Berberine Synergy™



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 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.

Insulin and Blood Glucose Management

The most prominent of berberine's pharmacological properties are its beneficial effects on insulin and blood glucose management. Berberine exerts its effects independently of the mechanisms of metformin and other

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

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.¹ When added to the existing medication regimens of patients with poorly controlled diabetes, berberine significantly reduced fasting and postprandial blood glucose, insulin, HbA1c and HOMA-IR. These changes were observed after just five weeks of berberine supplementation.¹

In a separate study on newly diagnosed type-2 diabetics with dyslipidemia, berberine supplementation resulted in favorable changes to triglycerides, uric acid, total cholesterol, HOMA-IR, fasting insulin, LDL-C, HbA1c, fasting glucose, blood glucose and plasma insulin after a glucose loading test.²

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.³ 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.³

There are multiple mechanisms behind berberine's influence on blood glucose control and insulin sensitivity. In diabetics using insulin, the addition of berberine resulted in increased fasting and postprandial C-peptide, which suggests that long-term use of berberine might improve insulin secretion in patients who fail to respond, or respond poorly, to oral hypoglyce-mic agents.¹¹ In addition to increased insulin secretion, berberine has been shown to increase insulin receptor expression, indicating that it may improve glycemic control by supporting the endogenous production of insulin while also facilitating clearance of the hormone. Cultured human liver and muscle cells show increased insulin receptor protein expression when exposed to berberine.³ Moreover, contrary to thiazolidinedione drugs (TZDs), berberine "suppresses the differentiation of preadipocytes, and reduces the accumulation of lipid droplets."³ This suggests berberine might be especially useful in cases of overweight or obese diabetics, where the potential for additional weight gain and edema associated with conventional pharmaceuticals would be undesirable.

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 non-diabetic 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.⁴

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. 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 human macrophages exposed to lipopolysaccharide (LPS, a potent endotoxin) showed that berberine led to reduced superoxide radical levels, compared to LPS-treated controls without berberine. At 24-hours of incubation with berberine, superoxide levels in LPS-treated cells were even lower than controls untreated with LPS.5

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.

Serving Size 1 capsule	
Amount Per Serving	% Daily Valu
Berberine (as Berberine HCI) (<i>Berberis an</i>	400 mg ristata)(bark)
Alpha Lipoic Acid	100 mg

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

Made with Non-GMO ingredients

Berberine upregulates the expression of LDL receptor mRNA and increases liver expression of LDL receptors, allowing for more effective clearance of LDLs from the bloodstream.^{6,7} Diabetic, dyslipidemic rats supplemented with berberine showed favorable changes to total cholesterol, triglycerides, LDL-C, ApoB, and HDL-C. For some parameters, the effects were more powerful than those achieved with rosiglitazone and fenofibrate.⁸

In rats fed a fatty liver-inducing diet, supplemental berberine resulted in decreased total body weight, visceral adiposity, total cholesterol, LDL-C and triglycerides, while also reducing serum ALT and AST, which suggests a protective effect for liver function. These markers were reduced compared to fatty liver rats not supplemented with berberine, but more notably, some of these parameters were reduced to levels seen in a healthy control group fed a normal diet. Rats supplemented with berberine had lower liver weights and lower triglyceride content in the liver. Researchers concluded that berberine has direct effects upon the methylation status of genes involved in deposition of triglycerides in the liver.⁹

Berberine has also been demonstrated to reduce fibrosis in chemically induced liver damage. 10,11 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. 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. A study involving type-2 diabetics showed that oral lipoic acid resulted in insulin sensitivity and glucose disposal rates that were not significantly different from those of healthy, non-diabetic controls.

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," ¹⁶ as it can regenerate vitamins E and C, coenzyme Q10 and glutathione. In fact, lipoic acid has an even greater redox potential than glutathione. ^{16,17} 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://mkt.s.designsforhealth.com/techsheets/Berberine-Synergy-References.pdf