

Original article

Sensitization and lung function in workers occupationally exposed to natural thickening products

Background: Three workers engaged in the manufacture of natural thickener products (*Cassia* spp., guar, and tamarind flour) were occupationally sensitized to *Cassia* spp. Therefore, a cross-sectional study on the prevalence of sensitization among and respiratory health of the employees of this plant was conducted.

Methods and Results: Sixty-two workers (36 with high, 26 with low exposure) participated in the survey. Skin prick tests and specific IgE tests with extracts of these components revealed that 11.3% were sensitized to *Cassia* spp. and 9.7% to at least one species of storage mites, with a significantly higher portion of atopic subjects in the sensitized group. Overall, 55% of the subjects reported work-related symptoms (upper and lower airways, eyes, or skin). FVC % pred. was significantly lower in highly exposed workers, while RV % pred. and RV%TLC % pred. were significantly higher in this group. In the multivariate model, sensitization was not a risk factor for impairment of lung function.

Conclusions: Dust exposure to flours may not only cause allergic sensitization but also induce chronic changes in lung function.

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Natural products such as guar, tamarind, and *Cassia* spp. flour are used to produce thickener products for dyes and foods. Products of *Cassia* spp. are widely used as a treatment for constipation (1). *Cassia* spp. (Leguminosae) are indigenous to India and are widespread in tropical countries. Sensitization to *Cassia* spp. has been described among workers exposed to dust in the process of manufacturing bulk laxatives (2) but also among people environmentally exposed to *Cassia* pollen (3). Whereas the study by Marks et al. (2) found that exposure to *Cassia* spp. mainly caused upper respiratory, eye, and skin symptoms with a low prevalence of occupational asthma, some case reports of occupational asthma due to *Cassia* exposure have been published (4, 5).

Guar gum is mainly used in the paper, food, cosmetic, pharmaceutical, textile, printing, polishing, and atomic metal processing industries, as well as being used as a thickener and emulsifier. Three or four species of guar (*Cyamopsis psoraloides*, syn. *Cyamopsis tetragonoloba*) are found in regions of Africa, Arabia, India, Pakistan, the USA, and northern Australia (6). Malo et al. (7) found 14 subjects with sensitization to guar gum (skin prick test or specific IgE) among 162 employees at a carpet-manufacturing plant using guar gum. In two of them, occupational asthma was confirmed. We have previously described one case of occupational asthma from guar gum (8), and Kanerva

et al. (9) published a paper on three cases of occupational allergic rhinitis from guar gum.

The tamarind tree (*Tamarindus indica*) grows mainly in India and tropical Africa. Like *Cassia* spp., its seeds are used for their laxative property. A case report (10) on occupational allergy to tamarind flour and a paper on the sensitizing effect of tamarind seeds have been published in Italy (11).

After the diagnosis of occupational sensitization among the staff of a plant producing natural thickeners, we conducted a study of respiratory health and allergic sensitization in this work force in October/November 1998. One aim of the study was to estimate the prevalence of sensitization to the natural products *Cassia* spp., guar, tamarind, polyzim (enzyme), and cornstarch, as well as to storage mites, in this population. In addition, the prevalence of respiratory symptoms and lung-function results were evaluated and compared with an internal control group.

Material and methods

Subjects

The cross-sectional survey was carried out in the autumn of 1998 on the site of a plant producing thickener. All 65 members of the factory's work force were invited to participate voluntarily in the cross-

sectional study. One subject was on annual leave, and two refused to participate. Of the remaining 62 participants, 36 production workers (mixing department, depolymerization, rolling mill, and enzyme section using polyzim) were supposed to be highly exposed, while 26 subjects working mainly in the laboratory and office were classified as less exposed (internal control group).

A control measurement of dust concentrations taken with personal samplers over one working day in the production area had shown concentrations of 23.9 mg/m³ for total dust and 0.35 mg/m³ for respirable dust (about PM₁₀=particles <10 µm in aerodynamic diameter).

Measurements were taken during the day shifts between 8 am and 5 pm.

All subjects were asked about their smoking habits, age, length of employment, job title, and respiratory symptoms within the last year. Work-related symptoms were defined as reporting at least one occurrence of symptoms at work of upper and lower airways, eyes, or skin. Asthma was defined as reporting at least one asthma attack within the last year or using asthma medication. Atopy was defined as having at least one positive skin prick test or one positive specific IgE result to any nonoccupational allergen.

