

Short communication

Protein and allergen content of various natural latex articles

Baur X, Chen Z, Raulf-Heimsoth M, Degens P. Protein and allergen content of various natural latex articles.
Allergy 1997; 52: 661-664. © Munksgaard 1997.

Proteins remaining in products made of natural rubber latex are potential sensitizers. In the present work, we quantified the releasable protein and allergen contents in 37 brands of latex gloves and 26 other latex products. Our results demonstrate the presence of widely varied protein and allergen contents in various latex articles and the lack of a correlation between the protein and allergen values. These findings may assist hospital management and medical staff to take effective preventive measures.

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Key words: allergy; gloves; latex.

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Accepted for publication 11 December 1996

Type I allergy to proteins released by articles made of natural latex has become a growing problem in recent years (1-8). High-risk populations include medical staff and patients with spina bifida or urogenital disorders undergoing multiple medical investigations and operations. Latex proteins cause sensitization due to direct skin contact as well as to inhalative uptake after absorption of glove powder that has become airborne (6, 9-13). Because of different production procedures, which include protein degradation and/or leaching by various methods, a broad range of allergens exists in latex-made products. Our study aimed to measure releasable allergens and proteins from commercially available gloves and other latex articles.

Material and methods

The amount of total water-extractable proteins associated with natural rubber products was determined by the modified Lowry method, according to the recommendation of the American Society for Testing and Materials (ASTM) (the standard test method for analyzing proteins in natural rubber and its products; ASTM D 5712-95, Annual Book of ASTM Standards, Vol. 14.02, June 1995). Briefly, 6-10 g of latex glove material or other latex products was cut into small pieces ($\approx < 1 \text{ cm}^2$) and extracted in distilled water (8 ml per gram of

natural rubber specimen) for 2 h at 37°C. After removal of rubber particles by centrifugation at 1000 g for 10 min, the extract containing aqueous soluble proteins was passed through a low protein-binding filter (Millipore) of 0.45 μm pore size. For removal of the interfering substances, a precipitation of proteins in the extract was carried out by adding 0.1 ml of 0.15% (w/v) sodium deoxycholate (DOC) to 1 ml of test protein extract. After vortexing and standing for 10 min at room temperature, 0.1 ml of 72% (w/v) trichloroacetic acid (TCA) and 0.1 ml of 72% (w/v) phosphotungstic acid (PTA) were added. After another 20 min at room temperature, the extract mixture was centrifuged for 15 min at 6000 g, and the supernatant was removed. The protein pellet was completely redissolved in 0.1 N NaOH. The protein content was then determined with a Lowry reagents kit from Bio-Rad (catalog no. 500-0116) and the ovalbumin as standard protein.

The quantitative analysis of latex allergens in the extracts of latex articles was achieved by a competitive RAST-immunoinhibition assay using the Pharmacia CAP System. As source antibodies, a serum pool (latex-IgE value: 11.4 kU/l in CAP) from five latex-allergic health-care workers was used. All five patients were shown by clinical history to have suffered from workplace-related urticaria, and four also had rhinitis, conjunctivitis, and bronchial

asthma. All five showed a positive skin prick test to latex and the presence of specific IgE antibodies to latex in their sera by latex RAST. A latex protein extract containing 0.8 mg protein per milliliter, prepared by centrifugation of a nonammoniated natural rubber tree latex from Sri Lanka, was used as reference allergen. A standard inhibition curve was constructed by competition of the reference allergen with the solid-phase ImmunoCAP latex allergen for specific IgE binding, in which the pooled serum (40 μ l) was preincubated individually with 10 μ l of the latex reference allergen at different dilutions, before reacting with the ImmunoCAP allergen. Quantification of latex allergen in sample extracts was achieved by preincubating 20 μ l of extract solution with 80 μ l of pooled serum to compete with ImmunoCAP latex allergen in the inhibition assay (in duplicate). The inhibition capacity of the sample extract was then compared with that of the reference allergen. The latex allergen content in rubber articles was expressed as protein mass per gram rubber latex. The extracts with very low protein content (lower than 5 μ g/ml) were lyophilized and redissolved in 1 ml water. The allergen content in the concentrated extract was then determined as described above. The detection sensitivity of the assay was 20 ng allergen, corresponding to 2 μ g allergen/g rubber.

