Fem Adapt

A Natural Solution for Menopausal Symptoms

- Helps reduce hot flashes and night sweats while also promoting mood balance
- Helps balance hormones, reducing the risk of post-menopausal diseases
- Provides four of the most effective and research-backed phytoestrogens

Details
Fem Adapt is AOR’s premium menopause formula that is especially useful for hot flashes. While many formulas on the market contain ingredients with minimal research in menopausal women, doses that are too low or unstandardized botanical extracts, Fem Adapt provides the most powerful, clinically studied, standardized phytoestrogens in research-backed doses. Fem Adapt contains flax lignans, soy isoflavones, black cohosh and a standardized hops extract, which collectively can reduce the severity and frequency of hot flashes and other menopausal concerns.

AOR’s Fem Adapt formula not only provides safe and effective relief from menopausal symptoms, but also provides protection against health problems for which the risk increases after menopause, such as cardiovascular complications, osteoporosis and others. This is due to the mild estrogenic activity of the phytoestrogens in the product, which can serve as natural hormone replacement therapy.

Additionally, some of the ingredients in Fem Adapt have been used in herbal medicine to help relieve premenstrual symptoms, including abdominal cramps, muscle and joint pain, nerve pain like sciatica and nervous tension.

Label Info
Discussion
Fem-Adapt contains herbs which are traditionally used to help relieve premenstrual symptoms, joint, and nerve pain. This synergistic formula is also beneficial in helping to relieve symptoms associated with menopause.

Product Variation
Product Code  Size
AOR04002  60 VEGI-CAPS

Supplements Facts
Serving Size: 2 Capsules  Amount
Linum usitatissimum L. extract (25-65:1)  168 mg
Soy Isoflavone extract  60 mg
Total isoflavones  18.2 – 27.4 mg AIE†
Genistein/Genistin  0.5 – 0.8 mg AIE†
Black Cohosh extract (15-20:1)  80 mg
LIFENOL®* (Hops extract (15-25:1)  120 mg

†AIE: Aglycone Isoflavone Equivalents.
*LIFENOL® is a registered trademark of Naturex, Inc.

Non-medical ingredients:
microcrystalline cellulose, silicon dioxide, maltodextrin, tricalcium phosphate, sodium stearyl fumarate. Capsule: hypromellose.

Guarantees
AOR™ guarantees that all ingredients have been declared on the label. Contains no wheat, gluten, peanuts, sulphites, dairy, eggs, shellfish or any animal byproduct.

Adult Dosage
Take 2 capsules daily with/without food, or as directed by a qualified health care practitioner. Take a few hours before or after taking other medications or natural health products.

Cautions
Ensure you are up-to-date on mammograms and gynecological evaluations prior to use. Consult a health care practitioner prior to use if you are breastfeeding, taking blood thinners, have a history of hormonal or gynecological disease including ovarian cancer, endometriosis or uterine fibroids, have a liver disorder or develop liver-related symptoms (e.g. abdominal pain, jaundice, dark urine), are taking hormone replacement therapy (HRT) including thyroid hormone replacement therapy or have depression or related diseases. Discontinue use and consult a health care practitioner if you experience breast pain, discomfort or tenderness or if you experience a recurrence of menstruation and/or uterine spotting. Do not use if you are pregnant, if you currently have or previously had breast cancer or breast tumours, have a predisposition to breast cancer as indicated by an abnormal mammogram, biopsy or have a family member with breast cancer. Consumption with alcohol, other medications or natural health products with sedative properties is not recommended. Some people
may experience drowsiness. Exercise caution if operating heavy machinery, driving a motor vehicle or involved in activities requiring mental alertness. Hypersensitivity such as an allergy has been known to occur in rare cases, in which case discontinue use. Consult a health care practitioner if symptoms persist or worsen, or for use beyond 1 year. This product contains soy.

Source
Natural botanical extracts
Non-GMO soy

Main Application
Menopause
PMS
Women's health

Disclaimer
The information and product descriptions appearing on this website are for information purposes only, and are not intended to provide or replace medical advice to individuals from a qualified health care professional. Consult with your physician if you have any health concerns, and before initiating any new diet, exercise, supplement, or other lifestyle changes.

