Berberine Synergy™

designs for health®

*Support for healthy blood sugar levels, insulin sensitivity and cardiovascular health**

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Berberine Synergy™ combines 400 mg of the plant alkaloid berberine (from *Berberis aristata*) along with 100 mg of alpha lipoic acid per capsule, in order to help support the management of healthy blood sugar levels and insulin sensitivity.* As downstream effects of these main actions, berberine may also help improve dyslipidemia, as well as other features of metabolic syndrome.[1]

Berberine Synergy™ may be beneficial for the support of*:

- Diabetes and pre-diabetes
- Insulin resistance/hyperinsulinemia
- Elevated triglycerides
- Non-alcoholic fatty liver
- PCOS linked to elevated insulin

Supplement Facts

Serving Size 1 capsule

Amount Per Serving		% Daily Value
Berberine (as Berberine HCl) (*Berberis aristata*)(root)	400 mg	*
Alpha Lipoic Acid	100 mg	*

*Daily Value not established.

Other Ingredients: Vegetable cellulose (capsule), calcium sulfate, microcrystalline cellulose, vegetable stearate, hydroxypropyl cellulose (HPC).

Insulin and Blood Glucose Management

The most prominent of berberine's beneficial properties are its positive effects on insulin and normal blood glucose management. Berberine exerts its effects independently of the mechanisms of metformin and other common hypoglycemic agents, so the compound may be used alone or in conjunction with conventional pharmaceutical drugs. In fact, berberine has been shown to be as effective as metformin in lowering fasting blood glucose and hemoglobin A1c (HbA1c), LDL-C, triglycerides, and fasting insulin.[2] When added to the existing medication regimens of patients with poorly controlled diabetes, berberine significantly reduced FBG, HOMA-IR, TNF-alpha, IL-6, and CRP compared with oral hypoglycemic agents alone.[3]

In a separate study on type-2 diabetics with dyslipidemia, 1g of berberine supplementation per day for 3 months resulted in favorable changes to fasting blood glucose and insulin levels, triglycerides, total cholesterol, LDL-C, HbA1c, and blood glucose, as well as an increase in glucose disposal rate.[3]

Research supports berberine's impressive effects on diabetes management and shows that it may be especially effective for diabetic patients with compromised liver function, for whom the potential adverse side-effects of conventional hypoglycemic drugs may not be an option.[4] In study subjects with chronic hepatitis, berberine supplementation resulted in decreased enzyme markers for liver damage (ALT and AST), as well as decreased gamma-glutamyl transferase (GGT) in subjects without liver damage.[4]

There are multiple mechanisms behind berberine's influence on blood glucose control and insulin sensitivity.[5] In diabetics with damaged pancreatic islet function, berberine's antioxidant promoting activity protected islet cells and promoted insulin secretion. Other mechanisms involved include the upregulation of insulin receptor (InsR) expression via increased InsR mRNA and protein expression via protein kinase C activation, increased GLUT1 expression which stimulated glucose uptake, inhibition of retinol binding protein-4, and promotion of GLP-1 secretion.[3] In another study of diabetic and myocardial necrotic induced mice, berberine treatment exhibited significant cardio-protective and anti-diabetic effects by restoring CPK-MB, HbA1c, and blood glucose levels while favorably modulating lipid levels.[6]

Another biochemical mechanism behind berberine's impressive effects is the inhibition of intestinal carbohydrate-digesting enzymes. Diabetic rats supplemented orally with berberine showed significant, dose-dependent decreases in disaccharidase activity and sucrase-isomaltase complex mRNA expression in the intestines. Similar effects were observed in nondiabetic rats, suggesting that berberine may be helpful for pre-diabetic patients, as well as others presenting with indicators of carbohydrate intolerance. Notably, compared to healthy controls, the diabetic rats had up to a 7-fold increase in sucrase activity and a 2.5-fold increase in maltase activity in the small intestine, suggesting that an intervention targeting reduced activity of these enzymes may have impressive effects on postprandial blood glucose levels. Two-hour area under the curve (AUC) for blood glucose levels after sucrose and maltose loading were lower in non-diabetic, berberine treated rats than in untreated controls. Similar findings for berberine's influence on carbohydrate-digesting enzymes are supported by observations in cultured human cell lines.[7]

