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Prevention of latex allergy among health care workers and in the general population: latex protein content in devices commonly used in hospitals and general practice

Received: 3 November 2004 / Accepted: 14 December 2005
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Abstract *Background:* In this study the latex protein content in devices commonly used in hospitals and general practice were investigated. The main aim was to acquire information for preventing latex allergy in health care workers and in the general population. *Methods:* About 22 different types of medical devices and 23 devices commonly used in general practice were examined evaluating the total allergenic potency by a modified RAST-inhibition assay and quantitative determination of single allergens (Hev b1, Hev b5 and Hev b6.02) by using commercial ELISA kit. *Results:* A high level of inhibition was found in medical devices, such as elastic bandage (81.57%), tourniquet (74.09%), Foley urinary catheter (68.35%), Penrose drainage (67.25%) and taping (39.6%), and in common devices, such as rubber inner-sole (84.20%), toy balloon (78.62%), latex mattress (74.27%), household rubber gloves (49.10%), working gloves (38.25%), inflatable floating mattress (32.10%). Concentrations of latex extractable proteins and Hev b1, Hev b5 and Hev b6.02 antigens were high in some medical and general devices. *Conclusions:* Latex exposure sources were found in hospitals and the home. These findings, though only preliminary and far from conclusive, could enable sensitized persons to avoid risky exposures and prevent allergic reactions. From the point of view of prevention, the time may come when every natural rubber object could be systematically labelled as “containing latex” together with the warning that “this item may cause allergic reactions in sensitized subjects.”

Keywords Health care workers · Latex allergy · Latex device · Prevention

Introduction

Natural rubber devices are widely used in the workplace and in everyday environments; therefore, many people are exposed to latex everyday. The growing use of latex gloves in health care practice since the 1980s has been associated with an increase of irritant and allergic diseases related to their use. Epidemiological studies indicate a prevalence of latex allergy among health care workers between 3 and 12% (Liss et al. 1997; Shahar et al. 2001; Ohlson et al. 2001; Holness and Mace 2001; Larese Filon et al. 2001). The prevalence is highest among dental personnel, general and operating room nurses (Kujala 1999).

Many medical devices other than gloves are made of natural rubber, such as tourniquets, elastic bandages, ventilation balloons, urinary catheters, and so on, and are commonly used in the operating theatre, emergency room and other departments. All these devices and also gloves could constitute a hazard for latex-sensitized workers and patients.

Other occupations can involve substantial latex exposure, such as the rubber industry, with a prevalence of sensitization of 11% (Tarlo et al. 1990) and a prevalence of allergy of 9% (Orfan et al. 1994), and hairdressers, where a prevalence of allergy of 9.7% has been reported (Van der Walle and Brunsveld, 1995).

Moreover, the general population is also exposed to latex, with the widespread use of natural rubber products in normal life. The prevalence of latex allergy in the general population is about 1% (Moneret-Veutrin et al. 1993; Brehler et al. 2002) but it is much higher in hyper-susceptible subjects, reaching 3% in atopic subjects (Arellano et al. 1992), 4.5% in atopic subjects with asthma (Hadjiliadis et al. 1995) and 32–50% in children with spina bifida (Moneret-Veutrin et al. 1993; Kelly

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et al. 1993). Prolonged contact with natural rubber toys and food allergies to cereals, bananas and other fruits may constitute a further risk factor for latex allergy (Axelsson et al. 1988; Sorva et al. 1995; Ylitalo et al. 1996).

IgE-mediated allergic reactions (hypersensitivity type I) due to latex sensitization are particularly important from a clinical point of view, since they may cause skin symptoms and ocular, respiratory or systemic symptoms (Levy et al. 1992; Sinha et al. 1998; Liss et al. 1997; Kujala 1999). Eczematous reactions to latex, similar to "protein contact dermatitis," have also been reported (Sommer et al. 2002; Larese Filon and Bagnato 2003).

Latex allergy is therefore an appreciable problem not only for exposed workers but also for the general population and preventive measures are needed to limit the number of new sensitizations and avoid clinical manifestation in already sensitized subjects. It is consequently interesting to know the content and release of allergenic proteins in a range of natural rubber devices widely used in health care institutions and general practice. The aim of this study was to acquire such information which, even if not conclusive, could be useful in the management of latex allergy.

