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# Levels of nickel and other potentially allergenic metals in Ni-tested commercial body creams

Short communication

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#### Abstract

It is extensively well-known that Ni and other metals occurring as impurities in cosmetic products might give rise to contact dermatitis in subjects with pre-existing allergy. The present study on the content of 13 metals (Cd, Co, Cr, Cu, Hg, Ir, Mn, Ni, Pb, Pd, Pt, Rh, and V) in moisturizing creams, labelled as "Ni-tested" (i.e., Ni content <100 ng g<sup>-1</sup>) and available on the Italian market, provides a basis for assessing their safety for consumers. Quantification of metals was performed by sector field inductively coupled plasma mass spectrometry after microwave-assisted acid digestion of products. The developed method had limits of quantification less than 0.8 ng g<sup>-1</sup> for all the elements; recovery was in the interval 88% (Cd, Co) to 110% (Hg), and precision was always under 7%. Nickel was present in all the products with levels between 17.5 and 153 ng g<sup>-1</sup>; three skin creams were slightly above the concentration reported on the label. The other elements were at levels below 1  $\mu$ g g<sup>-1</sup>. The highest concentrations, in ng g<sup>-1</sup>, of Co, Cr, Cu, and Mn were 222, 303, 51.2, and 59.9, respectively. Mean Cd, Pb, and V were below 5 ng g<sup>-1</sup>, while Hg was absent in all the samples. Among the new emergent allergens, Ir and Rh were in traces or even undetectable, while Pt had levels of 2.65 and 6.28 ng g<sup>-1</sup> in two creams and Pd was equal to 1.07 ng g<sup>-1</sup> in one product. The overall results are below the sensitizing limit proposed for consumer products and, thus, probably have no significant toxicological effects. Nevertheless, some creams presented amounts of Co and Cr comparable to those of Ni and therefore they have to be monitored in consideration of their cross-reactivity as well. © 2007 Elsevier B.V. All rights reserved.

Keywords: Ni-tested body creams; Metals; Allergic contact dermatitis; SF-ICP-MS

# 1. Introduction

Metals are well-recognized causes of allergic contact dermatitis (ACD) both at occupational and environmental level. The key metals involved in this pathology are, in order of incidence, Ni, Co, and Cr, either taken alone or in their association [1–3]. As regards Ni, this element is considered the primary source in causing ACD with a prevalence of 20% in females and 1% in males [4]. This is mainly due to the free Ni ions released from objects containing Ni – which daily came in contact with the skin (i.e., piercing, jewels, buttons, clasps, coins, etc.) – corroded by the human sweat. In order to reduce the Ni ACD, the release of this metal from various objects has been regulated by the Council Directive 94/27/EC [5]. Differently from Ni, Co and Cr ACD was mainly caused by occupational exposures. Allergy

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to cobalt chloride was associated to workers employed in construction, electronic and electroplating industries or exposed to glass, ceramics, and paints [1,3]. In addition, the presence of Co in Ni-alloys can cause skin sensitization when this material is used to produce jewels [6]. As regards Cr, people who working as photograph developer or with ceramics, constructions and tannery industry, or those dressing tanned leather might all develop ACD to this metal [1,7,8]. In particular, the hexavalent Cr compounds seem to be more associated to skin sensitization respect to trivalent compounds because penetrates the skin more easily [3].

A certain degree of sensitization was shown by the salts of platinum group elements (PGEs), i.e., Pt, Pd, Rh, and Ir, because of their large use in dental devices, jewellery, and automotive catalysts [9–11]. Moreover, a synergic action between Pd and Ni, pertaining to the same periodic group, has been suggested as being the cause of cross-sensitization [9]. Moreover, Cu and Mn are rare skin sensitizers; anyway, immune reactions due to Cu exposure from intrauterine devices or by handling euro coins

have been described, whereas the use of prosthetic materials in dentistry has created a risk of sensitization for both Cu and Mn [12,13]. Considering toxic metals such as Cd and Hg little was known on their dermatological activities. Cases of ACD due to Cd exposure from cement dust emission [14] and ceramics material [7] and to Hg present as ammoniated mercury (HgNH<sub>2</sub>Cl) in skin lightening creams have been reported [15]. One case of sensitization to V was found in an enameller employed in a ceramics industry [7]. Another important way of skin exposure to metals is the use of cosmetic products such as moisturizing creams, lipsticks, eye cosmetics, shampoos, cleansing milk, henna dye, etc. In these make-up products metals are present as impurities due to the particular sample formulation or the release from metallic devices used during their manufacture. In fact, the Directive 76/768/EEC and further revisions banned the use of Cd, Co, Cr, Ni, and Pb as metallic ions or salts in the preparation of cosmetic formulations [16]. Considering the prolonged contact time of cosmetic products with the skin the risk of ACD might be increased [17,18]. As a support to this, there are several studies evidencing the presence of Co, Cr, Ni, and Pb at levels of  $\mu g g^{-1}$  in henna dye, eye shadows, and lip liners with frequent positive reactions to patch tests [17,19–21]. Some authors revealed the presence of Cd, Cr, Cu, Hg, Pb, and metal oxides in body or sunscreen creams [22-24]. If the cosmetic products are formulated as dry, this will minimize the risk of skin penetration of metal, whereas those based on fat-soluble substances (for example moisturizing creams) promote the percutaneous absorption much more. On the other hand, adverse reactions to metal-containing cosmetic products were mostly observed in patients with manifestation of pre-existing allergy to metals. Patch tests revealed that a threshold limit equal to  $5000 \text{ ng g}^{-1}$  or – for a more protection equal to  $1000 \text{ ng g}^{-1}$  – for Ni, Co, and Cr excluded the risk of elicitation in sensitized people [25,26]. Given these facts and the increased frequency of allergy to Ni, the challenge of the cosmetic industry was to manufacture products to be used by people pre-sensitized to Ni. For this reason, manufacturers made available on the market creams labelled with the phrase "Ni-tested" together with a declared Ni concentration of < 0.00001%, i.e., 100 ng g<sup>-1</sup>, thus guaranteeing levels 50 times below the risk of causing allergy reactions.