Lung-function tests

Lung-function measurements were carried out on site in our mobile laboratory equipped with a body plethysmograph (Jaeger Masterlab, Würzburg, Germany [12]). Respiratory volumes (forced vital capacity [FVC], expired volume after 1 s [FEV₁], total lung capacity [TLC], residual volume [RV], and intrathoracic gas volume [ITGV]) were measured, as well as specific airway resistance (*sRaw*). The measuring procedure started with whole-body plethysmography with the subjects sitting in the cabin and respiring normally. Subsequently, at least three forced expiration maneuvers were performed, as recommended by the American Thoracic Society (13). Lung-function results were compared to age, sex, and height adjusted reference values, as proposed by the ECSC (14), and given as percentage of predicted (% pred.).

Skin prick tests

Skin prick tests were performed on the forearm of each subject. The allergens tested were 10 common inhalative allergens (*Dermatophagoides pteronyssinus*, *D. farinae*, cat, birch, mugwort, *Phleum pratense*, rye, *Penicillium notatum*, *Cladosporium herbarum*, and *Aspergillus fumigatus*) and three storage mites (*Acarus siro*, *Tyrophagus putrescentiae*, and *Lepidoglyphus destructor*) (Fa. Allergopharma, Reinbek, Germany; Fa. Bencard, Munich, Germany), as well as extracts of

Cassia spp., guar, tamarind, polyzim (enzyme), and cornstarch.

These extracts were prepared by dissolving 0.8% test suspension in 0.9% saline solution at 30°C for 1 h. After cooling to room temperature, the solution was centrifuged for 15 min (2800 rpm). To liquefy the *Cassia* spp. and guar extracts, an additional dilution with saline solution was performed (1:4). Prick extracts were preconserved in 0.5% phenol. Extracts were subsequently tested on 10 unexposed volunteers. None of them showed a positive skin reaction.

For all skin tests, histamine dihydrochloride (10 mg/ml) and saline solution were used as positive and negative controls. After 20 min, the largest diameter was measured, and the reaction was considered positive if the wheal size was at least as large as the diameter of the histamine wheal and at least 3 mm larger than the negative control.

Specific IgE determination

Blood samples were collected and analyzed for specific IgE to the same common aeroallergens as used for skin prick test. For the noncommercially available work-related allergens (*Cassia* spp., guar, tamarind, polyzim, and cornstarch), the skin prick solution was used. The analyses were done by the chemiluminescent method MagicLite[®], as described by Mazur & Pethran (15) (Ciba Corning, Fernwald, Germany).

Statistical analysis

Standard methods of statistical analyses were used, such as Fisher's exact test, the Mann-Whitney U test, and the multiple regression analysis. All statistical tests were done with a significance level of *P*=0.05.

Results

Study population

The characteristics of the groups are shown in Table 1. No significant difference between the two exposure groups could be observed in the demographic data, with the exception of a lower proportion of men in the less exposed group (*P*<0.001). The 12 exsmokers under study had stopped smoking at least 1 year before the study and were thus considered nonsmokers for the following analyses.

About one-half of the subjects complained of work-related symptoms. Ten workers reported wheezing, while six reported asthma, four of them also reporting wheezing. The prevalences of symptoms did not differ between the two groups.

Skin prick test and specific IgE

The prevalence of atopic subjects was 38.7% (Table 2). Ten subjects were sensitized to at least one work-related

Table 1. Characteristics of subjects by exposure group

	Less exposed group	Highly exposed group
Total number	26	36
Age [years], mean (range)	40 (18–59)	44 (25–63)
Male sex, (n [%])	15 [57.7***]	35 [97.2]
Length of employment [years], mean (range)	11 (0–35)	13 (0.1–35)
Current smokers ^a (n [%])	10 [38.5]	17 [47.2]
Ex-smokers (n [%])	3 [11.5]	9 [25.0]
Work-related symptoms (n [%])	13 [50.0]	21 [58.3]
Wheezing (n [%])	5 [19.2]	5 [13.9]
Asthma (n [%])	2 [7.7]	4 [11.1]
Cough (n [%])	1 [3.9]	7 [19.4]
Phlegm (n [%])	1 [3.9]	5 [13.9]
Atopic subjects ^b (n [%])	9 [34.6]	15 [41.7]

^aWorkers smoking within last year.^bAt least one positive skin prick test or specific IgE to non-work-related aeroallergens.*** $P < 0.001$ (Fisher's exact test) vs highly exposed group.

allergen, seven of them to *Cassia* spp., and six to storage mites. Of these workers, two were also sensitized to house-dust mites (Fig. 1).

