EndoStasis





Clinical Applications

- Supports Balance of the Female Hormone Cycle*
- May Ease Common Symptoms Associated with PMS and Menopause*
- Promotes Estrogen Detoxification*
- Provides Antioxidant Activity and Cellular Support*

EndoStasis delivers biologically active folate and other key methylation vitamins in combination with a targeted blend of ingredients to encourage hormone balance, help modify xenoestrogen activity, and restore tranquility. Vitex and black cohosh provide traditional hormone-balancing support; DIM, calcium D-glucarate, and 8-prenylnaringenin (from hops extract) promote estrogen detoxification; and rosemary, resveratrol, grape seed extract, and green tea extract provide antioxidant activity.*

All The 3rd Opinion Inc Formulas Meet or Exceed cGMP Quality Standards

Discussion

Whether it be during menstruation, ovulation, or menopause, the hormones in the female cycle fluctuate throughout a woman's lifetime. Hormonal imbalances contribute to the irritability and cramping commonly associated with premenstrual syndrome (PMS) and the hot flashes, sleep problems, and vaginal dryness associated with menopause. Hormonal imbalances may be exacerbated by xenoestrogens, a subcategory of endocrine disruptors that specifically have estrogen-like effects. Xenoestrogens have the capability to alter hormonal function in tissues, including breast, uterus, and cervix. Xenoestrogens may disrupt neurotransmitter balance, glucose homeostasis, normal reproduction, and healthy metabolism. ^[1,2] Additionally, improper aromatase conversion of excess estrogens has been associated with certain forms of hormone-dependent cancers. EndoStasis¹⁶ provides supplemental ingredients that have been traditionally and clinically used to support healthy hormone balance and promote detoxification of excess estrogens.*

Chaste Tree Berry Extract

Chasteberry (*Vitex* agnus-castus) has been used for centuries to support women with hormone-related gynecologic complaints. Chasteberry is well-known for its balancing effect on female hormones, prompting more regular cycles. Modern research has validated this traditional use by showing that various preparations of chasteberry demonstrate positive effects in women with PMS.^[3,4] The German Commission E approves the use of chasteberry to support menstrual cycle regularity, breast tenderness, and PMS; and it is widely recommended by family physicians and gynecologists in Germany for these issues.^[5] Chasteberry iridoids and flavonoids are thought to exert benefits through indirect effects on various hormones, especially prolactin and progesterone.^[5,6] Chasteberry also supports a normal, healthy attitude during the perimenopausal transition. It appears to significantly compete for binding at the estrogen receptors. Chasteberry has normalized short luteal phases and progesterone synthesis. The popular herb may help ease the common, transient symptom of mild breast tenderness possibly by inhibiting prolactin secretion.*^[7]

Black Cohosh Extract

Black cohosh (*Cimicifuga racemosa*) is an herb traditionally used by American Indians for support of gynecological issues, including menstrual cramping and related low-back discomfort. It is commonly used to address menopausal symptoms, which can be attributed to its gentle phytoestrogenic activity and ability to decrease the production of luteinizing hormone. Simply put, phytoestrogens are naturally occurring compounds in plants that have the ability to block estrogen receptor sites. Research suggests that black cohosh effectively maintains a sense of calmness and healthy outlook, and it may help address menopause-associated vasomotor symptoms.^[8,9] According to Ruhlen et al, black cohosh may exert its benefits through selective estrogen receptor modulation, serotonergic pathways, antioxidant activity, or inflammatory pathways.^[10] Various studies demonstrate that black cohosh may also reduce hot flashes, night sweats, vaginal dryness and thinning, sleep disturbances, and emotional symptoms.*^[11,12]

8-prenylnaringenin (8-PN)

Hops are the female seed cones of the hop species *Humulus lupulus*. The prenylflavonoid 8-PN, obtained from the lupulin glands of hop cones, appears to provide greater phytoestrogenic activity than other commonly used isoflavone phytoestrogens, such as daidzein and genistein.^[13] In vitro and in vivo studies indicate a potential role for 8-PN in easing common menopausal concerns.^[14,15] In pilot and prospective studies that were randomized and placebo-controlled, postmenopausal women who took 100-250 mcg/day of 8-PN experienced reductions in vasomotor symptoms and other common menopausal discomforts.^[15,16] 8-PN has also been observed to affect aromatase, a cytochrome P450 isoenzyme responsible for the conversion of circulating androgens into estrogens. Aromatase is expressed in several tissues, such as breast tissue, where estrogens exert physiological activity.^[17] Research has suggested that prenylflavonoids interact with aromatase in a manner that positively affects endogenous estradiol biosynthesis.*^[18]

Diindolylmethane (DIM) and Glucoraphanin

Healthy metabolism of exogenous and endogenous estrogens can be pivotal for hormonal balance. DIM (3,3'-diindolylmethane) is the stable, bioactive metabolite formed when stomach acid breaks down indole-3-carbinol (I3C), a sulfur-containing glucosinolate present in cruciferous vegetables. DIM has been found to support hormone metabolism and immune activity and stimulate antioxidant and detoxification systems. DIM helps maintain safe estrogen levels by aiding the conversion of dangerous estrogen fractions to more favorable metabolites and by promoting restoration of healthy hormone ratios. It promotes metabolism of estrogen into the favorable and protective 2-hydroxyestrone (2-OHE) metabolite versus production of 4-hydroxyestrone (4-OHE) and 16-alpha-hydroxyestrone (16-alphaOHE) metabolites.