As regards metal quantification, the quadrupole inductively coupled plasma mass spectrometry (Q-ICP-MS) technique has been successfully adopted in pharmaceutical and biomedical analysis [27–29]. In fact it has been proved to be advantageous respect to more traditional techniques like atomic absorption spectrometry or neutron activation analysis for its simultaneity, wide dynamic concentration range, very low detection limits. Notwithstanding this, Q-ICP-MS analyses needed a careful selection of correction procedures in order to overcome or reduce polyatomic interferences [30]. The sector field (SF)-ICP-MS represented a considerable advance respect to Q-ICP-MS because operated at higher mass resolution (up to  $m/\Delta m$  10,000) and physically shifted away from the analyte peak the polyatomic interferences improving, therefore, method specificity [31–33].

In this context, well-known (Ni, Co, Cr) and potential (Cd, Cu, Hg, Ir, Mn, Pd, Pb, Pt, Rh, and V) allergenic metals were

evaluated in commercial "Ni-tested" body creams in order to assess their safety for consumers. To this end, a microwave (MW) digestion procedure for sample dissolution and a SF-ICP-MS-based method for quantification were developed.

# 2. Experimental

#### 2.1. Samples and reagents

Eleven commercial hydratant body creams labelled "Nitested" destined, in particular, to people proved to be sensitized to Ni were selected for the study. The creams were produced by 11 different industries (i.e., nos. 1–8 from Italy, no. 9 from France, no. 10 from Switzerland, and no. 11 from USA). All the specimens were purchased from pharmacies located in Rome and stored at room temperature until their analysis. Singleelement standard solutions (SPEX, Edison, NJ, USA) at the concentration of 1 mg mL<sup>-1</sup> were used to prepare calibrants and internal standards (ISs). All the ISs were at the concentration of 1 ng mL<sup>-1</sup> in the analytical solutions. High-purity deionized water (EASY-pure, PBI, Milan, Italy) was used for dilution of samples and standards, and 67% HNO<sub>3</sub> of ultrapure-grade (ROMIL Ltd., Cambridge, UK) and 40% HF of suprapure-grade (Merck, Darmstadt, Germany) for digestions.

# 2.2. Instrumentation

A Milestone Ethos 900-Mega II microwave oven (FKV Milestone, Milan, Italy) with a PTFE-vessel rotor was employed for digesting samples.

A Thermo Finnigan Element II (Bremen, Germany) sector field inductively coupled plasma mass spectrometry (SF-ICP-MS), equipped with Meinhard-type glass nebulizer, water-cooled Scott spray chamber, torch with guard electrode device and nickel interface cones, was used for metals quantification. The measurement parameters of the spectrometer were: radiofrequency power, 1200 W; plasma flow, 14.0 L min<sup>-1</sup>; auxiliary flow, 0.90 L min<sup>-1</sup>; sample gas flow, 0.85 L min<sup>-1</sup>; mass resolution, 300  $m/\Delta m$  (low resolution, LR) for Cd, Hg, Ir, Pb, Pt and 4000  $m/\Delta m$  (medium resolution, MR) for Co, Cr, Cu, Mn, Ni, Pd, Rh, and V. Two ISs were used to correct for possible instrumental drifts: <sup>115</sup>In for Cd, Hg, Ir, Pb and Pt, and <sup>69</sup>Ga for Co, Cr, Cu, Mn, Ni, Pd, Rh, and V.

#### 2.3. Sample treatment

Aliquots of ca. 1 g of each moisturizing cream were weighed into PTFE-vessels. A mixture of 5 mL of HNO<sub>3</sub> and 1 mL of HF was added to each vessel and then MW irradiated. The cycle was as follows: 10 min at 250 W; 5 min at 400 W; 5 min at 500 W; 5 min at 600 W. After cooling, samples were quantitatively transferred into polystyrene liners and diluted up to 30 mL with high-purity deionized water. Samples were digested in triplicate and reagent blanks run together with matrices and have been considered in the final evaluation. In order to keep under control matrix effects, the standard addition approach on five concentration levels was used. Adequate amounts of each element were added to a pool of digested samples. In particular, for Cd, Co, Cu, Hg, Ir, Mn, Pb, Pd, Pt, Rh, and V the concentration levels of 0.10, 0.25, 0.50, 1.0, and 2.5 ng mL<sup>-1</sup> and one order of magnitude higher for Cr and Ni were selected.

# 3. Results and discussion

#### 3.1. Method performances

Considering that the samples have very complex composition with large organic matter content, the total digestion of the matrix is mandatory to assure a complete metals solubilization. For this reason both concentrated HNO<sub>3</sub> and HF were used. The former is a strong oxidizing acid able to destroy the organic matter and this capability is enhanced at high temperatures while the latter is able to dissolve silica and silicates compounds largely present in the matrix and to complex elements as their stable fluorides.

