

Work-Related Allergy and Asthma in Spice Mill Workers – The Impact of Processing Dried Spices on IgE Reactivity Patterns

Anita van der Walt^a Andreas L. Lopata^{b, c} Natalie E. Nieuwenhuizen^b
Mohamed F. Jeebhay^a

^aCentre for Occupational and Environmental Health Research, School of Public Health and Family Medicine, and

^bAllergy and Asthma Research Group, Division of Immunology, Institute of Infectious Diseases and Molecular Medicine, University of Cape Town, Cape Town, South Africa; ^cSchool of Applied Science, Allergy Research Group, RMIT University, Melbourne, Vic., Australia

Key Words

Work-related allergy • Allergy • Asthma • Garlic • Processed allergens • Spices

Abstract

Background: Three spice mill workers developed work-related allergy and asthma after prolonged exposure to high levels (>10 mg/m³) of inhalable spice dust. Patterns of sensitization to a variety of spices and putative allergens were identified. **Methods:** Work-related allergy and asthma were assessed on history, clinical evaluation, pulmonary function and fractional exhaled nitric oxide. Specific IgE reactivity to a range of common inhalant, food and spice allergens was evaluated using ImmunoCAP and allergen microarray. The presence of non-IgE-mediated reactions was determined by basophil stimulation (CAST-ELISA). Specific allergens were identified by immunoblotting to extracts of raw and dried processed garlic, onion and chili pepper. **Results:** Asthma was confirmed in all 3 subjects, with work-related patterns prominent in worker 1 and 3. Sensitization to multiple spices and pollen was observed in both atopic workers 1 and 2, whereas garlic and chili pepper sensitization featured in all 3 workers. Microarray analysis demonstrated prominent profilin reactivity in atopic worker 2. Immunoblotting demonstrated a 50-kDa cross-reactive allergen in garlic and on-

ion, and allergens of approximately 40 and 52 kDa in chili pepper. Dry powdered garlic and onion demonstrated greater IgE binding. **Conclusions:** This study demonstrated IgE reactivity to multiple spice allergens in workers exposed to high levels of inhalable spice dust. Processed garlic and onion powder demonstrated stronger IgE reactivity than the raw plant. Atopy and polysensitization to various plant profilins, suggesting pollen-food syndrome, represent additional risk factors for sensitizer-induced work-related asthma in spice mill workers.

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Introduction

The food industry employs a large proportion of workers exposed to potential allergens capable of causing occupational allergies and asthma [1]. Among consumers reporting food allergies, affecting 2% of the adult population in the industrialized world, spice allergy represents 2% of such cases [2]. Since spices are derived from plants, they have allergenic potential due to the bioactive ingredients present in processed vegetable dusts capable of inducing symptoms ranging from mild local to severe systemic allergic reactions [3]. Workers in the spice-related industry are exposed to a variety of different respi-

ratory sensitizers that may cause sensitization through inhalation or skin contact. Inhalation of spice dust has the potential to cause respiratory allergies such as rhinoconjunctivitis and asthma, contact dermatitis and occasionally anaphylaxis. Furthermore, irritant reactions in addition to these allergic responses in workers handling spices have also been reported [4]. Occupational asthma has been reported to a range of spices including garlic, onion, paprika, mace and coriander [5, 6].

Garlic (*Allium sativum*) belongs to the Alliaceae family (formerly Liliaceae), with the first report of garlic-induced asthma dating back to 1940, when Henson [7] described an atopic foreman with ragweed pollinosis whose asthmatic symptoms disappeared after the garlic 'powder' was replaced with 'kernels'. Inhalation-related garlic allergy has since been reported in different occupational settings including food preparation and catering, sausage making, harvesting and storing of garlic bulbs, spice manufacturing, as well as packing and selling of spices [8–11]. While garlic (*A. sativum*) is known to be one of the most frequent causes of dermatitis of the fingertips in caterers [12], occupational airborne allergic contact dermatitis with concurrent type 1 allergy has also been described due to garlic dust exposure [13]. Although considered rare, reports of allergic reactions after the ingestion of foods belonging to the Liliaceae family have been described [10, 14]. Other members of this family such as onion, leek and asparagus have also been reported to cause allergic reactions among exposed individuals. Immunological evidence of cross-reactivity between garlic and other related members of the Liliaceae family such as onion in patients with occupational asthma has also been described [6, 10]. Work-related respiratory symptoms in chili grinders have also been reported, although it was considered to be probably due to the irritant nature of the dust [15].

