



# HerbClip™

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**FILE: ■Hot Flashes  
■Menopause  
■Natural Remedies**

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**RE: Review of Natural and Pharmacological Remedies for Hot Flashes**

Himov-Kochman R, Hochner-Celnikier D. Hot flashes revisited: Pharmacological and herbal options for hot flashes management. What does the evidence tell us? *Acta Obstet Gynecol Scand.* 2005;84:972–979.

Hot flashes are a common complaint among menopausal women. According to the authors of this study, "most epidemiological studies from North America and Europe found that the incidence of hot flashes is highest in the peri-menopausal years, ranging from 58% to 93% after menopause and from 28 to 65% in pre-menopausal women." Conventional medical treatments are limited to hormone replacement therapy (HRT). However, recent data have indicated that conventional HRT increases a woman's risk of cardiovascular disease.<sup>1,2</sup> In a search for alternative treatment to HRT for relief of menopausal symptoms, women frequently turn to natural remedies. Natural treatments include diet, exercise, vitamin and mineral supplements, and botanical medicines. The current study is a review of research into some of these alternative therapies for the treatment of hot flashes.

The reviewers searched the MEDLINE database for placebo-controlled trials of pharmacological and botanical treatments for hot flashes between 1975 and 2004. Search terms used included "hot flashes/flush, vasomotor symptoms, menopause, and climacteric" combined with the search terms "alternative medicine, nonhormonal therapy, progesterone, anti-hypertensive therapy, anti-depressants, anti-convulsant therapy, phytoestrogens, and herbal medicine." Only English-language publications were included. Reviewed were studies that used progesterone, alpha adrenergic agonists, anti-depressants, anti-convulsants, soy products, black cohosh (BC), red clover, dong quai, ginseng root, evening primrose oil, vitamin E, and wild yam.

## **Progesterone**

Progesterone is commonly added to estrogen therapy to reduce the risk of endometrial hyperplasia and endometrial cancer in women with intact uteri; however, progesterone therapy might have benefit by itself. Medroxyprogesterone (MPA) has been shown in

"several double-blind, placebo-controlled studies" to decrease hot flash frequency. Specifically, 150 mg per month MPA administered by intramuscular injection reduced the frequency and severity of hot flashes by 90% compared with 25% for placebo; the effect of MPA was comparable to that of 0.625 mg conjugated equine estrogen. MPA therapy does have some adverse side effects, including unfavorably altering blood lipids, producing irregular uterine bleeding, bloating, and depression. Transdermal progesterone administered as a cream in a dose of 20 mg/day also decreased hot flash symptoms in one study, while 32 mg progesterone cream did not significantly alter the frequency or severity of hot flashes. Additionally, using progesterone alone "was recently associated with an increase in breast cancer seen among women treated by combined estrogen/progesterone therapy."

### **Alpha adrenergic agonists**

Alpha adrenergic agonists are a class of pharmacological agents commonly used to reduce blood pressure. These agents include  $\alpha$ -methyldopa, clonidine, and lofexidine. Hot flashes decreased by 50% in women taking 250–500 mg methyldopa twice daily, while a second study showed no benefit from taking methyldopa once daily. Clonidine has not shown consistent benefits, and "was intolerable by many patients because of nausea, depression, headache, and fatigue." Lofexidine, primarily used to treat heroin addiction reduced hot flashes by 60–70% in one study (dosage not reported).

### **Anti-depressants**

Selective serotonin-uptake inhibitors (SSRI) may provide relief to some women. A multicenter, randomized, double-blind, controlled, parallel group study of 165 menopausal women with at least 2–3 hot flashes per day were administered 12.5 or 25.0 mg/day of paroxetine CR for 6 weeks. Those in the paroxetine group experienced a significant 62–64% reduction in the frequency and severity of hot flashes compared to 38% in those receiving placebo. Fluoxetine, another SSRI, was also subjected to a placebo-controlled trial. Fluoxetine 20 mg/day decreased hot flashes, and the authors concluded that "fluoxetine resulted in a modest improvement in hot flashes."

Other antidepressants, such as venlafaxine, a selective norepinephrine reuptake inhibitor (SNRI), have also been shown to decrease hot flashes. Venlafaxine 37.5–150 mg/day decreased median hot flash scores after 4 weeks by 37%, 61% and 61% in the groups taking 37.5 mg/day, 75 mg/day, and 150 mg/day venlafaxine, respectively. In comparison, those in the placebo group experienced a median 27% reduction. However, those on venlafaxine also experienced more adverse effects, including mouth dryness, decreased appetite, nausea, and constipation. The authors of this review wrote, "It was concluded that venlafaxine is an effective nonhormonal treatment for hot flashes, although the efficacy must be balanced against the drug's side-effects."

### **Anti-convulsants**

Anti-convulsants studied for hot flashes have shown positive results. Gabapentin 900 mg/day was administered to 59 menopausal women for 12 weeks, and reduced hot flash frequency and severity by 54% and 67%, respectively. However, adverse effects caused 13% of study participants to withdraw from the study.

