



Original article

Evaluation of heavy metals in cosmetic products and their health risk assessment

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ABSTRACT

Heavy metals' contamination in cosmetic products is a serious threat. Present study was conducted to evaluate the concentrations of heavy metals (HMs) in various brands of cosmetic products with special emphasis on their health risk assessment. Five heavy metals including Cd, Cr, Fe, Ni and Pb were quantified in different brands of lotions, foundations, whitening creams, lipsticks, hair dyes and sunblock creams using atomic absorption spectrometry. Risk to the consumer's health was determined using systemic exposure dosage (SED), margin of safety (MoS), hazard quotient (HQ), hazard index (HI) and lifetime cancer risk (LCR).

On comparative basis, different brands of sunblock creams depicted highest concentration of Ni, Pb and Cr (7.99 ± 0.36 , 6.37 ± 0.05 and 0.43 ± 0.01 mg/kg, respectively), whereas lipsticks had elevated levels of Fe at 12.0 ± 1.8 mg/kg, and Cd was maximum in lotions (0.26 ± 0.02 mg/kg). Multivariate analysis revealed strong associations among Cr, Ni and Pb, while Cd and Fe showed disparity in distribution and sources of contamination. MoS, HQ and HI values were within the permissible limit apart from lotions and sunblock creams, while LCR value was higher than the permissible limit in all cosmetic products except lipsticks. Regular use of these products can cause serious threat to human health, particularly skin cancer on long time exposure. Therefore, continuous monitoring of cosmetic products, particularly with reference to HMs adulteration should be adopted to ensure the human safety and security.

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1. Introduction

Application of different cosmetics for personal care is as old as human civilization. With the passage of time, demand of cosmetics has increased many folds throughout the world. This is mainly owing to the increased awareness about methods to enhance the outlook of the body (Ullah et al., 2017). Today the use of cosmetics for personal grooming and body care has become the norm throughout the world (OJEU, 2009). The global market for beauty products has shown an average increase of about 5% per year. It

is an interesting fact that the market for cosmetics and personal care products has shown constant and stable growth ever since its origin and has progressed even in unstable economies (Barbalova, 2011).

Cosmetic products are composed of different organic and inorganic materials including hydrophilic and hydrophobic substances. In the manufacturing of coloured cosmetics, mineral pigments are commonly used which leads to the contamination of cosmetic products with heavy metals (HMs) such as, Cu, Ni, Co, Pb, Cr, Cd and other elements. These HMs become a part of cosmetic product intentionally in the form of pigments, preservatives, UV filters as well as antiperspirant, antifungal and antibacterial agents (Burger et al., 2016). It has been reported that human exposure to UV radiations can cause chronic as well as acute health effects on human skin, eye and immune system. Thus, cosmetic manufacturers use UV filters as important ingredients in sunscreens and other daily used cosmetic products. Though, UV filters are designed for the cosmetic products that are intended to apply on topical skin surface but derivatives of the products can bind to plasma protein and get circulated in

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the blood, then through phase I and II biotransformation reaction that get metabolized in the liver. Afterwards they may either be excreted through urine or they can be bio-accumulated within the organism (Locatelli et al., 2019). Some metals as well as parabens are incorporated as preservatives in cosmetic products because they possess antibacterial and antifungal properties. Through recent studies it has been evaluated that metals and parabens used as preservatives are also endocrine disruptors and can get easily absorbed through skin thus causing adverse effects on human health (Tartaglia et al., 2019; Iavicoli et al., 2009). Some metallic compounds are routinely used in the cosmetics as they possess properties to peel and whiten the skin (Burger et al., 2016). However, use of metals components are based on regulatory laws of a particular country (OJEU, 2009). Heavy metals are also added accidentally as impurities at various stages of cosmetic production. As the sort of raw material used in the manufacturing process, particularly the addition of additives and colour minerals cause contamination. In addition, water used for their preparation may also contain metallic impurities. Moreover, use of different instrumentation in cosmetic industries during sorting, manufacturing and packaging processes may also cause HMs contamination (Łodyga Chruścińska et al., 2018).