Most of the studies on occupational asthma caused by inhalation of garlic dust, have investigated IgE reactivity patterns only to a selected spice [7, 9–11, 16, 17], whereas in spice mills, spice workers have concurrent exposures to multiple spices during work activities. An added complexity in identifying putative allergens in spice mill workers is the wide variation of spice blends produced that is dependent on local availability, geographic tradition and recipes of popular manufacturers. Recent reports of a number of cases of work-related asthma from a spice mill prompted detailed investigation of 3 index cases by analysing their immune responses to an extensive range of spices and to identify the allergens responsible for their allergic symptoms.

Methods

Pulmonological Assessment

Work-related allergy and asthma were assessed on history and clinical evaluation using a standard respiratory questionnaire adapted for the spice dust work environment [18]. Spirometry and assessment of reversible airway obstruction were done according to guidelines of the American Thoracic Society/European Respiratory Society [19]. Work-relatedness of symptoms was determined by serial peak expiratory flow rate monitoring 4 times daily at work (2 weeks), away from work (2 weeks) and back at work (2 weeks). A portable fractional exhaled nitric oxide (FENO) sampling device (NIOX MINO® Airway Inflammation Monitor, Aerocrine AB, Solna, Sweden) was used to obtain serial FENO concentrations across the work shift [20].

Immunological Assessment

Specific IgE reactivity to a range of common inhalant and food allergens as well as 31 different spices was evaluated using ImmunoCAP (Phadia, Uppsala, Sweden). A cut-off point of <0.1 kU/l was used as the lowest limit for detecting specific IgE antibodies. The list of spices was compiled after obtaining an inventory of raw ingredients with allergenic potential used in the spice mill for which a specific ImmunoCAP test was available. Skin prick tests used a battery of common inhalant allergens (ALK-Abello) including grass pollens, house dust mites, cockroaches, cat, dog and various moulds. Atopy was defined as a positive skin prick test to common inhalant allergens. Specific IgE to defined natural and recombinant pollen and food allergens was quantified by allergen microarray (ISAC version CRD-79b, VBC-Genomics, Vienna, Austria) according to previously described methods [21]. Allergen-induced activation of basophils by preservatives (sodium benzoate and K-metabisulphite) was determined using the CAST-ELISA (Bühlmann, Switzerland) for sulphidoleukotriene release according to the manufacturer's manual.

Garlic Extract and Immunoblotting

Extracts were prepared from raw onion and garlic as well as garlic powder, onion flakes, chili pepper, whole chili and cayenne pepper freshly collected from the spice mill. Homogenized raw onion and garlic as well as spices were extracted in phosphate-buffered saline overnight at 4°C. The spice extracts were then centrifuged to remove large particulate matter. The extracts were separated by electrophoresis on 5–16% sodium dodecyl sulphate polyacrylamide gradient gels and transferred onto a polyvinylidenedifluoride membrane (Hybond-PVDF, Amersham). Membranes were incubated with patients' sera, and IgE-binding proteins were detected using alkaline-phosphatase-labeled monoclonal antihuman IgE antibody (Sigma, USA) with the chromogenic substrate 5-bromo-4-chloro-3-indolyl phosphate/nitroblue tetrazolium (Sigma, USA).

Results

History and Clinical Examination

All 3 workers reported work-related rhinitis and asthma symptoms that developed within 6–8 months of ex-

posure to various spice blends (table 1). There was, however, no history of food or spice allergy due to ingestion in any of these workers. Although garlic powder dust was the main spice reported by the workers to be causing their symptoms, other spice blends containing onion, cayenne and chili pepper as well as soya were implicated.

The occupational history indicated that aside from the variety of spices belonging to different families and species, spice mill workers were also exposed to grain flour dust (wheat and maize) as well as preservatives (sodium benzoate and K-metabisulphite). The production area of the spice mill is a general area where all the processing activities such as blending and packing of spice product are conducted except for milling, which occurs in a separate department. Dry materials such as peppercorns, coriander, paprika and chili peppers (*Capsicum annuum*) are crushed and ground in this milling area. Only hot peppers as opposed to bell peppers are used in this plant. Garlic is also used in a dried form as flakes, powder or granules during the blending of spice in the spice mill. An independent supplier manufactures the garlic product used in the spice mill. During this manufacturing process, garlic flakes are produced by a steam heat process at 65°C for 5 h. A report from a recent industrial hygiene survey conducted in the plant revealed that the inhalable dust levels ranged from 8.7 to 29.9 mg/m³ in the blending area and from 1.0 to 26.4 mg/m³ in the packing area, indicating that the extraction ventilation system in this spice mill was dysfunctional and inadequate in reducing spice dust exposures. The specific job histories obtained from these index cases revealed that worker 1 and 2 worked as feeder operators in the blending area, feeding raw spice into mixing bins, and worker 3 was a packer of raw spice product.