## **Soy**

Soy (*Glycine max*) foods and extracts studied for relief of menopausal symptoms have shown inconsistent results. Much of the evidence for soy comes from epidemiological data showing that Indonesian and Chinese women experience less hot flashes than western women (10–20% and 10–25% vs. 58–93%, respectively). In Taiwan, Japan, Korea, and Indonesia, approximately 17–36 g/day soybeans are consumed, compared to 4 g/day in the USA. The dietary goals for soy consumption are 25–60 g/day of soy protein or 40–60 mg/day isoflavones.

Soy contains phytoestrogens, which have estrogen-like activities in humans. The effects in people, though, are much weaker than pharmaceutical estrogen replacement therapy. According to the authors of this review, "There are over 20 different compounds of phytoestrogens in over 300 plants and herbal products such as garlic, parsley, wheat, rice, dates, cherries, apples, wine, and coffee; however, soy beans are by far the richest source of phytoestrogens." Isoflavones are a category of bioactive compounds that include daidzein and genistein. While there have been studies of soy for hot flashes, they "suffer from high placebo response, [and] inconsistent treatment dosage as a result of various extraction procedures and interindividual variation of isoflavone serum level following intake of equal dose." Clinical trials of soy products resulted in a 45% reduction in hot flashes compared to 30% for placebo, while an analysis of 11 different studies provided inconsistent results (4 showed a reduction in hot flashes, 5 showed no effect, and 2 showed a partial benefit). No effect on hot flashes was shown in 2 clinical trials using 42–58 mg and 72 mg/day isoflavones, respectively. There are different possible reasons for the various outcomes, including "the length of time soy-rich diet is consumed, life-long versus several weeks to months."

## **Black cohosh**

Black cohosh (*Actaea racemosa* syn. *Cimicifuga racemosa*) has been used "by native Indians for centuries." Most research has been conducted with one particular formula, Remifemin® (Shaper & Brümmer, GmbH & CoKG, Salzgitter, Germany). The mechanism of action for black cohosh is not completely understood. It does not act by binding estrogen receptors. Remifemin has been the subject of multiple clinical trials. Positive results were shown in 3 of 4 clinical trials. And another study on women with breast cancer taking tamoxifen treated for 12 months with black cohosh extract showed that "almost half of the patients" in the treatment group "were free of hot flashes, while severe hot flashes were reported by 24.4% of patients of the treated group." In contrast, 73.9% of those in the placebo group reported severe hot flashes.

## **Red clover**

Red clover (*Trifolium pratense*) is native to the USA and is used in traditional Native American medicine as a skin remedy. Phytoestrogens in red clover are formononetin, biochanin A, daidzein, genistein, and coumestrol. Clinical trials are inconsistent, and treatment with Promensil® (Novogen; Australia), a proprietary red clover extract, at doses ranging from 40 mg/day isoflavones to 160 mg/day isoflavones, showed no benefit. Additional studies are currently being conducted.

### **Dong quai**

Dong quai (*Angelica sinensis*) is a plant used extensively in traditional Chinese medicine (TCM). Its use dates back at least 20 centuries, and is reported to regulate menses and alleviate dysmenorrhea (painful menses). Like black cohosh, dong quai is not estrogenic. While frequently recommended in the popular press, the one clinical trial reported in this review did not find any benefit of dong quai for hot flashes. The dosage used in that study was 1500 mg dong quai (exact formula not reported) three times daily for 12 weeks.

### **Ginseng root**

Asian ginseng (*Panax ginseng*) has also been promoted to treat hot flashes. It is a "revered East-Asian aphrodisiac with estrogenic activity that is claimed to improve menopausal symptoms." American ginseng (dosage not specified) was not superior to placebo for hot flashes in one study.

### **Vitamin E**

Vitamin E has been promoted in popular and scientific literature to treat hot flashes. It is specifically recommended for hot flashes in breast cancer survivors. The authors found only one randomized placebo-controlled trial of vitamin E for hot flashes, which showed "a marginal decrease of hot flashes frequency, resulting in one less hot flash per day."

### **Evening primrose oil**

Evening primrose oil (EPO; *Oenothera biennis*) is an excellent source of essential fatty acids. It contains relatively large amounts of gamma linolenic acid (GLA), an omega-6 fatty acid, which is reported to account for its therapeutic effects. One clinical trial was reviewed, which showed "no difference in frequency of hot flashes between the treated and control groups." The dosage and duration of the study were not reported.

### **Wild (Mexican) yam**

Wild yam (*Dioscorea villosa*) contains phytoestrogens notably diosgenin which has been transformed into active progesterone-based oral contraceptives by laboratory synthesis. No effect of wild yam cream (not processed in the lab) on hot flashes was found in one clinical trial.

—John Neustadt, ND

### **References**

<sup>1</sup>Lemaitre RN, Heckbert SR, Psaty BM, Smith NL, Kaplan RC, Longstreth WT, Jr. Hormone replacement therapy and associated risk of stroke in postmenopausal women. *Arch Intern Med.* Sep 23 2002;162(17):1954-1960.

<sup>2</sup>Manson JE, Hsia J, Johnson KC, et al. Estrogen plus Progestin and the Risk of Coronary Heart Disease. *N Engl J Med.* August 7, 2003 2003;349(6):523-534.

The American Botanical Council has chosen not to reprint the original article.

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