

Cosmetic Use in Nigeria May Be Safe: A Human Health Risk Assessment of Metals and Metalloids in Some Common Brands

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Synopsis

Twenty different brands of cosmetic products were purchased from supermarkets in Port Harcourt, Rivers State, Nigeria, with the aims to determine the levels of metals and assess the health risk to humans through long-term usage. The concentration of metals (arsenic, lead, mercury, cadmium, and nickel) in the cosmetic samples was measured with atomic absorption spectrophotometry after acid digestion. The concentration of metals in these brands of cosmetic studied ranged from As: 0.001–0.0161 mg/kg, Pb: 0.289–2.873 mg/kg, Hg: 0.001–0.0014 mg/kg, Cd: 0.001–0.334 mg/kg, and Ni: 0.007–2.748 mg/kg. The metal and metalloid contents were less than the regulatory limits set for both metal impurities and as color additives. The target hazard quotient, hazard index, and cancer risk were less than the acceptable limit, indicating a measure of safety. Cosmetics sold in Nigeria may not add to the body burden of metals and metalloids.

INTRODUCTION

The pursuit for beauty has led to the rapid increase in utilization of cosmetics by millions of people (both men and women) all over the world (1). Cosmetic is a cocktail of chemicals that is intentionally applied to the skin surface for the purpose of promoting attractiveness or beautification. Heavy metals such as lead, cadmium, and mercury can be deliberately used as active ingredients in the formulations of cosmetics or may exist as impurities in cosmetics products because of their persistence and ubiquitous nature (2). The natural occurrence of these metals in rock, soil, and water can cause them to be present in the manufacturing of pigments and other raw materials used in cosmetics industries (3). Although a limited number of ingredients such as lead acetate in hair dyes are

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permitted under strict conditions of use, the existence of heavy metals in cosmetics as an ingredient has been banned by legislation of most developed countries because they have been found to be harmful and usage of these cosmetics can be injurious to human health (4). The most significant route of exposure to heavy metals in cosmetics is through the dermal route because cosmetics are mostly applied on the skin surface. Oral exposure can occur when it is used around the mouth, as well as hand to mouth contact after exposure to cosmetics containing those heavy metals (5). Oral exposure can also occur in children who tend to rub their eyes during cosmetics irritation and put contaminated finger in the mouth (6). Inhalation exposure to cosmetics is usually considered negligible but may be possible through aerosol cosmetics application (7).

Metals are of environmental and public health significance because they can initiate a wide range of toxic and chronic health effects such as cancer, reproductive development and neurological disorders, kidney and liver problem, lungs damage, contact dermatitis, brittle hair, and hair loss. Many are also implicated as endocrine disruptors (3). Despite all the regulations and safety systems in place for cosmetics today, the question still remains about the safety of cosmetic ingredients and impurities and the standard associated with them. There seems to be no legislation regarding contaminants in cosmetics in Nigeria (1). Many studies have provided scientific data on the level of heavy metals in cosmetics but there is a paucity of data regarding the health risk assessment of heavy metals in cosmetics to which the population may be exposed to. This study was undertaken to determine the concentrations of lead, cadmium, mercury, arsenic, and nickel in cosmetic products and to evaluate the human health risk involved in the daily usage of these cosmetics.

MATERIALS AND METHODS

SAMPLE COLLECTIONS

In January 2014, 20 brands of cosmetic samples (body cream, facial cream, hand cream, lip balm, and hair cream), were purchased from supermarkets and cosmetic shops in Port Harcourt, Rivers State, Nigeria, and used in the study.

METAL ANALYSIS

Using our previous method (8), the samples were ashed and digested in Teflon labware that had been cleaned in a high-efficiency particulate air-filtered (class 100), trace metal-clean laboratory to minimize contamination. This protocol involved sequential cleaning of the labware in a series of baths in solutions (1 wk each) and rinses (five per solution) in a three-step order, namely, a detergent solution bath and deionized water rinses, then 6-NHCl (reagent grade) solution bath and ultrapure water rinses, and finally, 7.5 N HNO₃ (trace metal grade) solution bath and ultrapure water rinses (8). The labware was air-dried in a polypropylene laminar airflow-exhausting hood. A dry ashing method was used by adding 30 ml of each sample into a conical flask and heating on a hot plate at 200°C for 45 min, and then in a furnace at 500°C until the volume was drastically reduced to near dryness. Digestion was performed by an addition of 10 ml concentrated

aqua regia (HCl:HNO₃, 3:1); this was heated to dryness. Then, 20 ml deionized water was added, stirred, and the mixture filtered. The filtrate was made up in a standard volumetric flask, and lead, cadmium, and nickel concentrations were assayed with atomic absorption spectrophotometry at 205 Å (8). Arsenic was measured with direct flow injection through a hydride generation system (9), with a limit of detection (LOD) of 0.11 µg/l. Mercury was determined by the cold vapor technique after reduction with stannous chloride (SnCl₂), to release the mercury in the sample solution. Precaution was taken at all times because of the toxic nature of mercury. A stock standard solution was prepared by dissolving 1.080 g of mercury (II) oxide, in a minimum volume of 1:1 HCL, and diluted to 1 l with deionized water. This solution was then analyzed by the AAS using an air-acetylene, oxidizing (lean, blue) flame at a wavelength of 253.7 nm.

Appropriate quality procedures and precautions were carried out to assure the reliability of the results. All reagents used in the study were of analytical grades.

A spike-and-recovery analysis was performed to assess the accuracy of the analytical techniques used. Post-analyzed samples were spiked and homogenized with varying amounts of the standard solutions of different metals. The spiked samples were then processed for analysis by the dry ashing method (1). The LOD for arsenic, mercury, cadmium, and nickel was 0.001, whereas the LOD for lead was 0.01 ppm, with blank values reading as 0.00 ppm for all the metals in deionized water with an electrical conductivity value of less than 5 µS/cm. Samples were analyzed in triplicate.

HEALTH RISK ASSESSMENT

The human health risk models including carcinogenic and noncarcinogenic ones raised by United States Environmental Protection Agency were adopted. These models and their threshold values were used to assess the potential human health risks posed by heavy metal contamination for this study. Human beings could be exposed to heavy metal from cosmetic products via dermal contact with cosmetic particles. The chronic dermal exposure to lead, cadmium, mercury, arsenic, and nickel was calculated using the equation according to Environmental Protection Agency (EPA) (10) (Table I).

$$CDE_{\text{dermal}} = \frac{CS \times SA \times AF \times ABS \times EF \times ED \times CF}{Bw \times AT}$$

Table I
Parameters used for Calculation of Chronic Daily Exposure of Heavy Metals in Cosmetics (11)

Parameters	Unit	Child	Adult
Body weight (BW)	kg	15	70
Exposure frequency (EF)	days/year	350	350
Exposure duration (ED)	years	6	30
Skin surface area (SA)	cm ²	2,100	5,700
Adherence factor (AF)	mg/cm ²	0.2	0.07
Dermal absorption factor (ABS)	none	As (0.03) other metals (0.001)	As (0.03) other metals (0.001)
Conversion factor (CF)	kg/mg	10 ⁻⁶	10 ⁻⁶
Average time (AT)	days	365 × 70	365 × 70
For carcinogens		350 × ED	350 × ED
For noncarcinogens			

The risk effect is made up of carcinogenic and noncarcinogenic risk assessments for all the metals through the dermal exposure pathway. Cancer risk can be evaluated from the following formula:

$$\text{Cancer risk} = \text{CDE} \times \text{SF},$$

where cancer risk represents the probability of an individual lifetime health risks from carcinogens, CDE is the chronic daily exposure of carcinogens (mg/kg/d), and SF is the slope factor of hazardous substances (mg/kg/d). The noncarcinogenic risk from individual heavy metal can be expressed as the hazard quotient (HQ):

$$\text{HQ} = \text{CDE}/\text{RfD},$$

where the non-cancer HQ is the ratio of exposure to hazardous substances, and RfD is the chronic reference dose of the toxicant (mg/kg/d).

$$\text{Hazard index due to heavy metals} = \sum \text{CDE}/\text{RfD},$$

where the hazard index (HI) is the sum of more than one HQ for multiple substances, CDE is the chronic daily exposure of heavy metal, and RfD is the chronic reference dose for the heavy metal. The acceptable value for the HI is <1. For the present study, the following reference doses were used: As: 3.00E-04, Pb: 5.2E-04, Hg: 3.00E-04, Ni: 5.60E-03, and Cd: 5.70E-5; and cancer slope for As: 1.5 (12,13).

