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**FILE: ■Milk Thistle (*Silybum marianum*)
■Cancer**

HC 020444-262

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RE: Beyond Liver Conditions: Other Uses for Milk Thistle with Clinical Guidelines

Abascal K, Yarnell E. The many faces of *Silybum marianum* (milk thistle).

Part 1 — Treating cancer and hyperlipidemia and restoring kidney function. *Alternative & Complementary Therapies*. 2003 Aug.:170-175.

Part 2 — Clinical uses, safety, and types of preparations. *Alternative & Complementary Therapies*. 2003 Oct.:251-256.

Milk thistle (*Silybum marianum*) is frequently used for liver-related ailments and detoxification (see HCs 020442.258, 111194.168, 120322.230, 010237.235, 061726.216 and 030431.240). In these two articles, Abascal and Yarnell undertake a survey of other potential uses, along with clinical guidelines for use. Milk thistle has been used medicinally at least since Greco-Roman times (see HC 100890.167), and is still used in Basque traditional medicine as a digestive aid, anti-inflammatory, antineoplastic, hypotensive, styptic, diuretic, and general tonic. Nineteenth century Eclectic physicians used it for problems of the liver, kidney, and spleen; gallstones; problems in pregnancy and menstruation; and other conditions; the herb was specific for "sallow faces; capricious appetites; nervous irritability; despondency..." and more.

In the late 1950s, silymarin, a flavonolignan complex, was isolated from milk thistle. Silymarin includes silybin, silydianin, and silychristin, and usually composes about 4-6% of milk thistle seed. Nearly all milk thistle research has used either silymarin or silybin, and it is generally dispensed in standardized capsules with a content of about 70-80% silymarin. Yarnell and Abascal argue that despite a lack of clinical evidence, milk thistle seed and seed oil, as well as tinctures, teas, and decoctions, have some history of effective use. Studies suggest silymarin provides benefits at very low levels, despite poor solubility in water and poor absorption, but these preparations are not interchangeable with preparations containing concentrated amounts of silymarin for most clinical uses.

A number of studies, both in vitro and in vivo, suggest that milk thistle is potentially beneficial in treating or preventing various cancers: inhibiting prostate cancer cells and increasing apoptosis (programmed cell death) in them; inhibiting growth and stimulating regression of skin tumors with topical application; inhibiting induction of tongue squamous-cell cancer; decreasing incidences of bladder neoplasms; inhibiting growth and DNA synthesis in breast and cervical cancer cells; reducing frequency of drug-induced colon adenocarcinomas, and inhibiting proliferation in

leukemia cells. Silybin may be useful in hormone-refractory human prostate cancer and may enhance the efficacy of tumor necrosis factor (TNF)-alpha-based chemotherapy.

Indeed, its liver protectant effects in chemo- and radiation therapies may be as valuable to cancer patients as milk thistle's antineoplastic effects, especially in drug-resistant cancers (see HC 030439.240). Silybin has inhibited growth of drug-resistant ovarian and breast cancer cell lines. Silymarin has increased the effectiveness of the chemotherapy drugs daunomycin and doxorubicin, inhibited their cellular efflux, and protected heart cells against doxorubicin-induced lipid peroxidation. Some studies combining silybin with cisplatin, another chemotherapy drug, have also found positive effects, but the authors note studies indicating that silybin, while protecting against renal damage, was not synergistic with cisplatin or ifosfamide against testicular cancer cells. Nephroprotective effects have been observed when silymarin is given prior to radiation treatment and before or after paracetamol or vincristine. Patients with metastasizing brain tumors who received milk thistle and omega-3 fatty acids before radiation had improved survival times and fewer side effects. The authors suggest, based on a number of pharmacological studies, that topical silymarin would be a beneficial addition to sunscreens in protecting against ultraviolet-B-induced skin cancers and recommend that practitioners include standardized milk thistle products in cancer treatment regimens, especially where there is damage or potential damage to liver or kidneys from allopathic treatment.

