

Allergy to kiwi: A double-blind, placebo-controlled food challenge study in patients from a birch-free area

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Background: Allergy to kiwi fruit is being increasingly reported, but it has never been evaluated by means of a double-blind, placebo-controlled food challenge (DBPCFC) study.

Objective: We sought to assess kiwi allergy on the basis of a DBPCFC and identify the patterns of allergen recognition in sensitized patients from a birch-free area.

Methods: Forty-three patients with allergy symptoms who were sensitized to kiwi were evaluated by means of clinical history, skin tests, IgE determinations, and DBPCFCs. The pattern of allergen recognition was assessed by means of IgE immunoblotting. Sequence analysis of IgE-binding bands was performed by using Edman degradation.

Results: DBPCFCs were performed in 33 patients; 4 patients had experienced severe anaphylaxis, and 6 patients declined informed consent. DBPCFC results were positive in 23 patients and negative in 10 patients. The most frequent clinical manifestation was oral allergy syndrome. Twenty-one percent of the patients were not allergic to pollen. Forty-six percent of patients experienced systemic symptoms, and this happened with higher frequency in patients not allergic to pollen (100%). Twenty-eight percent of the patients were sensitized to latex. The IgE-binding bands in kiwi extract more frequently recognized by patient sera were those of 30, 24, 66, and 12 kD, and they could not be associated with any pattern of kiwi-induced allergic reactions.

Conclusion: The results provide evidence that kiwi allergy is not a homogeneous disorder because several clinical subgroups can be established. No definite allergen-recognition pattern was associated with the type of allergic reactions to kiwi. One of 5 patients with kiwi allergy was not allergic to pollen, and these patients had the highest risk of systemic reactions to kiwi. (*J Allergy Clin Immunol* 2004;113:543-50.)

Key words: Food allergy; double-blind, placebo-controlled food challenge; kiwi fruit allergy; oral allergy syndrome

Abbreviations used

DBPCFC: Double blind, placebo-controlled, food challenge

OAS: Oral allergy syndrome

Kiwi fruit belongs to the Actinidiaceae family. The first reports of allergic reactions to kiwi fruit occurred relatively late in 1981.¹ Allergic reactions to kiwi were associated with birch² or grass³ pollen hypersensitivity. Gall et al² suggested that kiwi allergy was a new manifestation of birch pollen-associated food allergy and that it was due to cross-reactive antigens in the kiwi fruit. Thus kiwi allergy could be expected in patients with birch pollen allergy exhibiting high levels of IgE to birch pollen. In addition, with the methodology followed by these authors, specific IgE to kiwi would be found only in patients with severe generalized reactions.² Kiwi allergens have been recently identified and characterized.^{4,5} However, several questions regarding kiwi allergy remain unknown, such as the evaluation of kiwi allergy by means of the double-blind, placebo-controlled food challenge (DBPCFC) and the development of kiwi allergy by subjects living in birch-free areas.

The purpose of this study was to provide a clinical and immunologic evaluation of kiwi allergy among patients from a birch-free area on the basis of the results of DBPCFCs performed in 43 consecutive patients with IgE sensitization to kiwi fruit.

METHODS

Patients

Patients reporting symptoms on eating kiwi and IgE sensitization to kiwi (prick by prick) were recruited from the Allergy Department at Fundación Jiménez Díaz (Madrid, Spain). The clinical history of hypersensitivity reactions to kiwi was documented by a medical questionnaire. Written informed consent was obtained from all patients enrolled in the study.

DBPCFCs with kiwi fruit

DBPCFCs were performed following the recipe designed by Dr Cuesta-Herranz (Table I). Two different drinks were prepared for the test meal, an active drink (with kiwi) and a placebo drink (without kiwi). All ingredients were mixed in a blender. They were similar in color, flavor-taste, consistency, and texture so as not to be differentiated by the patients. Increasing amounts (7.5, 25, 75, and 150 mL) of either active or placebo drink were administered in a random

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TABLE I. Recipe for DBPCFCs with kiwi

Active drink (250 mL)	Ingredient	Placebo drink (250 mL)
50 g	Fresh kiwi pulp*	No added
10 g	Wheat semolina	10 g
3.5 g	Vanilla	3.5 g
150 mL	Pineapple juice	100 mL
No added	Green liquid coloring	0.1 mL
No added	Yellow liquid coloring	0.15 mL
No added	Pear pulp	75 g

*Without tiny seeds.

manner every 30 minutes, except if the patient reported a higher latency period from the clinical history. The challenge result was considered positive if the subject had symptoms after provocation with the active substance and no symptoms after the placebo challenge. If the oral challenge result with masked kiwi was negative, an open oral challenge test with a fresh kiwi fruit was performed.

