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Contact allergy to spices

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A group of 103 patients suspected of contact allergy was tested with the European standard series, wood tars and spices: paprika, cinnamon, laurel, celery seed, nutmeg, curry, black pepper, cloves, white pepper, coriander, cacao and garlic. 32 patients (Group I) were selected on the basis of positive tests to one or more of possible indicators for allergy to spices: colophony, balsam of Peru, fragrance-mix and/or wood tars. 71 patients (Group II) showed no response to these indicators. In Group I ($n=32$) a statistically significantly higher % of patients (47%) showed positive reactions to 1 or more spices, compared with 15% in Group II ($N=71$). Among the spices, the highest numbers of reactions were found to nutmeg (28%), paprika (19%) and cloves (12%) in the indicator-positive Group I. Fragrance-mix turned out to be a particularly important indicator allergen, especially for paprika, nutmeg and cloves. The contact allergy in 11 out of 32 (Group I) and 7 out of 25 patch-tested patients (recruited from Group II) appeared to be directed mainly against the ether-extractable volatile fractions of the spices.

Key words: spices; nutmeg; paprika; cloves; fragrance-mix; colophony; balsam of Peru; wood tars; allergic contact dermatitis; ether extraction.

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The increasing use of spices and flavours in foods and cosmetics in Western countries (1) led us to investigate the occurrence of contact allergy to spices. Investigation of contact or delayed-type hypersensitivity to herbs and spices is important for several reasons.

First, in some patients the cause of cheilitis, gingivostomatitis, gastro-intestinal or perianal problems may be elucidated (2–4). Cinnamon oil and cinnamic aldehyde in dentifrices, toothpastes and medical and cosmetic preparations, and cardamom, oil of mustard, oil of cloves, allspice, ginger, coriander, nutmeg and curry have all been reported as causes of allergic contact dermatitis (2–5).

Second, in growers and handlers of spices, and housepersons who have frequent contact with spices, hand eczema may be due to contact allergy to spices (6). Garlic and onion cause contact dermatitis in food handlers, and vegetables such as lettuce, endive, parsley and carrots are also reported as being responsible for contact dermatitis in housepersons and catering workers (6).

Third, there are interesting reports of severe attacks of angioedema and urticaria after ingestion of aromatic plants such as celery in atopic patients with immediate-type skin reactions to mugwort pollen extract (7). Delayed-type allergy, which is defective in atopy (10), was not assessed in these patients. Therefore, the relationship between delayed-type contact allergy and IgE-mediated immediate-type reactions to spices in patients with suspected food allergies is an interesting subject for study (8, 9).

In addition to the occurrence of contact allergy to spices, we also studied whether the

allergy was directed against the volatile or the solid fractions of certain spices. This was investigated by patch testing with powdered spices and a modified European standard series.

Patients and Methods

A group of 103 patients was patch tested with the European standard series and wood tars (11), included as a possible indicator of allergy to spices, as are colophony, balsam of Peru and fragrance-mix. All 103 patients were also tested with a series of 10 spices (Group A spices, Table 1). The group of 103 patients comprised 79 patients randomly selected during 1989 for allergic contact dermatitis of different origin and 24 patients selected because of a known positive reaction to one or more of the above-mentioned indicators during 1987 or 1988.

Group I ($n=32$) was composed of these 24 patients plus 8 of the 79 patients found to be positive to one of the indicators. In Group I, 6 patients were positive to colophony, 8 to balsam of Peru, 24 to fragrance-mix and 8 to wood tars. Group II consisted of 71 patients negative to the indicators.

Apart from the European standard and spices series, Group I and 25 patients of Group II were also tested with cacao and garlic, and ether extracts of certain spices (Group B spices, Table 1). Tests with ether extracts were performed to see whether contact allergy to spices was directed against volatile ether-extractable substances or against the solid fractions of the spices.

