

Factors related to the development of sensitization to green coffee and castor bean allergens among coffee workers

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Summary

Background Occupational allergic respiratory symptoms in coffee workers have been frequently reported, but the ultimate cause of sensitization is still debated, castor bean being considered besides green coffee beans. Atopy and cigarette smoking have been suggested as promoting factors of sensitization for several occupational allergens.

Objective This study was carried out to assess the prevalence of allergic respiratory symptoms and of sensitization to both green coffee beans and castor bean in the whole workforce of a coffee manufacturing plant. Furthermore we wanted to ascertain both the presence of castor bean antigens in the settled dust of the green coffee beans warehouse and the possible crossreactivity between the two beans. Meanwhile, the effect of smoking and atopy was considered.

Method Two-hundred and eleven workers were examined. A questionnaire on oculorhinitis and asthma was administered and skin-prick tests for green coffee beans, castor bean and 15 common inhalant allergens were carried out. Isoelectric focusing, isoelectric focusing immunoblot and radioallergosorbent assay (RAST) inhibition were performed on samples of settled environmental dust from the green coffee area, as well as on castor bean and green coffee beans.

Results Ten per cent of the workers complained of oculorhinitis alone and 16% of asthma (nearly always associated with oculorhinitis). The overall prevalence of skin-sensitization was: 15% for green coffee beans, 22% for castor bean, 22% for common allergens. Evidence of sensitization to occupational allergens was more common in smokers, with a more than twofold increase in relative risk. The strong association between skin positivity to common and occupational allergens suggests that atopy acts as an enhancing host factor towards occupational sensitization. The analysis of the dust confirmed the presence of castor bean antigens.

Conclusion Our findings indicate that castor bean is the major cause of occupational sensitization among coffee workers, whereas smoking and atopy act as enhancing factors.

Keywords: sensitization, green coffee bean, castor bean, coffee workers, atopy, smoking habits

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Introduction

Occupational exposure to coffee dust has often been reported as being responsible for allergic respiratory

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symptoms [1–3]. However, extensive epidemiological surveys are scanty and the prevalence of sensitized workers varies from one study to another [3–8]. Moreover, the ultimate cause of the respiratory allergy is debated: besides green coffee bean (GCB), castor bean (CB) has been shown to be a distinct primary cause of sensitization in coffee workers [2, 3]. CB is thought to be an accidental contaminant of GCB, as some coffee sacks may have once contained CB or may have been stored in contaminated ship containers [6, 9]. However, in the last few years, coffee producers have started using new burlap or plastic sacks and/or specific containers; such measures should, in theory, have reduced the relevance of CB contamination [7].

Some studies reported an increased risk of developing occupational allergy in smokers in as much as they generally have higher levels of specific IgE antibodies and a higher prevalence of occupational asthma compared with non-smokers. Such findings were related to occupational exposure to tetrachlorophthalic anhydride [10], platinum salts [11], ispaghula and senna [12], ispaghula and green coffee/castor bean [13], *Bacillus subtilis* enzymes [14] and urinary proteins shed by laboratory animals [15]. Moreover, the latency required for sensitization has been reported to be shorter among smokers in an industrial population exposed to ethylene diamine [16].

This study was carried out in an attempt to assess the prevalence of allergic respiratory symptoms and of sensitization to both GCB and CB in the whole workforce currently exposed in a coffee manufacturing plant.

An attempt was also made to ascertain both the presence of CB antigens in the settled dust of the GCB warehouse, where bags are split open and emptied, and a possible crossreactivity between the two beans.

Materials and methods

Patients

Two hundred and eleven employees currently exposed in a coffee manufacturing plant were examined at the Department of Traumatology, Orthopaedics and Occupational Medicine of Turin University. The sample was subdivided into two groups: those who had been or were working in the green coffee department even for short periods and those who never did.

As far as smoking habits are concerned, ex-smokers were subdivided according to time from stopping; those who had stopped at least 5 years prior to investigation were considered non-smokers and those who had stopped thereafter were considered smokers. No one

had been previously exposed to coffee beans in other factories.

A simple allergic symptom questionnaire dealing with either seasonal or perennial oculorhinitis and asthma was administered to all the subjects, who were subsequently skin tested. Informed consent was obtained from all patients before the study.