One milliliter of active drink contained 0.2 g of fresh kiwi pulp. The total amount of kiwi pulp administered to each patient before considering a negative DBPCFC result was 51.5 g, which is equivalent to 2 kiwi fruits.

Food challenge was not performed when a patient denied informed consent or when a patient had a convincing history of recent severe anaphylaxis to kiwi, which was defined as marked laryngeal edema, significant wheezing, or hypotension developing immediately after the ingestion of kiwi.

Kiwi extract

Kiwi fruits were bought at a local market. Whole kiwi was homogenized in 0.01 mol/L PBS (pH 7.4, 1:2 wt/vol) and processed according to a method previously described.⁴ Skin prick test solutions were prepared at a concentration of 20 mg of freeze-dried material per milliliter. The final protein content of the extract was 79.25 µg of protein per milligram of lyophilized extract (Lowry-Biuret method; Sigma Diagnostics, St Louis, Mo).

Skin testing

Skin prick tests were performed with fresh kiwi pulp (prick-by-prick technique),⁶ 2 commercially available kiwi extracts (CBF Leti SA, Madrid, Spain, and Bial-Aristegui, Bilbao, Spain), and the aforementioned homemade kiwi extract. Skin prick tests were also performed with other commercially available fruit extracts: avocado (Stallergènes, Anthony, France), banana and peach (ALK-Abelló, Madrid, Spain), melon (Bial-Aristegui), and chestnut (CBF Leti), with papain (Bial-Aristegui), natural rubber latex (ALK-Abelló), and common aeroallergens, including birch pollen (ALK-Abelló).

A wheal diameter 3 mm or greater with erythema compared with that produced by using the saline control was defined as a positive reaction.⁷ Skin prick test wheal areas were measured by using the technical software Mac Draft v. 4.3 and pencil Wacom.

Specific IgE determinations

Measurements of serum-specific IgE to kiwi, latex, and papain were carried out by using the CAP FEIA system (Pharmacia, Uppsala, Sweden). Direct ELISA was performed to determine specific IgE levels to kiwi extract, as previously described.⁸ Three individual sera from nonallergic patients were used as negative controls. Optical densities 4 times higher than the mean value of the negative control sera were considered positive.

SDS-PAGE

SDS-PAGE analysis was used to determine the protein composition of kiwi extract. The sample was run in SDS-PAGE gel (2.67% C and 15% T acrylamide), as described by Laemmli.⁹ An amount of 150 µg of lyophilized kiwi extract was diluted in reducing buffer containing β-mercaptoethanol (5%), denatured at 100°C for 10 minutes, centrifuged for 1 minute at 10,000 rpm, and loaded into the gels. Reference markers with known molecular weights (14.4, 21.5, 31, 45, 66.2, and 97.4 kd) from BioRad Laboratories (Hercules, Calif) were run in the same gel. After electrophoresis, the gels were fixed for 45 minutes and silver stained (BioRad Laboratories). Afterward, the gel was stained with Coomassie Blue.

Immunoblotting

Separated bands were electrophoretically transferred to P-Immobilon membrane (polyvinylidene difluoride; Millipore, Bedford, Mass). After being transferred, the membrane was dried at room temperature for 4 hours. The membrane was incubated overnight with individual sera from patients and with a pool of sera from patients with positive IgE levels, as evaluated by means of direct ELISA, and diluted in 0.01 mol/L PBS Tween 2%. Specific IgE binding was detected with peroxidase-conjugated monoclonal anti-human IgE (Ingenasa, Madrid, Spain) for 2 hours diluted 1:100 in 0.01 mol/L PBS, 15% FCS, and 1% heparin. The reaction was developed with tetramethylbenzidine and stopped with bidistilled water. Afterward, the membrane was dried overnight at room temperature. Sera from all subjects were tested individually by means of IgE immunoblotting after SDS-PAGE of the crude extract.