Reactions were considered positive (+) only if they strictly fulfilled the clinical criteria for an allergic reaction: extension of the reaction beyond the test chamber; erythema and papules or vesicles; increased strength of reaction at 72 h compared with 48 h. Reactions recorded as ± represent dubious irritant or allergic reactions (Table 2).

Spices were patch tested as dry powders moistened with a drop of water. The following spices were tested (Table 1): paprika, cinnamon, laurel, celery seed, nutmeg, curry, black pepper, cloves, white pepper, coriander, cacao and garlic. They were all obtained from a local grocery store, each being packed in a small plastic container as a dry powder by Silvo, Van Sillevoldt, Papendrecht, The Netherlands.

Ether extraction of cloves, nutmeg, paprika,

Table 1. Spices patch tested in indicator-positive (I) and -negative (II) populations

	Spice	Group I ($n=32$)	Group II ($n=71$)
Group A	paprika cinnamon laurel celery seed nutmeg curry black pepper cloves white pepper coriander	patch tested $n=32$	patch tested $n=71$
Group B	cacao garlic paprika (ether extract) cinnamon (ether extract) nutmeg (ether extract) cloves (ether extract) black pepper (ether extract)	patch tested $n=32$	patch tested $n=25$

cinnamon and black pepper was performed as previously described (8). After this procedure, volatile and certain coloured substances were found to be absent from the original spices.

Statistical analysis was performed by the χ^2 test for 2 independent variables.

Results

In the indicator-positive Group I, 15 of the 32 patients (47%) were positive to one or more of the spices. This frequency was significantly higher ($p < 0.001$) than in the indicator-negative Group II, in which only 15% (11 out of 71 cases) were positive. In 13 patients of Group I who were positive to > 1 indicator, 7 patients were found to be positive $\geqslant 1$ spices.

The patterns of reactions to the various spices in each group are shown in Table 2. In the indicator-positive Group I, the highest number of reactions were to nutmeg (28%), paprika (19%) and cloves (12%). The indicator-negative Group II showed significantly lower frequencies of positive reactions to these spices (Table 2).

Group I showed 3 to 12% of $\pm$ responders. The incidence was similar in Group II (1 to 18%). In Group II, 13 patients (18%) showed a $\pm$ response to nutmeg (Table 2).

In the 32 patients of Group I, positive reactions to paprika, nutmeg and cloves coincided in 5 out of 6, 8 out of 9 and 4 out of 4 cases with a reaction to fragrance-mix, respectively (Table 3). Coincidence with colophony was also quite frequent.

Group I ($n = 32$) and 25 patients recruited from Group II ($n = 71$) were tested with original and ether-extracted preparations of cinnamon, cloves, nutmeg, paprika and black pepper. In 11 out of 32 and 7 out of 25 patients from Groups I and II, respectively, positive reactions to $\geqslant 1$ spices were found (Table 4).

In 8 out of 11 patients and 4 out of 7 patients from Groups I and II, respectively, the contact allergy was directed to ether-extractable volatile substances of black pepper, cloves, nutmeg and/or paprika. One nutmeg, one paprika, one cinnamon and one clove allergy were found to be directed against the solid spice fractions in Group I, whereas in Group II, only one contact allergy to the solid fraction of nutmeg was observed.

3 allergic reactions to the ether-extracted but not to the original preparations were observed, indicating the exposure of hidden antigens by ether extraction: one nutmeg allergy in Group I and one nutmeg and one cinnamon allergy in Group II (Table 4).