Skin tests

Skin-prick test was carried out using: (a) extracts of 15 common allergens (CA) (Hollister Stier): grass, mugwort, ragweed, plantain, birch, beech (10 000 pnu/mL) and pellitory (5 000 pnu/mL) pollen; aspergillus mix, penicillium mix (10 000 pnu/mL); mites (*Dermatophagoides farinae*, *D. pteronyssinus*) (5 000 pnu/mL), animal danders (cat, dog, cow, horse) (5% w/v); and histamine solution (10 mg/mL); (b) castor bean (CB) (extracts prepared by Lofarma, Milan, Italy). The seeds were prepared as follows: ground with homogenizer, defatted with several changes of diethylether and dried, dry powder extracted at 2% w/v ratio with stirring in phosphate buffered saline (PBS) (pH 7.2, 0.125 M) for 24 h at 5°C. The suspension was centrifuged and the clear supernatant collected and heated at 100°C for 30 min, according to Lehrer [17] to inactivate ricin, which could provoke pseudo-inflammatory reactions [18]. The solution was centrifuged and the clear supernatant collected and dialysed (cut-off 3500 Da) against several changes of saline and 0.8% phenol added. The extract was diluted 1 in 2 with glycerin and sterilized through 0.22 micron membranes (Pal) resulting in a final w/v ratio of 1%; (c) the 12 green coffees in use in the plant (extracts prepared by Lofarma, Milan, Italy) coming from different countries: Brazil (three varieties: Conilon, S. Paulo, Santos), Columbia, Costarika, Guatemala, Ivory Coast, Kenia, Nicaragua, San Salvador, Tanzania (two varieties: mixed Tanzania and Bukoba). The extracts were prepared according to the same procedure used for CB, with the following modifications: the extraction w/v ratio was 4%, and therefore the final ratio 2%; heating at 100°C had been omitted.

The skin-test positivity was evaluated by comparing the allergen weal size to histamine size. Each weal was quantified as the mean of the greatest diameter and the one perpendicular in its middle point. Allergen weal values were then scored as multiples or fractions of histamine weal value and reactions were deemed positive when the ratio to histamine was at least one quarter, according to Nelson [19]. All values lower than that were considered negative without further defining doubtful categories. The prevalence of skin positivity to CB in the general population from the same area

Table 3. Distribution of skin-test results for occupational allergens (OA) according to atopic status

	Occupational allergens +	Occupational allergens -	Odds ratio
Common allergens +	25	20	8.18
Common allergens -	22	144	

$$\chi^2 = 31.42; P < 0.001.$$

was measured. Three hundred subjects consecutively attending the outpatient department for allergological screening of rhinitic and/or asthmatic symptoms were skin-prick tested for CB. No one had positive results.

Isoelectric focusing (IEF) and IEF immunoblot

Samples of CB, GCB and settled environmental dust from the green coffee working area (ED) were extracted in phosphate buffered saline (PBS) (PBS: 0.85% NaCl, 0.087% Na₂HPO₄, 0.1% NaN₃, 0.012% KH₂PO₄) diluted to: CB, 82 600 pnu/mL; GCB, 73 000 pnu/mL; ED, 32 000 pnu/mL. One and half millilitres of GCB and CB extracts and 3 mL of ED extract were dialysed overnight at 4°C against distilled water using 3500 Da membrane tubing. After dialysis 500 µL aliquots were dispersed into preweighed freeze-drying vials. Of the remaining undialysed materials 3 × 250 µL of the GCB and CB extract and 5 × 250 µL of the ED extract were also dispersed into freeze-drying vials. All vials were freeze-dried for 2 days; weights of freeze-dried materials were 13.7, 3.3, 3.5 mg/vial respectively. IEF was performed according to the standard procedure described by Ibsen and Lowenstein [20]. Briefly, samples (35 mg/mL, 20 µL) were applied in duplicate to the polyacrylamide gel plate (LKB-Pharmacia); each run was performed with a prefocusing of 7 min and a sample run time of 1 h 40 min.

