

Research Article

Risk of Exposure to Trace Elements through the Application of Facial Makeup Powders

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The study aimed to ascertain the levels of trace elements present in the face powders marketed in Ghana. Fifteen different brands of facial makeup powders were purchased from a local market in Ghana. The samples were analyzed using an X-ray fluorescence (XRF) analyzer to determine the concentrations of 16 elements (Pb, As, Hg, Zn, Fe, Mn, Cr, Ti, Cu, Ni, Co, Sb, Cd, Ag, Sn, and Au). The contents of the trace elements were ordered in the following descending order according to the maximum concentrations: Fe > Zn > Ti > Mn > Cr > Hg > As > Pb > Cu, Ni, Co, Sb, Cd, Ag, Sn, and Au. Pearson correlation statistics showed strong positive relationships between Pb and Zn ($r = 0.71$), Pb and Cr ($r = 0.57$), Hg and Zn ($r = 0.63$), Hg and Fe ($r = 0.73$), Hg and Cr ($r = 0.61$), Zn and Fe ($r = 0.69$), Zn and Cr ($r = 0.88$), Fe and Cr ($r = 0.67$), and Fe and Ti ($r = 0.62$). Except for Pb and Cr, all the other elements had their margin of safety (MOS) values less than 100. The hazard indices (HIs) for Pb, Mn, Cr, and Ti were less than 1, indicating no risk. However, the HIs for As, Hg, Zn, and Fe were more than 1, indicating a potential risk of usage in adults. As a result, using face powders could put users at risk of exposure to trace elements. Dermal exposure to trace elements from cosmetics resulted in a lifetime cancer risk (LCR) that was higher than what was considered tolerable ($LCR > 10^{-6}$) due to the presence of Pb, As, and Cr. Mercury was identified as a potential skin sensitizer in the cosmetic samples examined by an exposure-based sensitization quantitative risk assessment (SQRA).

1. Introduction

Cosmetics are ubiquitously used worldwide for regular self-care. To increase the beauty of human skin and body, cosmetics are frequently used daily. Creams, face lotions, face powder, lipsticks, eye mascara, and hair makeup are among these cosmetics [1, 2]. The existence of dangerous substances in these items is a source of concern. Trace elements such as lead, cadmium, cobalt, chromium, copper, manganese, nickel, titanium, iron, zinc, mercury, and arsenic are among the toxic ingredients in cosmetics [3, 4].

Because their use represents a possible source of human exposure, the elemental concentrations in skin hygiene products are a serious health concern. The presence of trace

elements is widespread in colored cosmetics. As a result, cosmetics are one of the most significant sources of trace elements released into the environment.

While some elements and their salts are banned (such as tin, arsenic, cadmium, nickel, and lead), others are either permitted with restrictions or are only permitted in certain salt forms (e.g., cobalt, chromium, gold, mercury, and selenium among others) [5]. These additions might not be deliberate since some elements come from natural sources [6]. Numerous other raw materials that might be used to make cosmetics that are regarded as natural products have also been found to contain trace elements like cadmium (Cd), lead (Pb), nickel (Ni), arsenic (As), and mercury (Hg). These include olive oil, honey, argan oil, and citrus essential oils [7, 8].

Different skin care products have different uses and different exposure scenarios as a result. Certain cosmetics are applied to specific body parts, such as the hands, face, scalp, and armpits. Examples of such cosmetics are lipstick, hydroalcoholic gels, cream foundations, eye mascara, and scalp care treatments. Other products, such as soaps and lotions, are applied to the entire body surface [9].

Human pollutants' health risks are evaluated on the basis of the mechanistic assumption that they may be cancerous or not. For the estimation of harmful health impacts, numerous researchers have used this method extensively in the literature [2, 4, 9–11]. Most research on the possible health impacts of exposure to contaminants has focused on ingestion, with less attention paid to skin absorption and inhalation.

Cosmetics expose people to a variety of situations. In some instances, such as with shampoos and toothpaste, cosmetics are removed quickly after use. In other cases, such as with body lotions or lipsticks, these chemicals are rubbed into the skin and may stay in contact with it for extended periods [2].

An ad hoc comparative risk assessment technique has historically been used to assess the safety of substances that have the potential to produce skin sensitization through contact. In recent years, general toxicology has largely accepted the principles of exposure-based risk assessment as an extrapolation of quantitative risk assessment approaches [12].

