
In vitro cross-reactivity between tomato and other plant allergens

M. Ángeles López-Matas, PhD*; Ángel Ferrer, PhD†; Carlos H. Larramendi, MD‡; Ángel Julio Huertas, MD§; Juan Antonio Pagán, MD¶; José Luis García-Abujeta, MD‡; Joan Bartra, PhD||; José Ramón Lavín, MD#; Carmen Andreu, MD†; and Jerónimo Carnés, PhD*

Background: Cross-reactivity among fruits and different pollen and fruit species has been extensively reported.

Objectives: To investigate the in vitro cross-reactivity between tomato and pollen, fruit, and latex extracts and to identify the proteins involved.

Methods: A serum pool was prepared from 18 individuals residing on the Spanish Mediterranean coast (9 men and 9 women; mean [SD] age, 27.4 [10.1] years) who had positive skin prick test reactions to tomato peel. Extracts from 10 pollens, 12 fruits, and latex were tested. Levels of specific IgE to each extract were measured. The allergenic profile was evaluated by means of immunoblot. The percentage of inhibition between extracts and tomato peel extract was analyzed by means of CAP inhibition, and the allergens implicated were elucidated by immunoblot inhibition.

Results: For pollens, the highest specific IgE values were obtained for grasses. Most pollen extracts showed a capacity of inhibition similar to that of tomato peel extract; high percentages were obtained with *Artemisia vulgaris* and *Poa pratensis*. The most strongly inhibited allergens in tomato corresponded to bands of 32 and 45 kDa. For fruits, the highest value of specific IgE was detected for peach. High percentages of inhibition were obtained with peach and hazelnut. No inhibition was detected with latex. Peach, chestnut, and melon inhibited high molecular weight bands (32 and 45 kDa) and a band of approximately 10 kDa.

Conclusions: Cross-reactivity between tomato and pollen and fruit extracts has been demonstrated. Allergens with a high molecular weight range seem to be responsible in pollen extracts. A 10-kDa band seems to be responsible in *Platanus acerifolia*, *Salsola kali*, peach, chestnut, and melon.

Ann Allergy Asthma Immunol. 2009;103:425–431.

INTRODUCTION

Cross-reactivity among fruits and other allergens from plants has been extensively studied. The association among them has been called *pollen-food syndrome*.^{1–5} Several studies have suggested that the basis of this phenomenon is the homology between allergens present in pollens and fruits. As previous studies point out, the primary sensitizer agent would be, mainly, the pollen, and the IgE antibodies directed to pollen could induce an allergic reaction in the presence of homologous fruit allergens.⁶ Sensitization to pollen allergens differs according to the patients' place of residence, indicating a specific geographic distribution in the different pollen-food syndromes that can also be influenced by the local eating habits.⁵

Tomato (*Lycopersicon esculentum*) is a frequently ingested fruit worldwide. The prevalence of sensitization to tomato in a population residing on the Spanish Mediterranean coast, has

been estimated to be 6.5%,⁷ and different studies^{4,8–10} have reported that tomato sensitization is usually associated with sensitization to other food allergens.

Tomato extracts have been characterized, and their allergenicity has been reported. Until now, 3 different allergens have been described and analyzed: profilins (Lyc e 1),^{10,11} β -fructofuranosidase (Lyc e 2),¹² and nonspecific lipid transfer proteins (LTPs) (Lyc e 3),¹³ considered as major allergens. Other proteins with the capacity to bind IgE have also been described, such as glucanase,⁹ peroxidase,¹⁴ polygalacturonase 2A (PG2A),^{13,15} pectinesterase,^{13,15} superoxide dismutase,¹⁵ chitinase,¹⁶ and patatin.⁸ Some of these allergens have been involved in the cross-reactivity among foods and pollens, especially profilin,¹⁰ LTPs,¹⁷ and PG2A.¹⁸ In tomato, cross-reactivity has been reported with grass pollen,¹⁹ latex,⁸ potato,⁸ Japanese cedar pollen,¹⁸ *Platanus acerifolia* pollen,²⁰ and *Cannabis sativa* leaves.²¹ However, cross-reactivity with other common fruits or pollens of the Mediterranean area has not been analyzed in detail. Identification of the proteins and allergens involved in cross-reactivity is relevant to diagnosis (design of standardized allergen extracts and component resolved diagnosis) and treatment. In addition, identification of major allergens may allow the development of hypoallergenic varieties of fruits that lack these proteins. The aims of this study are to investigate the in vitro cross-reactivity between tomato and pollen, fruit, and latex extracts in a Spanish Mediterranean population and to identify the potential allergens implicated in this phenomenon.