SAFETY EVALUATION OF COSMETIC PRODUCTS

The risk associated with the exposure to metallic impurities in cosmetic products can be evaluated using the uncertainty factor called the margin of safety (MoS), and it 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) Scientific Committee on Consumer Safety (SCCS) (14).

$$\text{MoS} = \frac{\text{NOAEL}}{\text{SED}}$$

The systemic availability of the cosmetic substance is estimated by taking into account the daily amount of the finished product applied, the concentration of the substance under study, dermal absorption of that particular contaminant, and a human body weight value (14).

The SED is given by the following expression:

$$\text{SED}(\mu\text{g kg}^{-1}\text{bw day}^{-1}) = \frac{\text{Cs} \times \text{AA} \times \text{SSA} \times \text{F} \times \text{RF} \times \text{BF}}{\text{BW}} \times 10^3$$

where Cs is the concentration of the substance in the cosmetic product (mg kg⁻¹), AA is the amount of the cosmetic product applied, SSA is the skin surface area, RF is the retention factor (1.0 for leave-on cosmetic products), BF is the bioaccessibility factor, 10³ is the unit CF, BW is the body weight (kg). A default body weight of 60 kg was assumed in this study. The AA, SSA, and RF values adopted for this study were the standard values established by the SCCS (14) and the values are shown in Table II. The reference dose (RfD)

Table II
Product Type and Parameters Used for Calculation of Systemic Exposure Dose (14)

Product type	AA (amount applied in gram)	SSA (skin surface area in cm ²)	F (frequency in day)	RF (retention factor)
Body cream	7.82	15,670	2.28	1.0
Facial cream	1.54	565	2.14	1.0
Hand cream	2.16	860	2	1.0
Lip balm	0.057	4.8	2	1.0
Hair cream	4.0	1,010	1.14	0.1

for the studied metals was used to derive their respective NOAEL values. The RFD is defined as an estimate of the daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during lifetime. Hence, the relation between NOAEL and RFD is $\text{NOAEL} = \text{RFD} \times \text{UF} \times \text{MF}$, where UF and MF are the uncertainty factors (reflecting the overall confidence in the various datasets) and modifying factors (based on the scientific judgment used), respectively. In this case, the default values of UF and MF are 100 and 1, respectively. The RFDs (in mg/kg/d) used are shown in Table V. The World Health Organization (WHO) proposed a minimum value of 100, and it is generally accepted that MoS should at least be 100 to conclude that a substance is safe for use (14). The SCCS also noted the fact that in many convection computations of MoS, the oral bioavailability of the substance is assumed to be 100% if oral absorption data are available. However, it is considered appropriate to assume that not more than 50% of an orally administered dose is systemically available (14). For the purpose of this study, two scenarios were considered, i.e., dermal absorption of the metal not exceeding 50% and 100% of the measured concentrations of the substance in the cosmetic products.

RESULTS

Table III shows the concentrations of heavy metals, namely, As, Pb, Hg, Cd, and Ni, respectively. The concentration of As ranged from 0.001 to 0.016 mg/kg. Least heavy metal concentration of arsenic was found in Authentic herbal cream, Cyndy herb crystal, New Jerusalem, Dr Elechi omega 7, and Heel herbal, whereas the highest concentration of arsenic was found in Aquasulf. Fifty-five percent of samples had concentrations of Arsenic less than the detectable limit, whereas 45% had concentrations between 0.001 and 0.016.

Pb concentration was 0.283 mg/kg and 2.873 mg/kg in heel balm and Tee Tee 3 d, respectively. Ten percent of the samples, namely Chioral restoration and Lip balm feel, had concentrations of Pb that were in the detectable limit. Thirty percent of the samples had concentrations less than 1.000 mg/kg, whereas 60% of the cream samples had concentrations greater than 1.000 mg/kg.

The concentration of Hg in the cream samples ranged from 0 to 0.001 mg/kg. Seventy-five percent of the samples had concentrations of Hg less than the detectable limit, whereas 25% of the samples had Hg concentrations of 0.001 mg/kg.

Cadmium concentration in the cream samples stood at 0.001–0.334 mg/kg in Candy anti-spot and Chioral restoration. Notably, 45% of the samples had Cd concentration less than the detectable limit, whereas 55% had concentrations less than 1.000 mg/kg.

Table III
Metal Concentration in Cosmetics (mg/kg)

S/N	Sample identity	As	Pb	Hg	Cd	Ni	Σ Metals
1	BJ 7 d	ND	1.694	0.001	0.042	0.798	2.535
2	Tee Tee 3 d	ND	2.873	ND	0.255	0.842	3.97
3	Aquasulf	0.016	2.607	ND	0.276	1.163	4.046
4	Skin Guard Aloe vera	0.012	2.827	ND	0.171	1.389	4.387
5	Acrec way	ND	1.056	ND	0.069	2.745	3.87
6	Ceedyd acne	0.002	1.774	ND	ND	0.411	2.185
7	Authentic herbal cream	0.001	0.896	0.001	ND	0.872	1.769
8	Chioral restoration	ND	ND	ND	0.334	ND	0.334
9	Magic herb	ND	1.669	ND	ND	1.323	2.992
10	Cyndy herb crystal	0.001	0.769	ND	ND	0.596	1.365
11	New Jerusalem	0.001	1.437	ND	0.006	0.372	1.815
12	Dr Elechi omega 7	0.001	1.026	0	ND	2.492	3.518
13	Grace palm herbal balm	ND	0.428	0.001	ND	1.673	2.102
14	Anti-wrinkles cream	0.002	2.116	ND	0.011	1.946	4.073
15	Hip up cream	ND	1.367	ND	0.003	0.748	2.118
16	Hand D cream	ND	0.695	ND	0.001	1.192	1.888
17	Heel balm	0.001	0.283	ND	0.005	0.348	0.636
18	Lip balm feel	ND	ND	ND	ND	0.94	0.94
19	Deep relief	ND	1.422	ND	ND	0.413	1.835
20	Candy anti-spot	ND	0.647	0.001	ND	0.287	0.935

As: arsenic, Pb: lead, Hg: mercury, Cd: cadmium, Ni: nickel.

Nickel in the cream samples ranged from 0.287 to 2.745 mg/kg in Candy anti spot and Acreway, respectively. Fifty-five percent of the creams' samples had concentrations less than 1.000 mg/kg and 40% had concentrations greater than 1.000 mg/kg, whereas only Chioral restoration had concentration less than the detectable limit.

