Milk Thistle

*Photo © Steven Foster*

*Silybum marianum* (L.) Gaertn.

Text by Armando González Stuart, Ph.D., 2005

**Botanical family:** Asteraceae (Compositae).

**Other common names:** Marian thistle, St. Mary’s Thistle.

**Common names in Spanish:** Cardo mariano, Cardo lechoso.

**Medicinal parts:** The dried, ripe fruits or achenes (“seeds”).

**History**

The ripe fruits or achenes (“seeds”) of this plant have been employed in Europe for many centuries for the treatment of liver and gall bladder dysfunctions (Schulz et al., 2004; Wichtl, 2004; Blumenthal, 2003). Originally form the European continent, this herb has been introduced to diverse parts of North America (Boon and Smith, 2004).

**Active Principles**

- The main active principles contained in milk thistle are silybin (silbinin), sylchrisitin and silydianin, commonly referred to collectively as *sylimarin* (Boon and Smith, 2004; Blumenthal. 2003).
The compounds mentioned above are phenolic compounds known as flavonolignans, which have antioxidant, anti-inflammatory, and free radical scavenging properties (Gruenwald, 2004; Tumova et al., 2004; Flora et al., 1998).

The plant also contains fatty acids, silbonol and apigenin, as well as quercetin, taxifolin and biogenic amines (Boon and Smith, 2004; Skenderi, 2004).

**Applications in Herbal Therapy**

Milk thistle is used primarily to treat various liver diseases and dysfunctions including alcoholic cirrhosis, hepatitis (due to viral infections or drug-induced), as well as hepatic problems related to diabetes (Gruenwald, 2004; Lieber et al., 2003; Jacobs et al., 2002; Blumenthal, 2000; Flora et al., 1998).

Sylimarin has liver regenerative effects by stimulating the enzyme known as RNA polymerase in the nucleus of liver cells. This results in an increase of ribosomal protein synthesis which helps to regenerate hepatocytes. A practical application is the antidotal effect that sylimarin possesses against Amanita mushroom (death cap) poisoning. When injected intravenously, sylimarin blocks the toxic effect of the mushroom toxin alpha-amantin (Gruenwald, 2004).

Preparations made from milk thistle have been approved by the German Commission E to treat mild gastrointestinal dysfunctions (Barrett, 2004; Blumenthal, 1998).

Milk thistle has also been used to treat minor cases of hypotension (Skenderi, 2004).

**Clinical Studies Employing Milk Thistle**

In a meta analysis of clinical trials employing milk thistle as a hepatoprotective agent, it was concluded that treatment with milk thistle appeared to be safe and well tolerated, although no reduction in mortality, no improvements in histology at liver biopsy, or in biochemical markers of liver function among patients with chronic liver disease was found (Jacobs et al., 2002).

In another meta analysis of clinical trials evaluating sylimarin, it was concluded from the available evidence that it could be useful in the treatment of alcoholic liver cirrhosis, and that this phytochemical has a good safety record with only rare cases of gastrointestinal disturbances and allergic skin rashes having been reported (Saller et al., 2001).
• Although sylimarin appears to offer a hepatoprotective effect in humans and baboons (Lieber et al., 2003), it apparently does not do so significantly in certain ruminants (Tedesco et al., 2004).

• A study was made investigating the possible modifying effect of dietary administration of the silymarin on AOM-induced colon carcinogenesis in male F344 rats. The researchers concluded that there was a clear indication of chemopreventive ability of dietary silymarin against chemically induced colon tumorigenesis. These results may provide a scientific basis for progression to clinical trials of the chemoprevention of human colon cancer (Kohno et al., 2002).

• Recent evidence that dietary silibinin can inhibit the growth of certain cancers in rodents suggests that this agent could certainly have clinical potential as an IKKbeta inhibitor. The beta subunit of the signalsome - IKKbeta, a vital catalyst of NF-kappaB activation is an obligate mediator of the disruption of insulin signaling induced by the excessive exposure of tissues to free fatty acids, as well as by adipocyte hypertrophy. For this reason, compounds which safely inhibit or suppress the activation of IKKbeta could be useful in reversing insulin resistance syndrome and help to curb type 2 diabetes. Silibinin, one of the active principles contained in milk thistle is one of the natural agents which has possesses this effect in-vitro (McCarty, 2005).

