What Makes Releaves® Unique?

Releaves®

A non-synthetic whole food dietary supplement that provides natural vitamins and precursors for all animals with suspected hormonal imbalances.

Ingredients: A proprietary blend of sustainable red palm fruit oil enhanced with organic red raspberry leaves and organic red raspberry extract

Empirical results suggest Releaves may have application for:

- Suspected hormonal imbalances in all animals
- Chronic egg-laying in birds and reptiles
- Feather picking behavior with a hormonal cause
- Other reproductive disorders in all animals
- Behavioral problems due to hormonal stress
- Ferret adrenal disease†
- Mammary gland tumors†
- Uterine tumors†
- Cushing's disease†

Releaves Mode of Action

There is much research on the antioxidant, anti-inflammatory, antimicrobial, antitumor and pro-cardiovascular effects of polyphenols found in raspberries.[7,8] The ability of the polyphenols to counteract an animal's hormonal imbalances include the following factors:

- **Ellagic acid is a breakdown product derived from ellagitannins,** which are compounds found in abundance in red raspberries.[6,8,9-12] This metabolite can act as a selective estrogen receptor modulator (SERM). Because there are different types of estrogen receptors (ER alpha and beta), ellagic acid can act as an agonist (ER alpha) in some cells and antagonist (ER beta) in other cells, depending on the distribution of estrogen receptor types in that cell.[13] This is similar to the effects of the drug tamoxifen.
- **There is evidence in mammals that ellagic acid can be further metabolized to urolithins by bacteria in the lower gut,** which are more potent ER-binding ligands.[14]
- **Raspberry ketone,** besides having effects on fat metabolism, can also act as an androgen antagonist.[15-17]
- **Protocatechuic acid (PCA)** is a bacterial breakdown product in gut microflora of anthocyanin, a polyphenol that is abundant in raspberry extracts.[9,10,12,18] A growing body of evidence supports the concept that PCA can exert a variety of biological effects by acting on different molecular targets. It has been shown that PCA possesses antioxidant and anti-inflammatory as well as antihyperglycemic and neuroprotective activities. Interestingly, PCA was shown to prevent damage to reproductive markers in male rats exposed to tetrachlorodibenzo-p-dioxin (TCDD), an environmental contaminant.[19]
- **Polyphenols in the berry can also** act as antagonists of the epidermal growth factor receptor (EGFR). In chickens (and other animals) activation of this receptor plays a critical role in the supply of follicle cells that are required for further egg development.[20-23] Berry polyphenols appear to block activation of EGFR, at least in cancer models, so it is possible that this may also happen at the level of the follicle cells and could slow or interrupt a continuous egg-laying situation.[24]

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†Further research being conducted