Research
Background

Symptoms of Menopause
Menopause refers to the permanent cessation of ovulation and menstrual periods in women, which can occur either naturally or as a result of medical or surgical intervention. It is a natural physiological event that results in a decreased production of sex hormones – estrogen and progesterone – by the ovaries. The primary symptoms of menopause include hot flashes and night sweats. Secondary symptoms can include anxiety, mood swings, depression, loss of libido and vaginal dryness. Hot flashes are thought to result from a decline in circulating estradiol (E2) that induces a thermoregulatory dysfunction mediated by the hypothalamus.

Hormonal Balance
Studies have shown that phytoestrogens such as lignans from flax and genistein from soy isoflavones have direct effects on some of the hormonal pathways that are involved in menopausal symptoms. This combination may also be effective in reducing the risks of post-menopausal-related osteoporosis and cardiovascular disease. AOR’s Fem Adapt formula provides safe and effective relief for menopausal symptoms such as hot flashes and night sweats and protection against diseases for which the risk increases after menopause like cardiovascular disease and osteoporosis.

Hot Flashes and Genistein
In Asia, only 10-20% of menopausal women experience hot flashes, while in North America 70-80% of women experience hot flashes. Researchers have hypothesized that this difference is due to dietary factors, including the consumption of isoflavones found in soy. Genistein is one of the key isoflavones found in soy and has been researched in menopausal women due to its structural similarity to estrogen, making it a phytoestrogen. During menopause the production of estrogen declines which is why genistein has been used, due to its structural similarity to estrogen. Many clinical trials have shown genistein supplementation to reduce the number and severity of hot flashes during menopause.

**Black Cohosh**

Black Cohosh is a flowering plant native to North America originally used by the Native Americans. It has been traditionally used in herbal medicine for the relief of menstrual-associated pain and the pain associated with neuralgia conditions such as sciatica. It has been effective in relieving the muscle and joint pain associated with rheumatic conditions such as osteoarthritis, fibrositis and rheumatoid arthritis. As it has a calmative effect, it is also useful in nervous conditions. Recent research has found that black cohosh may actually have mood boosting and anti-osteoporotic activities, which help reduce some of the secondary symptoms associated with menopause.

**Lignans and menopause**

Lignans are naturally occurring compounds found in the cell walls of plants such as fruits, vegetables, nuts and seeds such as flax (Linum usitatissimum). They are transformed in the colon to enterodiol and enterolactone which are then absorbed into the body via enterohepatic circulation. Studies show that enterolactone and enterodiol are helpful in conditions associated with estrogen deficiency. Lignan supplementation has also been shown to increase the production of 2-hydroxyestrogen. Research shows having a higher ratio of 2-hydroxyestrogen to 16?-hydroxyestrogen has a protective effect in women.

**Hops and Estrogen**

Lifenol is a patented hops extract which has been clinically studied in France in menopausal women. Hops have been used in the beer industry for hundreds of years but in 1988 one of the active components of hops – 8-prenylnaringenin (8PN) was identified as having estrogenic properties; it is considered the most potent phytoestrogen. 8PN has been shown to have a higher affinity for estrogenic receptors than coumesterol from clover or genistein or dadzein from soy due to a unique side chain.

**PMS and Menstrual Migraines**

Some of the ingredients in Fem Adapt such as soy isoflavones and black cohosh have also been traditionally used to treat PMS symptoms and have been clinically found to reduce the frequency of migraine attacks associated with menstruation. This makes Fem Adapt helpful for peri-menopausal and menopausal women dealing with the uncomfortable symptoms of hormone fluctuations.
Research

Genistein and Estrogen

Genistein has been shown in laboratories to have estrogenic effects by weakly binding to estrogen receptors (ER). For this reason it is commonly referred to as a phytoestrogen. It binds more strongly to ER-? than ER-?, which then competes with estradiol for binding to these estrogen receptors. The ?-estrogen receptor predominates in the heart, vasculature, bone, and bladder and may account for some of genistein’s beneficial effects. Genistein binds weaker to ERs than estradiol, and induces estrogenic effects with less potency than estradiol. This suggests that genistein selectively binds to estrogen receptors, serving as a natural alternative to conventional hormonal therapy, which has been associated with an increased risk of breast cancer, stroke, venous thromboembolism and coronary heart disease.