Table 2. Delayed-type hypersensitivity reactions to spices in indicator-positive (I) and -negative (II) populations. +: clinically allergic reaction; $\pm$: dubious irritant or allergic reaction; −: no reaction. Reactions observed 48 and 72 h after application of patches

	Group I ($n = 32$)			Group II ($n = 71$)		
Spice	+ (%)	$\pm$ (%)	− (%)	+ (%)	$\pm$ (%)	− (%)
paprika*	6 (19)	4 (12)	22 (69)	–	7 (10)	64 (90)
cinnamon	2 (6)	1 (3)	29 (91)	–	1 (1)	70 (99)
laurel	1 (3)	1 (3)	30 (94)	–	1 (1)	70 (99)
celery	3 (9)	4 (12)	25 (79)	2 (3)	3 (4)	66 (93)
nutmeg*	9 (28)	1 (3)	22 (69)	6 (8)	13 (18)	52 (74)
curry	1 (3)	3 (9)	28 (88)	1 (1)	5 (7)	65 (92)
black pepper	1 (3)	3 (9)	28 (88)	2 (3)	–	69 (97)
cloves*	4 (12)	3 (9)	25 (79)	1 (1)	1 (1)	69 (98)
white pepper	–	3 (9)	29 (91)	1 (1)	–	70 (99)
coriander	–	4 (12)	28 (88)	1 (1)	3 (4)	67 (95)
cacao	–	–	32 (100)	–	–	25 (100)
garlic	–	2 (6)	30 (94)	–	2 (8)	23 (92)

* Significantly different distribution between Groups I and II using the χ^2 test ($p < 0.05$).

Discussion

In this paper, we report the occurrence of delayed-type hypersensitivity to various spices commonly used in the European kitchen. The spices were patch tested in the above-mentioned indicator-positive and -negative populations. Significantly higher frequencies were found for nutmeg, paprika and cloves in the indicator-positive group . Compared with the data of Niinimäki (5, 6), the frequencies found by us for these spices were high. The test procedures used, especially with regard to concentration and vehicle, may explain this discrepancy.

Difficulties in distinguishing between irritant and allergic reactions may arise. Niinimäki (5, 6) has also pointed out these difficulties. In our study, the high number of dubious irritant or allergic (±) responses to nutmeg, and the difference between Group I (3%) and Group II (18%) with regard to those reactions, were striking. We cannot explain this discrepancy. Reactions were considered positive only if they strictly fulfilled the clinical criteria for delayed-type allergy. In addition to the clinical criteria, the many negative reactions among those tested support the fact that the reactions recorded as + represented true allergic reactions. These considerations stress the need for standardized (non-irritant) patch test concentrations for nutmeg in particular.

Another important explanation for the differences in frequency between our study and those of Niinimäki (5, 6) may be the indicators chosen. Niinimäki (5) selected only balsam of Peru as an indicator for delayed-type hypersensitivity to spices. In our study, colophony, balsam of Peru, fragrance-mix and wood tars coincided with positive reactions to spices. We found fragrance-mix to be an especially important indicator allergen for paprika, nutmeg and cloves in particular. Our selection of 4 indicators related to plants detected more spice allergies and apparently accounted for the different incidence and distribution of allergies to cloves, cinnamon, curry, white pepper and paprika.

The high incidence of nutmeg allergy in our groups may reflect the increasing use of nutmeg (and other spices) in cosmetics in Western society (1). Nutmeg oil is used not ony as a flavour in food, but also as a drug (carminative) and in soaps and parfumes (2, 12). It is conceivable that the current trend to develop new perfumes is related to the increasing use of nutmeg oil in cosmetic preparations.

Nutmeg (Myristica fragrans) consists of 5–10% volatile and 25–30% non-volatile oils (12). Oleum myristicae aethereum contains 2 main groups of chemical compounds: monoterpenes (pinenes, camfene, limonenes, geraniol, alpha-terpineol) and phenylpropane derivatives (myristicine, elemicine, safrol, eugenol, methoxy-eugenol, iso-eugenol, methylisoeugenol) (13). Both groups contain sensitizers.

