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## Allergy to Persimmon (*Diospyros kaki*), A Chitinase and Thaumatin-Like Protein: 2 Newly Identified Allergens

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Persimmon, or sharon fruit (*Diospyros kaki*), is a sweet tropical fruit from the Ebenaceae tree family. It is commonly cultivated in warm regions of the world, including China, Japan, Brazil, Turkey, and Italy. Although it is widely consumed in industrialized countries owing to its beneficial properties, few cases of allergy to persimmon have been reported. No persimmon allergens have been officially recognized (allergen.org), although 4 allergens have been identified as being involved in isolated allergic reactions, namely, nsLTP, Bet v 1 protein–like, profilin, and isoflavone reductase (the last 3 are recognized in allergome.org) [1-3].

We present 2 case reports of systemic immediate reactions after ingestion of persimmon. The first involved a 34-year-old woman (P1) with a personal background of intermittent mild asthma due to mold (*Alternaria alternata*) and grass pollen allergy. She reported an episode of generalized urticaria, periocular angioedema, and rhinitis a few minutes after ingestion of a whole fresh persimmon fruit. The second patient (P2) was an 18-year-old woman who reported generalized urticaria, abdominal pain, and shortness of breath while eating a fresh persimmon fruit. Both patients were treated in the emergency department with intramuscular antihistamines and corticosteroids, and their symptoms resolved quickly.

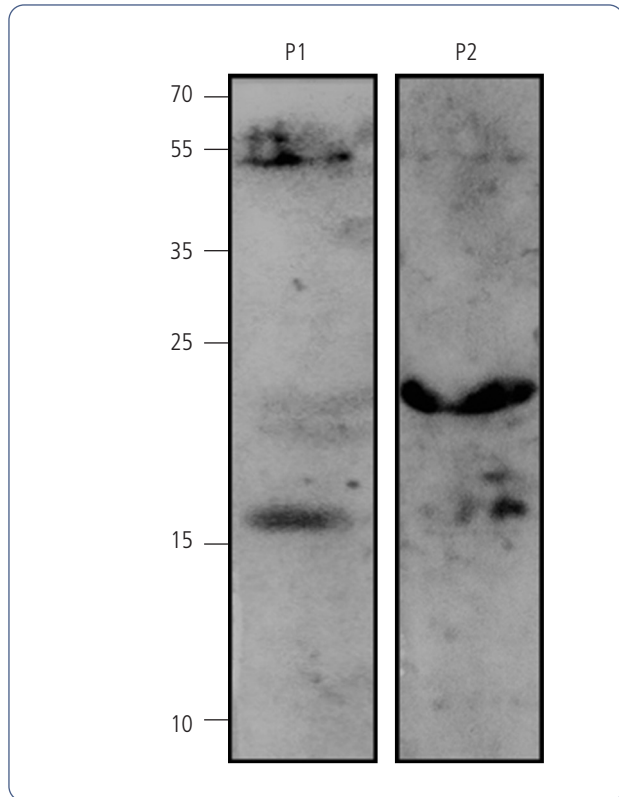
Skin prick testing (SPT) with a battery of commercially available aeroallergen extracts (ALK, Spain) and prick-by-prick testing with natural persimmon were performed. Total serum IgE levels and persimmon-specific IgE were measured using ImmunoCAP (Thermo Fisher Scientific). Immunoblot was performed with natural persimmon extract. Oral food challenges were not performed owing to the systemic allergic symptoms, the clear correlation with persimmon ingestion, and the positive result to both persimmon-specific IgE and prick-by-prick with natural persimmon. After the allergic reaction,

both patients tolerated other plant-derived foods, such as fruit, nuts, and vegetables.

SPT with aeroallergens was positive for *Lolium* species (5×7 mm) and *Alternaria alternata*, (4×4 mm) in P1 and *Secale cereale* (4×3 mm) and *Cupressus arizonica* (7×4 mm) in P2. Negative results were obtained for other pollens, dust mites, and animal dander. Skin prick tests with purified allergens (Pho d 2 [ALK] and Pru p 3 [Roxall]) were negative in both patients.