References

1. McFarlin BL, Gibson MH, O'Rear J, Harman P: A national survey of herbal preparation use by nurse-midwives for labor stimulation. Review of the literature and recommendations for practice. J Nurse Midwifery, 44:205-16, 1999.
2. Jing Z, Pistilli MJ, Holloway AC, Crankshaw DJ: The effects of commercial preparations of red raspberry leaf on the contractility of the rat's uterus in vitro. Reprod Sci, 17:494-501, 2010.
3. Bamford DS, Percival RC, Tothill AU: Raspberry leaf tea: a new aspect to an old problem. Br J Pharmacol, 40:161P-2P, 1970.
4. Rojas-Vera J, Patel AV, Dacke CG: Relaxant activity of raspberry (*Rubus idaeus)* leaf extract in guinea-pig ileum in vitro. Phytother Res, 16:665-8, 2002.
5. Makaji E, Ho SH, Holloway AC, Crankshaw DJ: Effects in rats of maternal exposure to raspberry leaf and its constituents on the activity of cytochrome p450 enzymes in the offspring. Int J Toxicol, 30:216-24, 2011.
6. Rao AV, Snyder DM: Raspberries and human health: a review. J Agric Food Chem, 58:3871-83, 2010.
7. Landete JM: Updated knowledge about polyphenols: functions, bioavailability, metabolism, and health. Crit Rev Food Sci Nutr, 52:936-48, 2012.
8. Gonzalez-Barrio R, Edwards CA, Crozier A: Colonic catabolism of ellagitannins, ellagic acid, and raspberry anthocyanins: in vivo and in vitro studies. Drug Metab Dispos, 39:1680-8, 2011.
9. Kahkonen MP, Hopia AI, Heinonen M: Berry phenolics and their antioxidant activity. J Agric Food Chem, 49:4076-82, 2001.
10. Koponen JM, Happonen AM, Mattila PH, Torronen AR: Contents of anthocyanins and ellagitannins in selected foods consumed in Finland. J Agric Food Chem, 55:1612-9, 2007.
11. Borges G, Degeneve A, Mullen W, Crozier A: Identification of flavonoid and phenolic antioxidants in black currants, blueberries, raspberries, red currants, and cranberries. J Agric Food Chem, 58:3901-9, 2010.
12. Kahkonen M, Kylli P, Ollilainen V, et al: Antioxidant activity of isolated ellagitannins from red raspberries and cloudberries. J Agric Food Chem, 60:1167-74, 2012.
13. Papoutsi Z, Kassi E, Tsiapara A, et al: Evaluation of estrogenic/antiestrogenic activity of ellagic acid via the estrogen receptor subtypes ERalpha and ERbeta. J Agric Food Chem, 53:7715-20, 2005.
14. Larrosa M, Gonzalez-Sarrias A, Garcia-Conesa MT, et al: Urolithins, ellagic acid-derived metabolites produced by human colonic microflora, exhibit estrogenic and antiestrogenic activities. J Agric Food Chem, 54:1611-20, 2006.
15. Morimoto C, Satoh Y, Hara M, et al: Anti-obese action of raspberry ketone. Life Sci, 77:194-204, 2005.
16. Park KS: Raspberry ketone increases both lipolysis and fatty acid oxidation in 3T3-L1 adipocytes. Planta Med, 76:1654-8, 2010.
17. Ogawa Y, Akamatsu M, Hotta Y, et al: Effect of essential oils, such as raspberry ketone and its derivatives, on antiandrogenic activity based on in vitro reporter gene assay. Bioorg Med Chem Lett, 20:2111-4, 2010.
18. Kassim A, Poette J, Paterson A, et al: Environmental and seasonal influences on red raspberry anthocyanin antioxidant contents and identification of quantitative traits loci (QTL). Mol Nutr Food Res, 53:625-34, 2009.
19. Beytur A, Ciftci O, Aydin M, et al: Protocatechuic acid prevents reproductive damage caused by 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in male rats. Andrologia, 44 Suppl 1:454-61, 2012.
20. Tan TQ, Ge C, Mi Y, et al: Ginsenosides promote proliferation of granulosa cells from chicken prehierarchical follicles through PKC activation and up-regulated cyclin gene expression. Cell Biol Int, 34:769-75, 2010.
21. Lin JX, Jia YD, Zhang CQ: Effect of epidermal growth factor on follicle-stimulating hormone-induced proliferation of granulosa cells from chicken prehierarchical follicles. J Zhejiang Univ Sci B, 12:875-83, 2011.
22. Jin Y, Zhang C, Zeng W, et al: Interactive actions of prostaglandin and epidermal growth factor to enhance proliferation of granulosa cells from chicken prehierarchical follicles. Prostaglandins Other Lipid Mediat, 83:285-94, 2007.
23. Hernandez AG, Bahr JM: Role of FSH and epidermal growth factor (EGF) in the initiation of steroidogenesis in granulosa cells associated with follicular selection in chicken ovaries. Reproduction, 125:683-91, 2003.
24. Meiers S, Kemeny M, Weyand U, et al: The anthocyanidins cyanidin and delphinidin are potent inhibitors of the epidermal growth-factor receptor. J Agric Food Chem, 49:958-62, 2001.

Additional references available upon request.

Each carefully selected ingredient in the HEALx products has beneficial properties and health benefits individually; therefore, references are provided on the various components; however, it is the combination of ingredients that works synergistically to produce results.

Harrisons PET PRODUCTS

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