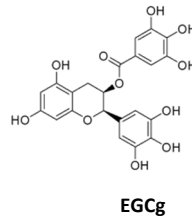
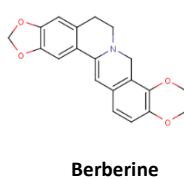
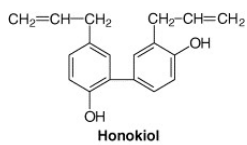


Adrenal Cortisol Support™

TECHNICAL SUMMARY

Everyday life stress can impact adrenal production of cortisol and trigger stress-related eating. Adrenal Cortisol Support™ is a botanical and nutritional formulation that naturally supports a normal adrenal response and helps to promote healthy blood sugar management.* Adrenal Cortisol Support™ features Relora®, a proprietary herbal combination that has clinically demonstrated that it can support healthy cortisol levels, temporarily relieve perceived daily stress, and help manage

Structure formula: Relora® is standardized to no less than 1.5% honokiol and 0.1% berberine.



Chemical name:

Honokiol [2-(4-hydroxy-3-prop-2-enylphenyl)-4-prop-2-enylphenol]; (from *Magnolia officinalis*)

Berberine [9,10dimethoxy-2,3-(methylenedioxy)-7,8,13,13a-tetrahydroberberinium]; (from *Phellodendron amurense*)

EGCg [(2R,3R)-5,7-dihydroxy-2-(3,4,5-trihydroxyphenyl)-3,4-dihydro-2H-chromen-3-yl] 3,4,5-trihydroxybenzoate. (from green tea extract)

Magnolol [5,5'-diallyl-2,2'-dihydroxybiphenyl]; (from *Magnolia officinalis*)

Allergen and Additive Disclosure: Not manufactured with wheat, gluten, milk, egg, fish, shellfish, or tree nut ingredients. Produced in a GMP facility that processes other ingredients containing these allergens.

Delivery Form: Vegetable Capsules

ROLE AS NUTRIENT/FUNCTION

- Preclinical research suggests that magnolol and honokiol may possess central nervous system (CNS) modulating activities.* Magnolol has been shown to influence cortisol metabolism.* Honokiol and its metabolite dihydrohonokiol have demonstrated the capability of interacting with gamma-aminobutyric acid-A (GABA-A) and muscarinic receptors.* More recent studies suggest that the behavioral effects observed after oral administration of a magnolol and honokiol mixture in a rodent model simulating a stressful situation may be attributed to the attenuation of reduced levels of the serotonin precursor 5-hydroxytryptamine (5-HT), while increasing 5-hydroxyindoleacetic acid (5-HIAA) levels in several area of the animal's brain; additionally, a reduction in previously elevated corticosterone serum concentrations was observed.*
- Berberine-containing herbs have a long history of use by traditional herbalists for a multitude of indications. In recent years, berberine has been recognized for its potential effects on

Supplement Facts

Serving Size 1 Veg Capsule

	Amount Per Serving	% Daily Value
Vitamin C (from Calcium Ascorbate)	33 mg	37%
Pantothenic Acid (from Calcium Pantothenate)	10 mg	200%
Calcium (from Calcium Carbonate and Ascorbate)	12 mg	1%
Magnesium (from Magnesium Oxide)	8 mg	2%
Chromium (from Chromium Nicotinate Glycinate (Albion™))	20 mcg	57%
Relora® (Proprietary blend of <i>Magnolia officinalis</i> bark extract and <i>Phellodendron amurense</i> bark extract)	200 mg	†
Green Tea Extract (<i>Camellia sinensis</i>) (Leaf) [min. 50% EGCg (Epigallocatechin Gallate)]	90 mg	†
Ashwagandha Extract (<i>Withania somnifera</i>) (Root and Leaf)	20 mg	†
Holy Basil Extract (<i>Ocimum tenuiflorum</i>) (Leaf)	20 mg	†
Reishi Mushroom Powder (<i>Ganoderma lucidum</i>)	20 mg	†
Rhodiola Extract (<i>Rhodiola rosea</i>) (Root)	20 mg	†

† Daily Value not established.

Other ingredients: Hypromellose (cellulose capsule), Ascorbyl Palmitate and Silicon Dioxide.

