EVALUATING RISKS OF ALLERGY TO CHROMIUM RELEASED FROM FOOTWEAR

MIRELA PANTAZI 1, GABRIELA MACOEVSCU 1, SIMINA STEFAN 2, ANA MARIA VASILESCU 1

1 INCDTP – Division: Leather and Footwear Research Institute, 93 Ion Minulescu St., Bucharest, Romania, email: icpi@icpi.ro
2 Faculty of Applied Chemistry and Material Science, University Politehnica of Bucharest, No 1-7, Polizu Street, Sector 1, 011061, Bucharest, Romania

Chromium tanning of leather is the most important tanning method and is used in over 80% of tanneries in the world. Several studies have indicated that leather products, when worn, can release chromium as Cr(VI) or Cr(III), compounds which can cause allergic reactions and severe foot eczema. Development of allergy to chromium, among patients with eczema, was investigated in different EU countries (Denmark, Germany, Italy, etc.). The main purpose of this study is to clarify whether the compounds of Cr(VI) and Cr(III) are released from leather shoes in a quantity leading to a risk of causing allergic reactions. In order to highlight chromium content in leather, footwear samples were analyzed according to SR EN ISO 5398/1-2008 to determine total chromium and according to SR EN ISO 17075:2010 for the detection and quantification of soluble chromium VI with a detection limit of 3 mg/kg Cr(VI). The results are a measure of the total potential exposure to Cr(VI) and were used to identify shoes that may present a risk of allergy.

Keywords: leather footwear, chromium, allergy to chromium.

INTRODUCTION

Leather must be tanned in order to get durability, softness and flexibility, properties that make it usable for shoes. Chromium tanning is the most important tanning method and it is over 80% used in the leather industry worldwide. The chemical used in the tanning process is alkaline chromium(III) sulphate. This chemical reacts with the hide and stabilizes certain proteins, making it more resistant to degradation. Hexavalent chromium (Cr(VI)) is not used in the tanning industry and has no effect in the tanning process (Rydin, 2002). Chromium(III) salts can, under certain conditions, be converted into compounds of Cr(VI). It is known that light, UV radiation and heat, combined with the presence of oxidized fatty acids, can cause the conversion of Cr(III) to Cr(VI), in certain types of hides. Also, it is known that the pH value significantly influences the state of chromium. Trivalent chromium oxidation in air may be favoured by elevated pH during neutralization or dyeing processes.

Studies have shown that, under certain conditions, chemicals in leather may release compounds of Cr(VI). Previously, this was not thought possible, because Cr(VI), under the influence of many organic compounds at a low pH value was expected to be reduced to compounds of Cr(III) (Hauber & Germann, 1999). However, it is now known that chemicals in leather are capable of releasing compounds of Cr(VI) due to aging and UV radiation, which is a big problem, because hexavalent chromium compounds are contact allergens. Cr(VI) is considered one of the best known allergens.

Contact allergy develops when reactive substances, with low molecular weight, such as Cr(VI), penetrate human skin and activate the immune system. Activating the immune system means that it is able to recognize and respond to the specific substance when exposed to it again.

Most studies have focused on allergies caused by Cr(VI). However, exposure to chromium, through chromium-tanned leather may also include exposure to trivalent...
Evaluating Risks of Allergy to Chromium Released from Footwear

chromium compounds. After tanning, most Cr(III) compounds are bound to the collagen fibres in the leather, but it was proved that an excess of trivalent chromium compounds may be released from leather during the use of footwear.

In 2006 Hansen et al. studied the connection between foot eczema and exposure to Cr(III). It was found that patients with contact allergy, both to Cr(III) and Cr(VI) presented a higher risk of developing foot eczema than patients who responded positively only to Cr(VI). This indicated that Cr(III) plays a role in the development of foot eczema. However, Cr(VI) is considered a more potent allergen than Cr(III).

The main purpose of this study is to clarify whether Cr(VI) and Cr(III) compounds are released from leather shoes made in Romania, in amounts which may lead to risks that could cause allergic reactions.

METHODS

Determining Soluble Cr(VI) in Leather

International Standard SR EN ISO 17075:2008 establishes the method used to determine Cr(VI) in solutions obtained by washing leather under certain conditions. Soluble Cr(VI) is extracted from the sample in phosphate buffer at 7.5-8.0 pH and if necessary, substances that influence detection are eliminated by solid phase extraction. Cr(VI) in solution oxidizes 1,5-diphenylcarbazide to 1,5-diphenylcarbazone to form a red/purple complex, with chromium, which can be measured photometrically at 540 nm. The results obtained by the method described are strictly dependent on extraction conditions. The results obtained using other extraction procedures (extraction solution, pH, extraction time, etc.) cannot be compared with results obtained using the procedure described in this standard.

This method is recommended in order to quantify Cr(VI) content in leather; according to the method, the detection limit is 3 mg/kg. This method is applied to leather from any animal tanned using chromium salts.