Affiliations: * R&D Department, Laboratorios LETI S.L., Tres Cantos, Madrid, Spain; † Allergy Unit, Hospital de la Vega Baja, Orihuela, Alicante, Spain; ‡ Allergy Unit, Hospital Marina Baixa, Villajoyosa, Alicante, Spain, and Centro de Especialidades Foidetes, Benidorm, Alicante, Spain; § Allergy Section, Hospital Santa María del Rosell, Cartagena, Murcia, Spain; ¶ Allergy Unit, Hospital Virgen de la Arrixaca, Murcia, Spain; || Allergy Service, Hospital Clínico de Barcelona, Barcelona, Spain; # Allergy Unit, Hospital General Básico de la Defensa, Valencia, Spain.

Disclosures: Authors have nothing to disclose.

Received for publication March 11, 2009; Received in revised form June 4, 2009; Accepted for publication June 7, 2009.

MATERIALS AND METHODS

Patient Population

This study was conducted with the approval of the Hospital de la Vega Baja ethics committee. A serum pool was prepared from 18 individuals (9 men and 9 women; mean [SD] age, 27.4 [10.1] years) enrolled for a previous study of prevalence of tomato allergy on the Spanish Mediterranean coast.⁷ Serum samples were collected from each patient after obtaining their oral consent. Sera were included from patients with positive skin prick test (SPT) reactions to tomato peel extract (10 mg/mL) and specific IgE levels higher than 0.5 OD to at least 1 of the tested tomato extracts (peel and pulp).

All the patients underwent SPT with a battery of common standardized aeroallergens (Laboratorios LETI S.L., Tres Cantos, Spain), including pollens such as *Olea europaea*, *Artemisia vulgaris*, a mixture of grasses, *Parietaria judaica*, *Cupressus arizonica*, *Salsola kali*, *Chenopodium album*, *Betula alba*, *P. acerifolia*, and *Plantago lanceolata* as well as mites, molds, and epithelia. The patients also underwent SPT with different foods, including nuts, peach, apple, banana, kiwi, melon, and pineapple, and a latex extract (Laboratorios LETI S.L.). Wheal sizes greater than 7 mm² were considered positive.

All the patients were sensitized to aeroallergens; 17 individuals (94%) had rhinitis, asthma, or both, and 11 (61%) reported symptoms after contact with or ingestion of tomato. All the patients were sensitized to pollens, 10 (56%) to mites, 7 (39%) to epithelia, and 2 (11%) to molds. Among pollens, sensitization to *A. vulgaris* and *Chenopodiaceae* pollen (*S. kali* and *C. album*) were the most prevalent, with 13 sensitized individuals (72%), followed by 10 (56%) to *O. europaea* and 7 (39%) to grasses (Table 1).

Sixteen individuals (89%) were sensitized to some of the studied foods: 14 (78%) to peach, 13 (72%) to kiwi, 12 (67%) to pineapple, 8 (44%) to nuts, 6 (33%) to melon, and 2 (11%) to banana, although most of them did not report symptoms after ingestion (Table 1). Only 2 patients were sensitized to latex (Table 1). Eleven patients (61%) reported urticaria, and 6 (33%) experienced oral allergy syndrome related to food allergy. The pool of sera was prepared after mixing the same quantity of each individual serum, aliquoted, and frozen at -20°C.

Extract Manufacturing

Commercially available pollen and food extracts were prepared following internal manufacturing procedures. Canary variety tomatoes were purchased at a local market in optimal conditions for human consumption. Peel and pulp extracts were individually prepared and extracted. After dialysis, individual extracts were sterile filtered, frozen, and freeze-dried.²² The protein content was measured using the Lowry-Biuret method (BioRad Laboratories, Hercules, California). For the in vitro cross-reactivity studies, 10 pollen extracts (*O. europaea*, *P. acerifolia*, *P. lanceolata*, *C. album*, *S. kali*, *B. alba*, *A. vulgaris*, *Phoenix dactylifera*, *Avena sativa*, and *Poa pratensis*), 12 food extracts (peach [peel and pulp], potato,

Table 1. Sensitizations in the 18 Study Patients

Sensitivity	Patients, No. (%)	Reported symptoms, No.
Pollens	18 (100)	NA
<i>Olea europaea</i>	10 (56)	NA
Grasses	7 (39)	NA
<i>Artemisia vulgaris</i>	13 (72)	NA
<i>Parietaria judaica</i>	4 (22)	NA
<i>Chenopodiaceae</i>	13 (72)	NA
<i>Platanus acerifolia</i>	6 (33)	NA
<i>Plantago lanceolata</i>	6 (33)	NA
<i>Phoenix dactylifera</i>	3 (17)	NA
Fruits	16 (89)	NA
Peach peel	14 (78)	5
Melon	6 (33)	2
Kiwi	13 (72)	3
Nuts	8 (44)	8
Banana	2 (11)	4
Pineapple	12 (67)	3
Other fruits/vegetables	8 (44)	8
Latex	2 (11)	1
Mites	10 (56)	NA
Fungi	2 (11)	NA
Epithelia	7 (39)	NA

Abbreviation: NA, not applicable.

carrot, kiwi, pineapple, banana, melon, avocado, chestnut, hazelnut, and almond), and latex were used.

