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Milk Thistle-An Overview

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ABSTRACT

Milk thistle (Silybum marianum, family-Compositae) is widespread throughout the world. Milk thistle's common name comes from the white markings on the leaves and its milky white sap used traditionally by nursing mothers to increase milk. Milk thistle appears to be safe and have multiple health benefits on various liver conditions viz; liver cirrhosis, alcoholic hepatitis, alcoholic fatty liver, liver poisoning, and viral hepatitis. Primary chemical constituents of Milk Thistle include flavolignans (silymarin), tyramine, histamine, gamma linoleic acid, essential oil, mucilage, and bitter principle. Available evidence is not sufficient to suggest whether milk thistle may be more effective for some liver diseases than others or if effectiveness might be related to duration of therapy or chronicity and severity of liver disease.

Keywords: Milk Thistle, Liver diseases, Liver poisoning, Silymarin, Tyramine, Histamine

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INTRODUCTION

Milk Thistle is a thistle of the genus Silybum, a flowering plant of daisy family (Asteraceae). The plant is native to Mediterranean regions of Europe, North Africa and the Middle East[1]. The name milk thistle derives from a feature of the leaves, which are prominently banded with splashes of white. Milk thistle (silybummarianum) has been used for 2000 years as an herbal remedy for variety of ailments, particularly liver, kidney and gall bladder problems.

Many years of research shows the active– lignin (flavanolignan) group of constituents called Silymarin, contained onlyin the seed shell have liver protective and regenerative properties, as well as antioxidant effect. Milk thistle protects the liver from toxins, including certain drugs such as acetaminophen (Tylenol), which can cause liver damage in high doses. Silymarin has antioxidant and anti inflammatory properties and it may help the liver repair itself by growing new cells. The liver protective effects were known and written about in an ancient leading to active chemicals, pharmacological and safety research beginning in Germany in the 1950's. Clinical use for a variety of liver elements such as Hepatitis, has also proposed throughout parts of the world.

Milk Thistle

Figure:1

Figure:2

Figure:3

(Figure:1, 2 and 3 show Silybum marianum Flower)

Scientific Classification

Kingdom	Plantae
(unranked)	Angiosperms
(unranked)	Eudicots
(unranked)	Asterids

Order	Asterales
Family	Asteraceae
Subfamily	Carduoideae
Tribe	Cynareae
Genus	Silybum

Species
• Silybumeburneum
• Silybummarianum
• Silybum× gonzaloi

Plant Description and Classification

Members of this genus grow as annual or biennial plants. It is now found throughout the world. This stout thistle usually grows in dry, sunny areas. They are commonly found in hedge banks and waste places in Europe. The large, dark green alternate leaves are waxy lobed, toothed and thorny, with white blotches or veins. Milk Thistle gets its name from the milky white gap that comes from the leaves when they are crushed. The spiny stems branch at the top and read a height of 5-10 feet. The plant shows reddish purple flowers having spiny apex. The small, hard skinned fruit is brown, spotted and shiny. Milk thistle spread quickly and it matures quickly, in less than a year. Only two species are currently classified in this genus.

- Silybum eburneum-Known as the silver Milk Thistle, Elephant thistle or Ivary Thistle.
- Silybum marianum-The Blessed Milk Thistle, which has a large members of other common names, such as Variegated thistle.

The two species hybridise naturally, the hybrid being known as Silybum x gonzaloi.

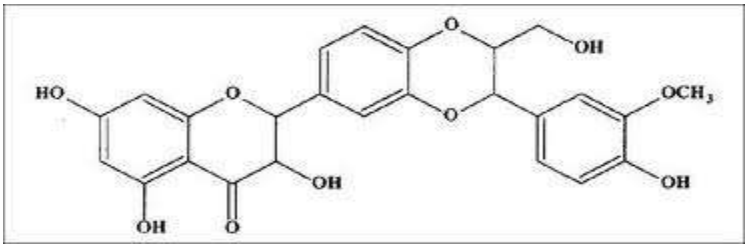
Plant Description: Silybum marianum flower

Thistle flower **Dried thistle flowers at the end of summer**

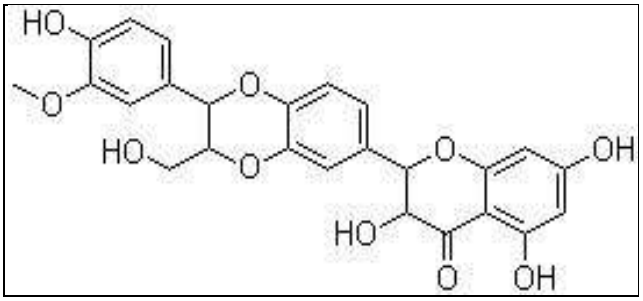
Nomenclature

Traditional milk thistle extract is made from the seeds, which contain approximately 4-6% silymarin. The extract consists of about 65-80% silymarin[2] which is a flavanolignan complex and