Workers sensitized to *Cassia* spp. and/or storage mites were younger (35.2 vs 43.4 years; $P < 0.05$) and had shorter periods of employment than workers without these sensitizations (5.4 vs 13.8 years; $P < 0.05$). In the group of sensitized subjects, the prevalence of atopy was significantly higher. No significant differences could be observed between sensitized and unsensitized employees in exposure status, prevalence of work-related symptoms, and smoking status (Table 3).

Lung-function results

The mean levels of lung function are shown in Fig. 2 according to exposure group. Highly exposed workers had significantly lower mean FVC % pred. values and significantly higher mean RV % pred. and RV%TLC % pred. results than less exposed subjects ($P < 0.05$). There was a tendency for higher ITGV % pred. in highly exposed subjects (107.1 vs 98.4; $P = 0.11$). The other lung-function parameters did not differ significantly

between the two groups. A trend for higher *sRaw* values was seen in the highly exposed subjects (0.78 vs 0.64; $P = 0.09$). A multiple regression model using lung-function end points with significant differences between the two groups as dependent variables and exposure status, prevalence of work-related symptoms, work-related sensitization, length of employment, and smoking status as predictor variables was applied by the stepwise forward method (Table 4). FVC % pred. was significantly lower in subjects with higher exposure and workers reporting work-related symptoms. RV % pred. and RV%TLC % pred. were significantly elevated in highly exposed workers and those reporting work-related symptoms. Length of employment was positively correlated with RV % pred. and RV%TLC % pred. No influence of smoking status or sensitization to *Cassia* spp. and/or storage mites was seen.

Discussion

This study has shown a high prevalence of sensitization to *Cassia* spp. (11.3%) and storage mites (9.7%) among a group of workers in a plant producing thickener. The sensitization to *Cassia* spp. did not differ significantly from the prevalence found in a group of pharmaceutical workers by Marks et al. (2) (15.3%; $P = 0.51$, Fisher's exact test). There is only one study describing the prevalence of sensitization to *Cassia* pollen, among 140 patients environmentally exposed in India (3). The prevalence in that study of 12.3% sensitization to *Cassia* spp. in skin tests is not directly comparable to our study because all of these subjects suffered from respiratory allergies.

Work-related sensitization to storage mites has been found in several studies. For example, among bakers, a sensitization rate comparable to our study to at least one type of storage mite has been described (17.7%; $P = 0.18$, Fisher's exact test) (16). Similar prevalences of sensitization were observed in grain elevator workers (17) and farmers (18, 19). The latter study reported a prevalence of storage mite sensitization in the general population of about 6% and thus remarkably lower than in our study group. Kroidl (20) found a ratio of 2:1 of sensitization to house-dust mites to that of storage mites in patients undergoing skin prick testing. A cross-reactivity between these two families of Acaridae mites has been shown by Luczynska et al. (21). In the present study, only two of the six subjects sensitized to storage mites also showed sensitization to house-dust mites. A similar number of workers were sensitized to house-dust mites and storage mites. Thus, it is likely that the sensitization to storage mites found in our study was mainly work-related. All workers sensitized to storage mites had positive skin prick tests only. Of those workers sensitized to *Cassia* spp., 42.9% had positive skin prick test and specific IgE. Thus, the skin prick test

Table 2. Frequency of sensitization to nonoccupational and occupational aeroallergens in skin prick test and specific IgE

Number [%]	Only prick	Only specific IgE	Both	Total
Atopic subjects ^a	8 [12.9]	7 [11.3]	9 [14.5]	24 [38.7]
<i>Cassia</i> spp.	4 [6.5]	0 [0.0]	3 [4.8]	7 [11.3]
Guar	0 [0.0]	0 [0.0]	0 [0.0]	0 [0.0]
Tamarind	0 [0.0]	0 [0.0]	0 [0.0]	0 [0.0]
Polyzim	0 [0.0]	0 [0.0]	0 [0.0]	0 [0.0]
Cornstarch	0 [0.0]	0 [0.0]	0 [0.0]	0 [0.0]
Storage mites	6 [9.7]	0 [0.0]	0 [0.0]	6 [9.7]

^aAt least one positive skin prick test or specific IgE to non-work-related aeroallergens.