Specific IgE

Specific IgE levels to all previously mentioned extracts were determined using the pool of sera. Briefly, microplates (Immulon IV; Thermo Fisher Scientific, Milford, Massachusetts) were coated with all the extracts (2 µg of protein per well), and the pool of sera was incubated 2 hours at room temperature. After 3 washes, peroxidase-conjugated monoclonal anti-human IgE (Ingenasa, Madrid, Spain) was added; after 2 hours, the reaction was developed, stopped, and read at 450 nm. Extracts with OD less than 0.2 were considered to be negative and were not used for further assays (Fig 1).

Immunoblot Experiments

Twenty micrograms of protein of each extract was electrophoresed by means of sodium dodecyl sulfate—polyacrylamide gel electrophoresis and was electrotransferred to a polyvinylidene difluoride membrane (Millipore, Bedford, Massachusetts). Membranes were incubated overnight with the sera pool (1:2 dilution in phosphate-buffered saline Tween 0.1%). After washing, membranes were incubated with anti-human IgE-peroxidase (Ingenasa), developed with luminol solutions (Immun-Star HRP Chemiluminescent Kit; Bio-Rad Laboratories), and detected using chemiluminescence (ChemiDoc XRS; Bio-Rad Laboratories). Extracts without visible bands were excluded from further studies (Fig 1).

Inhibition Experiments

CAP and immunoblot inhibition experiments were conducted using tomato peel extract in the solid phase. Briefly, different

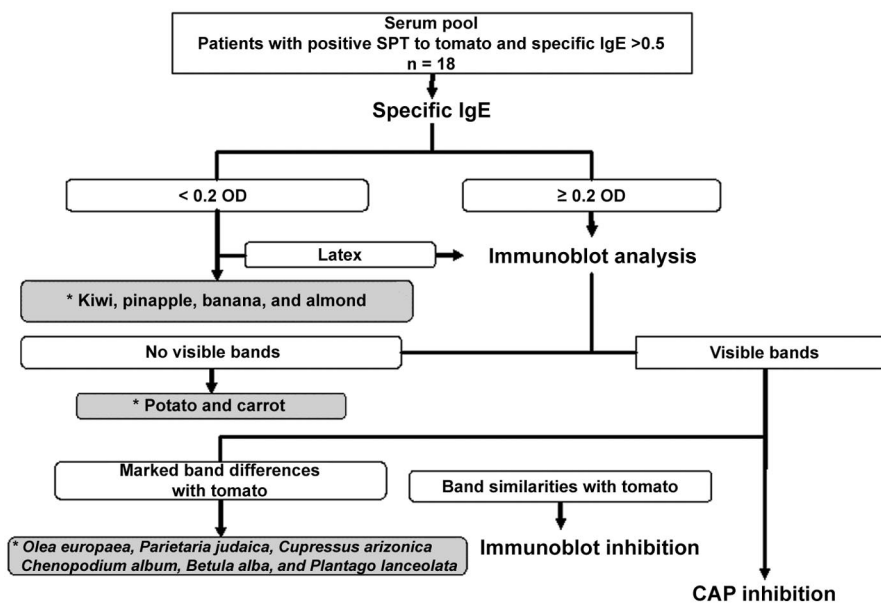


Figure 1. Flowchart of the study. Extracts with negative results were excluded from further analysis, except for latex, which was included in all the experiments, even if specific IgE was negative. SPT indicates skin prick testing. *Excluded from further analysis.

allergen extracts (previously described) were inhibited with the sera pool. After reaction, the complexes of antigen (food or pollen extract)–antibody (pool of sera) were individually incubated with the solid phase containing tomato peel extract. Cross-reactivity and percentage of inhibition were evaluated considering the capacity of food and pollen extracts to “erase” the IgE-binding tomato bands or to reduce in percentage the capacity of inhibition, determined in noninhibited controls.