The main objective of this study was to determine elemental concentrations and evaluate the risk of trace elements that cause noncancer, cancer, or sensitization in facial powders.

2. Methodology

2.1. Sampling and Sample Preparation. A total of fifteen (15) facial cosmetic powder products were bought from a local market in Ghana. Before analysis, the lumpy samples were reduced to a fine powder in a clean, sterile mortar and placed in labelled Ziploc bags.

2.2. Sample Analysis. The concentrations of trace elements were determined using a Niton XRF analyzer (Mobile Test S, NDTr-XL3t-86956, com 24) from Thermo Scientific. The instrument was calibrated with a standard calibration disc before analysis. Half of the sample holder was filled with the powdered samples, each weighing approximately 1.50 g. The sample holder was cupped, covered with Mylar film, and subjected to an XRF scan for 180 seconds. Pb, As, Hg, Zn, Fe, Mn, Cr, Ti, Cu, Ni, Co, Sb, Cd, Ag, Sn, and Au were examined in the samples. All samples were treated the same and analyzed in triplicates. Mean concentrations were reported.

2.3. Statistical Analysis. The mean and standard deviation were used to express all results. Using the Microsoft Excel 2019 program, the maximum and minimum elemental concentrations were also determined.

2.4. Noncarcinogenic Risk Assessment. The margin of safety (MOS), which is derived from formula (1), can be used to represent the amount of risk for the noncarcinogenic risk assessment.

$$MOS = \frac{NOAEL}{SED}, \quad (1)$$

where NOAEL is no observed adverse effect level (NOAEL) and SED is systemic exposure dose.

$$SED = A(\text{mg/kg} - \text{B.W.} \cdot \text{day}^{-1}) \times \frac{C_{\max}(\%)}{100} \times \frac{DAp(\%)}{100}, \quad (2)$$

where C_{\max} is the highest concentration of the ingredient in the final cosmetic at the point of application, A is the expected daily exposure to the cosmetic product per kg of body weight, based on the amount applied and frequency of application, and DAp is dermal absorption [13].

The hazard index (HI) was estimated as a ratio of the systemic exposure dose (SED) to the reference dose (RfD).

2.5. Carcinogenic Risk Assessment. Based on previous animal carcinogenicity research, the margin of exposure (MOE) and the lower limit of the benchmark dose (BMDL) values were established [2].

The margin of exposure (MOE), which is determined using the equation $MOE = BMDL_{10}/SED$, can be used to express the amount of risk. The US EPA considers a cancer risk of more than 10,000 to be tolerable [14, 15].

The lifetime cancer risk (LCR) can be used to evaluate the potential cancer risks caused by measured doses of chemical contaminants [13]. The LCR is calculated by

$$LCR = SED \times \text{cancer slope factor (CSF)}. \quad (3)$$

The LCR was determined using linear extrapolation from the following equation based on daily lifetime SED:

$$LCR = \frac{SED}{HT25/0.25}. \quad (4)$$

Based on the comparative metabolic rates, the animal dosage descriptor (T25) is transformed to the human dose descriptor (HT25) using the following equation:

$$HT25 = \frac{T25}{(\text{Body weight}_{\text{human}}/\text{Body weight}_{\text{animal}})^{0.25}}, \quad (5)$$

where human body weight = 70 kg, rat body weight (male) = 0.5 kg, female = 0.35 kg, mouse body weight (male) = 0.03 kg, and female = 0.025 kg [16].

2.6. Dermal Sensitization Risk Assessment. The assessment of the risk of dermal sensitization was estimated by assessing the ratio between the acceptable consumer level (AEL) and the consumer exposure level (CEL), where $AEL \geq CEL$ is considered acceptable [12]. The AEL is expressed as dose/unit area/day. The AEL was determined as a ratio of no expected sensitization induction level (NESIL) to the sensitization assessment factor (SAF).

TABLE 1: Elemental concentrations (mean \pm SD, minimum and maximum) of facial powders ($\mu\text{g/g}$).

