



K05

ESTROVITE®

Optimizes Estrogen Metabolism and Receptor Site Response

BENEFITS OF PRODUCT

- Provides key compounds that support healthy estrogen receptor site response
- Provides important nutrients that improve estrogen metabolism

USE OF PRODUCT

This product is recommended for healthy estrogen balance in both men and women. Estrogen dominance is a very common hormonal imbalance that exists in all industrialized countries. Estrogen dominance can be determined by elevated levels of estrogen, or by the progesterone:estrogen ratio in women or the testosterone:estrogen ratio in men.

Estrovite® is useful in cases that require maintaining healthy estrogen metabolism such as premenstrual syndrome, menopause, etc. This product can also be used to support estrogen balance during follicular phase or luteal phase variations.

MECHANISM OF ACTION

This product optimizes/improves estrogen receptor sensitivity and cellular response with natural compounds such as isoflavones, herbal adaptogens, and vitamins. It also contains various compounds that support estrogen metabolism by means of supporting healthy concentration of sex hormone binding globulin, thus supporting healthy the levels of unbound active estrogens, encouraging proper detoxification of estrogen by further supporting methylation, hydroxylation, and balancing of estrogen receptor response.

KEY INGREDIENTS RESEARCH COMMENTARY:

The research information presented here should not be construed as claims regarding performance of this product.

ISOFLAVONES (DAIDZEIN AND GENISTEIN) Soy contains compounds called isoflavones. The biological active isoflavones include the compounds daidzein and genistein. Isoflavones have been classified as phytoestrogens because of their estrogenic properties, however this classification may not be appropriate. The term "Selective Estrogen Receptor Modulator" is the term that has gained recent acceptance due to the adaptive nature of these compounds on estrogen receptor sites. Isoflavones are not just compounds that have the ability to bind to estrogen receptors and induce an estrogen-like response. Their pharmacology is much more advanced. It appears that isoflavones have the ability to exert both agonistic and anti-agonistic effects on estrogen receptor sites depending on the circumstance. For example, isoflavones have demonstrated an estrogenic effect on receptor sites in tissues absent of proper estrogen levels and an anti-estrogenic effect on receptor sites in the presence of excess estrogen.¹

This explains their acknowledged clinical effectiveness in both low and high estrogen cases. These compounds have also been shown to have modulating impacts on estrogen metabolism that are not direct receptor mediated due to their impact on sex hormone-binding globulin (SHBG). Isoflavones have the ability to support the production of SHBG, which has the ability to bind to the cell surface receptors resulting in the regulation and the bioavailability and activity of hormones.² Isoflavones have also demonstrated in studies to have many positive impacts on both male and female metabolism,^{3 4 5} antiviral properties,⁶ anti-inflammatory properties,⁷ antioxidant properties,^{8 9} and cardioprotective properties.¹⁰

DIRECTIONS

Take 1-2 capsules, 3 times a day, or as directed by your healthcare practitioner.

Supplement Facts

Serving size 1 vegetarian capsule
Servings per container 90

Amount Per Serving	% Daily Value
Vitamin B6 (as pyridoxal 5 phosphate) 12 mg	600%
Folic Acid 700 mcg	175%
Vitamin B12 (as cyanocobalamin) 50 mcg	833%
Magnesium (as magnesium citrate) 60 mg	15%
Indol 3 Carbinol 50 mg	*
Genistein (from soy isoflavone) 10 mg	*
Daidzein (from soy isoflavone) 10 mg	*
Black Cohosh root 150 mg	*
Dong Quai root 100 mg	*
Proprietary Blend: 23 mg	*
Red Clover leaf extract	*
Cellulase (plant enzyme)	*
Peptidase (plant enzyme)	*

*Daily value not established.

Other Ingredients: vegetable cellulose (vegetarian capsule), silicon dioxide.

