

# Berberine SAP

Science-based berberine for optimal metabolic function

Berberine is an active constituent found in a variety of species of plants. Newer studies have found berberine has biological effects in several pathways in the body, indicating it may be a potential treatment for metabolic syndrome.<sup>[1]</sup> Metabolic syndrome is hypothesized as beginning with an accumulation of lipids in nonadipose tissues, known as nonalcoholic fatty liver disease (NAFLD).<sup>[1]</sup> Berberine also has studies supporting its ability to reduce symptoms associated with NAFLD, as well as showing significant antidiabetic effects and lipid-lowering capability.<sup>[2, 3, 4]</sup> Historically, berberine has been used for its antimicrobial activity, as berberine is active against a wide range of organisms including bacterial viruses, fungi, helminths, and chlamydia.<sup>[1]</sup>

## ACTIVE INGREDIENTS

Each capsule contains:

Berberine hydrochloride . . . . . 300 mg

**This product is non-GMO.**

**Contains no:** Gluten, soy, wheat, corn, eggs, dairy, yeast, citrus, preservatives, artificial flavour or colour, starch, or sugar.

**Berberine SAP** contains 90 capsules per bottle.

## DIRECTIONS FOR USE

**Take 1 capsule three times daily** or as directed by your healthcare practitioner. Consult a healthcare practitioner for use beyond 3 months.

## INDICATIONS

**Berberine SAP** may be effective:

- In reducing nonalcoholic fatty liver disease (NAFLD).
- In regulating symptoms associated with metabolic syndrome.
- and supports healthy:
  - Cholesterol and glucose levels in patients with type 2 diabetes or hypercholesterolemia.
  - Microbial activity against bacterial, viruses, helminths, and fungi, without having a negative impact on beneficial bacteria.

## SAFETY AND SIDE EFFECTS

There is a long history of safe usage of berberine clinically. However, some adverse effects have been reported, including gastrointestinal concerns, allergic skin reactions, and arrhythmia.<sup>[1]</sup> There are some reports that indicate berberine may induce apoptosis in hepatoma cells; however, these cytotoxic effects were not seen in healthy hepatocytes.<sup>[1]</sup>

In a recent study, berberine supplemented in oral dosages of 500 mg three times per day was associated with gastrointestinal symptoms in 34.5% of participants.<sup>[3]</sup> However, at the reduced dose of 300 mg of berberine three times per day, gastrointestinal side effects were eliminated while observing similar beneficial effect on glucose and lipid control. For this reason and optimal patient safety, **Berberine SAP** is dosed at 300 mg per capsule of berberine hydrochloride.

## PURITY, CLEANLINESS, AND STABILITY

All ingredients listed for each **Berberine SAP** lot number have been tested by an ISO 17025-accredited third-party laboratory for identity, potency, and purity.



Scientific Advisory Panel (SAP):  
adding nutraceutical research  
to achieve optimum health



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Berberine is an isoquinoline alkaloid present in a variety of plant species including *Hydrastis canadensis*, *Coptis chinensis*, *Berberis aquifolium*, and *Berberis vulgaris*.<sup>[1]</sup> Historically, berberine is well-known for its use as an antimicrobial; however, more recent research has demonstrated that this alkaloid has a multitude of therapeutic applications, including metabolic diseases like obesity, metabolic syndrome, and type 2 diabetes.<sup>[1]</sup>

## BERBERINE METABOLISM

Berberine metabolites become widely distributed within the body, with kinetic studies showing berberine is found in the liver, kidneys, spleen, lung, and brain. It is found in its highest concentration in the liver at about a 70-fold increase versus plasma.<sup>[1]</sup>

## BERBERINE AND CHOLESTEROL

Berberine has been reported to inhibit both triglyceride and cholesterol synthesis in human hepatoma cells, as well as from primary hepatocytes.<sup>[1]</sup> Multiple animal studies have demonstrated that berberine can alleviate hyperlipidemia and fatty liver in obese and obese and diabetic rats.<sup>[2]</sup> In another study, mice consumed a high-fat diet to induce fatty liver, and after sixteen weeks of berberine supplementation there was a 14% reduction in liver lipid content as well as an alleviation of hepatic stenosis.<sup>[1]</sup>

Human clinical investigations have shown that berberine supplementation may reduce aspartate and alanine transaminase levels in patients with type 2 diabetes, indicating that berberine may improve liver function.<sup>[1]</sup> Berberine has also been shown to reduce liver necrosis in both steatosis due to hepatitis C infection as well as non-alcoholic steatosis.<sup>[1]</sup> Another study demonstrated berberine's positive effect on its ability to lower hypercholesterolemia, specifically LDL-C, in elderly hypercholesterolemic patients who were statin-intolerant.<sup>[1]</sup>