The blot was performed according to the method described by Baldo and Tovey [21]. Briefly, a serum pool obtained by mixing several sera from subjects positive to GCB and/or CB (SP) was incubated for 3 h with the blot, washed with 0.15 M NaCl and incubated overnight at 20°C with anti-human IgE ¹²⁵I lot Bg 80 at 32 355 CPM/50 µL. The blot was then washed with 0.15 M NaCl and distilled water and allowed to air-dry before being exposed to KODAK XOMAT S X-ray film for 3 days at ambient temperature. All samples were detected by infra-red scanning.

Table 4. Distribution of perennial symptoms (asthma and/or oculorhinitis) and skin-test results for occupational allergens

	Occupational allergens +	Occupational allergens -	Odds ratio
Perennial symptoms +	20	23	4.54
Perennial symptoms -	27	141	

$$\chi^2 = 16.608; P < 0.001.$$

Inhibition radioallergosorbent assay (RAST)

Allergen discs of GCB, CB and ED were prepared, according to the method described by Ceska [22], with distilled water and stored in PBS pH 7.4 containing 0.1% sodium azide. Each extract of GCB, CB and ED was reconstituted to give a concentration of 0.5 mg/mL in RAST buffer. Fifty microlitres of each were plated out in duplicate four times. For maximum binding control 50 µL aliquots of RAST buffer were plated out, while 100 µL RAST buffer aliquots were used for non-specific binding controls. Fifty microlitres of SP diluted 1:1 with RAST buffer were added to all sets of the duplicates. The plate was incubated overnight at 4°C with mixing. After washing 100 µL anti IgE ¹²⁵I lot Bg 81 at 50 490 CPM was added and the plate incubated overnight at 20°C. The discs were then washed and counted for 2 min on an NE 1600 gamma counter.

Statistical methods

Simple chi-squared statistics and odds ratios (as a measure of relative risk) were used to study the relationship between skin sensitization to occupational allergens and both sensitization to common allergens and the prevalence of respiratory symptoms. The effect of smoking on skin sensitization was examined allowing for differences in working departments, i.e. exposure to green or roasted coffee respectively. A stratified analysis was, therefore, carried out according to the Mantel Haenszel (MH) method, resulting in a combination of fourfold tables. The whole set of data was subdivided into two strata (green or roasted coffee), for which single odds ratios (OR), and 1 degree of freedom (d.f.) chi-squared were computed. Summary odds ratios and chi-squared for the associations were also calculated, together with chi-squared test for the homogeneity of the OR across the strata. The same procedure was used

Table 1. Distribution of symptoms according to type of exposure and smoking habits

	Total	Green coffee workers		Roasted coffee workers	
		Smokers	Non-smokers	Smokers	Non-smokers
	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)
No symptoms	155 (74)	17 (66)	20 (77)	42 (71)	76 (76)
Oculorhinitis (without asthma)	22 (10)	4 (15)	1 (4)	6 (10)	11 (11)
Perennial	15 (7)	3 (11)	1 (4)	2 (3)	9 (9)
Seasonal	7 (3)	1 (4)	0 (0)	4 (7)	2 (2)
Asthma (alone or associated to oculorhinitis)	34 (16)	5 (19)	5 (19)	11 (19)	13 (13)
Perennial	30 (14)	5 (19)	4 (15)	9 (15)	12 (12)
Seasonal	4 (2)	0 (0)	1 (4)	2 (4)	1 (1)
Total	211 (100)	26 (100)	26 (100)	59 (100)	100 (100)

to assess whether there was a significant association between atopy and skin sensitization to occupational allergens (OA), allowing for differences in smoking habits.

Results

As many as 25% of the subjects under study were considered exposed, at least for some time, to green coffee. This subgroup (52 men) had an exposure duration (9.0 ± 5.0 years) similar to that (10.2 ± 5.5 years) of the roasted coffee workers (55 men and 104 women). Green coffee workers (GCW) were slightly younger (36.2 ± 8.1 years) than roasted coffee workers (RCW) (42.2 ± 9.4 years).

Table 1 reports the distribution of the symptoms according to job and to smoking habits. Asymptomatic subjects were 74% of the whole group, whereas 10% complained of oculorhinitis alone and 16% of asthma (associated in all cases but one with oculorhinitis).

Symptoms were reported to be perennial by the majority of the subjects affected particularly as far as asthma was concerned (14%).

