

Melon sensitivity shares allergens with *Plantago* and grass pollens

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Possible associations between allergy to pollen and that to food allergens were studied in 262 patients sensitized to pollen. Forty-four patients (16.7%) showed some allergic symptoms after testing with fruits and vegetables, melon being the food most frequently involved (24 patients), followed by sunflower seed (12 patients). Skin testing was done by the prick method with natural fruit or vegetable, and also with commercial food extracts. We found in our region that the distribution of sensitivity to pollens in the group of patients with allergy to fruits or vegetables does not coincide with the prevalence in pollen-allergic subjects in general, since in the first group – subjects allergic to food – there was a major prevalence of allergy to *Plantago* ($P < 0.01$). In particular, in the group of subjects allergic to melon, the prevalence of sensitivity to grass and especially to *Plantago* was larger than in pollen-allergic subjects in general ($P < 0.05$ and $P < 0.001$, respectively). The use of fresh food produced better results than commercial extracts. A positive skin test to fresh melon closely correlated with positive CAP results. CAP inhibition experiments were carried out, and we found that *Dactylis* and *Plantago* extracts inhibited the binding of the melon-positive pool to solid-phase melon. The results suggest the existence of common antigenic epitopes in melon and *Plantago* pollen, and in melon and grass pollen.

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Patients with pollinosis may have oral and systemic manifestations because of allergy to certain fruits and vegetables. This correlation has been observed between the allergy to birch pollen and that to apple (9), and between allergies to mugwort pollen and celery (17); moreover, melon and banana seem to be associated with ragweed hay fever (1). More recently, watermelon has been connected with ragweed (8). The reason for these associations may probably be explained by structural similarities between pollen antigens and vegetables or fruits (4, 8, 10, 17).

It is unknown whether there are new associations in areas where certain types of pollens are of clinical importance. It seems obvious that, depending on the food habits and on the predominant pollens in each region, a certain association may appear. In our area, besides grass and olive, the pollens of some weeds such as mugwort, *Parietaria*, and *Plantago* have special importance. The objective of this study was to analyze the relationship between the most important pollens in our area and the fruits and vegetables usually consumed by our population.

Material and methods

Patients

A total of 262 patients, 142 women and 120 men, mean age 20.3 years (range 5–66 years) was included in this survey. All of them attended consecutively for the first time at our hospital and had a typical history of seasonal rhinoconjunctivitis and/or asthma, as shown by prick-test sensitivity to at least one type of local pollen. The tested allergens included pollen of grasses, weeds (*Parietaria judaica*, *Artemisia vulgaris*, *Rumex acetosella*, *Plantago lanceolata*, and *Chenopodium album*) and trees (*Olea europaea*). We did not test with birch pollen because birch is not a common tree in our area. We also tested other inhalant allergens such as *Dermatophagoides pteronyssinus*, *D. farinae*, cat and dog epithelia, *Alternaria tenuis*, *Cladosporium herbarum*, and *Aspergillus fumigatus*. The glycerin-preserved extracts were obtained from a commercial supplier (Abelló SA, Madrid, Spain).

Each patient was asked about oropharyngeal symptoms and other kinds of allergic symptoms

(urticaria, difficulty in breathing, cough, or digestive problems) in relation to specific fruits and vegetables. Food histories were considered to be positive only if the patient had experienced the same symptoms on at least two occasions and if the symptoms began less than 1 h after food ingestion.

Skin tests (ST) for food allergens

Skin testing was carried out by the prick method with natural fruit or vegetable, according to the method of Dreborg & Foucard (6), on the palmar surface of the forearm, in all the patients with symptoms related to these foods. We used a prick lancet (Bloodlancet, TSK Laboratory, Tokyo, Japan). Both a positive (histamine 10 mg/ml) and negative (saline solution) control were included. The reactions were read after 15 min and were considered to be positive in the presence of a wheal with the same diameter as that caused by histamine. Any medication was withdrawn at least 10 days before skin testing. Following the same criteria, we also used in all our patients commercial extracts of the food tested (10 mg/ml) (Leti SA, Barcelona and Abelló SA, Madrid, Spain). All these extracts were tested in 20 control subjects: 10 normal nonallergic subjects and 10 subjects allergic only to *D. pteronyssinus*, *D. farinae*, or both (average age, 23.1 years; range, 12–44 years).