In all 20 cream samples, the total analyzed metal concentration ranged from 0.334 mg/kg in Chioral restoration to 4.387 mg/kg in Skin guard aloe vera. Twenty percent of the cream samples had concentrations of analytes less than 1.000 mg/kg, whereas 80% had concentrations greater than 1.000 mg/kg (1.000–4.387 mg/kg).

Table IV shows the CDE from heavy metals in the creams. The CDE to arsenic ranged from 4.22E-10 to 6.75E-09 mg/kg/d for adults and 4.14E-10 to 6.63E-09 mg/kg/d for children. The highest CDE to arsenic was from Aquasulf.

The CDE to Pb from the cream ranged from 9.28E-09 to 9.42E-08 mg/kg/d and 9.12E-09 to 9.26E-08 mg/kg/d for adults and children, respectively. The least CDE value due to Pb exposure was found in Heel balm, whereas the highest CDE value for Pb was found in Tee Tee 3 d.

The CDE ranges for Hg, Cd, and Ni were 3.28E-11–0 mg/kg/d and 3.22E-12–0 mg/kg/d, 4.41E-11–4.69E-09 mg/kg/d and 1.38E-11–4.61E-09 mg/kg/d, and 4.03E-09–3.50E-08 mg/kg/d and 3.96E-09–3.44E-08 mg/kg/d for adults and children, respectively. The least CDEs from Cd and Ni were found in hand cream and candy anti spot, respectively, whereas the highest CDEs were found in Chioral restoration and Dr Elechi omega 7.

Table V shows the noncarcinogenic risk, namely, target HQ (THQ) and hazard indices, respectively. The THQ ranged from As exposure was 2.53E-13–2.02E-12 and 2.49E-13–1.99E-12 for adults and children, respectively.

Table IV
Chronic Daily Intake of Metals in Cosmetics for Adults and Children (mg/kg/day)

S/N	Sample identity	As		Pb		Hg		Cd		Ni	
		ADL	CHL	ADL	CHL	ADL	CHL	ADL	CHL	ADL	CHL
1	BJ 7 d	ND	ND	5.56E-08	5.46E-08	3.28E-11	3.22E-12	5.90E-10	5.80E-10	1.12E-08	1.10E-08
2	Tee Tee 3 d	ND	ND	9.42E-08	9.26E-08	ND	ND	3.58E-09	3.52E-09	1.18E-08	1.16E-08
3	Aquasulf	6.75E-09	6.63E-09	8.55E-08	8.40E-08	ND	ND	3.88E-09	3.81E-09	1.63E-08	1.61E-08
4	Skin Guard Aloe vera	5.06E-09	4.97E-09	9.27E-08	9.11E-08	ND	ND	2.40E-09	2.36E-09	1.95E-08	1.92E-08
5	Accec way	ND	ND	3.46E-08	3.40E-08	ND	ND	9.70E-10	9.53E-10	3.86E-08	3.79E-08
6	Ceedym acne	8.43E-10	8.28E-10	5.82E-08	5.72E-08	ND	ND	ND	ND	5.78E-09	5.68E-09
7	Authentic herbal cream	4.22E-10	4.14E-10	2.94E-08	2.89E-08	3.28E-11	3.22E-12	ND	ND	1.23E-08	1.20E-08
8	Chioral restoration	ND	ND	ND	ND	ND	ND	4.69E-09	4.61E-09	ND	ND
9	Magic herb	ND	ND	5.47E-08	5.38E-08	ND	ND	ND	ND	1.86E-08	1.83E-08
10	Cyndy herb crystal	4.22E-10	4.14E-10	2.52E-08	2.48E-08	ND	ND	ND	ND	8.38E-09	8.23E-09
11	New Jerusalem	4.22E-10	4.14E-10	4.71E-08	4.63E-08	ND	ND	8.43E-11	8.28E-11	5.23E-09	5.14E-09
12	Dr Elechi omega 7	4.22E-10	4.14E-10	3.36E-08	3.31E-08	0	0	ND	ND	3.50E-08	3.44E-08
13	Grace palm herbal balm	ND	ND	1.40E-08	1.38E-08	3.28E-11	3.22E-12	ND	ND	2.35E-08	2.31E-08
14	Anti-wrinkles cream	8.43E-10	8.28E-10	6.94E-08	6.82E-08	ND	ND	1.55E-10	1.52E-10	2.74E-08	2.69E-08
15	Hip up cream	ND	ND	4.48E-08	4.40E-08	ND	ND	4.22E-11	4.14E-11	1.05E-08	1.03E-08
16	Hand D cream	ND	ND	2.28E-08	2.24E-08	ND	ND	1.41E-11	1.38E-11	1.68E-08	1.65E-08
17	Heel balm	4.22E-10	4.14E-10	9.28E-09	9.12E-09	ND	ND	7.03E-11	6.90E-11	4.89E-09	4.81E-09
18	Lip balm feel	ND	ND	ND	ND	ND	ND	ND	ND	1.32E-08	1.30E-08
19	Deep relief	ND	ND	4.66E-08	4.58E-08	ND	ND	ND	ND	5.80E-09	5.70E-09
20	Candy antri-spot	ND	ND	2.12E-08	2.08E-08	3.28E-11	3.22E-12	ND	ND	4.03E-09	3.96E-09

CHL: children (body weight = 15 kg), ADL: adults (body weight = 70 kg), As: arsenic, Pb: lead, Hg: mercury, Cd: cadmium, Ni: nickel.