Table 2 refers to the skin-test results according to allergen associations, type of exposure and smoking habits. The overall prevalence of sensitization was: 15% for GCB, 22% for CB, 22% for CA. Skin-test negative subjects were 50% of GCW and 74% of RCW. CB accounted for the greatest number of positive cases (35% of GCW and 18% of RCW), then followed

by CA (35% of GCW and 17% of RCW) and GCB (27% of GCW and 11% of RCW).

CB positivity was not associated with GCB positivity in 32% of the cases. GCB positive workers were almost always CB positive. There was no appreciable difference in the frequency of skin positivity to the 12 varieties of coffee used in the plant. The mean diameter of weals for the different classes of allergens was distributed as follows: CB = 10.27 mm, GCB = 5.97, CA = 5.60 (histamine = 6.63).

The prevalence of positivity to CA was twice as high in GCW compared with RCW. In the whole group dust mites accounted for the greatest number of positive cases ($n = 21$), followed by grass pollen ($n = 11$), penicillium ($n = 4$), mugwort ($n = 3$), pellitory ($n = 3$), beech ($n = 1$).

The prevalence of skin positivity to at least one CA (i.e. atopic status), for smokers and non-smokers taken together, was 53% among workers sensitized to OA vs 12% among non-sensitized workers. Table 3 shows a strong and highly significant association ($\chi^2 = 31.42$, $P < 0.001$) between atopic status and skin-test results for OA. This association was not modified by smoking habit, when subdividing all cases into smokers and non-smokers (not reported in the Table for simplicity) and adopting the above mentioned MH procedure, which showed no difference of the odds ratios across smoking categories.

As far as symptoms are concerned, asthma and oculorhinitis were considered together. The great majority

Table 2. Skin-test positive cases according to allergen grouping, type of exposure and smoking habits

	Total	Green coffee workers		Roasted coffee workers	
		Smokers	Non smokers	Smokers	Non smokers
	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)
Castor bean	3 (1)	0 (0)	0 (0)	3 (5)	0 (0)
Castor bean and green coffee	19 (9)	6 (23)	2 (8)	5 (8)	6 (6)
Castor bean and common allergens	12 (6)	1 (4)	3 (11)	5 (8)	3 (3)
Castor bean Green coffee and common allergens	13 (6)	5 (19)	1 (4)	4 (7)	3 (3)
Green coffee	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Green coffee and common allergens	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Common allergens	20 (10)	3 (11)	5 (19)	4 (7)	8 (8)
Negative cases	144 (68)	11 (43)	15 (58)	38 (65)	80 (80)
Total	211 (100)	26 (100)	26 (100)	59 (100)	100 (100)

of skin-negative cases were asymptomatic, except for 15% of the subjects, who mostly reported perennial symptoms. The pattern of symptoms complained of by subjects positive only to CA was in agreement with the type of skin positivity.

Thirty-six per cent of subjects positive to OA alone

Table 5. Distribution of the skin-test results for occupational allergens according to smoking habits arranged in two strata related to working department

	Smokers	Non-smokers	Odds ratio
Green coffee workers			
Occupational allergens +	12	6	2.86
Occupational allergens -	14	20	
Roasted coffee workers			
Occupational allergens +	17	12	2.97
Occupational allergens -	42	88	

χ^2 MH: 8.913 ($P < 0.01$)

RR MH: 2.931 (95% C.L.: 1.447–5.937)

χ^2 hom: 0.0093 (NS.)

(CB and GCB taken together) were symptomatic and mainly affected by perennial symptoms.

Subjects positive to both OA and CA were symptomatic to a greater extent (64%). Approximately one half of these subjects had perennial symptoms while 12% (three subjects) reported seasonal symptoms and showed skin positivity to seasonal allergens (grass pollen).

Table 4 shows the distribution of perennial symptoms (of most interest due to their possible occupational origin) according to skin-test results for OA (whether or not associated with CA). In spite of the strong and highly significant association, it must be stressed that only 47% of symptomatic subjects had positive skin-test results, which is about the same proportion (43%) of OA skin-positive subjects with symptoms. Therefore, the presence of symptoms can only partly be predicted from skin tests.

Table 5 shows the distribution of the cases according to OA skin-positivity and smoking habits arranged in two strata related to working department. Globally, there was a significant effect of smoking on skin sensitization. Moreover, the smoking effect was consistent across occupational exposure categories (d.f.1 χ^2 for homogeneity over the strata: 0.009 statistically not significant).