## BERBERINE AND INSULIN

Berberine has been shown to regulate glucose metabolism both in vitro and in vivo.<sup>[3]</sup> In a pilot study comparing the efficacy of berberine versus metformin in newly diagnosed type 2 diabetic patients, researchers demonstrated that after 3 months, the hypoglycemic effect of berberine (500 mg three times per day) was similar to metformin.<sup>[3]</sup> Clinical effects in the berberine group included statistically significant decreases in fasting blood glucose, postprandial blood glucose, hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) and plasma triglycerides.<sup>[3]</sup> In a follow-up study of adults with poorly controlled type 2 diabetes, patients were administered berberine for 3 months.<sup>[3]</sup> Berberine was able to lower fasting blood glucose and postprandial blood glucose from week 1 through to the end of the trial. In addition, statistically significant decreases in HbA<sub>1c</sub> and fasting plasma insulin as well as in total cholesterol and low-density lipoprotein cholesterol were observed.<sup>[3]</sup> During the trial, 34.5% of patients experienced transient gastrointestinal adverse effects; however, functional liver or kidney damages were not observed in any patients.<sup>[3]</sup> When berberine dosages were reduced to 300 mg three times per day, gastrointestinal symptoms improved significantly.<sup>[3]</sup> Researchers concluded that berberine is a potent oral hypoglycemic agent with beneficial effects on lipid metabolism.<sup>[3]</sup>

Berberine may impact insulin levels by upregulating insulin receptor expression. In patients treated with berberine, researchers found a significant elevation in the percentage of peripheral blood lymphocytes that express insulin receptors.<sup>[4]</sup> Berberine was also effective at lowering fasting blood glucose in patients

with chronic hepatitis B or C and type 2 diabetes, with patients also demonstrating improvement in liver function observed via a reduction in liver enzymes.<sup>[4]</sup>

Berberine has the ability to stimulate insulin secretion in pancreatic islet cells as well as HIT-T15 cells, which may also play a role in its anti-diabetic activity. When Hep G2 cells produce interleukin-6 (IL-6) and tumour necrosis factor- $\alpha$  (TNF- $\alpha$ ), this results in a state of inflammation which in turn impairs the insulin pathways. Berberine treatment inhibits the production of both IL-6 and TNF- $\alpha$ , associated with an improvement in the insulin-signaling cascade. Therefore, berberine may have its effect on enhancing insulin secretion through its anti-inflammatory activity.<sup>[1]</sup> Berberine may also promote activation of messenger RNA transcription of the insulin receptor, contributing to berberine's ability to regulate insulin sensitivity.<sup>[1]</sup>

## BERBERINE AS AN ANTIMICROBIAL

Berberine has been shown to have significant antimicrobial activity against bacteria, fungi, parasites, helminths, and viruses.<sup>[1]</sup> Berberine has considerable data against several bacteria including *Streptococcus*, *Salmonella*, *Klebsiella*, *Clostridium*, *Pseudomonas*, *Proteus*, *Shigella*, *Vibrio*, and *Cryptococcus* species, as well as being effective in treating *Escherichia coli* diarrhea.<sup>[1]</sup> Data also shows that berberine exerts this positive effect without harming indigenous *Lactobacilli* and *Bifidobacteria* in the intestinal system.<sup>[1]</sup>

Berberine has also been researched as a treatment for multidrug-resistant *E. coli*.<sup>[5]</sup> Five multidrug-resistant (MDR) STEC/EPEC and five MDR ETEC isolates from yaks with hemorrhagic diarrhoea were selected for the study.<sup>[5]</sup> Antibacterial activity of berberine was evaluated, and researchers concluded that berberine may be a good antibacterial treatment against MDR *E. coli*.<sup>[5]</sup>

## BERBERINE AND GUT FLORA

A study exploring the role of berberine's effect on endotoxemia in mice found that pretreating cells with berberine protected the endothelial tight junctions against disruption which could potentially have a similar effect on human Caco-2 cells.<sup>[1]</sup> Therefore, berberine treatment may block endotoxemia from entering into circulation, and thus reduce hepatic inflammation and progression of NAFLD.

Researchers have also hypothesized that part of berberine's beneficial effect in patients with diabetes mellitus is due to its ability to modulate gut flora.<sup>[6]</sup> Recent evidence suggests that gut flora composition may be associated with obesity and type 2 diabetes, both ailments associated with low-grade inflammation.<sup>[6]</sup> Since berberine is poorly absorbed, it acts topically in the gastrointestinal system and is able to inhibit bacterial cell division which may play a role in regulating gut flora.<sup>[6]</sup>

## REFERENCES

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