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Milk Thistle

Silybum marianum

The Milk Thistle

by Steven Foster

In June of 1997, I saw an excellent news report aired by ABC 20/20 on St. John's wort's usefulness in treating mild to moderate depression. One of the physicians interviewed for the piece said that St. John's wort was the flagship of herbal medicine, and the best-researched herb in the world. I sat there in my chair and said to myself. "Wrong." When I think of the best-researched herb in the world from the standpoint of known active constituents, proven pharmacological mechanisms of action, proven clinical effectiveness through dozens of controlled clinical studies and decades of experience, and an excellent safety record, there is only one herb that can fit all of those criteria. It is milk thistle.

Milk thistle preparations are from the seeds of *Silybum marianum*, a member of the sunflower family native to a narrow area of the Mediterranean, but grown for centuries throughout Europe and naturalized on that continent. It is also naturalized in the United States. In fact, it is a common weed in California. From time to time, I see television ads, obviously shot in California in a field. Milk thistle is often seen in the ads. It was brought to America by early settlers, probably as a food plant, and became established in the eastern United States, as well as the West.

By the turn of the century, it was already common in California, in abandoned fields, old pastures, and by roadsides. It is also naturalized in some areas of South America, and Australia, where it is a nuisance weed forming thickets.

Milk Thistle has black shiny seeds, crowned with feathery tufts like those of dandelion seeds. It is the seed that have been the subject of interest among herbalists. Traditionally, seeds have been roasted for use as a coffee substitute, but it is their historical and modern use in the supportive treatment of liver disease that has attracted attention. Use of the plant as a liver protecting agent dates at least to the first century.

Dioscorides, a first century Greek physician who served the Roman army, gave the name *Silybum* to a number of edible thistles. Now the genus name *Silybum* is given to two species originating from the Mediterranean region, including our subject *Silybum marianum*. The name milk thistle refers to the white streaks along the leaf veins. In Germany where the plant is often depicted as a religious symbol associated with the Virgin Mary, legend ascribes the white mottling to a drop of the Virgin Mary's milk. The species name "*marianum*" honors the symbolic association of the plant with the Virgin Mary.

Modern use of milk thistle in medicine is limited to the seeds. The plant has gained prominence based on scientific research in the past thirty years. However, its use is not the result of new biological screening that catapults it into prominence as a "new" medicinal plant. Rather, its use as a liver-protecting herb dates to the earliest Greek references to the plant. Pliny the Elder (A.D. 23-79), the first century Roman physician/naturalist wrote about use of the plant as a vegetable, but warned it was not worth the effort to boil it, as it was troublesome to cook. He also mentioned that the juice of the plant, mixed with honey, is excellent for "carrying off bile." This is perhaps the first reference to the use of Milk Thistle for liver-related conditions.

A thousand years later, the plant was already well-known in Germany. It is mentioned in an important medieval German manuscript, the *Physica* of Hildegarde of Bingen, the first herbal written by a woman, composed about 1150 then first published in 1533. Hildegarde, theologian, music composer, and writer was herself a "renaissance women," before the age of the Renaissance. She wrote about the uses of the roots, whole plant and leaves of Milk Thistle, which she called "*vehedistel*" or Venus Thistle.

Still used in the eighteenth century, Culpepper (1787 ed.) notes that it is effectual "to open the obstructions of the liver and spleen, and thereby is good against the jaundice." He also writes, "The seed and distilled water are held powerful to all the purposes aforesaid, and besides, it is often applied both inwardly to drink, and outwardly with cloths or spunges [sic.], to the region of the liver, to cool the distemper thereof…"

Reinvestigating the value of traditional herbal remedies, in 1929, H. Schultz, a German scientist, began to look into the value of milk thistle. He found that a famous eighteenth century German physician, Rademacher, had advocated use of milk thistle preparations for chronic liver diseases, acute hepatitis, and jaundice. By the 1930s once again clinical interest in

milk thistle was beginning to emerge.

Intensive research into the liver-protecting (hepatoprotectant) properties of the plant, the responsible chemical components, and mechanisms of action, began about 30 years ago. Attempts to isolate the active components of the seed were begun in 1958. Ten years later a research team headed by H. Wagner at the University of Munich was successful in isolating a compound termed silymarin, which was believed to be a single compound. Improved chemical separation methods later revealed that silymarin was not a single component but a complex of chemicals known as flavonolignans. The primary components isolated and structurally characterized from silymarin include silybinin, silydianin and silychristin. Collectively, these isoflavonolignans are found in concentrations of 4 to 6 percent in the ripe seeds. European Milk Thistle products, some of which are available on the American market, are standardized to 70 - 80 percent silymarin.