Trace quantities of some toxic metals (such as Cd and Pb) have been found in many products including toothpastes, face makeup and lipsticks etc. (Li et al., 2015). It has also been reported that natural ingredients like plant based materials are the major source of heavy metal contamination in cosmetics (Bocca et al., 2014). It has been recommended by The International Organizations to measure the quantity of toxic metals in the plants used as raw material as well as in the final products. As previously reported that toxic metals may be present in herbs and plants as a result of pre-existing use of fertilizers, insecticides or due to their cultivation near industrial zones. Therefore principal analytical procedures should be followed to reduce heavy metal concentration in raw material and to ensure the quality of final products (Locatelli et al., 2014).

In past it was assumed that the cosmetics are only associated with local effects but in the last few decades concerns were raised after the fact that certain substances in cosmetics may penetrate deep into the skin and get exposed to the organs. This stirred skin tests to check the penetration/adsorption capability of certain substances from the products as well as their toxicity (Nohynek et al., 2010). Although the outer most protective layer of skin (stratum corneum) does not allow large penetration, traces of HMs present in cosmetic products may reach the circulatory system (Bocca et al., 2014). Some of the metals have tendency to get accumulated with stratum corneum and cause allergic effects while others are diffusible in sweating, tears and sebum excretion and may penetrate through the skin appendages or through trans-cellular and intracellular pathways and reach blood circulatory system of human body. Therefore, daily application of many cosmetic products may result in increasing exposure of HMs to human body (Brzówska et al., 2018).

Elevated exposure to the heavy metals may result in numerous health problems including skin allergies, severe redness, swelling/skin ulcers, cellular death, DNA damage, oxidative stress, neurotoxicity, memory loss, reproductive failure and carcinogenic health effects (Kim et al., 2015; Bocca et al., 2014; Senesse et al., 2004; Agoramoorthy et al., 2008; Amry et al., 2011; Smith et al., 2015). In this context, the present study was focused on the determination of heavy metal concentrations in selected cosmetic products and to appraise health risks associated with exposure to the metals in cosmetic products. It is anticipated that the present study would provide pivotal information related to the health risks associated with the prolonged use of the cosmetic products.

2. Material and methods

2.1. Sample collection

Most commonly used cosmetic products (more than 70% frequency) were considered and collected for analysis in the present study. The usage frequency was calculated based on the data extracted from the questionnaire filled by more than 100 users during this study. It was ensured that the selected samples were representatives of most available, popular and commonly used product types. Locally manufactured and imported cosmetic products ($n = 189$) were collected in triplicates from local community and markets of Abbottabad, Haripur and Mansehra, Pakistan. The cosmetic products were sampled into six different groups; lotions (30 brands), foundations (9 brands), whitening creams, lipsticks, hair dyes and sunblock (6 brands each). Samples were stored at room temperature before analysis.

2.2. Washing

Washing is the most critical step for accurate heavy metal analysis. Washing of all accessories was done following the protocol of Olmedo et al. (2010). All glassware were washed first with detergent and then rinsed repeatedly with tap water. Afterwards, glassware were soaked in a solution of HNO_3 (5%) for about 24 h. Then rinsing was done using deionised water and dried at 80°C for 48 h before use.

2.3. Sample preparation

The collected samples were digested using acids mixture (HNO_3 , H_2SO_4 and HClO_4 in ratio of 1:1:1) following the procedure reported by Saeed et al. (2011) and Ayenimo et al. (2010) with modifications. Approximately, 1.0 g of each sample (in triplicate) was taken in 50 mL conical flask, followed by the addition of 5 mL of HNO_3 and the mixture was kept overnight at room temperature. Subsequently, the contents were heated on a hot plate by slowly increasing the temperature up to 90°C and after appearance of brown fumes, mixture was allowed to cool. Then H_2SO_4 (5 mL) was added and heated again for 30–60 min followed by cooling to room temperature. Finally, then 5 mL of HClO_4 was added and the contents were digested until clear solution was obtained. After digestion, the samples were cooled to room temperature and filtered through Whatman filter paper No. 41 and the final volume (50 mL) was adjusted by deionised water. Blanks were also prepared following the same procedure with each batch of samples ($n = 5$). All the digested samples were stored in refrigerator till further analysis.