Table 1 shows the isotopes selected for quantification and the resolution used to separate relevant interferences from the analytes. Mercury, Ir, Pb, and Pt were free from interferences and thus quantified in the LR resolution setting using their most abundant isotope to obtain the highest instrumental sensitivity, whereas Cd was determined at mass 111 because of the isobaric overlapping of <sup>114</sup>Sn on its most abundant mass (i.e., m/z = 114). Elements such as Co, Cr, Cu, Mn, Ni, Pd, Rh, and V were quantified at MR to avoid serious interfering species. In fact, a part from interferences produced by the plasma, the addition of HNO<sub>3</sub> and HF as decomposition reagents and the matrix with high content of metals created not negligible interferences. For example, the formation of ArN<sup>+</sup>, ArNH<sup>+</sup> overlapped the signals of Cr, Mn and V; ArF<sup>+</sup> heavily (i.e., 99.6%) covered the signal of Co, and CaF<sup>+</sup> interfered with the chosen mass of Cu. The high content of elements in the matrix such as Ca, K, Na, Mg, and Zn (mainly under the form of ascorbates and phosphates) - forming several oxides, argides and chlorides - also posed problems for the quantification of Co, Cu, Mn, Ni, Pd, and Rh, leading to incorrect high values. In this study, by using the MR mode, all these interferences were shifted far from the analytical peak and thus unequivocally separated. Moreover, the oxides formation

Table 1	
Method	parameters

Table 2	
Method	performances

Element	$LoQ (ng g^{-1})$	Recovery	Precision (%)	
		Spike <sup>a</sup> (ng g <sup>-1</sup> )	Found $(ng g^{-1})$	
Cd	0.014	5	$4.45\pm0.32$	5.21
Co	0.010	5	$4.40 \pm 0.43$	3.62
Cr	0.13	50	$50.3 \pm 4.6$	3.50
Cu	0.83	50	$48.7\pm5.2$	4.96
Hg	0.16	1	$1.10\pm0.12$	6.80
Ir	0.003	1	$0.97\pm0.05$	3.52
Mn	0.12	50	$49.6 \pm 3.5$	2.56
Ni	0.15	50	$52.2 \pm 4.1$	5.20
Pb	0.20	5	$4.56\pm0.53$	1.59
Pd	0.030	1	$0.92\pm0.06$	5.60
Pt	0.010	1	$0.99\pm0.05$	3.71
Rh	0.010	1	$1.03 \pm 0.14$	6.23
V	0.020	5	$5.32\pm0.47$	4.18

<sup>a</sup> Amount spiked on raw material.

was daily minimized by adjusting the BaO<sup>+</sup>/Ba<sup>+</sup> ratio, usually maintained below 0.002 (equal to 0.2%). These instrumental settings permitted to avoid the use of mathematical correction factors usually applied in Q-ICP-MS analysis, which anyway, would have been inadequate in case of such a great amount of interferences. As for the LR, the most abundant isotopes were selected for each element with the exception of Ni which, at mass 58, was hampered by the isobaric  ${}^{58}$ Fe, and of Pd that, at mass 106 (the most abundant one), was interfered by ArZn<sup>+</sup>. In order to show how the SF-ICP-MS neutralized the interferences and unequivocally distinguished among analyte and interferents, the spectra of Co and Ni in MR have been reported in Fig. 1a and b, respectively. In both cases the interferents were on the right of analyte signal. The signal of Co resulted to be well separated from the signals of ArF<sup>+</sup>, CaO<sup>+</sup>, ArNa<sup>+</sup>, and KO<sup>+</sup> (Fig. 1a), and that of Ni from CaO<sup>+</sup>, NaCl<sup>+</sup>, and ArMg<sup>+</sup> (Fig. 1b).

Table 2 shows the data on limits of quantification (LoQs), recovery and precision of the proposed method. The LoQs were calculated by using the  $10\sigma$  criterion on reagent blanks. Because of the lack of a cream-based certified reference material, accuracy was checked throughout recovery tests. To this end, the cream was added with known amounts of the elements of inter-

	Main interferences separated			
Cd 111 12.8 300 <sup>a</sup>				
Co 59 100 4000 $^{40}Ar^{19}F$ , $^{43}Ca^{16}O$ , $^{41}K^{18}$	<sup>3</sup> O, <sup>36</sup> Ar <sup>23</sup> Na, <sup>42</sup> Ca <sup>16</sup> O <sup>1</sup> H			
Cr 52 83.8 4000 $4^{40}$ Ar <sup>12</sup> C, ${}^{36}$ Ar <sup>16</sup> O, ${}^{38}$ Ar <sup>1</sup>	<sup>14</sup> N, <sup>35</sup> Cl <sup>17</sup> O, <sup>37</sup> Cl <sup>15</sup> N, <sup>35</sup> Cl <sup>16</sup> O <sup>1</sup> H			
Cu 63 69.2 4000 $4^{40}$ Ar <sup>23</sup> Na, ${}^{31}$ P <sup>16</sup> O <sup>16</sup> O, ${}^{42}$	<sup>4</sup> Ca <sup>19</sup> F			
Hg 202 29.8 300 <sup>a</sup>				
Ir 193 62.7 300 <sup>a</sup>				
Mn 55 100 4000 ${}^{37}Cl^{18}O$ , ${}^{40}Ar^{15}N$ , ${}^{39}K^{16}$	$^{5}O, ^{40}Ar^{14}N^{1}H$			
Ni 60 26.1 4000 $^{44}Ca^{16}O, {}^{23}Na^{37}Cl, {}^{36}A$	r <sup>24</sup> Mg			
Pb 208 52.4 300 <sup>a</sup>	6			
Pd 105 22.3 4000 <sup>40</sup> Ar <sup>65</sup> Cu, <sup>68</sup> Zn <sup>37</sup> Cl				
Pt 195 33.8 300 <sup>a</sup>				
Rh 103 100 4000 $^{40}$ Ar <sup>63</sup> Cu $^{68}$ Zn <sup>35</sup> Cl $^{662}$ Zn	Zn <sup>37</sup> Cl			
V 51 99.8 4000 <sup>35</sup> Cl <sup>16</sup> O, <sup>37</sup> Cl <sup>14</sup> N, <sup>36</sup> Ar <sup>1</sup>	$^{4}N^{1}H$			

<sup>a</sup> No relevant interference for the matrices considered.



