St. Mary's Thistle

Silybum marianum

BOTANICAL FAMILY:	Asteraceae/Compositae
PARTS USED:	Fruit (seed)
OTHER COMMON NAMES:	Milk thistle, mariendistelfruchte (German), chardon-Marie (French), carduo nariano (Italian)

OVERVIEW[1]

St Mary's Thistle is a member of the daisy family, and is closely related to globe artichoke. It's spiny leaves have white veins, giving it a mottled splotched appearance. St. Mary's Thistle is native to the Mediterranean region, but is widely cultivated throughout the West. It has been used medicinally for over 2000 years, and was recommended by Dioscorides and Culpepper.

Constituents	Flavonolignans silybin, silychristin and silydianin, collectively known as silymarin Fixed oil, flavonoids, taxifolin, sterols
Major Actions	Hepatoprotective, hepatic trophorestorative
Other Actions	Antioxidant, choleretic, galactogogue
Indications	Indigestion; Hepatitis, fatty liver, liver fibrosis and cirrhosis; Liver problems associated with pregnancy such as cholestasis; Gallstones and gallbladder conditions; Hepatotoxicity induced by medications, toxins, chemicals and pollutants; Lactation; Type II diabetes mellitus; Haemochromatosis, beta-thalassaemia and thalassaemia major; As an adjunct in cancer treatments.
Traditional Use	St. Mary's Thistle has been used in liver and gallbladder disease for centuries. Historically, it was also used for snake bites, haemorrhoids, dropsy (oedema), catarrh and pleurisy.
Preparations	Liquid extract 2:1/69% ethanol or glycetract 1:1/0% ethanol or tablet.
Applications	Practitioners can consider prescribing St. Mary's Thistle in the context of: Sluggish liver and gallbladder function; Liver disease; Gallbladder disease; Exposure to hepatotoxic substances; Exposure to oxidative stress; Metabolic conditions including diabetes; Excessively high iron levels; Supporting adequate breast milk production; Support during cancer treatment.

SUMMARY OF RESEARCH

Clinical Studies

Hepatotoxicity	A systematic review involving 19 clinical trials concluded that it was reasonable to use silymarin as a supportive strategy in Amanita phalloides poisoning and liver cirrhosis. In alcoholic liver disease, serum aspartate aminotransferase (AST) levels were significantly reduced with silymarin supplementation compared to placebo. In liver cirrhosis, total mortality was significantly lower with silymarin treatment.[2]
Non-Alcoholic Liver Disease	In an early uncontrolled study involving 2000 patients with toxic liver damage from various causes, St Mary's Thistle supplementation significantly reduced serum levels of hepatic enzymes, a marker of liver damage. Symptoms including nausea, discomfort and itching were improved in 83% of patients.[3]
	In a randomised controlled trial, 90 patients undergoing treatment with potentially hepatotoxic medications were given oral silymarin extract 800 mg daily for 90 days. The trial found that silymarin reduced the lipoperoxidative liver damage associated with butyrophenone or phenothiazine medications.[4]
Alcoholic Liver Disease	A randomised controlled trial utilising 420 mg silymarin extract per day for 4 years significantly increased survival rates in patients with alcoholic cirrhosis.[5] A similar study in 170 patients with cirrhosis of differing aetiologies found silymarin 420 mg per day for 2 years significantly reduced mortality, and that this effect was more pronounced in alcoholic cirrhosis.[6]
	In a double blind controlled trial, patients with alcoholic cirrhosis were treated with silymarin 420 mg per day for 6 months. Hepatic enzymes and bilirubin levels were significantly reduced in the treatment group compared to placebo. There were also positive changes in liver histopathology in the treatment group.[7]
Chronic Liver Disease	A post-marketing surveillance study investigated the effects of silymarin 280-420 mg per day for 12 weeks in patients with chronic liver diseases of different aetiologies. The study found that the patients experienced a clinically relevant decrease in subjective symptoms including nausea, anorexia and upper abdominal pressure. There was also a significant reduction in markers of liver fibrogenesis in the subgroup of patients who had elevated levels at baseline.[8]
	A clinical trial in patients with chronic persistent hepatitis found that silybin treatment for three months significantly reduced serum liver enzyme levels.[9]
	An observational study looked at 1049 patients with advanced hepatitis C related liver disease who were non-responsive to antiviral therapy. The study found that silymarin use was associated with a reduced progression from liver fibrosis to cirrhosis.[10]
	A clinical trial examined the effects of silymarin plus standard antiviral therapy versus antiviral therapy alone in patients with hepatitis C over three months. The trial found that clinical symptoms of hepatitis C disappeared 7-10 days sooner in the silymarin group. Cytolytic syndrome was resolved in the herbal group, and the number of patients considered cured at the end of the study was 20% higher in the silymarin plus antiviral group.[11]
Acute Liver Disease	Two clinical trials investigated the effects of silymarin in patients with acute viral hepatitis. The trials found a significant decrease in serum liver enzymes and bilirubin compared to placebo.[12,13]
	In a randomised controlled trial 105 participants with acute hepatitis were given 420 mg silymarin per day or placebo for four weeks. The study found that silymarin resulted in an earlier improvement on subjective and clinical markers of biliary excretion, including jaundice, dark urine, scleral icterus and indirect bilirubin.[14]
Diabetes	In 2 randomised controlled trials, patients with type II diabetes mellitus were given standard therapy plus silymarin or placebo for 4 months. Both studies found that the addition of silymarin led to significant improvements in glycaemic control compared to placebo. Significant improvements in fasting glucose, glycosylated haemoglobin (HbA1c), lipid profiles, liver enzymes and body mass index were seen in the silymarin groups.[15,16]

