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| |  | | --- | | Natural Medicines in the Clinical Management of Menopausal Symptoms | |
| |  | | --- | |  | |  | | |  |  |  | | --- | --- | --- | | |  |  | | --- | --- | | Introduction | [return to top](http://naturaldatabase.therapeuticresearch.com.mainehealth.idm.oclc.org/ce/CECourse.aspx?cs=naturalstandard&s=ND&pm=5&pc=16-111#top) | | | |  | | --- | | A hundred years ago menopause was not as big of a concern as it is today. In 1900, women typically lived to about age 50. The typical age of menopause was 51. Today, the typical age of menopause is still 51, but life expectancy is closer to 80 years. Women now spend much more time in menopause and post-menopause.  Conjugated estrogens (*Premarin*) were introduced in 1942. But it didn't become popular until 1966 when Dr. Robert Wilson promoted it in his book, *Feminine Forever*. The discovery of the connection between estrogen and uterine cancer resulted in the addition of a progestin in the 1980s to help protect against endometrial hyperplasia. In the 1990s, long-term "hormone replacement therapy" (HRT) was being used by millions of women to prevent osteoporosis, cardiovascular disease, Alzheimer's disease, and other postmenopausal disorders.  This all changed in 2000. The study results from the huge Women's Health Initiative (WHI) and the Heart and Estrogen/Progestin Replacement Study (HERS II) found conjugated estrogen plus medroxyprogesterone actually INCREASES the risk of myocardial infarction, stroke, venous thromboembolism, and breast cancer.10958,10959,10960,10961 Since HERS II, additional findings have added concerns about an INCREASED risk for dementia and urinary incontinence.10962,10963 Estrogen/progestin also does NOT seem to improve quality of life in older postmenopausal women without menopausal symptoms.10964 Estrogen still has its place, but is no longer considered a drug for all problems of menopause.  Estrogen/progestin therapy is now only recommended short-term for controlling menopausal symptoms. Most experts recommend not using it for more than five years. And many women are now turning to alternatives. | | | | |  |  |  | | --- | --- | --- | | |  |  | | --- | --- | | Menopausal Changes | [return to top](http://naturaldatabase.therapeuticresearch.com.mainehealth.idm.oclc.org/ce/CECourse.aspx?cs=naturalstandard&s=ND&pm=5&pc=16-111#top) | | | |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | | The menopause transition is the transition between fertility and menopause when menses becomes less frequent. It is also often called perimenopause or climacteric. Menopause is defined as the cessation of menstrual cycles for 12 consecutive months. Unlike other endocrine glands which function life-long, the ovaries are programmed to shut down after about 50 years. The age of natural menopause ranges from about 40 to 58 years.10965,10966  Menopausal symptoms can persist for weeks, months, or years. Symptom severity varies greatly among women. Early signs are irregular or prolonged menstrual bleeding that can become severe. As estrogen levels decline, vasomotor symptoms, including hot flashes and night sweats (hot flashes with drenching sweats) can also occur. This can set up a domino effect where the night sweats interfere with sleep, causing exhaustion, leading to irritability and adverse effects on mood. Up to 85% of women have hot flashes with widely varying intensity and frequency. Some women report "triggers" that affect the frequency and/or severity of hot flashes.   |  | | --- | | **Potential Hot Flash "Triggers"** | | * Alcohol * Hot or spicy foods * Caffeine * Stress * Hot drinks * Warm environment |   Women can also experience many non-vasomotor symptoms.10965,10966   |  | | --- | | **Non-vasomotor Symptoms of Menopause** | | * Anxiety * Depression * Difficulty with concentration * Difficulty with decision making * Difficulty with memory * Headaches * Insomnia * Irritability * Joint pain * Loss of libido * Mood swings * Tiredness * Vaginal dryness |  |  | | --- | | What menopausal symptoms are your patients concerned with the most? | | | | | |  |  |  | | --- | --- | --- | | |  |  | | --- | --- | | Lifestyle Modifications | [return to top](http://naturaldatabase.therapeuticresearch.com.mainehealth.idm.oclc.org/ce/CECourse.aspx?cs=naturalstandard&s=ND&pm=5&pc=16-111#top) | | | |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | | Lifestyle modification is the first step in managing menopausal symptoms. Women who are overweight with a body mass index (BMI) greater than 30 kg/m2 are more than twice as likely to experience moderate to severe hot flashes compared to women whose BMI is less than 25 kg/m2. Cigarette smoking also increases the frequency and severity of hot flashes.10967 Recommend exercise, a healthy diet with adequate fruits and vegetables, and quitting smoking. These lifestyle changes decrease menopausal symptoms, increase sense of well-being, and lower the risk for cardiovascular disease, breast cancer, and osteoporosis.10965,10966   |  | | --- | | **Practice Pearl** | | Women looking for "natural" healthy approaches for menopause might be interested in [**yoga**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=1241), [**Qi gong**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=1186), [**acupuncture**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=1219), or [**moxibustion**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=1446). Participating