

Anaphylaxis Induced by Milk Thistle (*Silybum marianum*) Seed Ingestion: A Case Report

Planas-Vinos M¹, Sala-Cunill A^{1,2,3}, Luengo O^{1,2,3}, Castillo Fernandez M⁴, Galvan-Blasco P^{1,2}, Cardona V^{1,2}, Guilarte M^{1,2,3}, Labrador-Horrillo M^{1,2,3}, Gil-Serrano J^{1,2,3}

¹Allergy Department, University Hospital Vall d'Hebron, Barcelona, Spain

²Allergy Research Unit, Vall d'Hebron Research Institute (VHIR), Barcelona, Spain

³Universitat Autònoma de Barcelona, Barcelona, Spain

⁴Diater Pharmaceutical Laboratories, Madrid, Spain

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Milk thistle (*Silybum marianum*), a flowering herb from the Asteraceae family, is known for its seeds, which are rich in tocopherol, a potent antioxidant. Milk thistle is commonly used for medicinal purposes in Mediterranean regions and has traditionally been taken for liver diseases, diabetes, and weight loss [1-3]. Allergy to herbs from the Asteraceae family usually causes respiratory symptoms such as rhinitis, especially in the case of mugwort (*Artemisia vulgaris*) and dandelion (*Taraxacum officinale*). Mugwort and dandelion plants are also involved in pollen-food syndrome, causing reactions to certain fruits, such as melon, watermelon, banana, and tomato, owing to cross-reactivity between pollen and the proteins these foods contain.

We present the case of a 55-year-old Ukrainian woman with no relevant previous medical history who has been living in Barcelona for the last 5 years. She was referred to our outpatient clinic from the emergency department for assessment of previous anaphylactic shock. She reported a reaction that started 5-10 minutes after drinking a milk thistle seed infusion for weight loss. Her symptoms included generalized urticaria, facial angioedema, shortness of breath, abdominal pain with diarrhea, and dizziness. She was treated with intravenous antihistamines (dexchlorpheniramine 5 mg) and corticosteroids (methylprednisolone 60 mg) and intramuscular adrenaline 500 µg. Recovery was fast and complete. Serum tryptase levels peaked at 70 µg/L at 60 minutes after the acute reaction and at 40 µg/L after 120 minutes. The patient denied ingesting any other food or medication that day, could not recall any associated cofactors, and did not report previous reactions upon food ingestion.

Following this acute reaction, the patient did not consume milk thistle (*S marianum*) or cardoon (*Cynara cardunculus*). However, she tolerates artichoke (which belongs to the Asteraceae family). No other symptoms were reported with any other foods after this episode. As for other allergic symptoms, the patient only reported rhinitis in spring and autumn.

Written informed consent for additional studies and for the publication of this article was obtained from the patient. We performed an allergy work-up including skin prick tests (SPTs) for common inhalant allergens; these were positive for house dust mites and mugwort. The panel included house dust mites, molds, animal dander, and pollens common in our geographical area, such as *Parietaria judaica*, *Olea europaea*, *Platanus acerifolia*, grasses, mugwort, *Salsola kali*, *Chenopodium* species, *Cupressus* species, purified peach lipid transfer protein, and purified palm tree profilin. Testing with a comprehensive panel of food allergens including nuts, fruits, legumes, cereals, meats, milk, fish, seafood, egg, *Anisakis simplex*, and latex yielded negative results. Given the lack of a standardized thistle seed extract, prick-by-prick testing with a thistle seed infusion and the seed itself was performed, yielding positive results (7×15 mm and 6×10 mm, respectively). The results were negative in 5 nonallergic controls. Blood tests revealed the following results: baseline serum tryptase, 4.54 µg/L; total IgE, 671 kU/L; specific IgE for *A vulgaris*, 1.65 kU_A/L; and specific IgE for *Dermatophagoides pteronyssinus*, 12 kU_A/L. ImmunoCAP ISAC analysis revealed positive specific IgE to Cyn d 1, Phl p 1, Amb a 1, Art v 1, Fel d 1, Der f 1, Der f 2, Der p 1, Der p 2, and Lep d 2. SDS-PAGE and immunoblotting with the milk thistle seed extract (Figure)

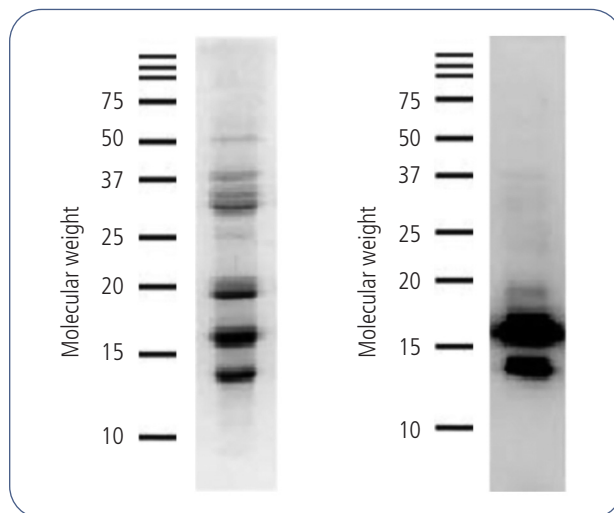


Figure. SDS-PAGE of milk thistle (*Silybum marianum*) seed extracts (left) and immunoblotting (right) performed with patient serum showing the IgE-binding protein.

identified 2 IgE-binding proteins with an approximate molecular weight of 17 kDa and a 14 kDa. Mass spectrometry (Mascot, 2.5.1 [Bruker]) identified these proteins as a small hydrophilic plant seed protein (12 peptides with 54.9% protein coverage) and an 11-S seed storage protein (23 peptides with 23.9% protein coverage) with homology to *C cardunculus*.

Milk thistle seeds contain flavonolignans, primarily silymarin, known for its anti-inflammatory and immunomodulatory properties, which are mediated through the suppression of cytokine and adhesion molecule release, as well as by inhibition of NF- κ B signaling [1,4]. Despite the relatively widespread use of milk thistle, reports of allergic reactions are rare. Cross-reactivity within the Asteraceae family has been suggested, including plants such as ragweed, mugwort, daisy, and artichoke, although no cases have been reported to date. Few cases of allergy to the Asteraceae family have been described. In Poland, Wojas et al [5] reported a case of allergy to *S marianum* and *Eragrostis tef* in a patient exposed to these allergens at work (anaphylaxis upon consuming both products). In Spain, Davila Fernández et al [6] reported the case of a patient with allergy to cardoon (*C cardunculus*), an Asteraceae family member (angioedema upon consuming raw, but not cooked, cardoon) [6]. Furthermore, a case of acute generalized exanthematous pustulosis has been attributed to milk thistle [7].

We report the first documented anaphylactic reaction to milk thistle seed, identifying the candidate allergen as a small hydrophilic plant seed protein (12 peptides with 54.9% protein coverage) and an 11-S seed storage protein (23 peptides with 23.9% protein coverage) with homology to *C cardunculus* (another member of the Asteraceae family). The potential cross-reactivity between *S marianum* and other members of the Asteraceae family should be further investigated (the patient tolerated other members of Asteraceae). This clinical case also highlights the importance of recognizing natural supplements as potential allergens.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Johana Gil-Serrano

University Hospital Vall d'Hebron
Passeig Vall d'Hebron 119-129
08035 Barcelona, Spain
E-mail: johana.gil@vallhebron.cat