Materials and methods

In this study 22 different types of medical devices and 23 devices commonly used by the general population (Table 1) were examined, measuring the allergenic

Table 1 Devices tested for latex protein content

Medical devices	Other devices
Foley urinary catheter	Diving mask (black rubber)
Kehr tube	Diving mask strap (black rubber)
Tourniquet	Diving nose piece
Urinary condom texas	Household rubber gloves
Abdominal drain	Work gloves
Penrose drain	Electric plug cover
Pezzer probe	Gas pipe
Malecot	Window wiper
Rusch	Bike inner tube
Stethoscope	Rubber eraser
Mask for anaesthetics	Toy
Sphygmomanometer band	Baby's dummy
Sphygmomanometer pump	Inflatable floating mattress
Cpap balloon	Hot water bottle
Balloon connector for cpap	Rubber inner sole
ECG electrode	Latex mattress
Thermodilution balloon probe	Toy balloon
Defluxion connector	Unlined rubber gloves for housework
Oxygen-nitrogen monoxide feeding tube	Truck inner tube
Fogarty balloon	Car tyre
Tape	Scooter tyre
Elastic bandage	Truck tyre
	Feeding Bottle Teat

potency of latex devices by a modified RAST-inhibition assay, using these devices as solid phase (Villalta et al. 2000). The results are expressed as the average percentage inhibition $\pm$ SD. Allergen content determination of Hev b1, Hev b5 and Hev b6.02 present in the extractable protein latex of devices was performed by ELISA method using commercial kit. The procedures used to obtain latex extracts from devices and to perform ELISA assay are described below.

Latex extract

Fresh latex sap (provided by Dr. Yeang, the Rubber Institute of Malaysia, Kuala Lumpur, Malaysia) was collected in chilled containers surrounded by crushed ice before being centrifuged at 20,000g at 4°C for 1 h. The rubber cream was eliminated and the aqueous fraction was alternately frozen and thawed to break up lutoid membranes and allow the release of allergens. The preparation was centrifuged and the supernatant (a mixture of fractions B and C, called latex serum extract) was used for further experiments.

Preparation of extract from latex devices

Each device has been cut into small pieces and put into proper containers. Extraction was performed at 10% (w/v) using TES (*N*-tris-hydroxymethyl-methyl-2-aminoethanesulfonic acid) buffer at 0.1 M, pH 7.4, under stirring at 4°C. After 2 h of extraction, liquid fraction was separated from the solid fraction by centrifugation at 10,000g for 20 min. at 4°C. Subsequently liquid fraction was dialysed against distilled water, filtered through a 0.22 μ m membrane, lyophilized and stored at -20° until use.

Preparation of latex-coated solid phases (beads)

One thousand polystyrene beads (Precision Plastic Balls, USA) were activated by treatment with a solution of glutaraldehyde (2% v/v) in PBS. The beads were then washed and coated with latex extract (diluted 1:250 in PBS) by overnight incubation at room temperature. The coated beads were washed again 1 h before treatment with NaBH₄, 0.01 M, in order to stabilize the linkage with the latex proteins. Finally, the beads were saturated with bovine serum albumin (BSA) (1% p/v in PBS-Tween 20, 0.05%). After further washings the beads were kept at 4°C until use.

Preparation of latex IgE positive-human pool serum

Ten sera from latex-allergic subjects, selected on the base of their clinical history and the positiveness to the prick test, were checked by RAST assay to establish their

positiveness class: 50 μ L of each serum was added in tubes containing latex-coated beads. After 6 h of incubation and subsequent washings with PBS-BSA, 50 μ L of a solution of ^{125} I-labelled goat anti-human IgE serum (Sferikit, Lofarma, Milan, Italy) was added and incubated overnight. The beads were then washed and residual radioactivity (expressed as counts per minute, cpm) was measured with a gamma counter and compared with a positive standard curve. Sera showing positiveness class 3 or 4 were pooled and used for further experiments.

Rast-inhibition assay

Villalta et al.'s (2000) modification of the traditional RAST-inhibition assay developed by Ceska et al. (1975) was used. Pieces of gloves and different materials were directly used as solid phase. The procedure was as follows: 50 μ L of latex IgE-positive pooled serum + 50 μ L PBS or 50 μ L of non-allergic patients' pooled serum plus 50 μ L PBS, as negative control, were added to tubes containing a piece of glove or sample of the device (1 cm²) for a 2-h pre-contact. This meant that part or all of the latex-specific IgE antibodies could be lost depending on the presence of latex allergens on the sample. As positive control, we used tubes containing 50 μ L of latex IgE-positive pool serum and 50 μ L PBS without any sample.