in a yoga program for 8 to 10 weeks seems to significantly decrease some measures of hot flash frequency and severity and improve sleep quality.16270,16279,89007 Qi gong practiced for 30 minutes daily for 12 weeks also appears to reduce menopausal symptoms and improve sleep.18218 Preliminary research also shows that moxibustion and acupuncture can improve symptoms in some women.29806,88584,88585 However, another alternative treatment modality, [**reflexology**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=1182), doesn't seem to help.15842 |  |  | | --- | | **Commonly Used Conventional and Natural Medicines Used for Menopausal Symptoms\*** | | **Centrally-acting Agents**   * **Conventional Medications**   + Clonidine (*Catapres*)   + Gabapentin (*Neurontin*)   + Methyldopa (*Aldomet*)   + SSRIs (*Prozac*, *Paxil*, etc)   + Venlafaxine (*Effexor*) * **Natural Medicines**   + [**St. John's wort**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=329) (*Hypericum perforatum*)   + [**Valerian**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=870) (*Valeriana officinalis*) | | **Hormonal**   * **Conventional Medications**   + Estrogen (*Premarin*, etc)   + Estrogen/progestin (*Prempro*, etc)   + Medroxyprogesterone acetate (*Depo-Provera*)   + Megestrol acetate (*Megace*) * **Natural Medicines**   + [**Alfalfa**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=19) (*Medicago sativa*)   + Bio-identical hormones   + [**Black cohosh**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=857) (*Actaea racemosa*)   + [**Chasteberry**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=968) (*Vitex agnus-castus*)   + [**DHEA**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=331) (*Dehydroepiandrosterone*)   + [**Dong quai**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=936) (*Angelica sinensis*)   + [**Flaxseed**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=991) (*Linum usitatissimum*)   + [**Hops**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=856) (*Humulus lupulus*)   + [**Kudzu**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=750) (*Pueraria lobata*)   + [**Licorice**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=881) (*Glycyrrhiza glabra*)   + [***Panax ginseng***](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=1000)   + [**Red clover**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=308) (*Trifolium pratense*)   + [**Sage**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=504) (*Salvia officinalis*)   + [**Soy**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=975) (*Glycine max*)   + [**Wild yam**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=970) (*Dioscorea villosa*) | | **Miscellaneous**   * [**Acupuncture**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=1219) * [***Amberen***](http://naturaldatabase.therapeuticresearch.com.mainehealth.idm.oclc.org/ce/ceNDMono.aspx?onlinece=ceMENO&brand_id=91659&view=bn) * [**Evening primrose oil**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=1006) (*Oenothera biennis*) * [**Moxibustion**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=1446) * [**Qi Gong**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=1186) * [**Reflexology**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=1182) * [**Vitamin E**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=954) * [**Yoga**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=1241) | | | | | |  |  |  | | --- | --- | --- | | |  |  | | --- | --- | | Hormone Therapy | [return to top](http://naturaldatabase.therapeuticresearch.com.mainehealth.idm.oclc.org/ce/CECourse.aspx?cs=naturalstandard&s=ND&pm=5&pc=16-111#top) | | | |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | Hormone therapy still has an important role for short-term treatment of menopausal symptoms. It is VERY effective for hot flashes.228,10968 But you'll see a more tailored approach to using hormone therapy these days. The best time to use hormone therapy is right when menopausal symptoms start. Using the lowest effective dose for the shortest duration is the best approach. An example of a low-dose product is drospirenone 0.25 mg / estradiol 0.5 mg (*Angeliq*). The duration of treatment should usually be limited to about 5 years. Longer duration treatment is associated with increased breast cancer risk. When discontinuing hormone therapy, use a taper over several months to reduce discontinuation symptoms.18014  Some women are still trying "bioidentical hormones" which are often compounded in specialty pharmacies. These are estrogens that are the same or similar as those produced endogenously and are prepared in customized doses. Although many women swear by these compounds, there's no proof that they are safer or more effective than commercially available products.  We have a nice comparison chart showing all the different [postmenopausal hormone therapy products](http://naturaldatabase.therapeuticresearch.com.mainehealth.idm.oclc.org/ce/ceCourseLinks.aspx?page=view_ddpu&dd=280506).  