Sequence analysis

The sequence analysis of protein bands (Edman degradation) was performed according to a previously described method.¹⁰ Briefly, polyvinylidene difluoride membranes (ProBlott) with CAPS buffer (3-cyclohexylamino-1-propanesulfonic acid) were used to transfer the proteins, according to the manufacturer's recommendations (Applied Biosystems, Foster City, Calif). Proteins were stained with Coomassie Blue, cut out with a razor, and sequenced in a Procise sequencer (Applied Biosystems). Fifteen N-terminal amino acid residues were determined for each band. The N-terminal sequences obtained were analyzed by using the BLAST Program (Expasy; www.expasy.ch) to identify the protein in the databases.

Statistical analysis

The geometric means and medians of the wheal sizes induced by the kiwi extracts and fresh kiwi fruit were calculated. The Shapiro-Wilks test was used to determine normal distribution, and the Wilcoxon test was used to evaluate the differences between the wheal sizes induced by skin prick testing with different kiwi extracts.

RESULTS

Patients

Forty-three patients (31 female and 12 male patients) aged 5 to 54 years (median, 31.2 years) were enrolled in the study. Clinical history with regard to kiwi allergy revealed that 31 (72%) patients had experienced oral allergy syndrome (OAS) after consumption of kiwi fruit; 12 (28%) patients had urticaria, angioedema, or both; 5 (12%) patients had contact urticaria; 4 (9%) patients had anaphylaxis; 2 (5%) patients had abdominal cramps; and 1 (2%) patient had rhinitis, conjunctivitis, and moderate dyspnea. The characteristics of the patients are shown in Table II.

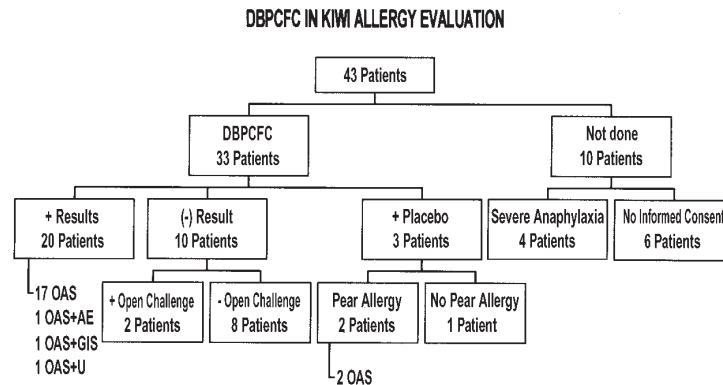


FIG 1. Results of DBPCFC with kiwi.

Skin testing

The results of skin testing performed by means of the prick-by-prick method with kiwi were positive in 100% of the patients, whereas positive skin responses with the 2 commercial extracts and the homemade kiwi extract were observed in 40%, 28%, and 35% of the patients, respectively. Skin prick test responses to other plant-derived food extracts were positive to chestnut in 16 (37%) patients, melon and peach in 11 (25.6%) patients, avocado and banana in 8 (18.6%) patients, and papain in 7 (16%) patients.

Twelve (28%) patients had positive skin test responses to latex, and 10 of them had clinical manifestation with latex particles.

Up to 35 (81%) patients were allergic to pollen (34 to grasses, 31 to *Olea europaea*, 28 to *Cupressus arizonica*, 27 to *Platanus hybrida*, 23 to *Plantago lanceolata*, 19 to *Artemisia vulgaris*, and 18 to *Betula verrucosa*).

Eight patients were not sensitized to pollen: 5 (12%) were exclusively monosensitized to kiwi, and 3 (7%) were sensitized to kiwi along with other fruits. All but one of the patients not allergic to pollen had experienced previous systemic reactions to kiwi fruit.

DBPCFCs with kiwi fruit

Oral food challenges were not performed in 10 patients: 6 patients declined informed consent, and 4 had experienced severe anaphylaxis according to clinical history. DBPCFCs with kiwi were performed in 33 patients (Fig 1 and Table II). Twenty (66%) of 33 patients had positive DBPCFC results with kiwi and negative results with placebo. Seventeen (85%) of the 20 patients complained of symptoms strictly localized to the oral cavity (OAS). In addition, one patient complained of OAS and angioedema, one patient experienced OAS and gastrointestinal symptoms, and one patient experienced OAS and urticaria. None of the patients had severe reactions during the challenge test. The median of the provocative dose eliciting a positive challenge was that corresponding to 1.5 g of fresh kiwi pulp.

Three patients had positive DBPCFC results with placebo. These patients were also investigated for pear allergy because this fruit was contained in the placebo recipe. Two of them complained of OAS and had positive prick-prick and open challenge results to pear.

