# FlashArrest®

### Targeting Estrogen Activity for Men and Women\*



Available in 60 capsules

### **Discussion**

As scientific knowledge advances, it is becoming more evident that a balance of estrogenic and antiestrogenic activities within the body is normal and optimal, has important effects on the health of estrogen-sensitive tissues, and can help relieve normal menopausal symptoms. Reducing abundant estrogenic activity is one way to support balance. Another approach is to offer the body a "weak" estrogen that can support estrogenic activity when it is low or can replace more potent endogenous or exogenous estrogens. [1] Research suggests that the ingredients in FlashArrest do both.\*

Prenylnaringenins (PNs) Hops are the female seed cones of the hop species *Humulus lupulus*, a medicinal plant that offers a wide range of biologically active components that are used for a variety of purposes. More recently, prenylflavonoids obtained from the lupulin glands of hop cones have become the focus of research. The prenylflavonoid 8-PN has been identified as one of the most potent phytoestrogens because it provides greater activity than other commonly used isoflavone phytoestrogens, such as daidzein and genistein.\*<sup>[2]</sup>

In vitro and in vivo studies conducted in recent years indicate a potential role for PNs in relieving common menopausal concerns. [3,4] In pilot and prospective studies that were randomized and placebo-controlled, postmenopausal women who took 100-250 mcg/day of standardized PNs experienced reductions in vasomotor symptoms and other common menopausal discomforts. [4,5] Although further studies are needed, animal and in vitro research with PNs indicates a mild estrogenic effect in vaginal and uterine tissues [6] and shows promising effects in cardiovascular, [7,8] bone, [9,10] prostate, [11] and breast health. [12,13]\*

Not only do PNs offer phytoestrogenic activity, but they have 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. [12] New research suggests that prenylflavonoids interact with aromatase in a manner that positively affects endogenous estradiol biosynthesis [1] and, therefore, the relative balance of other hormones, such as testosterone. [14] Of the flavonoids studied, 8-PN has demonstrated the greatest impact on estrogen biosynthesis during in vitro experimentation. [1,12] It has been postulated that providing phytoestrogens while modulating the production of

## **Clinical Applications**

- » Supports the Body's Natural Process of Healthy Aromatase Activity\*
- » May Support Bone, Breast, and Prostate Tissue Health\*
- » Helps to Relieve Normal Menopausal Symptoms, Such as Hot Flashes\*
- » Supports Cardiovascular Health\*

FlashArrest® delivers a unique, proprietary blend of 8-prenylnaringenin (8-PN) from hops and plant-lignan extract at clinically relevant levels. Research suggests lignans and 8-PN can support the body's natural process of healthy aromatase activity and exert phytoestrogen (e.g., enterolactone) and antioxidant activity. This all-natural formula may support cardiovascular, bone, breast, and prostate health and help relieve normal menopausal discomforts.\*

potent endogenous estrogens may result in safer, more balanced estrogenic activity. Brunelli et al.<sup>[15]</sup> investigated the influences of PNs on epidermal growth factor (EGF)-elicited pathways in certain breast cells and demonstrated that 8-PN interferes with EGF-induced cell proliferation in estrogen-receptor positive cells.\*

HMRlignan™ Plant lignans are phytonutrients commonly found in small amounts in unrefined whole grains, seeds, nuts, vegetables, berries, and beverages, such as tea and coffee. The friendly bacteria in our intestines convert plant lignans into the "human" lignans called enterodiol and enterolactone. HMRlignan is a concentrated, naturally occurring plant lignan called 7-hydroxymatairesinol, which is derived from the Norway spruce (*Picea abies*). In humans, 7-hydroxymatairesinol is a direct metabolic precursor of enterolactone.\*<sup>[16]</sup>

Enterolactone is a phytoestrogen that binds to estrogen receptors and has both weak estrogenic and weak antiestrogenic effects. The latter accounts for much of its cell-protective capacity. Additionally, in vitro work has demonstrated that enterolactone affects aromatase and the biosynthesis of estrogen and has strong free radical scavenging and antioxidant properties. He protective effect of lignans and enterolactone on tissues, including those of the prostate and breast, is encouraging. At the same time, the estrogenicity of HMR and enterolactone, although milder than estradiol, offers promising applications for women with menopausal concerns. For instance, in a randomized, single-blind, parallel group pilot study, 20 menopausal women taking 50 mg/d of hydroxymatairesinol for eight weeks experienced half as many hot flushes as compared to pretreatment. He Furthermore, high serum enterolactone has repeatedly been associated with cardiovascular health.\*

#### FlashArrest® Supplement Facts

Serving Size: 2 Capsules

FlashArrest® Proprietary Blend 193 mg \*\*

Hops Extract (*Humulus lupulus*) (flower)
(0.15% 8-prenylnaringenin) and Norway Spruce Extract
(*Picea abies*)(knotwood)(81% hydroxymatairesinol
potassium acetate adduct and other lignans)

\*\* Daily Value not established.

Other Ingredients: Microcrystalline cellulose, capsule (hypromellose and water), stearic acid, magnesium stearate, and silica.

**DIRECTIONS:** Take one to two capsules daily, or use as directed by your healthcare professional.

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

**STORAGE:** Keep closed in a cool, dry place out of reach of children.

**FORMULATED TO EXCLUDE:** Wheat, gluten, corn, soy, animal and dairy products, fish, shellfish, peanuts, tree nuts, egg, sesame, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, and artificial preservatives.