Genistein and Osteoporosis

Genistein structurally resembles estrogen and acts as a selective estrogen receptor modulator. Genistein may help control bone cell metabolism by its higher affinity for ?-estrogen receptors, which are found more in bone than ?-estrogen receptors, which are found more in reproductive tissue. Genistein has been shown to directly inhibit osteoclast activity, which is involved in the destruction of bone and increase osteoblastic proliferation, which is involved in bone formation. Studies have shown genistein to decrease bone resorption markers and increase bone formation markers, leading to a net gain in bone mass. These findings have been confirmed using the urinary excretion markers pyridinoline and deoxypyridinoline (markers of bone resorption), which were found to be decreased in research subjects taking genistein. In one clinical trial lasting over two years in duration, subjects supplemented with genistein and experienced an improvement in bone mineral density (BMD), as well as a significant decrease in bone fracture risk.

Flax Lignans

SDG or secoisolariciresinol diglucoside from flax (Linum usitatissimum) is specialized lignan that has high bioavailability due to the monomers compared to the large polymers usually found in traditional flax supplements. SDG is converted by mammalian bacteria in the colon into enterodiol (END) and enterolactone (ENL) which are the active human lignans. These lignans (remarkably similar to the human estrogens) are extensively studied for their cardioprotective, menopausal, bone density and inflammatory effects in humans. A recent study in women using 500mg of SDG for 6 weeks was found to reduce ultra-sensitive C-reactive protein, one of the inflammatory markers. Another study showed that women had significantly reduced cholesterol and other heart health indices when taking SDG monomers. Animal studies have confirmed the benefits of SDG for tissues in the breast, colon, ovary and the endometrium. An important finding was that SDG exerts a potent anti-angiogenesis effect particularly by inhibiting the vascular endothelial growth factor (VEGF) and promoting apoptosis. It is also hypothesized that lignans stimulate sex hormone binding globulin (SHBG) from the liver, inhibiting aromatase activity.

Hops
A double blind randomized cross over study (specifically designed to take into account the high degree of “placebo” effect common with menopausal studies) showed that 8PN reduced hot flashes and night sweats and may be a good adjunct to other post-menopausal treatments.

Black Cohosh

The effects of black cohosh on menopausal symptoms such as hot flashes and night sweats are under scrutiny, as are its traditional uses for pain related to PMS and its content of estrogen-like compounds. However, more recent research has revealed that black cohosh may have serotonin-like compounds that activate serotonin receptors. This is important because low mood can be secondary symptoms to menopause and PMS. In addition, newer clinical studies have shown that compounds in black cohosh may inhibit the formation of osteoclasts which are cells that break down bone. Bone loss is one of the top concerns among post-menopausal women. For these reasons, black cohosh is still considered to be advantageous for menopausal women.

Menstrual Migraines

Several older studies also found some of these ingredients helpful for reducing migraines associated with menstruation. One study found that a blend of the phytoestrogens black cohosh, dong quai and soy isoflavones significantly reduce the frequency of migraine attacks versus placebo from months 2-6. Another study administered genistein and daidzein, two phytoestrogens found in soy isoflavones and found reduced frequency of migraine attacks over 3 months.

Market Trends

Many women turn to conventional hormone therapies to manage physical difficulties experienced during menopause, or to over-the-counter pain killers, anti-inflammatories or birth control pills to alleviate the symptoms of PMS. Unfortunately some of the therapies and medications have undesirable side effects.

There is confusion as to whether phytoestrogens increase the risk of estrogen-dependent cancers. Many recent studies have found that phytoestrogens do not increase the risk of cancer.

AOR Advantage

AOR’s Fem Adapt includes standardized clinically tested natural ingredients that have been demonstrated to safely and effectively alleviate some of the uncomfortable and undesirable symptoms associated with menopause. There is also some evidence to suggest that phytoestrogens, and those from soy in particular, can help alleviate the symptoms of PMS including menstrual migraines.

References


Abstract

A randomized, double-blind, placebo-controlled, cross-over pilot study on the use of a standardized hop extract to alleviate menopausal discomforts.


OBJECTIVES: To examine the efficacy of a hop extract (standardized at 100μg 8-prenylnaringenin per day) for relief of menopausal discomforts.

METHODS: A 16-week randomized, double-blind, placebo-controlled, cross-over study was conducted with 36 menopausal women. The participants were randomly allocated to either placebo or active treatment (hop extract) for a period of eight weeks after which treatments were switched for another eight weeks. The Kupperman Index (KI), the Menopause Rating Scale (MRS) and a multifactorial Visual Analogue Scale (VAS) were assessed at baseline, and after eight and sixteen weeks.