Specific IgE determination

IgE was measured by the Pharmacia CAP System, which was used, according to the manufacturer's instructions, for the following allergens: grass, olive, mugwort, *Parietaria*, *Chenopodium*, *Plantago*, *Rumex*, and melon. The results were expressed in kU/l. Values that were higher than 0.35 kU/l were considered to be positive.

CAP inhibition experiments

We carried out immunoinhibition in liquid phase in the CAP system to prove a partial identity between melon and some pollens. We used extracts of *Dactylis*, *Plantago*, and olive pollens (Abelló SA, Madrid, Spain) as allergens in liquid phase, and melon and *Plantago* as allergens in solid phase (immunoCAP, Pharmacia). We used a pool of serum positive for melon (4.76 kU/l), *Plantago* (36.8 kU/l), *Dactylis* (45.5 kU/l), and olive (32.8 kU/l).

Serial dilutions were used from an initial concentration of 10 biologic units (BU). A volume of each dilution was reacted with an identical volume from the "pool" (1:1), and these were incubated at 37°C for 1 h. A portion of the pool was used as a control against another from the free diluent of allergen. With all the immunodistributed samples incubated

with the different dilutions of the three allergens in liquid phase, quantification of IgE related to melon (solid phase) was carried out by the standard technique.

As a quality control of this experiment, the *Plantago*, in liquid phase and in different dilutions, from 100 BU, was matched with the same *Plantago* in solid phase.

Statistical analysis

The statistical associations of foods with pollen allergens were investigated by the chi-square test. A *P* value of 0.05 was taken as the limit of significance.

Results

Epidemiologic and clinical data

Of the 262 patients with pollinosis, 214 (81.6%) had a convincing grass allergy, and 143 (54.5%) were allergic to olive pollen, 111 (42.3%) to *Plantago*, 94 (35.8%) to mugwort, 75 (28.6%) to *Chenopodium*, 56 (21.3%) to *Rumex*, and 46 (17.5%) to *Parietaria*. Food hypersensitivity was reported by 44 patients (16.7%) with an outstandingly high frequency of problems with melon (24 patients), followed by sunflower seed (12 patients) and watermelon (10 patients) (Table 1).

The distribution of the sensitivity to pollens in the group of patients with allergy to fruits or vegetables did not reflect the prevalence in pollen-allergic subjects in general in our region, since in the first patients there was a major prevalence of allergy to *Plantago* (*P* < 0.01) (Table 2). In particular, in the group of subjects allergic to melon, the prevalence of sensitivity to grass and especially to *Plantago* was larger than in pollen-allergic subjects in general (*P* < 0.05 and *P* < 0.001, respectively) (Table 2). In fact, all the patients with symptoms related to the intake of melon showed hypersensitivity to *Plantago* and grass pollen. For the other pollens, there were no significant differences.

Table 1. Individual foods associated with allergy to pollen (262 patients with pollinosis)

	<i>n</i>	%		<i>n</i>	%
Melon	24	(9.1%)	Pear	3	(1.1%)
Sunflower seed	12	(4.5%)	Peanut	3	(1.1%)
Watermelon	10	(3.8%)	Apple	2	(0.7%)
Peach	7	(2.6%)	Strawberry	2	(0.7%)
Walnut	7	(2.6%)	Orange	2	(0.7%)
Almond	6	(2.2%)	Chestnut	2	(0.7%)
Banana	5	(1.9%)	Kiwi	1	(0.3%)
Hazelnut	5	(1.9%)	Grape	1	(0.3%)
Pistachio	5	(1.9%)	Pineapple	1	(0.3%)
Cherry	4	(1.5%)	Potato	1	(0.3%)
Tomato	4	(1.5%)	Pine nut	1	(0.3%)