Lots of women and their prescribers have abandoned hormone therapy. Many women are searching for alternatives, often for "natural" health products. Even before the big studies, many women were using natural products to treat menopausal symptoms. In 2000, before results from the big studies were known, women spent $600 million on these products.10970 Since hormone therapy has fallen out of favor, natural approaches have become even more popular. In fact, three of the top 10 best-selling herbal products in the U.S. are commonly used for menopausal symptoms.18015 Women who take natural products often consider them safer than other approaches.10971,10972   |  | | --- | | Are your patients using any natural medicines or alternative modalities to help with menopausal symptoms? Which ones do they use most often? |   **Phytoestrogens**  The most commonly used group of natural products for vasomotor symptoms are phytoestrogens or "plant estrogens." The three main kinds of phytoestrogens are isoflavones, lignans, and coumestans.  Isoflavones are the most potent and the most common phytoestrogens in supplements. Phytoestrogens are also found in many common food sources.7655   |  |  | | --- | --- | | **Phytoestrogen Class** | **Food Source** | | Isoflavones | legumes ([**soy**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=975), chickpeas or garbanzo, [**red clover**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=308), lentil, beans) | | Lignans | [**flaxseed**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=991), lesser amounts in lentils, whole grains, beans, fruits, vegetables | | Coumestans | [**red clover**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=308), sunflower seeds, sprouts |   Phytoestrogens are not structurally related to estrogen, but phytoestrogens contain a phenolic ring that allows them to bind to estrogen receptors. Phytoestrogens are 100 to 10,000 times weaker than endogenous estrogen. Depending on the tissue type and location in the body, phytoestrogens can act as estrogens OR antiestrogens. In fact, phytoestrogens have activity similar to selective estrogen receptor modulators (SERMs) such as tamoxifen and raloxifene (*Evista*).7655 For example, the estrogenic activity of soy varies with the level of endogenous estrogen. In premenopausal women with normal endogenous estrogen levels, soy phytoestrogens have an antiestrogen effect since soy isoflavones can displace endogenous estrogen from receptors. In postmenopausal women with low endogenous estrogens, soy phytoestrogens are more likely to act as weak estrogens.  Interest in phytoestrogens for vasomotor symptoms began when researchers noticed that only about 10% of Asian women report experiencing hot flashes. The Asian diet contains significantly more soy protein than the typical North American diet. Some researchers speculate that Asian women are less likely to have hot flashes due to this high soy consumption.7655,10973  Since phytoestrogens have estrogenic effects, women often wonder if phytoestrogens also increase the risk of breast cancer or have other adverse effects similar to prescription estrogen. There is a lot of debate about the potential risks associated with phytoestrogens. Research findings are conflicting.  On one hand, soy is thought to be beneficial due to preliminary evidence that suggests soy isoflavones have antioxidant, antiproliferative, and antiangiogenic activity.2296,3983 Soy also contains other anticarcinogenic compounds such as saponins, phytates, protease inhibitors, and phytosterols.9346 This suggests that phytoestrogens could DECREASE the risk of breast cancer. However, other laboratory evidence suggests that phytoestrogens from soy can stimulate proliferation of normal human breast tissue.3980,3981 This suggests that phytoestrogens could INCREASE the risk of breast cancer.  Population studies suggest that consuming phytoestrogens such as soy in the diet modestly DECREASES the risk of breast cancer.5939,7334,7335,7336,11038,11807,14363 But most of this research is in Asian populations. There is less evidence about the effects of soy in Western populations and the evidence is conflicting. One analysis of epidemiological research suggests that increased soy intake is associated with a reduced risk of breast cancer development in Western-culture women.75377 Also, a population study suggests that eating tofu once weekly reduces the risk of premenopausal bilateral breast cancer in Western-culture women compared to not eating tofu.75590 However, other population studies show that dietary intake of soy isoflavones among Western-culture middle-aged women is NOT associated with a decreased risk of breast cancer.11391, 17109, 90955 In a multiethnic population, dietary intake of soy isoflavones was NOT associated with a reduced risk of breast cancer.90967 The reason for the disparate findings is unclear; however, the effects of soy might vary based on ethnic differences in response.7663  There is also research showing that soy intake DECREASES breast cancer recurrence in patients with existing breast cancer. Two analyses of evidence from observational research show that increased intake of soy food following breast cancer diagnosis is associated with a 21% to 25% reduction in breast cancer recurrence.90956,90969 This effect appears to be greatest for women with estrogen receptor-negative, estrogen receptor-positive/progesterone receptor-positive, or postmenopausal breast cancer.90956   |  | | --- | | **Practice Pearl** | | Because there is insufficient reliable information about the effects of soy preparations, patients with breast cancer, a history of breast cancer, or a family history of breast cancer should avoid or use phytoestrogens cautiously. Foods containing phytoestrogens are probably safe, but advise patients with breast cancer concerns to avoid excessive intake of concentrated phytoestrogen SUPPLEMENTS.9346 There are also concerns that some