After overnight incubation, beads were washed and 100 μ L of ^{125} I-labelled goat anti-human IgE serum was added to each tube. After another overnight incubation and further washing, residual radioactivity on the beads was determined with a gamma counter. The percentage inhibition was calculated as follows: per cent inhibition = (positive control cpm – sample cpm)/(positive control cpm – negative control cpm) $\times$ 100.

Using a pool of human sera from patients with positive RAST for mites and grass extracts and negative RAST for latex extract, experiments were also done to exclude that any decreases in the inhibition were due to a non-specific link between IgE antibodies and glove latex proteins. In this case mites or grass extract-coated beads

were used instead of latex extract beads. Inhibition was calculated as described previously.

RAST-inhibition experiments were also done with glove extracts. For the 2-h pre-contact, 30 μ L of glove extract and 20 μ L of latex IgE positive pool serum were mixed in a tube. Then the procedure described earlier was used but 30 μ L of PBS instead of 30 μ L of glove extract was added to the positive control and 20 μ L of normal human serum instead of 20 μ L of latex IgE-positive pooled serum was added in the negative control.

ELISA

Hev b1, Hev b5, and Hev b6.02 were determined using the FITkit (Fit-Biotech, Tampere, Finland). A standard curve was plotted for each latex allergen following the manufacturer's instructions. The allergen content in samples was determined by interpolation of the optical density on the reference curve. Results have been expressed in mcg/g device.

Results

Latex devices used in our hospital and other latex devices used in general practice and those which are commonly available on the Italian market have been tested; in particular in this study only powder-free gloves have been taken into consideration because the powdered gloves have been already analysed by Crippa et al. (2003). For the test validation, we had tested by RAST inhibition some latex gloves known to have a high latex protein content (samples B, E, S analysed in the study of Crippa et al. (2003) and to establish a cut-off for positive results we had tested some certified latex-free (silicon) devices by RAST inhibition. The RAST inhibition on the three samples of gloves (average of the three measurements on each sample) confirmed a high content of latex-extractable proteins in latex gloves (Fig. 1). An inhibition percentage lower than 10.90% was detected in "latex-free" devices, probably mainly due to unspecific binding; the cut-off for positive results was set at 11%

Fig. 1 Extractable latex proteins in medical gloves

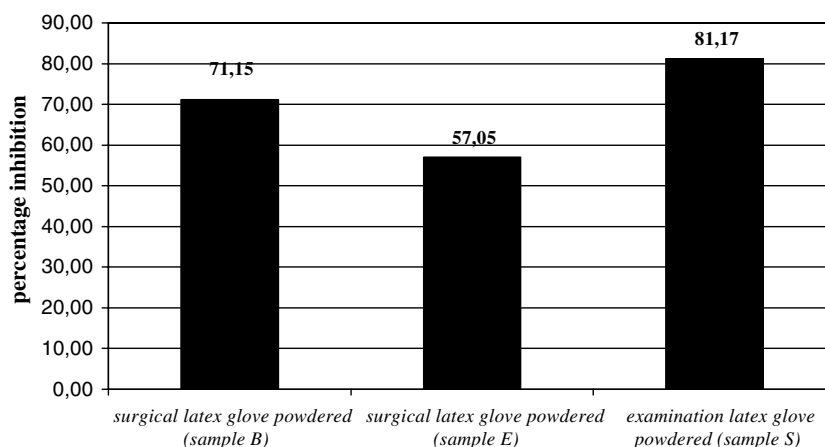
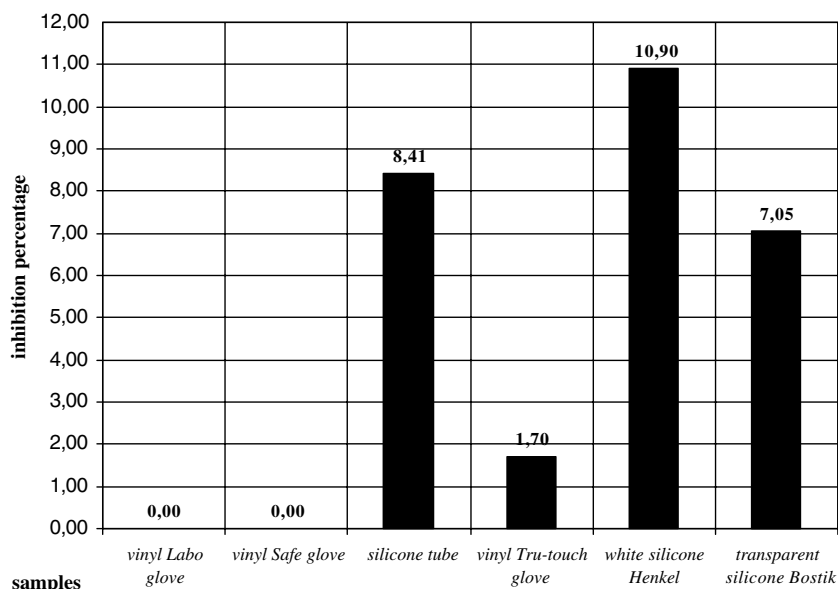