Table 2. Distribution of pollinosis and its comparison between pollen-allergic subjects in general and subjects allergic to fruits and vegetables in general and to melon in particular

Pollens	General (n=262)	Total foods (n=44)	Melon (n=24)
Grass	214 (81.6%)	40 (90.9%)	24 (100%)**
Olive	143 (54.5%)	23 (52.2%)	15 (62.5%)
<i>Plantago</i>	111 (42.3%)	30 (68.1%)*	24 (100%)***
<i>Artemisia</i>	94 (35.8%)	21 (47.7%)	7 (29.1%)
<i>Chenopodium</i>	75 (28.6%)	16 (36.3%)	9 (37.5%)
<i>Rumex</i>	56 (21.3%)	8 (18.1%)	4 (16.6%)
<i>Parietaria</i>	46 (17.5%)	9 (20.4%)	7 (29.1%)

* $P < 0.01$; ** $P < 0.05$; *** $P < 0.001$.

Of the patients sensitized to *Plantago*, 21.6% had problems with melon. For the other pollens, this incidence was smaller. For grass, it was 11.2%.

Table 3 shows the main clinical data on patients with allergy to fruits and vegetables in general, and, in particular, to the two kinds of food most frequently involved, melon and sunflower seed. Sunflower seed appears to be the most dangerous food because it was implicated in four of the five cases of systemic anaphylaxis. In contrast, outstanding as a main symptom in those patients allergic to melon was itching of the oral mucosa and of the pharynx (91.6%), with absence of systemic symptoms (0%). Of these patients, 45.8% (11/24) individuals were sensitive only to melon, and among those who had problems with other fruits, the most frequent association was with watermelon (eight patients, 33.3%), which, like melon, belongs to the Cucurbitaceae family, followed by banana and peach (both in four patients).

The age of the subjects with allergy to melon was 8–50 years (mean age = 23 years). Five subjects were younger than 10 years, 11 were aged 10–20 years, six were aged 21–30, and only two were older than 30 years. Of these subjects, 66.6% showed symptoms before they were 21 years old.

Skin test to foods

All the patients with allergy to melon showed immediate reactions to fresh food under skin prick test-

Table 3. Incidence of symptoms with single and total foods

Symptoms	Melon	Sunflower seed	Total foods
Oral pruritus	22	8	35
Angioedema lips/mouth	2	4	10
Gastrointestinal symptoms	1	3	4
Rhinoconjunctivitis	0	1	2
Asthma	0	0	0
Urticaria	0	2	11
Anaphylaxis	0	4	5

Table 4. Results of skin test (ST) in 44 patients with clinical history of hypersensitivity to fruits and vegetables

	ST (natural)	ST (commercial extracts)
Melon (n=24)	24	3
Sunflower seed (n=12)	5	1
Watermelon (n=10)	6	2
Peach (n=7)	2	1
Walnut (n=7)	4	0
Almond (n=6)	3	1
Banana (n=5)	4	0
Hazelnut (n=5)	2	1
Pistachio (n=5)	0	0
Cherry (n=4)	1	0
Tomato (n=4)	3	0
Pear (n=3)	2	0
Peanut (n=3)	1	0
Apple (n=2)	1	1
Strawberry (n=2)	0	0
Orange (n=2)	2	0
Chestnut (n=2)	0	0
Kiwi (n=1)	1	0
Grape (n=1)	0	0
Pineapple (n=1)	0	0
Potato (n=1)	1	0
Pine nut (n=1)	0	0

ing. Control skin test with the same food was negative in control subjects, indicating that the positive reactions were specific. In only three patients was the prick test with commercial extract of melon positive. In the rest of the food, the sensitivity of the prick test changed extensively, depending on the food tested, although, in general, fresh food yielded better results than did commercial extracts (Table 4).