Table V
HQ and HI of Metals in Cosmetics for Adults and Children

S/N	Sample identity	As		Pb		Hg		Cd		Ni		HI	
		ADL	CHL	ADL	CHL	ADL	CHL	ADL	CHL	ADL	CHL	ADL	CHL
1	BJ 7 d	ND	ND	2.89E-11	2.84E-11	9.84E-15	9.67E-16	3.36E-14	3.31E-14	6.28E-11	6.17E-11	9.17396E-11	9.01E-11
2	Tee Tee 3 d	ND	ND	4.9E-11	4.81E-11	ND	ND	2.04E-13	2.01E-13	6.63E-11	6.51E-11	1.15469E-10	1.13E-10
3	Aquasulf	2.02E-12	1.99E-12	4.45E-11	4.37E-11	ND	ND	2.21E-13	2.17E-13	9.15E-11	8.99E-11	1.38239E-10	1.36E-10
4	Skin Guard Aloe vera	1.52E-12	1.49E-12	4.82E-11	4.74E-11	ND	ND	1.37E-13	1.35E-13	1.09E-10	1.07E-10	1.59188E-10	1.56E-10
5	Acnec way	ND	ND	1.8E-11	1.77E-11	ND	ND	5.53E-14	5.43E-14	2.16E-10	2.12E-10	2.34114E-10	2.3E-10
6	Ceedym acne	2.53E-13	2.49E-13	3.03E-11	2.97E-11	ND	ND	ND	ND	3.23E-11	3.18E-11	6.28538E-11	6.18E-11
7	Authentic herbal cream	1.26E-13	1.24E-13	1.53E-11	1.5E-11	9.84E-15	9.67E-16	ND	ND	6.86E-11	6.74E-11	8.40483E-11	8.26E-11
8	Chioral restoration	ND	ND	ND	ND	ND	ND	2.68E-13	2.63E-13	ND	ND	2.67575E-13	2.63E-13
9	Magic herb	ND	ND	2.85E-11	2.8E-11	ND	ND	ND	ND	1.04E-10	1.02E-10	1.32591E-10	1.3E-10
10	Cyndy herb crystal	1.26E-13	1.24E-13	1.31E-11	1.29E-11	ND	ND	ND	ND	4.69E-11	4.61E-11	6.01496E-11	5.91E-11
11	New Jerusalem	1.26E-13	1.24E-13	2.45E-11	2.41E-11	ND	ND	4.81E-15	4.72E-15	2.93E-11	2.88E-11	5.39156E-11	5.3E-11
12	Dr Elechi omega 7	1.26E-13	1.24E-13	1.73E-11	1.72E-11	0	0	ND	ND	1.96E-10	1.93E-10	2.1376E-10	2.1E-10
13	Grace palm herbal balm	ND	ND	7.3E-12	7.17E-12	9.84E-15	9.67E-16	ND	ND	1.32E-10	1.29E-10	1.38985E-10	1.37E-10
14	Anti-wrinkles cream	2.53E-13	2.49E-13	3.61E-11	3.55E-11	ND	ND	8.81E-15	8.66E-15	1.53E-10	1.5E-10	1.8951E-10	1.86E-10
15	Hip up cream	ND	ND	2.33E-11	2.29E-11	ND	ND	2.4E-15	2.36E-15	5.89E-11	5.78E-11	8.21868E-11	8.07E-11
16	Hand D cream	ND	ND	1.19E-11	1.16E-11	ND	ND	8.01E-16	7.87E-16	9.38E-11	9.22E-11	1.05671E-10	1.04E-10
17	Heel balm	1.26E-13	1.24E-13	4.83E-12	4.74E-12	ND	ND	4.01E-15	3.94E-15	2.74E-11	2.69E-11	3.23465E-11	3.18E-11
18	Lip balm feel	ND	ND	ND	ND	ND	ND	ND	ND	7.4E-11	7.27E-11	7.39844E-11	7.27E-11
19	Deep relief	ND	ND	2.42E-11	2.38E-11	ND	ND	ND	ND	3.25E-11	3.19E-11	5.67555E-11	5.58E-11
20	Candy anti-spot	ND	ND	1.1E-11	1.08E-11	9.84E-15	9.67E-16	ND	ND	2.26E-11	2.22E-11	3.36321E-11	3.3E-11

CHL: children (body weight = 15 kg), ADL: adults (body weight = 70 kg), As: arsenic, Pb: lead, Hg: mercury, Cd: cadmium, Ni: nickel.

The THQ for Pb, Hg, Cd, and Ni was $9.84\text{E-}15$ – 0 and $9.67\text{E-}16$ – 0 , $4.83\text{E-}12$ – $4.90\text{E-}11$ and $4.74\text{E-}12$ – $4.81\text{E-}11$, $9.38\text{E-}16$ – $2.68\text{E-}13$ and $9.22\text{E-}16$ – $2.63\text{E-}13$, and $2.26\text{E-}11$ – $1.96\text{E-}10$ and $2.22\text{E-}11$ – $1.93\text{E-}10$ for adults and children, respectively.

HI range was $2.67\text{E-}13$ – $2.34\text{E-}10$ and $2.63\text{E-}13$ – $2.30\text{E-}10$ for adults and children, respectively. The least HI value was calculated from Chioral restoration, whereas the highest was found in Acreway creams, respectively.

Cancer risk from the different brands of cream is shown on Table VI. The highest cancer risk value for adults was $1.011\text{E-}08$, whereas the least was $6.324\text{E-}10$. These concentrations were found in Aquasulf and Authentic herbal cream, Cyndy herb crystal, New Jerusalem, Dr Elechi omega 7, and Heel balm. Cancer risk for children ranged from $6.213\text{E-}10$ to $9.941\text{E-}09$ in the same cream samples, respectively.

The estimated SED and MoS associated with the use of these brands of cosmetic products are shown in Tables VII and VIII.

DISCUSSION

The presence of toxic metals in cosmetics is inevitable because of their ubiquitous and persistent nature in the environment. But their presence in cosmetics as an ingredient has been prohibited by some countries, whereas there is no international standard on their impurity level. There might not be international standards, but most ingredients prone to contain heavy metals (such as colorants) have established purity requirements.

Table VI
Cancer Risk of Metal in Cosmetics (mg/kg)

S/N	Sample identity	As	
		ADL	CHL
1	BJ 7 d	ND	ND
2	Tee Tee 3 d	ND	ND
3	Aquasulf	$1.01195\text{E-}08$	$9.94192\text{E-}09$
4	Skin Guard Aloe vera	$7.58959\text{E-}09$	$7.45644\text{E-}09$
5	Acrec way	ND	ND
6	Ceedym acne	$1.26493\text{E-}09$	$1.24274\text{E-}09$
7	Authentic herbal cream	$6.32466\text{E-}10$	$6.2137\text{E-}10$
8	Chioral restoration	ND	ND
9	Magic herb	ND	ND
10	Cyndy herb crystal	$6.32466\text{E-}10$	$6.2137\text{E-}10$
11	New Jerusalem	$6.32466\text{E-}10$	$6.2137\text{E-}10$
12	Dr Elechi omega 7	$6.32466\text{E-}10$	$6.2137\text{E-}10$
13	Grace palm herbal balm	ND	ND
14	Anti-wrinkles cream	$1.26493\text{E-}09$	$1.24274\text{E-}09$
15	Hip up cream	ND	ND
16	Hand D cream	ND	ND
17	Heel balm	$6.32466\text{E-}10$	$6.2137\text{E-}10$
18	Lip balm feel	ND	ND
19	Deep relief	ND	ND
20	Candy anti-spot	ND	ND

As: arsenic.

Table VII.
Systemic Exposure Dosage and Margin of Safety of Metals in Cosmetics Obtained by Using 100% Bioaccessibility

Sample (brand name and type)	Systemic exposure dosage					Margin of safety				
	As	Pb	Hg	Cd	Ni	As	Pb	Hg	Cd	Ni
BJ 7 d (body cream)	ND	7.8881	0.0065	0.1956	3.716	ND	0.0066	4.6019	0.0292	0.1507
Tee Tee 3 d (facials)	ND	0.089	ND	0.0079	0.0261	ND	0.5843	ND	0.72156	21.469
Aquasulf (body cream)	0.075	12.139	ND	1.2852	5.4155	0.4002	0.0043	ND	0.00444	0.1034
Skin Guard Aloe vera (body cream)	0.0573	13.164	ND	0.7963	6.4679	0.5238	0.004	ND	0.00716	0.0866
Acree way (body cream)	ND	4.9173	ND	0.3213	12.782	ND	0.0106	ND	0.01774	0.0438
Ceedym acne (facials)	7E-05	0.055	ND	ND	0.0127	461.15	0.9462	ND	ND	43.983
Authentic herbal cream (body cream)	0.0065	4.1722	0.0051	ND	4.0605	4.6019	0.0125	5.8569	ND	0.1379
Chioral restoration (body cream)	ND	ND	ND	1.5553	ND	ND	ND	ND	0.00366	ND
Magic herb (body cream)	ND	7.7717	ND	ND	6.1605	ND	0.0067	ND	ND	0.0909
Cyndy herb crystal (hair cream)	8E-06	0.059	ND	ND	0.0047	3,908.3	8.809	ND	ND	122.41
New Jerusalem (body cream)	0.0061	6.6914	ND	0.0279	1.7322	4.9559	0.0078	ND	0.20402	0.3233
Dr Elechi omega 7 (body cream)	0.0088	4.7776	0.0047	ND	11.604	3.3908	0.0109	6.4426	ND	0.0483
Grace palm herbal balm (hand cream)	ND	0.0265	ND	ND	0.1036	ND	1.9608	ND	ND	5.4058
Anti-wrinkles cream (body cream)	0.0098	9.8531	ND	0.0512	9.0615	3.0679	0.0053	ND	0.11128	0.0618
Hip up cream	ND	6.3654	ND	0.014	3.4831	ND	0.0082	ND	0.40803	0.1608
Hand D cream (hand cream)	ND	ND	ND	6E-05	0.0738	ND	ND	ND	92.0543	7.5872
Heel balm (heel balm)	1E-07	3E-05	ND	5E-07	3E-05	299,043	2,014.8	ND	12,500	17,645
Lip balm feel (lip balm)	ND	ND	ND	ND	9E-05	ND	ND	ND	ND	6,532.3
Deep relief (body cream)	ND	6.6229	ND	ND	1.9231	ND	0.0079	ND	ND	0.2912
Candy anti-spot (facials)	ND	0.02	3E-05	ND	0.0089	ND	2.5936	880.37	ND	62.986