20-35% fatty acids including linoleic acid[3]. Silymarin is a complex mixture of polyphenolic molecules including three isomeric flavanolignans called silybin, silycrystin and silydianin and one flavonoid, silibinin , a semi purified fraction of silymarin is a primarily a mixture of two diastereoisomerssilybin A and Silybin B in a roughly 1:1 ratio[3,4]. Milk Thistle seeds also contain other flavanolignans namely dehybrosilybin, desocrysilycristin, desoxysilydianin, silyhermin, neosilyhermin, silybinome and silandrin. Other constituents present are betaine, apigenin and silybonol.[5]



Silybin



Silymarin

Uses

For many centuries extracts of thistle milk have been recognized as "liver tonics."[3] Research into the biological activity of silymarin and its possible medical uses has been conducted in many countries since the 1960s [6] but the quality of the research has been uneven.[7] Milk thistle has been reported to have protective effects on the liver and to greatly improve its function. It is typically used to treat liver cirrhosis, chronic hepatitis (liver inflammation), toxin-induced liver damage including the prevention of severe liver damage from *Amanita phalloides* ('death cap' mushroom poisoning), and gallbladder disorders.[2,8]

A review examining studies with a double-blind protocol concluded that milk thistle and its derivatives has no significant effect on mortality or course of disease in individuals with alcoholic and/or hepatitis B or C disease.[9]

Hepatoprotective

- **Toxin induced liver damage**

Research suggests that milk thistle extracts both prevent and repair damage to the liver from toxic chemicals and medications. Workers who had been exposed to vapors from toxic chemicals (toluene and/or xylene) for 5-20 years were given either a standardized milk thistle extract (80% silymarin) or placebo for 30 days.[10] The workers taking the milk thistle extract showed significant improvement in liver function test (ALT and AST) and platelet counts versus the placebo group.

The efficacy of silymarin in preventing drug-induced liver damage in patients taking phychotropic drugs long term has been investigated.[11] Most studies show milk thistle improves liver function and increases survival in people with cirrhosis and chronic hepatitis.

A clinical trial in humans showed that silymarin (140mg orally 3 times daily) was not effective when used for one year in combination with ursodeoxycholic acid (UDCA) for the treatment of primary biliary cirrhosis.[12] A study in baboons indicated that continuous intragastric infusion of silymarin retarded the development of alcohol induced hepatic fibrosis over a three year period. The authors suggested that the failure of silymarinto show beneficial effects in other clinical trials may have been due to poor compliance with treatment, resulting in insufficient dosing.[13]

In a 2010 study published in journal Cancer, milk thistle was associated with a trend towards reducing the liver damaging effect of chemotherapy in a randomized double- blind placebo controlled study of 50 children.[14]

- **Amanita mushroom poisoning**

Based on traditional use, milk thistle has been used as an emergency antidote to poisoning by deathcap mushroom (*Amanita phalloides*)-silymarin block the receptor site of outer liver cell membrane.There has been no controlled clinical study of any treatment suggested for mushroom poisoning.The efficacy of thirty different treatments was analyzed in a retrospective study of 205 cases of *Amanita phalloides* (death cap) mushroom poisoning.[15] Both penicillin and hyperbaric oxygen independently contributed to a higher rate of survival. When [silybin silibinin] was added to the penicillin treatment, survival was increased even more. In another 18 cases of death cap poisoning, a correlation was found between the time elapsed before initiation of silybin therapy, and the severity of the poisoning. The data appear to indicate that severe liver damage in *Amanita phalloides* poisoning can be prevented effectively when administration of silybin begins within 48 hours of mushroom intake.[16]Animal studies have found that milk thistle extract completely counteracts the toxic effects of the mushroom when given within 10 minutes of ingestion.

- **Viral hepatitis**

Milk thistle is widely used in the treatment of viral hepatitis (particularly hepatitis C). However, studies show mixed results. Some found improvements in liver function, while others did not. In one study of 16 patients who didn't respond to interferon and ribavirin therapy, milk thistle significantly reduced the viral load of hepatitis C. In 7 of the subjects the virus decreased to undetectable levels after 14 days of therapy.

Silymarin also shows hepatoprotective effects against D-galactosamine,carbontetrachloride and thioacetamide. It has been reported that therapeutic utility of silimarin is due to stabilization of cell membrane, stimulation of protein synthesis and accelerating the process of regeneration of hepatic cells. [5]

Cancer

Early laboratory studies also suggest that silymarin and other active substances in milk thistle may have anticancer effects. These substances appear to stop cancer cells from dividing and reproducing, shorten their lifespan, and reduce blood supply to tumours. Some studies suggest silymarin may favourably supplement sunscreen protection and may help reduce the risk of skin cancer. More studies are needed, however, to show whether milk thistle has any effects in the body (not just in test tubes).

Antioxidant and anti inflammatory activity

Diabetic nephropathy

The potential efficacy of silymarin in the treatment of diabetic nephropathy has been demonstrated in several animal studies so far.[17] It has also been found to be effective in reducing proteinuria in type 2 diabetes patients with overt nephropathy in a recent randomized controlled trial.[18] This reduction in proteinuria was attributed to antioxidant and anti-inflammatory effects of silymarin.