INDOLE-3-CARBINOL Estrogen hormones are metabolized initially in the liver by hydroxylation at phase I of the detoxification process. This hydroxylation takes place primarily on one of three carbons. The 2-carbon, which yields 2-hydroxyestron (2-OH), the 4-carbon which yields 4-hydroxyestron (4-OH) or on the 16-alpha-carbon which yields 16-alpha-hydroxyestron (16-alpha-OH).

The 2-OH metabolite has a very weak estrogenic response and is therefore the preferential estrogen metabolite. On the other hand, 16-alpha-OH and the 4-OH exert a powerful and persistent mitogenic estrogen receptor response. Therefore, modifying metabolism to yield more 2-OH metabolites and less 16-alpha-OH and the 4-OH metabolites would be optimal, especially for those that are estrogen dominant. A natural compound derived from cruciferous vegetables called Indole-3-Carbinol (I3C) has the ability to shift the ratio of 2-OH to 16-alpha-OH in favor of 2-OH. I3C promotes 2-OH formation by inducing phase I cytochrome P450-1A1 and P450-1A2, which facilitates 2-hydroxylation of estrogen. In addition, I3C also has shown some ability to decrease 4-OH production. Improving the ratios of phase I hydroxylation metabolites may have positive impacts on the influence of healthy estrogen metabolism.^{11 12}

13 14 15 16 17

Statements in this flyer have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.

Formula
Info Page

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As Prepared by Apex Energetics, Inc.

PYRIDOXAL-5-PHOSPHATE (B6) Vitamin B-6 has been shown to reduce tissue hypersensitivity to estrogen. Evidence shows that vitamin B6 interacts with the steroid hormone receptor complex and the binding of this complex to DNA. This binding will then turn off the transmission of the hormonal signal to the nucleus of the cell. A B-6 deficiency may explain why there may be exaggerated symptoms of estrogen dominance with normal or slightly increased estrogen levels. It may not be the level of estrogens causing estrogen excess symptoms, but rather the exaggerated transcriptional response that induces the expression of estrogen excess symptoms and patterns. An active form of B-6 such as pyridoxal-5-phosphate should be considered anytime a nutritional approach is used to optimize estrogen or other hormonal patterns.¹⁸

BLACK COHOSH (CIMICIFUGA RACEMOSA) contains triterpene glycosides which have estrogen modulating impacts on metabolism. The active components of black cohosh appear to improve estrogen deficient type symptoms without the adverse risks of estrogen replacement therapy. It has shown to decrease hot flashes, increase blood flow to the pelvic area, relieve spasms, and improve hormone related mood depression, but it does not stimulate the uterine tissues the way estrogen does or alter the release of prolactin or follicle-stimulating hormone. Therefore, it lacks the complete properties of estrogen, which makes it a safe and natural compound to use in support of estrogen balance.^{20 21 22 23 24}

DONG QUAI (ANGELICA SINENSIS) is another herb that has "Selective Estrogen Receptor Modulator" properties. It contains compounds that exhibit estrogenic expression. However, their activity is as low as a 1:400 ratio compared to human estrogens and have no true estrogen impact on cells. It is its chemical influence on receptor sites that have made this herb useful in both estrogen deficient and estrogen excess cases. In estrogen deficient patterns, angelica compounds have the ability to exert some influence on estrogen receptor site expression and improve symptoms of low estrogen. In estrogen excess type patterns, angelica compounds have the ability to compete with estrogens on receptor sites and reduce the influence of estrogen receptor binding. Therefore, it may be useful in both excess and deficient type patterns.²⁵ Angelica has many other favorable qualities including qualities as a hemotonic for treating anemia, analgesic properties, anti-inflammatory

and anti-allergenic actions, cardioprotective influence, mild laxative property, as well as its ability to increase vagina lubrication.^{26 27 28 29 30 31}

MAGNESIUM is an essential nutrient for the phase II detoxification of estrogens. Once estrogens are hydroxylated by phase I detoxification they become catechol estrogens with the potential to become oxidized to quinone estrogens. Quinone estrogens can induce genotoxic damage and promote carcinogenesis.³² Magnesium is an essential cofactor for the enzyme catechol-O-methyltransferase (COMT) which converts catechol estrogens into water soluble metabolites before they become potential carcinogenic quinone estrogens.³³ Magnesium also helps phase II glucuronidation by up-regulating the enzyme glucuronyl transferase which helps detoxify estrogens.