Table VIII
Systemic Exposure Dosage and Margin of Safety of Metals in Cosmetics Obtained by Using 50% Bioaccessibility

Sample (brand name and type)	Systemic exposure dosage					Margin of safety				
	As	Pb	Hg	Cd	Ni	As	Pb	Hg	Cd	Ni
BJ 7 d (body cream)	ND	3.9441	0.0033	0.1956	3.716	ND	0.0066	4.6019	0.0292	0.1507
Tee Tee 3 d (facials)	ND	0.0445	ND	0.0039	0.013	ND	1.1685	ND	1.44312	42.938
Aquasulf (body cream)	0.0375	6.0697	ND	0.6426	2.7078	0.8003	0.0086	ND	0.00887	0.2068
Skin Guard Aloe vera (body cream)	0.0286	6.582	ND	0.3981	3.2339	1.0476	0.0079	ND	0.01432	0.1732
Acree way (body cream)	ND	2.4586	ND	0.1606	6.391	ND	0.0211	ND	0.03548	0.0876
Ceedym acne (facials)	3E-05	0.0275	ND	ND	0.0064	922.29	1.8924	ND	ND	87.966
Authentic herbal cream (body cream)	0.0033	2.0861	0.0026	ND	2.0302	9.2037	0.0249	11.714	ND	0.2758
Chioral restoration (body cream)	ND	ND	ND	0.7776	ND	ND	ND	ND	0.00733	ND
Magic herb (body cream)	ND	3.8858	ND	ND	3.0803	ND	0.0134	ND	ND	0.1818
Cyndy herb crystal (hair cream)	4E-06	0.003	ND	ND	0.0023	7,816.6	17.619	ND	ND	244.81
New Jerusalem (body cream)	0.003	3.3457	ND	0.014	0.8661	9,911.7	0.0155	ND	0.40803	0.6466
Dr Elechi omega 7 (body cream)	0.0044	2.3888	0.0023	ND	5.802	6.7817	0.0218	12.885	ND	0.0965
Grace palm herbal balm(hand cream)	ND	0.0133	ND	ND	0.0518	ND	3.9215	ND	ND	10.812
Anti-wrinkles cream (body cream)	0.0049	4.9266	ND	0.0256	4.5308	6,135.8	0.0106	ND	0.22256	0.1236
Hip up cream	ND	3.1827	ND	0.007	1.7415	ND	0.0163	ND	0.81606	0.3216
Hand D. cream (hand cream)	ND	ND	ND	3E-05	0.0369	ND	<0.001	ND	184.109	15.174
Heel balm (heel Balm)	5E-08	1E-05	ND	2E-07	2E-05	598,086	4,029.5	ND	25,000	35,289
Lip balm feel (lip balm)	ND	ND	ND	ND	4E-05	ND	ND	ND	ND	13,065
Deep relief (body cream)	ND	3.3115	ND	ND	0.9616	ND	0.156	ND	ND	0.5824
Candy anti-spot (facials)	ND	0.01	2E-05	ND	0.0044	ND	5.1872	1,760.7	ND	125.97

These might vary by country (US, CANADA, EU, and Asia), but they are established. The impurity level can be reduced with adherence to good manufacturing practices (4). In the present study, the heavy metal and metalloids concentrations in analyzed samples arranged in descending order were $Pb > Ni > Cd > As > Hg$, respectively. This may have been from impurities and contaminants from the raw materials; lead was the most predominant. Its concentration was higher than that of all the other metals investigated. Similar findings have been reported by other workers, showing the predominance of lead in different brands of kohl samples purchased in local markets in Tunisia and Pakistan, respectively (15,16). The lead concentration range of 0.283–2.873 mg/kg is higher than the threshold limit value of 0.05 mg/l set by the American Conference of Governmental Industrial Hygienist for inorganic lead and lead chromate (17).

The concentration of lead was within a safe range when compared with 10, 20, and 10 mg/kg limits set by Health Canada and the Indian Government Ministry of Health and Family Welfare and the Cosmetics Section Committee of the Bureau of Indian Standards (18). Previous studies in cosmetics and body creams in Nigeria have reported similar concentrations of lead. Studies carried out by Oyedele *et al.* (19) and Sani *et al.* (20) found concentrations of 0.1–0.9 mg/kg and 0.05–0.14 mg/kg of lead in cosmetics which are lower than the concentrations found in the present study. However, Orisakwe and Oturaku (1), Iwegbue *et al.* (2), Nduka *et al.* (8), and Omenka and Adeyi (21) found 1.2–9.2 mg/kg, 12–24 mg/kg, 0.1–4.12 mg/kg, and ND–468 mg/kg concentrations of lead in cosmetic products in Nigeria which were higher than those found in the present study. In cosmetics from Saudi markets, Pakistan, and Malaysia, respectively, Al-Saleh *et al.* (4), Ullah *et al.* (15), and Rusmadi *et al.* (22) found 0.49–1.793 mg/kg, 1.74–1,071 mg/kg, and 0.002–0.114 mg/kg of lead, respectively.

Lead poisoning has been recognized as a major public health risk. Exposure to lead produces various deleterious effects on the hematopoietic, renal, reproductive, and central nervous system, mainly through increased oxidative stress (23). Chronic toxicity is characterized by persistent vomiting, encephalopathy, lethargy, delirium, convulsions, and coma (24). Once lead enters the body, it is distributed in organs such as the brain, kidneys, liver, and bones. The body stores lead in the teeth and bones where it accumulates over time. Lead stored in bone may be remobilized into the blood during pregnancy, thus exposing the fetus. Undernourished children are more susceptible to lead because their bodies absorb more lead if other nutrients, such as calcium, are lacking (25).

