

# Milk Thistle

## A Historical Liver Treatment

Milk thistle is a plant with a long history in medicine, having been mentioned in every important medicinal record of herbs.<sup>1</sup> It was widely used as a medicinal plant in traditional European medicine, and its seeds have been used for over 2000 years for a variety of purpose.<sup>2</sup> Traditional uses have mainly focused on the treatment of liver diseases, but have also included gallbladder disorders such as hepatitis, cirrhosis and jaundice.<sup>1</sup> Milk thistle was brought to North America with European immigration, and was used there as a treatment for such various ailments as gallstones, morning sickness, uterine hemorrhage, and congestion of the liver, spleen or kidneys.<sup>3</sup>



Figure 1. Milk Thistle

Currently, milk thistle is still a staple in natural medicine. It is commonly included in detoxification regimes due to its ability to support and protect the liver.<sup>4</sup> However, its applications have been extended to other purposes including support for the pancreas, the lungs and the kidneys, prostate disorder, and

dermatology and cosmetics.<sup>1</sup> It has also begun to gain attention for its activities against cancer cells and for its effects in the regulation of cholesterol levels.<sup>1</sup> Although its actions are somewhat disputed and still not fully understood, the potentials of this remarkable plant for dealing with a wide variety of disorders have caused it to become one of the most studied plants in natural medicine.

### Silymarin- the Active Ingredient

The active ingredient in milk thistle is a flavonoid complex known as silymarin, which is extracted from the seeds of the plant.<sup>1,2</sup> The standardized seed extract contains approximately 70-80% of silymarin flavolignans, and around 20-40% of a fraction of polymeric and oxidized polyphenolic compounds which has not been chemically defined.<sup>1</sup> The six major flavolignans are silybin A and B, isosilybin A and B, silychristin, and silydianin. These compounds are likely the main contributors to silymarin's beneficial effects.<sup>5</sup> In particular, silybin, also known as silibinin, has been studied for its effectiveness in liver treatment and other applications.<sup>1</sup>

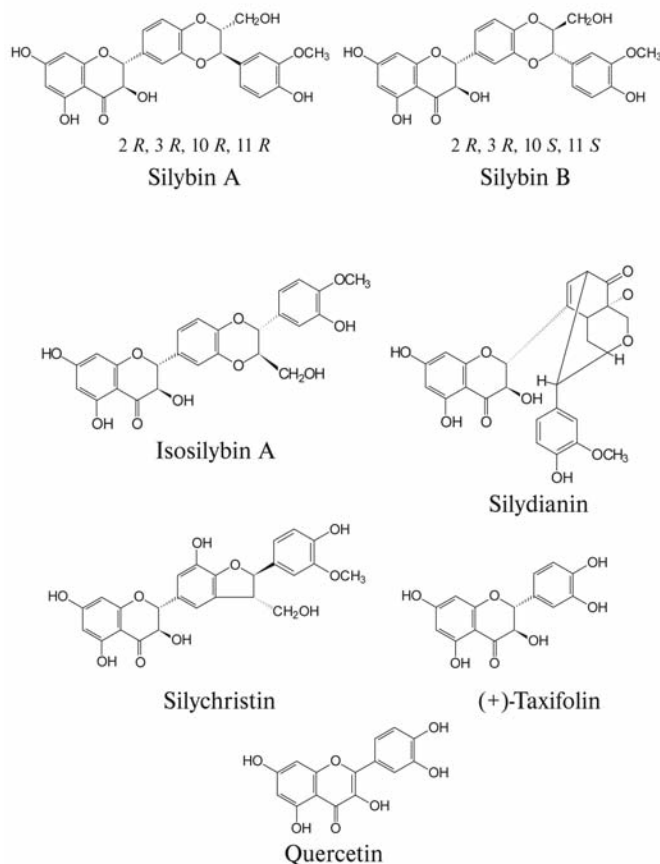


Figure 2. Active components present in milk thistle

The precise mechanism of action of silymarin is currently not well defined, although several mechanisms have been suggested in scientific studies.<sup>1</sup> Silymarin is known to have antioxidant qualities, stopping the damage caused by free radicals, which are highly reactive by-products of cellular metabolism.<sup>1</sup> It also has anti-inflammatory and immunomodulatory effects.<sup>5</sup> Furthermore, it appears to have an influence on cholesterol metabolism.<sup>1</sup>