The action of DIM is complemented by glucoraphanin, a compound isolated from broccoli seed that breaks down into sulforaphane glucosinolate (SGS). Researchers have shown that when SGS is broken down to sulforaphane (its active form), it safely and effectively upregulates the Nrf2 system, activates the antioxidant response element (ARE), enhances the production of important antioxidants, and activates vital phase

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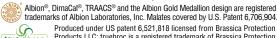
Supplement Facts

Amount	Per Serving %	Naily Val
Vitamin B6 (as pyridoxine HCl and pyridoxal 5'-phosphate)	15 mg	882%
	200 mcg DFE	50%
Vitamin B12 (as MecobalActive™ methylcobalamin)	200 mcg	8333%
Calcium (as DimaCal® dicalcium malate, calcium D-glucarate, and TRAACS® calcium bisglycinate chelate)	60 mg	5%
Magnesium (as Albion® dimagnesium malate)	25 mg	6%
Calcium D-Glucarate	100 mg	**
Diindolylmethane (DIM)	50 mg	**
Green Tea Extract (<i>Camellia sinensis</i>)(leaf)(98% polyphenols, 75% catechins, and 45% EGCG)	50 mg	**
Black Cohosh Extract (<i>Cimicifuga racemosa</i>)(root and rhizome)(2.5% triterper glycosides)	ie 50 mg	**
Chaste Tree Extract (<i>Vitex agnus-castus</i>)(berry)(0.6% aucubin and 0.5% agnuside)	50 mg	**
Turmeric Extract (<i>Curcuma longa</i>)(root)(95% curcuminoids)	25 mg	**
Rosemary Extract (Rosmarinus officinalis)(leaf)(5% rosmarinic acid)	25 mg	**
trans-Resveratrol (from Polygonum cuspidatum)(root)	20 mg	**
Grape Seed Extract (Vitis vinifera)(seeds)(95% proanthocyanidins)	12.5 mg	**
truebroc® Glucoraphanin (from broccoli extract)(Brassica oleracea italica)(seed	d) 4.5 mg	**
8-prenylnaringenin (from hops extract)(Humulus lupulus)(cones)	100 mcg	**
** Daily Value not established.		

Other Ingredients: Capsule (hypromellose and water), maltodextrin, ascorbyl palmitate, microcrystalline celluose, silica, L-leucine, tricalcium phosphate, and hydroxypropyl cellulose



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Mecobal Active is a trademark of Ferrer Health Tech.

Calcium D-glucarate is licensed from Applied Food Sciences, Inc. and is protected by US

II detoxification enzymes.[23] These mechanisms provide protection from toxins, xenoestrogens, and reactive intermediates formed after phase I detoxification.*

Additional Antioxidant Activity and Detoxification Support

EndoStasis provides additional ingredients that provide antioxidant activity and support detoxification. Calcium D-glucarate (CGT), produced naturally in very small amounts in the body and found in many fruits and vegetables, is included for its support of glucuronidation (phase II oxidation). Green tea catechins have been found to assist in free radical scavenging and support detoxification through modification of phase I and phase II enzymes. Turmeric extract provides curcumin, a phytonutrient valued for its promotion of antioxidant activity and support of metabolic detoxification. While resveratrol (Polygonum cuspidatum) may be best known for its antioxidant activity, it also provides phytoestrogenic activity. Both rosemary and grape seed extracts also provide antioxidant activity."

Folate, Methylcobalamin (B12), Vitamin B6, Calcium, and Magnesium Readily available forms of B vitamins, including 5-methyltetrahydrofolate (folate), methylcobalamin (B12), and pyridoxal 5'-phosphate (B6) are included for their role in supporting methylation. Highly bioavailable forms of calcium and magnesium are included for their role in muscle contraction and relaxation *