Results and Discussion

Our test results with 21 different brands of commercial gloves can be compared with the findings of other authors (Table 1) (14–17). Although the methods used were different, there is a moderate overall similarity in the releasable protein contents found by most authors. Discrepancies exist in protein content of the glove brands Biogel[®] M (no. 5), Exam No Powder (no. 7), Gammex[®] (no. 9), and Sempermed[®] (no. 20). According to Alenius et al. (14), the Bradford method always produces a much lower protein content than the Lowry method.

With regard to allergen concentrations, generally heterogeneity exists between results of different investigators. This is especially true of Triflex[®] (no. 21), Conform (no. 6), Biogel M (no. 5) and Neutalon[®] (no. 14).

The cause of these discrepancies is unknown. They may be due to the application of different analysis methods and antibody sources. Therefore, standardization of analysis methods is urgently necessary. Changes in production procedure and/or latex sap are also likely to exist. They may result in a great variation of the protein and/or allergen content from batch to batch (examined gloves did not belong to the same batches).

In our own investigations, a total of 62 different natural latex articles were investigated (Fig. 1). In 12 products, neither protein nor allergen was measurable. We found remarkable differences between protein and allergen contents in the latex articles such as latex mattress 1 (n), latex pad F sterile (w), mattress cover 1 and 2 (q and r), and chlorinated rectum catheter (k), as well as in the glove brands NuTex sterile (no. 16), NuTex non-sterile (no. 15), Exam no powder (no. 7), Gammex (no. 9), Safeskin[®]-Supra (no. 25), and Safeskin (no. 26), all of which have a moderate to high protein content but no detectable allergen. Moreover, in several products, e.g., nos. 2, 3, 13, 15, etc., a low protein content but no allergen was measurable. In the latter products, an allergenic potential could not be definitely excluded since, so far, determination of allergenicity in these gloves has been estimated with our IgE source from five patients only. Furthermore, experiences with subjects who have been in contact with these products for a longer period of time will be necessary. Results of statistical analysis showed no significant correlation between the measurable protein and allergen contents in the latex products investigated ($r^2=0.40$).

In view of the uncertainty of the risk of sensitization, we recommend that the protein content in latex products be used for orientation purposes only and the allergen content for detailed information and decisions on preventive measures. Moreover, the allergen content should be quantitated by use of a larger number of representative sera (or serum pools).

At present, no definite borderline for the concentration or amount of latex allergens eliciting allergic reactions and sensitization can be given. Like Kwangskuth & Maibach (18), we have even observed immediate-type cutaneous reactions to Biogel gloves, the inner side of which is coated with polyhydroxyethyl-methacrylate (PHEMA). This shows that a polymer protection layer currently used for the reduction of contact with latex materials is not sufficient. Furthermore, our previous cross-sectional study revealed that the respiratory sensitization to latex was observed exclusively in hospital areas with detectable airborne latex allergens (19). These allergens, which can be eliminated by leaching and other treatment of latex articles (20), were significantly associated with the presence of latex type I allergy. Our preliminary data suggest a dose-response relationship between the allergen load on the one hand and the risk of sensitization on the other hand (19). Detailed studies are necessary to describe such a relationship objectively, enabling hospital management and medical staff to take the required preventive measures on a validly cost-effective consideration.

Table 1. Releaseable protein and allergen concentrations of various surgical gloves (comparison with results in literature)

