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Risk assessment of allergen metals in cosmetic products

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Synopsis

Cosmetics are one of the most common reasons for hospital referrals with allergic contact dermatitis. Because of the increased use of cosmetics within the population and an increase in allergy cases, monitoring of heavy metals, especially allergen metals, is crucial. The aim of this study was to investigate the concentration of allergen metals, nickel (Ni), cobalt (Co), and chromium (Cr), in the most commonly used cosmetic products including mascara, eyeliner, eye shadow, lipstick, and nail polish. In addition, for safety assessment of cosmetic products, margin of safety of the metals was evaluated. Forty-eight makeup products were purchased randomly from local markets and large cosmetic stores in Istanbul, Turkey, and an atomic absorption spectrometer was used for metal content determination. Risk assessment of the investigated cosmetic products was performed by calculating the systemic exposure dosage (SED) using Scientific Committee on Consumer Safety guideline. According to the results of this investigation in all the samples tested, at least two of the allergen metals, Ni and/or Co and/or Cr were detected. Moreover, 97% of the Ni-detected products, 96% of Cr- and 54% of Co-detected products, contained over 1 μg/g of this metals, which is the suggested ultimate target value for sensitive population and thereby can be considered as the possible allergen. On the basis of the results of this study, SED of the metals was negligible; however, contact dermatitis caused by cosmetics is most probably due to the allergen metal content of the products. In conclusion, to assess the safety of the finished products, postmarketing vigilance and routine monitoring of allergen metals are very important to protect public health.

INTRODUCTION

Cosmetic products are commonly used by millions of consumers to keep their body in good condition, to change their appearance, or to correct body odors (1). On the other hand, increased use of cosmetics and/or continuous use over prolonged time may also lead to unwanted adverse health effects, in particular, local dermal effects (2). It was reported that, cosmetics are one of the most common reasons for hospital referrals with allergic contact dermatitis (3).

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Nickel (Ni), cobalt (Co), and chromium (Cr) are the metals most commonly responsible for allergic contact dermatitis (4). Duarte *et al*. reported that 33.5% of 1208 patients in their study had at least one positive reaction to Ni and/or Co and/or Cr in patch test for diagnosis of contact dermatitis (5). Also, it should be consider that contact allergens may cause a mild response on the first few exposures, but after the allergy develops, the response worsens with subsequent exposures and eventually, even short exposures to low concentrations can cause very severe reactions (6).

Because of the increased use of cosmetics within the population and an increase in allergy cases, monitoring of heavy metals especially allergen metals is crucial. The objective of our study was to investigate the concentration of allergen metals, Ni, Co, and Cr, in the most commonly used cosmetic products such as mascara, eyeliner, eye shadow, lipstick, and nail polish. In addition, for safety assessment of cosmetic products, margin of safety (MoS) of the metals was evaluated.

MATERIALS AND METHODS

SAMPLING

Commonly used makeup products were purchased randomly from local markets and large cosmetic stores in Istanbul, Turkey. Forty-eight samples were divided into seven groups: mascara (n = 5), eye shadow (12), eyeliner (7), lipstick (6), blush (4), nail polish (10), and body cream (4).

REAGENTS

All reagents were of analytical grade. All aqueous solutions were prepared with deionized water obtained by using ultrapure water system (Aqua-Nova Hepta Distillated, resistivity 0.34 MΩ×cm, Kristianstad, Sweden). HNO_3 (65%) and HF (40%) from Merck suprapure grade (Darmstadt, Germany) were used for digestion of the samples and dilution. Plastic bottles, autosampler cups, teflon vessels, vials for collecting samples, and glassware were cleaned by soaking in HNO_3 (10% v/v) for a day, rinsing four times with ultrapure water and drying in an oven at 40°C. All prepared solutions were stored in high-density polypropylene bottles. Autosampler washing solution containing HNO_3 (0.2% v/v) was used to avoid clogging of the autosampler sampling capillary tip and to improve dispersion of sample solution onto the graphite tube. Stock standard solutions of analytes (1 g/l each) were obtained from Merck. Standard solutions were freshly prepared by diluting the stock standard solutions to the desired calibration ranges in 0.2% HNO_3.

APPARATUS

An atomic absorption spectrometer (AAS) technique with a Perkin Elmer AS-800 AAS (MA), equipped with transversely heated graphite furnace (BO 504033), a longitudinal Zeeman background correction system, and an autosampler, was used for metal determination. Argon was used as inert gas for graphite furnace measurements. Samples were injected into the graphite furnace using an autosampler (Perkin Elmer AS-800). Digestion was carried out using Milestone MLS 1200 Mega high-performance microwave digestion unit (Shelton, CT).