Element	Mean concentration ($N=15$)	Minimum concentration	Maximum concentration	Maximum acceptable concentration	Limit of detection (LOD)
Pb	$7.6 \times 10^{-1} \pm 2.93 \times 10^0$	<LOD	1.13×10^1	10.00	1.74
As	$3.87 \times 10^0 \pm 4.71 \times 10^0$	<LOD	1.57×10^1	3.00	1.22
Hg	$2.82 \times 10^0 \pm 7.50 \times 10^0$	<LOD	2.36×10^1	3.00	3.46
Zn	$1.12 \times 10^4 \pm 2.36 \times 10^4$	1.73×10^1	7.17×10^4	20.00	15.80
Fe	$6.18 \times 10^4 \pm 5.99 \times 10^4$	1.40×10^4	1.83×10^5	20.00	116.94
Mn	$3.86 \times 10^1 \pm 4.26 \times 10^1$	<LOD	1.14×10^2	20.00	21.09
Cr	$2.16 \times 10^1 \pm 2.68 \times 10^1$	<LOD	8.37×10^1	20.00	4.75
Ti	$1.42 \times 10^3 \pm 3.12 \times 10^3$	1.10×10^2	1.23×10^4	20.00	18.23
Cu	<LOD	<LOD	<LOD	20.00	6.24
Ni	<LOD	<LOD	<LOD	20.00	10.89
Co	<LOD	<LOD	<LOD	20.00	6.79
Sb	<LOD	<LOD	<LOD	5.00	3.60
Cd	<LOD	<LOD	<LOD	3.00	3.31
Ag	<LOD	<LOD	<LOD	20.00	2.21
Sn	<LOD	<LOD	<LOD	-	2.35
Au	<LOD	<LOD	<LOD	20.00	1.93

<LOD is less than the limit of detection.

The following equation estimated the CEL:

$$\text{CEL} = C \text{ max \%} \times \text{pro du ct exposure} \times 1000. \quad (6)$$

3. Results and Discussion

The mean concentrations and the range of elements measured in cosmetic products are shown in Table 1. Cu, Ni, Co, Sb, Cd, Ag, Sn, and Au concentrations were below the detection limits of the XRF used. Fe concentrations ranged from 13989.44 to 182558.66 $\mu\text{g/g}$. The levels of Zn ranged from 17.34 to 71658.02 $\mu\text{g/g}$, and Ti ranged from 110.29 to 12294.77 $\mu\text{g/g}$. Pb concentrations ranged from <LOD–11.34 $\mu\text{g/g}$, Mn, <LOD–114.81 $\mu\text{g/g}$, and Cr, <LOD–83.67 $\mu\text{g/g}$. As concentration ranged from <LOD–15.67 $\mu\text{g/g}$ and Hg, <LOD–23.62 $\mu\text{g/g}$. All the elements detected had their maximum concentrations exceeding the maximum acceptable concentrations (MACs) in cosmetics. Fe had the highest maximum concentration and Pb had the least concentration among the detected elements.

Trace elements enter the body through dermal or topical application when cosmetic items are used. Both local and systemic impacts of these elements on humans are possible [17]. Due to their affinity for keratin, trace elements at the application site may bind to the stratum corneum and deposit there, creating local reactions that can manifest as allergic contact dermatitis [17].

The formation of free radicals and an inflammatory response are considered the main causes of skin damage caused by trace elements, while the exact mechanism is still unclear [18]. Elements could build up over time if contaminated cosmetics were used repeatedly. Skin inflammation in the systemic system can worsen as a result of exposure of the skin to trace elements [18]. A metalloid that is a common environmental pollutant is arsenic. Long-term dermal exposure to arsenic can cause hyperpigmentation and *in situ* keratosis, but systemically it may induce

carcinogenesis and vascular disorders [7]. Arsenic is generally not a significant pollutant, according to numerous studies, and the quantities of this metalloid rarely go above the 3 ppm threshold. However, it has been found in large amounts in cosmetics from the underground market [19]. Face cosmetics, such as foundations and creams, contain minimal quantities of arsenic, reported as up to 1.0 and 0.171 ppm, respectively [2, 20].

One of the trace elements frequently included in cosmetic formulae is mercury [21]. It has skin-lightening qualities in its inorganic form, such as ammoniated mercury, while its organic forms, such as phenyl and ethyl mercuric salts, are utilized as preservatives in mascaras and eye makeup removal treatments [22, 23]. After dermal application, Hg enters the skin through sweat glands and hair follicles [7, 24]. During this process, part of the Hg is converted to metallic form, which builds up in the skin tissue. Tyrosinase is inhibited *in situ* by mercury's inhibition of the melanin-producing enzyme [25], hence its use in skin-lightening creams [17]. Hg toxicity may display various symptoms, including nausea, vomiting, and kidney damage, as well as effects on the central nervous system such as irritability, tremors, weakness, agitation, exhaustion, and memory loss. It may also affect the sensorial systems, that is, loss of hearing, taste, and vision [7]. A high Hg content can lead to death [26, 27].