Pulmonological Assessment

Spirometry results of workers 1 and 2 demonstrated mild airway obstruction with significant reversibility of FEV₁ after bronchodilator administration (table 1). Although worker 3 had normal spirometry, the methacholine challenge test was positive (PC₂₀ = 2.3 mg/ml). A chest radiograph revealed no evidence of allergic alveolitis in all 3 workers. Serial peak expiratory flow rate measurements confirmed a work-related pattern in workers 1 and 3, with an OASYS work effect index for asthma symptoms of 2.75 observed in worker 3 (a value of <2.5 is considered to have a low probability of being work-related). FENO measurement was distinctly raised (>50 ppb) in worker 2 across the entire shift.

Immunological Assessment

Skin prick testing to a standard panel of common aeroallergens revealed that only workers 1 and 2 were atopic (table 1). Garlic and chili pepper sensitization featured in all 3 workers. Worker 2 demonstrated very high specific IgE reactivity to garlic (208 kU/l) and chili pepper, and was also sensitized to most of the spices tested, including grain flours. Worker 1 demonstrated moderate reactivity to garlic, chili pepper and wheat, and was sensitized to several other spices as well. Worker 3 showed low levels of specific IgE antibody (<0.7 kU/l) to garlic and chili pepper only. All 3 workers demonstrated sensitivity to either one or both preservatives. High specific IgE reactivity to birch pollen and moderate levels to mugwort pollen was observed for worker 2, whereas worker 1 showed relatively low levels of IgE reactivity to these pollens.

Microarray analysis demonstrated that worker 2 reacted to a variety of plant profilins from birch tree (Bet v 2), olive and palm tree, bermuda and timothy grass, sunflower and other weeds as well as the latex (Hev b 8) profilin (table 2). In addition, worker 2 also had elevated specific IgE to peach lipid transfer protein (Pru p 3). Worker 1 only displayed reactivity to perennial rye (Lol p 1) and timothy grass (Phl p 1, Phl p 2, Phl p 5, Phl p 6) allergens, none of which are profilins. Worker 3 did not recognise any of the allergens tested, confirming the non-atopic status observed on skin prick testing. All 3 workers displayed no reactivity to bromelain, regarded as a marker for cross-reactive carbohydrate determinants.

Sodium dodecylsulfate-polyacrylamide gel electrophoresis (SDS-PAGE) demonstrated a dominant protein of approximately 50 kDa for garlic powder and onion flakes, while a 40-kDa protein was the most prominent in the extract of chili pepper (fig. 1). Immunoblotting demonstrated a similar pattern of allergen recognition in workers 1 and 2 with the major IgE-binding protein for both garlic and onion extracts at 50 kDa, the garlic allergen showing the stronger band. Furthermore, greater IgE reactivity was demonstrated to the powdered form compared to the raw form for both garlic and onion. In chili (whole, processed and cayenne pepper), IgE-binding proteins with molecular weights of 51–52 and 40 kDa were recognised by both workers 1 and 2. IgE binding was not observed in worker 3 (data not shown), probably due to the very low levels of specific IgE as determined by ImmunoCAP.

Table 1. Clinical, pulmonological and immunological assessment of spice mill index cases with work-related asthma

