

Table 1
Exercise and Photosensitivity Tests

Exercise challenge test	Acetylsali- cyclic acid	Antigen	UVA	UVB	Visible light + UVA	Visible light	Reaction
only exercise	none	none	none	none	none	none	negative
only exercise	✓	none	none	none	none	none	negative
only exercise	✓	none	✓	none	none	none	negative
exercise 3 min after taking antigen	none	lemon	none	none	none	none	negative
exercise 3 min after taking antigen	✓	lemon	none	none	none	none	negative
exercise 3 min after taking antigen	✓	lemon	✓	none	none	none	positive
exercise 3 min after taking antigen	✓	lemon	none	✓	none	none	negative
exercise 3 min after taking antigen	✓	lemon	none	none	✓	none	positive
exercise 3 min after taking antigen	✓	lemon	none	none	none	✓	negative
exercise 60 min after taking antigen	✓	lemon	✓	none	none	none	negative
exercise 3 min after taking of antigen	✓	orange	✓	none	none	none	negative

Abbreviations: UVA, ultraviolet A; UVB, ultraviolet B.

urticaria of the upper body, eyelid edema, and dyspnea with stridor within 10 minutes of ending the exercise test.

She exhibited no signs of skin photosensitivity after the above 2 exercise stress tests. She had no allergic symptoms after the exercise test while exposed to UVB or visible light stimulation 3 min after ingesting sliced lemon and 60 minutes after taking aspirin. She experienced no anaphylaxis after exercise when exposed to UVA 60 minutes after ingesting sliced lemon and 60 minutes after taking aspirin, or 3 minutes after ingesting sliced orange and 60 minutes after taking aspirin (Table 1).

Lemon, orange, watermelon, and tomato were cross-reactive with orchardgrass.⁷ Cucumber and watermelon were cross-reactive with ragweed, and kiwi was cross-reactive with mugwort. A few reports have linked anaphylaxis to orchardgrass¹ and lemon.² Citrus foods, such as lemon and orange contain furocoumarins, which act as skin photosensitizers.⁸

We diagnosed this patient with food-dependent exercise-induced anaphylaxis, modified by UVA stimulation. We believe that furocoumarins present in lemon and tomato cross-react with orchardgrass to induce anaphylaxis. Lemon contains furocoumarins, such as bergapton and psoralen.⁹ It has been reported that 5-methoxypsoralen might cause anaphylaxis.¹⁰

We instructed the patient to refrain from exercise and avoid exposure to light for an hour after ingesting these foods and she has not had any anaphylactic symptoms for more than 2 years.

To our knowledge, this is the first report of anaphylaxis caused by the cross-reactivity of furocoumarins, present in lemon, with orchardgrass.

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Anaphylaxis to flaxseed in a non-atopic adult patient



Flaxseeds are consumed added to cereals and cooked foods, used for their laxative effect and high content of omega-3 fatty acids. At the dietary level, 15 g of flaxseeds provides 135% of the daily requirement of omega-3 fatty acids revealing a beneficial effect. Possibly related to its increased consumption over the last few

years, although infrequent, allergic reactions to flaxseeds have been reported.^{1–9}

A 64-year-old man with no personal history of atopy was referred for an allergological study owing to 3 episodes of anaphylaxis in the last 4 years. The previous episode took place immediately after ingestion of a flaxseed preparation with cow's milk and wheat bread. He developed oropharyngeal pruritus, abdominal pain, dyspnea, vomiting, diarrhea, generalized urticaria, and

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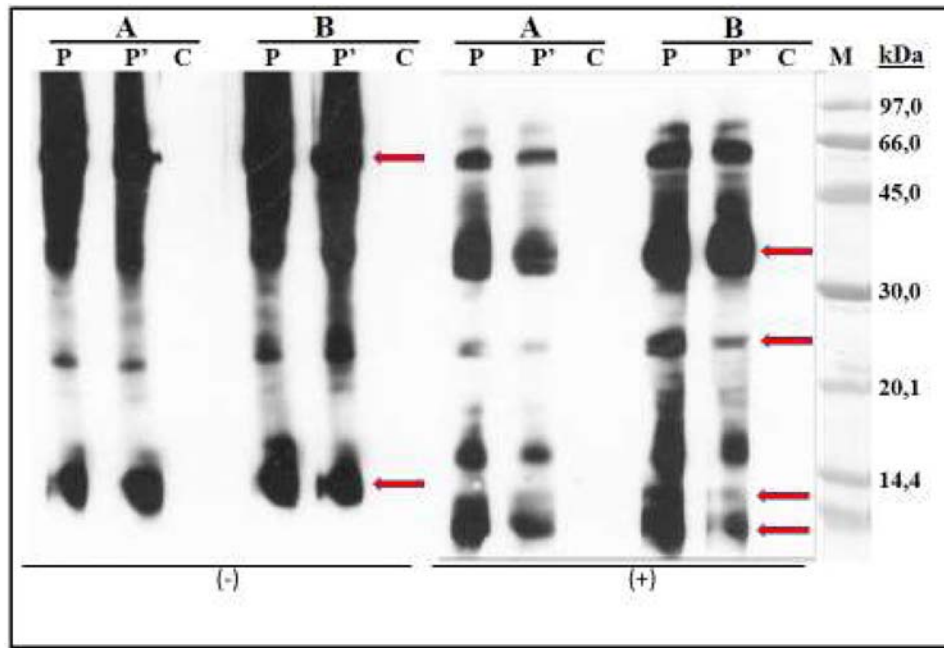