Other uses

Beside benefits for liver disease, other unproven treatment claims include:

- Lowering cholesterol levels[19]
- Reducing insulin resistance in people with type 2 diabetes who also have cirrhosis,[19,20]
- Reducing the growth of cancer cells in breast, cervical, and prostate cancers.[21]
- Clinical study has shown that liver function tests can be improved in active hepatitis patients.[22]
- Bitter tonic[5]
- Anti depressant[5]
- In homeopathy for treatment of jaundice and bronchitis.[5]

Use as food

Milk thistle has also been known to be used as food.[23] Around the 16th century the milk thistle became quite popular and almost all parts of it were eaten. The roots can be eaten raw or boiled and buttered or par-boiled and roasted. The young shoots in spring can be cut down to the root and boiled and buttered. The spiny bracts on the flower head were eaten in the past like globe artichoke, and the stems (after peeling) can be soaked overnight to remove bitterness and then stewed. The leaves can be trimmed of prickles and boiled and make a good spinach substitute or they can also be added raw to salads.

Dose

- In clinical trials silymarin has typically been administered in amounts ranging from 420–480 mg per day in two to three divided doses.[24]
- High doses of 600 mg daily in the treatment of type II diabetes[25,26]
- 600 or 1200 mg daily in patients chronically infected with hepatitis C virus[26]

An optimal dosage for milk thistle preparations has not been established. Milkthistle, along with dandelion and other extracts are often referred to as hangover cures as the bitter tincture helps organs rid toxins after heavy drinking.[27]

Available forms[28]

- Capsules of standardized dried herb (each capsule contains about 120 - 140 mg silymarin)
- Liquid extract
- Tincture
- Silymarin phosphatidylcholine complex - may be absorbed more easily than regular standardized milk thistle. Phosphatidylcholine is a key element in cell membranes. It helps silymarin attach easily to cell membranes, which may keep toxins from getting inside liver cells. People who have alcohol-related liver disease should avoid alcohol extracts.

How to take it ?[28]

Paediatric

There are no studies showing whether it is safe to give milk thistle to a child. Liver problems can be serious and should be diagnosed by a physician. Talk to your child's health care provider before giving milk thistle to a child.

Adult

If you think you have a liver problem, you should see a health care provider. Liver disease can be life threatening.

Precautions[29]

The use of herbs is a time honoured approach to strengthening the body and treating disease. Herbs, however, can trigger side effects and can interact with other herbs, supplements, or medications. For these reasons, you should take herbs with care, under the supervision of a health care practitioner.

Milk thistle is generally regarded as safe. Side effects are usually mild and may involve stomach upset and diarrhoea. Some people may get a rash from touching milk thistle plants.

Milk thistle should not be used by pregnant or breastfeeding women.

People with a history of hormone related cancers, including breast, uterine, and prostate cancer, should not take milk thistle. Do not take milk thistle if you are allergic to ragweed, chrysanthemums, marigolds, chamomile, yarrow, or daisies.

Possible Interactions

If you are being treated with any of the following medications, you should not use milk thistle without first talking to your health care provider.

- **Antipsychotics** -- includes butyrophenones (such as haloperidol) and phenothiazines (such as chlorpromazine, fluphenazine, and promethazine)
- **Phenytoin(Dilantin)** -- a medication used for seizures
- **Halothane** -- a medication used during general anaesthesia
- **Birth control pills or hormone replacement therapy**

Milk thistle may interfere with the following medications, because both milk thistle and these medications are broken down by the same liver enzymes:

- **Allergy drugs** -- such as fexofenadine (Allegra)
- **Drugs for high cholesterol** -- including statins such as lovastatin (Mevacor, Altocor)[30]
- **Antianxiety drugs** -- including alprazolam (Xanax), diazepam (Valium), and lorazepam (Ativan)[30]
- **Antiplatelet and anticoagulant drugs (blood thinners)** -- including clopidogrel (Plavix) and warfarin (Coumadin)[30]
- **Some cancer drugs**[30]
- **Drugs broken down by the liver** -- because milk thistle works on the liver, it may affect drugs broken down by the liver, of which there are many. Speak with your health care provider.[30]

Alternative names

Silybummarianum; St. Mary's thistle

CONCLUSION

Clinical efficacy of milk thistle is not clearly established. Interpretation of the evidence is hampered by poor study methods and/or poor quality of reporting in publications. Problems in study design include heterogeneity in etiology and extent of liver disease, small sample sizes, and variation in formulation, dosing, and duration of milk thistle therapy. Possible benefit has been shown most frequently, but not consistently, for improvement in aminotransferases and liver function tests are overwhelmingly the most common outcome measure studied. Survival and other clinical outcome measures have been studied least often, with both positive and negative findings. Available evidence is not sufficient to suggest whether milk thistle may be more effective for some liver diseases than others or if effectiveness might be related to duration of therapy or chronicity and severity of liver disease. Regarding adverse effects, little evidence is available regarding causality, but available evidence does suggest that milk thistle is associated with few, and generally minor, adverse effects. Despite substantial in vitro and animal research, the mechanism of action of milk thistle is not fully defined and may be multifactorial. A systematic review of this evidence to clarify what is known and identify gaps in knowledge would be important to guide.

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