Fig. 2 Percentage inhibition in latex-free devices



inhibition (Fig. 2) and it was calculated by the value of the negative control $\pm$ the value of the standard deviation.

Latex-extractable proteins were measured in the devices listed in Table 1. The highest values were in elastic bandages with 81.57% inhibition, followed by tourniquets 74.09%, Foley urinary catheter 68.35%, Penrose drain 67.25% and tape 39.6%. The following devices, however, also had inhibition higher than the cut-off: Fogarty balloon, oxygen–nitrogen monoxide feeding tube, sphygmomanometer pump, sphygmomanometer band, mask for anaesthetic, stethoscope, Rusch, Malecot, abdominal drain, urinary condom texas and Kehr tube (Fig. 3).

In widely used devices high percentages of inhibition were found in rubber inner sole (84.20%), toy balloon (78.62%), latex mattress (74.27%), household rubber gloves (49.10%), work gloves (38.25%), inflatable floating mattress (32.10%). However, several other devices, such as feeding bottle teat, scooter tire, car tire, truck inner tube, unlined rubber gloves for housework, household glove, hot water bottle, bike inner tube, window wiper, diving nose piece, and black diving mask had inhibition higher than the cut-off (Fig. 4).

We used an ELISA method to assess the presence of allergens Hev b1, Hev b5, and Hev b6.02 in devices with a high content of latex-extractable proteins and some latex gloves with a high latex protein content: samples B, E, S analysed in the study of Crippa et al. (2003). In all these products we were able to determine antigen Hev b6.02 in the extract as such, but to measure the other allergens we had to concentrate the extract from 50 to 200 times.

Hev b6.02 allergen was found in all the devices listed, with particularly high levels in powdered surgical latex gloves (sample B), elastic bandage, rubber inner sole and the Penrose drain. Hev b1 and Hev b5 have been detected in very low concentrations. Figure 5 shows the

concentration of Hev b1, Hev b5 and Hev b6.02 in the sample extracts of the devices analysed.

Discussion

Latex allergy is a problem that needs effective preventive measures in the workplace, particularly in health care practice, and at home. It is not always easy to avoid contact with latex devices since natural rubber is found not only in gloves but in many other widely used products too. Since the risk of sensitization is exposure-related while the onset of symptoms in already sensitized subjects is evident even after short or low exposure, it could be important to know the amount of latex proteins released by devices commonly used in hospitals or in general practice.

This study confirmed that many natural rubber items commonly used in the operating theatre, emergency room, or other hospital departments, or in the home, can release substantial amounts of latex proteins.

Our results are only preliminary and obviously not conclusive since we could only test a small sample of natural rubber devices and aware of the variability of the latex protein content in similar products we think to extend, in the future, our investigations to same devices made by different manufacturers and, if possible, to verify also intra-lots variability. Anyway the variability of the results on the same extract of a single device can change according to the method.