phytoestrogens from soy and red clover might interfere with the effectiveness of tamoxifen.7072,8192,14362,90973 |   Some women also ask if phytoestrogens "unopposed" by a progestin will increase the risk of endometrial cancer just like conventional estrogens. There's not much known about this, but some evidence suggests that dietary intake of soy phytoestrogens DOESN'T stimulate endometrial growth.2429,7358,7654,9676,9917 Some evidence suggests that women in countries with a diet high in isoflavones actually have a lower incidence of endometrial cancer.7338,10372,90954 Other epidemiological research suggests that higher intake of soy food and isoflavones is NOT associated with a reduced risk of endometrial cancer in Japanese women.90954  The effects might be different with concentrated soy isoflavone extract. Soy extracts providing 120 mg/day of isoflavones for 6 months does not seem to stimulate endometrial thickening.13209 But taking 150 mg/day for 5 years does seem to increase the risk of endometrial hyperplasia.12105 It is unclear if this is a significant clinical concern, however, because there is no evidence that this dose of soy isoflavones increases the risk of ATYPICAL hyperplasia. Atypical hyperplasia has a much higher risk of developing into endometrial cancer than simple endometrial hyperplasia.12105,90973 Tell women that the safest bet is to stick with foods containing phytoestrogens rather than concentrated supplements.  [**Soy**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=975) and soy isoflavones are the most commonly used phytoestrogens and the best studied. Consuming soy protein, 20 to 60 grams daily, providing 34 to 100 mg of isoflavones, seems to MODESTLY decrease the frequency and severity of hot flashes in menopausal women.2296,2297,3978,3986,3987,7653,9917,11805,75478,75486,75649,92661 Soy extracts in tablet form, providing 35 to 120 mg of isoflavones daily, also seem to have beneficial effects.4751,6455,7802,9916,10460,11805,11993,11994,13209,15220,15850,75478 Some evidence shows that soy extracts are more effective in women who have a greater frequency of hot flashes.15220 Additionally, there appears to be a dose-response relationship with isoflavone content and efficacy. In one study, taking 100-200 mg of isoflavones (Novasoy 400, Archer Daniels Midland Company) daily in two to three divided doses reduces hot flashes more than lower doses or less frequent dosing intervals.90950  Soy extracts have also been compared to conventional estrogens in preliminary trials. In one trial, a soy extract providing 54 mg daily of the isoflavone genistein reduced hot flashes by 22% to 29% compared to about 53% with 17-beta-estradiol 1 mg daily.11994 Another trial suggests that a soy extract providing 60 mg of isoflavones twice daily is comparable to conjugated estrogens 0.625 mg daily; however, conjugated estrogens appear to work more quickly.13209 More evidence is needed to accurately compare the effectiveness of soy extracts to conventional estrogens.  Not all research on soy has been positive. Several studies have found no benefit with soy extracts used for hot flashes.7801,11806,14062,15038,15851 The reason for these conflicting findings is not clear, but it may be due to high placebo response rates in some trials. Patient expectations of treatments can significantly impact perceived benefits. According to one analysis, inconsistent results might also be due to differences in the isoflavones composition of the soy extracts. Studies using products that provide at least 15 mg of the genistein isoflavone daily consistently show positive outcomes. Studies using products containing a lower concentration of genistein have produced inconsistent findings.15133  Explain to patients that eating soy foods or taking soy supplements might provide modest relief, but it's no magic bullet. If patients take a soy supplement, aim for one providing at least 15 mg of genistein.   |  | | --- | | **Practice Pearl** | | Breast cancer survivors often have significant problems with hot flashes. Although soy seems to be helpful for some women with hot flashes, it doesn't seem to be effective for women who have hot flashes related to breast cancer treatment.3991,7054,7658 |  |  | | --- | | **Practice Pearl** | | Caution patients on warfarin about adding soy to their diet. Soy might reduce warfarin effectiveness.9672 |   Some women might ask about [**ipriflavone**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=310). It's a synthetic soy isoflavone derivative. Some research suggests that it reduces bone loss. But it doesn't have any effect on hot flashes.7655  [**Red clover**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=308) is widely promoted and used for hot flashes. It contains isoflavones similar to soy. A few preliminary studies suggest that red clover may reduce hot flashes.10991,19545,19552 However, most clinical research, including a pooled analysis of 7 trials, shows that taking red clover extract does not seem to significantly reduce hot flashes compared to placebo.8925,10975,10976,10991,92661 Don't recommend red clover for menopausal symptoms.   |  | | --- | | **Practice Pearl** | | Caution women on warfarin about using red clover. Red clover contains coumarins which can have anticoagulant effects.9553,19557,19558,19559 Taking high doses of red clover might have additive effects with warfarin and potentially increase the risk of bleeding. |   [**Flaxseed**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=991) is a rich source of lignan phytoestrogens, as well as the omega-3 fatty acid, alpha-linolenic acid, and fiber. Some research suggests that consuming dietary flaxseed 40 to 90 grams daily in place of other dietary fats significantly improves MILD menopausal symptoms such as hot flashes.10978,12910,21200 But not all research has been positive. Some research shows that flaxseed is no more effective than taking a placebo such as wheat germ.16762,12910,18224,22176 It is possible that flaxseed has not been effective when lower doses were used.  Flaxseed is a healthy alternative to other fats and it is safe. Some women may be interested in giving it a try, but let them know that it might not provide much, or any, relief from hot flash symptoms.   |  | | --- | | **Practice Pearl** | | Explain that 40 grams (4 tablespoons) of flaxseed contains about 16 grams of fat and up to 200 calories. Tell women to use flaxseed INSTEAD of other dietary fats, not in addition to them, to avoid packing on the calories. |  |  | | --- | | **Practice Pearl** | | Caution patients on warfarin and other anticoagulants about using flaxseed. High doses of flaxseed can decrease platelet aggregation.5898 Theoretically, this could increase the risk of bleeding in patients who also take warfarin. You can get all the details about interactions by using the [*Interaction Checker*](http://naturaldatabase.therapeuticresearch.com.mainehealth.idm.oclc.org/nd/search.aspx?s=nd&pt=7). Just enter all the drugs and natural products a patient is taking and click "Check Interactions" to get a detailed report. |   [**Black cohosh**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=857) is among the top-selling herbs in the U.S. Its primary use is for menopausal symptoms. But there has been debate over the years whether black cohosh actually has estrogenic effects or if it works by some other mechanism. It appears to have estrogen-like effects.4618,4619,14330 But it does NOT directly bind estrogen receptors, up-regulate estrogen-dependent genes, or stimulate the growth of estrogen-dependent tumors in experiments.4619,7860,9996,10979,11030 It might act as an agonist at serotonin receptors and it appears to increase markers of bone formation.11030,14330 There is speculation that black cohosh has SERM-like activity. In experimental models it seems to have estrogenic activity in some tissue types such as bone, but not in others such as the endometrium.   |  | | --- | | **Practice Pearl** | | Do not confuse black cohosh with two unrelated plants, blue cohosh and white cohosh, which have toxic effects.4,12 Blue cohosh is especially dangerous in pregnant women as some of its constituents can result in teratogenic effects.1122,7110 |   Despite the popularity of black cohosh, the data are lukewarm. The most consistent evidence is for a specific commercial extract called [*Remifemin*](http://naturaldatabase.therapeuticresearch.com.mainehealth.idm.oclc.org/ce/ceNDMono.aspx?onlinece=ceMENO&brand_id=4070&view=bn) (Phytopharmica/Enzymatic Therapy). This extract is standardized to contain 1 mg triterpene glycosides, calculated as 27-deoxyacetin, per 20 mg tablet. Evidence shows that it significantly reduces menopausal symptom indices and hot flash frequency compared to placebo.9437,13143,13184,14423,35824,35853,35964 Preliminary evidence suggests that it is comparable to low-dose transdermal estradiol (*Estraderm*) 25 mcg every 7 days, tibolone 2.5 mg, and conjugated equine estrogens 0.625 mg (for relieving hot flashes).13184,15889,35964  Research using other formulations of black cohosh is less consistent. A different commercial black cohosh extract CR BNO 1055 (*[Klimadynon/Menofem](http://naturaldatabase.therapeuticresearch.com.mainehealth.idm.oclc.org/ce/ceNDMono.aspx?onlinece=ceMENO&brand_id=14627&view=bn" \t "monograph)*, Bionorica AG) 40 mg/day was comparable to taking conjugated estrogens 0.6 mg/day for relieving hot flashes in one study; however, neither treatment was significantly more effective than placebo.10987 Studies using other non-commercial black cohosh extracts have been mostly negative.14424,15038,15158,35875 In fact, a high quality study found that a non-commercial black cohosh extract 160 mg daily standardized to 2.5% triterpene glycosides did not significantly reduce hot flash frequency or other vasomotor symptoms after 3, 6, or 12-months of treatment.15158 The problem is, this product is different than all of the others, which makes it difficult to make an apples-to-apples comparison of the findings.  When the results of all studies are analyzed together, it appears that black cohosh does not significantly reduce hot flash frequency or menopausal symptoms.89467,92661 However, these analyses do not evaluate data specific to certain formulations or account for potential differences among products.  Overall, some formulations of black cohosh appear to provide modest relief for some women. If a woman wants to try black cohosh, recommend the product with the best evidence of potential benefit, *Remifemin*.  Even though black cohosh might help some menopausal women with hot flashes, like soy, black cohosh does NOT seem to be effective for relieving hot flashes in breast cancer survivors.7054,15161  There are also lingering concerns about long-term safety. Based on clinical trials, black cohosh appears to be very safe. However, there have been several reports of liver damage, sometimes requiring liver transplantation, in women taking black cohosh products.4383,10692,11909,12006,13144,14469,35857 It's unclear if black cohosh is the cause of liver problems in these cases. Some experts speculate that product contamination or substitution of a hepatotoxic plant might be responsible. Until more is known, advise patients who take black cohosh to consider getting liver function tests periodically.  [**Dong quai**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=936) is commonly used in traditional Chinese medicine, usually in combination with other herbs. In the U.S., dong quai is often used as a single-ingredient remedy for hot flashes. There's contradictory evidence regarding whether or not dong quai has estrogenic effects.738,6180,7860,10979 There is some evidence that it does stimulate the growth of breast cancer cells similar to estrogen.7860,10979  Some preliminary clinical research suggests that taking dong quai in combination with other ingredients might reduce hot flashes in menopausal women.22371,48445,48522 However, when used alone, dong quai does not appear to be beneficial.738  There are also safety concerns with dong quai. It contains constituents such as bergapten, safrole, and isosafrole, which are considered to be carcinogenic. Whether taking dong quai results in the accumulation of enough of these constituents to cause cancer is not known. Tell women not to use it, especially long term.7162   |  | | --- | | Which natural medicines for menopause would you tell your patients to avoid? Why? |   [**Chasteberry**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=968) (*Vitex agnus-castus*) is a well-known "women's herb." In addition to menopausal symptoms it is used in women for premenstrual syndrome and infertility. Chasteberry appears to have a variety of effects on neurotransmitters including dopamine and acetylcholine.7014,7015,10122 It also appears to have estrogen and progestin activity.10979,11456 Although there is some evidence that it might help for symptoms of premenstrual syndrome,41490,41494 there's no reliable evidence that it helps for menopausal symptoms.   |  | | --- | | **Practice Pearl** | | Chasteberry appears to stimulate the growth of breast cancer cells *in vitro*.10979 Like other phytoestrogens, tell women with a history of breast cancer that chasteberry might not be safe. |   Lots of other herbs have estrogenic activity and are used to treat menopause, for example: [**kudzu**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=750), [**alfalfa**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=19), [**hops**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=856), and [**licorice**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=881). They each have varying degrees of estrogenic activity.7860,10979,10980 But there's no reliable evidence that these are effective for menopausal symptoms.  [**Panax ginseng**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=1000), or Asian ginseng, is commonly just called "ginseng." It is sometimes used for vasomotor symptoms due to suspected estrogenic effects. Whether ginseng has any true estrogenic effect is controversial.590,592,7860,10981,10982,10983 The ginsenoside constituents in ginseng do appear to stimulate breast cancer cells in laboratory studies. And some women who take ginseng can have estrogen-like side effects.10984  Research on Panax ginseng for menopausal symptoms is preliminary and contradictory. Taking a low dose of Panax ginseng, 200 mg daily, does not seem to reduce hot flashes.10981 However, in a study using Panax ginseng 1000 mg three times daily symptoms of hot flashes were significantly reduced.89749 Some preliminary research also suggests that taking Panax ginseng helps menopausal symptoms such as fatigue, insomnia, and depression.3863   |  | | --- | | Have your patients taken Panax ginseng, Chasteberry, or Dong quai teas? What can you tell them about their safety and effectiveness? |   Women sometimes ask about [**DHEA**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=331) ([**dehydroepiandrosterone**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=331)), which is sometimes hyped as a "miracle hormone" to prevent aging. DHEA is a precursor to sex steroids such as testosterone and estrogen. Low doses of DHEA increase testosterone levels and may very slightly increase estrogen levels.6011,10985  DHEA hype far exceeds DHEA research. There is contradictory evidence on the effects of DHEA on menopausal symptoms. Some evidence suggests that taking DHEA orally 10 mg to 25 mg daily decreases hot flashes, as well as psychological symptoms.11464,21417 But other evidence suggests no benefit of DHEA 50 mg daily on mood, fatigue, cognition, or sense of well-being in perimenopausal women.6011,21361 And other clinical research suggests that DHEA does not improve menopause-related decreased libido in women.88492 Tell women that it is too soon to recommend DHEA for menopausal symptoms.  