RESULTS: After 8 weeks, both active treatment and placebo significantly improved all outcome measures when compared to baseline with somewhat higher average reductions for placebo than for the active treatment. After 16 weeks only the active treatment after placebo further reduced all outcome measures, whereas placebo after active treatment resulted in an increase for all outcome measures. Although, the overall estimates of treatment efficacy (active treatment-placebo) based on linear mixed models do not show a significant effect, time-specific estimates of treatment efficacy indicate significant reductions for KI (P = 0.02) and VAS (P = 0.03) and a marginally significant reduction (P = 0.06) for MRS after 16 weeks.

CONCLUSIONS: Whereas the first treatment period resulted in similar reductions in menopausal discomforts in both treatment groups, results from the second treatment period suggest superiority of the standardized hop extract over placebo. Thus, phytoestrogen preparations containing this standardized hop extract may provide an interesting alternative to women seeking relief of mild vasomotor symptoms.
Soy isoflavones, estrogen therapy, and breast cancer risk: analysis and commentary.


Messina MJ, Wood CE.

….soyfoods are essentially a unique dietary source of isoflavones, compounds which bind to estrogen receptors and exhibit weak estrogen-like effects under certain experimental conditions. In recent years the relationship between soyfoods and breast cancer has become controversial because of concerns–based mostly on in vitro and rodent data–that isoflavones may stimulate the growth of existing estrogen-sensitive breast tumors. This controversy carries considerable public health significance because of the increasing popularity of soyfoods and the commercial availability of isoflavone supplements. In this analysis and commentary we attempt to outline current concerns regarding the estrogen-like effects of isoflavones in the breast focusing primarily on the clinical trial data and place these concerns in the context of recent evidence regarding estrogen therapy use in postmenopausal women. Overall, there is little clinical evidence to suggest that isoflavones will increase breast cancer risk in healthy women or worsen the prognosis of breast cancer patients. Although relatively limited research has been conducted, and the clinical trials often involved small numbers of subjects, there is no evidence that isoflavone intake increases breast tissue density in pre- or postmenopausal women or increases breast cell proliferation in postmenopausal women with or without a history of breast cancer. The epidemiologic data are generally consistent with the clinical data, showing no indication of increased risk. Furthermore, these clinical and epidemiologic data are consistent with what appears to be a low overall breast cancer risk associated with pharmacologic unopposed estrogen exposure in postmenopausal women. While more research is required to definitively allay concerns, the existing data should provide some degree of assurance that isoflavone exposure at levels consistent with historical Asian soyfood intake does not result in adverse stimulatory effects on breast tissue.

In vitro serotonergic activity of black cohosh and identification of N(omega)-methylserotonin as a potential active constituent.


Cimicifuga racemosa (L.) Nutt. (syn. Actaea racemosa L., black cohosh) is used to relieve menopausal hot flashes, although clinical studies have provided conflicting data, and the active constituent(s) and mechanism(s) of action remain unknown. Because serotonergic receptors and transporters are involved with thermoregulation, black cohosh and its phytoconstituents were evaluated for serotonergic activity using 5-HT7 receptor binding, cAMP induction, and serotonin selective re-uptake inhibitor (SSRI) assays. Crude extracts displayed 5-HT7 receptor binding activity and induced cAMP production. Fractionation of the methanol extract led to isolation of phenolic acids and identification of N(omega)-methylserotonin by LC-MS/MS. Cimicifuga triterpenoids and phenolic...
acids bound weakly to the 5-HT7 receptor with no cAMP or SSRI activity. In contrast, N(omega)-methylserotonin showed 5-HT7 receptor binding (IC50 = 23 pM), induced cAMP (EC50 = 22 nM), and blocked serotonin re-uptake (IC50 = 490 nM). These data suggest N(omega)-methylserotonin may be responsible for the serotonergic activity of black cohosh.

Effects of the phytoestrogen genistein on bone metabolism in osteopenic postmenopausal women: a randomized trial.


BACKGROUND: Observational studies and small trials of short duration suggest that the isoflavone phytoestrogen genistein reduces bone loss, but the evidence is not definitive.

OBJECTIVE: To assess the effects of genistein on bone metabolism in osteopenic postmenopausal women.