Fig. 1. SF-ICP-MS spectra of Co (a) and Ni (b) obtained in medium resolution.

est, digested with acids in the MW oven and then SF-ICP-MS analyzed. Levels added and found recoveries were reported in Table 2.

Precision was expressed as the relative standard deviation (R.S.D.) on 10 replicated measurements of a pool of digested samples, so it represented the repeatability of the method. The LoQ values were around  $0.02 \text{ ng g}^{-1}$  for Cd, Co, Ir, Pd, Pt, Rh, and V, and approximately 10 times higher for Cr, Hg, Mn, Ni, and Pb. Copper had LoQs higher than  $0.5 \text{ ng g}^{-1}$  but this was not a problem as the level of this element was usually well above in all the analyzed creams. Recoveries, in the interval 88% (Cd, Co) to 110% (Hg), were satisfactory considering that they were calculated on concentrations equal or below 1.5 ng mL<sup>-1</sup> in the analytical solution. This result gave assurance that the matrix mineralization process avoided significant analyte loss or contamination. Precision was below 10% for all the elements testifying a good homogeneity of the digests.

# 3.2. Metal quantification

The concentration of metals in the 11 types of moisturizing creams is presented in Table 3. Each product was given a running number.

Table 3 Metal content (mean concentration and S.D., in ng  $g^{-1}$ ) obtained in different samples of body creams (number of independent replicates = 3)