### References

- 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]
- 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]
- 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]
- 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]
- Erkkola R, Vervarcke S, Vansteelandt S, et al. A randomized, double-blind, placebocontrolled, 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]
- Rimoldi G, Christoffel J, Wuttke W. Morphologic changes induced by oral long-term treatment with 8-prenylnaringenin in the uterus, vagina, and mammary gland of castrated rats. Menopause. 2006 Jul-Aug;13(4):669-77. [PMID: 16837889]
- Böttner M, Christoffel J, Wuttke W. Effects of long-term treatment with 8-prenylnaringenin and oral estradiol on the GH-IGF-1 axis and lipid metabolism in rats. *J Endocrinol*. 2008 Aug;198(2):395-401. [PMID: 18499805]
- Di Vito C, Bertoni A, Nalin M, et al. The phytoestrogen 8-prenylnaringenin inhibits agonistdependent activation of human platelets. *Biochim Biophys Acta*. 2012 Nov;1820(11):1724-33. [PMID: 22766195]
- Miyamoto M, Matsushita Y, Kiyokawa A, et al. Prenylflavonoids: a new class of non-steroidal phytoestrogen (Part 2). Estrogenic effects of 8-isopentenylnaringenin on bone metabolism. Planta Med. 1998 Aug;64(6):516-19. Erratum in: Planta Med. 1998 Dec;64(8):769. [PMID: 9741296]
- Sehmisch S, Hammer F, Christoffel J, et al. Comparison of the phytohormones genistein, resveratrol and 8-prenylnaringenin as agents for preventing osteoporosis. *Planta Med*. 2008 Jun;74(8):794-801. [PMID: 18537073]
- Delmulle L, Bellahcène A, Dhooge W, et al. Anti-proliferative properties of prenylated flavonoids from hops (Humulus lupulus L.) in human prostate cancer cell lines. *Phytomedicine*. 2006 Nov;13(9-10):732-34. [PMID: 16678392]
- Monteiro R, Faria A, Azevedo I, ert al. Modulation of breast cancer cell survival by aromatase inhibiting hop (Humulus lupulus L.) flavonoids. J Steroid Biochem Mol Biol. 2007 Jun-Jul;105(1-5):124-30. [PMID: 17643984]
- Hemachandra LP, Madhubhani P, Chandrasena R, et al. Hops (Humulus lupulus) inhibits oxidative estrogen metabolism and estrogen-induced malignant transformation in human mammary epithelial cells (MCF-10A). Cancer Prev Res (Phila). 2012 Jan;5(1):73-81. [PMID: 21997247]
- Burnett-Bowie SA, McKay EA, Lee H, et al. Effects of aromatase inhibition on bone mineral density and bone turnover in older men with low testosterone levels. J Clin Endocrinol Metab. 2009 Dec;94(12):4785-92. [PMID: 19820017]
- Brunelli E, Pinton G, Chianale F, et al. 8-Prenylnaringenin inhibits epidermal growth factorinduced MCF-7 breast cancer cell proliferation by targeting phosphatidylinositol-3-0H kinase activity. J Steroid Biochem Mol Biol. 2009 Feb;113(3-5):163-70. [PMID: 19103290]
- Cosentino M, Marino F, Ferrari M, et al. Estrogenic activity of 7-hydroxymatairesinol potassium acetate (HMR/lignan) from Norway spruce (Picea abies) knots and of its active metabolite enterolactone in MCF-7 cells. *Pharmacol Res*. 2007 Aug;56(2):140-47. [PMID: 17572100]
- 17. Barlow RN, Johnson JP. Fact sheet on the phytoestrogen enterolactone. Breast Cancer & The Environment Research Centers. 2007 Nov:31-37. http://www.zerobreastcancer.org/research/bcerc\_factsheets\_phytoestrogen\_enl.pdf. Accessed October 19, 2012.
- Brooks JD, Thompson LU. Mammalian lignans and genistein decrease the activities of aromatase and 17beta-hydroxysteroid dehydrogenase in MCF-7 cells. J Steroid Biochem Mol Biol. 2005 Apr;94(5):461-67. [PMID: 15876411]
- HMRlignan<sup>™</sup>—Direct Enterolactone Precursor [press release]. Locarno, Switzerland and Easton, PA: Linnea SA; August 17, 2005. http://www.hmrlignan.com/images/PressRelease\_ Launch.pdf. Accessed October 24, 2012.
- Kangas L, Saarinen N, Mutanen M, et al. Antioxidant and antitumor effects of hydroxymatairesinol (HM-3000, HMR), a lignan isolated from the knots of spruce. Eur J Cancer Prev. 2002 Aug;11 Suppl 2:S48-57. [PMID: 12570335]
- Bylund A, Saarinen N, Zhang JX, et al. Anticancer effects of a plant lignan 7-hydroxymatairesinol on a prostate cancer model in vivo. Exp Biol Med (Maywood). 2005 Mar;230(3):217-23. [PMID: 15734725]
- Olsen A, Knudsen KE, Thomsen BL, et al. Plasma enterolactone and breast cancer incidence by estrogen receptor status. *Cancer Epidemiol Biomarkers Prev.* 2004 Dec;13(12):2084-9. [PMID: 15598765]
- Miura D, Saarinen NM, Miura Y, et al. Hydroxymatairesinol and its mammalian metabolite enterolactone reduce the growth and metastasis of subcutaneous AH109A hepatomas in rats. Nutr Cancer. 2007;58(1):49-59. [PMID: 17571967]
- 24. Udani J, Hardy M. 7-Hydroxymatairesinol (7-HMR) New pharmacokinetic data and effect on enterolactone metabolites and hot flashes in menopausal women. Scripps Integrative Medicine 5th Annual Natural Supplements Conference; January 17-20, 2008; San Diego, CA. http://www.hmrlignan.com/images/Research.pdf. Accessed October 19, 2012.

Additional references available upon request

