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Berb-Evail™ contains 400 mg of the plant alkaloid berberine (from *Berberis aristata*) for the primary purpose of supporting healthy blood sugar levels and enhancing insulin sensitivity.* As downstream effects of these main actions, berberine may also help improve dyslipidemia and other features of metabolic syndrome. Additionally, berberine has been shown to exhibit antimicrobial properties.

The Designs for Health Evail™ Process – for enhanced absorption of berberine

Berb-Evail™ is manufactured using the Designs for Health Evail™ technology, which is an all-natural formulation that improves the absorption and delivery of berberine. This process uses a proprietary blend of MCT oils, non-soy derived lecithin, and vitamin E, without the use of potentially harmful surfactants.

Insulin and Blood Glucose Management

The most prominent of berberine's clinical properties are its beneficial effects on insulin and 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 the popular drug 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 fasting blood glucose and insulin levels, triglycerides, uric acid, total cholesterol, HOMA-IR, LDL-C, HbA1c, and 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 levels, which suggests that long-term use of berberine might improve endogenous insulin secretion in patients who fail to respond, or who respond poorly, to oral hypoglycemic agents.¹¹ In addition to increasing insulin secretion, berberine has been shown to increase insulin receptor expression in cultured human liver and muscle cells, which may improve insulin sensitivity.³ Moreover, contrary to thiazolidinedione drugs (TZDs), berberine "suppresses the differentiation of preadipocytes, and reduces the accumulation of lipid droplets."¹³ 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 intestinal disaccharidase activity. Even in non-diabetic rats treated with berberine, two-hour area under the curve (AUC) blood glucose levels after sucrose and maltose loading were lower than those of untreated controls. Similar observations have been made in cultured human cell lines, which suggests berberine may be helpful for pre-diabetic patients and others presenting with early indicators of carbohydrate intolerance or metabolic syndrome that has not yet progressed to overt diabetes.⁴

Additional effects of berberine are achieved via inhibition of dipeptidyl peptidase IV (DPP IV). As DPP IV degrades incretin hormones—which stimulate post-prandial insulin secretion—increasing the half-life of incretins may help increase endogenous insulin secretion in response to a meal.⁵ Berberine also exerts blood glucose lowering effects by stimulating glycolysis via inhibition of mitochondrial glucose oxidation (specifically at complex I of the electron transport chain), and by increasing cellular glucose uptake independently of insulin.⁶ (The DPP IV inhibitor category of drugs is becoming more popular due to the efficacy of this mechanism in contributing to type-2 diabetes management.⁷) Berberine increases phosphorylation of AMP-kinase (AMPK), which occurs naturally in response to physical exercise, fasting, and caloric restriction.⁸ In this sense, berberine may be thought of as a "calorie restriction mimetic," which again mirrors the effects of metformin. In this sense, the combined effects of berberine in lowering blood glucose, increasing insulin sensitivity, and reducing mitochondrial oxygen consumption may have anti-aging properties.

Blood Lipids and Liver Health

Berberine has been shown to exert favorable effects on blood lipids and nonalcoholic fatty liver. Unlike statin drugs, berberine does not affect the complex cholesterol biosynthesis pathway, and therefore does not present the same undesirable side-effects. 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.^{9,10} 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.¹¹

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.¹²

Berberine has also been demonstrated to reduce fibrosis in chemically induced liver damage.^{13,14} 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.

Antimicrobial Effects

Beyond its role as a powerful agent for blood sugar regulation, berberine has long been recognized as an antimicrobial, antiviral, and anti-parasitic compound. Berberine extracts have demonstrated bactericidal effects against diarrhea-causing strains of *Vibrio cholera* and *Escherichia coli*, and anti-parasitic effects against *Giardia lamblia*, *Entamoeba histolytica*, and *Trichomonas vaginalis*.¹⁵ Berberine may be as effective as the common antibiotic Flagyl against giardiasis.¹⁶ Other common organisms shown to be subject to the antimicrobial action of berberine include *Candida*, *Chlamydia*, *Salmonella*, *Klebsiella*, *Clostridium*, *Shigella*, and *Cryptococcus*.¹⁷

When to consider Berb-Evail™

- **Blood Glucose:** Consider using Berb-Evail™ when additional support for blood sugar management and insulin resistance is desired, and the preference is for a standalone berberine supplement (in lieu of Berberine Synergy™, which contains added alpha-lipoic acid).
 - Berb-Evail™ should be added to a protocol that first includes Metabolic Synergy™, our foundational glucose support formula, along with Sensitol™, which helps with insulin resistance.
 - Additional glucose support formulas may be included, such as Chromium Synergy™, while GlucoSupreme™ Herbal may be added if an increase in insulin output is needed.
- **Antimicrobial Effects in the GI:** Consider Berb-Evail™ when short term (4-6 weeks) adjunctive therapy to a foundational regimen of GI Microb-X™ and Oil of Oregano may be warranted.

Recommended Use:

- As a dietary supplement, take one softgel per day, or as directed by a health care practitioner.

Cautions

- Due to the potential for additive effects resulting from inhibition of DPP IV by berberine, special consideration should be given when adding this product to the supplement regimen of patients who may already be taking a DPP IV inhibitor.
- Due to berberine's antimicrobial activity, it is recommended that long-term use of this product be accompanied by monitoring of the GI microbiota, such as with the DFH GI-MAP™ molecular stool analysis through Diagnostic Solutions Labs, to assure that changes to intestinal microflora, which may benefit from probiotic supplementation, can be addressed with Probiotic Synergy™, Probiotic Supreme™ or Probiophage DF™.

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

http://catalog.designsforhealth.com/assets/itemresources/Berb_Evail_References.pdf

Berb-Evail™ may be beneficial for the support of*:

- Diabetes and pre-diabetes
- Insulin resistance/hyperinsulinemia
- Elevated triglycerides
- Non-alcoholic fatty liver

Supplement Facts

Serving Size 1 softgel

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

*Daily Value not established.

Other Ingredients: Medium chain triglycerides, vitamin E, high gamma tocopherol, sunflower lecithin; bovine gelatin, purified water, glycerine, annatto (natural color) (softgel ingredients).



*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.

To contact Designs for Health, please call us at (860) 623-6314, or visit us on the web at www.designsforhealth.com.