Beyond these roles in helping to regulate blood glucose and insulin, berberine may also support a healthy metabolism and lighten overall body burden by easing oxidative stress and restoring cellular redox efficiency.[8] With mitochondrial dysfunction being increasingly tied to a host of poor health outcomes, supporting mitochondrial flexibility may be of particular importance in hyperinsulinism and metabolic syndrome, with their various downstream effects on multiple organs and tissue systems. A study employing cultured mouse macrophages treated with lipopolysaccharides (LPS, a potent endotoxin) or palmitic acid (PA) showed that berberine significantly inhibited pro-inflammatory cytokine expression, COX-2, and LPS- and PA- induced activation of endoplasmic reticulum oxidative stress.[9]

Another animal study found that LPS-induced mice had suppressed cytochrome P450 enzyme activity in the liver and that pretreatment with berberine inhibited inflammatory biomarkers (TNF-a & IL-1B) in the serum, as well as inflammatory marker and iNOS mRNA expression in the liver, and significantly increased bile acid concentration in the liver demonstrating berberine's potent anti-inflammatory actions.[10]

Blood Lipids and Liver Health

Berberine has been shown to exert favorable effects on blood lipids and non-alcoholic fatty liver. Unlike statin drugs, berberine does not affect the complex cholesterol biosynthesis pathway, and therefore does not present the same undesirable side-effects.[11]

Berberine upregulates the expression of LDL receptor mRNA and increases liver expression of LDL receptors while downregulating lipogenic enzymes like fatty acid synthase.[12, 13] Furthermore, berberine reduces triglyceride and total cholesterol levels by modulating adipogenic transcription factor expression.[14]

Hyperlipidemic hamsters given berberine for 10 days had significantly reduced levels of total cholesterol, triglycerides, and LDL-C by day 7 demonstrating berberine's ability to promote the excretion of cholesterol from the liver into the bile.[15]

A meta-analysis demonstrates berberine's favorable effects on humans with non-alcoholic fatty liver disease (NAFLD). Those treated with berberine showed significant improvements in AST, ALT, and GGT liver enzyme levels compared to lifestyle interventions and other drugs alone.[16] Additionally, berberine alone significantly lowered triglycerides and LDL-C, increased HDL-C levels, and decreased hepatic fat content in NAFLD patients.[16, 17] In mice fed a high-fat, high-sucrose diet, berberine improved hepatic steatosis in vitro by inducing SIRT1-dependent autophagy and suppressing palmitate-induced lipid accumulation.[18]

Berberine has also been demonstrated to reduce fibrosis in chemically induced liver damage.[19] Because the liver is a key player in glycemic control, compounds that aid in blood sugar handling while simultaneously conferring significant protection to liver function may be powerful tools in the arsenal against metabolic syndrome.

Lipoic Acid: Antioxidant and Blood Sugar Support

Lipoic acid is best known as a lipid and water-soluble antioxidant, but it also powerfully influences insulin secretion and sensitivity.[20, 21] The combination of lipoic acid and berberine has a strong potential to help patients improve their glycemic control. Like berberine, lipoic acid exerts effects upon the insulin receptor, but also aids in glucoregulation by facilitating recruitment of insulin-sensitive glucose transporters (GLUT-4 and GLUT-1) to muscle and adipose cell membranes.[22] An in vitro study demonstrated alpha-lipoic acid's (ALA) protective effects against glucose-induced myoglobin glycation. Administration of ALA significantly reduced fructosamine levels, a direct association with decrease advanced glycation end product (AGE) formation, reduced free iron release from myoglobin, and showed significant protective effects from oxidative damage.[23]

Related to its antioxidant function, lipoic acid is a key cofactor for mitochondrial enzymes involved in cellular metabolism and energy (ATP) production, specifically pyruvate dehydrogenase and α-ketoglutarate dehydrogenase. Lipoic acid is sometimes called an "antioxidant of antioxidants,"[24] as it can regenerate vitamins E and C, coenzyme Q10 and glutathione.[25] In fact, lipoic acid has an even greater redox potential than glutathione.[22, 25] Mitochondrial oxidative stress may be both a cause and an effect of impaired carbohydrate tolerance, and lipoic acid may be beneficial for comprehensively addressing this issue.

Recommended Use:

- Take one capsule per day with a meal, or as directed by a health care practitioner.
- Note: Patients taking this product should be monitored closely, as their medication may require adjustment to account for the efficacy of berberine regarding blood glucose and insulin levels.

For a list of references cited in this document, please visit:
http://catalog.designsforhealth.com/assets/itemresources/Berberine_Synergy_References.pdf

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.