2.4. Quantification of HMs

Quantification of selected metals was done using atomic absorption spectrophotometer (Perkin Elmer AAnalyst 700) at their specific wavelength. Calibration line method was employed under optimum analytical conditions (Table S1) for the analysis of selected HMs. Standard stock solutions (1000 mg/L) of the metals were used to prepare the working standards freshly on the day of analysis. Countercheck of the results was ensured through the internal standard analysis as well as by standard reference materials (NIST SRM 1515) which showed very good recovery (97–102%). Blanks were routinely analysed for the metals contents and the final results were appropriately corrected. All the measurements were made in triplicate.

2.5. Statistical analysis

The statistical parameters related to the distribution of metals in the cosmetic products were computed using STATISTICA (Stat-Soft Inc, 1999). Other statistical analyses including correlation and ANOVA were done using SPSS (V13.0), while graphs were plotted through Sigma Plot (V1 2.5) and Bio-Vinci (1.1.5). The analytical data were presented as mean \pm SD for triplicate analysis of each sample.

2.6. Health risk assessment

2.6.1. Margin of safety (MoS)

Health risk to humans as a result of exposure to heavy metal impurities present in the cosmetics can be computed in terms of Margin of Safety (MoS), which can be calculated by taking a ratio of No Observed Adverse Effect Level (NOAEL) of the product under study by its systemic exposure dosage (SED) as reported previously (SCCS, 2012).

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

The SED predicts amount of chemicals that enter into human body by various exposure means. It is calculated based on the metal concentration present in the product under study, amount of the product applied per day, frequency of application, surface area of the skin on which the product is applied and average body weight (SCCS, 2012). The SED value was calculated by an expression:

$$SED(mg/kg/d) = \frac{Cs \times AA \times SSA \times F \times RF \times BF}{BW} \times 10^{-3} \quad (2)$$

where, Cs indicates metal concentration in the sample (mg/kg), SSA is the surface area of skin onto which the product is applied (cm²), AA shows the quantity applied (g/cm²), RF is the retention factor, F indicates the application frequency of a product/day, BF is the bioaccessibility factor, 10⁻³ (mg/kg) is used as unit conversion factor, BW is the average body weight (70 kg) (El-Aziz et al., 2017; SCCS, 2012).

A level of exposure where no adverse effect is observed is called NOAEL and its value was calculated based on dermal reference doses (RfDs) as reported by (USEPA, 2006) using following expression:

$$NOAEL = RfD \times UF \times MF \quad (3)$$

where, UF is uncertainty factor (reflects overall confidence in the various data sets), MF is modifying factor (based on the scientific judgment). Default values for MF and UF are 1 and 100 respectively. RfDs represents dermal reference doses ($\mu\text{g kg}^{-1}\text{d}^{-1}$) of different metals. According to USA risk-based concentration table, dermal reference doses for Cd, Cr, Fe, Ni and Pb are 0.005, 0.015, 140, 5.4 and 0.42 $\mu\text{g/kg/d}$ (Achary et al., 2016).

According to World Health Organization (WHO), MoS value up to 100 is acceptable and product with MoS value above 100 is considered safe for use. The scientific committee on consumer's safety (SCCS) recognizes that in many conventional calculations of MoS, oral bioavailability of an element is assumed to be 100%, if oral absorption data are not available. Standard values of skin surface area (SSA) and amount applied (AA) established by SCCS for cosmetic products are given in Table S2. However, it is considered suitable to assume that not more than 50% of an orally administered dose is systemically accessible (SCCS, 2012).