Pb is considered a pollutant that has negative health impacts on people. Lead is neurotoxic, nephrotoxic, and hepatotoxic when it contacts important organs [28, 29] and can also affect the reproductive system [30]. Through the placenta, lead can potentially affect fetal growth [31]. According to several studies, it is considered a possible human carcinogen [2, 4, 9, 17, 32]. The World Health Organization established a limit of 10 ppm [7].

Chromium concentrations detected far exceeded the maximum allowed levels set by various regulatory organizations [7, 15, 33]. Cr^{6+} is more toxic than Cr^{3+} [34]. However, the presence of Cr^{6+} as an ingredient in cosmetics

TABLE 2: Pearson's correlation for trace elements.

	Pb	As	Hg	Zn	Fe	Mn	Cr	Ti
Pb	1.00							
As	0.24	1.00						
Hg	-0.10	0.14	1.00					
Zn	0.71	0.29	0.63	1.00				
Fe	0.21	0.31	0.73	0.69	1.00			
Mn	-0.25	0.29	0.24	-0.03	-0.04	1.00		
Cr	0.57	0.33	0.61	0.88	0.67	0.29	1.00	
Ti	-0.05	0.07	0.06	0.02	0.62	-0.33	0.03	1.00

TABLE 3: Estimated noncancer risk assessment of trace elements in facial makeup.

Element	DAp (%)	NOAEL (mg/kg bw/d)	RfD	Maximum concentration ($\mu\text{g/g}$)	SED (mg/kg/d)	MOS (NOAEL/SED)	HI (SED/RfD)
Pb	0.30	8.00×10^0	0.01	1.13×10^1	1.00×10^{-2}	3.23×10^3	0.71
As	1.90	8.00×10^{-4}	0.01	1.57×10^1	2.00×10^{-2}	4.00×10^{-2}	72.35
Hg	1.00	6.30×10^{-1}	0.01	2.36×10^1	2.00×10^{-2}	3.68×10^1	57.40
Zn	0.20	9.10×10^{-1}	0.30	7.17×10^4	1.05×10^1	9.00×10^{-2}	34.83
Fe	1.00	1.25×10^2	0.70	1.83×10^5	1.33×10^2	9.40×10^{-1}	190.12
Mn	1.00	1.40×10^{-1}	0.14	1.14×10^2	8.00×10^{-2}	1.67×10^0	0.60
Cr	1.20	1.80×10^3	1.50	8.37×10^1	7.00×10^{-2}	2.46×10^4	0.05
Ti	0.10	6.25×10^1	3.00	1.23×10^4	8.9×10^{-1}	6.97×10^1	0.30

TABLE 4: Estimated cancer risk assessment of Pb, As, Hg, and Cr in facial makeup.

Element	CSF	BMDL ₁₀ (mg/kg bw/d)	SED (mg/kg b.w./d)	MOE	LCR	
					SED \times CSF	$\frac{SED}{HT25/0.25}$
Pb	8.5×10^{-3}	6.3×10^{-5}	0.01	0.25	2.11×10^{-5}	3.84×10^{-5}
As	1.50	3.0×10^{-4}	0.02	0.01	0.03	NA
Hg	—	6.0×10^{-2}	0.02	3.49	NA	NA
Cr	0.50	1.4×10^{-1}	0.07	1.91	0.04	1.48

TABLE 5: Estimated dermal sensitization quantitative risk assessment of Hg in facial makeup.

Element	Product exposure (mg/cm ² /d)	CEL ($\mu\text{g/cm}^2$)	SAF	NESIL ($\mu\text{g/cm}^2/\text{d}$)	AEL (NESIL/SAF) ($\mu\text{g/cm}^2$)	$\frac{AEL}{CEL}$
Hg	3.17	748.75	300	46.60	0.16	2.1×10^{-4}

is not restricted by law. Therefore, Cr must be controlled as an impurity in cosmetics because it is harmful to humans.

Manganese is an essential mineral necessary for mitochondrial oxidative activities and is found in its natural form in the Earth's crust. Increased absorption occurs with oxidized manganese and in acidic media. In the lowest food chain, its bioconcentration is highest. In addition, it is used to make multivitamin supplements [35].