METHYLATION COFACTORS - Vitamin B12 and folic acid help support the essential methylation detoxification pathway which helps convert the estrogens to methyl ester metabolites which can then be excreted via bile elimination or urination.

OTHER PRODUCTS TO CONSIDER

Other products can be used in conjunction with Estrovite® (K05) to balance hormone physiology. Progestaid™ (K04) is a broad spectrum herbal and nutritional product used to support progesterone balance. Testanex™ (K17) can be used to normalize the enzyme aromatase which converts testosterone into estrogen. Elevated cortisol can suppress leutinizing hormone and cause estrogen dominance. AdrenaStim™ (K16) can be used to cortisol release. Metacrin-DX™ (K10) and Methyl-SP™ (K14) can be used to support estrogen detoxification. Super EFA Complex™ (K08) supplies essential fatty acids that are selective estrogen receptor modulators. Opticrine™ (K03) can be used to support the gonadal-hypophyseal feedback loop which may be helpful in cases with low estrogen.

REFERENCE INFO

¹ Adlercreutz H, Mazur W. Phyto-oestrogens and Western diseases. *Ann Med* 1997;29:95-120.

² Price KR, Fenwick GR. Naturally occurring oestrogens in foods – a review. *Food Addit Contam* 1985;2:73-106.

³ Hirano T, Fukuoaka K, Oka K, et al. Antiproliferative activity of mammalian lignan derivatives against the human breast carcinoma cell line, ZR-75-1. *Cancer Invest* 1990;8:595-602.

⁴ Hartman PE, Shenkel DM. Antimutagens and anticarcinogens: a survey of putative interceptor molecules. *Environ Mol Mutagen* 1990;15:145-182.

⁵ Hirano T, Gotoh M, Ika K. Natural flavonoids and lignans are potent cyto-static agents against human leukemic HL-60 cells. *Life Sci* 1994; 55:1061-1069.

⁶ MacRae WD, Hudson JB, Towers GH. The antiviral action of lignans. *Plant Med* 1989;55:531-535.

⁷ Wu ES, Loch JT 3rd, Toder BH, et al. Flavones. 3. Synthesis, biological activities, and conformational analysis of isoflavone derivatives and related compounds. *J Med Chem* 1992;18:3519-3525.

⁸ Jha HC, Recklinghausen G, Zilkah F. Inhibition of in vitro microsomal lipid peroxidation by isoflavonoids. *Biochem Pharmacol* 1985;34:1367-1369.

⁹ Wei H, Wei L, Frenkel K, et al. Inhibition of tumor promoter-induced hydrogen peroxide formation in vitro and in vivo by genistein. *Nutr Cancer* 1993;20:1-12.

¹⁰ Wagner JD, Cefalu WT, Anthony MS, et al. Dietary soy protein and estrogen replacement therapy improve cardiovascular risk factors and decrease aortic cholesteryl ester content in ovariectomized cynomolgus monkeys. *Metabolism* 1997;46:698-705.

¹¹ Bradlow HL, Sepkovic DW, Telang NT, et al. Multifunctional aspects of the action of indole-3-carbinol as an anti tumor agent. *Ann NY Academy Sci* 1997;28-29:111-116.

¹² Michnovicz JJ, Bradlow HL. Altered estrogen metabolism and excretion in humans following consumption of indole-3-carbinol. *Nutr Cancer* 1991;16(1):59-66.