DESIGN: Randomized, double-blind, placebo-controlled trial.

SETTING: 3 university medical centers in Italy. PATIENTS: 389 postmenopausal women with a bone mineral density (BMD) less than 0.795 g/cm2 at the femoral neck and no significant comorbid conditions.

INTERVENTION: After a 4-week stabilization period during which participants received a low-soy, reduced-fat diet, participants were randomly assigned to receive placebo (n = 191) or 54 mg of genistein (n = 198) daily for 24 months. Both the genistein and placebo tablets contained calcium and vitamin D.

MEASUREMENTS: The primary outcome was BMD at the anteroposterior lumbar spine and femoral neck at 24 months. Secondary outcomes were serum levels of bone-specific alkaline phosphatase and insulin-like growth factor I, urinary excretion of pyridinoline and deoxypyridinoline, and endometrial thickness. Data on adverse events were also collected.

RESULTS: At 24 months, BMD had increased in genistein recipients and decreased in placebo recipients at the anteroposterior lumbar spine (change, 0.049 g/cm2 [95% CI, 0.035 to 0.059] vs. -0.053 g/cm2 [CI, -0.058 to -0.035]; difference, 0.10 g/cm2 [CI, 0.08 to 0.12]; P < 0.001) and the femoral neck (change, 0.035 g/cm2 [CI, 0.025 to 0.042] vs. -0.037 g/cm2 [CI, -0.044 to -0.027]; difference, 0.062 g/cm2 [CI, 0.049 to 0.073]; P < 0.001). Genistein statistically significantly decreased urinary excretion of pyridinoline and deoxypyridinoline, increased levels of bone-specific alkaline phosphatase and insulin-like growth factor I, and did not change endometrial thickness compared with placebo. More genistein recipients than placebo recipients experienced gastrointestinal side effects (19% vs. 8%; P = 0.002) and discontinued the study. Limitations: The study did not measure fractures and had limited power to evaluate adverse effects.
CONCLUSION: Twenty-four months of treatment with genistein has positive effects on BMD in osteopenic postmenopausal women.

Isoflavone treatment for acute menopausal symptoms.


OBJECTIVE: The onset of climacteric symptoms (hot flashes and night sweats) is the primary reason for perimenopausal women to start hormone therapy. The association of a lower incidence of postmenopausal symptoms with high intake of soybeans in Asian women suggests that phytoestrogens are an alternative to estrogen therapy. The main effective compounds in soybean are isoflavones, which have a higher binding affinity to estrogen receptor beta than to estrogen receptor alpha. The aim of present study was to evaluate the effects of isoflavone treatment in postmenopausal women.

DESIGN: This was a double-blind prospective study. Sixty healthy postmenopausal women were randomly assigned by computer into two groups to receive 60 mg isoflavones or placebo daily for 3 months. Before and after treatment, climacteric symptoms were recorded; serum was collected to measure the levels of lipoprotein lipids, estradiol, and follicle-stimulating hormone; and biopsy specimens from endometrium and breast were analyzed to investigate the expression level of steroid receptors and proliferation. Endometrial thickness was measured by ultrasound.

RESULTS: Fifty-one women finished the 12-week study. In women receiving 60 mg isoflavones daily, hot flashes and night sweats were reduced by 57% and 43%, respectively. The treatment did not change the levels of circulating estradiol or follicle-stimulating hormone. Immunohistochemical staining of endometrial and breast biopsy specimens revealed that isoflavones did not affect expression levels of steroid receptors; estrogen receptors alpha, beta, and betacx; progesterone receptors A and B; or the proliferation marker Ki67. No side effects on body weight or lipoprotein lipids were observed.

CONCLUSIONS: This short-term prospective study implies that isoflavones could be used to relieve acute menopausal symptoms.

A triterpene glycoside from black cohosh that inhibits osteoclastogenesis by modulating RANKL and TNFalpha signaling pathways.


Qiu SX, Dan C, Ding LS, Peng S, Chen SN, Farnsworth NR, Nolta J, Gross ML, Zhou P.