2.6.2. Hazardous quotient (HQ) and hazard index (HI)

Hazard quotient (HQ) is the ratio of systemic exposure dosage (SED) of a substance to the dermal reference dose (RfD) of each

metal (USEPA, 2011; Liu et al., 2013). The HQ value <1 is considered to be safe while the greater than 1 is unsafe for human health. The HQ level was calculated using formula:

$$HQ = SED/RfD \quad (4)$$

Hazard index (HI) is the summation of hazard quotients for all the metals under study. It is computed in order to evaluate human health risk due to the exposure of all metallic impurities. The HI value was calculated using following relationship as reported previously (El-Aziz et al., 2017):

$$HI = \sum HQ = HQ_{Cd} + HQ_{Cr} + HQ_{Ni} + HQ_{Fe} + HQ_{Pd} \quad (5)$$

2.6.3. Lifetime cancer risk (LCR)

Lifetime cancer risk is usually investigated for carcinogenic metals. In the current study, LCR was determined by using following relationship (El-Aziz et al., 2017):

$$LCR = SED \times SF \quad (6)$$

where, SF represents the carcinogenicity slope factor (mg/kg/d)⁻¹ and it approximates the cancer risk per unit intake dose of an agent to cause cancer over an average lifetime. The reported slope factor for Pb, Cr, Ni and Cd are 0.0085, 0.5, 0.91 and 6.7 (mg/kg/d)⁻¹, respectively (IRIS, 2007; USEPA, 2010; WHO, 2008).

3. Results and discussion

3.1. Heavy metals' distribution in lotions

In total 30 different brands of lotions (n = 90) were analysed and measured levels of HMs were significantly different at $p < 0.05$ from one brand to another (Table 1). L1 depicted highest level of Cd (2.13 \pm 0.15 mg/kg), followed by L19 and L20 (0.27 \pm 0.02 and 0.26 \pm 0.01 mg/kg, respectively), while in L4 to L11, L22 and L23 brands Cd metal was below the detectable limit. Measured levels of Cd in all samples of lotion were within the permissible limit of 3 mg/kg set by Canadian authority in cosmetic products (HCSC, 2012). Range of Cd observed in the current study was almost comparable as reported earlier by Ababneh and Al-Momani (2018), but was lower than the reported by Borowska and Brzóska (2015). Results showing Cr concentration revealed that in 12 brands of lotions (L4 to L13, L22 and L23), Cr level was below the detection limit. Maximum concentration of Cr was quantified in L20 (0.69 \pm 0.02 mg/kg). Comparatively, Cr level was slightly higher in our samples than a previous report (Borowska and Brzóska, 2015). However, Cr was within the safe limit of 50 mg/kg set by USFDA (USFDA, 2013). Generally Fe is considered as essential mineral but its exceeding level may cause serious health issues (Miyajima et al., 2002). In all samples of lotion, measured levels of Fe varied from 0.27 to 7.01 mg/kg. The highest concentration was detected in L24 (7.01 \pm 0.14 mg/kg), while lowest was in L23 (0.27 \pm 0.19), imported from South Africa.

Concentration of Ni was maximum in L17 (6.29 \pm 0.12 mg/kg), whereas lowest level was calculated in L27 (0.01 \pm 0.05 mg/kg). However, in L18 Ni was below the detectable limit (Table 1). It was noted that Ni concentration in our samples was comparable with previous reports (Ababneh and Al-Momani, 2018; Borowska and Brzóska, 2015). Recommended level of Ni set by USFDA and Cosmetics Italia is 200 mg/kg (USFDA, 2013) in cosmetics. However, it is suggested that for skin protection Ni and Cr concentration should be <1.0 mg/kg in cosmetic products, particularly that come in direct contact with skin and 0.5 mg/kg of Ni concentration is enough to cause dermatitis (Basketter et al., 2003). Measured level of Pb ranged from 0.07 to 8.29 mg/kg. Highest concentration of Pb was in L20 (8.29 \pm 0.09 mg/kg), followed by L19

Table 1
Measured levels of HMs (mg/kg) in the cosmetic products.