MEASUREMENT OF CR, NI, AND CO LEVELS

Cosmetic samples (100 mg) were wet weighted and digested with 3 ml of 65% HNO_3 and 1 ml of 40% HF in microwave digestion system (digestion conditions for microwave system were applied as 2 min for 250 W, 2 min for 0 W, 6 min for 250 W, 5 min for 400 W, 5 min for 650 W, vent: 8 min). The digested samples were filled with double-glass distilled water up to 5.0 ml. These samples were applied to AAS for element determination. The operation parameters for the investigated elements were set as recommended by the manufacturer (Table I). Of sample aliquot, 20 μl was injected into the graphite furnace, and then the chemical modifier was added for Cr and Co by the autosampler. Each experimental datum was the arithmetic average of two determinations.

RESULTS AND DISCUSSION

In this study, the level of the most notable allergen metals, Cr, Ni, and Co was investigated in 48 cosmetic products (Tables II and III). The highest level of Ni (37.95 μg/g) and Co (48.19 μg/g) was found in same eyeliner, whereas the highest Cr level (62.19 μg/g) was detected in a lipstick sample. The European Union (EU) and Turkey legislations have prohibited nickel in cosmetic products (7,8). However, according to our results, Ni was detected in 69% of the investigated samples. The lowest level was found in nail polish samples, and Ni in body creams was under the limit of detection (0.3 ng/ml). Almost all the eye cosmetic samples contained varying amounts of Ni (1.75–37.95 μg/g). The Ni content of eye cosmetics was found higher than those of other type of products. These levels were found lower than the FDA limitation for Ni impurities in color additives (9). However, as the skin of the eyelid is thin, the most vulnerable and sensitive areas of the body, eczemas of the eyelids are common (10); such observations in eye cosmetic

Table I
Instrumental Conditions of Atomic Absorption Spectrometer

Instrumental conditions	Cr	Ni	Co
Argon flow (ml/min)	250	250	250
Sample volume (μl)	20	20	20
Modifier (μl)	5	-	5
Heating program temperature (°C; ramp time [s], hold time [s])			
Drying 1	110 (1–30)	110 (1–30)	110 (1–30)
Drying 2	130 (15–30)	130 (15–30)	130 (15–30)
Ashing	1500 (10–20)	1100 (10–20)	1400 (10–20)
Atomization	2300 (0–5)	2300 (0–5)	2400 (0–5)
Cleaning	2450 (1–3)	2500 (1–5)	2450 (1–3)

Table II
Concentrations of Allergen Metals in Cosmetics

Metal	Number of samples with detectable metals[a]	Mean ± SD (μg/g)	Range (μg/g)
Ni	33	6.79 ± 7.15	0.93–37.95
Cr	48	18.07 ± 19.10	0.51–62.19
Co	47	3.60 ± 7.93	0.15–48.19

SD: Standard deviation.
[a]Non-detectable values were not taken into account.

products is alarming and should be considered in future risk assessments. Although the lipstick samples contained relatively less amount of Ni compared to other types, it should be considered that Ni in lipsticks was reported to be the most common and relevant allergen in the patients referred for lip dermatitis (11). Furthermore, 97% of the Ni-detected products in this study contained Ni levels over 1 μg/g, which is the suggested ultimate target value for sensitive population (4) and thereby can be considered as the possible allergen.

In our previous study, we determined Ni in 94.29% of the 105 hair care products commercially available in Turkey (12), and unfortunately, Ni content of 17.14% of the samples was above the limit of allergic contact dermatitis. In the general population, estimated prevalence of contact sensitization because of Ni allergy has been reported to be 8.6% worldwide (13). And we are exposed to Ni not only with these cosmetic products but also in various components of clothing such as zippers and buckles, by jewelry, household items, electronics, and medical and dental devices (14). So it is important to evaluate cumulative exposure.

It was reported that when consumer products contained a level more than 1 μg/g of Cr, the risk of the induction of sensitization was higher (15). Similarly, Basketter *et al*. (16) showed in their study with 17 chromium-allergic healthy individuals, that the patch test threshold was 10 ppm for Cr but in the presence of an irritant such as sodium lauryl sulfate, the threshold should be considered as 1 ppm. In this study, Cr was detected in all the investigated samples and levels were found higher than 1 μg/g except two mascara samples.