¹³ Michnovicz JJ, Adlercreutz H, Bradlow HL. Changes in levels of urinary estrogen metabolites after oral indole-3-carbinol treatments in humans. *J Natl Cancer Inst* 1997;89(10):718-23.

¹⁴ Wong GY, Bradlow L, Sepkovic D, et al. Dose-ranging study of indole-3-carbinol for breast cancer prevention. *J Cell Biochem Suppl* 1997;28-29:111-116.

¹⁵ Yuan F, Chen DZ, Liu K, et al. Anti-estrogenic activities of indole-3-carbinol in cervical cells: implications for prevention of cervical cancer. *Anticancer Res* 1999;19(3A):1673-80.

¹⁶ Michnovicz JJ, Bradlow HL. Induction of estradiol metabolism by dietary indole-3-carbinol in humans. *J Natl Cancer Inst* 1990;82:947-949.

¹⁷ Telang NT, Kaldare M, Bradlow HL, et al. Inhibition of proliferation and modulation of estradiol metabolism: novel mechanisms for breast cancer prevention by the phytochemical indole-3-carbinol. *Proc Soc Exp Bio Med* 1997;216:246-252.

¹⁸ Tully DB, Allgood VE, Cidlowski JA. Modulation of steroid receptor-mediated gene expression by vitamin B6. *FASEB J* 1994;8(3):343-49.

¹⁹ Brucker A. Essay on the phytotherapy of hormonal disorders in women. *Med Welt* 1960;44:231-2333.

²⁰ Warnecke G. Influencing menopausal symptoms with a phytotherapeutic agent. *Med Welt* 1985;36:871-874.

²¹ Stoll W. Phytopharmakon influences atrophic vaginal epithelium. Double-blind-study – Cimicifuga vs. estrogenic substances. *Therapeuticum* 1987; 1:23-31.

²² Lieberman S. A review of the effectiveness of Cimicifuga racemosa for the symptoms of menopause. *J Women's Health*. 7(5):525-529, 1998.

²³ Miksicek RJ. Commonly occurring plant flavonoids have estrogenic activity. *Molecular Pharmacology* 1993;44:37-43.

²⁴ Duker EM, et al. Effects of extracts from Cimicifuga racemosa on gonadotropin release in menopausal women and ovariectomized rats. *Planta Medica* 1991;57:420-424.

²⁵ Hirata JD, et al. Does dong quai have estrogenic effects in postmenopausal women? A double-blind placebo-controlled trial. *Fertil Steril* 68(6):981-986, 1997.

²⁶ Ozaki Y. Antiinflammatory effect of tetramethylpyrazane and ferulic acid. *Chem Pharm Bull* 1992;40(4):954-956.

²⁷ Bensky D, et al. *Chinese Herbal Medicine Materia Medica*, Seattle, WA:East-land Press, 1986.

²⁸ Sherman JA. *The Complete Botanical Prescriber*. Portland OR: John Sherman, 1993.

²⁹ Hikino H. Recent research on Oriental medicinal plants. *Econ Med Plant Res* 1985;1:53-85.

³⁰ Thastrup O, Fjaland B, Lemmich J. Coronary vasodilatory, spasmolytic and cAMP-phosphodiesterase inhibitory properties of dihydropyranocoumarins and dihydrofuranocoumarins. *Acta Pharmacol et Toxicol* 1983;52:246-53.

³¹ Yamada H, Kiyohara H, Cyong JC, et al. Studies on polysaccharides from Angelica. *Planta Medica* 1984;48:163-167.

³² Yager JD, Liehr JG. Molecular mechanisms of estrogen carcinogenesis. *Annu Rev Pharmacol Toxicol* 1996;36:203-32.

³³ Bullerworth M, Lau SS, Monks TJ. 17 Beta-estradiol metabolism by hamster hepatic microsomes. Implications for the catechol-O-methyl transferase-mediated detoxification of catechol estrogens. *Drug Metab Dispos* 1996;24(4):588-94.