It was recently found that eugenol, a major constituent of nutmeg, inhibited prostaglandin

Table 3. Coincidence of delayed-type hypersensitivity reactions to spices and indicator allergens in Group I ($n=32$)

Spice	Colophony	Balsam of Peru	Fragrance-mix	Wood tars
paprika ($n=6$)	2	1	5	1
cinnamon ($n=2$)	1	1	1	1
laurel ($n=1$)	1	–	–	–
celery ($n=3$)	1	1	3	1
nutmeg ($n=9$)	3	2	8	2
black pepper ($n=1$)	1	–	–	–
cloves ($n=4$)	1	2	4	1
curry ($n=1$)	–	1	1	–

synthesis (14). Such effects of different nutmeg constituents may help to explain its toxicity. Another component of nutmeg, the solid triglyceride of myristinic acid is used in cosmetics such as isoprenyl myristate. 6 patients with contact dermatitis from this compound have been recorded (15).

The composition of nutmeg may depend upon its country of origin and also on the quality of the nutmeg harvest. Thus, the occurrence of antigens and the incidence of nutmeg allergy may vary with different nutmeg preparations. However, in the Netherlands, Silvo products are known for their good and constant quality. Testing with the separate constituents of nutmeg will provide more insight into this contact allergy.

When questioned, 5 out of 44 patients described clinical signs or symptoms after eating spices. One patient (Group I), with a positive patch test to paprika, had eczema of the hands and perianal area and often used paprika. When she stopped using paprika, the hand eczema gradually disappeared, but her perianal condition persisted. Another patient (Group II) with contact allergy to nutmeg complained of discomfort in the mouth after eating nutmeg. A 3rd and 4th patient (both Group II), both with contact allergy to celery and nutmeg, experienced generalized itching after eating celery (Patient no. 3) or spicy pork (Patient no. 4). A 5th patient (Group II) with positive tests to black pepper and coriander also complained of itching after eating black pepper. When patients suffer from suspected contact eczema, allergic stomatitis or the above-mentioned problems, it is worthwhile testing for contact allergy to spices.

Another question is whether both immediate and delayed-type sensitivities to food allergens are induced against the same antigens. We have shown previously that coriander and celery are potent inducers of an IgE antibody response (8, 9), and that ether extraction of the coriander did not affect its IgE-binding capacity. In contrast, coriander exhibited a

Table 4. Delayed-type hypersensitivity reactions [positive (+) or negative (−)] to original (o) and ether-extracted (e) spices in 18 out of 57 patients

		Reaction to				
Group	Patient no.	Black pepper o,e	Cinnamon o,e	Cloves o,e	Nutmeg o,e	Paprika o,e
I ($n=32$)	1	−,−	−,−	−,−	+,−	−,−
	2	−,−	−,−	+,−	−,−	−,−
	3	+,−	−;−	+,−	+,−	+,+
	4	−,−	−,−	−,−	+,−	−,−
	5	−,−	−,−	−,−	+,−	+,−
	6	−,−	−,−	+,−	+,−	−,−
	7	−,−	+,+	−,−	−,−	−,−
	8	−,−	−,−	−,−	−,+	−,−
	9	−,−	−,−	+,+	+,−	−,−
	10	−,−	−,−	−,−	−,−	+,−
	11	−,−	−,−	−,−	+,+	−,−
II ($n=25$)	1	−,−	−,−	−,−	+,−	−,−
	2	−,−	−,−	−,−	+,−	−,−
	3	+,−	−,−	−,−	−,−	−,−
	4	−,−	−,−	−,−	+,+	−,−
	5	−,−	−,−	−,−	−,+	−,−
	6	−,−	−,−	−,−	+,−	−,−
	7	−,−	−,+	−,−	−,−	−,−

particularly low incidence of delayed-type hypersensitivity in our study (Table 2). The majority of the positive patch tests against spices appeared to be directed against the ether-extractable volatile fractions of the spices. These facts may suggest that IgE-mediated immediate-type hypersensitivity responses are directed against different antigens in spices from those that elicit delayed-type hypersensitivity. Further studies to relate delayed-type reactions to specific serum IgE antibodies to spices are in progress.

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