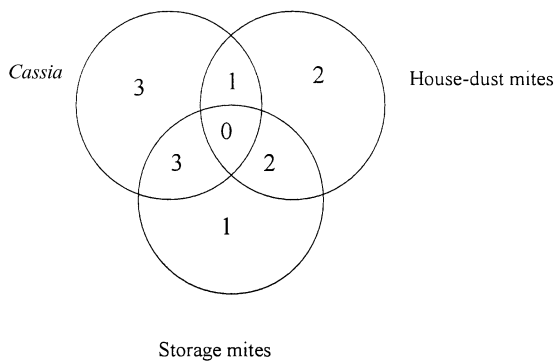


Figure 1. Sensitization (number) to house-dust mites, *Cassia* spp., and/or storage mites in skin prick test and/or specific IgE ($n_{\text{total}}=62$).

was shown to be more sensitive than specific IgE, as found by other authors (22). Theoretically, allergy tests using only partly standardized allergen extracts may underestimate the prevalence of sensitization. Thus, we cannot entirely exclude false negative results.

Some studies have reported a work-related allergy to guar gum (7–9) and tamarind (10), but none of the subjects under study had been sensitized to these agents or to polyzim and cornstarch. The percentage of atopic subjects was comparable to that in general population studies (23). When subjects with work-related sensitization to *Cassia* spp. and/or storage mites were compared to the workers not sensitized, the proportion of atopic subjects was higher among workers with sensitization.

Table 3. Differences between study subjects sensitized to *Cassia* spp. and/or storage mites and unsensitized subjects

Sensitization to <i>Cassia</i> spp. and/or storage mites	No	Yes
Total number (<i>n</i>)	52	10
Age (years) (mean [minimum–maximum])	43.4 [18–63]	35.2 [25–43]
Length of employment (years)	13.8 [0–35] [§]	5.4 [0–18]
Atopy (<i>n</i> [%])	17 [33]	7 [70] [*]
Highly exposed subjects (<i>n</i> [%])	30 [58]	6 [60]
Work-related symptoms (<i>n</i> [%])	26 [50]	8 [80]
Asthma (<i>n</i> [%])	3 [6]	3 [30] [*]
Current smokers (<i>n</i> [%])	20 [38]	7 [70]

$P<0.05$, Mann–Whitney U-test.

^{*} $P<0.05$, Fisher's exact test.

[§] $n=51$.

This has also been described in the previous report of Marks et al. (2), but they found this effect to be limited to the nonsmoking subjects. Therefore, atopic subjects seem to be more likely to develop work-related sensitization to *Cassia* spp. and/or storage mites. In addition, 30% of the sensitized subjects had asthma attacks and/or had been using asthma medication within the preceding year. The finding of a similar percentage of highly exposed subjects in sensitized and unsensitized subjects is probably due to the fact that the workers of the less exposed group were not completely unexposed. It would be interesting to investigate whether there is a dose-response relationship between