Since DHEA can be converted to estrogen, there are also concerns about breast cancer. In fact, epidemiological studies associate higher serum concentrations of DHEA with increased breast cancer risk in postmenopausal women. Tell women with hormone responsive tumors such as breast cancer to avoid taking DHEA.9437,10370   |  | | --- | | **Practice Pearl** | | Since DHEA can be converted to androgens such as testosterone, it can sometimes cause unwanted cosmetic side effects such as an increase in facial hair, acne, and deepening of the voice.2113,4242,7559 |   [**Sage**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=504) is now also being marketed for menopause symptoms. Sage is thought to have some estrogenic activity due to its constituent geraniol. In preliminary clinical research a specific, thujone-free sage extract (*Sage Menopause*, Bioforce AG, Switzerland) significantly improved menopausal symptoms, especially hot flashes. Capsules containing 280 mg of the sage extract were taken once daily for 56 days. The mean number of hot flashes decreased by about 40% per day, and those which did occur had reduced intensity.17177 Additional preliminary clinical evidence suggests that tablets containing sage extract 120 mg plus alfalfa extract 60 mg taken daily for 3 months can also reduce hot flashes and night sweating compared to pretreatment.72695 Advise women that the sage should be free of thujone which can be toxic if enough is consumed.1304 | | | | |  |  |  | | --- | --- | --- | | |  |  | | --- | --- | | Centrally-acting Treatments | [return to top](http://naturaldatabase.therapeuticresearch.com.mainehealth.idm.oclc.org/ce/CECourse.aspx?cs=naturalstandard&s=ND&pm=5&pc=16-111#top) | | | |  |  |  | | --- | --- | --- | | Alternatives to hormonal treatments are now becoming more popular due to the negative studies associated with HRT. Venlafaxine, gabapentin, clonidine, and methyldopa are used.10966 Selective serotonin-reuptake inhibitors (SSRIs) and other antidepressants are also used, but none of these treatments seems to be as effective as estrogen for hot flashes.10969 Also, SSRIs sometimes have bothersome side effects such as drowsiness, dry mouth, constipation, and sexual dysfunction.10966  Women also use many centrally-acting natural products, mostly for non-vasomotor menopausal symptoms. [**Valerian**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=870) is often used for insomnia.17577,19406 Although valerian can be effective for insomnia, there's no reliable evidence that it helps when insomnia is associated with menopause.  [**St. John's wort**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=329) is often used for depression related to menopausal symptoms. There is some clinical research showing that combining St. John's wort with black cohosh reduces symptoms.15037,15893 But it's not known if this benefit is due to St. John's wort, black cohosh, or the combination. There is no reliable evidence that taking St. John's wort by itself is effective for reducing menopausal symptoms.   |  | | --- | | **Practice Pearl** | | Always use caution with St. John's wort since it can cause many drug interactions. For example, St. John's wort is a potent inducer of cytochrome P450 3A4 (CYP3A4). Over 50% of drugs on the market are affected by CYP3A4. St. John's wort also induces p-glycoprotein and other cytochrome P450 enzymes. Click to see a full list of [St. John's wort interactions with drugs](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=329). | | | | | |  |  |  | | --- | --- | --- | | |  |  | | --- | --- | | Miscellaneous | [return to top](http://naturaldatabase.therapeuticresearch.com.mainehealth.idm.oclc.org/ce/CECourse.aspx?cs=naturalstandard&s=ND&pm=5&pc=16-111#top) | | | |  | | --- | | [**Evening primrose oil**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=1006) is sometimes promoted to relieve hot flashes. It's sometimes advertised as an "estrogen promoter," but there's no evidence of any effect on estrogen levels in humans and it doesn't seem to be effective for relieving hot flashes.274,15038,21002 Don't recommend it.  [**Wild yam**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=970) is often promoted as a source of "natural hormones." It is often used as a topically applied cream for menopausal symptoms. Promoters falsely claim that a component of wild yam, diosgenin, is converted by the body to progesterone and/or dehydroepiandrosterone (DHEA). Diosgenin can be converted to hormones in the laboratory but NOT in the body.  Wild yam does not have estrogenic effects and is not effective for hot flashes.10989 Tell women not to waste their money on wild yam creams.  [**Vitamin E**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=954) supplements are sometimes recommended for menopausal symptoms. But there's no reliable evidence that vitamin E helps menopausal women.  [***Amberen***](http://naturaldatabase.therapeuticresearch.com.mainehealth.idm.oclc.org/ce/ceNDMono.aspx?onlinece=ceMENO&brand_id=91659&view=bn) is a commercial dietary supplement that's been heavily marketed for menopausal women. It's promoted for hot flashes, insomnia, irritability, low libido and weight loss. The product contains an odd mix of ingredients including ammonium succinate, [**calcium**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=781), monosodium glutamate, [**glycine**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=1072), [**magnesium**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=998), [**zinc**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=982), and [**vitamin E**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=954). It gets its name from the succinate (or succinic acid) component. An older name for succinic acid is "amber acid."  The manufacturer claims that succinate activates the central nervous system in a way that affects the neuroendocrine system and helps the body cope with physical and emotional stress.  