CAP inhibition. A total of 700 μ g of protein of tomato peel extract was previously labeled using a biotin kit (Roche Diagnostics, Mannheim, Germany) and was used in the solid phase. Aliquots of 50 μ L of tomato peel biotin-labeled extract were incubated in streptavidin uniCAP disks (Phadia, Uppsala, Sweden) for 30 minutes. The pool of sera was preincubated (2:3 dilution) with each extract, previously recognized by the pool of sera ($OD \geq 0.2$, as indicated in the “Specific IgE” subsection) at a concentration of 5 mg/mL of freeze-dried material for 2 hours at room temperature. Afterward, the preincubated extracts were added to the previously tomato peel–coated uniCAP disks. The experiment was performed using the ImmunoCAP 100E system (Phadia). A standard curve was obtained with tomato peel extract. Results are expressed as percentage of inhibition of each extract with respect to tomato peel extract.

Immunoblot inhibition. Immunoblot inhibition experiments were conducted to identify the cross-reactive bands between tomato peel extract and the selected food and pollen extracts. Tomato peel extract (20 μ g of protein) was used in the solid phase, electrophoresed, and electrotransferred to a polyvinylidene difluoride membrane following the same procedure previously described. A total of 200 μ g of protein from peach

peel, melon, avocado, chestnut, hazelnut, latex, *A vulgaris*, *P acerifolia*, *P pratensis*, and *S kali* was incubated for 2 hours at room temperature with the pool of sera (2:3 dilution). These 4 pollens were selected according to the percentage of CAP inhibition and the similarities of bands recognized in the immunoblot experiments (Fig 1). Afterward, the complex extract–pool of sera was added to the membranes and incubated overnight. Results were visualized by means of chemiluminescence.

RESULTS

Specific IgE

Positive specific IgE was detected to all pollens and most tested foods. The highest IgE values were obtained with peach peel extract in fruits (with values higher than those obtained with tomato peel) and grasses in pollen extracts. Specific IgE values to tomato and peach were significantly higher (5 and 6 times, respectively) in peel than in pulp extracts. The specific IgE level to some foods (kiwi, pineapple, banana, and almond) was less than 0.2, and these extracts were not used for further experiments. The specific IgE to latex was also negative, but it was included in further experiments because of its interest in cross-reactivity (Fig 2).

Immunoblot Experiments

The pool of sera recognized several bands in a molecular weight (MW) range of 10 to 100 kDa in pollen (Fig 3A) and food (Fig 3B) extracts.

In pollen extracts, only a band of approximately 10 kDa was recognized in *A vulgaris*. Several bands in an MW range of 30 to 60 kDa were vividly recognized, especially in

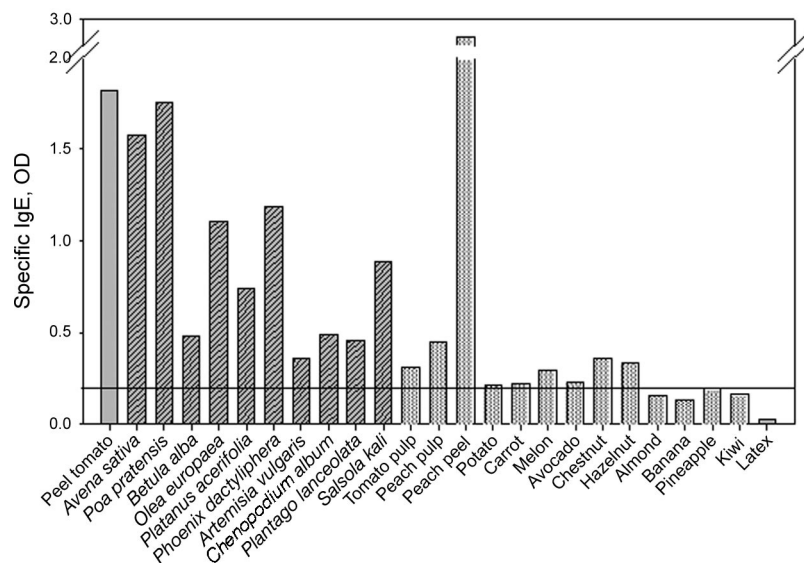


Figure 2. Specific IgE levels of the pool of sera determined by direct enzyme-linked immunosorbent assay to different analyzed pollen and food extracts. The line at 0.2 OD defines the cutoff value for positivity.