In perhaps the best book on clinical use of phytomedicine, *Herbal Medicine* (English edition 1988) by the late physician, Rudolf Fritz Weiss, he notes that compared with silymarin, few plant principles have been as extensively researched in recent years. According to Weiss, the efficacy of silymarin has been confirmed by the extensive laboratory, histological and clinical data. Numerous well-designed clinical trials have been conducted in Europe, primarily Germany, on the therapeutic efficacy of silymarin in the treatment of metabolic liver damage, chronic hepatitis, and bile duct inflammation, often induced by alcohol, drugs (psycopharmaceuticals), and chronic liver disease including certain forms of hepatitis. The hepatoprotective effects of silymarin have been demonstrated in accelerating normalization of impaired liver function. Accelerated improvement in measures of liver function, including serum levels of GOT (glutamic&emdash;oxalacetic transaminase), GPT (glutamic&emdash;pyruvic transaminase) and Gamma&emdash;GT (gamma&emdash;glutamyl&emdash;transpeptidase) have been consistently observed. Dosages involved in clinical trials have often been 420 mg./day, used for a period of 4 to 8 weeks.

The therapeutic efficacy is based on several separate mechanisms of action. Silymarin alters the outer liver membrane cell structure in such a way that certain toxins, as demonstrated with the toxins of the Deathcap mushroom, cannot enter the cell. Silymarin also stimulates RNA polymerase A (also known as polymerase I), enhancing ribosome protein synthesis, resulting in activating the regenerative capacity of the liver through cell development. Clinical use of silymarin today applies to toxic liver damage for the supportive treatment of chronic inflammatory liver disorders and cirrhosis of the liver, such as in chronic hepatitis, and fatty infiltration of the liver by alcohol and other chemicals.

According to a recent review article by Morazzoni and Bombardelli (1995), in Germany the primary causes of liver intoxication include alcohol (71 percent), psychopharmaceuticals (18 percent) and industrial exposure to chemicals (11 percent). While removal of the liver disease-causing substance is important in management of toxic liver situations, silymarin is the best documented drug for treatment of liver intoxication. Previously, oral clinical application of silybin has been limited by bioavailability. These

authors report on a new silybin complex that has been shown to have markedly improved bioavailability, hence pharmacodynamic activity in both animal and human studies.

The German Health Authorities, equivalent to the U.S. FDA, have established a separate panel, known as Commission E to develop acceptable uses, contraindications, and dosages for well-defined herbal medicines in Germany. The Commission E monographs serve as the basis for regulation of herb products in Germany, and serve as the model for European Union harmonization of laws on phytomedicines. Their positive monograph on milk thistle seed allows preparations of the seeds for the supportive treatment of chronic inflammatory liver disorders and cirrhosis of the liver, such as chronic hepatitis, and fatty infiltration of the liver by alcohol and other chemicals. The monograph also notes that pretreatment with silymarin inhibits alcohol&emdash;induced liver damage, suggesting that it is useful in both a preventative and curative sense.

In 1996, I recall a case that hit the news in which an Asian immigrant died from mistakenly wild-harvesting a death-cap (Amanita) mushroom, thinking it was an edible mushroom. It was sad to realize that special milk thistle preparations were unavailable to treat this case in California. Let me explain. A few years ago I was sitting in a meeting with a friend of mine in Germany, a physician who is a hepatologist - a specialist in liver disease. Our meeting was interrupted several times by phone calls. An emergency room in Prague was attempting to arrange for her to get a milk thistle preparation to them as soon as possible to treat a case of deathcap mushroom poisoning. She made several phone calls and arranged for a pilot on a commercial airline to deliver the preparation to Prague on the next flight in an hour. In western Europe a special water soluble chemical fraction derived from the seeds of Milk Thistle, known as silibinin (not to be confused with silymarin or other oral dosage forms), is stocked in most emergency rooms and poison control centers for use as an adjunct therapy to the treatment of Amanita (Deathcap) mushroom poisoning. If administered in time, the use of this preparation in intravenous drip infusion therapies has helped lower mortality rates from Deathcap mushroom poisoning below any levels that have previously been achieved.

Milk Thistle seed preparations have been used for the treatment of liver disease since antiquity. At one time or another, virtually all parts of the plant have been used as both food and medicine with virtually no reports of toxicity, aside from a mild laxative effect in some patients. The extensive chemical, pharmacological, and clinical research that has been conducted over the past thirty years, has revealed the active components, mechanism of action, and proven its efficacy in human liver disease. Milk Thistle is one of those fascinating plants, whose use, supported by 2000 years of historical use, has emerged as an important example of how traditional information can be used for the development of modern herb products.

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