Ten (33%) of 30 patients had negative DBPCFC results. Two of these 10 patients with a negative DBPCFC result had a positive open challenge result with kiwi, and the 8 remaining patients tolerated the ingestion of fresh kiwi fruit without any ill effect.

The results of the DBPCFCs with kiwi among the 10 patients who were allergic to latex were positive in 6 patients and negative in 2 patients, and 2 patients refused the oral challenge test.

Five of 8 patients not allergic to pollen were finally considered to be allergic to kiwi: 3 had a positive DBPCFC result, and 2 were given the diagnosis on the basis of a history of previous anaphylactic reaction to kiwi. One patient had a negative DBPCFC result, and the remaining 2 patients refused the challenge test.

Specific IgE

Fifty percent of patients with kiwi allergy had specific IgE to kiwi, as determined by means of direct ELISA. Detailed results of specific IgE levels in several groups are shown in Table III. Up to 20 (47%) individuals had a positive CAP determination to latex, although only 10 patients were clinically allergic to latex.

SDS-PAGE and sequence analysis

Several protein bands were detected in a molecular weight range of 12 to 70 kD (Fig 2). The N-terminal amino acid sequence found for the 24-kD band was A-T-F-N-I-I-N-N-?-P-F-T-V-V-A. A search of the Swiss Protein Bank showed that this was the sequence of amino acids of a thaumatin-like protein that had been recently described.⁵ On the data bank, position 9 corresponds to a cysteine that sometimes is missed in Edman degradation.

The band at approximately 12 kD yields a mixture of heterogeneous amino acids without any identifiable sequence.

TABLE II. Demographic, clinical, and immunologic characteristics of the study patients

Patient no.	Age (y)	Sex	Symptoms	Positive SPT response to pollen	Other positive SPT response	DBPCFC to kiwi	Immunoblot binding bands (kd)
1	19	F	OAS, UA	Yes	No	ND	66, 30, 24
2	36	F	OAS	Yes	BAN	+	Negative
3	51	F	UA	No	No	+	66, 30, 24, 12
4	51	F	OAS	Yes	No	ND	Negative
5	17	M	OAS	Yes	AVO, CHES, BAN, PEA	Negative	30
6	54	M	OAS, UA	No	BAN	ND	Negative
7	45	F	R, A	No	No	Negative	Negative
8	52	M	OAS	No	LAT, CHES	ND	Negative
9	29	F	OAS, UA	Yes	LAT	ND	30, 12
10	22	M	UA	No	PAP, AVO, CHES	+	30, 12
11	39	M	OAS	Yes	PAP, LAT, AVO, CHES	+	30
12	19	F	OAS, UA	Yes	No	ND	30
13	27	M	OAS	Yes	AVO, PEA, MEL, CHES	+	Negative
14	32	M	OAS	Yes	No	+	30
15	20	F	OAS	Yes	PAP, LAT, AVO, CHES, BAN, MEL, PEA	+	24
16	27	F	UA, R, A	Yes	CHES, PEA, PEAR	+ Placebo	30, 24
17	39	M	OAS	Yes	CHES, MEL, PEA	Negative	24
18	52	F	OAS	Yes	LAT	Negative	24, 30, 12
19	19	F	OAS	Yes	MEL	+	Negative
20	29	F	OAS	Yes	PEA	Negative	30
21	21	F	OAS, GI	Yes	No	+	30
22	26	F	Anaphylaxis	No	No	ND, anaphylaxis	24, 30
23	35	F	OAS	Yes	PAP, LAT, AVO, CHES, BAN, PEA	+	30
24	16	F	OAS	Yes	CHES, MEL, PEA	+ Placebo	66, 30, 24
25	36	F	UA, GI	No	No	+	Negative
26	24	M	OAS	Yes	CHES, PEA	+	30, 24
27	27	F	OAS	Yes	LAT, MEL	+	Negative
28	43	F	OAS	Yes	No	Negative	24, 12
29	20	F	UA	Yes	PAP, LAT, AVO, CHES	+	Negative
30	28	F	OAS	Yes	PEA, PEAR	+ Placebo	Negative
31	43	F	OAS	Yes	CHES, MEL	Negative	Negative
32	28	F	OAS	Yes	MEL, CHES, LAT	+	66, 30, 24
33	36	F	Anaphylaxis	No	No	ND, anaphylaxis	Negative
34	25	F	OAS	Yes	PAP, LAT, AVO, CHES, PEA	+	66, 30, 24
35	25	F	OAS	Yes	No	+	30
36	5	F	Anaphylaxis	Yes	No	ND, anaphylaxis	66, 30, 24
37	34	M	OAS	Yes	MEL	Negative	Negative
38	25	F	OAS, UA	Yes	No	+	Negative
39	49	F	OAS	Yes	PAP, LAT, AVO, CHES, BAN	+ Open	Negative
40	27	F	UA	Yes	LAT, BAN, MEL	+ Open	Negative
41	35	M	Anaphylaxis	Yes	No	ND, anaphylaxis	Negative
42	21	M	OAS, U	Yes	BAN	+	30
43	35	M	UA	Yes	MEL	+	Negative