Directions

Take two capsules twice daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

References

- 1. Singleton DW, Khan SA. Xenoestrogen exposure and mechanisms of endocrine disruption. Front Biosci. 2003 Jan 1;8:s110-8. Review. [PMID: 12456297]
- 2. Nadal A, Ropero AB, Laribi O, et al. Nongenomic actions of estrogens and xenoestrogens by binding at a plasma membrane receptor unrelated to estrogen receptor alpha and estrogen receptor beta. Proc Natl Acad Sci U S A. 2000 Oct 10:97(21):11603-8. [PMID: 11027358]
- 3. Schellenberg R, Zimmermann C, Drewe J, et al. Dose-dependent efficacy of the Vitex agnus castus extract Ze 440 in patients suffering from premenstrual syndrome. Phytomedicine. 2012 Nov 15;19(14):1325-31. [PMID: 230223911
- 4. Zamani M. Neghab N. Torabian S. Therapeutic effect of Vitex agrus castus in patients with premenstrual syndrome, Acta Med Iran, 2012;50(2):101-06, IPMID: 223590781
- 5. Roemheld-Hamm B. Chasteberry. Am Fam Physician. 2005 Sep 1;72(5):821-24. [PMID: 16156340]
- 6. Schellenberg R. Treatment for the premenstrual syndrome with agnus castus fruit extract: prospective, randomised, placebo controlled study. BMJ. 2001 Jan 20;322(7279):134-37. [PMID: 11159568]
- 7. Chopin LB. Vitex agnus castus essential oil and menopausal balance: a research update. Complement Ther Nurs Midwifery. 2003 Aug;9(3):157-60. [PMID: 12852933]
- 8. Geller SE, Studee L, Botanical and dietary supplements for menopausal symptoms; what works, what does not, J Womens Health (Larchmt), 2005 Sep:14(7):634-49, [PMID: 16181020]
- 9. Nappi RE, Malavasi B, Brundu B, et al. Efficacy of Cimicifuga racemosa on climacteric complaints: a randomized study versus low-dose transdermal estradiol. Gynecol Endocrinol. 2005 Jan;20(1):30-5. [PMID: 15969244] 10. Ruhlen RL, Sun GY, Sauter ER. Black cohosh: insights into its mechanism(s) of action. Integr Med Insights. 2008;3:21-32. [PMID: 21614156]
- 11. Lieberman S. A review of the effectiveness of Cimicifuga racemosa (black cohosh) for the symptoms of menopause. J. Women's Health. 1998 June;7(5):525-9. [PMID: 9650153]
- 12. Mohammad-Alizadeh-Charandabi S, Shahnazi M, Nahaee J, et al. Efficacy of black cohosh (Cimicifuga racemosa L.) in treating early symptoms of menopause: a randomized clinical trial. Chin Med. 2013 Nov 1;8(1):20. [PMID: 24499633]
- 13. Overk CR, Yao P, Chadwick LR, et al. Comparison of the in vitro estrogenic activities of compounds from hops (Humulus lupulus) and red clover (Trifolium pratense). J Agric Food Chem. 2005 Aug 10;53(16):6246-53 [PMID: 16076101]
- 14. Bowe J, Li XF, Kinsey-Jones J, et al. The hop phytoestrogen, 8-prenylnaringenin, reverses the ovariectomy-induced rise in skin temperature in an animal model of menopausal hot flushes. J Endocrinol. 2006 Nov;191(2):399-405. [PMID: 17088409]
- 15. Heyerick A, Vervarcke S, Depypere H, et al. 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, [PMID: 16321485]
- 16. Erkkola R, Vervarcke S, Vansteelandt S, et al. A randomized, double-blind, placebo controlled, cross-over pilot study on the use of a standardized hop extract to alleviate menopausal discomforts. Phytomedicine. 2010 May:17(6):389-96, [PMID: 20167461]
- 17, Monteiro R, Faria A, Azevedo I, et al. Modulation of breast cancer cell survival by aromatase inhibiting hop (Humulus Lubulus L.) flavonoids, J Steroid Biochem Mol Biol, 2007 Jun-Jul:105(1-5):124-30, IPMID: 176439841 18. van Meeuwen JA, Nijmeijer S, Mutarapat T, et al. Aromatase inhibition by synthetic lactones and flavonoids in human placental microsomes and breast fibroblasts—a comparative study. Toxicol Appl Pharmacol. 2008 May 1:228(3):269-76, [PMID: 18201740]
- 19. Lord RS, Bongiovanni B, Bralley JA. Estrogen metabolism and the diet-cancer connection: rationale for assessing the ratio of urinary hydroxylated estrogen metabolites. Altern Med Rev. 2002 Apr;7(2):112-29. [PMID:
- 20. Bradlow HL. Review. Indole-3-carbinol as a chemoprotective agent in breast and prostate cancer. In Vivo. 2008 Jul-Aug;22(4):441-5. [PMID: 18712169]
- 21. Riby JE, Xue L, Chatterji U, et al. Activation and potentiation of interferon-gamma signaling by 3,3'-diindolylmethane in MCF-7 breast cancer cells. Mol Pharmacol. 2006 Feb;69(2):430-9. [PMID: 16267208]
- 22. Cavalieri E, Frenkel K, Liehr JG, et al. Estrogens as endogenous genotoxic agents—DNA adducts and mutations. J Natl Cancer Inst Monogr. 2000;(27):75-93. [PMID: 10963621]
- 23. Keum YS. Regulation of the Keap1/Nrf2 system by chemopreventive sulforaphane: implications of posttranslational modifications. Ann N Y Acad Sci. 2011 Jul;1229:184-89. [PMID: 21793854]

Does Not Contain

Wheat, gluten, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

> *These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