Nevertheless, we are able to draw some conclusions:

- Latex exposure in hospitals is complex and many devices besides gloves contain latex, and could constitute a risk factor for health care workers and patients;
- A lot of these devices, such as elastic bandages or Foley urinary catheters, and so on with a high extractable protein content are used for prolonged contact with skin or mucous membranes. This could

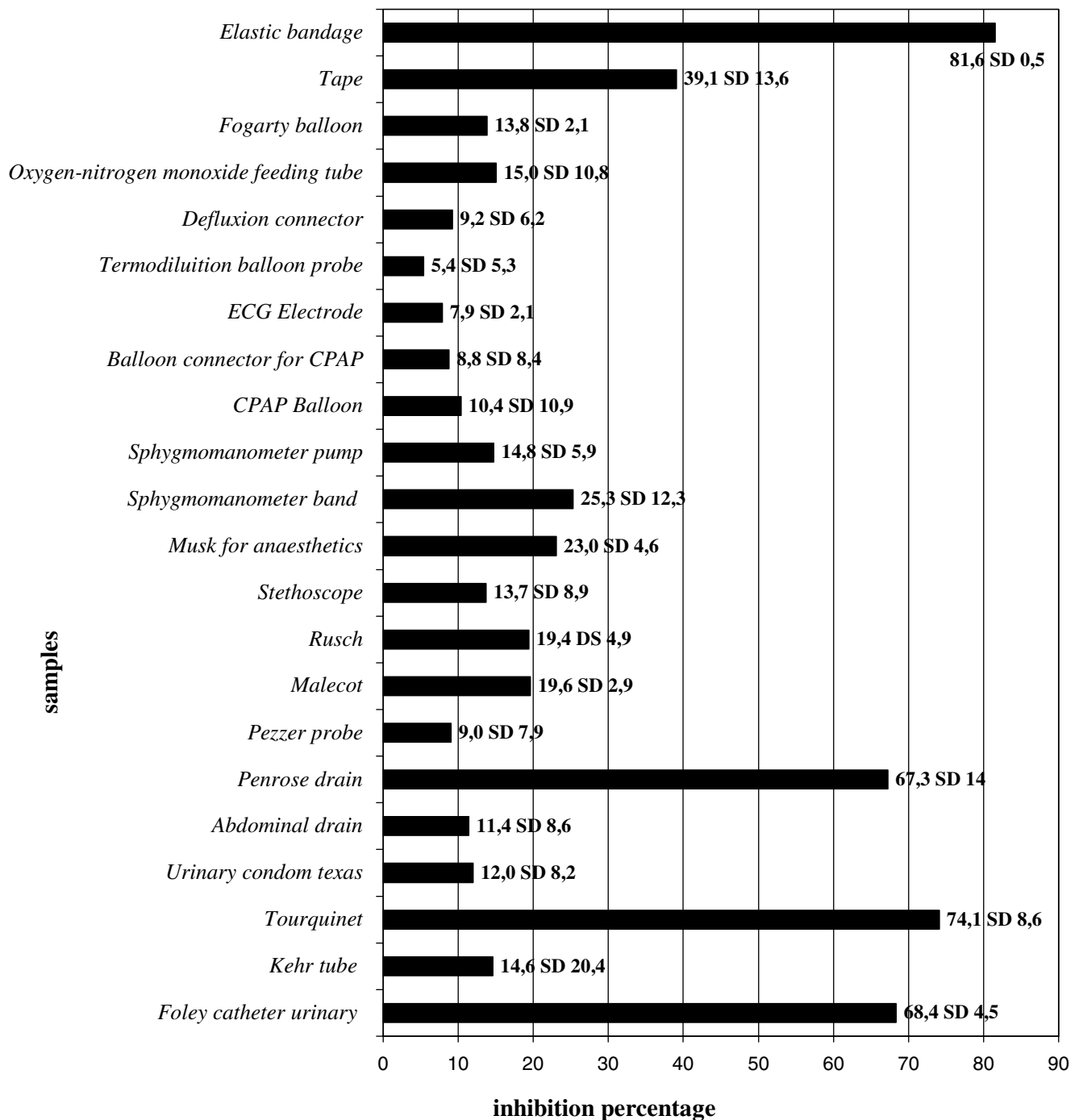


Fig. 3 Latex-extractable proteins in medical devices

- pose a risk for non-allergic patients and also sensitized subjects;
- Other devices, such as tourniquets or tape, have a high extractable protein content but they are usually only in contact with the skin for a short time, so they should involve a risk mainly for sensitized patients;
- Most of the commonly used devices we tested, such as the toy balloon, rubber inner sole, household glove or feeding bottle teat have a high extractable protein content and involve prolonged contact with skin or mucous membranes;
- We detected Hev b6.02 with the FITkit ELISA in all the devices and Hev b5 in almost all. These major allergens are involved in allergic reactions in children with spina bifida, and in health care personnel (Poley and Slater 2000; Niggemann and Breiteneder 2000, Kostyal et al. 1998; Schmid-Grendelmeier and Cramer 2001);