Figure 1. A SDS-PAGE immunoblotting in 2 electrophoresis conditions: nonreducing (without 2-mercaptoethanol) and reducing (with 2-mercaptoethanol). A, roasted flaxseed extract; B, flaxseed extract; P, P', patient's serum; C lane, control serum; M, molecular mass pattern. (+) Samples with 2-mercaptoethanol. (–) Samples without 2-mercaptoethanol. SDS-PAGE, sodium dodecyl sulfate–polyacrylamide gel electrophoresis.

hypotension. He was attended by the emergency service at home, requiring intramuscular adrenaline, parenteral dexchlorpheniramine, and methylprednisolone and intravenous fluid therapy with progressive resolution of symptoms. The patient did not remember the food that was involved in the previous reactions except for seed bread. The rest of the foods from the previous reaction were subsequently tolerated after this episode. He brought the flaxseed preparation, which contained the following: 100% flaxseed and traces of soy, nuts, and sesame.

Skin prick tests were performed with a battery of commercial extracts (ROXALL Laboratories, Bilbao, Spain) of aeroallergens, foods, and panallergens (milk, egg white, egg yolk, tuna, shrimp, hake, lentil, *Anisakis*, veal, peach nsLTP [Pru p 3]), flour (rice, corn, barley, rye, wheat, gluten), nuts and seeds (peanut, walnut, almond, hazelnut, sunflower seed, pistachio, soybean), pollen profilin (Pho d 2), and birch pollen with positive results to almond and hazelnut. A prick-by-prick test with ground flaxseeds was also performed with a positive result (15 × 15-mm papule).

Laboratory test results were as follows: basal tryptase, 3.4 µg/mL; total immunoglobulin IgE (IgE), 56 IU/mL; and specific IgE by ImmunoCAP (Thermo Fisher Scientific, Uppsala, Sweden): hazelnut 4.3 kUA/L, Cor a 9 5.81 kUA/L, almond 3.8 kUA/L, sesame 2.87 kUA/L, soybean 0.6 kUA/L, and Pru p 3 0.02 kUA/L. The patient tolerated walnuts and hazelnuts in open oral challenge test. He had already tolerated peanuts, chestnuts, almonds, and soybeans. A flaxseed elimination diet was recommended with no further reactions. Owing to ethical reasons and to avoid unnecessary risk, an oral challenge test with flaxseeds was not performed. Extract from flaxseed was prepared by delipidation with acetone, homogenization in phosphate-buffered saline (20% W/V) (50 mM phosphate buffer, 100 mM NaCl, pH 7.5) with magnetic stirring, centrifugation to remove the insoluble materials, dialysis of the supernatants against distilled water, and lyophilization.

Sodium dodecyl sulfate–polyacrylamide gel electrophoresis immunoblotting with flaxseed extract was performed according to the Laemmli method under reducing (with 2-mercaptoethanol) and nonreducing (without 2-mercaptoethanol) conditions. After

incubating polyvinylidene difluoride membrane with patient's serum, 3 bands of approximately 13, 24, and 57 kDa were detected under nonreducing conditions. Furthermore, 6 bands of approximately 58 kDa, 34 kDa, 25 kDa, 16 kDa, 10 kDa, and 5 kDa were found under reducing conditions (Fig 1).