		Age: Gender: Smoking status:	Worker 1 28 years male smoker	Worker 2 29 years male non-smoker	Worker 3 28 years female non-smoker
Exposure history	Exposure duration Job type Spice causing symptoms		2 years feeder operator garlic, onion, chili pepper	2 years feeder operator garlic, onion, soya pepper	8 years packer garlic, black pepper, cayenne pepper
Work-related symptoms	Asthma-related Ocular-nasal		yes (6 months) yes	yes (8 months) yes	yes (2 months) yes
Pulmonological assessment	Chest radiograph Spirometry: – FEV ₁ pre-BD/post-BD, ml – FVC pre-BD/post-BD, ml Methacholine challenge test PC ₂₀ , mg/ml Work-related changes on serial PEFr FENO serial, ppb: day 1 pre-shift/post-shift/day 2 pre-shift		NAD 3,430/3,750 4,440/4,690 N/A yes 22/22/22	NAD 2,890/3,530 4,740/5,060 N/A N/A 84/76/65	NAD 2,820/2,690 3,070/3,160 2.3 (positive) yes 17/13/–
Immunological assessment (in vivo)	Skin prick test common aeroallergens		positive	positive	negative
Immunological assessment (in vitro)	Specific IgE, kU/l				
Pollens					
<i>Betula verrucosa</i>	common silver birch		0.88	>100	<0.10
<i>Artemisia vulgaris</i>	mugwort		1.45	35.70	<0.10
Spice family					
Alliaceae	garlic onion		2.37 2.05	208.00 33.00	0.63 <0.10
Solanaceae	chili pepper paprika		0.89 0.68	53.10 2.89	0.51 <0.10
Zingiberaceae	cardamon ginger		1.23 0.89	6.60 4.71	<0.10 <0.10
Lamiaceae	marjoram oregano sage thyme mint basil		1.90 0.52 0.86 <0.10 0.29 0.12	5.31 2.23 1.42 3.24 0.81 0.38	<0.10 <0.10 <0.10 <0.10 <0.10 <0.10
Brassicaceae	mustard white		0.91	4.09	<0.10
Apiaceae	fennel anise celery caraway coriander parsley		1.33 0.46 0.76 0.55 0.45 1.17	6.29 2.75 9.26 1.34 1.75 10.10	0.12 <0.10 <0.10 <0.10 <0.10 <0.10
Myrtaceae	allspice cloves		0.12 0.14	0.52 0.32	<0.10 <0.10
Piperaceae	black pepper		0.96	3.42	<0.10
Lauraceae	bayleaf cinnamon		0.14 <0.10	0.51 0.19	<0.10 <0.10
Myristicaceae	mace nutmeg		1.87 0.18	8.36 0.32	<0.10 <0.10
Grains	wheat maize		1.71 0.97	8.03 11.80	<0.10 <0.10
Soya bean	soya		2.21	7.07	<0.10
Other foods	Santa Maria curry tomato		0.83 0.86	8.78 37.10	<0.10 <0.10
Preservatives	CAST ELISA Sodium benzoate (negative cut-off: 90 pg/ml) K-metabisulphite (negative cut-off: 40 pg/ml)		260 160	70 50	140 20

NAD = No abnormality detected; N/A = not applicable; PEFr = peak expiratory flow rate.

Table 2. Microarray IgE analysis of sera of spice mill index cases with work-related asthma to selected pollen and food allergens

Species name	Allergen	Function	Worker 1 IgE, kU/l	Worker 2 IgE, kU/l	Worker 3 IgE, kU/l
Tree pollen					
<i>Betula verrucosa</i> (birch)	Bet v 1	ribonuclease	<0.01	<0.01	<0.01
<i>Betula verrucosa</i>	Bet v 2	profilin	<0.01	28.10	<0.01
<i>Olea europaea</i> (olive)	Ole e 1	trypsin inhibitor	<0.01	1.37	<0.01
	Ole e 2	profilin	<0.01	25.66	<0.01
<i>Phoenix dactylifera</i> (date palm)	Pho d 2	profilin	<0.01	17.26	<0.01
Weeds					
<i>Helianthus annuus</i> (sunflower)	Hel a 2	profilin	<0.01	26.06	<0.01
<i>Mercurialis annua</i> (annual mercury)	Mer a 1	profilin	<0.01	21.48	<0.01
<i>Parietaria judaica</i> (wall pellitory)	Par j 3	profilin	<0.01	37.29	<0.01
Food					
<i>Malus domestica</i> (apple)	Mal d 1	ribonuclease	<0.01	<0.01	<0.01
<i>Prunus persica</i> (peach)	Pru p 3	lipid transfer protein	<0.01	7.38	<0.01
<i>Apis graveolens</i> (celery)	Api g 1	ribonuclease	<0.01	<0.01	<0.01
<i>Daucus carota</i> (carrot)	Dau c 1	PR-10 protein	<0.01	<0.01	<0.01
Grass					
<i>Cynodon dactylon</i> (bermuda grass)	Cyn d 12	profilin	<0.01	20.92	<0.01
<i>Lolium perenne</i> (perennial rye grass)	Lol p 1	expansin	15.42	49.17	<0.01
<i>Phleum pratense</i> (timothy grass)	Phl p 1		10.59	48.96	<0.01
	Phl p 5		22.07	14.02	<0.01
	Phl p 12	profilin	<0.01	13.30	<0.01
	Phl p 2		30.98	<0.01	<0.01
	Phl p 6		2.41	36.84	<0.01
Latex					
<i>Hevea brasiliensis</i>	Hev b 8	profilin	<0.01	17.87	<0.01
Bromelain					
<i>Ananas comosus</i>	Ana c 2	CCD marker	<0.01	<0.01	<0.01