Health Canada, the Bureau of Indian Standards, and the United States Food and Drug Administration have set 3, 2, and 3 mg/kg, respectively, as the safe concentration of arsenic through dermal exposure (18,26). All cosmetic cream samples in this study were within this safe limit set for arsenic. Nduka *et al.* (8) and Nasirudem and Amaechi (27) found 0.002–0.005 mg/kg and 0.11–1.00 mg/kg, respectively, in cosmetic samples in Nigeria. In Sudan, Sabah *et al.* (28) found 1.504–6.796 mg/kg range of arsenic in cosmetic products which is significantly higher than the concentration found in the present study. Arsenic is a widely distributed environmental pollutant with known carcinogenic and neurotoxicant effects (29). Arsenic occurs in inorganic and organic forms. Inorganic arsenic compounds (such as those found in water) are highly toxic, whereas organic arsenic compounds (such as those found in seafood) are less harmful to health. The immediate symptoms of acute arsenic poisoning include vomiting, abdominal pain, and diarrhea. These are followed by numbness and tingling of the extremities, muscle cramping, and death, in extreme cases. Skin lesions and hard patches on the palms and soles of the feet

(hyperkeratosis), skin cancers, developmental effects, neurotoxicity, diabetes, pulmonary and cardiovascular diseases, and arsenic-induced myocardial infarction are some chronic effects of As toxicity (25).

Cadmium concentration in the present study did not violate the 3 mg/kg standard set by Health Canada (19). Several studies have reported a significantly higher concentration of cadmium in cosmetic samples in Nigeria. Nduka *et al.* (8), Iwegbue *et al.* (2), Sani *et al.* (22), and Omenka and Adeyi (21) reported 0.01–1.32 mg/kg, 3.1–8.4 mg/kg, 0.14–1.32 mg/kg, and ND–36.3 mg/kg concentrations of cadmium. Notably, similar concentrations have been obtained in studies outside Nigeria. Ullah *et al.* (15), Rusmadi *et al.* (24), and Sabah *et al.* (28) reported 0.41–0.942 mg/kg, 0.002–0.114 mg/kg, and 0.1559–0.6179 mg/kg concentrations of cadmium in cosmetics from Pakistan, Malaysia, and Sudan, respectively. Exposure to cadmium can lead to a variety of adverse health effects including cancer. Acute inhalation exposure (high levels over a short period of time) to cadmium can result in flu-like symptoms (chills, fever, and muscle pain) and can damage the lungs. Chronic exposure (low level over an extended period of time) can result in kidney, bone, and lung disease (30). There are three possible ways of cadmium resorption in the human body, namely, gastrointestinal, pulmonary, and dermal (31). Binding of a free cadmium ion to sulfhydryl radicals of cysteine in epidermal keratins, or an induction and complexing with metallothioneins are two mechanisms that facilitate cadmium absorption through the skin (32).

There is no international guidelines or limits for nickel in cosmetic products. However, several studies have shown the presence of irritants following repeated exposure to nickel greater than 10 µg/g (33–35). Concentrations of Ni (18–288 mg/kg, 0.05–17.34 mg/kg, 3.68–11.03 mg/kg, and ND–107 mg/kg) reported by Iwegbue *et al.* (2), Nduka *et al.* (8), Sani *et al.* (20), and Omenka and Adeyi (21) were all higher than the concentration in the present study. The most common harmful health effect of nickel in humans is an allergic reaction. Approximately 10–20% of the population is sensitive to nickel. The most serious harmful health effects from exposure to nickel are chronic bronchitis, reduced lung function, and cancer of the lung and nasal sinus (36).

There was no violation of the 1.00 mg/kg standard set by Health Canada for mercury. Nduka *et al.* (8) and Nasirudem and Amaechi (27) reported mercury at the range of 0.003–0.007 mg/kg and 30.00–90.32 mg/kg, respectively, in cosmetic samples in Nigeria. Mercury is considered by the WHO as one of the top 10 chemicals or groups of chemicals of major public health concern. Elemental mercury and methylmercury are toxic to the central and peripheral nervous systems. The inorganic salts of mercury are corrosive to the skin, eyes, and gastrointestinal tract, and may induce kidney toxicity if ingested (37). The concentration of mercury in this study ranged from 0.001 to 0.0014 mg/kg; this value was less than 3 µg/g set by Canada authority (18). Mercury concentration in this study was comparable to the values reported by other workers (8,38). Notwithstanding the low levels of mercury in these cosmetics, chronic exposure may pose a public health risk. It has been observed that mercury is absorbed through the skin and used in skin whiteners because the metal is able to block the production of melanin, which gives hair and skin pigmentations (39). Mercury is ranked a top three priority pollutant that has become a serious health concern because of its high capacity for bioaccumulation and the variety of its effects on biological systems (40,41).

As reflected by the results of the study, the THQ and HI values for both adults and children were all less than 1.0 for all metals analyzed. In a study by Rusmadi *et al.* (22), the

THQ of nickel and cadmium in skin-lightening creams in Malaysia was <1 , whereas THQ for Pb in the same study was >1 . HQ in the study of cosmetic brands in Nigeria by Nduka *et al.* (8) were all <1 for mercury and arsenic. This is an indication of a relatively low noncarcinogenic risk from heavy metals in the cosmetics analyzed. THQ is the ratio of the potential exposure to the substance and the level at which no adverse effects are expected. HQ less than or equal to one indicates that adverse non-cancer effects are not likely to occur, and thus can be considered to have negligible hazard. HQs greater than one are not statistical probabilities of harm occurring. Instead, they are a simple statement of whether (and by how much) an exposure concentration exceeds the reference concentration (RfC) (42). HI is the sum of HQs for substances that affect the same target organ or organ system. Because different pollutants (air toxics) can cause similar adverse health effects, combining HQs associated with different substances is often appropriate. The HI is only an approximation of the aggregate effect on the target organ (e.g., the lungs) because some of the substances might cause irritation by different (i.e., nonadditive) mechanisms. An HI equal to or greater than 1.0, however, does not necessarily suggest a likelihood of adverse effects. Because of the inherent conservatism of the RfC methodology, the acceptability of exceedances must be evaluated on a case-by-case basis, considering such factors as the confidence level of the assessment, the size of the uncertainty factors used, the slope of the dose-response curve, the magnitude of the exceedance, and the number or types of people exposed at various levels greater than the RfC (42,43).

The carcinogenic risk for children and adults was all lower than the acceptable and priority risk of $1\text{-E-}04$ and $1\text{-E-}06$. The result of cancer risk for arsenic in the study of cosmetic brands in Nigeria by Nduka *et al.* (8) was $1.781\text{E-}13$ and $1.95\text{E-}12$. The risk associated with the potential to develop cancer after exposure to chemicals is often expressed as a probability or a fraction in a range from zero to one ($0.0\text{--}1.0$). Usually the numbers are very small and shown in fractions of 1 million or fractions of 100,000. $1.0\text{E-}1$ means one in 10, $1.0\text{E-}2$ means one in 100, $1.0\text{E-}3$ means one in 1,000, $1.0\text{E-}4$ means one in 10,000, $1.0\text{E-}5$ means one in 100,000, $1.0\text{E-}6$ means one in a million, and $1.0\text{E-}9$ means one in a billion, respectively (44).

Cosmetics have often been considered by many dermatologists to be more harmful than good (15). These contain more than 10,000 ingredients which are linked to many diseases, such as cancer, birth defects, and developmental and reproductive harm. Dermal exposure is expected to be the most significant route because most of the cosmetic products are directly applied to the skin. Oral exposure can occur from wearing of cosmetics products containing heavy metal impurities around the mouth and also from hand-to-mouth contact (5). Many factors can affect the numerical value that is used to represent the degree of dermal absorption, such as exposure time, product formulation, dose, and the fate of the chemical in the skin. Information on the exposure to metal toxins through dermal contact is very scanty, and few data exist on the personal care products (45).