Brand	CN	SC	Cd	Cr	Fe	Ni	Pb
Lotions (n = 90)							
Nivea	Dubai	L1	2.1 ± 0.2 ^a	0.08 ± 0.01 ^{cdef}	2.42 ± 0.38 ^{cd}	3.24 ± 0.41 ^b	4.57 ± 0.31 ^d
Mother care	Pakistan	L2	0.17 ± 0.17 ^{bcde}	0.42 ± 0.37 ^b	1.72 ± 1.33 ^{cdefghi}	6.11 ± 0.24 ^a	4.32 ± 0.59 ^{de}
Vaseline	Indonesia	L3	0.03 ± 0.02 ^{efghij}	0.04 ± 0.01 ^{cdefg}	0.36 ± 0.02 ^{hi}	1.97 ± 0.07 ^{bcde}	1.02 ± 0.33 ^{kl}
Olivia	Pakistan	L4	bdl	bdl	0.58 ± 0.03 ^{fghi}	0.83 ± 0.04 ^{def}	0.77 ± 0.21 ^{klm}
Care Natural Honey Lotion	Pakistan	L5	bdl	bdl	0.29 ± 0.03 ⁱ	0.47 ± 0.12 ^{ef}	1.22 ± 0.25 ^{ijk}
Jergens	Dubai	L6	bdl	bdl	0.40 ± 0.39 ^{hi}	2.50 ± 0.38 ^{bcd}	1.87 ± 0.22 ^{hi}
Vaseline	South Africa	L7	bdl	bdl	0.27 ± 0.19 ⁱ	1.19 ± 1.21 ^{cdef}	1.45 ± 0.16 ^{hij}
Hollywood Style	USA	L8	bdl	bdl	0.50 ± 0.13 ^{ghi}	2.27 ± 1.35 ^{bcd}	1.67 ± 0.03 ^{hij}
Rivaj UK	Pakistan	L9	bdl	bdl	0.67 ± 0.01 ^{efghi}	2.33 ± 1.17 ^{bcd}	1.89 ± 0.20 ^h
Bath & Body Work	USA	L10	bdl	bdl	0.62 ± 0.10 ^{fghi}	1.70 ± 0.53 ^{bcdef}	3.18 ± 0.04 ^g
Garnier body lotion	London	L11	bdl	bdl	0.38 ± 0.52 ^{hi}	3.21 ± 0.47 ^b	3.30 ± 0.16 ^{fg}
Vaseline dry skin repair	South Africa	L12	0.01 ± 0.05 ^{efghij}	bdl	0.68 ± 0.08 ^{efghi}	3.41 ± 0.67 ^b	3.87 ± 0.32 ^{ef}
Vaseline Olvera	Malaysia	L13	0.03 ± 0.03 ^{efghij}	bdl	0.58 ± 0.08 ^{fghi}	1.83 ± 1.16 ^{bcde}	4.14 ± 0.04 ^{de}
Remembrance	Ireland	L14	0.21 ± 0.02 ^{bcd}	0.59 ± 0.01 ^{ab}	2.10 ± 0.30 ^{cdef}	6.15 ± 0.15 ^a	6.97 ± 0.21 ^c
Dove	India	L15	0.25 ± 0.03 ^{bc}	0.62 ± 0.04 ^{ab}	2.71 ± 0.63 ^c	6.24 ± 0.10 ^a	7.19 ± 0.16 ^c
Olay	Malaysia	L16	0.23 ± 0.04 ^{bcd}	0.61 ± 0.03 ^{ab}	1.88 ± 0.57 ^{cdefgh}	5.95 ± 0.08 ^a	7.30 ± 0.30 ^{bc}
Enchanteur	Dubai	L17	0.25 ± 0.04 ^{bc}	0.66 ± 0.01 ^a	2.23 ± 0.70 ^{cde}	6.29 ± 0.12 ^a	7.53 ± 0.31 ^{bc}
Ponds	Pakistan	L18	bdl	0.01 ± 0.04 ^{cdefg}	0.89 ± 0.04 ^{defghi}	bdl	0.68 ± 0.08 ^{klmn}
Johnson's baby lotion	Italy	L19	0.27 ± 0.02 ^b	0.67 ± 0.03 ^a	2.01 ± 0.72 ^{cdefg}	6.16 ± 0.33 ^a	7.94 ± 0.10 ^{ab}
Natural fresh watermelon	France	L20	0.26 ± 0.01 ^{bc}	0.69 ± 0.02 ^a	2.42 ± 0.31 ^{cd}	6.15 ± 0.13 ^a	8.29 ± 0.09 ^a