Osteoporosis is a major age-related source of morbidity and mortality. Increased bone resorption mediated by osteoclasts is central to its pathogenesis. Cytokines, particularly RANKL and TNFalpha, are often increased under pathologic conditions, leading to enhanced osteoclastogenesis. Black
cohosh (Actaea/Cimicifuga racemosa L), a popular herbal supplement for the treatment of menopausal symptoms, was recently shown to have the beneficial effect of preventing bone loss. Here, we demonstrate that 25-acetylcimigenol xylopyranoside (ACCX), a triterpenoid glycoside isolated from black cohosh, potently blocks in vitro osteoclastogenesis induced by either RANKL or TNFalpha. This blockage of osteoclastogenesis elicited by ACCX results from abrogation of the NF-kappaB and ERK pathways induced by either RANKL or TNFalpha, respectively. Importantly, this compound attenuates TNFalpha-induced bone loss in vivo. Therefore, ACCX represents a potential lead for the development of a new class of antiosteoporosis agents.

Isoflavone supplements containing predominantly genistein reduce hot flash symptoms: a critical review of published studies.
Menopause; 2006, 13(5): 831-9

Williamson-Hughes PS, Flickinger BD, Messina MJ, Empie MW.

OBJECTIVE: Several reviews have evaluated the clinical evidence relating isoflavone treatment to the relief of menopausal hot flash symptoms. The majority of these reviews included a variety of isoflavone sources, often without discriminating between the identities of individual isoflavones contained in the study product. An evaluation of published studies using well-characterized isoflavone-containing supplements was conducted to determine whether the observed effects, or lack thereof, were attributable to differences in the composition of isoflavones in study products.

DESIGN: Eleven studies that met the inclusion criteria were stratified according to specific isoflavone composition.

RESULTS: All 11 studies contained similar total isoflavone doses. In five studies, involving a total of 177 treated participants, the study product provided more than 15 mg genistein (calculated as aglycone equivalents) per treatment. Each of these five studies consistently reported a statistically significant decrease in hot flash symptoms. In the six studies involving a total of 201 treated participants that provided less than 15 mg genistein per treatment, only one reported a statistically significant decrease in hot flash symptoms. Thus, the reduction in hot flashes was related to genistein dose, not total isoflavone content of the treatments.

CONCLUSION: Reports concluding that isoflavone supplements do not significantly reduce hot flash symptoms may be incorrect. The lack of discrimination between individual isoflavones contained in heterogeneous isoflavone mixtures from differing sources can be misleading when designing studies, interpreting results, and conducting reviews. In light of these observations, evaluation of isoflavone effects should focus greater attention to the specific composition within supplements in future studies.

A first prospective, randomized, double-blind, placebo-controlled study on the use of a standardized hop extract to alleviate menopausal discomforts.

Maturitas. 2006 May 20;54(2):164-75.
Heyerick A, Vervarcke S, Depypere H, Bracke M, De Keukeleire D.

**OBJECTIVES:** To examine the efficacy of a hop extract enriched in 8-prenylnaringenin (8-PN, the phytoestrogen in hops, Humulus lupulus L.) on relief of menopausal discomforts.

**METHODS:** A prospective, randomized, double-blind, placebo-controlled study over 12 weeks with 67 menopausal women, who were administered a hop extract standardized on 8-PN (100 or 250 microg). The responses were determined by means of a modified Kupperman index (KI) and a patients’ questionnaire.

**RESULTS:** All groups, including placebo, showed a significant reduction of the KI both after 6 weeks and after 12 weeks. The hop extract at 100 microg 8-PN was significantly superior to placebo after 6 weeks (P=0.023) but not after 12 weeks (P=0.086). No dose-response relationship could be established, as the higher dose (250 microg) was less active than the lower dose both after 6 weeks and after 12 weeks. Still, a trend for a more rapid decrease of KI was noticed for both active groups as compared to placebo. In particular, the decrease in hot flush score (isolated from the KI) was found significant for both treatment groups after 6 weeks (P.CONCLUSIONS: Daily intake of a hop extract, standardized on 8-PN as a potent phytoestrogen, exerted favorable effects on vasomotor symptoms and other menopausal discomforts. Hop-derived prenylated flavonoids may provide an attractive addition to the alternative treatments available for relief of hot flushes and other menopausal discomforts.

Effect of consumption of soy isoflavones on behavioural, somatic and affective symptoms in women with premenstrual syndrome.

**Br J Nutr. 2005 May;93(5):731-9.**

Bryant M, Cassidy A, Hill C, Powell J, Talbot D, Dye L.