Prick-by-prick testing with natural persimmon was positive for peel in both patients (P1, 7×5 mm; P2, 10×6 mm) and pulp (P1, 6×4 mm; P2, 8×7 mm). Total IgE was 39.4 kU/L for P1 and 1200 kU/L for P2. Specific IgE to persimmon was 0.7 kU<sub>A</sub>/L for P1 and 0.95 kU<sub>A</sub>/L for P2. Specific IgE to rPru p 1, rPru p 3, rPru p 4, Bet v 1, Bet v 2, Phl p 12, and Heb b 8 was negative in both patients.

Persimmon extract was prepared as previously reported [4]. Sodium dodecyl sulfate–polyacrylamide gel electrophoresis (SDS-PAGE) of persimmon extract revealed multiple protein bands with molecular weights ranging from 10 to 100 kDa (Figure in Supplementary Material). Immunoblotting was performed under reducing conditions, and incubation with the patients' serum revealed an IgE-binding band of 16 kDa in P1 and another of 24 kDa in P2 (Figure). These bands were extracted from the gel, and proteins were identified by mass spectrometry, as well as by searching a nonredundant protein sequence database (NCBI) using the Mascot program (<http://www.matrixscience.com>) in the Proteomic Service of Complutense University



**Figure.** In vitro study with persimmon extract in both patients. Immunoblotting revealed an IgE protein band of 16 kDa in patient 1 (left) and 24 kDa in patient 2 (right).

of Madrid, which is a member of the ProteoRed Network, as previously reported [4]. The results obtained revealed that the 16-kDa band corresponded to a thaumatin-like protein, while the 24-kDa protein corresponded to chitinase.

Although persimmon allergy is not frequent, it can elicit allergic reactions in sensitized patients. LTP was identified for the first time as persimmon allergen in 2015 [5]. In a series of 3 patients with persimmon allergy, the IgE-inhibition assay revealed partial inhibition by a glycopeptide derived from bromelain (carbohydrate determinants) in all patients and by Bet v 2 (profilin) in 1 of the patients, suggesting their role as persimmon allergens [2]. Bolhaar et al [1] reported Bet v 1 as a persimmon allergen in 2 patients with a previous history of birch- and grass pollen-induced rhinoconjunctivitis and plant food-related allergy (apple). The authors pointed to the role of birch pollen as a primary sensitizer in persimmon allergy.

Two isolated cases of persimmon allergy have been reported, although no allergen was identified in either of them. A 30-kDa and a 60-kDa IgE protein band were demonstrated in a Japanese child with persimmon allergy [6], and a case of anaphylaxis induced by this fruit was demonstrated by Martinez et al [7], who used in vivo and in vitro tests.

Homologous Bet v 6 (an isoflavone reductase) protein bands have been found in persimmon. This allergen is responsible for cross-reactivity between birch pollen and some plant foods. Nevertheless, its role as an allergen was not demonstrated in persimmon, as it was in other plant foods, such as apple, peach, and carrot [1,3].

In the present study, we identified 2 new allergens in persimmon, namely, thaumatin and chitinase. In recent years, thaumatin has gradually gained clinical relevance in pollens and plant-derived food and is considered a panallergen. However, its cross-reactivity profile has yet to be elucidated. Thaumatin is a heat-stable, acid-resistant, and intensely sweet-tasting 23-kDa protein present in pollens (cypress, birch, mugwort, olive, and plane), fruits (Mal d 2, Pru av 2, Act c 1, and Cap a 1), and other plant-derived foods (Cap a 1) [8]. Chitinases are a relatively small group of resistant proteins weighing around 30 kDa. They are classified into various families and classes for which structural analyses and identification of epitopes have been only partially carried out. Chitinases have been identified as allergens in some fruits (banana, raspberry, pomegranate, avocado), vegetables (tomato), nuts (chestnuts), cereals (rice, wheat), insects (silkworm), aeroallergens (*Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*), and latex. These proteins are the main cause of latex-fruit syndrome [9].

In conclusion, we report 2 persimmon allergens weighing 16 kDa and 24 kDa that were identified as thaumatin-like protein and chitinase, respectively. To the best of our knowledge, this is the first time that thaumatin and chitinase have been reported as allergens in persimmon. More studies are needed to fully characterize persimmon allergens and their cross-reactivity with other pollens.

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### Conflicts of Interest

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