SUMMARY OF RESEARCH	
Diabetes (continued)	A randomised trial in 60 patients with diabetes induced by alcoholic liver cirrhosis investigated the effects of silymarin 600 mg per day on glycaemic control. The study found silymarin significantly improved fasting blood glucose levels, glycosuria, HbA1c levels, fasting insulin levels and the need for exogenous insulin, compared to baseline and to matched controls.[17]
Iron-Related Disorders	In a clinical trial, 59 iron-loaded patients with beta-thalassaemia were randomised to receive standard desferrioxamine therapy plus silymarin 420 mg or placebo daily for 3 months. Silymarin plus desferrioxamine was better tolerated and more effective in reducing serum ferritin than desferrioxamine alone or in combination with placebo. The silymarin group also had significant improvements in alkaline phosphatase and glutathione levels compared to placebo.[18]
Osteoarthritis	An eight week randomised controlled trial compared the effects of silymarin and the non-steroidal anti-inflammatories (NSAIDS) piroxicam and meloxicam on inflammatory markers in 220 patients with osteoarthritis of the knee. Both the silymarin alone and silymarin plus piroxicam groups had significant reductions in the inflammatory markers interleukin-α1, interleukin-8, complement C3 and C4 compared to meloxicam and placebo.[19]
Haemodialysis	In 2 clinical trials, silymarin supplementation significantly increased haemoglobin levels in patients undergoing haemodialysis.[20,21] One of these also found significant improvements in antioxidant status and reductions in oxidative stress markers in the silymarin group.[20]
Galactagogue Effects	In a group of 50 healthy lactating women, supplementation increased breast milk production by 85%, compared to 32% in the placebo group.[22]
Experimental Studies	
Hepatoprotective Activity	A range of experimental studies suggest that St Mary's Thistle protects the liver via a number of mechanisms, including: Antioxidant protection;[23] Enhancing hepatic cellular regeneration at a DNA level;[24] Antifibrotic activity.[25]
	High dose silymarin supplementation resolved hepatic fibrosis induced by carbon-tetrachloride in rats. It also significantly reduced elevated liver enzymes and reversed the altered expression of actin in liver cells.[32]
	An experimental study in rats found that treatment with silymarin and Terminalia chebula after toxic doses of paracetamol reduced the significant elevations in blood lipids, blood urea nitrogen, serum creatinine and liver enzymes, suggesting both hepatoprotective and nephroprotective activity.[33] Another study found that silymarin administered for 2-4 days after a lethal dose of paracetamol significantly reduced mortality rates in mice.[34]
	An animal study found that silymarin protected against iron-induced hepatotoxicity, significantly reducing the number of necrotic hepatic cells after iron overload. This effect was comparable to the iron chelator desferrioxamine.[35]
Metabolic Effects	A small study examined the effects of silybin 231 mg per day for 4 weeks in patients with type II diabetes. Silybin treatment led to a significant reduction in red blood cell sorbitol, but did not reduce fasting glucose levels. This suggests that silybin may act as an aldose reductase inhibitor and improve diabetes outcomes by downregulating the polyol pathway.[36]
	An animal study found that silymarin supplementation significantly reduced blood glucose and cholesterol levels, corrected hypoproteinaemia, inhibited hepatic lipoxygenase products and corrected oxidative phosphorylation disturbances in hepatic mitochondria in experimentally-induced diabetes.[37]
	Silymarin treatment protected rats against non-alcoholic fatty liver disease, by reducing insulin resistance, increasing antioxidant protection and reducing oxidative damage, preserving mitochondrial function, and reducing elevated liver enzymes.[38,39]
	Two animal studies found silymarin supplementation reduced cholesterol absorption, improved blood lipid parameters and reduced liver cholesterol levels in rats fed a high cholesterol diet.[40,41]