The SED of arsenic from the use of these cosmetic products ranged from $5\text{E-}08$ to 0.075 $\mu\text{g/kgbw/d}$ for both 50% and 100% bioaccessibility scenario. This value was less than the provisional tolerable daily intake (PTDI) of arsenic set as 0.002 mg/kg by JECFA (46).

The SED of lead ranged from $1\text{E-}05$ to 13.164 $\mu\text{g/kgbw/d}$ for both 50% and 100% bioaccessibility. The PTDI for lead was withdrawn by the FAO/WHO joint committee because it could no longer be considered health protective, but nevertheless, a PTDI value of 3.6 $\mu\text{g/kgbw/d}$ was used as an indicator to compare with the results of the estimated

daily intake (47). The SED for some of the brands of cosmetics product sampled (body creams) were greater than the PTDI value, whereas SED of brands of cosmetic products grouped as facials, hand creams, and lip balm were less than the PTDI value.

The SED of cadmium from the use of these cosmetics ranged from $2\text{E-}07$ to $1.5553\text{ }\mu\text{g/kgbw/d}$ for both 50% and 100% bioaccessibility scenario. The PTDI of cadmium is set at $1\text{ }\mu\text{g/kgbw/d}$; however, the European food and safety authority (EFSA) set the provisional tolerable weekly intake of cadmium as $2.5\text{ }\mu\text{g/kgbw/wk}$ (48). The SED value of cadmium from the use of these brands of cosmetic products was less than 0.1% of the EFSA provisional intake, except for some brands of cosmetic products grouped as body cream, such as Aquasulf body cream and Cloral restoration cream, which had SED value greater than $1\text{ }\mu\text{g/kgbw/d}$.

The estimated value of Hg and Ni from the use of these brands of cosmetic products for both 50% and 100% bioaccessibility scenario ranged from $2\text{E-}05$ to $0.0065\text{ }\mu\text{g/kgbw/d}$ and $2\text{E-}05$ to $12.782\text{ }\mu\text{g/kgbw/d}$, respectively. The tolerable daily intake of Hg and Ni are $0.20\text{ }\mu\text{g/kgbw/d}$ (49) and $720\text{ }\mu\text{g/kgbw/d}$ (46), respectively. The estimated SED for Hg and Ni in this study were less than their respective tolerable daily intake.

The estimated MoS value for metals in these brands of cosmetics (body creams and hand creams) were lower than the proposed value of 100 set by the WHO, indicating that a significant risk might be associated with the long-term use of these cosmetic products, whereas brands of cosmetic products such as lip balms, hair creams, and some facial creams had a value greater than the proposed MoS value by the WHO, which indicates a nonsignificant risk associated with the concentration of metals in these products.

CONCLUSION

This study has revealed that the heavy metal contaminants in cosmetic creams analyzed may not pose significant health risk as individual concentrations are less than standard limits set by Health Canada, Food and Drug Administration, and the Cosmetics Section Committee of the Bureau of Indian Standards. Cancer risk from this study was within safe limits. Taken together, cosmetic use in Nigeria may not constitute a significant source of body burden of these metals.

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REFERENCES

- (1) E. Orisakwe and J. O. Otaruku, Metal concentrations of cosmetic commonly used in Nigeria, *Sci. World J.*, 2013, 959637 (2013).
- (2) C. M. A. Iwegbue, F. I. Bassey, G. Obi, G. O. Tesi, and B. S. Martincigh, Concentration and exposure risk of some metals in facial cosmetics in Nigeria, *Toxicol. Rep.*, 3, 468–472 (2015).
- (3) B. Bocca, A. Pino, A. Alimonti, and G. Forte, Toxic metals contained in cosmetics: a status report, *Regul. Toxicol. Pharmacol.*, 68, 447–467 (2014).
- (4) I. Al-Saleh and S. Al- Enazi, Trace metal in lip sticks, *Toxicol. Environ. Chem.*, 96(6), 1149–1165 (2011).

- (5) E. L. Sainio, R. Jolanki, E. Hakata, and L. Kanerva, Metal and arsenic in eye shadows, *Contact Dermatitis*, **42**, 5–10 (2000).
- (6) A. D. Hardy, H. H. Sutherland, and R. Vaishnav, A study of the composition of some eye cosmetics (kohl) used in the United Arab Emirates, *J. Ethnopharmacol.*, **80**(2–3), 137–145 (2002).
- (7) *Risk Assessment Guidance for Superfund, Volume I: Human Health Evaluation Manual, Part E: Supplemental Guidance for Dermal Risk Assessment* (Office of Superfund Remediation and Technology Innovation, U.S. Environmental Protection Agency, Washington, DC, 2004). EPA/540/R/99/005, OSWER 9285.7-02EP PB99-963312.
- (8) J. K. Nduka, I. O. Oduba, O. E. Orisakwe, L. D. Ukaegbu, C. Sokaibe, and N. A. Udowelle, Human health risk assessment of heavy metals in cosmetics in Nigeria, *J. Cosmet. Sci.*, **66**, 233–246 (2015).
- (9) F. Gil, L. F. Capitán-Vallvey, E. De Santiago, J. Ballesta, A. Pla, and A. F. Hernández, Heavy metal concentrations in the general population of Andalusia, south of Spain: a comparison with the population within the area of influence of Aznalcollar mine spill (SW Spain), *Sci. Total Environ.*, **372**, 49–57 (2006).
- (10) U.S. Environmental Protection Agency, *Risk Assessment Guidance for Superfund Volume I: Human Health Evaluation Manual (Part E, Supplemental Guidance for Dermal Risk Assessment)* (USEPA, Washington, DC, 2004).
- (11) L. Kexin, L. Tao, W. Lingqing, and Y. Zhiping, Contamination and health risk assessment of heavy metals in road dust in Bayan Obo mining region in inner Mongolia, north China, *J. Geogr. Sci.*, **25**(12), 1439–1451 (2015).
- (12) L. Ferreira-Baptista and E. De Miguel, Geochemistry and risk assessment of street dust in Luanda, Angola: a tropical urban environment, *Atmos. Environ.*, **39**(25), 4501–4512 (2005).
- (13) N. Zheng, J. Liu, and Q. Wang, Health risk assessment of heavy metal exposure to street dust in the zinc smelting district, northeast of China, *Sci. Total Environ.*, **408**(4), 726–733 (2010).
- (14) Scientific Committee on Consumer Safety (SCCS), *The SCCS's Notes of Guidance for Testing of Cosmetic Substances and Their Safety Evaluation*(SCCS/1501/12), 8th Ed. (Scientific Committee on Consumer Safety, European Union, Belgium, 2012). The SCCS adopted this opinion at the 17th plenary meeting of 11 December, 2012.
- (15) H. Ullah, S. Noreen, A. Fozia Rehman, A. Waseem, S. Zubair, M. Adnan, and I. Ahmad, Comparative study of heavy metals content in cosmetic products of different countries marketed in Khyber Pakhtunkhwa, Pakistan, *Arabian J. Chem.*, **10**, 10–18 (2017).
- (16) M. A. Nouioui, S. Mahjoubi, A. Ghorbel, M. B. H. Yaha, D. Amira, H. Ghorbel, and A. Hedhili, Health risk assessment of heavy metals in traditional cosmetics sold in Tunisha local markets, *Int Scholarly Res. Not.*, **2016**, 6296458 (2016).
- (17) H. Fu and H. Boffeta, Cancer and occupational exposure to inorganic lead compounds: a metal analysis of published data, *Occup. Environ. Med.*, **52**, 73–81 (1995).
- (18) Health Canada-Santé Canada (HC-SC), *Guidance on Heavy Metal Impurities in Cosmetics* (Health Canada-Santé Canada, Canada, 2012), accessed October 16, 2014, <http://www.hc-sc.gc.ca/cps-spc/pubs/indust/heavymetals-metiaux lourds/index-eng.php>.
- (19) F. Oyediji, G. Hassan, and B. Adeleke, Hydroquinone and heavy metals levels in cosmetics marketed in Nigeria, *Trends Appl. Sci. Res.*, **6**(7), 622–639 (2011).
- (20) A. Sani, M. B. Gaya, and F. A. Abubakar, Determination of some heavy metals in selected cosmetic products sold in Kano metropolis, Nigeria, *Toxicol. Rep.*, **3**, 866–869 (2016).
- (21) S. Omenka and A. Adeyi, Heavy metal content of selected personal care products (PCPs) available in Ibadan, Nigeria and their toxic effects, *Toxicol. Rep.*, **3**, 628–635 (2016).
- (22) S. Rusmadi, S. Ismail, and S. Praveena, A case study of selected heavy metals (lead, cadmium, and nickel) in skin-lightening creams and dermal health risk in Malaysia, *Ann. Trop. Med. Public Health*, **10**(1), 95 (2017).
- (23) G. Flora, D., Gupta, and A. Tiwari, Toxicity of lead: a review with recent updates, *Interdiscip. Toxicol.*, **5**(2), 47–58 (2012).
- (24) J. Pearce, Burton's line in lead poisoning, *Eur. Neurol.*, **57**(2), 118–119 (2006).
- (25) World Health Organization, *Lead Poisoning and Health*, 2016, retrieved May 1, 2017, <http://www.who.int/mediacentre/factsheets/fs379/en/>.
- (26) U.S. EPA, *The Risk Assessment Guidelines of 1986* (Office of Health and Environmental Assessment, Washington, DC, 1987). EPA/600/8-87/045.
- (27) M. Nasirudeen and A. Amaechi, Spectrophotometric determination of heavy metals in cosmetics sourced from Kaduna metropolis, Nigeria, *Sci. World J.*, **10**(3), 1–5 (2015).
- (28) E. Sabah, M. Hassan, and Y. Almoeiz, The hazards of hidden heavy metals in face make-ups, *Br. J. Pharmacol. Toxicol.*, **4**(5), 188–193 (2013).