						• •							
Sample	Cd	Со	Cr	Cu	Hg	Ir	Mn	Ni	Pb	Pd	Pt	Rh	V
1	$0.57\pm0.05$	$4.87\pm0.19$	$303 \pm 11$	$7.31 \pm 1.03$	<loq< td=""><td><math display="block">0.055\pm0.004</math></td><td><math display="block">38.2\pm2.8</math></td><td><math>153\pm 8</math></td><td><math display="block">0.71\pm0.08</math></td><td><math display="block">0.32\pm0.03</math></td><td><loq< td=""><td><math display="block">0.025\pm0.002</math></td><td><math display="block">4.00\pm0.03</math></td></loq<></td></loq<>	$0.055\pm0.004$	$38.2\pm2.8$	$153\pm 8$	$0.71\pm0.08$	$0.32\pm0.03$	<loq< td=""><td><math display="block">0.025\pm0.002</math></td><td><math display="block">4.00\pm0.03</math></td></loq<>	$0.025\pm0.002$	$4.00\pm0.03$
2	$0.20\pm0.01$	$0.13\pm0.01$	$16.8\pm1.6$	$3.27\pm0.29$	<loq< td=""><td><loq< td=""><td><loq< td=""><td><math display="block">17.5\pm1.4</math></td><td><math display="block">1.14\pm0.09</math></td><td><loq< td=""><td><loq< td=""><td><loq< td=""><td><math display="block">0.29\pm0.02</math></td></loq<></td></loq<></td></loq<></td></loq<></td></loq<></td></loq<>	<loq< td=""><td><loq< td=""><td><math display="block">17.5\pm1.4</math></td><td><math display="block">1.14\pm0.09</math></td><td><loq< td=""><td><loq< td=""><td><loq< td=""><td><math display="block">0.29\pm0.02</math></td></loq<></td></loq<></td></loq<></td></loq<></td></loq<>	<loq< td=""><td><math display="block">17.5\pm1.4</math></td><td><math display="block">1.14\pm0.09</math></td><td><loq< td=""><td><loq< td=""><td><loq< td=""><td><math display="block">0.29\pm0.02</math></td></loq<></td></loq<></td></loq<></td></loq<>	$17.5\pm1.4$	$1.14\pm0.09$	<loq< td=""><td><loq< td=""><td><loq< td=""><td><math display="block">0.29\pm0.02</math></td></loq<></td></loq<></td></loq<>	<loq< td=""><td><loq< td=""><td><math display="block">0.29\pm0.02</math></td></loq<></td></loq<>	<loq< td=""><td><math display="block">0.29\pm0.02</math></td></loq<>	$0.29\pm0.02$
3	$1.00\pm0.07$	$0.64\pm0.03$	$39.7\pm2.9$	$13.2\pm1.3$	<loq< td=""><td><math display="block">0.060\pm0.006</math></td><td><math display="block">11.0\pm0.4</math></td><td><math>147 \pm 11</math></td><td><loq< td=""><td><math display="block">0.33\pm0.03</math></td><td><loq< td=""><td><math display="block">0.080 \pm 0.008</math></td><td><math display="block">1.31\pm0.11</math></td></loq<></td></loq<></td></loq<>	$0.060\pm0.006$	$11.0\pm0.4$	$147 \pm 11$	<loq< td=""><td><math display="block">0.33\pm0.03</math></td><td><loq< td=""><td><math display="block">0.080 \pm 0.008</math></td><td><math display="block">1.31\pm0.11</math></td></loq<></td></loq<>	$0.33\pm0.03$	<loq< td=""><td><math display="block">0.080 \pm 0.008</math></td><td><math display="block">1.31\pm0.11</math></td></loq<>	$0.080 \pm 0.008$	$1.31\pm0.11$
4	$0.12\pm0.01$	$0.84 \pm 0.11$	$41.7\pm4.3$	$28.7\pm2.5$	<loq< td=""><td><loq< td=""><td><math display="block">5.15\pm0.15</math></td><td><math display="block">28.0\pm3.0</math></td><td><math display="block">1.05\pm0.12</math></td><td><loq< td=""><td><math display="block">6.28\pm0.13</math></td><td><math display="block">0.024 \pm 0.001</math></td><td><math display="block">11.4\pm0.2</math></td></loq<></td></loq<></td></loq<>	<loq< td=""><td><math display="block">5.15\pm0.15</math></td><td><math display="block">28.0\pm3.0</math></td><td><math display="block">1.05\pm0.12</math></td><td><loq< td=""><td><math display="block">6.28\pm0.13</math></td><td><math display="block">0.024 \pm 0.001</math></td><td><math display="block">11.4\pm0.2</math></td></loq<></td></loq<>	$5.15\pm0.15$	$28.0\pm3.0$	$1.05\pm0.12$	<loq< td=""><td><math display="block">6.28\pm0.13</math></td><td><math display="block">0.024 \pm 0.001</math></td><td><math display="block">11.4\pm0.2</math></td></loq<>	$6.28\pm0.13$	$0.024 \pm 0.001$	$11.4\pm0.2$
5	$2.23\pm0.18$	$5.83 \pm 0.31$	$64.9\pm2.8$	$19.8 \pm 1.1$	<loq< td=""><td><loq< td=""><td><math display="block">7.53 \pm 1.6</math></td><td><math display="block">88.7\pm6.2</math></td><td><math display="block">2.80\pm0.20</math></td><td><loq< td=""><td><loq< td=""><td><math display="block">0.029 \pm 0.002</math></td><td><math display="block">4.47\pm0.51</math></td></loq<></td></loq<></td></loq<></td></loq<>	<loq< td=""><td><math display="block">7.53 \pm 1.6</math></td><td><math display="block">88.7\pm6.2</math></td><td><math display="block">2.80\pm0.20</math></td><td><loq< td=""><td><loq< td=""><td><math display="block">0.029 \pm 0.002</math></td><td><math display="block">4.47\pm0.51</math></td></loq<></td></loq<></td></loq<>	$7.53 \pm 1.6$	$88.7\pm6.2$	$2.80\pm0.20$	<loq< td=""><td><loq< td=""><td><math display="block">0.029 \pm 0.002</math></td><td><math display="block">4.47\pm0.51</math></td></loq<></td></loq<>	<loq< td=""><td><math display="block">0.029 \pm 0.002</math></td><td><math display="block">4.47\pm0.51</math></td></loq<>	$0.029 \pm 0.002$	$4.47\pm0.51$
6	$1.17\pm0.06$	$1.33\pm0.13$	$148 \pm 11$	$33.7\pm5.08$	<loq< td=""><td><math display="block">0.20\pm0.03</math></td><td><math display="block">59.9 \pm 0.29</math></td><td><math>128 \pm 14</math></td><td><math display="block">0.93\pm0.15</math></td><td><loq< td=""><td><math display="block">0.81\pm0.16</math></td><td><math display="block">0.15\pm0.02</math></td><td><math display="block">1.07\pm0.10</math></td></loq<></td></loq<>	$0.20\pm0.03$	$59.9 \pm 0.29$	$128 \pm 14$	$0.93\pm0.15$	<loq< td=""><td><math display="block">0.81\pm0.16</math></td><td><math display="block">0.15\pm0.02</math></td><td><math display="block">1.07\pm0.10</math></td></loq<>	$0.81\pm0.16$	$0.15\pm0.02$	$1.07\pm0.10$
7	$4.39\pm0.10$	$110 \pm 5$	$44.4\pm2.9$	$11.7\pm1.2$	<loq< td=""><td><loq< td=""><td><math display="block">20.2\pm0.3</math></td><td><math display="block">43.7\pm3.0</math></td><td><math display="block">8.67 \pm 0.56</math></td><td><math display="block">0.060\pm0.010</math></td><td><loq< td=""><td><loq< td=""><td><loq< td=""></loq<></td></loq<></td></loq<></td></loq<></td></loq<>	<loq< td=""><td><math display="block">20.2\pm0.3</math></td><td><math display="block">43.7\pm3.0</math></td><td><math display="block">8.67 \pm 0.56</math></td><td><math display="block">0.060\pm0.010</math></td><td><loq< td=""><td><loq< td=""><td><loq< td=""></loq<></td></loq<></td></loq<></td></loq<>	$20.2\pm0.3$	$43.7\pm3.0$	$8.67 \pm 0.56$	$0.060\pm0.010$	<loq< td=""><td><loq< td=""><td><loq< td=""></loq<></td></loq<></td></loq<>	<loq< td=""><td><loq< td=""></loq<></td></loq<>	<loq< td=""></loq<>
8	$3.49\pm0.26$	$222\pm 8$	$21.1\pm4.5$	$9.09 \pm 1.10$	<loq< td=""><td><loq< td=""><td><math display="block">14.3\pm1.1</math></td><td><math display="block">67.8\pm2.7</math></td><td><math display="block">7.06\pm0.29</math></td><td><math display="block">0.21\pm0.06</math></td><td><loq< td=""><td><loq< td=""><td><loq< td=""></loq<></td></loq<></td></loq<></td></loq<></td></loq<>	<loq< td=""><td><math display="block">14.3\pm1.1</math></td><td><math display="block">67.8\pm2.7</math></td><td><math display="block">7.06\pm0.29</math></td><td><math display="block">0.21\pm0.06</math></td><td><loq< td=""><td><loq< td=""><td><loq< td=""></loq<></td></loq<></td></loq<></td></loq<>	$14.3\pm1.1$	$67.8\pm2.7$	$7.06\pm0.29$	$0.21\pm0.06$	<loq< td=""><td><loq< td=""><td><loq< td=""></loq<></td></loq<></td></loq<>	<loq< td=""><td><loq< td=""></loq<></td></loq<>	<loq< td=""></loq<>
9	$0.82\pm0.17$	$2.75\pm0.26$	$39.9 \pm 1.9$	$23.7\pm3.91$	<loq< td=""><td><loq< td=""><td><math display="block">4.78\pm0.6</math></td><td><math display="block">63.2\pm4.6</math></td><td><math display="block">1.22\pm0.17</math></td><td><loq< td=""><td><loq< td=""><td><loq< td=""><td><math display="block">2.55\pm0.11</math></td></loq<></td></loq<></td></loq<></td></loq<></td></loq<>	<loq< td=""><td><math display="block">4.78\pm0.6</math></td><td><math display="block">63.2\pm4.6</math></td><td><math display="block">1.22\pm0.17</math></td><td><loq< td=""><td><loq< td=""><td><loq< td=""><td><math display="block">2.55\pm0.11</math></td></loq<></td></loq<></td></loq<></td></loq<>	$4.78\pm0.6$	$63.2\pm4.6$	$1.22\pm0.17$	<loq< td=""><td><loq< td=""><td><loq< td=""><td><math display="block">2.55\pm0.11</math></td></loq<></td></loq<></td></loq<>	<loq< td=""><td><loq< td=""><td><math display="block">2.55\pm0.11</math></td></loq<></td></loq<>	<loq< td=""><td><math display="block">2.55\pm0.11</math></td></loq<>	$2.55\pm0.11$
10	$0.77\pm0.01$	$0.61\pm0.10$	$39.2\pm3.4$	$51.2\pm0.5$	<loq< td=""><td><loq< td=""><td><math display="block">6.91 \pm 1.1</math></td><td><math display="block">80.6\pm5.7</math></td><td><math display="block">6.29 \pm 0.44</math></td><td><loq< td=""><td><loq< td=""><td><loq< td=""><td><math display="block">3.08\pm0.36</math></td></loq<></td></loq<></td></loq<></td></loq<></td></loq<>	<loq< td=""><td><math display="block">6.91 \pm 1.1</math></td><td><math display="block">80.6\pm5.7</math></td><td><math display="block">6.29 \pm 0.44</math></td><td><loq< td=""><td><loq< td=""><td><loq< td=""><td><math display="block">3.08\pm0.36</math></td></loq<></td></loq<></td></loq<></td></loq<>	$6.91 \pm 1.1$	$80.6\pm5.7$	$6.29 \pm 0.44$	<loq< td=""><td><loq< td=""><td><loq< td=""><td><math display="block">3.08\pm0.36</math></td></loq<></td></loq<></td></loq<>	<loq< td=""><td><loq< td=""><td><math display="block">3.08\pm0.36</math></td></loq<></td></loq<>	<loq< td=""><td><math display="block">3.08\pm0.36</math></td></loq<>	$3.08\pm0.36$
11	$5.11\pm0.42$	$2.26\pm0.42$	$59.6\pm4.2$	$34.2\pm2.3$	<loq< td=""><td><loq< td=""><td><math display="block">51.4\pm3.3</math></td><td><math display="block">58.5\pm5.2</math></td><td><math display="block">3.24\pm0.26</math></td><td><math display="block">1.07\pm0.19</math></td><td><math display="block">2.65\pm0.06</math></td><td><loq< td=""><td><math display="block">6.03\pm0.48</math></td></loq<></td></loq<></td></loq<>	<loq< td=""><td><math display="block">51.4\pm3.3</math></td><td><math display="block">58.5\pm5.2</math></td><td><math display="block">3.24\pm0.26</math></td><td><math display="block">1.07\pm0.19</math></td><td><math display="block">2.65\pm0.06</math></td><td><loq< td=""><td><math display="block">6.03\pm0.48</math></td></loq<></td></loq<>	$51.4\pm3.3$	$58.5\pm5.2$	$3.24\pm0.26$	$1.07\pm0.19$	$2.65\pm0.06$	<loq< td=""><td><math display="block">6.03\pm0.48</math></td></loq<>	$6.03\pm0.48$