## The Effects of Milk Thistle

### Protection for the Liver

Silibinin's effectiveness as a liver protective agent has been documented throughout history. Its protective effects appear to be at least partially mediated by its antioxidant activity.<sup>1</sup> It is also thought to intercede with cell signaling pathways, blocking the production of pro-inflammatory molecules in order to avoid an excessive inflammatory response. It has been found to do so at a lower concentration than the well-known anti-inflammatory agent salicylate.<sup>1</sup> Furthermore, its antioxidant effect helps to decrease the damaging cytotoxic effects of various drugs and other compounds that can damage the liver.<sup>1</sup> In animal studies, silymarin and silibinin were found to be able to protect mice or rats against liver damage caused by such factors as acute ethanol intoxication, carbon tetrachloride, cisplatin and acetaminophen.<sup>2</sup> Milk thistle is currently recommended by the German Commission E for dyspeptic complaints, toxin-induced liver damage, and hepatic cirrhosis as well as for a supportive therapy for chronic inflammatory liver conditions.<sup>6</sup>

### Effects on Cholesterol Levels

Silibinin has been found to have beneficial effects on cholesterol levels. It is thought that its antioxidant activity helps to protect cholesterol-transporting lipoproteins.<sup>1</sup> It has also been found to influence cholesterol metabolism, and can block a key enzyme involved in the synthesis of cholesterol.<sup>7</sup> In rats, milk thistle seed oil was found to reduce serum total cholesterol and triglyceride levels by 84 and 60%.<sup>4</sup> Silibinin's potential in helping to deal with cancer has been the focus of many recent studies. Its ability to interact with cellular pathways includes the ability to modulate various regulators of the cell cycle.<sup>1</sup> This is important in cancerous cells, which have deranged cell cycles and divide too quickly. Cell studies with silibinin have found that it is able to inhibit and to kill abnormal cells of various forms of cancer without damaging

healthy cells.<sup>1,8</sup> It is also thought to block the proliferation of cancerous cells.<sup>8</sup> For instance, prostate cancer cells incubated with silibinin showed a dose and time-dependent decrease in viability and motility.<sup>8</sup> Silibinin's antioxidant effects also help to protect against cellular damage, such as in the case of skin damage caused by UV radiation. This has been tested in both cell and animal studies, in which silibinin was found to have beneficial effects when used both topically and when fed in the diet.<sup>9</sup> Other studies have suggested that silibinin's ability to protect against the toxicity of various drugs may be able to lessen the toxicity of anticancer agents and enhance the effectiveness of chemotherapy treatments.<sup>2</sup> Studies have suggested several areas of potential for silibinin, including cleansing and detoxification after chemotherapy, the prevention of chemotherapy-caused liver damage, and dealing with liver damage after chemotherapy.<sup>2</sup> While the results that have been discovered so far suggest that silibinin has a fairly strong anticancer effect, more studies are needed to confirm these results.<sup>10</sup>

### Other Effects

Silibinin's effects may be beneficial in other areas as well. Its anti-inflammatory effects can help protect neurons from over inflammation, as well as from toxicity associated with drugs such as acetaminophen, cisplatin and cyclosporin.<sup>10</sup> Silibinin has been suggested to have protective effects in allergic asthma, likely due to its interference with pro-inflammatory pathways, and its ability to help stabilize cellular membranes, thus blocking the release of pro-inflammatory molecules.<sup>1</sup> Other studies have suggested that silibinin may help to reduce insulin resistance.<sup>11</sup>

### Clinical Trials

The effectiveness of milk thistle has been tested in several scientific studies and clinical trials.

