P.O. Box 144345 Austin, TX 78714-4345 ▪ 512.926.4900 ▪ Fax: 512.926.2345 ▪ www.herbalgram.org

HerbClip™

File: ■ Milk Thistle (*Silybum marianum*)
■ Silymarin
■ β-thalassemia Major

HC 061363-484

Date: November 15, 2013

RE: Silymarin Modulates Immune Markers in Patients with β-thalassemia Major

Gharagozloo M, Karimi M, Amirghofran Z. Immunomodulatory effects of silymarin in patients with β-thalassemia major. *Int Immunopharmacol*. June 2013;16(2):243-247.

The genetic disease known as β-thalassemia is characterized by abnormal hemoglobin, leading to increased red blood cell (RBC) turnover and severe anemia. Blood transfusion is a common treatment; however, lysis (breaking down) of RBCs along with transfusions often result in excess iron, oxidative stress, and subsequent immune problems. Milk thistle (*Silybum marianum*) contains a combination of structurally related flavonolignans (silybin A, silybin B, isosilybin A, isosilybin B, silychristin, isosilychristin, and silydianin), which are found in an extract of the seeds that is known as silymarin. Silymarin has shown anti-inflammatory, antioxidant, and iron-chelating bioactivity in previous studies, and has also been reported to modulate the immune system. This observational study investigates the potential effects of silymarin on those with β-thalassemia major.

Included patients had β-thalassemia and received blood transfusions, and 25 took the pharmaceutical iron chelator desferrioxamine, while 5 did not. Those under 12 years, with hepatitis B, C, or HIV, kidney or heart problems, were pregnant, taking additional chelators, or had trouble with oral absorption were excluded. Patients were given Legalon® (Rottapharm|Madaus; Monza, Italy) for 12 weeks. Legalon consists of milk thistle standardized to 80% silymarin. Patients were assigned to either a combination therapy group (desferrioxamine at 40 mg/kg/day along with 140 mg of Legalon 3 times daily) or a silymarin-only group (140 mg of Legalon 3 times daily). Patients kept track of their dosages, and these "diaries," as well as pill count, served to assess compliance. At baseline and endpoint, cell counts and immunology markers were assessed, and function variations in immune cells plus serum levels of markers were compared.

This study placed most patients with β-thalassemia (n=25; mean age of 20.0 ± 5.3 years old) into the combination group. Average desferrioxamine dose was 40.0 ± 2.1 mg/kg/day 5 to 7 days per week. Those in the silymarin group (n=5) had not taken desferrioxamine for the prior 6 months. The compliance in both groups was rated as "excellent," and no dropouts were reported. Platelets and RBCs, hemoglobin, hematocrit (HCT), and mean (average) hemoglobin per red blood cell (MCH), red blood cell volume

(MCV), and concentration of hemoglobin per red blood cell (MCHC) measurements were not different between groups at baseline.

Immune cell percentages, including lymphocytes, natural killer (NK) cells, and CD3, 4, and 8 co-receptors, were unchanged in both groups as compared to baseline. In addition, immunoglobulins were not different at the end of the study in either group. In both groups, tumor necrosis factor-α (TNFα) concentrations were significantly less as compared to baseline values ($P<0.05$), and neopterin was significantly elevated in both groups as compared to baseline ($P<0.05$). Also, both interleukin-4 (IL-4) and interferon-γ (IFNγ) cytokines from peripheral blood mononuclear cells stimulated in vitro with phytohemagglutinin significantly increased in both groups at the end of the study ($P<0.05$).

Evidence in this study suggests that silymarin supports aspects of the immune system in patients with β-thalassemia. Specifically, it is surmised that the stimulation of neopterin, a marker of cellular immune system activation, may help explain the benefits of silymarin in protecting the liver. Also, it is mentioned that silymarin may be an immunostimulant at low doses or an immunosuppressant at high doses, an important factor to consider in comparing studies, as silymarin in most formulations is not readily absorbed in the intestine. Despite positive results, and even though baseline levels allowed each patient in the combination therapy group to serve as their own control to compare with effects of desferrioxamine alone, the inclusion of a desferrioxamine arm by itself in this study would have further clarified silymarin's efficacy as an immune support. In summary, this study shows that silymarin may have potential in supporting the immune system of those suffering from iron excess, such as in patients with β-thalassemia.

—Amy C. Keller, PhD

The American Botanical Council has chosen not to include the original article.