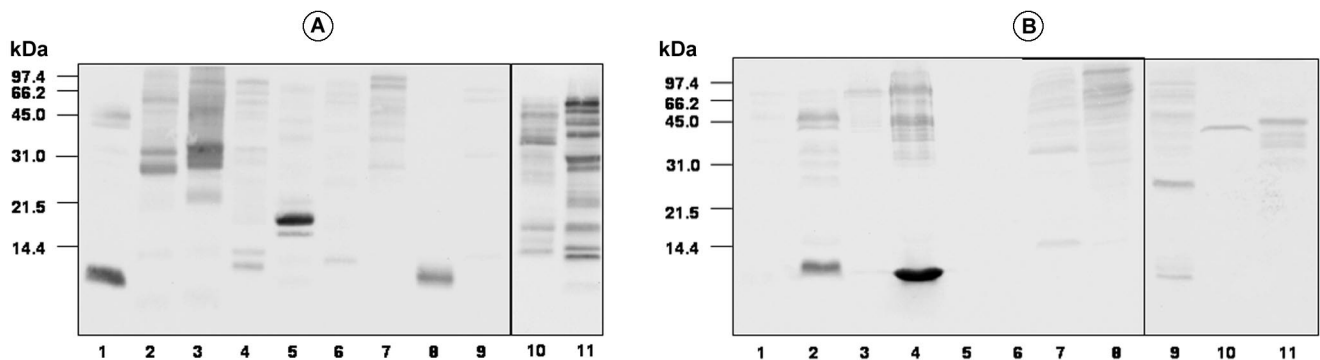


Figure 3. Results of IgE immunoblot. Twenty micrograms of protein per lane of each extract were used in the solid phase. Membranes were incubated with the specific pool of sera (1:2 dilution). A, Pollens. Lane 1 is tomato peel; 2, *Avena sativa*; 3, *Poa pratensis*; 4, *Betula alba*; 5, *Olea europaea*; 6, *Platanus acerifolia*; 7, *Phoenix dactylifera*; 8, *Artemisia vulgaris*; 9, *Chenopodium album*; 10, *Plantago lanceolata*; and 11, *Salsola kali*. B, Foods and latex. Lane 1 is tomato pulp; 2, tomato peel; 3, peach pulp; 4, peach peel; 5, potato; 6, carrot; 7, melon; 8, avocado; 9, chestnut; 10, hazelnut; and 11, latex.

grasses, *P. lanceolata*, and *S. kali*. In *O. europaea*, a band of 20 kDa was clearly recognized. Very weak reactivity was detected with *C. album*.

In food extracts, the pool of sera recognized in peach peel and chestnut extracts a band of approximately 10 kDa, probably corresponding to LTPs, and several bands with an MW higher than 30 kDa. The pool of sera did not recognize any bands in potato and carrot extracts, and they were excluded from further experiments. Several bands with an MW higher than 35 kDa and a band of 14 kDa were visualized in melon extracts. Bands in the high MW range (>30 kDa) were slightly recognized in avocado, and only a band of approximately 45 kDa was detected in hazelnut. Only 4 bands with MWs of 40 to 45 kDa were recognized in latex extract.

Inhibition Experiments

CAP inhibition. The rate of inhibition was mild to moderate in all cases (17.7%–62.6%) (Fig 4).

In pollens, the highest capacity of inhibition was obtained with *A. vulgaris* (54%) and *P. pratensis* (47%). In contrast, *P. dactylifera* showed a capacity of inhibition of only 23%. The remaining analyzed pollen extracts had a similar inhibition capacity: *A. sativa*, 37%; *B. alba*, 34%; *O. europaea*, 36%; *P. lanceolata*, 33%; *P. acerifolia*, 37%; and *S. kali*, 39%.

In fruits, the capacity of inhibition was more variable: peach peel inhibited 63% of the tomato peel extract, and hazelnut and chestnut showed similar capacities of inhibition (46% and 45%, respectively). A 39% capacity of inhibition

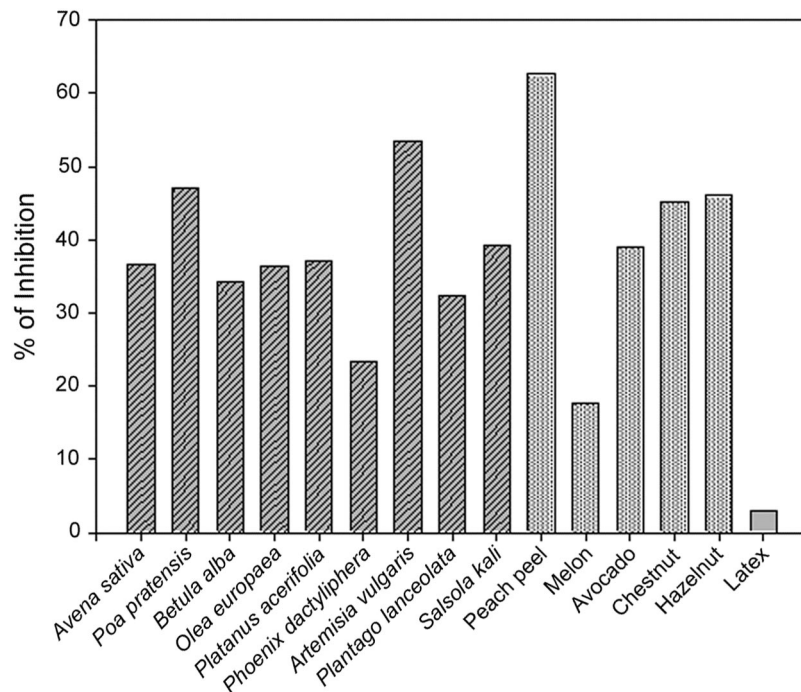


Figure 4. Percentage of inhibition of different extracts by CAP. Tomato peel extract was used in the solid phase. The pool of sera was preincubated (2:3 dilution) with each extract at 5 mg/mL of freeze-dried material. A standard curve was prepared with tomato peel extract. Results are expressed as percentage of inhibition of each extract with respect to tomato peel extract.