SPT, Skin prick test; UA, urticaria-angioedema; ND, not done; BAN, banana; AVO, avocado; CHES, chestnut; PEA, peach; R, rhinitis; A, asthma; LAT, latex; PAP, papain; MEL, melon; GI, gastrointestinal symptoms; U, urticaria.

Immunoblot analysis

A pool of sera recognized several bands in a molecular weight range between 12 to 70 kd (Fig 2). Specific IgE-binding bands recognized by individual sera are shown in Fig 3 and Table II. The most frequent IgE-binding band was recognized by 13 (54%) individual sera of 24 patients with kiwi allergy corresponding to actinidin (Act c 1), the major

kiwi allergen.⁴ Seven (29%) patients recognized the band of 24 kd, corresponding to a thaumatin-like protein,⁵ and this should be considered as an important kiwi allergen. Eight percent of patients recognized the 12-kd band, and 16% recognized the 66-kd band. Nonetheless, among patients not allergic to kiwi, 8 (42%) recognized the actinidin band, 26% reacted to the thaumatin-like protein, 16% reacted to the 12-kd band, and 10% reacted to the 66-kd band.

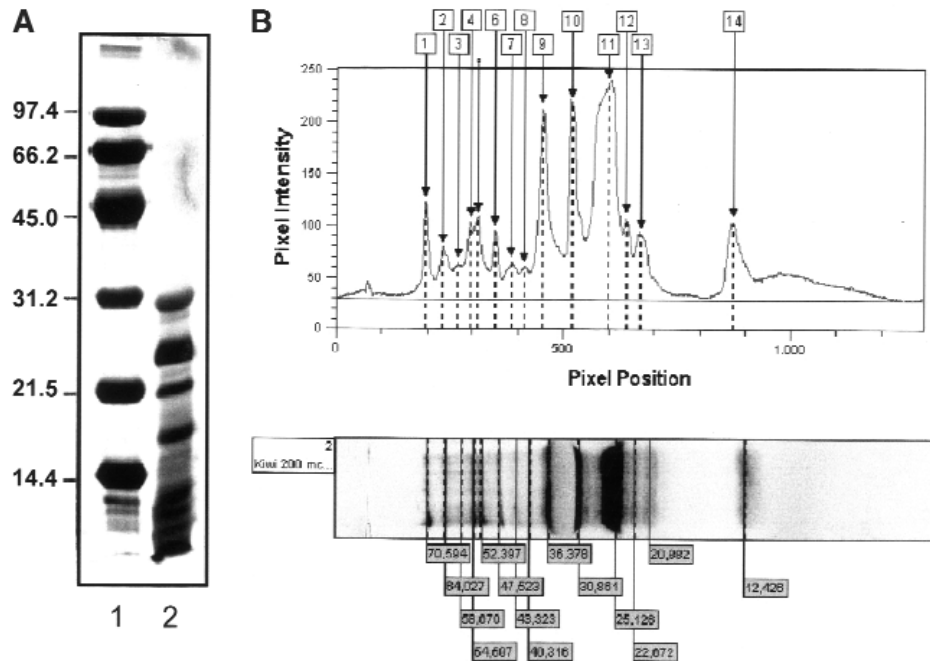


FIG 2. A, SDS-PAGE of kiwi extract: *lane 1*, molecular weight markers; *lane 2*, kiwi extract (150 μ g). Combined silver/Coomassie Blue staining is shown. B, IgE immunoblot with pooled sera from patients allergic to kiwi.