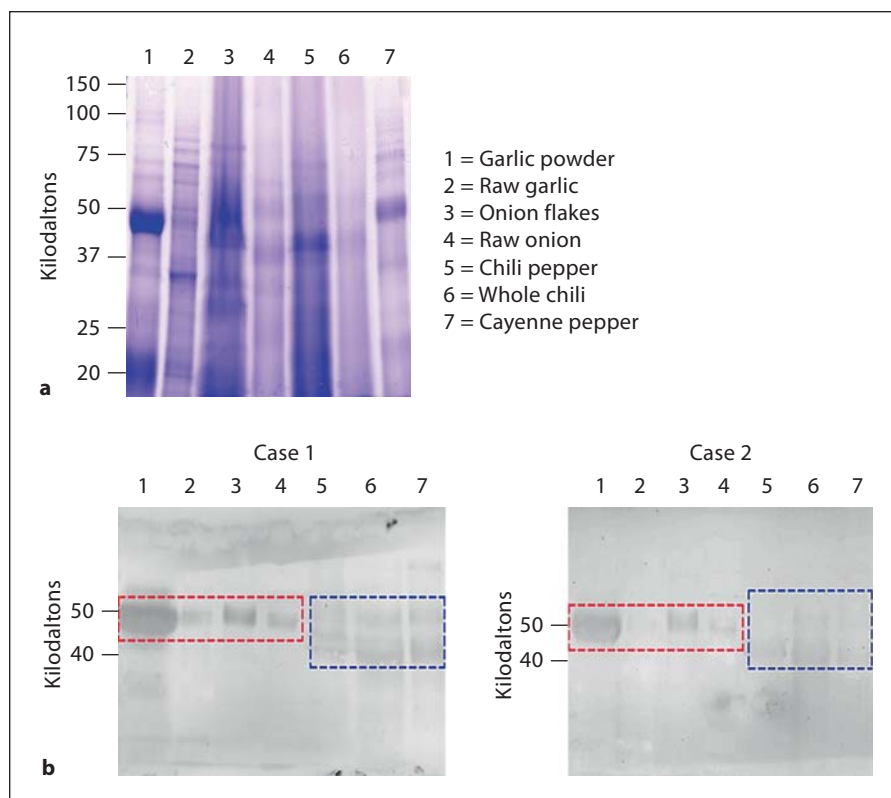
CCD = Cross-reactive carbohydrate determinant.

Discussion

In this study, we report work-related allergy and asthma among 3 spice mill workers, likely due to garlic, onion and chili pepper sensitization after exposure to a multitude of airborne spices, with no previous history of spice or food allergy. Food allergy to Liliaceae vegetables (garlic, onion, leek and asparagus) and spices is relatively rare, but allergic reactions to garlic on ingestion and work-related asthma secondary to inhalation of garlic dust have been reported [7, 9–11, 16, 17]. Potentially fatal adverse reactions, including anaphylaxis, have also been described after the ingestion of garlic [10, 22]. In one case, anaphylaxis occurred after ingestion of young unripe garlic in a woman with a previous history of allergy to pollen and dried fruit, and food-dependent, exercise-induced ana-

phylaxis. As is the finding in this study, Falleroni et al. [11] also reported a case of work-related asthma due to garlic dust exposure in which the patient tolerated ingestion of cooked garlic and onion without symptoms. It is possible that this may have been due to either inactivation or alteration of the allergenicity of the antigen through the heating process or gastric digestive processes.

In this study, immunoblotting revealed a 50-kDa cross-reactive allergen in garlic and onion, garlic being the most prominent. Several garlic protein allergens have been identified in previous studies of allergy due to garlic. In a study by Anibarro et al. [8], two major protein bands were demonstrated at approximately 12 and 54 kDa by electrophoresis of garlic extract. The latter proved to be the major IgE-binding protein and shared similar allergenic epitopes with onion. The allergenic components of



garlic were also shown to be shared by several Liliaceae with SDS-PAGE immunoblotting when IgE-binding proteins of 12 kDa were found in young garlic, garlic, onion and leek extracts [22]. Two main IgE-binding proteins with molecular weights of 55 and 35 kDa were revealed in extracts of fresh garlic and onion, and only the 35-kDa protein showed strong IgE binding with serum from a worker with occupational asthma due to onion [6]. Alliin lyase, a 56-kDa IgE-binding protein, has recently been identified as a major garlic allergen in a group of Taiwanese patients aged 7–48 years with garlic allergy. This protein is widely distributed in other *Allium* species, namely leek, shallot, onion, and has been described as a potentially new cross-reactive allergen [16].