Up to 80 % of the Western female population experience premenstrual syndrome (PMS). Long-term pharmacological therapy is unacceptable to most women, and is not warranted for moderate symptoms. Nutritional therapies are popular, but lack a clear evidence base. Anecdotal evidence suggests beneficial effects of soy isoflavones because of their influence on endogenous oestrogen and actions on specific tissues. The effect of isolated soya protein (ISP) containing 68 mg/d (aglycone equivalents) soy isoflavones (IF) on premenstrual symptom severity was studied in a seven-menstrual cycle, double-blind, placebo-controlled, crossover intervention study in twenty-three women with prospectively confirmed PMS aged 18-35 years and BMI 19-30 kg/m(2). ISP containing IF or milk protein placebo was consumed for two complete menstrual cycles. ISP containing IF (genistein, daidzein, equol) were measured in 24 h urine samples. After two cycles of ISP containing IF intervention, total symptoms (F(2,36) 8.20, P=0.000) and physical symptoms (F(2,36) 8.18, P=0.000) were significantly reduced compared with baseline after both active and placebo treatments, although differences between active and placebo treatment were non-significant. Specific premenstrual symptoms, headache (F(2,32) 4.10, P=0.026) and breast tenderness (F(2,32) 4.59, P=0.018), were reduced from baseline after soy IF, but not milk protein placebo. Cramps (F(2,32) 4.15, P=0.025) and swelling (F(2,32) 4.64, P=0.017) were significantly lower after active treatment compared with placebo. Concentrations of genistein and daidzein were increased following soy IF consumption, but
equol production did not enhance symptom reduction. The present study showed that ISP containing IF may have potential to reduce specific premenstrual symptoms via non-classical actions.

**Black cohosh acts as a mixed competitive ligand and partial agonist of the serotonin receptor.**


Extracts of the rhizome of black cohosh [Actaea racemosa L., formerly called Cimicifuga racemosa (L.) Nutt.] were evaluated for potential mechanisms of action in the alleviation of menopausal hot flashes. Ovariectomized Sprague-Dawley rats were administered a 40% 2-propanol extract of black cohosh [4, 40, and 400 mg/(kg.day)] by gavage for 2 weeks with or without estradiol [50 microg/(kg.day)] to determine if black cohosh could act as an estrogen or antiestrogen on the basis of an increase in uterine weight or vaginal cellular cornification. No effects were observed on uterine weight or on vaginal cellular cornification in rats treated with black cohosh alone or in combination with 17beta-estradiol, indicating this black cohosh extract had no estrogenic or antiestrogenic properties in the ovariectomized rat model. To evaluate other potential pathways by which black cohosh might reduce menopausal hot flashes, serotonin activity was first assessed by the inhibition of radioligand binding to cell membrane preparations containing recombinant human serotonin receptor (5-HT) subtypes. A 40% 2-propanol extract of black cohosh was tested against 10 subtypes of the serotonin receptor, revealing the presence of compounds with strong binding to the 5-HT(1A), 5-HT(1D), and 5-HT(7) subtypes. Subsequent binding studies were carried out using 5-HT(1A) and 5-HT(7) receptors because of their association with the hypothalamus, which has been implicated in the generation of hot flashes. The black cohosh 40% 2-propanol extract inhibited [(3)H]lysergic acid diethylamide (LSD) binding to the human 5-HT(7) receptor (IC(50) = 2.4 /- 0.4 microg/mL) with greater potency than binding of [(3)H]-8-hydroxy-2-(di-N-propylamino)tetralin to the rat 5-HT(1A) receptor (IC(50) = 13.9 /- 0.6 microg/mL). Analysis of ligand binding data indicated that components of a black cohosh methanol extract functioned as a mixed competitive ligand of the 5-HT(7) receptor. In addition, a black cohosh methanol extract elevated cAMP levels in 293T-5-HT(7)-transfected HEK cells, suggesting the extract acted as a partial agonist at the receptor. The elevation in cAMP mediated by the black cohosh extract could be reversed in the presence of the antagonist methiothepin, indicating a receptor-mediated process. These data suggest that reductions in hot flashes in some women taking black cohosh may not be due to estrogenic properties. This study identifies other possible biological targets of black cohosh that could account for reported biological effects.