was obtained with avocado and 18% with melon. Tomato peel extract was not inhibited by latex extract.

Immunoblot inhibition. Results are shown in Figure 5. Pollen extracts had a significant capacity and pattern of inhibition. In all cases, the inhibition was mediated by bands with an MW range of 30 to 60 kDa. The 10-kDa band was only slightly inhibited by *P acerifolia* and *S kali*, whereas the other pollens did not significantly inhibit this band. *A vulgaris* had the lowest inhibition capacity.

In fruits, melon and peach peel extract showed the highest capacity of inhibition. They were capable of partially inhibiting all the allergens in the tomato extract, especially those with a high MW. Chestnut also showed a high capacity of inhibition, mainly the high MW bands and with significant inhibition of LTPs. Avocado inhibited only high MW bands, whereas hazelnut did not significantly inhibit any bands. Latex extract only slightly inhibited high MW bands.

DISCUSSION

The existence of cross-reactivity among different plant sources has been extensively analyzed, and clinically relevant cross-reactivity between tomato and other fruits, pollen, and latex has been reported.^{8,18,19,23} However, there are not many available data with respect to the allergens involved and the co-sensitization among tomato and other plant extracts. In this study, we analyzed cross-reactivity among tomato and other plant allergens using 18 serum samples from tomato-

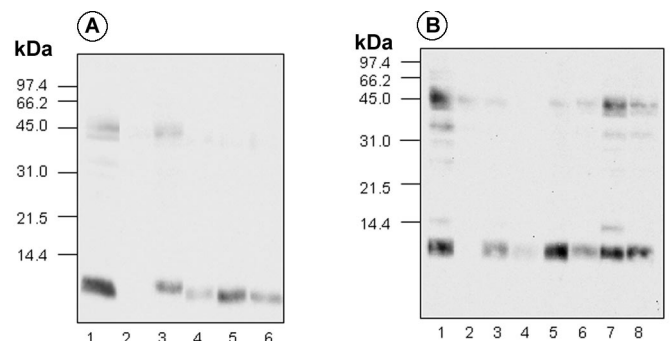


Figure 5. Results of IgE immunoblot inhibition. Tomato peel extract was used in the solid phase (20 µg of protein per lane). The pool of sera was preincubated (2:3 dilution) with each extract (200 µg of protein). A, Pollens. Lane 1 is no inhibition; 2, tomato peel; 3, *Artemisia vulgaris*; 4, *Platanus acerifolia*; 5, *Poa pratensis*; and 6, *Salsola kali*. B, Foods and latex. Lane 1 is no inhibition; 2, tomato peel; 3, peach peel; 4, melon; 5, avocado; 6, chestnut; 7, hazelnut; and 8, latex.

sensitized individuals residing on the Mediterranean coast of Spain. Sensitized individuals were previously selected using SPT with a tomato peel extract in a previous study⁷ of the prevalence of tomato sensitization.

Ten pollens, including relevant local pollens, such as *O europaea*, grasses, and *S kali*, as well as other pollens not relevant in our area, such as *B alba*, latex, and foods, includ-

ing peach and nuts, were chosen to investigate the levels of specific IgE in the pool of sera and the cross-reactivity with tomato. High levels of specific IgE were obtained, especially for the most common local allergens, such as peach peel and grasses, *O europaea*, and *S kali* in pollens. These results demonstrate that tomato and peach peel extracts were more antigenic than were pulp extracts. Specific IgE levels to kiwi, pineapple, banana, and almond were less than 0.2, and these extracts were not included in the inhibition experiments.