Three products had Ni concentration around or slightly above  $100 \text{ ng g}^{-1}$ , while the remaining showed levels lower than 89 ng  $g^{-1}$ . Chromium was present at levels of tens of ng  $g^{-1}$  in all the products, with maximum levels of 148 and 303 ng  $g^{-1}$  in the creams nos. 1 and 6. Cobalt content was not higher than  $6 \text{ ng g}^{-1}$ , but two samples (nos. 7 and 8) had much higher concentrations (i.e., 110 and 222 ng  $g^{-1}$ ). Vanadium was higher than 10 ng  $g^{-1}$ in one sample, the other products showing concentrations from 0.29 to 6.03 ng  $g^{-1}$ . Mercury was below the LoQ in all products; Ir and Pd were under the LoQ for 8 out of 11 samples and Pd and Rh were undetectable in 55% of the products. Only two products (nos. 4 and 11) contained Pt at levels of a few ng  $g^{-1}$ , one of these (no. 11) presented also a relatively high content of Pd. Except for one cream, Mn and Pb were always detectable with concentrations varying between 5.15 and 59.9 ng  $g^{-1}$  and 0.71 and 8.67 ng  $g^{-1}$ , respectively. Copper ranged 3.27–33.7 ng  $g^{-1}$ . Product no. 6 which presented a high content of Cr, showed the highest levels of Ir, Mn, and Rh and also a relatively high concentration of Ni. On the contrary, product no. 2 presented the lowest concentration for several elements, i.e., Co, Cr, Cu, Mn, Ni, and V.

