has been some concern for adverse effects on wound healing and lipid peroxidation.^{37,38}



Vitamin E

Vitamin E is an essential lipid-soluble antioxidant found in vegetable oils, nuts, seeds, and green leafy vegetables.⁴⁰ Good sources of vitamin E include sunflower seeds, almonds, peanuts, olive oil, spinach, and broccoli.⁴⁰ There are some studies that show vitamin E may reduce VMS in menopausal women.^{28,29} In an 8-week randomized controlled trial among 93 menopausal women, there was a reduction in hot flashes after 4 weeks in the vitamin E group given 200 IU capsules twice daily.^{28,29} Vitamin E has known anti-inflammatory effects that are believed to be the mechanism for alleviating VMS.^{28,29} Side effects reported were GI symptoms (ie, abdominal pain and discomfort, vomiting, diarrhea), headache, allergy, and skin rash.^{28,29} There are concerns that vitamin E toxicity can lead to increased bleeding. Therefore patients on anticoagulants should use caution when taking vitamin E as a supplement.^{28,29}

Implications for clinical practice

Menopause is an individual experience and nurse practitioners can support menopausal women by individualizing care to each

woman's concerns, beliefs, and preferences.^{10-14,41} Offering menopause counseling that includes discussing changes in physiology, menopause-related symptoms, psychosocial issues, and treatment options facilitates informed decision making.^{10-14,41} CIH supplements may be a viable option for women who wish to avoid the side effects of or are unable to take HT and non-hormonal prescription medication for VMS. When suggesting over-the-counter (OTC) supplements, it is important to remember that regulation of dietary supplements by the FDA is extremely limited.¹⁰⁻¹⁴ The amount, composition, and quality of supplements will vary depending on brand.¹² When choosing CIH supplements, contraindications should be assessed and current medications reviewed to ensure that the selected CIH supplement does not result in detrimental interactions.^{10,12} Potential side effects and dose-related toxicity should be discussed.

It is important to note that phytoestrogens, vitamin E, curcumin, and omega-3 fatty acids may be introduced into the diet via food sources, rather than OTC CIH supplements.^{16,28,29,37,41} A diet rich in plant-based foods (ie, fruits, vegetables, whole grains, nuts) may aid menopausal women in the self-management of VMS.¹⁰⁻¹⁴

Promoting lifestyle modifications may be beneficial for menopausal women with VMS.¹⁰⁻¹² For example, although efficacy has not been supported by empiric evidence, some women report relief by avoiding identified triggers such as caffeine and alcohol, drinking cool liquids, using fans and air conditioning, and the layering of light cotton clothing. Nurse practitioners will want to stay apprised of ongoing study findings regarding efficacy and safety of herbal and dietary

supplements for management of VMS. As well, they may want to become knowledgeable about other CIH options that women might be considering for VMS so as to provide evidence-based information to aid in decision making. ■

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