Titanium dioxide (TiO₂) is used in a variety of products, including paints, cosmetics, orthodontic materials, and food. TiO₂ can be used as an inorganic ultraviolet (UV) filter or as a white pigment primarily in sunscreens, but it can also be used in various day creams, foundations, and lip balms to protect against the known carcinogenic effects of UV radiation [36]. Most in vitro, in vivo, and ex vivo research in humans or animals revealed that the stratum corneum was the site of penetration of nano-TiO₂. Nano-TiO₂ could not reach the general circulation or penetrate the layers of the skin surface to reach viable cells, whether the skin was healthy or impaired.

Following application to healthy, intact, or sunburned skin, SCCS found that nano-TiO₂ in concentrations up to 25% as a UV filter in sunscreens can be considered not to pose any danger of negative effects in people [13].

Pearson's correlation statistics (Table 2) reveal strong positive relationships between Pb and Zn ($r=0.71$), Pb and Cr ($r=0.57$), Hg and Zn ($r=0.63$), Hg and Fe ($r=0.73$), Hg and Cr ($r=0.61$), Zn and Fe ($r=0.69$), Zn and Cr ($r=0.88$), Fe and Cr ($r=0.67$), and Fe and Ti ($r=0.62$).

3.1. Noncancer Risk Assessment of Trace Elements in Cosmetics. Table 3 summarizes the findings of the risk assessment for noncarcinogenic trace elements. The SED was calculated to be between 0.002 and 133.09 mg/kg bw/d, assuming the maximum amount used in cosmetics, based on the concentrations of Pb, As, Hg, Zn, Fe, Mn, Cr, and Ti in cosmetics. A MOS of more than 100 would indicate no obvious risk to humans [13]. Except for Pb and Cr, all of the

elements had MOS values less than 100. The hazard indices (HIs) for Pb, Mn, Cr, and Ti were less than 1, indicating no risk. However, the HIs for As, Hg, Zn, and Fe were more than 1, indicating a potential risk of usage in adults. As a result, using the items could put users at risk of exposure to trace elements.

3.2. Cancer Risk Assessment of Trace Elements in Cosmetics. The cancer risk assessment results for Pb, As, Hg, and Cr in cosmetics are presented in Table 4. The SED for Pb, As, Hg, and Cr contained in facial makeup powders was 0.0025, 0.022, 0.017, and 0.073 mg/kg bw/d, respectively. MOE ranged from 0.014 to 3.485, with As having the lowest MOE and Hg having the highest MOE. The life cancer risk (LCR) was above 10^{-6} , indicating unsafe levels for humans.

3.3. Sensitization Quantitative Risk Assessment of Trace Elements in Cosmetics. The SQRA results are presented in Table 5. The percentage concentration of trace elements in a product type is acceptable if the AEL exceeds the CEL. The AEL: CEL ratio for Hg was less than 1, which is unacceptable because the CEL exceeded the AEL. Therefore, Hg is a potential skin sensitizer.

4. Conclusions

The findings obtained from the study are essential to understanding the risks of trace element exposure and their occurrence in cosmetics used for facial makeup. The contents of the trace elements were ordered in the following descending order according to the maximum concentrations: Fe > Zn > Ti > Mn > Cr > Hg > As > Pb > Cu, Ni, Co, Sb, Cd, Ag, Sn, and Au. In general, the investigated samples had trace element concentrations significantly higher than the MOS and cancer risk criteria (10^{-6}). Out of the 16 trace elements, the hazard indices (HIs) for As, Hg, Zn, and Fe were more than 1, indicating a potential risk of usage in adults. According to this study on the trace element content of facial makeup, the presence of harmful elements in cosmetics must be regulated to protect consumer health.

Data Availability

The corresponding author will provide supplementary data upon request.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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References