In chili (whole, processed and cayenne pepper), IgE-binding proteins with molecular weights of 51–52 and 40 kDa were recognised during IgE immunoblotting for both workers 1 and 2, whereas SDS-PAGE demonstrated a band of about 40 kDa as the most prominent for chili pepper extract. The particular molecular weights of these proteins, and whether they are related to the protein allergens identified for garlic and onion, can only be confirmed with the sequencing thereof. However, Schöll et al. [3] have suggested that the hotter spices, as is the case with

chili, are the more likely to act as adjuvants for sensitization by promoting transport of molecules below a molecular mass of 70 kDa. This molecular size corresponds to the size of molecules relevant for sensitization and IgE binding in spice-related allergy as observed in this study. It is possible that in addition to the dried product, an adjuvant effect may also have contributed to the multiple sensitizations observed in two of these three workers.

Another novel finding of this study is the role of processing techniques on the IgE reactivity patterns observed. One of the major allergen families that appears to lose its capacity to elicit allergic reactions in processed foods is the Bet v 1 superfamily of plant food allergens. The food matrix itself and processing procedures may be responsible for the apparent thermolability of Bet v 1 homologues in foods such as apple [23]. However, this is not so for other foods such as celery root which retains its allergenicity after cooking [24]. Recent studies of Bet v 1 have shown it to be relatively thermostable, the protein unfolding only at temperatures above 68°C [25]. Furthermore, the dry heating of food (e.g. roasting) can result in enhanced allergenicity as has been demonstrated for other plant allergens such as peanuts [26]. In this non-enzymatic reaction, called Maillard reaction, free amino groups on

proteins bind to the aldehyde or ketone groups of sugars and these glycated proteins can undergo further structural re-arrangements called Amadori products (important for flavour and aroma). The roasted peanut allergens have demonstrated over 100-fold increased allergenicity as well as increased stability against gastric digestion. These effects have not been previously demonstrated for dried spices, and could well be one of the effects leading to the enhanced IgE-binding reactivity of the heat dried garlic and onion flakes observed in this study as none of the workers displayed reactivity to bromelain, a known marker for cross-reactive determinants. SDS-PAGE and IgE immunoblotting demonstrated a prominent band of approximately 50 kDa for both raw and processed garlic and onion, with the garlic powder being most dominant. This suggests that this allergenic protein is cross-reactive, heat stable and enriched in the extracts after processing. Altered and enhanced allergenicity was therefore evident in both garlic and onion processed in its dried form.

In this study, worker 2 showed marked reactivity on allergen microarrays to a number of tree and weed pollens in addition to other plant-derived food allergens, mainly from the allergen protein family of profilins [27]. Patients with pollinosis often display sensitization to various plant-derived foods (class 2 food allergies). These reactions are the result of IgE cross-reactivity to profilins and lipid transfer proteins, but may also be due to high-molecular-weight glycoproteins [28]. Clinical pollen-food syndromes such as the mugwort-mustard allergy, celery-mugwort-spice allergy and the celery-birch-mugwort-spice syndrome have been previously described [29, 30]. Patients with food allergies specifically to Liliaceae (garlic, onion, leek) have also been found to have celery-mugwort-spice syndrome [31]. Birch tree (*Betula verrucosa*) profilin Bet v 2 and mugwort (*Artemisia vulgaris*) profilin Art v 4 have been identified as significant contributors to allergic reactions to pollen and plant-derived food within the celery-birch-mugwort association due to cross-reaction with celery profilin Api g 4 [32, 33]. In this study, both workers 1 and 2 were sensitized to common silver birch tree and mugwort weed pollens as well as to celery (by ImmunoCAP) and grass pollens (by microarray). Anibarro et al. [8] found that IgE binding to garlic allergens was almost completely inhibited by cross-reacting timothy grass (*Phleum pratense*) pollen extracts. However, Leitner et al. [34] investigated allergens originating from pepper (Piperaceae) and paprika (Solanaceae) and showed that IgE cross-reactivity in the celery-birch-mugwort-spice syndrome to spices other than Apiaceae is not exclusively caused by Bet v 1 homologs and/or

profilins. Worker 2 also tested positive to Pru p 3 allergen (7.38 kU/l), a lipid transfer protein from peach which is associated with sensitization to taxonomically diverse pollens [35]. While it is well known that cross-reactive pan-allergens are implicated in pollen-food syndromes, the exact role of profilins in triggering allergic symptoms is still unclear [28]. Pan allergen reactivity was clearly demonstrated for worker 2 who was sensitized to multiple plant-derived spices probably due to inhalation. In addition, profilin appeared to act as a cross-reactive pan-allergen in this worker and pollinosis may therefore pose as a risk factor in the development of spice allergy. The class 2 allergy, particularly the celery-birch-mugwort-spice association may be of importance in this worker, and the relationship between pan-allergens and garlic allergens needs further investigation at a molecular level.