The effect of different occupational exposure itself was not significant (summary odds ratios, not reported in Table, for GCW to RCW: 2.15, χ^2 3.63).

Table 6. Percentage of inhibition of the RAST results at 0.5 mg/mL among green coffee bean, castor bean and environmental dust systems

	Green coffee bean	Castor bean	Environmental dust
Green coffee bean	62.2	3.5	54.3
Castor bean	6.9	34.4	51.8
Environmental dust	51.3	14.5	56.2

Inhibition RAST results are shown in Table 6. A negligible inhibition by CB in GCB system and by GCB in CB system was observed, which suggested a slight or absent crossreactivity between the two. A clear inhibition was produced by both GCB and CB in ED system and by ED in all three systems.

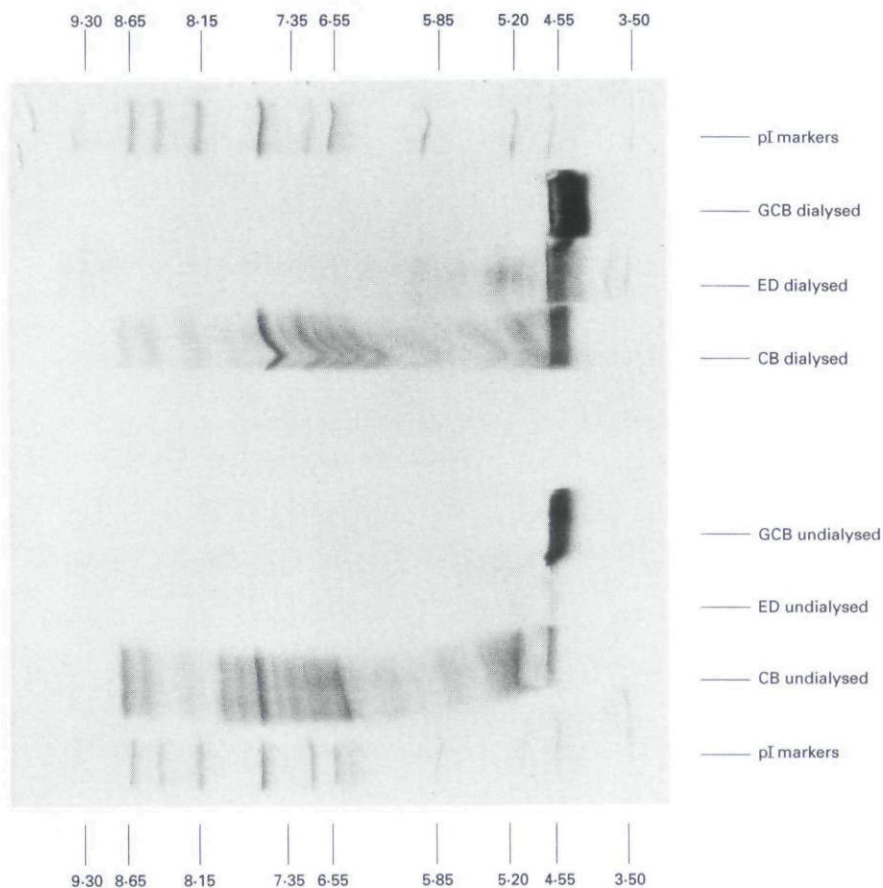
IEF results are shown in Fig. 1. Most of the GCB material is concentrated at pI 4.5 with slight, but perfectly detectable by infra-red scanning, stained component dispersed throughout the pI range. The CB

extract gave a very strong stained profile throughout the pI range, with the strongest serum binding components at approximately pHs 4.55–5.30, 6.20, 6.55, 7.5 and 8.70. The ED extract gave a profile containing many components with pIs common to those in the CB extract. The two bands found in the ED between pH 8.65 and 9.30, are not present in the CB but in the GCB extract. As previously underlined, all the components were perfectly detectable by infrared scanning, even though occasionally poorly visible on gel slide image, due to the low protein concentration.

IEF immunoblot confirmed the above results, and in particular that ED extract contained a number of components with common pIs to those present in CB extract, even if the binding properties were not very strong.