**Randomized, controlled trial of phytoestrogen in the prophylactic treatment of menstrual migraine.**


Burke BE, Olson RD, Cusack BJ.
Approximately 30% of women afflicted with migraine have menstrually associated attacks. These migraines are often refractory to treatment. Evidence suggests estrogen and progestin fluctuations may influence menstrual migraine. Phytoestrogens have demonstrated estrogenic effects in some tissues, but are without stimulation of the endometrium, suggesting decreased risk with long-term use. This study was undertaken to assess the efficacy of a phytoestrogen combination in the prophylactic treatment of menstrual migraine. Forty-nine patients were randomized to receive either placebo, or a daily combination of 60 mg soy isoflavones, 100 mg dong quai, and 50 mg black cohosh, with each component standardized to its primary alkaloid. Patients received study medication for 24 weeks. Average frequency of menstrually associated migraine attacks during weeks 9-24 was reduced from 10.3 /- 2.4 (mean /- s.e.m.) in placebo treated patients to 4.7 /- 1.8 (P < 0.01) in patients treated with the phytoestrogen preparation.

Genistein, the dietary-derived angiogenesis inhibitor, prevents LDL oxidation and protects endothelial cells from damage by atherogenic LDL.


Kapiotis S, Hermann M, Held I, Seelos C, Ehringer H, Gmeiner BM.

....In this study, genistein, a compound derived from a soy diet with a flavonoid chemical structure (4?,5,7-trihydroxyisoflavone), which was found to inhibit angiogenesis, has been evaluated for its ability to act as an LDL antioxidant and a vascular cell protective agent against oxidized LDL. The results showed that genistein was able to inhibit the oxidation of LDL in the presence of copper ions or superoxide/nitric oxide radicals as measured by thiobarbituric acid-reactive substance formation, alteration in electrophoretic mobility, and lipid hydroperoxides. Bovine aortic endothelial cell- and human endothelial cell-mediated LDL oxidation was also inhibited in the presence of genistein. The 7-O-glucoside of genistein, genistin, was much less effective in inhibiting LDL oxidation in the cell-free and cell-mediated lipoprotein-oxidating systems. Incubating human endothelial cells in the absence or presence of genistein and challenging the cells with already oxidized lipoprotein revealed that in addition to its antioxidative potential during LDL oxidating processes, genistein effectively protected the vascular cells from damage by oxidized lipoproteins. The tyrosine kinase inhibitor genistein was found to block upregulation of two tyrosine-phosphorylated proteins of 132 and 69 kDa in endothelial cells induced by oxidized LDL. Parallel experiments with the inactive analogue daidzein, however, showed that the cytoprotective effect of the isoflavones seems not to be dependent on tyrosine phosphorylation. Our findings will support the suggested and documented beneficial action of a soy diet in preventing chronic vascular diseases....

Lignans and flavonoids inhibit aromatase enzyme in human preadipocytes.

J Steroid Biochem Mol Biol; 1994, 50(3-4):205-12

Wang C, Mäkelä T, Hase T, Adlercreutz H, Kurzer MS.

Lignans and flavonoids are naturally-occurring diphenolic compounds found in high concentrations in
whole grains, legumes, fruits and vegetables. Seven lignans and six flavonoids were evaluated for their abilities to inhibit aromatase enzyme activity in a human preadipose cell culture system. The lignan, enterolactone (Enl) and its theoretical precursors, 3-demethoxy-3O-demethylmatairesinol (DMDM) and didemethoxymatairesinol (DDMM) decreased aromatase enzyme activity, with Ki values of 14.4, 5.0 and 7.3 microM, respectively. The flavonoids, coumestrol, luteolin and kaempferol also decreased aromatase enzyme activity, with Ki values of 1.3, 4.8 and 27.2 microM, respectively. Aminoglutethimide, a pharmaceutical aromatase inhibitor, showed a Ki value of 0.5 microM. Kinetic studies showed the inhibition by all compounds to be competitive. Smaller decreases in aromatase activity were observed with the lignan, enterodiol (End) and its theoretical precursors, O-demethylsecoisolariciresinol (ODSI), demethoxysecoisolariciresinol (DMSI) and didemethylsecoisolariciresinol (DDSI). The flavonoids, O-demethylangolensin (O-Dma), fisetin and morin showed no inhibitory effects. The inhibition of human preadipocyte aromatase activity by lignans and flavonoids suggests a mechanism by which consumption of lignan- and flavonoid-rich plant foods may contribute to reduction of estrogen-dependent disease....