- [1] H. Arshad, M. Z. Mehmood, M. H. Shah, and A. M. Abbasi, "Evaluation of heavy metals in cosmetic products and their health risk assessment," *Saudi Pharmaceutical Journal*, vol. 28, no. 7, pp. 779–790, 2020.
- [2] D. S. Lim, T. H. Roh, M. K. Kim et al., "Non-cancer, cancer, and dermal sensitization risk assessment of heavy elements in cosmetics," *Journal of Toxicology and Environmental Health Part A: Current Issues*, vol. 81, no. 11, pp. 432–452, 2018.
- [3] C. Kulal, R. K. Padhi, K. Venkatraj, K. K. Satpathy, and S. H. Mallaya, "Study on trace elements concentration in medicinal plants using EDXRF technique", biological trace element research," *Biological Trace Element Research*, vol. 198, no. 1, pp. 293–302, 2020.
- [4] A. K. Salama, "Assessment of metals in cosmetics commonly used in Saudi Arabia," *Environmental Monitoring and Assessment*, vol. 188, no. 10, p. 553, 2016.
- [5] E. Łodyga-Chruścińska, A. Sykuła, and M. Więdołcha, "Hidden metals in several brands of lipstick and face powder present on polish market," *Cosmetics*, vol. 5, no. 4, p. 57, 2018.
- [6] S. B. Kumar, R. K. Padhi, A. K. Mohanty, and K. K. Satpathy, "Elemental distribution and trace metal contamination in the surface sediment of south east coast of India," *Marine Pollution Bulletin*, vol. 114, no. 2, pp. 1164–1170, 2017.
- [7] T. Attard and E. Attard, "Heavy elements in cosmetics", environmental impact and remediation of heavy elements," 2022, <https://www.intechopen.com/chapters/80103>.
- [8] T. Eticha, H. Getachew, G. Kahsay, and H. Gebretsadik, "Elements contamination in face powders and their associated health risks to the users in mekelle, Ethiopia," *Journal of Environmental and Analytical Toxicology*, vol. 8, no. 1, p. 1, 2018.
- [9] U. P. Gnonsonoro, Y. E. D. Ake Assi, N. S. Sangare, Y. U. Kouakou, and A. Trokourey, "Health risk assessment of heavy elements (Pb, Cd, Hg) in hydroalcoholic gels of abidjan, côte d'Ivoire," *Biological Trace Element Research*, vol. 200, no. 5, pp. 2510–2518, 2022.
- [10] V. K. Bolor, N. O. Boadi, L. S. Borquaye, and S. Afful, "Human risk assessment of organochlorine pesticide residues in vegetables from Kumasi, Ghana," *Journal of Chemistry*, vol. 2018, Article ID 3269065, 11 pages, 2018.
- [11] F. Forkuoh, N. O. Boadi, L. S. Borquaye, and S. Afful, "Risk of human dietary exposure to organochlorine pesticide residues in fruits from Ghana", scientific reports," *Scientific Reports*, vol. 8, no. 1, pp. 16686–16695, 2018.
- [12] A. M. Api, D. A. Basketter, P. A. Cadby et al., "Dermal sensitization quantitative risk assessment (QRA) for fragrance ingredients," *Regulatory Toxicology and Pharmacology*, vol. 52, no. 1, pp. 3–23, 2008.
- [13] SCCS, "Revision of the SCCS notes of guidance for the testing of cosmetic ingredients and their safety evaluation," *European Commission*, vol. 1564, p. 151, 2016.
- [14] European Food Safety Authority Scientific Committee, "Use of the benchmark dose approach in risk assessment," 2016, <https://efsa.onlinelibrary.wiley.com/doi/10.2903/j.efsa.2017.4658>.
- [15] USEPA, "Exposure factors handbook," 1997, <https://www.epa.gov/expobox/about-exposure-factors-handbook>.
- [16] T. Sanner and E. Dybing, "Comparison of carcinogen hazard characterisation based on animal studies and epidemiology," *Basic and Clinical Pharmacology and Toxicology*, vol. 96, no. 1, pp. 66–70, 2005.