Golden pearl lotion	Pakistan	L21	0.10 ± 0.03 ^{cdefghi}	0.01 ± 0.02 ^{cdefg}	0.51 ± 0.09 ^{ghi}	1.73 ± 0.39 ^{bcdef}	0.57 ± 0.18 ^{klmn}
Cream 21	Germany	L22	bdl	bdl	0.35 ± 0.08 ^{hi}	2.63 ± 0.19 ^{bc}	1.071 ± 0.002 ^{ijkl}
Vaseline Petroleum jelly	Pakistan	L23	bdl	bdl	0.34 ± 0.05 ^{hi}	2.35 ± 0.29 ^{bcd}	1.49 ± 0.03 ^{hij}
Salon 7 day protection	Pakistan	L24	0.17 ± 0.01 ^{bcde}	0.13 ± 0.01 ^c	7.01 ± 0.14 ^a	0.08 ± 0.01 ^f	0.34 ± 0.02 ^{mn}
MIEIVIC	China	L25	0.14 ± 0.02 ^{bcdefg}	0.12 ± 0.01 ^{cde}	5.81 ± 0.42 ^{ab}	0.08 ± 0.04 ^f	0.30 ± 0.02 ^{mn}
Cream 24 Hour	England	L26	0.16 ± 0.02 ^{bcdef}	0.11 ± 0.02 ^{cdef}	5.64 ± 0.46 ^{ab}	0.07 ± 0.02 ^f	0.22 ± 0.04 ^{mn}
Floral Rush	Dubai	L27	0.07 ± 0.06 ^{defghij}	0.07 ± 0.02 ^{cdefg}	4.85 ± 1.34 ^b	0.01 ± 0.05 ^f	0.07 ± 0.17 ^{mn}
Cucumber Melon	USA	L28	0.12 ± 0.02 ^{bcdefgh}	0.08 ± 0.01 ^{cdefg}	5.20 ± 0.71 ^b	0.05 ± 0.02 ^f	0.26 ± 0.11 ^{mn}
Glysolid	Italy	L29	0.14 ± 0.02 ^{bcdefg}	0.07 ± 0.01 ^{cdefg}	5.48 ± 0.20 ^{ab}	0.066 ± 0.004 ^f	0.35 ± 0.06 ^{mn}
Meijer Moisturizing lotion	USA	L30	0.15 ± 0.01 ^{bcd}	0.12 ± 0.02 ^{cd}	5.31 ± 0.35 ^b	0.08 ± 0.02 ^f	0.44 ± 0.05 ^{lmn}
		Max.	2.13	1.00	7.01	6.29	8.29
		Min.	0.007	0.008	0.271	0.012	0.068
		Mean	0.257	0.283	2.140	2.592	2.809
		SE	0.015	0.009	0.070	0.076	0.091
Hair Dyes (n = 18)							
Olivia (non-metallic dye)	Pakistan	D1	bdl	bdl	0.27 ± 0.33 ^a	2.5 ± 1.8 ^{ab}	4.72 ± 0.05 ^d
Revlon	Italy	D2	0.001 ± 0.021 ^b	0.05 ± 0.02 ^{cd}	0.32 ± 0.18 ^a	3.79 ± 1.00 ^a	5.02 ± 0.15 ^{cd}
Garnier Black	London	D3	bdl	0.08 ± 0.01 ^{bc}	0.26 ± 0.30 ^a	3.06 ± 0.88 ^a	5.33 ± 0.18 ^{bc}
Color Pro	Greece	D4	0.03 ± 0.02 ^b	0.12 ± 0.02 ^{ab}	0.28 ± 0.27 ^a	3.82 ± 0.27 ^a	5.67 ± 0.23 ^{ab}
Keune	Holland	D5	0.03 ± 0.03 ^b	0.13 ± 0.02 ^a	0.42 ± 0.22 ^a	4.17 ± 0.23 ^a	5.84 ± 0.19 ^a
Garnier Dark Brown	France	D6	0.17 ± 0.02 ^a	0.06 ± 0.02 ^d	bdl	0.08 ± 0.02 ^b	0.40 ± 0.11 ^e
		Max.	0.169	0.130	0.416	4.167	5.835
		Min.	0.001	0.048	0.263	0.081	0.402
		Mean	0.057	0.086	0.310	2.900	4.496
		SE	0.013	0.006	0.011	0.252	0.341
Foundations (n = 27)							
Dermacol	Europe	F1	0.06 ± 0.03 ^b	0.19 ± 0.03 ^d	45.4 ± 12.0 ^a	4.79 ± 1.33 ^b	3.38 ± 0.26 ^{ab}
