

Berberine Synergy™

Healthy Glucose Metabolism*

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This information is provided as a medical and scientific educational resource for the use of physicians and other licensed health-care practitioners ("Practitioners"). This information is intended for Practitioners to use as a basis for determining whether to recommend these products to their patients. All recommendations regarding protocols, dosing, prescribing, and/or usage instructions should be tailored to the individual needs of the patient considering their medical history and concomitant therapies. This information is not intended for use by consumers.

Berberine Synergy™ is a targeted formula featuring berberine and alpha-lipoic acid (ALA) designed to help support healthy blood glucose metabolism and antioxidant status.* Berberine, a botanical extract from *Berberis aristata*, is an isoquinoline alkaloid compound found in plants, such as goldenseal, Oregon grape, and barberry. In addition to berberine's supportive metabolic effects, it also promotes healthy blood vessels and cardiovascular function.* Berberine may also support a normal inflammatory response.* ALA is added to promote a normal inflammatory response, healthy metabolism and weight management, and vascular tone.* Together, berberine and ALA may support individuals with dysregulated glucose and insulin-related inflammatory conditions.*

Formula Highlights

- Provides a clinically relevant amount of berberine and alpha-lipoic acid to support metabolic health, blood sugar metabolism, weight management, cardiovascular support, and antioxidant status*
- Berberine (*Berberis aristata*) supports optimal metabolic health by reducing GLP-1 breakdown*
- Gluten-free, dairy-free, soy-free, non-GMO

Berberine

Glucose, Insulin, and Lipid Metabolism Support*

Berberine (*Berberis aristata*) is a compound highly regarded for its efficacy in supporting blood glucose regulation and healthy insulin metabolism.* Evidence indicates berberine may be supportive in lowering numerous markers of metabolic dysfunction, including fasting blood glucose (FBG), hemoglobin A1C (HbA1c), low-density lipoprotein-cholesterol (LDL-C), triglycerides (TGs), and fasting insulin.¹⁻³ One of the main ways berberine may support metabolic health is through its ability to facilitate glucagon-like peptide-1 (GLP-1) secretion in vitro.⁴ GLP-1 is a peptide hormone that promotes healthy body composition and weight by supporting insulin and inhibiting glucagon secretion, which stimulates glucose production in the liver.⁵ Two berberine metabolites, berberrubine (BBB) and palmatine (PMT), have been reported to have significant pharmacological effects on GLP-1, namely, increasing the production of the GLP-1 peptide in mechanistic studies.⁴ A systematic review and meta-analysis of randomized controlled trials (N = 4,158) published in 2021 investigated the efficacy of berberine intervention alone (between 1.5 to 2 g/day) or with standard conventional therapies in treating diabetes (type 2 diabetes mellitus [T2DM] or prediabetes) compared to control groups.⁶ The primary and secondary outcomes assessed were HbA1C, FBG, and 2-hour post-prandial plasma glucose (2hPG); and fasting insulin (FINS), Homeostatic Model Assessment for Insulin Resistance (HOMA-IR), and body mass index (BMI), respectively. Significant reductions in HbA1C (MD = -0.73), FBG (MD = -0.86), 2hPG (MD = -1.26), FINS (MD = -2.05), HOMA-IR (MD = -0.71), and BMI (MD = -1.43) were reported (all P < 0.05).⁶

Berberine attenuates several pathways involved in blood lipid metabolism. Berberine can upregulate adenosine triphosphate (ATP)-binding cassette transporter 1 and hepatic LDL-c receptor messenger RNA expression, facilitating the removal of cholesterol from cells and supporting the liver's capacity to clear LDL-C from the blood.^{7,8} Berberine has also been shown to increase the fecal excretion of cholesterol and promote the synthesis of bile acids, further supporting its lipid-regulating role.^{2,9} A review of clinical trials reported that patients (n = 887) with various conditions such as T2DM, metabolic syndrome, hyperlipidemia, and non-alcoholic fatty liver disease who were given daily berberine (900 to 1,500 mg/day for three to 16 weeks) experienced improved glucose and insulin control, decreases in waist circumference, triglyceride levels, total cholesterol, and LDL-C, and an increase in high-density lipoprotein cholesterol (HDL-C).² Data show that these effects may be more supportive when berberine is combined with statins.⁹ A systematic review and meta-analysis investigated the efficacy of berberine plus simvastatin treatment compared to simvastatin alone to attenuate triglyceride levels, total cholesterol, LDL-C, and HDL-C.⁹ The groups (n = 223) given berberine (0.5 to 1.5 g/day) plus statins (10 mg to 20 mg/day) for one month to six months experienced improved levels of triglycerides and total cholesterol while attenuating adverse side effects of statin use, such as muscle aches and elevated liver enzymes.⁹

Benefits*

- Supports healthy blood glucose and insulin metabolism^{1-3,5,6,9-13,15,16,18,19,22}
- Helps support normal glucagon-like peptide-1 (GLP-1) secretion^{4,5,11}
- May help support healthy weight management^{2,6}
- Promotes cardiovascular health^{1-3,5-9,15,22}
- Supports antioxidant status¹⁷⁻²¹
- Helps support overall cellular health^{13,15-21}

Supplement Facts

Serving Size 1 capsule

Amount Per Serving	% Daily Value
Berberine HCl (<i>Berberis aristata</i>)(root)	400 mg *
Alpha Lipoic Acid	50 mg *

*Daily Value not established.

Other Ingredients: Cellulose (capsule), dicalcium phosphate, microcrystalline cellulose, vegetable stearate, silicon dioxide, ascorbyl palmitate.