- Supports Healthy Adrenal Response*
- Appetite Management*

SUGGESTED USAGE: Take 1 capsule 3 times daily, or as directed by your healthcare practitioner.

glucose metabolism and central nervous health.* Animal studies suggest that berberine administration leads to significantly increased levels of norepinephrine, serotonin, and dopamine in the brain ($p < 0.001$).* Another rodent study found that the oral administration of berberine led to improved cognitive performance, glucose metabolism, oxidative stress, and cholinesterase activity.*

- EGCg has been shown to support weight management efforts by inhibiting digestive lipases, resulting in reduced fat absorption, decreased adipocyte differentiation, as well as promotion of lipolysis and thermogenesis in humans.* The latter has been ascribed to EGCg's ability to interfere with noradrenaline degradation leading to prolonged sympathetic stimulation and thermogenesis.*

NATUROKINETICS®

Liberation: Disintegration time for Adrenal Cortisol Support™ vegetable capsules is less than 60 min. in water.

Absorption: In laboratory settings, in rats, after oral ingestion magnolol is rapidly absorbed with an initial T_{max} at 15 min, with a second peak 8 hours post-ingestion. Honokiol and magnolol appear to be absorbed by passive diffusion, mainly in the duodenum. The absorption of berberine and EGCg after oral ingestion are relatively low. For EGCg, T_{max} ranges from 60 to 115 min.

Distribution: Magnolol and honokiol are extensively metabolized in the liver. Additionally, elevated concentrations of magnolol have been

detected in the kidney, brain, lung, and heart tissue. After intragastric dosing, berberine is widely distributed in various organs, including liver, kidney, spleen, lung, and the brain; hepatic tissue showed the highest concentration, which was approximately 70-fold greater than that of plasma. Pharmacokinetic studies have revealed that after entering the bloodstream in its free form, EGCg is extensively metabolized by the liver. Some researchers have also detected EGCg bound to protein, as well as minor fractions in brain, lung, heart, kidney, and other tissues.

Metabolism: Magnolol, honokiol, and berberine undergo extensive first-pass metabolism, generating various glucuronide and sulfate conjugates, as well as methylated and hydroxylated metabolites. Likewise, the biotransformation of EGCg leads to the formation of glucuronide and sulfate conjugates, and its mono- or di-methylated metabolites in the liver.

Elimination: Liver metabolic biotransformation is the primary route of elimination for magnolol. A minute amount of magnolol is eliminated intact in urine while about 20% of orally administered magnolol is detected in feces. The excretion pattern of honokiol is unknown. Berberine is primarily excreted via bile and feces. EGCg is excreted in its methylated and glucuronidated metabolite forms primarily via bile and feces.

CLINICAL VALIDATION

- In a double-blind, placebo-controlled trial with 28 volunteers, Relora® supplementation (750 mg/d for 6 weeks) resulted in significant support of healthy weight associated with support of normal cortisol levels, as compared with placebo.*
- In a follow-up randomized, parallel, placebo controlled clinical trial with 26 premenopausal women, Relora® supplementation (750 mg/d for 6 weeks) resulted in significant support of energy level and mood measured by several standardized questionnaires as compared to placebo.*

SAFETY INFORMATION

Tolerability: In clinical studies, the ingredients in Adrenal Cortisol Support™ have been well tolerated.

Contraindications: Patients with allergies to any of its constituents should not take this product.

INTERACTIONS

Drug Interactions: While no adverse events have yet been reported, magnolia might cause central nervous system depressant effects and as such, might interact with alcohol, barbiturates, and benzodiazepines, increasing the risk of drowsiness and motor reflex depression. Berberine may potentiate the blood glucose lowering effect of anti-diabetes agents. Additionally, berberine may theoretically alter the pharmacokinetics of several medications utilizing the CYP3A4 pathway (i.e., lovastatin, clarithromycin, indinavir, sildenafil, triazolam), thus increasing their levels and prolonging their plasma half-lives.

Supplement Interactions: None known.

Interaction with Lab Tests: None known.

STORAGE

Store in cool, dry, and dark environment in original sealed container. Protect from extended exposure to direct sunlight, heat, and moisture.