Its liver protective effects have been the area of the most research. A study of patients with hepatitis C found that milk thistle, along with the antioxidant alpha lipoic acid and selenium and with dietary and lifestyle changes, helped to reduce disease markers such as serum transaminase levels and viral load.<sup>12</sup> In a randomized double-blind study, patients suffering from alcoholic cirrhosis of the liver were found to have a significantly higher survival rate when given silymarin compared to control groups.<sup>13</sup>

Silibinin's effects on cholesterol have also been tested. In 15 patients who had had their gallbladders removed, the administration of 420 mg of milk thistle extract per day for 30 days resulted in a significant decrease in the concentrations of biliary cholesterol compared to patients who were given a placebo. Researchers suggested that the silibinin may have helped to decrease cholesterol synthesis in the liver.<sup>12</sup> In another study, 14 type II hyperlipidemic patients were given 420 mg of milk thistle extract per day for seven months. The milk thistle was suggested to have an effect on decreased total cholesterol in the serum and an increase in high-density (good) cholesterol levels in the blood.<sup>14</sup>

In a controlled study of insulin-treated patients, 600 mg of milk thistle extract per day for 12 months appeared to significantly reduce fasting glucose levels, mean daily glucose levels and decrease fasting insulin levels compared to controls.<sup>11</sup> In a randomized controlled trial of alcoholic diabetic patients, 600 mg of milk thistle extract per day for 6 months was associated with significant decreases in the mean levels of fasting blood glucose, daily blood glucose and daily insulin need compared with controls and the patients' own baseline levels.<sup>13</sup>

In 30 patients with end-stage diabetic nephropathy, milk thistle extract appeared to help normalize the regulatory effects in the immune system, for instance, by helping to activate T cells and significantly decrease the release of a key pro-inflammatory molecule.<sup>15</sup>

## Beneficial Actions of Milk Thistle

- Liver protection
- Support for liver disorders, including hepatitis C and cirrhosis
- Reduction of the toxicity of chemotherapy drugs
- Anti-cancer effects
- Anti-inflammatory actions
- Cholesterol reduction
- Blood sugar balancing effects
- Immune system support

## Safety Profile

Overall, milk thistle is considered to be extremely safe.<sup>1</sup> Side effects in clinical trials have been mainly limited to a very low frequency of gastrointestinal symptoms.<sup>1</sup> The majority of people have no adverse reactions. It has been suggested that up to 1.44 g of silibinin administered daily in an oral form for over a week is safe.<sup>2</sup>

Silibinin undergoes metabolism by both phase I and phase II enzymes. Its interaction with these enzymes has led to fears of its effect on the metabolism of other drugs. Most studies in this area have found that silibinin does not interact significantly with many other drugs. Studies with several common drugs found a general lack of associated toxicity and a low interference in their metabolism when combined with milk thistle<sup>16</sup>; however, a physician should be consulted before taking milk thistle with other medications due to the potential for interference.<sup>2</sup>

## Milk Thistle- the Past and the Future

While milk thistle has a long history of medicinal use, its effectiveness in human studies has been somewhat controversial because of occasionally conflicting results in scientific literature.<sup>1</sup> This is likely due to the fact that studies in the past have tended to use variably composed silymarin preparations.<sup>1</sup> As the ingredient becomes more standardized, and as its mechanism of action becomes better understood, its effectiveness will be more clearly determined. Thus far, its potential is acknowledged by many clinical trials, as well as by its historical record. It is a plant that will continue to hold interest for those looking to optimize the health of their liver.