No.	Glove brand	Protein concentration			Allergen or antigen concentration						
		Over (Lowry) µg/g glove	Beckhold (15) (BCA) µg/glove	Yunginger et al. (16) (Nitehydri) µg/ml	Alenius et al. (14) (Lowry) µg/g glove	Alenius et al. (14) (Bradford) µg/g glove	Over (CAP inhibition) µg/g glove	Wrangö & Lundberg (17) (LEAP) µg/ml	Wrangö & Lundberg (17) (EA) U/ml	Beckhold (15) (LEAP) µg/glove	Yunginger et al. (16) (EA) AU/ml
1	Alcoquel (E)*	<					<				
2	Biogel (S)	25	450	<15	15	3	<	0.03–0.25	<0.1–2	25	71<5
3	Biogel Diagnostic (E)	55					<				
4	Biogel Super-Sensitive (S)	<					<				
5	Biogel M (S)	44	700	<15		28	28			0.6	<5
6	Conform (E) (p)	107		78/24		15	15	6.8	0.1	126	<5
7	Exam Glo Powder (E)	76		<15			<				<5
8	Flexarm Powder-free (E)	<					<				
9	Gammex (S) (p)	155			68	20	<	4.5	0.1		
10	GloSkin Powder-free (E)	<					<				
11	Latex powderfree (E)	50				13	13				
12	Malaysia (E) (p)	1000				816	816				
13	Menex (S)	37					<				
14	Naurition (S) (p)	593	1400	494			37	0.5–2.9	0.3–1.5	194	32
15	NuTact (E)	141					<				
16	NuTact (S)	182					<	5.6	0.1		
17	Pella soft (E)	32				18	18				
18	Pella microtex (S) (p)	522				398	398				
19	Serpermed classis (S) (p)	1034				525	525				
20	Serpermed (S) (p)	685			46	547	547				
21	Trifix (S) (p)	311	5750	246	337	81	173	19	70	2046	5910

*E: examination glove; S: surgical glove; p: powdered.

< = not measurable.

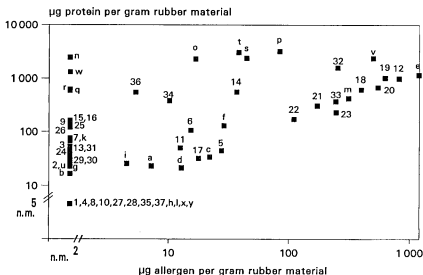


Fig. 1. Analyses of protein and allergen contents in various fragmented articles made of natural latex. *Commercial gloves*: 1) Absogel, Co. U.; 2) Biogel[®], Co. R.; 3) Biogel[®] Diagnostic, Co. R.; 4) Biogel[®] Super-Sensitive, Co. R.; 5) Biogel[®] M, Co. R.; 6) Conform, Co. A.; 7) Exam No Powder, Co. A.; 8) Flexam Powder-Free, Co. B.; 9) Gammex[®], Co. A.; 10) Glads powderfree, Co. M.; 11) Latex powderfree, Co. D.S.; 12) Malaysia (no name), Co. U.; 13) Manex[®], Co. B.; 14) Neutralon[®], Co. J & J; 15) NuTex, nonsterile, Co. A.; 16) NuTex, sterile, Co. A.; 17) Peha[®] soft, Co. H.; 18) Peha[®] microptic, Co. H.; 19) Sempermed[®] classic, Co. S.; 20) Sempermed[®], Co. S.; 21) Triflex[®], Co. B. 23) Safeskin[®]-Excel, Co. S.; 24) Safeskin-Supra, Co. S.; 25) Safeskin-Satin, Co. S.; 26) Safeskin, Co. S.; 27) Sterimed[®], Co. St.; 28) Contastop[®], Co. St.; 29–31) Gentle Skin[®], Co. Me.; 32) Sempermed[®], powdered, Co. A.; 33) Peha[®] Soft, powdered Co. H.; 34) Kannex[®], Co. K.; 35) Puritec[®], Co. M.; 36) Latex Exam, powdered, Co. S.; 37) Latex Exam, powderfree, Co. S. *Test glove*: 22) nonsterile test glove, Co. J & J. *Other rubber articles*: a) balloon catheter, nonchlorinated, Co. R.; b) balloon catheter, chlorinated, Co. R.; c) balloon catheter, chlorinated/prevalcanized, Co. R.; d) balloon catheter, silver-impregnated, Co. R.; e) balloon material, nonchlorinated; f) condoms, Co. M.; g) esophagus catheter, Co. J; h) pacifier, Co. N.; i) pacifier, Co. S.; k) rectum catheter chlorinated, Co. R.; l) rubber teat; m) textile rubber; n, o, and p) latex mattress 1–3, Co. P.; q and r) mattress cover 1–2, Co. P.; s and t) latex mattress, Co. N.; u) rubber tube, Co. V.; v) latex pad F; w) latex pad F sterile; x) latex pad W; y) latex pad W, sterile (all latex pads are from Co. Eu). n.m.: not measurable.

Acknowledgments

We thank Anne Flagg, Silke Maryska, and Maria Düser for their excellent technical assistance.

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