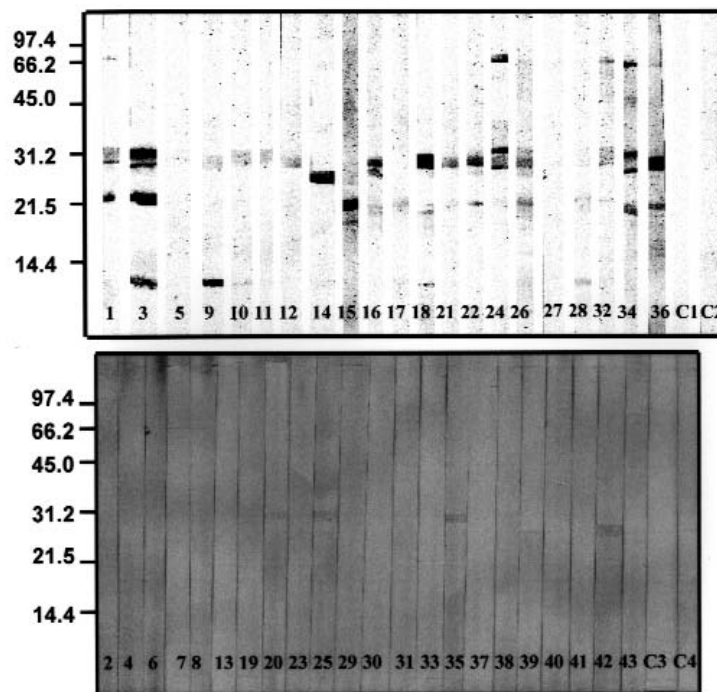


FIG 3. IgE immunoblots with individual sera. Numbers on lanes correspond to patient numbers in Table I. C1 and C3, Nonatopic sera; C2 and C4, sera from a patient allergic to peach.

DISCUSSION

In this study we have evaluated kiwi allergy on the basis of DBPCFC results among patients from a birch-

free area. The results of this study point out that kiwi allergy is not a homogeneous disorder and that efforts should be made to improve the quality of kiwi extracts. Several clinical subgroups could be established: patients

TABLE III. Number of patients with positive IgE determinations according to clinical data

Specific IgE results	DBPCFC +	DBPCFC –	Anaphylaxis	DBPCFC placebo +	Open food challenge +	Not done
ELISA kiwi +	9	3	3	2	0	4
ELISA kiwi –	11	5	1	1	2	2
CAP kiwi +	8	2	3	1	0	4
CAP kiwi –	12	6	1	2	2	2
CAP papain +	8	1	1	0	0	0
CAP latex +	11	2	3	1	1	2

with kiwi allergy with mild or moderate-severe allergic reactions, with or without associated pollinosis, or with or without concomitant latex allergy. No definite allergen-recognition pattern in kiwi extract was associated with the clinical profile of allergic reactions to kiwi.

This is the first report in which kiwi allergy was evaluated by means of DBPCFC. The design of the DBPCFC protocol with adequate vehicles and placebos is an important prerequisite to improve the usefulness of this procedure in confirming a history of adverse reactions to fresh fruits. In this regard we first developed several recipes to blind kiwi fruit, some characteristics of which are difficult to mask, such as flavor, taste, and particularly texture. Mashed fresh pear pulp was added to the placebo recipe to show that patients were unable to differentiate between the active and the placebo drink. Although pear pulp might elicit allergy reactions, it was finally added because pear allergy is a quite uncommon cause of fruit allergy in our area. However, this should be borne in mind on evaluating positive results with the placebo. The results obtained with this recipe provide evidence that the active drink was able to elicit positive reactions in patients with kiwi allergy. Negative results on DBPCFCs were not in contradiction with those from open oral challenge tests, with the exception of 2 cases. Thus it appears that the doses and concentrations administered were adequate and that the method to mask kiwi did not inactivate the kiwi allergens. However, there were 2 (6%) positive open oral challenge results after a negative DBPCFC result, which should not be strictly considered a false-negative DBPCFC result because this might happen as a consequence of a reaction to placebo. This finding has been described with variable frequency in several studies with other fruits and vegetables: 0% to melon¹¹ and chickpea,¹² 4% to carrot,¹³ 6% to hazelnut,¹⁴ or 13% to celery.¹⁵ Finally, 3 patients had positive DBPCFC results with placebo. Two of these reactions could be explained by pear allergy (positive prick-prick test results and open oral challenge results to pear).