SUMMARY OF RESEARCH

Iron Absorption	A small cross-over trial investigated the effects of silybin on iron absorption from food in 10 patients with haemachromatosis. On separate occasions, patients were given a meal containing a specific amount of non-haem iron, plus silybin or water or tea, and their serum iron levels were monitored. The post-prandial rise in serum iron levels was lowest after silybin compared to water or tea, suggesting that silybin acts as an iron chelator in the digestive tract.[42]
Bile Production and Secretion	Silymarin supplementation at 420mg per day for 30 days significantly reduced biliary cholesterol concentration and bile saturation index compared to placebo in patients with gallstones or prior cholecystectomy.[43]
	Silymarin supplementation increased bile flow and bile salt secretion in a dose dependant manner.[44]
	Silymarin prevented experimentally induced cholestasis in rats, counteracting the associated reduction in bile salt pool size.[45]
Anti-Inflammatory and Immune Modulating Effects	Silymarin reduces immune-mediated inflammation via inhibition of NF-κB (90), TNF-α and nitric oxide *in vitro*. It also inhibits the activation of microglia in response to bacterial lipopolysaccharide, and thereby reduces neurotoxicity in vitro.[46]
Cancer	*In vitro* and *in vivo* studies suggest that silymarin has many important anticancer actions, including the ability to inhibit cellular proliferation, increase apoptosis, decrease angiogenesis, block cell cycle regulators, enhance the expression of cell cycle inhibitors and inhibit transcriptional factors. Chemopreventative effects have been demonstrated in various cancer models, including skin, breast, lung, colon, bladder, kidney, prostate, ovarian, cervical and hepatocellular carcinomas.[47]
	Oral or topical silybin before or immediately after UVB exposure provided strong protection against carcinogenesis in hairless mice. Silybin significantly reduced tumour multiplicity, size and volume, and moderately reduced tumour incidence. It also increased tumour latency by up to 4 weeks.[48,49]
	In a long-term rat study, oral silymarin given during or after carcinogen exposure for 4 weeks significantly reduced the incidence and multiplicity of colonic adenocarcinoma.[50] Similar results have been seen in prostate[51] and bladder cancer.[52]
	In mice with skin papillomas, silymarin significantly reduced tumour growth and cell proliferation index, and improved the apoptotic index.[53] In a prostate cancer model, silymarin strongly inhibited the growth of advanced prostate tumours in immunodeficient mice.[54]
	Silymarin has been shown to reduce the toxic effects of chemotherapy treatments. Silymarin given to rats before a single dose of cisplatin prevented glomerula and proximal tubular damage. Treated rats also had significantly lower blood urea nitrogen and serum creatinine than rats given cisplatin alone.[55]
	Coadministration of silybin potentiated the antitumour effects of cisplatin in mice. The mice also recovered from chemotherapy earlier than mice treated with cisplatin alone, particularly in terms of weight loss.[56]

SAFETY PROFILE

Drug Interactions	Use cautiously alongside glucose-lowering drugs, due to additional hypoglycaemic effects. Monitor. Use cautiously alongside narrow therapeutic index p-glycoprotein substrates, including warfarin and digoxin. Separate doses and monitor.
Cautions	Use cautiously in those with known sensitivities to other plants in the Asteraceae/Compositae family. Use cautiously in patients with gallstones, due to the risk of gallstone impaction and bile duct obstruction.
Contraindications	Contraindicated in known allergy to St. Mary's Thistle.
Adverse Events	None expected.

SAFETY PROFILE

Pregnancy	No known cautions.
Lactation	No known cautions.
Children	No known cautions.

** For a full safety profile please contact Clinical Support*

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