The manufacturer also cites research in animals and preliminary clinical research from Russia. This research suggests that taking an *Amberen*-like product called "*Enerlit-Clima*" for 3 weeks can significantly reduce menopausal symptoms during the menopause transition.18051 But we're not convinced. More evidence about long-term safety and effectiveness is needed. | | | | |  |  |  | | --- | --- | --- | | |  |  | | --- | --- | | The Bottom Line | [return to top](http://naturaldatabase.therapeuticresearch.com.mainehealth.idm.oclc.org/ce/CECourse.aspx?cs=naturalstandard&s=ND&pm=5&pc=16-111#top) | | | |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | Due to the concern about the safety of estrogens and HRT, many more women are turning to phytoestrogens and other natural products for menopausal symptoms. In addition to questions about the effectiveness of natural products, women will want to know about risks, such as cardiovascular disease, and breast and uterine cancer.  Explain to women that natural medicines with estrogenic effects might not be any safer than conventional estrogenic drugs. At this point, there is not enough data from large-scale clinical trials to compare safety of phytoestrogens with conventional estrogen products. Women with a history of breast cancer should avoid supplements containing a phytoestrogen or suspected of having estrogenic effects.  Soy has the most evidence for effectiveness and some women might benefit from taking it. Soy protein-containing foods are preferred over soy extract supplements which have concentrated isoflavones. There is less known about the long-term safety of soy extract supplements.  Black cohosh might also help some women. Due to concerns about potential liver damage, women taking black cohosh should consider getting liver function tests.  Explain to women that these supplements are not "big guns." They seem to provide only modest relief, if any.  Don't recommend red clover, DHEA, flaxseed, chasteberry, kudzu, alfalfa, hops, licorice, evening primrose oil, *Panax ginseng*, wild yam, or vitamin E. There's not enough evidence that these are beneficial. Steer patients away from dong quai due to potential safety concerns.  What supplements are your patients taking for menopausal symptoms? Let us know…or start a conversation on [*Colleagues Interact*](http://naturaldatabase.therapeuticresearch.com.mainehealth.idm.oclc.org/ce/ceCourseLinks.aspx?page=colleaguesinteract).  Print a *Natural Medicines* [recommendation chart](http://naturaldatabase.therapeuticresearch.com.mainehealth.idm.oclc.org/ce/documents/ce_16111-02.pdf) as a reference for your practice site.   |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | | **Recommendation Chart for Natural Medicines Used for Menopausal Symptoms** | | | | | | | |  | **Likely Safe** | **Possibly Safe** | **Insufficient Evidence** | **Possibly Unsafe** | **Likely Unsafe** | **Unsafe** | | **Effective** |  |  |  |  |  |  | | **Likely Effective** |  |  |  |  |  |  | | **Possibly Effective** | [**-Soy foods**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=975) | [**-Black cohosh**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=857) [**-St. John's wort**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=329) (in combination with black cohosh) [**-Sage**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=504) [**-Soy extracts**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=975) |  |  |  |  | | **Insufficient Evidence** | [**-Chasteberry**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=968) [**-Flaxseed**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=991) [**-Ginkgo**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=333) [**-St. John's wort**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=329) (alone) [**-Vitamin E**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=954) [**-Yoga**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=1241) | [**-Alfalfa**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=19) [**-DHEA**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=331) (short-term use) [**-Hops**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=856) [**-Kudzu**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=750) [**-Licorice**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=881) [**-Red clover**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=308) [**-Valerian**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=870) | [***-Amberen***](http://naturaldatabase.therapeuticresearch.com.mainehealth.idm.oclc.org/ce/ceNDMono.aspx?onlinece=ceMENO&brand_id=91659&view=bn) | [**-DHEA**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=331)  (long-term use) |  |  | | **Possibly Ineffective** | [**-Evening primrose oil**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=1006) [**-Reflexology**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=1182) | [**-Dong quai**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=936) (short-term use) [***-Panax ginseng***](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=1000) [**-Wild yam**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=970) |  | [**-Dong quai**](http://naturalmedicines.therapeuticresearch.com.mainehealth.idm.oclc.org/databases/food,-herbs-supplements/professional.aspx?productid=936)  (long-term use) |  |  | | **Likely Ineffective** |  |  |  |  |  |  | | **Ineffective** |  |  |  |  |  |  | | | | | |  |  | | --- | --- | | |  | | --- | |  | | | |  | |  | |  | |  | |  | |
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