On Western blot of tomato extract, different tomato IgE binding bands were clearly visualized. A protein of approximately 10 kDa (Lyc e 3) was vividly recognized in tomato extracts, suggesting its effect on the sensitization profile of this population. This band was also clearly recognized in peach peel, chestnut, and *A vulgaris* extracts. This tomato allergen was not totally inhibited by any other extracts, although it was partially inhibited with peach peel, melon, chestnut, *A vulgaris*, *P acerifolia*, *P pratensis*, and *S kali* extracts. These results are in agreement with those of previous studies,^{24,25} in which the existence of LTPs as widespread fruit allergens has been described. However, the present results suggest that the homology between tomato LTPs and other LTPs from different fruits and pollens is only partial and that cross-reactivity may not be as significant as previous studies have suggested.⁵

Lyc e 2 (β -fructofuranosidase), a protein of 50 kDa, is an allergen described, until now, only in tomato. This band was clearly recognized in tomato extracts and in peach peel extract. Other bands with high MW (45–80 kDa) were visualized in food and pollen extracts showing all of them IgE binding capacity. The inhibition studies with tomato peel extract demonstrated that allergens in this MW range were totally inhibited by melon extract and also by *P acerifolia*, *P pratensis*, and *S kali* pollen extracts. These bands were also partially inhibited by the remaining extracts, except *A vulgaris*, hazelnut, and latex.

The minor allergen Lyc e 1 (profilin),¹⁰ a protein of approximately 14 kDa belonging to a commonly cross-reactive allergen family, has already been reported in tomato.¹⁹ However, the allergologic importance of profilins on the Mediterranean coast of Spain does not seem to be significant.²⁶ In the present study, a 14-kDa band was slightly recognized, suggesting that patients were not notably sensitized to tomato profilin. The pool of sera recognized bands only in the MW range of profilins (14 kDa approximately) in melon, *S kali*, *P lanceolata*, and *B alba*. Tomato peel extract Western blot further recognized other protein bands with MWs of approximately 25, 30, 35, and 42 kDa (Fig 3B).

Cross-reactivity between latex and tomato has been reported, and the involved allergens suggested are patatin homologous of 44 to 46 kDa.⁸ In the present population, only 2 individuals were sensitized to latex, and the specific IgE to this allergen was negative. A significant association between latex and tomato was not found in this population.

Pollens mainly inhibited allergens with high MWs. Although a good correlation was obtained when the inhibition

was analyzed by means of immunoblot and the percentage was calculated by means of CAP, we obtained discordance between both methods only in *A vulgaris*. In this case, bands were poorly inhibited, but we obtained the highest capacity of inhibition, determined by means of CAP assays (53%). This discordance cannot be easily explained and deserves further study. *P acerifolia*, *P pratensis*, and *S kali* completely inhibited bands between 30 and 60 kDa.⁹ In fruits, peach and chestnut showed the highest capacity of inhibition. Melon also inhibited almost completely the tomato allergens.

In general, these data are in agreement with those of previously published studies,^{4,8–10} in which tomato allergy has been associated with other food allergies. Cross-reactivity among tomato and the studied plant-derived allergens seems to be related to several different allergens, probably showing different cross-reacting profiles that should be further studied. This study adds information about the cross-reactive allergens and the co-sensitization patterns of tomato with other plant allergens in a Mediterranean population, stressing the importance of studies from different geographical areas.

In summary, we demonstrated cross-reactivity between tomato and other fruits, mainly peach peel, melon, and nuts, and pollens, *A vulgaris*, *P. acerifolia*, and grasses, in the studied population. According to these results, profilins do not seem to have a significant relevance in our area, LTPs may play only a partial role, and high MW allergens that could correspond to Lyc e 2 and PG2A seem to be important. More studies with purified allergens or families of allergens are needed to clarify the responsible allergens and the involved epitopes and the homology of these proteins.

REFERENCES

1. Vieths S, Scheurer S, Ballmer-Weber B. Current understanding of cross-reactivity of food allergens and pollen. *Ann N Y Acad Sci*. 2002;964:47–68.
2. Yagami T. Allergies to cross-reactive plant proteins: latex-fruit syndrome is comparable with pollen-food allergy syndrome. *Int Arch Allergy Immunol*. 2002;128:271–279.
3. Caballero T, Martín-Esteban M. Association between pollen hypersensitivity and edible vegetable allergy: a review. *J Investig Allergol Clin Immunol*. 1998;8:6–16.
4. Wagner S, Breiteneder H. The latex-fruit syndrome. *Biochem Soc Trans*. 2002;30:935–940.
5. Egger M, Mutschlechner S, Wopfner N, et al. Pollen-food syndromes associated with weed pollinosis: an update from the molecular point of view. *Allergy*. 2006;61:461–476.
6. Valenta R, Kraft D. Type 1 allergic reactions to plant-derived food: a consequence of primary sensitization to pollen allergens. *J Allergy Clin Immunol*. 1996;97:893–895.
7. Larramendi CH, Ferrer A, Huertas AJ, et al. Sensitization to tomato peel and pulp extracts in the Mediterranean Coast of Spain: prevalence and co-sensitization with aeroallergens. *Clin Exp Allergy*. 2008;38:169–177.
8. Reche M, Pascual CY, Vicente J, et al. Tomato allergy in children and young adults: cross-reactivity with latex and potato. *Allergy*. 2001;56:1197–1201.
9. Palomares O, Villalba M, Quirarte J, Polo F, Rodríguez R. 1,3- β -glucanases as candidates in latex-pollen-vegetable food cross-reactivity. *Clin Exp Allergy*. 2005;35:345–351.
10. Westphal S, Kempf W, Foetisch K, et al. Tomato profilin Lyc e 1: IgE cross-reactivity and allergenic potency. *Allergy*. 2004;59:526–532.
11. Willeroider M, Fuchs H, Ballmer-Weber BK, et al. Cloning and mo-