Although rare, several cases of hypersensitivity to flaxseed have been reported, most of them being described as anaphylactic reactions,^{1–4,10} as in this case. Storage proteins, such as the 11S globulin and the 2S albumin, are responsible for most cases of flaxseed allergy, as previously reported.^{5,6,10} By sodium dodecyl sulfate–polyacrylamide gel electrophoresis immunoblotting, several proteins from flaxseed were recognized by patient's specific IgE. The 13-kDa band found under nonreducing conditions most probably corresponds to the 2S albumin in its native state, Lin u 1, composed by 2 subunits bound by disulfide bridges. We assume that the 2 bands of 10 kDa and 5 kDa found under reducing conditions represent these 2 subunits (Fig 1).⁶ The band of 57 kDa found under nonreducing conditions would correspond to the 11S globulin in its native state (Fig 1). The 34-kDa band that appears in electrophoresis under reducing conditions could correspond to the large subunit of this 11S globulin. Lipid transfer proteins (LTP) sensitization has been reported in only 1 case of flaxseed anaphylaxis.² The patient we present was not sensitized to panallergens, such as pollen profilin or nsLTP. Moreover, unlike previously reported,^{1,2,6,7} our patient did not show sensitization to aeroallergens nor personal history of atopy.

Cross-reactivity between flaxseeds and other seeds (peanut, soybean, rapeseed, lupine, and wheat) has been described by Fremont et al⁸ and Bueno-Díaz et al⁵ through albumin 2S and globulin 11S; however, its clinical relevance, as Patel and Bahna¹⁰ described, was not assessed by a challenge test. Our patient has subclinical sensitization to other seeds and nuts tested (hazelnut, almond, sesame, and soya) but without clinical signs after ingestion.

In summary, we present a confirmed case of flaxseed anaphylaxis in an adult male patient, with no previously diagnosed allergic pathology. Food allergy is increasing in both developed

and underdeveloped countries, and new or infrequent foods are increasingly being diagnosed as a result of changes in consumption patterns owing to globalization. Seed allergy, specifically flaxseed allergy, should be considered in the differential diagnosis of food allergy.

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Should children with immunoglobulin E–mediated food allergy be screened for eosinophilic esophagitis?



Eosinophilic esophagitis (EoE) is a chronic inflammatory disease of the esophagus, involving an allergen-mediated process highly associated with other atopic conditions.^{1–3} Several studies have identified the significance of food antigens underlying EoE development, evidenced by treatment using food elimination diets and the emergence of EoE with oral immunotherapy.^{4,5} The progression from immunoglobulin E–mediated food allergy (IgE-FA) to EoE has been illustrated, either from the same or different food triggers.^{6,7} Still, EoE remains difficult to diagnose because of nonspecific or masking of symptoms, disease underrecognition, and the need for an invasive diagnostic procedure, resulting in diagnostic delay. This contributes to the risk of stricture formation and fibrostenosis.⁸ Currently, no interventional studies have evaluated the use of screening for EoE potentially relevant in higher-risk populations such as those with IgE-FA.⁷ Thus, we sought to determine the extent to which children with IgE-FA (but without a diagnosis of EoE) reported EoE symptoms through formal screening.

From April to October 2021, we surveyed all children with IgE-FA in our allergy practice using the Pediatric Eosinophilic Esophagitis Symptom Severity Module (PEESS) version 2.0, a validated pediatric-specific questionnaire to assess for symptoms of EoE in children ages 8 to 18 years and parent proxy ages 2 to 18 years.⁹ Dysphagia-specific scores were primarily evaluated given the established correlation of these scores with increased EoE activity histologically.⁹ In addition,

we included a supplemental question (“do you ever feel food going down after swallowing?”), which was considered a potentially substantial question relevant to EoE on the basis of the authors’ clinical experience. Surveys were administered at routine office visits. Children with previously established EoE and IgE-FA were included for comparative purposes. Patients with EoE but without IgE-FA were excluded. Our primary outcome was a positive response to dysphagia-specific items (items 7–12) on the PEESS, in which patients scored the frequency of symptoms as greater than or equal to “1 or more times a week” or severity as “kind of bad” or greater. A “yes” response to the supplemental questions was a co-primary outcome. Secondary outcomes included positive responses on non-dysphagia-specific PEESS items and the correlation between child and parent responses.

There were 263 families surveyed over a 6-month study period. We excluded 40 charts (4 with EoE but no IgE-FA and 36 incomplete surveys). The remaining 223 (210 with IgE-FA only and 13 with IgE-FA and EoE) were analyzed. The patients’ median age was 9 years (range 2–18) and 64% were boys. The patients were atopic, including 55%, 32%, and 23% with allergic rhinitis, asthma, and atopic dermatitis, respectively. Roughly 10% reported a family history of EoE.

For our primary outcome (Table 1), 26 children (16%) endorsed dysphagia symptoms (13% with IgE-FA only). An additional 25 patients responded affirmatively to our supplemental question, cumulatively equaling 31% of children with symptoms of dysphagia or abnormal feeding sensation, 28% in children with IgE-FA without EoE diagnosis. Positive parent responses were elicited in 22 (12%) overall and 12% in those with IgE-FA only. In total, 51 (24%) participants with IgE-FA without EoE elicited any positive (child or parent) response.

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