



Silybum marianum (Milk Thistle)

Description and Constituents

Silybum marianum (milk thistle) has been used for centuries as an herbal medicine for the treatment of liver disease. Its use for liver disorders dates back to Pliny the Elder, a Roman naturalist, who described milk thistle as being “excellent for carrying off bile.”¹ Milk thistle is an annual or biennial plant indigenous to Europe and is also found in some parts of the United States. It grows in rocky soils to a height of three to ten feet with an erect stem that bears large, alternating, prickly-edged leaves. The common name, milk thistle, is derived from the “milky white” veins on the leaves, which, when broken open, yield a milky sap. Flowering season is from June to August, and each stem bears a single, large, purple

flower ending in sharp spines. The fruit portion of the plant is glossy brown or grey with spots.²⁻⁴

Silybum marianum contains silymarin, which is composed of the flavanolignans silybin, silydianin, and silychristine, with silybin being the most biologically active. Silymarin is found in highest concentrations in the fruit portion of the plant but is also found in the leaves and seeds. The seeds also contain betaine, trimethylglycine and essential fatty acids, which may contribute to silymarin’s hepatoprotective and anti-inflammatory effects.

Mechanisms of Action

Silymarin’s hepatoprotective effects are accomplished via several mechanisms including antioxidation,⁸ inhibition of lipid peroxidation,⁹ enhanced liver detoxification via inhibition of Phase I detoxification and enhanced glucuronidation,^{10,11} and protection of glutathione depletion.¹² Studies have also shown silymarin exhibits several anti-inflammatory effects, including inhibition of leukotriene and prostaglandin synthesis, Kupffer cell inhibition, mast cell stabilization, and inhibition of neutrophil migration.¹³⁻¹⁷ In addition, silymarin has been shown to increase hepatocyte protein synthesis, thereby promoting hepatic tissue regeneration.¹⁸ Animal studies have also demonstrated silybin reduces the conversion of hepatic stellate cells into myofibroblasts, slowing or even reversing fibrosis.¹⁹ Clinical studies conducted in Hungary¹⁹ also demonstrated silymarin to have immunomodulatory effects on the diseased liver.^{20,21}

Pharmacokinetics

Silymarin is not water soluble, making tea preparations ineffective; therefore it is usually administered orally in encapsulated form. Because absorption of silymarin from the gastrointestinal tract is only moderate (23-47%), it is best administered as a standardized extract of 70-80 percent silymarin. In animals and humans, peak plasma levels are reached in four to six hours after an oral dose. Silymarin is excreted primarily via the bile but some clearance is also achieved via the kidneys. The clearance half-life of silymarin is six to eight hours.^{22,23}

Clinical Indications

Amanita Mushroom Poisoning

The most impressive use of silymarin is in the treatment of *Amanita phalloides* mushroom poisoning. The genus *Amanita* is widespread in Europe and North America with several edible species being prized by mushroom collectors. Unfortunately, many of the *Amanita* species are highly toxic, and ingestion results in severe liver damage and death in approximately 30 percent of cases.²⁴ In animal studies, silymarin given within 10 minutes after *amanita* toxin ingestion completely counteracted the toxic effects, and if given within 24 hours of toxin ingestion silymarin prevented death and greatly reduced liver damage.²⁵

Hepatitis

Studies have shown silymarin to be effective in the treatment of both acute and chronic hepatitis. In acute viral hepatitis, administration of silymarin shortened treatment time and lowered serum bilirubin, AST, and ALT. In patients with chronic hepatitis, 420 mg silymarin per day for six months also yielded improved serum liver enzymes.²⁶

Alcoholic Liver Disease and Cirrhosis

Studies conducted in Austria and Hungary have demonstrated silymarin administration resulted in a normalization of serum liver enzyme and total bilirubin levels in patients with alcoholic liver disease, in addition to improved liver tissue histology.²⁷ In patients with cirrhosis, long-term (41 months) administration of silymarin at 420 mg per day resulted in a significant increase in survival compared to the placebo group.²⁸

Hypercholesterolemia

An animal study found silymarin given to rats with diet-induced hypercholesterolemia demonstrated an anticholesterolemic effect similar to probucol, with an increase in HDL cholesterol and a decrease in total and biliary cholesterol.²⁹

Psoriasis

The value of silymarin in the treatment of psoriasis may be due to its ability to improve endotoxin removal by the liver, inhibit cAMP phosphodiesterase, and inhibit leukotriene synthesis. Abnormally high levels of cAMP and leukotrienes have been observed in patients with psoriasis and normalization of these levels may improve the condition.^{13,30}

Dosage/Toxicity

Silybum marianum is usually given as a standardized extract (70-80% silymarin) in encapsulated form, 100-300 mg three times daily being the typical adult dose. Both animal and human studies have shown silymarin to be non-toxic. At high doses (>1500 mg per day) a laxative effect is possible due to increased bile secretion and flow. Mild allergic reactions have also been noted but were not serious.

References

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