- (29) World Health Organization (WHO), *Guidelines for Drinking Water Quality, Volume 1-Recommendations*, 3rd Ed. (World Health Organization, Geneva, Switzerland, 2008) accessed January 21, 2012, http://www.who.int/water_sanitation_health/dwa/fulltext.pdf.
- (30) Occupational Safety and Health Administration, *Safety and Health Topics, Cadmium—Health Effects*, 2017, retrieved May 1, 2017, <https://www.osha.gov/SLTC/cadmium/healtheffects.html>.
- (31) J. Godt, F. Scheidig, C. Grosse-Siestrup, V. Esche, P. Brandenburg, A. Reich, and D. A. Gronenberg, The toxicity of cadmium and resulting hazards for human health, *J. Occup. Med. Toxicol.*, 1, 1–6 (2006).
- (32) C. Fasanya-Odeyemi, L. M. Latinwo, C. O. Ikediobi, L. Gilliard, G. Sponholtz, J. Nwoga, F. Stino, N. Hamilton, and G. W. Erdos, The genotoxicity and cytotoxicity of dermally-administered cadmium: effects of dermal cadmium administration, *Int. J. Mol. Med.*, 1, 1001–1006 (1998).
- (33) C. F. Allenby and B. Godwin, Influence of detergent washing powder on minimal eliciting patch test concentration of nickel and chromium, *Contact Dermatitis*, 9, 421–499 (1983).
- (34) D. J. Gawkrödger, Nickel dermatitis: how much nickel is safe? *Contact Dermatitis*, 35, 267–271 (1996).
- (35) D. A. Basketter, G. Angelini, R. A. Ingbe, P. S. Kern, and T. Merine Nickel, Cadmium and cobalt in consumer products: revisiting safe levels in new millennium, *Contact Dermatitis*, 49, 1–7 (2003).
- (36) Agency for Toxic Substances and Disease Registry, *Toxicological Profile for Arsenic*, 2007, accessed April 28, 2017, <https://www.atsdr.cdc.gov/toxprofiles>.
- (37) World Health Organization, *Mercury and health*, 2017, retrieved May 1, 2017, <http://www.who.int/mediacentre/factsheets/fs361/en/>.
- (38) A. A. Adepoju-Bello, O. O. Oguntibeju, R. A. Adebisi, N. Okpala, and H. A. B. Coker, Evaluation of the concentration of toxicmetals in cosmetic products in Nigeria, *Afr. J. Biotechnol.*, 11, 16360–11664 (2012).
- (39) M. H. Gbetoh and M. Amyot, Mercury, hydroquinone and clobetasol propionate in skin lightening products in West Africa and Canada, *Environ. Res.*, 150, 403–410 (2016).
- (40) P. B. Tchounwou, C. G. Yedjou, A. K. Patlolla, and D. J. Sutton, Heavy metal toxicity and the environment, *EXS*, 101, 133–164 (2012).
- (41) J. Laamech, A. Bernard, X. Dumont, B. Benazzouz, and B. Lyoussi, Blood lead, cadmium and mercury among children from urban, industrial and rural areas of Fez Boulemane region (Morocco): relevant factors and early renal effects, *Int. J. Occup. Med. Environ. Health*, 27(4), 641–659 (2014).
- (42) U.S. Environmental Protection Agency, *Toxics Release Inventory: Public Data Release Report*, 2001, accessed February 24, 2015, www.epa.gov/tri/tridata/tri01.
- (43) M. Callahan and K. Sexton, If cumulative risk assessment is the answer, what is the question? *Environ. Health Perspect.*, 115(5), 799–806 (2007).
- (44) In.gov, *Risk Assessment*, 2017, retrieved June 1, 2017, <http://www.in.gov/idem/airquality/2640.htm>, <https://www.statista.com/statistics/243742/revenue-of-the-cosmetic-industry-in-the-us/>.
- (45) J. Y. Ayenimo, A. Adekunle, and O. Makinde, Heavy metal exposure from personal care products, *Bull. Environ. Contam. Toxicol.*, 84(1), 8–14 (2009).
- (46) World Health Organization (WHO), *Summary and Conclusion of the 61st Meeting of the Joint FOA/WHO Expert Committee on Food Additives (JECFA) JECFA/Sc Rome* (World Health Organization, Italy, 2003), pp. 10–19 (June, 2013).
- (47) FAO/WHO, Joint FAO/WHO Food Standard Programme, *Codex Committee on Contaminant in Foods 5th Session*, The Hague, The Netherlands, March 21–25, 2011, pp. 90, accessed July 15, 2013, <http://www.64.76.123.202/cclac/CCCF/2011/3%Documentos/Documentos%20Ingles/cf05INF.pdf>.
- (48) European Food Safety Authority (EFSA), Scientific opinion statement on tolerable weekly intake for cadmium, *EFSA J.*, 9(2), 1–19 (1975).
- (49) Bureau of Chemical Safety, Health Canada, *Fish Consumption. Review and Recommendation of Current Intake Figures for Canadian Consumers* (2004).