Another interesting aspect of this study was the evaluation of kiwi allergy among patients from a birch-free area. Kiwi allergy has always been reported in areas in which patients were exposed to birch pollen.² Our results point out that kiwi allergy can develop without associated birch pollen allergy and, even more importantly, without associated pollinosis. In this regard approximately 21% of kiwi allergy occurred in patients not allergic to

pollen. Although these results are somehow different from those reported by other researchers,^{2,3,5,16} similar data have previously been reported for peach allergy because 19% of peach allergy occurred in patients not allergic to pollen.¹⁷ In addition, it should be highlighted that patients with kiwi allergy with associated pollen allergy have a high frequency (41%) of sensitization to birch pollen, which is unexpectedly high in a birch pollen-free area such as Madrid.¹⁸ Similar data have been previously reported in melon¹⁹ and peach¹⁷ allergy among patients with pollen allergy from this area, which is thought to be due to profilin sensitization and allergenic cross-reactivity between peach and several taxonomically unrelated pollens.²⁰

OAS to fruits is common among patients sensitized to pollens.^{11,21,23} The characteristics of kiwi-induced allergic reactions indicate that the most frequent clinical manifestation was OAS (100%), which was accompanied by an important number of systemic reactions (46%), some of them severe. Noticeably, the subgroup of patients not allergic to pollen experienced the highest percentage of systemic reactions (100%).

When comparing several methods to assess kiwi hypersensitivity, the prick-by-prick test with fresh kiwi appears to be the most sensitive test in comparison with skin testing with other kiwi extracts or with specific IgE determinations to kiwi by means of ELISA or commercial CAP testing. Interestingly, only 50% of the patients had a positive IgE result to kiwi extract determined by means of ELISA or CAP, a percentage similar to that found with skin prick tests with commercial or homemade extracts. These results are in agreement with those reported by Poon et al,²⁴ and these results therefore question the quality of the extracts used for the diagnosis of fruit allergy. Therefore efforts should be made to improve the quality of kiwi extract in the future, including assessment of the biologic activity of the extract,²⁵ measurement of the major allergen content of the extract,²⁶ or both.

Actinidin (Act c 1) has been identified as the major allergen of kiwi fruit.⁴ Recently, a thaumatin-like protein has been identified and characterized as another kiwi allergen.⁵ Among our patients with kiwi allergy from a birch-free area, it was found that only 50% had specific serum IgE to kiwi extract. The IgE-binding bands detected with higher frequency corresponded to Act c 1 (54%) and thaumatin-like protein (29%). Our results also demonstrate that sensitization to the thaumatin-like pro-

tein was found not only among patients reporting OAS but also in 3 (27%) of 11 patients who had experienced systemic reactions, which is in disagreement with the data from Gavrovic-Jankulovic et al.⁵ Our results are also different from those of Gall et al² because specific IgE to kiwi was found both in patients with and without systemic reactions or even in patients without sensitization to birch pollen.

Several reports have incriminated kiwi in the so-called latex-fruit syndrome.²⁷ Class I chitinases were responsible for cross-reactivity between latex and avocado, banana, and chestnut²⁸; however, these chitinases have not been found in kiwi extract. The discrepancy between the results of skin and serologic tests to latex might be due to the high frequency of positive CAP results to latex in patients allergic to pollens and fruits.²⁹ Moller et al³⁰ demonstrated by means of immunoblot inhibition that latex, avocado, and banana extracts and 2 components of 43 and 67 kd in kiwi fruit shared common IgE epitopes. In our study 6 patients recognized a 66-kd band in kiwi extract, 5 of whom were sensitized to latex, as determined by means of CAP, but the other 6 patients sensitized to latex did not recognize this band. Akasawa et al³¹ described Hev b 5, an acidic 16-kd allergen in natural latex that shows a high degree of homology in the amino acid sequence (47% sequence identity) to a 28-kd acidic protein from kiwi fruit, which could explain allergenic cross-reactions between kiwi and latex. However, the implications of this band have not yet been demonstrated.^{2,32,33}

In summary, the results of this study, on the basis of DBPCFCs, demonstrate that kiwi allergy is not a homogeneous disorder because several clinical subgroups can be identified. No definite allergen-recognition pattern could be associated with the clinical allergic reactions to kiwi. Actinidin, thaumatin-like protein, and 12- and 66-kd IgE-binding bands were the main kiwi allergens in a Spanish population living in a birch-free area. However, the presence of IgE to the thaumatin-like protein or actinidin did not always equate with positive DBPCFC results, raising questions for further investigations.

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