## References

1. Gazak R, Walterova D and Kren V. Silybinin and silymarin- new and emerging applications in medicine. *Current Medicinal Chemistry*. 2007;14:315-338.
2. Wu JW, Lin LC and Tsai TH. Drug-drug interactions of silymarin on the perspective of pharmacokinetics. *Journal of Ethnopharmacology*. 2009;121:181-193.
3. Abascal K, Yarnell E. The many faces of *silybum marianum* (milk thistle) part I. *Altern Complement Ther*. 2003;9:170-175.
4. Greenlee H, Abascal K, Yarnell E and Ladas E. Clinical applications of *silybum marianum* in oncology. *Integrative Cancer Therapies*. 2007;6:158-165.
5. Schrieber SJ, Wen Z, Vourvahis M, Smith PC, Fried MW, Kashuba ADM, Hawke RI. The pharmacokinetics of silymarin is altered in patients with hepatitis C virus and nonalcoholic fatty liver disease and correlates with plasma caspase-3/7 activity. *Drug Metabolism and Disposition*. 2008;36(9):1909-1916.

6. *The Complete German Commission E Monographs: Therapeutic Guide to Herbal Medicines 1st Ed.* Baltimore, MD: Lippincott Williams & Wilkins:1998.
7. Nassuato G, Iemmolo RM, Strazzabosco M, Lirussi F, Deana R, Francesconi MA, Muraca M, Passera D, Fragasso A, Orlando R et al. Effect of Silibinin on biliary lipid composition. *Experimental and clinical study.* *J Hepatol.* 1991;12(3):290-295.
8. Mokhtari MJ, Motamed N, Shokrgozar MA. Evaluation of silibinin on the viability, migration and adhesion of the human prostate adenocarcinoma (PC-3) cell line. *Cell Biology International.* 2008;32:888-892.
9. Gu M, Dhanalakshmi S, Singh RP and Agarwal R. Dietary feeding of silibinin prevents early biomarkers of UVB radiation-induced carcinogenesis in SKH-1 hairless mouse epidermis. *Cancer Epidemiology Biomarkers and Prevention.* 2005;14:1344-1349.
10. Dietzmann J, Thiel U, Ansorge S, Neumann KH, Tager M. Thiol-inducing and immunoregulatory effects of flavonoids in peripheral blood mononuclear cells from patients with end-stage diabetic nephropathy. *Free Radic Biol Med.* 2002;33(10):1347-1354.
11. Velussi M, Cernigoi AM, De Monte A, Dapas F, Caffau C, Zili M. Long-term (12 months) treatment with an anti-oxidant drug (silymarin) is effective on hyperinsulinemia, exogenous insulin need and malondialdehyde levels in cirrhotic diabetic patients. *J Hepatol* 1997;26(4):871-879.
12. Berkson BM. A conservative triple antioxidant approach to the treatment of hepatitis C: combination of alpha lipoic acid (thioctic acid), silymarin, and selenium: three case histories. *Med Klin.* 1999;94(suppl 3):84-89.
13. Velussi M, Cernigoi AM, Viezzoli L, et al. Silymarin reduces hyperinsulinemia, malondialdehyde levels, and daily insulin need in cirrhotic diabetic patients. *Curr Ther Res* 1993;53(5):533-545.
14. Somogyi A, Ecsedi GG, Blazovics A, Miskolczi K, Gergely P, Feher J. Short term treatment of type II hyperlipoproteinaemia with silymarin. *Acta Med Hung.* 1989;46:289-295.
15. Tamayo C and Diamond S. Review of clinical trials evaluating safety and efficacy of milk thistle (silybum marianum Gaertn.). *Integrative Cancer Therapies.* 2007;6:146.
16. Sridar C, Goosen TC, Kent UM et al. Silybin inactivates cytochromes P450 3A4 and 2C9 and inhibits major hepatic glucuronosyltransferases. *Drug Metabl. Dispos.* 2004;32(6):587-594.

# An Important Antioxidant



- Protects the heart
- Boosts levels of Glutathione
- Improves immunity
- Protects against toxins

**NAC Sustained™**