Discussion

The prevalence of workers with skin positivity to OA found in this study was substantial and identical to that reported by Osterman [8] (22%). Skin positivity for GCB appears to be randomly distributed among the 12 varieties used with no single type showing a higher presence of positive results.

**Fig. 1.** Isoelectric focusing gel for extracts of green coffee (GCB), castor bean (CB), environmental dust (ED).

The prevalence of CB sensitization (22%) was higher than that due to GCB (15%). CB can be considered a strong allergen which constantly produced weals larger than GCB and CA did.

Subjects employed in the processing of green coffee were skin positive to OA more frequently (35%) than those employed in roasted coffee areas only (18%), although the difference did not reach the statistical significance level. This finding may be partly explained by the high turnover in the factory which may have mislead our job classification. However, a contamination of roasted coffee areas by green coffee dust can not be ruled out. The immunological analysis of ED extract confirmed the definite, though slight, presence of CB antigens, as was shown by IEF profiles and RAST inhibition. In fact, the latter showed the presence in ED of both GCB and CB antigens. This last finding suggests that a low contamination of raw coffee by CB still occurs in the firm, at least occasionally. Therefore, working processes must be modified by means of both a more stringent and safer transporting system of green coffee to the factory and a strictly automated processing throughout the factory itself. Sensitization to OA was found to be more common in smokers, with a more than twofold increase in relative risk. This finding is in agreement with literature data, which suggest that smoking may increase allergen access to submucosal immunocompetent cells [10].

Skin positivity to CA was present in 22% of the whole group. Such a prevalence is considerably lower than that reported by Thomas [7] (54%), which is, however, based on less stringent diagnostic criteria (i.e. weals at least 1 mm greater in diameter than those of the negative controls were deemed positive in that paper). Data deriving from studies on general population from both Europe and the USA, showed a prevalence ranging from 28% to 36%, thus slightly higher than in this study [23–26]. This may be due to selective mechanisms entailing either the rejection of job applicants found skin-positive for CA at preliminary medical screening, or the withdrawal of subjects with respiratory complaints of a possible atopic origin.

The strong association between skin positivity to OA and CA suggests that atopy acts as an enhancing host factor for occupational sensitization. In this regard our findings are in agreement with Osterman's data [8] but disagree with Thorpe's [23] results. It should be stressed that atopy has been described as a promoting factor in developing sensitization to other occupational high molecular weight organic allergens, such as enzyme detergents, laboratory animal danders and flour dust [27, 28].

Considerable debate exists as to the policy to be

adopted for atopic subjects applying for these occupations. The choice is between either the exclusion of atopics from employment [29] or having them followed by very stringent environmental control and medical follow-up [30]. The question is not easy to resolve. Our data seem to suggest that, in this population, the exclusion of the 45 atopics (21% of the total sample) would have reduced the number of people sensitized to OA from 47 to 22, with a lowering of 53%. The suitability of such an exclusion rests, not only on medical, but also on social and ethical concern.

Similar considerations could apply to smoking habits, as, according to our results, smoking increases the relative risk of sensitization to OA. In this case, a policy of exclusion seems even more unrealistic (smokers being, by the way, considerably more than atopics). However, educational policies should be implemented and smoking during work hours should be strictly forbidden.

In our sample, the proportion of subjects sensitized to mites is consistent with Thorpe's findings [23], but unexpectedly high when using as reference our findings derived from symptomatic subjects. In fact skin-test positivity in our outpatient department over a 5-year period prior to this study, was distributed as follows: 41.2% grass pollen, 23% different pollens, 14.2% pellitory pollen, 14% mites, 7.6% animal danders and moulds (unpublished data).

Even if sensitization to dust mites may contribute in causing the perennial symptoms recorded in our group, the pattern is consistent with a prevailing occupational origin. However, it must be stressed that only about half the symptomatic workers are positive to OA. This finding could partly be explained by an irritative, rather than allergic nature of symptoms [8].

We should like to stress the high prevalence of oculorhinitic symptoms: these were reported by 26% of the total sample and almost invariably accompanied chest symptoms.

In conclusion, our findings indicate that CB is the major cause of occupational sensitization among coffee workers, whereas smoking and atopy act as enhancing factors. People at risk are not only those confined to the green coffee warehouse, in as much as sensitized workers were observed also in departments processing roasted coffee.

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