Clinical Applications

» Supports Glucose Metabolism and Insulin Sensitivity*
» Supports Healthy Blood Lipid Metabolism*
» Assists the Body in Maintaining Normal Levels of HbA1c*
» Positively Influences Adipocyte Differentiation and PPAR Expression Associated with Adipogenesis*
» Provides Antioxidant Support*

ALAmax™ Protect is designed to help support cardiometabolic health. It delivers alpha-lipoic acid (ALA), the plant alkaloid berberine, and biotin in one convenient formula. These ingredients have been observed to support insulin activity and glucose metabolism. Research also suggests a role for berberine in supporting normal A1C levels.*

Discussion
Berberine
As a naturally occurring botanical extract, berberine is commonly isolated from plants such as Oregon grape, barberry, and goldenseal. Two other berberine-containing plants that are familiar to practitioners of Chinese medicine are Phellodendron chinense and Phellodendron amurense—the latter being the source of berberine in ALAmax Protect. Berberine is known as an alkaloid, and plants containing berberine have traditionally been used for their various health-promoting properties. Research has demonstrated that berberine helps regulate glucose and lipid metabolism, positively influences cell signaling, provides antioxidant support, and impacts immune health.[1-3] Of more recent interest is the influence of berberine on cardiometabolic health, including its effects on adenosine monophosphate-activated protein kinase (AMPK), gene transcription and signaling factors that influence adipose tissue differentiation, and hemoglobin A1c (HbA1c) levels.*

Adenosine Monophosphate-Activated Protein Kinase (AMPK)
As the primary enzyme that induces an intracellular cascade of events, AMPK is responsible for maintaining and replenishing cellular energy stores. AMPK activation stimulates glucose uptake and fat oxidation while it suppresses lipogenesis and gluconeogenesis. Cumulatively, AMPK activation leads to beneficial metabolic states in liver, muscle, and peripheral tissues. Of the natural products known to activate AMPK, berberine is one of the most prominent. AMPK activation by berberine was reported as early as 2006.[4] Since that time, berberine-mediated AMPK activation has been repeatedly demonstrated, and this mechanism is thought to be central to the beneficial effects on glucose metabolism, insulin sensitivity, cytokine activity, and cardiovascular health observed in patients taking berberine.[5-6]

Adipocyte Differentiation and PPAR-Gamma Expression
In vitro, berberine positively influences fat cell size.[7] This effect is significant because it has been reported that fat tissue composed of a high number of small fat cells is more sensitive to insulin than fat tissue (with the same lipid content) composed of a low number of large fat cells. Berberine has also been shown to downregulate the adipogenesis-regulating transcription factors peroxisome proliferator-activated receptor (PPAR) gamma2 and CCAAT/enhancer-binding protein (C/EBP) alpha in preadipocytes isolated from human omental fat.[1] This downregulating effect on PPARs has been observed in other in vitro work and in animal research as well.[8] In a human study, individuals taking 900 mg/d of berberine for three months showed decreases in waist circumferences and BMI (body mass index) as well as significant decreases in leptin levels, leptin/adiponectin ratio, and the homeostatic model assessment of insulin resistance (HOMA-IR). There were no significant changes in adiponectin levels.[9]

Hemoglobin A1c (HbA1c)
Also known as glycated hemoglobin or glycosylated hemoglobin, HbA1c serves as the definitive measure of a person’s average blood sugar level for a three-month period. Maintaining HbA1c within a healthy range is an important aspect of cardiometabolic wellness. Recent studies on berberine show that doses of 1,000 to 3,000 mg/d have a positive effect on HbA1c levels. Yin et al demonstrated that 1,500 mg/d of berberine had significant beneficial effects on HbA1c, glucose metabolism, and triglyceride metabolism.[10] In a randomized placebo-controlled study (n = 116), 1,000 mg/d of berberine significantly decreased HbA1c and had positive effects on blood lipid metabolism.[11] This desirable effect on HbA1c by berberine has also been observed in animals.[5-6] Taken together, these research studies suggest that berberine has excellent potential as an agent that supports cardiometabolic health. Four capsules or one daily dose of ALAmax Protect provides 1,000 mg of berberine hydrochloride to achieve the range (1,000 to 1,500 mg/d) used in clinical studies.*

Alpha-Lipoic Acid (ALA)
ALA is a multifunctional antioxidant also known as thiotic acid. It has numerous effects that complement berberine. These effects include reducing oxidative stress, regenerating antioxidants, increasing glutathione synthesis, boosting antioxidant defense systems at the gene-expression level, stimulating AMPK activation,[12,13] affecting adipocyte differentiation,[14] and increasing insulin-stimulated glucose disposal.[12,14,15] Furthermore, ALA inhibits nuclear factor-κB (NF-κB), a transcription factor that activates many proinflammatory genes in the vasculature, making ALA an excellent pairing to berberine for cardiometabolic health.*

Biotin
Biotin has been added because chronic administration of lipic acid lowers the activities of pyruvate carboxylase and beta-methylcrotonyl-CoA carboxylase in vivo by competing with biotin.[16]

*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.
### ALAmax™ Protect Supplement Facts

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Amount Per Serving</th>
<th>% Daily Value</th>
</tr>
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<tbody>
<tr>
<td>Biotin</td>
<td>190 mcg</td>
<td>633%</td>
</tr>
<tr>
<td>Berberine HCl</td>
<td>500 mg</td>
<td>**</td>
</tr>
<tr>
<td>Alpha-Lipoic Acid</td>
<td>250 mg</td>
<td>**</td>
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**Daily Value not established.**

### Other Ingredients:
- HPMC (capsule), ascorbyl palmitate, L-leucine, silica, and medium-chain triglyceride oil.

### Directions:
Take two capsules twice daily, or as directed by your healthcare practitioner.

### CAUTIONS:
Consult your healthcare practitioner prior to use. Individuals taking medications, especially medications that are metabolized by cytochrome P450 enzymes or that affect blood glucose, should discuss potential interactions with their healthcare practitioner. Do not use if you are pregnant, nursing, or trying to conceive. Do not use if tamper seal is damaged.

### Storage:
Keep closed in a cool, dry place out of reach of children.

### Does Not Contain:
- Wheat, gluten, corn, yeast, soy, animal or dairy products,
- fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial enzymes or that affect blood glucose, should discuss potential interactions with medications, especially medications that are metabolized by cytochrome P450.

### References

Additional references available upon request.