Even if Ni actually represents the main cause of contact dermatitis, minimal amounts of other toxic metals can trigger a pre-existing allergy [18]. In some cases, in fact, reactions to Ni were not isolated but associated to Cr, Co, and Pd sensitivity [6,10,25,26]. On this basis, it has been proposed that consumers products should contain less than 5000 ng g<sup>-1</sup> – and preferably below 1000 ng g<sup>-1</sup> – of metals such as Co, Cr, and Ni to minimize the risk for allergenic reactions [18,25,26]. The levels of Pb should not exceed 20,000 ng g<sup>-1</sup> [34] and in cement the level of water-soluble Cr(VI) should be less than 0.0002% [35].

Taking into account these considerations, the first conclusion of this study is that the concentration of Ni was above  $100 \text{ ng g}^{-1}$  in 3 out of the 11 analyzed products. Despite this concentration appeared to be slightly higher than those declared on the label, it was 10 times below the concentration considered as allergologically safe for consumers [25].

As a second conclusion, the other metals considered presented levels lower than  $1000 \text{ ng g}^{-1}$  in all cases. In particular, Co and Cr, which are responsible together with Ni for the majority of cases of contact dermatitis, even at their highest concentrations (ca. 200 and 300 ng g<sup>-1</sup>, respectively) were lower than the limits proposed as safe [25]. Also Pb was very low and below the risk-free limit. Mercury, which is present in many skin-lightening creams causing facial dermatitis, was negative in all the samples [15].

This study was also devoted to weakly sensitizing agents, such as Cu, Cd, Mn, and V and PGEs [7,10]. Copper, Cd, Mn, and V were at relatively low levels, even if in one case it exceeded  $10 \text{ ng g}^{-1}$  for V and  $50 \text{ ng g}^{-1}$  for Cu and Mn. The concentrations of Ir, Pd, Pt, and Rh were at fractions of  $\text{ ng g}^{-1}$  or even undetectable in several cases; anyway two creams had both a certain content of Pt.

Finally, to the best of our knowledge, there are very few previous studies on the content of metals in moisturizing creams. The importance of such information is due to the fact that body creams contain fat-soluble substances which facilitate the absorption of metals through the skin and also because creams remain in contact with the skin for a long period of time. It is also worth remarking that some creams presented Cr and Co in amounts comparable to those of Ni and that these two elements are scarcely explored. Among the few published studies on creams, Conti et al. reported data for Cd, Cr, Hg, and Pb in five body creams. In particular, values of Cd and Pb here obtained were similar to the lower limit of the experimented ranges, Cr fully overlapped and Hg was found below the LoQ in both studies [24]. Another paper quantified Cu and Pb in various cosmetic products, creams included, founding these metals al levels of tens of  $\mu g g^{-1}$ , more than one order of magnitude higher than this study [22].

Other cosmetics such as make-up products, detergents, shampoos and foam baths, contained metals in quantity higher than those on creams because of their different formulations and the final uses. Some examples are: in henna, Ni and Co were ca.  $3 \ \mu g g^{-1}$  [17], and Pb ranged 2.2–19.9  $\ \mu g g^{-1}$  [20]; commercial foam bath had a content of Cr 22–199 ng g<sup>-1</sup> and Ni 26–287 ng g<sup>-1</sup> [36]; household products (i.e., liquid and powder detergents) contained 0.1–0.9  $\ \mu g g^{-1}$  of Ni, 0.1–1.1 of Cr, 0.1–0.2 of Co [25,37]; eye shadows had Co, Cr, Ni, and Pb in the range of 1–50  $\ \mu g g^{-1}$  and in one sample Cr was more than 300  $\ \mu g g^{-1}$  [19]; in a permanent lip-liner Ni was equal to 1.8  $\ \mu g g^{-1}$  [21].

# 4. Conclusions

The developed procedure based on MW assisted treatment and SF-ICP-MS quantification allowed the precise and accurate determination of chemical elements in body creams. Among the 11 products labelled as "Ni-tested" three cases had a Ni concentration above the declared value of  $100 \text{ ng g}^{-1}$ . However, the concentration of Ni in all the creams was much lower than the recommended safe level (< $1000 \text{ ng g}^{-1}$ ) for consumers. Mercury was less than LoQ in all cases and Co, Cr, and Pb were well below the limits suggested to be at risk of sensitization. Among the new allergenic metals, Ir, Rh, Pd, and Pt were at traces in the majority of cases. These results suggested that body creams contained metals at levels that are not likely to cause allergy reactions in subjects with contact allergy. Nevertheless, it should be convenient to monitor the concentration of other metals next to Ni, also considering the possibility of their cross-reactivity.