Melon-specific IgE

Positivity for melon CAP was observed in 21/24 subjects (87.5%), symptoms and skin test being positive. The range of positives fluctuated between 0.36 kU/l and 6.71 kU/l, with a mean of 2.2 kU/l (Table 5). Tests in the control group all elicited negative results.

Table 5. Melon-specific IgE determined by CAP

Patient no.	kU/l	Patient no.	kU/l
1	4	13	0.45
2	3.2	14	<0.35
3	0.95	15	1.60
4	5.30	16	3.35
5	0.54	17	0.52
6	0.62	18	4.76
7	1.20	19	0.52
8	0.36	20	2.32
9	0.96	21	2.56
10	<0.35	22	5.18
11	6.71	23	0.96
12	<0.35	24	0.90

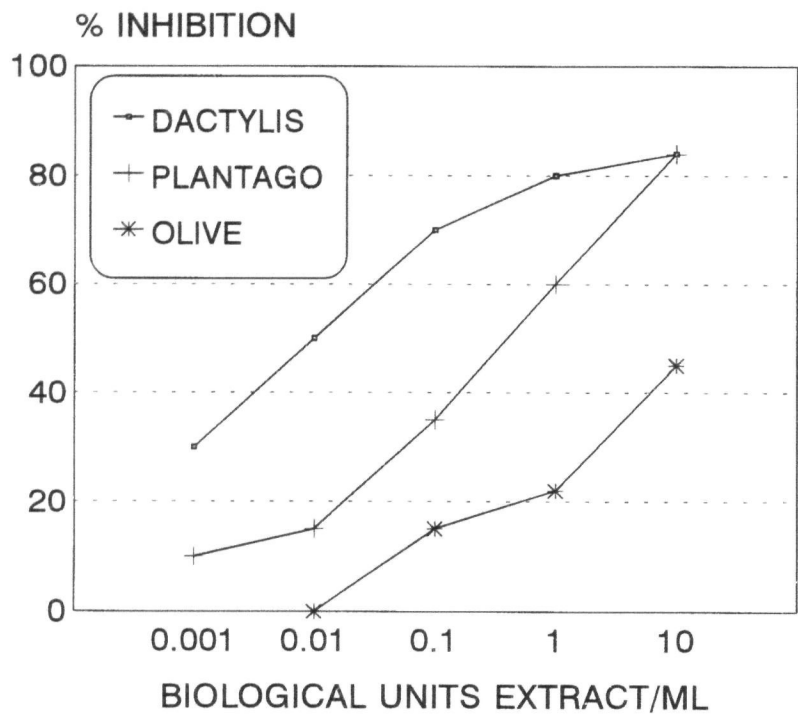


Fig. 1. CAP inhibition studies: melon-positive pool (class 3) inhibited by different dilutions of *Plantago* and *Dactylis* extracts. Olive extract did not reach 50% of inhibition.

CAP inhibition studies

Both the *Dactylis* and *Plantago* extracts readily inhibited the binding of melon-positive pool to solid-phase melon in a dose-dependent manner, as illustrated in Fig. 1 and Table 6. The inhibition was greater with *Dactylis*, indicating that the allergenic composition of melon, *Dactylis*, and *Plantago* is one of partial identity. The extract of olive with the dilution in a larger concentration (10 BU) did not reach 50% inhibition.

The previous control experiment, in which the *Plantago* in solid phase was inhibited by the *Plantago* in liquid phase, showed the reliability of the methodology, obtaining an inhibition of 86% with 100 BU, 66% with 10 BU, and 57% with 1 BU.