Determining Cr(III) Content in Leather

Total chromium content, expressed as chromium oxide (Cr₂O₃), was determined according to SR EN ISO 5398/1:2008. SR EN ISO 5398/1:2008 describes a method for the determination of chromium in aqueous solution obtained from leather. This is an analysis for total chromium in leather; it is not compound specific or specific to its oxidation state. This method describes the determination of chrome by iodometric titration and is to be applicable to chromium-tanned leathers which are expected to have chromic oxide contents in excess of 0.3 %. Cr(III) content was determined by subtracting Cr(VI) content from the total chromium content. This is possible due to the generally accepted assumption that chromium is present in the leather only as Cr(III) and Cr(VI). The result is expressed in mg Cr(III)/kg leather.

EXPERIMENTAL

Experiments were carried out on 10 pairs of leather shoes, made in Romania, as follows:
- 4 pairs of children's footwear;
• 3 pairs of women's footwear;
• 3 pairs of men's footwear.

Analysis of hexavalent chromium migration from leather samples was carried out according to SR EN ISO 17075:2008 Leather - Chemical Tests - Determination of Chromium(VI) Content, and determination of total chromium in leather was done according to SR EN ISO 5398/1:2008 Leather - Chemical Determination of Chromic Oxide Content - Part 1: Quantification by Titration.

Results of evaluating hexavalent and trivalent chromium content in leather footwear studied are presented in Table 1.

Table 1. Test results for Cr(VI) and total Cr

<table>
<thead>
<tr>
<th>Footwear type</th>
<th>Volatile matter</th>
<th>Chromium oxide</th>
<th>Total chromium mg/kg</th>
<th>Cr(VI) mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children's shoes n.1</td>
<td>9.83</td>
<td>3.26/3.62*</td>
<td>24768</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>Children's shoes n.2</td>
<td>11.56</td>
<td>2.72/3.08*</td>
<td>21073</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>Children's shoes n.3</td>
<td>11.65</td>
<td>3.98/4.50*</td>
<td>30789</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>Children's shoes n.4</td>
<td>8.89</td>
<td>3.28/3.60*</td>
<td>24631</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>Women's shoes n.5</td>
<td>14.45</td>
<td>4.27/4.77*</td>
<td>32636</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>Women's shoes n.6</td>
<td>10.23</td>
<td>3.96/4.41*</td>
<td>30173</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>Women's shoes n.7</td>
<td>12.05</td>
<td>4.07/4.63*</td>
<td>31679</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>Men's shoes n.8</td>
<td>13</td>
<td>4.73/5.44*</td>
<td>37221</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>Men's shoes n.9</td>
<td>10.31</td>
<td>2.52/2.81*</td>
<td>19215</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>Men's shoes n.10</td>
<td>11.69</td>
<td>3.53/4.00*</td>
<td>27368</td>
<td>&lt; 1</td>
</tr>
</tbody>
</table>

* Values related to chromium oxide are reported to leather free of volatile matter.

Since Cr(VI) concentrations were always under the detection limit of 3 mg/kg (showing values well below 1 mg/kg), values of Cr(III) content can be approximated with the values of total chromium.

The content of chromium (III) has been analysed as the total chromium content in the leather samples. Eventual hexavalent chromium in the products will also be included in these figures, but the content of hexavalent chrome is negligible in relation to the content of chromium (III).

The concentration is expressed as % Cr$_2$O$_3$, which is the normal unit in the leather industry. The content of chromium in leather depends on the product, but will normally
Evaluating Risks of Allergy to Chromium Released from Footwear

be between 3 - 5% of Cr₂O₃. The chromium content should generally not be below 2.5% Cr₂O₃ for chrome tanned leather in order to receive a good quality of the leather (UNIDO, 1994).

Health Evaluation – Allergy to Chromium

Contact allergy develops when the reagents, low molecular weight substances such as chromium, penetrate human skin and stimulate the immune system. This stimulation means that the immune system is able to recognize and react to a specific substance. Contact allergy is also called type IV allergy and consists of two phases. The first phase is called induction or sensitization phase, where changes in the immune system are induced. This phase is without symptoms. At subsequent exposure to sufficient amounts of allergens, the immune system will react to the substance and the symptoms will appear. This phase is called elicitation and its symptoms are eczema.

Chromium is a transition metal, which exhibits different oxidation states ranging from + 2 to + 6. However, only trivalent Cr(III) and hexavalent chromium Cr(VI) have stable enough oxidation states to act as contact allergens. To become an allergen, a substance with low molecular weight, should be able to bind to proteins in human skin.

Studies show that Cr(VI) does not react with proteins. It is believed that Cr(VI) penetrates the skin and is reduced to Cr(III) to act as an allergen.

Studies on Threshold Values for Allergy to Chromium

In risk assessment, existing data on people take precedence over the results of animal studies. A typical way of expressing threshold values regarding the effects of allergens is MET10% (minimal elicitation threshold) - which represents the estimated dose causing a reaction in 10% of sensitized individuals. MET10% derives from exposure to an allergen dose over an area of 0.5 cm² for 48 hours.