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#### References

- [1] J.F. Fowler, Curr. Probl. Dermatol. 10 (1998) 213-244.
- [2] L. Kanerva, R. Jolanki, T. Estlander, K. Alanko, A. Savela, Am. J. Contact Dermat. 3 (2000) 155–160.
- [3] C. Lidén, M. Bruze, T. Menné, in: J.P. Frosch, T. Menné, J.-P. Lepoittevin (Eds.), Contact Dermatitis, 4th ed., Springer-Verlag, Berlin, 2006, pp. 537–568.

- [4] A. Josefson, G. Färm, B. Styme, B. Meding, Contact Dermat. 55 (2006) 286–290.
- [5] Directive 94/27/EC of the European Parliament and of the Council of 30 June 1994. Official Journal of the European Communities, L 188, 22 July 1994, 1–2.
- [6] M. Hindsén, L. Persson, B. Gruvberger, Contact Dermat. 53 (2005) 350–351.
- [7] A. Motolese, M. Truzzi, A. Giannini, S. Seidenari, Contact Dermat. 28 (1993) 59–62.
- [8] M. Barré Hansen, T. Menné, J. Duus Johansen, Contact Dermat. 54 (2006) 140–144.
- [9] M. Hindsén, A. Spirén, M. Bruze, Contact Dermat. 53 (2005) 2-8.
- [10] B. Santucci, C. Valenzano, M. de Rocco, A. Cristaudo, Contact Dermat. 43 (2000) 333–338.
- [11] J.A. Marcusson, K. Cederbrant, J. Heilborn, Contact Dermat. 38 (1998) 297–298.
- [12] J.J. Hostynek, H.I. Maibach, Dermatol. Ther. 17 (2004) 328-333.
- [13] J. Pardo, M. Rodríguez-Serna, J. De La Quadra, J.M. Fortea, Contact Dermat. 50 (2004) 41.
- [14] B. Işikli, T.A. Demir, T. Akar, A. Berber, S.M. Ürer, C. Kalyoncu, M. Canbek, Chemosphere 63 (2006) 1546–1552.
- [15] C.C. Sun, Contact Dermat. 17 (1987) 306–309.
- [16] Directive 76/768/EEC of the Council of 27 July 1976. Official Journal of the European Communities, L 262, 27 September 1976, 169–200.
- [17] I.-J. Kang, M.-H. Lee, Contact Dermat. 55 (2006) 26–29.
- [18] C.F. Allenby, D.A. Basketter, Contact Dermat. 28 (1993) 129–133.
- [19] E.-L. Sainio, R. Jolanki, E. Hakala, L. Kanerva, Contact Dermat. 42 (2000) 5–10.
- [20] N. Lekouch, A. Sedki, A. Nejmeddine, S. Gamon, Sci. Total Environ. 280 (2001) 39–43.
- [21] C. Jager, U. Jappe, J. Dtsch. Dermatol. Ges. 3 (2005) 527-529.

- [22] Iu. Tsankov, I. Iordanova, D. Lolova, S. Uzunova, S. Dinoeva, Probl. Khig. 7 (1982) 127–136.
- [23] A. Salvador, M.C. Pascual-Martí, J.R. Adell, A. Requeni, J.G. March, J. Pharm. Biomed. Anal. 22 (2000) 301–306.
- [24] M.E. Conti, F. Botrè, F. Mazzei, J. Appl. Cosmetol. 14 (1996) 147-154.
- [25] D.A. Basketter, G. Angelini, A. Ingber, P.S. Kern, T. Menné, Contact Dermat. 49 (2003) 1–7.
- [26] D.A. Basketter, G. Briatico-Vangosa, W. Kaesner, C. Lally, W.J. Bontinck, Contact Dermat. 28 (1993) 15–25.
- [27] N. Lewen, S. Mathew, M. Schenkerberger, T. Raglione, J. Pharm. Biomed. Anal. 35 (2004) 739–752.
- [28] J. Huang, X. Hu, J. Zhang, K. Li, Y. Yan, X. Xu, J. Pharm. Biomed. Anal. 40 (2006) 227–234.
- [29] R. Nageswara Rao, M.V.N. Kumar Talluri, J. Pharm. Biomed. Anal. 43 (2007) 1–13.
- [30] H. Vanhoe, J. Goossens, L. Moens, R. Dams, J. Anal. Atom. Spectrom. 9 (1994) 177–185.
- [31] B. Bocca, A. Alimonti, G. Forte, F. Petrucci, C. Pirola, O. Senofonte, N. Violante, Anal. Bioanal. Chem. 377 (2003) 65–70.
- [32] C.S. Muñiz, J.M. Marchante-Gayón, J.I. García Alonso, A. Sanz-Medel, J. Anal. Atom. Spectrom. 14 (1999) 193–198.
- [33] B. Bocca, G. Forte, A. Ronchi, R. Gaggeri, A. Alimonti, C. Minoia, Rapid Commun. Mass Spectrom. 20 (2006) 3289–3294.
- [34] L. Motitshke, Parfümerie kosmetik 6 (1990) 71.
- [35] Directive 2003/53/EC of the European Parliament and of the Council of 18 June 2003. Official Journal of the European Communities, L 178, 17 July 2003, 24–27.
- [36] L. Ciaralli, R. Giordano, S. Cassina, A. Sepe, S. Costantini, Ann. Ist. Super. Sanità 32 (1996) 381–385.
- [37] H. Ebner, T. Luger, R. Binder, G. Machata, Wien. Klin. Wochenschr. 90 (1978) 311–313.