Garner BB Cream	Germany	F2	0.12 ± 0.03 ^{ab}	0.23 ± 0.04 ^{abcd}	5.6 ± 3.3 ^b	5.61 ± 0.38 ^{ab}	3.56 ± 0.13 ^{ab}
Cool Beauty	Pakistan	F3	0.16 ± 0.04 ^a	0.20 ± 0.01 ^{cd}	5.3 ± 2.0 ^b	5.46 ± 0.18 ^{ab}	3.69 ± 0.04 ^{ab}
Maybelline New York	France	F4	0.10 ± 0.02 ^{ab}	0.23 ± 0.01 ^{bcd}	7.0 ± 4.0 ^b	5.96 ± 0.21 ^{ab}	3.73 ± 0.20 ^{ab}
Flormar Perfect Coverage	Turkey	F5	0.12 ± 0.01 ^{ab}	0.28 ± 0.02 ^{ab}	3.0 ± 0.1 ^b	5.83 ± 0.10 ^{ab}	3.95 ± 0.15 ^a
BB Cream Fair & lovely	India	F6	0.13 ± 0.01 ^{ab}	0.19 ± 0.03 ^d	2.3 ± 1.0 ^b	5.66 ± 0.41 ^{ab}	2.78 ± 2.01 ^{ab}
Fenty Beauty	Italy	F7	0.12 ± 0.01 ^{ab}	0.26 ± 0.01 ^{abc}	8.3 ± 3.1 ^b	6.34 ± 0.33 ^a	1.94 ± 0.16 ^b
DMGM Secret Wonder	Italy	F8	0.12 ± 0.02 ^{ab}	0.26 ± 0.02 ^{abc}	6.3 ± 1.2 ^b	6.02 ± 0.17 ^{ab}	2.42 ± 0.06 ^{ab}
Yardley Foundation	London	F9	0.06 ± 0.02 ^{ab}	0.30 ± 0.02 ^a	4.0 ± 0.1 ^b	5.49 ± 0.29 ^{ab}	1.98 ± 0.29 ^{ab}
		Max.	0.157	0.300	45.42	6.336	3.952
		Min.	0.059	0.186	2.294	4.788	1.944
		Mean	0.109	0.238	9.638	5.684	3.047
		SE	0.003	0.004	1.507	0.049	0.087
Whitening creams (n = 18)							
Golden Pearl	Pakistan	W1	0.10 ± 0.03 ^a	0.27 ± 0.01 ^a	1.97 ± 0.44 ^a	6.30 ± 0.21 ^a	2.5 ± 0.2 ^c
Fair & Lovely	India	W2	0.12 ± 0.04 ^a	0.29 ± 0.01 ^a	2.6 ± 0.2 ^a	5.97 ± 0.55 ^a	3.0 ± 0.2 ^{bc}
Olay	UAE	W3	0.12 ± 0.03 ^a	0.32 ± 0.02 ^a	2.2 ± 0.4 ^a	6.29 ± 0.31 ^a	3.1 ± 0.2 ^b
YC Whitening Cream	Thailand	W4	0.13 ± 0.04 ^a	0.32 ± 0.03 ^a	2.5 ± 0.2 ^a	6.32 ± 0.15 ^a	3.43 ± 0.06 ^{ab}
Rivaj UK Whitening Cream	Pakistan	W5	0.13 ± 0.05 ^a	0.29 ± 0.03 ^a	1.80 ± 0.52 ^a	5.94 ± 0.41 ^a	3.44 ± 0.24 ^{ab}
Stallman's	USA	W6	0.14 ± 0.01 ^a	0.30 ± 0.03 ^a	1.86 ± 0.16 ^a	7.0 ± 0.1 ^a	4.0 ± 0.4 ^a
		Max.	0.138	0.321	2.598	6.599	4.015
		Min.	0.100	0.274	1.799	5.941	2.499
		Mean	0.123	0.297	2.154	6.237	3.250
		SE	0.002	0.003	0.057	0.041	0.085
Lipsticks (n = 18)							
Christine Princess	Pakistan	LS1	0.15 ± 0.03 ^a	0.32 ± 0.01 ^b	3.0 ± 2.0 ^{cd}	6.49 ± 0.14 ^b	4.72 ± 0.17 ^d
Be cute (Velvet sensation)	Pakistan	LS2	0.19 ± 0.01 ^a	0.33 ± 0.01 ^b	11.0 ± 5.00 ^b	6.48 ± 0.06 ^b	5.02 ± 0.19 ^{cd}