• A clinical trial in Germany evaluated a commercial herbal preparation containing milk thistle as well as other herbs; known as STW-5 for the treatment of dyspeptic symptoms. The results indicated that the herbal preparation was significantly better than placebo (Madisch et al., 2001).

• A review of sixteen placebo-controlled trials was undertaken related to the efficacy and safety of milk thistle in the treatment of liver dysfunctions. According to the authors, milk thistle's efficacy was not clearly established. The published evidence was clouded by poor experimental design and reporting. A possible benefit has frequently been shown, although inconsistently, for parameters such as aminotransferases, but laboratory tests are the most common outcome measure studied. Survival and other clinical outcomes have been less studied, giving mixed results. The authors concluded that future well controlled clinical studies are necessary in order to ascertain the therapeutic value of this plant and its potential effects (Mulrow et al., 2000).

• Research using various animal tumor models has shown that Silymarin possesses chemopreventive effects against chemical carcinogenesis as well as photocarcinogenesis. Topical application of silymarin inhibited 7,12-dimethylbenz(a)anthracene-initiated, as well as several tumor promoters, like 12-O-tetradecanoylphorbol-13-acetate, mezerein, benzoyal peroxide and okadaic acid, induced skin carcinogenesis in mice. Additionally, silymarin also prevented UVB-induced skin carcinogenesis. Results from various experiments suggest that silymarin could be a promising chemopreventive and safe phytochemical that
could be tested against skin cancer in humans, as well as a potential ingredient for sunscreens for protection against UV radiation (Katiyar, 2005).

- Silymarin has been evaluated for its protective effect against UV irradiation-induced apoptosis in human malignant melanoma cells (A375-S2 cells). Results from a clinical trial showed that treatment with silymarin 500 microM for 12 h significantly inhibited UV irradiation (2.4 J/cm(2), 5 min)-induced apoptosis in A375-S2 cells (Li et al., 2004).

- Research in vitro has shown that silibinin (one of the major constituents of sylimarin) has cancer protective potential, since it down-regulates the co-activator of the androgen receptor, the prostate epithelium-derived Ets transcription factor (PDEF) and subsequently the secretion of PSA. Due to the antiproliferative potential of this phytochemical, as well as its inhibition of telomerase activity that mediates cell immortality and carcinogenesis, it may be useful therapeutically in the treatment of prostate cancer (Thelen et al., 2004).1,2

- Studies in mice have shown that silibinin is efficacious in interfering with the growth of prostate cancer cells (PCA). This phytochemical compound also synergizes the therapeutic effects of doxorubicin in PCA cells, making it a potential candidate for use in combination chemotherapy (Singh and Agarwal, 2004).

- Silibinin is a natural chemopreventive agent that potentially offers the possibility of safe use in combination with chemotherapeutic agents such as doxorubicin, carboplatin or cisplatin in the treatment of breast cancer (Tyagi et al., 2004).

- Another major component of sylimarin; silybin, has potent antibacterial activity against gram-positive bacteria without hemolytic activity, although it does not possess antimicrobial activity against gram-negative bacteria or fungi. Laboratory tests show that silybin inhibits RNA and protein synthesis on gram-positive bacteria (Lee et al., 2003).