In similar exposure scenarios regarding chromium from cement and wood, nickel in jewellery and dimethyl fumarate, a shoe fungicide, elicitation data such as MET10% were used directly in risk assessment. It is not possible to predict precisely the level of induction for a sensitizing substance, based on knowledge of threshold values such as MET10% elicitation values. But thresholds are sufficiently low to protect against the induction of sensitized individuals (Basketter et al., 2001) and this is the primary and secondary preventive measure.

Threshold Value for Cr(VI)

There are data from several studies conducted on humans, regarding the elicitation threshold for Cr(VI). At a single 48 hour closed exposure MET10% was estimated to be between 0.02-0.9 g/cm², data given in Table 2.

The latest study was done in Denmark and it estimates that MET10% is 0.03 g/cm², which corresponds to 1 mg/kg Cr(VI) (Hansen et al., 2003). This is in accordance with the results of the largest published study, where MET10% was 3 mg/kg for a 2 day period (Nethercott, 1994). However, there are variations with both smaller values and 10 times higher than MET10% (Hansen et al., 2002).

The American Environmental Protection Agency has based its risk assessment of allergy to chromium in wood on the study of Nethercott et al. (1994), which was the largest study.
Table 2. Estimated Minimal Elicitation Threshold for 10% of sensitized individuals (MET10%)

<table>
<thead>
<tr>
<th>MET10%</th>
<th>Number of test subjects</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.09 g Cr(VI)/cm²/2 days = 3 mg/kg</td>
<td>54</td>
<td>Nethercott et al., 1994</td>
</tr>
<tr>
<td>0.35 g Cr(VI)/cm²/2 days = 11.67 mg/kg</td>
<td>14</td>
<td>Allenby &amp; Goodwin, 1983</td>
</tr>
<tr>
<td>0.90 g Cr(VI)/cm²/2 days = 30 mg/kg</td>
<td>17</td>
<td>Kosann et al., 1998</td>
</tr>
<tr>
<td>0.02 g Cr(VI)/cm²/2 days = 0.67 mg/kg</td>
<td>5</td>
<td>Wass &amp; Wahlberg, 1991</td>
</tr>
<tr>
<td>0.03 g Cr(VI)/cm²/2 days = 1 mg/kg</td>
<td>18</td>
<td>Hansen MB et al., 2003</td>
</tr>
</tbody>
</table>

Threshold Value for Cr(III)

There are few studies on Cr(III). Identified threshold levels for Cr(III) are much higher than for Cr(VI).

In the study by Nethercott et al. (1994), only 1 of 54 patients responded to Cr(III), which corresponds to a threshold concentration of 33 μg/cm², while MET10% for Cr(III) estimated in the study by Hansen et al. (2003) was 0.18 g/cm², at least 6 times higher than for Cr(VI).

DISCUSSIONS

We analyzed the amount of chromium in leather uppers, because the upper comes most often in contact with skin and because there seems to be a slight tendency for allergic reactions that occur on the foot in this area. Moreover, the skin of the foot is thinner than the skin on the sole, thus being more likely to develop allergic reactions.

Low levels of Cr(VI) can cause allergic contact dermatitis. Patients allergic to Cr(VI) may react to a single exposure of 1 mg/kg-3 mg/kg Cr(VI).

SR EN ISO 17075 is the international standard method for detection and quantification of Cr(VI) and has a detection limit of 3 mg/kg.

The results are a measure of total potential exposure to Cr(VI) and were used to identify shoes having a risk of allergy to Cr(VI).

For quantitative analysis, using SR EN ISO 17075, it was found that the content of Cr(VI) did not exceed 3 mg/kg in any of the ten pairs of shoes analyzed.

CONCLUSIONS

The risk of using shoes that release chromium can be influenced by wearability conditions such as humidity, pH, micro-biological contamination and pre-existing skin diseases. This means that, under certain conditions, shoes with low levels of Cr(VI) may present a risk of allergy to chromium. However, in general, the higher the dose of allergen, the greater the risk of allergy. People who have already developed an allergy to Cr(VI) can be so sensitive that they react to levels of Cr (VI) below the limit. In all pairs of shoes analyzed low levels of both Cr(VI) and Cr(III) were found, which demonstrates that, technically, it is possible to produce high quality tanned leather, which falls within the product standard limits, without the risk of allergy to chromium.

The results of this study suggest that there are no problems related to a high content of chromium in leather shoes made in Romania.
Evaluating Risks of Allergy to Chromium Released from Footwear

REFERENCES

Hansen, M.B. et al. (2002), “Quantitative Aspects of Contact Allergy to Chromium and Exposure to Chrome-tanned Leather”, Contact Dermatitis, 47, 127-134.
SR EN ISO 17075:2010 Leather - Chemical Tests - Determination of Chromium(VI) Content.