Discussion

Patients with allergy to pollen are also frequently sensitive to fruits and vegetables (1, 6). The inci-

dence of this kind of allergy in subjects with pollinosis varies according to the series reviewed, being 16.7% in our survey. Moreover, the kind of food most commonly involved varies in different reports. In patients monosensitized to grasses, De Martino et al. (5) found that the most common foods were tomato and peanut. For Ortolani et al. (16), apple was the most common fruit associated with the pollinosis, especially birch. This association has been described by other researchers (9, 12). It is possible that these relationships vary according to the prevalence of certain pollens in each area and the dietary habits of the population. Recently, some patients with associated sensitization to latex, banana, chestnut, and avocado have been described, and cross-reactivity among them has been shown by RAST inhibition (2, 13, 14, 18).

In this survey, we have found melon to be the fruit most frequently involved as the cause of food allergy, being responsible for 54.5% of the cases. This percentage contrasts with the 16% found by Ortolani et al. (16). The group with allergy to melon showed more prevalence of sensitivity to grasses and *Plantago*, which appeared in 100% of the cases, with a statistically significant difference in relation to the distribution of pollens in our general population ($P < 0.05$ and $P < 0.001$, respectively) (Table 2). The low number of subjects allergic to apple (only two cases) in comparison with other series is explicable, taking into account the absence of birch trees in our area. Watermelon was the third most common food involved, and this fruit is related to melon (family Cucurbitaceae). Besides, watermelon was the food which appeared to be more frequently associated with subjects allergic to melon. This probably shows cross-reacting antigens in these fruits.

The CAP method confirmed skin test results in subjects with allergy to melon, with 87.5% correlation with the fresh food. In spite of the known instability of the allergens of fruits and vegetables, CAP appeared to be useful in detecting IgE specific to melon and to be better than RAST, according to the data for this technique from other researchers (15). On the other hand, commercial fruit and vegetable extracts for prick testing were especially ineffective. Fresh food yielded better results than commercial extracts; to judge by skin test results (Table 4), commercial extracts are not worth using at present.

CAP inhibition experiments suggest that the associations of *Plantago* pollen and melon, and grass pollen and melon depend on the presence of cross-reacting IgE to common structures. The olive pollen hardly reached inhibition, confirming our data and the specificity of our finding.

The association of allergy to melon with grass hay fever has already been suggested by other researchers (16), but we have not found any research related

Table 6. Results of melon CAP inhibition by different dilutions of *Dactylis*, *Plantago*, and olive extracts. Control: CAP for melon on diluted pool with free diluent of allergen = 2733 FU

BU	<i>Dactylis</i>		<i>Plantago</i>		<i>Olive</i>	
	FU	%	FU	%	FU	%
10	438	84	436	84	1503	45
1	552	80	1104	60	2136	22
0.1	815	70	1775	35	2328	15
0.01	1366	50	2323	15	2710	0
0.001	1910	30	2470	10	-	-

FU=fluorescence units; %=percentage of inhibition.

to *Plantago*, with which, according to our results, melon allergy may have a close relation. Therefore, allergy to *Plantago* and grass seems to be a factor favoring sensitivity to melon. The epidemiologic importance of the *Plantago* pollen with regard to the symptoms of pollinosis is unknown since its pollination coincided with that of grass and the small number of monosensitized subjects (3), although, in our area, its diffusion is important, and it is the third pollen in frequency of sensitivity after grass and olive, causing 42.3% of positive reactions. Bousquet et al. (3) found it in 36% of the patients allergic to pollen.

Some surveys of molecular biology have found a relationship between the main allergen of birch, *Bet v* I, and apple and hazelnut proteins (7, 11). Moreover, it has been possible to clone the second allergen of birch, *Bet v* II, which represents the profilin of birch. Profilins are ubiquitous proteins present in plants, in pollen, fruit, leaves, and roots (19). Any of these circumstances may be a cause of the cross-reactivity in different vegetables.

In conclusion, in our area, melon is the main food related to pollinosis, with a special association with allergy to grass and *Plantago*. A new clustering of allergy to pollen and sensitivity to vegetables has been reported. Cross-reactivity between allergens can explain the association.

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