Co was detected in 98% of the samples with the concentration ranges from 0.15 to 48.19 μg/g. The highest concentration was found in one of the eyeliner samples whereas the lowest concentration was found in a lipstick sample. All five samples of lipsticks contained Co, with an average concentration of 0.58 μg/g and maximum of 1.44 μg/g. Previous studies conducted in cosmetic product showed relatively lower Co levels in cosmetics (17). But the point is, cosmetics are not the only source of exposure, jewelry, belts, leather goods, implants, cleaners, and detergents also contain these metals and continuous exposure may cause chronic dermatitis (18). There are no international standards for metals contained in cosmetics yet. However, according to EU and Turkey Cosmetic Regulations, Cr and Ni are listed as one of the substances that are prohibited in any amount in cosmetic products (7,8).

Dermal exposure is expected to be the most significant route for cosmetic products since the majority of cosmetics are applied to the skin. But in risk characterization, the last

Table III
Allergen Metal Concentrations in Different Cosmetic Products

Cosmetics	N	Ni (μg/g)	Cr (μg/g)	Co (μg/g)
		Mean ± SD (range)[a]		
Mascara	5	8.21 ± 8.20 (1.75–19.02)	3.62 ± 4.17 (0.51–10.15)	3.94 ± 3.83 (0.16–10.18)
Eye shadow	12	5.74 ± 2.03 (3.03–9.40)	6.33 ± 4.91 (1.62–19.04)	3.11 ± 1.97 (1.21–7.09)
Eyeliner	7	14.92 ± 14.50 (3.79–37.95)	11.12 ± 11.64 (1.42–31.03)	14.96 ± 18.98 (0.28–48.19)
Lipstick	6	3.17 ± 1.33 (1.65–4.10)	54.74 ± 8.03 (44.61–62.19)[b,c,d]	0.58 ± 0.50 (0.15–1.44)[c]
Blusher	4	7.65 ± 1.73 (6.54–10.23)[e]	40.76 ± 12.01 (28.84–55.79)[b,c,d]	3.05 ± 2.23 (0.32–5.05)
Nail polish	10	1.26 ± 0.23 (0.93–1.48)[b,c,d,e,f]	17.48 ± 12.63 (6.67–40.13)[b,c,e,f]	0.44 ± 0.28 (0.18–0.88)[c,d,f]
Body lotion	4	ND[a]	7.12 ± 7.26 (1.64–17.82)[e,f,g]	0.53 ± 0.23 (0.30–0.81)[c]

[a]Non-detectable values were not taken into account for statistical analysis.
[b]$p < 0.05$ versus mascara; [c]$p < 0.05$ versus eye shadow; [d]$p < 0.05$ versus eyeliner; [e]$p < 0.05$ versus lipstick; [f]$p < 0.05$ versus blush; [g]$p < 0.05$ versus nail polish.

phase in the safety evaluation of a cosmetic product is to calculate the MoS, which is calculated by dividing the lowest no observed adverse effect level (NOAEL) value of the cosmetic substance under study by its estimated systemic exposure dosage (SED) (19).

We also compared safety limits of these metals with estimated intakes to evaluate potential health risks. According to previous studies, on average, women used lipsticks 2.35 times per day and applied 10 mg at each use, and average daily use was estimated as 24 mg of lipstick products (20). We used maximum detected Ni (4.10 µg/g), Cr (62.19 µg/g), and Co (1.44 µg/g) levels in lipstick samples to calculate highest estimated intake values. Highest exposure was determined as 0.10 µg/day for Ni, 1.49 µg/day for Cr, and 0.03 µg/day for Co. Compared with the tolerable daily intake (TDI) of Ni, 2.8 µg/kg body weight (bw = 70 kg) derived from European Food Safety Authority, highest estimated intake of Ni from lipstick was quite low, which is 0.05% of TDI (21). On the basis of the acceptable daily intake (ADI) of 1.4 mg/day for Co, our sample included almost about 0.002% of ADI and according to ADI of 0.2 mg/day for Cr, even in highest exposure, Cr levels in our lipstick was 0.75% (22).

In general, local adverse effects are the most prevalent effects of cosmetics in contact with human skin. In addition, skin penetration may lead to systemic exposure. The systemic availability of a cosmetic substance is estimated by taking into account the daily amount of applied finished product, the concentration of the substance under investigation, the dermal absorption of that particular substance, and a mean human body weight value (19). In this study, risk assessment of the investigated cosmetic products was performed by calculating the SED, which was calculated according to Scientific Committee on Consumer Safety guideline (19) and the MoS, according to the formula, MoS = NOAEL/SED. The MoS value is used to extrapolate from a group of test animals to an average human being, and subsequently from average humans to sensitive subpopulations. The World Health Organization proposes a minimum value of 100, and it is generally accepted that the MoS should at least be 100 to conclude that a substance is safe for use (19).