- [17] S. Borowska and M. M. Brzóška, "Elements in cosmetics: implications for human health," *Journal of Applied Toxicology*, vol. 35, no. 6, pp. 551–572, 2015.
- [18] J. P. Thyssen and T. Menné, "Metal allergy—a review on exposures, penetration, genetics, prevalence, and clinical implications," *Chemical Research in Toxicology*, vol. 23, no. 2, pp. 309–318, 2010.
- [19] A. Saadatzaheh, S. Afzalan, R. Zadehdabagh et al., "Determination of heavy elements (lead, cadmium, arsenic, and mercury) in authorized and unauthorized cosmetics," *Cutaneous and Ocular Toxicology*, vol. 38, no. 3, pp. 207–211, 2019.
- [20] M. B. Nasirudeen and A. U. Amaechi, "Spectrophotometric determination of heavy elements in cosmetics sourced from Kaduna Metropolis, Nigeria," *Science World Journal*, vol. 10, no. 3, pp. 1–5, 2015.
- [21] A. Kader Mohiuddin, "Heavy metals in cosmetics: the notorious daredevils and burning health issues," *American Journal of Biomedical Science & Research*, vol. 4, no. 5, pp. 332–337, 2019.
- [22] I. Al-Saleh and I. Al-Doush, "Mercury content in skin-lightening creams and potential hazards to the health of Saudi women," *Journal of Toxicology and Environmental Health*, vol. 51, no. 2, pp. 123–130, 1997.
- [23] B. Ladizinski, N. Mistry, and R. V. Kundu, "Widespread use of toxic skin lightening compounds: medical and psychosocial aspects," *Dermatologic Clinics*, vol. 29, no. 1, pp. 111–123, 2011.
- [24] R. H. Guy, J. J. Hostýnek, R. S. Hinz, and C. R. Lorence, "Elements and the skin: topical effects and systemic absorption, elements and the skin," 2016, https://www.researchgate.net/publication/327304969_Metals_and_the_Skin_Topical_Effects_and_Systemic_Absorption.
- [25] J. J. Hostýnek, "Factors determining percutaneous metal absorption," *Food and Chemical Toxicology*, vol. 41, no. 3, pp. 327–345, 2003.
- [26] E. S. Agorku, E. E. Kwaansa-Ansah, R. B. Voegborlo, P. Amegbletor, and F. Opoku, "Mercury and hydroquinone content of skin toning creams and cosmetic soaps, and the potential risks to the health of Ghanaian women," *SpringerPlus*, vol. 5, no. 1, pp. 319–325, SpringerPlus, 2016.
- [27] R. D. Barr, B. A. Woodger, and P. H. Rees, "Levels of mercury in urine correlated with the use of skin lightening creams," *American Journal of Clinical Pathology*, vol. 59, no. 1, pp. 36–40, 1973.
- [28] V. Karri, M. Schuhmacher, and V. Kumar, "Heavy elements (Pb, Cd, As and MeHg) as risk factors for cognitive dysfunction: a general review of elemental mixture mechanism in brain," *Environmental Toxicology and Pharmacology*, vol. 48, pp. 203–213, 2016.
- [29] L. Patrick, "Lead toxicity, a review of the literature. Part 1: exposure, evaluation, and treatment," *Alternative Medicine Review: A Journal of Clinical Therapeutic*, vol. 11, no. 1, pp. 2–22, 2006.
- [30] A. S. Chauhan, R. Bhadauria, A. K. Singh, S. S. Lodhi, D. K. Chaturvedi, and V. S. Tomar, "Determination of lead and cadmium in cosmetic products," *Journal of Chemical and Pharmaceutical Research*, vol. 2, no. 6, pp. 92–97, 2010.
- [31] J. G. Ayenimo, A. M. Yusuf, A. S. Adekunle, and O. W. Makinde, "Heavy metal exposure from personal care products," *Bulletin of Environmental Contamination and Toxicology*, vol. 84, no. 1, pp. 8–14, 2010.
- [32] National Institute of Technology and Evaluation, "Basic manual for calculation of the estimated human exposure used in the risk assessment of consumer products," 2008, http://www.nite.go.jp/en/chem/risk/ghs_risk_consumer_guidance_ap1_e.pdf.
- [33] Health Canada, "Guidance on heavy elemental impurities in cosmetics," 2012, <https://www.canada.ca/en/health-canada/services/consumer-product-safety/reports-publications/industry-professionals/guidance-heavy-metal-impurities-cosmetics.html>.
- [34] U. L. Usman, S. A. Danhauwa, S. Sajad, and S. Banerjee, "Assessment of heavy elemental in some commonly used cosmetic product and associated health risk in Nigeria: threat to public health," *Macromolecular Symposia*, vol. 397, 2021.
- [35] C. Santos-Burgoa, C. Rios, L. A. Mercado et al., "Exposure to manganese: health effects on the general population, a pilot study in Central Mexico," *Environmental Research*, vol. 85, no. 2, pp. 90–104, 2001.
- [36] B. Dréno, A. Alexis, B. Chuberre, and M. Marinovich, "Safety of titanium dioxide nanoparticles in cosmetics," *Journal of the European Academy of Dermatology and Venereology*, Blackwell Publishing Ltd, Hoboken, NY, USA, 2019.