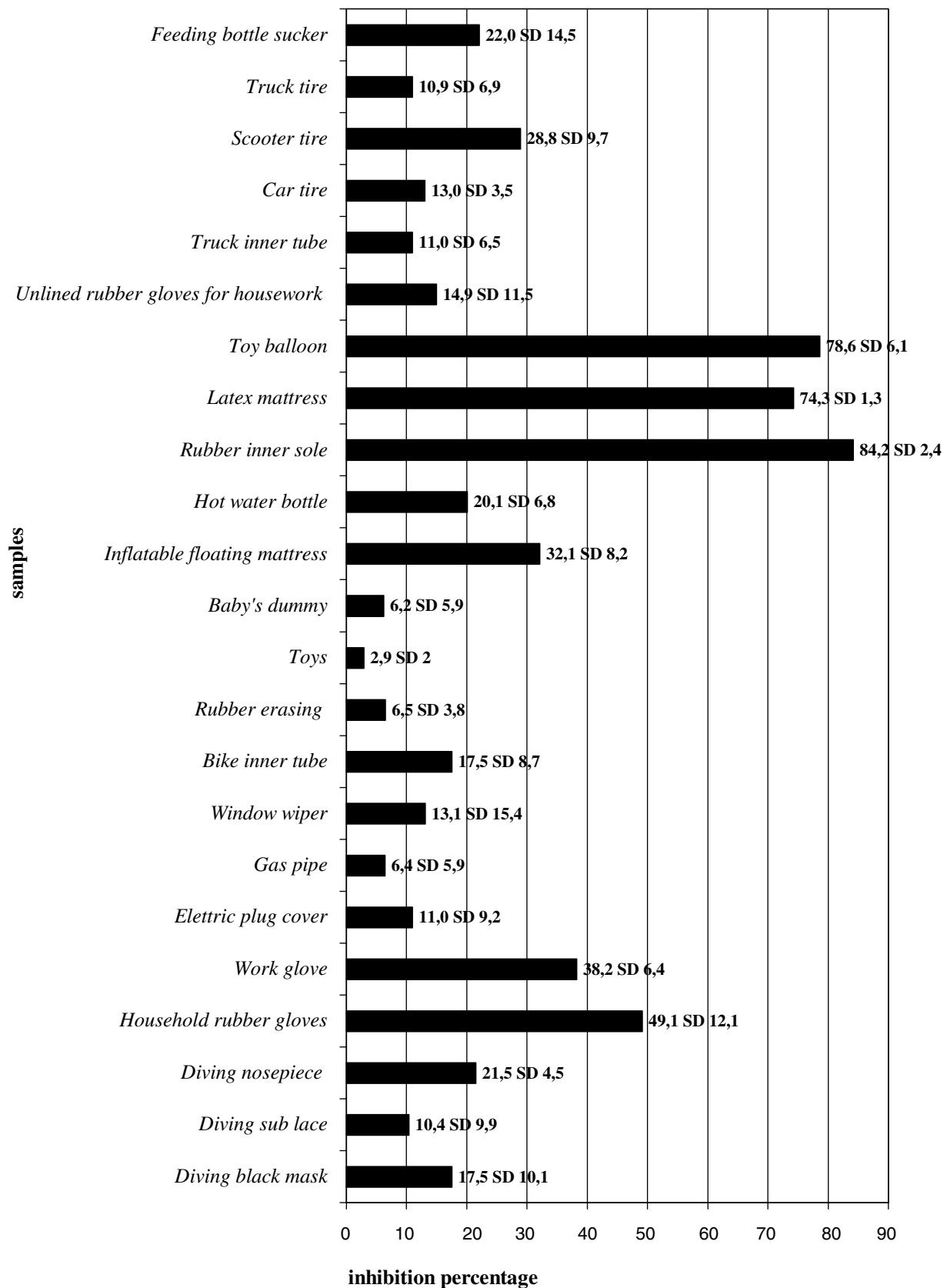


Fig. 4 Latex-extractable proteins in commonly used devices

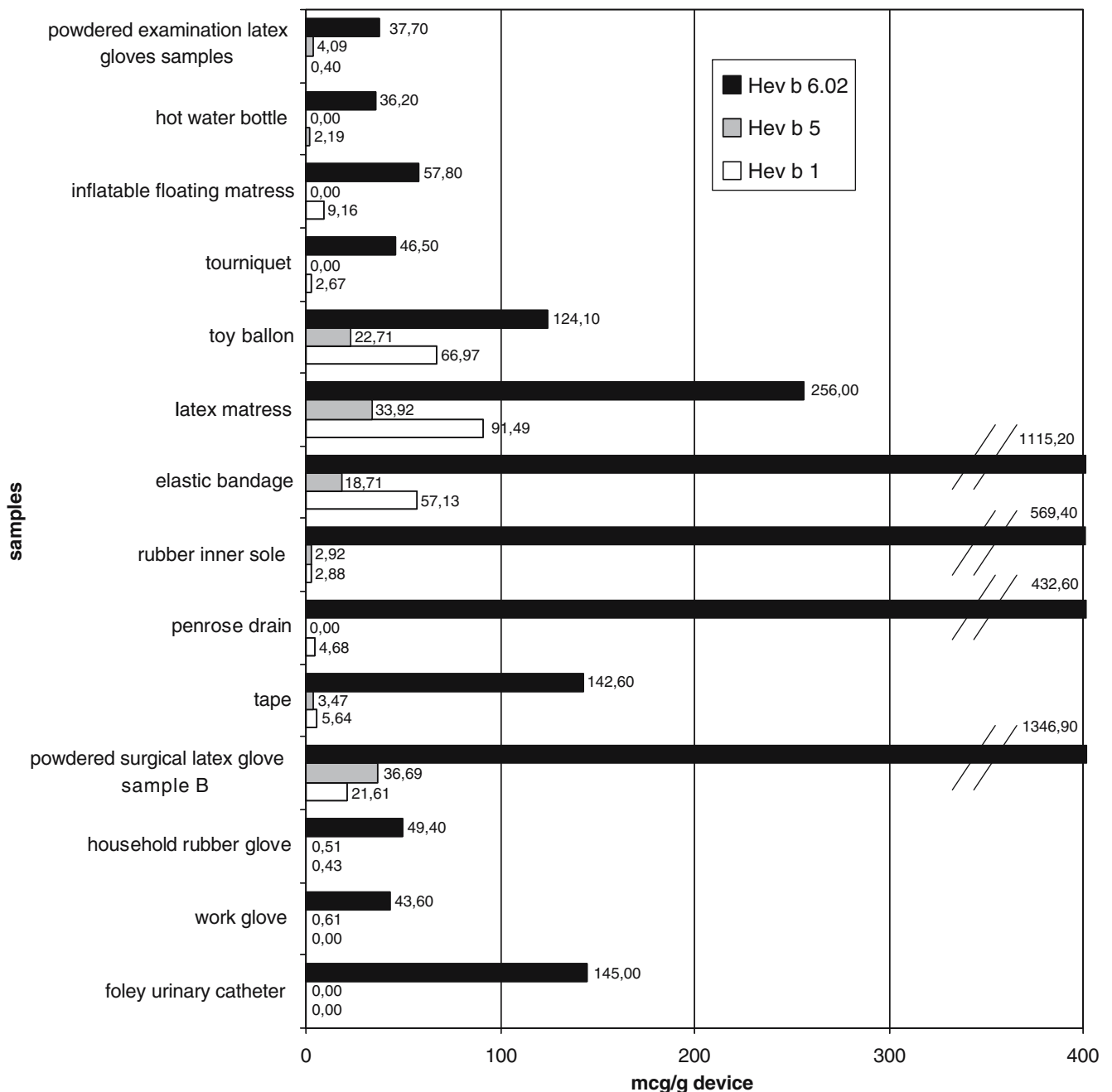


Fig. 5 Hev b1, Hev b5 and Hev b6.02 concentrations (mcg/g device) in sample extracts

- Contact with devices with a low percentage of inhibition cannot cause sensitization in non-allergic subjects but could be a risk for sensitized subjects.

In conclusion, for more effective prevention, devices containing latex should ideally be replaced with others made of synthetic polymers. If this is not possible, devices should be selected with the lowest possible content/release of latex, so as to avoid sensitization. It is in any case to be recommended that every natural rubber object will soon be systematically labelled as “containing latex” with the information “this item may cause allergic

reactions in sensitized persons. As regards to workplaces, these preventive measures must be associated with specific educational programs for workers and counseling for employers, whose effectiveness has also been demonstrated in recent studies (Latza et al. 2005).

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