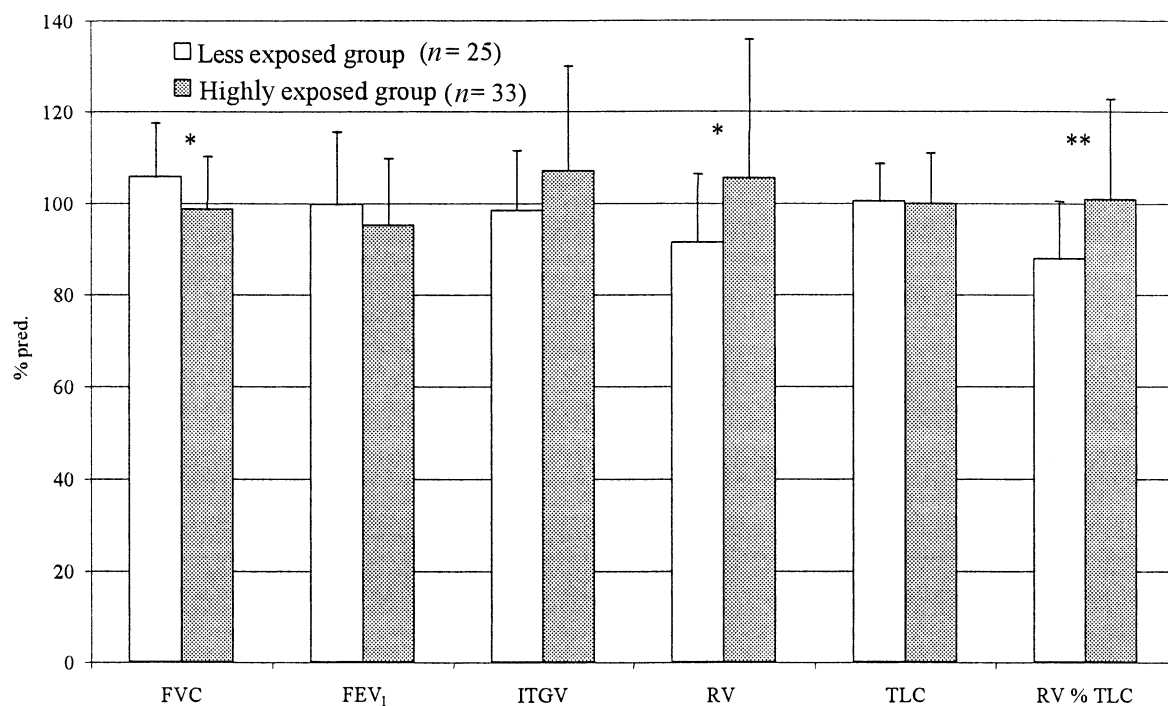


Figure 2. Mean lung-function results $\pm$ SD by exposure group. $*P<0.05$, Mann–Whitney U-test. $**P\leq 0.01$, Mann–Whitney U-test.

Table 4. Multiple regression models with lung-function results as dependent variables, and exposure status, prevalence of work-related symptoms, length of employment, and smoking status as possible predictor variables by stepwise forward method

<i>n</i> = 57		Exposure status (1 = low; 2 = high)	Work-related symptoms (0 = no; 1 = yes)	Sensitization to <i>Cassia</i> spp. and/or storage mites (0 = no; 1 = yes)	Length of employment (years)	Smoking (0 = no; 1 = yes)
FVC % pred.	β	−0.27	−0.30	0.13	—	—
R = 0.41	SE of β	0.13	0.13	0.13	—	—
<i>P</i> < 0.02	<i>P</i>	0.04	0.03	0.32	—	—
RV % pred.	β	0.25	0.27	—	0.22	—
R = 0.43	SE of β	0.12	0.12	—	0.12	—
<i>P</i> < 0.01	<i>p</i>	0.05	0.04	—	0.09	—
RV % TLC	β	0.30	0.37	—	0.23	—
R = 0.53	SE of β	0.12	0.12	—	0.12	—
<i>P</i> < 0.001	<i>p</i>	0.01	0.003	—	0.05	—

β : standardized multivariate regression coefficient; SE of β : standard error of β ; R: regression coefficient.

the concentration of the sensitizing agents under study and the sensitization of the exposed subjects. Moreover, no studies are known to have analyzed the prevalence of sensitization to natural thickener products in factories working with the end products produced in the factory under study (e.g., dye- or animal feed-producing factories).

Furthermore, among subjects with sensitization to work-related allergens, the length of employment was significantly shorter. It is possible that workers with work-related sensitization are more likely to develop work-related symptoms and thus leave the work force. This “healthy worker effect” has been described in many occupational studies (24) and is a general problem of the cross-sectional study design. It could be one reason for the lack of a higher proportion of highly exposed subjects or workers with work-related symptoms among the sensitized population. Suffering from symptoms is more likely to force workers to quit their jobs than a lung function decline, because symptoms might directly influence the quality of life. However, a loss of lung function is often recognized as delayed.

Thus, it is not surprising that we found no significant differences in the prevalence of symptoms between the two exposure groups, while a significant difference in lung function was observed. Length of employment had a negative effect on RV % pred. and RV%TLC % pred. (NS). The almost significantly increased *sRaw* in the highly exposed group may indicate a tendency to obstructive airway impairment due to occupational exposure. In line with this finding, the significant differences in FVC % pred., RV % pred., and RV%TLC % pred. suggest the development of hyperinflation.

Marks et al. (2) did not report the results of FEV₁ and FVC in their paper on asthma and allergy associated with occupational exposure to *Cassia* in a pharmaceutical work force. In some case reports on occupational sensitization to *Cassia* spp., the lung-function results of the patients were within normal ranges (4, 5). Sensitization had no significant influence on the lung-function results in the multiple regression model. Therefore, it may be hypothesized that exposure to dust, and not sensitization to work-related allergens, caused the observed changes in lung function in the participants. Thus, changes in lung function in the highly exposed group may be the result of a higher dust exposure, and not a result of sensitization resulting in occupational asthma. In addition, the prevalence of cough and phlegm tended to be higher in the production workers than the internal control group.

In conclusion, the risk of work-related sensitization in workers in a plant producing natural thickener was shown to be high (16.1%). Sensitized subjects had a shorter period of employment, possibly indicating job changes due to sensitization to occupational allergens. Impairment of lung function could be due to higher dust concentrations in the production area. Thus, dust reduction in this part of the plant should be strongly recommended.

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