In conclusion, the findings of this study suggest that spice mill workers are at increased risk of becoming sensitized to multiple spice allergens when exposed to inhalable spice dust levels of more than 1 mg/m³, suggesting that the currently recommended exposure limits of 10 mg/m³ (American Conference of Government Hygienists) for inhalable particulates not otherwise specified may be inadequate in protecting the health of exposed workers. However, the exact composition of the dust and the specific concentration of allergens present in the dust need further investigation. Furthermore, garlic and onion powder demonstrated enhanced allergenicity in the processed dry form and was more likely to become airborne. Atopy and simultaneous sensitization to various plant profilins may pose additional risk factors for sensitization to class 2 allergens and occupational asthma in these workers. Garlic, onion and chili pepper should be considered as potential allergens in spice mill workers presenting with work-related asthma and any individual exposed to aerosolized spices.

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References

- Jeebhay MF: Occupational allergy and asthma among food processing workers in South Africa. *Afr Newslett Occup Health Safety* 2002;12:59–62.
- Muhlemann RJ, Wüthrich B: Food allergies 1983–1987. *Schweiz Med Wochenschr* 1991; 121:1696–1700.
- Schöll I, Jensen-Jarolim E: Allergenic potency of spices: hot, medium hot, or very hot. *Int Arch Allergy Immunol* 2004;135:247–261.
- Zuskin E, Kanceljak B, Skuric Z, Pokrajac D, Schachter EN, Witek TJ, Maayani S: Immunological and respiratory findings in spice-factory workers. *Environ Res* 1988;47:95–108.
- Sastre J, Olmo M, Novalvos A, Ibanez D, Lahoz C: Occupational asthma due to different spices. *Allergy* 1996;51:117–120.
- Mansoor N, Ramafi G: Onion allergy – a case report. *Curr Allergy Clin Immunol* 2000;13: 14–15.
- Henson GE: Garlic: An occupational factor in the etiology of bronchial asthma. *J Florida Med Assoc* 1940;27:86.
- Anibarro B, Fontela JL, De La Hoz F: Occupational asthma induced by garlic dust. *J Allergy Clin Immunol* 1997;100:734–738.
- Seuri M, Taivanen A, Ruoppi P, Tukiainen H: Three cases of occupational asthma and rhinitis caused by garlic. *Clin Exp Allergy* 1993; 23:1011–1014.
- Lybarger JA, Gallagher JS, Pulver DW, Litwin A, Brooks S, Bernstein IL: Occupational asthma induced by inhalation and ingestion of garlic. *J Allergy Clin Immunol* 1982;69: 448–454.
- Falleroni AE, Zeiss R, Levitz D: Occupational asthma secondary to inhalation of garlic dust. *J Allergy Clin Immunol* 1981;68:156–160.
- Cronin E: Dermatitis of the hands in caterers. *Contact Dermatitis* 1987;17:265–269.
- Bassioukas K, Orton D, Cerio R: Occupational airborne allergic contact dermatitis from garlic with concurrent type 1 allergy. *Contact Dermatitis* 2004;50:39–50.
- Pires G, Pargana E, Loureiro V, Almeida MM, Pinto JR: Allergy to garlic. *Allergy* 2002;57:957–958.
- Uragoda CC: A comparative study of chili grinders with paprika splitters. *J Soc Occup Med* 1983;33:145–147.
- Shao-Hsuan Kao, Ching-Hsian Hsu, Song-Nan Su, Wei-Ting Hor, Wen-Hong Chang T, Lu-Ping Chow: Identification and immunologic characterization of an allergen, alliin lyase, from garlic (*Allium sativum*). *J Allergy Clin Immunol* 2004;113:161–168.
- Couturier P, Bousquet J: Occupational allergy secondary inhalation of garlic dust. *J Allergy Clin Immunol* 1982;70:145.
- Burney PGJ, Luczynska C, Chinn S, Jarvis D: The European Community Respiratory Health Survey. *Eur Respir J* 1994;7:954–960.