According to the EU Risk assessment documents, the available data indicate that absorption of Ni following dermal contact with either soluble or metallic Ni compounds can take place to a limited extent and 0.2% dermal absorption value should be used for risk characterization (23). MoS value for Cr was calculated based on the dermal absorption of 3% and NOAEL of 2.5 mg/kg bw/day for Cr (VI) (24), which is associated most strongly with skin sensitization (4). As shown in Tables IV and V, the MoS value for Ni and Cr was found greater than a factor of 100.

CONCLUSION

Because of the increase of allergy-related diseases, allergic metal in cosmetics might be a problem for the safeguard of public health. Despite dermal penetration of metals from cosmetics such as eyeliner, eye shadow, blush, mascara, and body cosmetics is negligible, local effects such as irritation, sensitization, or allergy are widely seen (15). Additionally, the continuous use of these cosmetics, swallowing of lipsticks or during sweating for the facial makeup, abraded skin, and use of cosmetic product under sunshine can also increase the absorption of these metals into the body from cosmetic products (25,26).

Table IV
Ni MoS Calculation

Cosmetic type	Maximum detected Ni (µg/g)	Maximum %Ni (g)	Estimated daily amount applied (g/day)	% Dermal absorption	SED (mg/kg/day)	NOAEL (mg/kg/day)	MoS (NOAEL/SED)
Mascara	19.02	0.001902	0.025	0.2	1.59×10^{-7}	2.2	13,880,126
Eye shadow	9.40	0.000940	0.02	0.2	6.27×10^{-7}	2.2	35,106,382
Eyeliner	37.95	0.003795	0.005	0.2	6.33×10^{-7}	2.2	34,782,609
Lipstick	4.10	0.000410	0.057	0.2	7.79×10^{-8}	2.2	28,241,335
Body lotion	ND[a]	ND[a]	7.82	0.2	ND[a]	2.2	ND[a]

[a]Non detectable values were not taken into account for calculation.

Table V
Cr MoS Calculation

Cosmetic type	Maximum detected Cr (μg/g)	Maximum %Cr (g)	Estimated daily amount applied (g/day)	% Dermal absorption	SED (mg/kg bw/day)	NOAEL (mg/kg bw/day)	MoS (NOAEL/SED)
Mascara	10.15	0.001015	0.025	3	1.27×10^{-6}	2.5	1,970,443
Eye shadow	19.04	0.001904	0.02	3	1.90×10^{-6}	2.5	1,313,025
Eyeliner	31.03	0.003103	0.005	3	7.76×10^{-7}	2.5	3,222,688
Lipstick	62.19	0.006219	0.057	3	1.77×10^{-5}	2.5	141,050
Body lotion	17.82	0.001782	7.82	3	6.98×10^{-4}	2.5	3588

To calculate the MoS of Co, we used a dermal absorption value of 0.13% for Co and used NOAEL of 0.01 mg/kg bw/day (Table VI) (23,24).

Table VI
Co MoS Calculation

Cosmetic type	Maximum detected Co (μg/g)	Maximum %Co (g)	Estimated daily amount applied (g/day)	% Dermal absorption	SED (mg/kg bw/day)	NOAEL (mg/kg bw/day)	MoS (NOAEL/SED)
Mascara	10.18	0.001018	0.025	0.13	5.51×10^{-8}	0.01	181,351
Eye shadow	7.09	0.000709	0.02	0.13	3.07×10^{-8}	0.01	325,486
Eyeliner	48.19	0.004819	0.005	0.13	5.22×10^{-8}	0.01	191,549
Lipstick	1.44	0.000144	0.057	0.13	1.78×10^{-8}	0.01	562,303
Body lotion	0.81	0.000081	7.82	0.13	8.23×10^{-5}	0.01	7286

According to our results, all the MoS values for the metals tested were found to be higher than 100 that is accepted as a minimum value for safe use of a substance (19).

It should be highlighted that in the first step of hazard identification, determination of the intrinsic factors that may produce potential risk to human health should be considered (1). Therefore, although removal of heavy metals from personal care products after manufacturing is not possible, careful selection of the raw material can improve the quality of the products (15). Moreover, postmarketing vigilance is very important to protect public health, although the regulation on cosmetovigilance system is handled differently in many countries (27).

Finally, it must be emphasized that contact dermatitis caused by cosmetics may be due to metal content; therefore, to assess the safety of the finished products, routine monitoring of allergen metal content is crucial.

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