Berberine helps support healthy glucose and insulin metabolism through multiple pathways and functions. Berberine's efficacy is attributed to increased endogenous insulin secretion and insulin receptor expression.¹⁰ Berberine regulates glucose metabolism through the GnRH-GLP-1 and mitogen-activated protein kinase (MAPK) signaling pathways by up-regulating the GLP-1 receptor and MAPK 10 gene while downregulating GnRHr and GnRH1.¹¹ Berberine is a natural dipeptidyl peptidase IV (DPP IV) inhibitor. This enzyme degrades incretin hormones, especially GLP-1, which may help increase endogenous insulin secretion in response to a meal.¹² Berberine also stimulates glycolysis by inhibiting mitochondrial glucose oxidation (specifically at complex I of the electron transport chain) and increasing cellular glucose uptake independently of insulin.¹³ Berberine increases the phosphorylation of AMP-kinase (AMPK), which is essential for proper cellular glucose metabolism and uptake.¹³ In this sense, berberine may mimic the supportive metabolic effects typically seen in response to physical exercise, fasting, and caloric restriction.¹⁴ It activates peroxisome proliferator-activated receptor (PPAR)-α and PPAR-γ, which play essential roles in glucose and lipid metabolism in adipose tissue.¹⁵ In animal studies, berberine alleviated hyperglycemic stress by inhibiting oxidative stress, glucose-provoked reactive oxygen species production, and apoptosis.¹⁶ Evidence also suggests that it can restore functional mass in pancreatic beta cells.¹⁵

Cardiovascular Support*

The cardiovascular-supportive properties of berberine are broad and well-established.* Berberine exhibited anti-arrhythmic effects in multiple animal studies.¹⁷ It has anti-atherosclerotic properties due to its supportive role in lipid metabolism, its inhibition of p38 mitogen-activated protein kinase and c-Jun N-terminal kinase signaling pathways, and its ability to modulate TNF-α, interleukin (IL)-1β, IL-6, and NF-kB.¹⁷ Berberine may support healthy blood pressure by promoting vasodilation and relaxation of vascular smooth muscle and inhibiting endothelial apoptosis.¹⁷ It also has been shown to support healthy heart function in the presence of ischemic heart disease, myocarditis, cardiomyopathy, and heart failure.¹⁷ Furthermore, a clinical trial exploring the effects of berberine supplementation for individuals with acute cerebral ischemic stroke as an adjunct treatment to the general therapy showed a significant reduction in the number of unstable carotid atherosclerotic plaques and inflammatory markers, including IL-6.²

Alpha-Lipoic Acid

Alpha-lipoic acid is a molecule that acts as a cofactor for enzymatic reactions related to blood sugar metabolism and cellular energy.¹⁸ It is found in the mitochondria of cells and has been shown to help support antioxidant status, a normal inflammatory response, and healthy metabolism.¹⁸ Evidence suggests that ALA may help support blood sugar homeostasis, antioxidant status, metabolic health, and a healthy inflammatory response.*

In preclinical studies, ALA has been shown to help promote healthy insulin signaling pathways and support healthy weight management.¹⁹ It may help support the activity of signaling molecules in the insulin/insulin-like growth factor-1 pathways, and specific proteins, such as insulin receptor substrate 1, phosphatidylinositol 3 kinase, and protein kinase B.¹⁹ ALA has been shown to downregulate the activity of pro-inflammatory cytokines, such as nuclear factor kappa light-chain-enhancer of activated B cells (NF-kB).¹⁹ It can scavenge reactive oxygen species and exhibit chelating activity for certain heavy metals.¹⁹ Additionally, rats fed a high-fat diet and given ALA exhibited reduced body weight via AMPK activation, showcasing the similarity to berberine's effects on promoting the phosphorylation of AMPK in cells.²⁰

ALA may help support healthy levels of glutathione and nuclear factor erythroid 2-related factor 2 activity (Nrf2).²¹ It also reduces the oxidized forms of glutathione and vitamins C and E and upregulates endothelial nitric oxide synthase (eNOS) expression, primarily expressed in the cardiovascular system.²¹ The activity of eNOS is believed to play a role in vascular homeostasis, vasodilation, and nitric oxide production.²¹ Several animal studies involving hypertensive murine models have reported that ALA helped attenuate increases in blood pressure.²¹

A systematic review and meta-analysis of randomized controlled trials published in 2022 investigated the efficacy of daily ALA intervention (200 mg to 1,200 mg for four to 52 weeks) in T2DM patients (N = 1,035) on various cardiometabolic measures, such as glycated hemoglobin, weight loss, and LDL-C.²² The patients who were given an extra 500 mg of ALA each day exhibited lowered glycated hemoglobin and body weight. The most significant weight loss (-0.5 pounds) was demonstrated when the patients took at least 600 mg/day of ALA.²² Based on these results, ALA may be clinically supportive to individuals with insulin and glucose-related inflammatory conditions, such as diabetes or metabolic syndrome.²²

Recommended Use: Take 1 capsule twice daily with a meal or as directed by your health-care practitioner.

Note: Work with a health-care practitioner to monitor blood glucose levels when taking this product, as medication for blood sugar regulation may require adjustment to account for the effects of berberine.

To gain an in-depth view of your patient's individual biochemistry and metabolism, consider **Designs for Health Metabolomics Spotlight™** functional wellness testing.

For a list of references cited in this document, please visit:

<https://www.designsforhealth.com/api/library-assets/literature-reference---berberine-synergy-tech-sheet-references>

Dosing recommendations are given for typical use based on an average 150-pound healthy adult. Health-care practitioners are encouraged to use clinical judgement with case-specific dosing based on intended goals, subject body weight, medical history, and concomitant medication and supplement usage.

***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.**

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