- Pellegrino R, Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R, Coates A, van der Grinten CPM, Gustafsson P, Hankinson J, Jensen R, Johnson DC, MacIntyre N, McKay R, Miller MR, Navajas D, Pedersen OF, Wanger J: Interpretative strategies for lung function tests. *Eur Respir J* 2005;26:948–968.
- American Thoracic Society/European Respiratory Society: ATS/ERS recommendations for standardized procedures for the on-line and offline measurement of exhaled lower respiratory nitric oxide and nasal nitric oxide. *Am J Respir Crit Care Med* 2005; 171:912–930.
- Deinhofer K, Sevcik H, Balic N, Harwanegg C, Hiller R, Rumpold H, Mueller MW, Spitzauer S: Microarrayed allergens for IgE profiling. *Methods* 2004;32:249–254.
- Pérez-Pimiento AJ, Moneo I, Santaolalla M, de Paz S, Fernández-Parra B, Domínguez-Lázaro AR: Anaphylactic reaction to young garlic. *Allergy* 1999;54:626–629.
- Mills ENC, Mackie AR: The impact of processing on allergenicity of food. *Curr Opin Allergy Clin Immunol* 2008;8:249–253.
- Ballmer-Weber BK, Hoffmann A, Wüthrich B, Lüttkopf D, Pompei C, Wangorsch A, Kästner M, Vieths S: Influence of food processing on the allergenicity of celery: DBP-CFC with celery spice and cooked celery in patients with celery allergy. *Allergy* 2002;57: 228–235.
- Mogensen JE, Ferreras M, Wimmer R, Petersen SV, Enghild JJ, Otzen DE: The major allergen from birch tree pollen, Bet v 1 binds and permeabilizes membranes. *Biochemistry* 2007;46:3356–3365.
- Maleki SJ, Chung SY, Champagne ET, Raufman JP: The effects of roasting on the allergenic properties of peanut proteins. *J Allergy Clin Immunol* 2000;106:763–768.
- Radauer C, Bublin M, Wagner S, Mari A, Breiteneder H: Allergens are distributed into few protein families and possess a restricted number of biochemical functions. *J Allergy Clin Immunol* 2008;121:847–852.
- Egger M, Mutschlechner S, Wopfner N, Gadermaier G, Briza P, Ferriera F: Pollen-food syndromes associated with weed pollinosis: an update from the molecular point of view. *Allergy* 2006;61:461–476.
- Figueroa J, Blanco C, Dumpiérrez AG, Almeida L, Ortega N, Castillo R, Navarro L, Pérez E, Gallego MD, Carrillo T: Mustard allergy confirmed by double-blind placebo-controlled food challenges: clinical features and cross-reactivity with mugwort pollen and plant-derived foods. *Allergy* 2005;60: 48–55.
- Bauer L, Ebner C, Hirschehr R, Wüthrich B, Pichler C, Fritsch R, Scheiner O, Kraft D: IgE cross-reactivity between birch pollen, mugwort pollen and celery is due to at least three distinct cross-reacting allergens: immunoblot investigation of the birch-mugwort-celery syndrome. *Clin Exp Allergy* 1996;26:1161–1170.
- Moneret-Vautrin DA, Morisset M, Lemerdy P, Croizier A, Kanny G: Food allergy and IgE sensitization caused by spices: CICBAA data (based on 589 cases of food allergy). *Allergy Immunol (Paris)* 2002;34:135–140.
- Scheurer S, Wangorsch A, Hausteiner D, Vieths S: Cloning of the minor allergen Api g 4 profilin from celery (*Apium graveolens*) and its cross-reactivity with birch pollen profilin Bet v 2. *Clin Exp Allergy* 2000;30: 962–971.
- Vallier P, Dechamp C, Vial O, Deviller P: A study of allergens in celery with cross-sensitivity to mugwort and birch pollens. *Clin Allergy* 1988;18:491–500.
- Leitner A, Jensen-Jarolim E, Grimm R, Wüthrich B, Ebner H, Scheiner O, Kraft D, Ebner C: Allergens in pepper and paprika. Immunologic investigation of the celery-birch-mugwort-spice syndrome. *Allergy* 1998;53:36–41.
- Fernández-Rivas M, González-Mancebo E, Rodríguez-Pérez R, Benito C, Sánchez-Monge R, Salcedo G, Alonso DM, Rosado A, Tejedor MA, Vila C, Casas ML: Clinically relevant peach allergy is related to peach lipid transfer protein, Pru p 3, in the Spanish population. *J Allergy Clin Immunol* 2003; 112:789–795.