



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.