- Certain anticancer agents employed in chemotherapy may induce short- and long-term toxicity to the liver. The active constituents in milk thistle may be useful in the prevention / treatment of liver dysfunction in patients currently undergoing chemotherapy (Ladas and Kelly, 2003).
<table>
<thead>
<tr>
<th>Reference</th>
<th>Plant / Plant product</th>
<th>Purpose of study</th>
<th>Number of subjects</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mills et al., 2005</td>
<td>Milk-thistle extract capsules (450 mg) taken 3 times/day</td>
<td>To determine whether ingestion of milk thistle affects the pharmacokinetics of indinavir in healthy volunteers</td>
<td>16</td>
<td>The milk thistle extract did not significantly reduce levels of Indinavir</td>
</tr>
<tr>
<td>Tanamly et al., 2004</td>
<td>Herbal supplement containing silymarin</td>
<td>To evaluate silymarin, in preventing complications of chronic hepatitis C virus infection</td>
<td>177</td>
<td>Silymarin improved symptoms and general well-being, but did not have any effect upon hepatitis C virus infection, serum ALT, or serum and ultrasound markers for hepatic fibrosis. A higher dose may have been needed.</td>
</tr>
<tr>
<td>Di Cenzo et al., 2003</td>
<td>Silymarin (160 mg 3 times/day); Indinavir 800 mg 3 times/day</td>
<td>To determine if milk thistle’s active principles (silymarin) alter the pharmacokinetics of indinavir</td>
<td>10</td>
<td>There was no apparent effect of silymarin on indinavir plasma concentrations.</td>
</tr>
<tr>
<td>Piscitelli et al., 2002</td>
<td>Milk thistle extract 175 mg (containing silymarin 153 mg)</td>
<td>To characterize the pharmacokinetics of indinavir in the presence and absence of milk thistle; as well as to determine the offset of any effect of milk thistle on indinavir disposition.</td>
<td>10</td>
<td>There was no interaction between milk thistle and indinavir in healthy patients.</td>
</tr>
<tr>
<td>Parés et al., 1998</td>
<td>Sylimarin</td>
<td>To determine the effect of silymarin in alcoholics with liver cirrhosis regarding survival, as well as clinical and laboratory changes</td>
<td>200</td>
<td>Silymarin did not have any significant effect on the course of the disease.</td>
</tr>
<tr>
<td>Ferenci et al., 1989</td>
<td>Silymarin (140 mg) three times per day</td>
<td>To determine the effect of silymarin on the outcome of patients</td>
<td>170</td>
<td>Effective</td>
</tr>
</tbody>
</table>

**Safety/Precautions**

- Milk thistle extracts are commonly regarded as safe, even for prolonged treatments (Mills and Bone, 2005; Gurley et al., 2004; Tanamley et al., 2004; Blumenthal, 2003, 1998; Boerth and Strong, 2002; Riley and Bhatti, 2001; Pepping, 1999).

- Only minor gastrointestinal discomfort has been experienced in rare cases (Saller et al., 2001; Blumenthal, 2000, 1998).

- Even though there are no adverse reports related to its use during pregnancy and lactation, as a precaution, consult a health professional before taking this herb if you are pregnant (Mill and Bone, 2005).

- In case of cyclopeptide mushroom poisoning, a physician should be consulted as to the possible application of the injectable preparations containing sylimarin; avoid giving milk thistle tea to any poisoned patient, as it has no therapeutic value for this purpose (Gehrmann et al., 2005).

**Potential Herb/Drug Interactions**

- In vivo and in vitro studies have shown that herbal products or supplements containing milk thistle seem to pose a minimal risk for CYP-mediated herb-drug
interactions in humans (Gurley et al., 2004; Patel et al., 2004; Di Cenzo et al., 2003; Zuber et al., 2002).

- Studies with healthy human subjects treated with indinavir and milk thistle extracts revealed that silymarin has no apparent effect on indinavir plasma concentrations Di Cenzo et al., 2003).

- Studies with patients infected with the HIV virus who are currently taking antiviral medication have shown that milk thistle in commonly administered dosages apparently does not interfere with indinavir therapy (Piscitelli et al., 2002).

- One case report mentions that milk thistle may offer protection from liver toxicity caused by the pharmaceutical drug dilantin (phenytoin) (Brinker, 2001).

- Experimental studies in vitro have shown that silybin inactivated purified, recombinant cytochromes P450 (P450) 3A4 and 2C9 via a mechanism-based manner. The researchers concluded that careful administration of silybin with drugs primarily cleared by P450s 3A4 or 2C9 would be advisable, due to potential drug-drug interactions (Sridar et al., 2004)

**Literature Cited**