-
- lecular and immunological characterisation of two new food allergens, Cap a 2 and Lyc e 1, profilins from bell pepper (*Capsicum annuum*) and tomato (*Lycopersicon esculentum*). *Int Arch Allergy Immunol.* 2003;131:245–255.
12. Westphal S, Kolarich D, Foetisch K, et al. Molecular characterization and allergenic activity of Lyc e 2 (β -fructofuranosidase), a glycosylated allergen of tomato. *Eur J Biochem.* 2003;270:1327–1337.
13. Foetisch K, Son D, Altmann F, et al. Tomato (*Lycopersicon esculentum*) allergens in pollen-allergic patients. *Eur Food Res Technol.* 2001;213:259–266.
14. Weangsripanaval T, Nomura N, Moriyama T, et al. Identification of suberization-associated anionic peroxidase as a possible allergenic protein from tomato. *Biosci Biotechnol Biochem.* 2003;67:1299–1304.
15. Kondo Y, Urisu A, Tokuda R. Identification and characterization of the allergens in the tomato fruit by immunoblotting. *Int Arch Allergy Immunol.* 2001;126:294–299.
16. Díaz-Perales A, Collada C, Blanco C, et al. Cross-reactions in the latex-fruit syndrome: a relevant role of chitinases but not of complex asparagine-linked glycans. *J Allergy Clin Immunol.* 1999;104:681–687.
17. Asero R, Mistrello G, Roncarolo D, et al. Detection of some safe plant-derived foods for LTP-allergic patients. *Int Arch Allergy Immunol.* 2007;144:57–63.
18. Kondo Y, Tokuda R, Urisu A, et al. Assessment of cross-reactivity between Japanese cedar (*Cryptomeria japonica*) pollen and tomato fruit extracts by RAST inhibition and immunoblot inhibition. *Clin Exp Allergy.* 2002;32:590–594.
19. Petersen A, Vieths S, Aulepp H, et al. Ubiquitous structures responsible for IgE cross-reactivity between tomato fruit and grass pollen allergens. *J Allergy Clin Immunol.* 1996;98:805–815.
20. Ibarrola I, Arilla MC, Martínez A, et al. Identification of a polygalacturonase as a major allergen (Pla a 2) from *Platanus acerifolia* pollen. *J Allergy Clin Immunol.* 2004;113:1185–1191.
21. Larramendi CH, Carnés J, García-Abujeta JL, et al. Sensitization and allergy to *Cannabis sativa* leaves in a population of tomato (*Lycopersicon esculentum*) sensitized patients. *Int Arch Allergy Immunol.* 2008;146:195–202.
22. Ferrer A, Carnés J, Gallego MT, et al. Characterization and improvement of apple extracts for the diagnosis of apple IgE-mediated allergy. *Ann Allergy Asthma Immunol.* 2005;95:462–467.
23. Tücke J, Posch A, Baur X, et al. Latex type I sensitization and allergy in children with atopic dermatitis: evaluation of cross-reactivity to some foods. *Pediatr Allergy Immunol.* 1999;10:160–167.
24. Asero R, Mistrello G, Roncarolo D, et al. Immunological cross-reactivity between lipid transfer proteins from botanically unrelated plant-derived foods: a clinical study. *Allergy.* 2002;57:900–906.
25. Díaz-Perales A, Lombardero M, Sánchez-Monge R, et al. Lipid-transfer proteins as potential plant panallergens: cross-reactivity among proteins of *Artemisia* pollen, *Castanea* nut and *Rosaceae* fruits, with different IgE-binding capacities. *Clin Exp Allergy.* 2000;30:1403–1410.
26. Barber D, de la Torre F, Feo F, et al. Understanding patient sensitization profiles in complex pollen areas: a molecular epidemiological study. *Allergy.* 2008;63:1550–1558.
- Requests for reprints should be addressed to:
Jerónimo Carnés, PhD
Laboratorios LETI S.L.
Calle del Sol 5.
Tres Cantos 28760
Madrid, Spain
E-mail: jcarnes@leti.com
-