Regarding the kidneys, milk thistle's effects on them "closely mirror the herb's effects on the liver," and intriguing clinical research shows normalized thiol status in patients with end-stage diabetic nephropathy, and in others receiving ambulatory peritoneal dialysis, with milk thistle treatment. Silymarin stimulates protein synthesis and cell regeneration in the kidneys just as in the liver. Silymarin has been observed to have a moderate diuretic effect in isotonic saline-loaded rats; however, there was also a marked decrease in potassium excretion, suggesting that it is a potassium-sparing diuretic. Abascal and Yarnell recommend use of milk thistle with any potentially kidney-damaging drug or treatment, as well as for patients with acute tubular necrosis or other situations involving acute epithelial cell loss.

Milk thistle shows promise in moderating some effects of a high-cholesterol or high-fat diet, especially in protecting against development of fatty livers and other liver damage. It appears to raise levels of high-density lipoprotein (HDL; "the good cholesterol"), thus decreasing risk of atherosclerosis. Milk thistle seed oil may reduce total serum lipid levels. Silybin reduced blood pressure and incidence of postocclusion arrhythmias in spontaneously hypertensive rats as much as tetrandrine (a constituent of *Stephania tetrandra*), implying potential usefulness in acute myocardial infarctions. Both silymarin and silybin decreased in vitro platelet aggregation in rats.

Given milk thistle's positive liver effects, it is logical to think that it might benefit hepatic diabetes. Indeed, at least two trials involving diabetic alcohol abusers found decreased fasting blood glucose, daily blood glucose, and daily glycosuria levels, and other improved outcomes. In another, silybin inhibited glucose-stimulated increase in vitro but did not affect blood glucose concentration, indicating a potential benefit in treating non-insulin-dependent diabetes mellitus. Diabetes secondary to alcoholic cirrhosis shares certain features with the diabetes which typically arises in pancreatic cancer, and pancreas protective effects have been observed with silymarin. Milk thistle may reduce insulin resistance in these types of diabetes, as well as preventing typical diabetic sequelae such as neuropathy and retinopathy.

Milk thistle may have potential as a neuroprotectant, and herbalists report its positive effects on carpal tunnel syndrome, myalgias, and multiple sclerosis; however, only in vitro studies support

these case reports. Yarnell and Abascal point out the difficulties of assessing results when it is not known if milk thistle's constituents reach the brain in sufficient concentrations to be efficacious in vivo. Again related, perhaps to milk thistle's hepatoprotective effects, animal studies consistently show that it helps protect the fetuses of rats on ethanol diets from fetal alcohol syndrome. However, the authors stress that this effect is at best only partial and that milk thistle should not be used to prolong alcohol abuse.

Milk thistle's effects on bile ducts and hepatic-bile synthesis may be clinically important in reducing biliary obstruction, and potentially useful in addressing obstruction secondary to pancreatic disorders, including cancer. Finally, a table lists several studies showing positive results for milk thistle against diseases as diverse as malaria and acute colitis.

Silymarin has very low toxicity, and milk thistle is not, as far as is known, embryotoxic. However, some studies have shown negative effects on cultured cells when silymarin or silybin are applied for a long period, and it may be that these isolated constituents are not completely safe. Some types of drug interactions clearly take place with milk thistle, or it could not exert its synergistic effects, and in vitro tests have shown that it inhibits drugs metabolized by CYP2D6, CYP2E1, and CYP3A4-mediated enzymes. However, concentrations necessary to achieve these effects are not reached with clinical use of silymarin supplements, and at least one study concluded that interactions with prescription drugs are unlikely at therapeutic doses. Some researchers recommend caution in combining milk thistle products with drugs metabolized through the CYP3A4 pathway in particular, and the authors say that caution is warranted with newer extracts whose increased bioavailability may not always be desirable. There is also a possibility that higher flavolignan concentrations in the gut could interfere with prescription medications.

— *Mariann Garner-Wizard*

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