Table 1 (continued)

Brand	CN	SC	Cd	Cr	Fe	Ni	Pb
KEUNA (MATTE)	France	LS3	0.2 ± 0.1 ^a	0.46 ± 0.03 ^a	30.0 ± 10.0 ^a	6.59 ± 0.18 ^{ab}	5.31 ± 0.29 ^{bc}
Etude Real Australian	Australia	LS4	0.14 ± 0.04 ^a	0.36 ± 0.01 ^b	11.0 ± 4.00 ^b	6.69 ± 0.22 ^{ab}	5.59 ± 0.07 ^{ab}
L'Oreal Paris	France	LS5	0.20 ± 0.04 ^a	1.0 ± 0.1 ^a	6.1 ± 1.2 ^{bc}	6.92 ± 0.02 ^a	5.89 ± 0.23 ^a
Toy lipstick	China	LS6	0.05 ± 0.01 ^b	0.07 ± 0.01 ^c	bdl	bdl	0.40 ± 0.02 ^e
		Max.	0.203	0.465	29.74	6.922	5.889
		Min.	0.051	0.074	2.530	6.483	0.404
		Mean	0.150	0.335	11.948	6.636	4.488
		SE	0.009	0.024	1.753	0.030	0.341
Sunblock (n = 18)							
Rivaj Sunblock	India	S1	0.13 ± 0.02 ^a	0.31 ± 0.03 ^b	2.75 ± 0.32 ^a	7.34 ± 0.86 ^b	6.03 ± 0.25 ^b
Neutrogena (SP525)	France	S2	0.12 ± 0.02 ^a	0.45 ± 0.02 ^a	2.44 ± 0.39 ^a	6.90 ± 0.19 ^c	6.07 ± 0.16 ^b
Soltan	UK	S3	0.12 ± 0.03 ^a	0.43 ± 0.02 ^a	2.77 ± 0.45 ^a	6.93 ± 0.12 ^c	6.31 ± 0.05 ^b
Sun care	Thailand	S4	0.14 ± 0.02 ^a	0.43 ± 0.02 ^a	2.30 ± 0.36 ^a	12.4 ± 0.12 ^a	6.40 ± 0.21 ^{ab}
Baby ganics sunscreen spray	USA	S5	0.12 ± 0.01 ^a	0.47 ± 0.03 ^a	2.31 ± 0.28 ^a	7.18 ± 0.48 ^b	6.53 ± 0.27 ^{ab}
Sunblock (SPF 60)	Pakistan	S6	0.16 ± 0.01 ^a	0.48 ± 0.02 ^a	2.57 ± 0.37 ^a	7.20 ± 0.15 ^b	6.89 ± 0.04 ^a
		Max.	0.155	0.481	2.774	12.37	6.889
		Min.	0.121	0.309	2.298	6.900	6.030
		Mean	0.132	0.428	2.522	7.989	6.372
		SE	0.002	0.010	0.035	0.359	0.053

CN. Country name, SC. Sample code, bdl, below detection limit, Alphabetical letters represents significant differences at $p < 0.05$.

(7.94 ± 0.10 mg/kg) and L17 (7.53 ± 0.31 mg/kg), while L27 had lowest level (0.07 ± 0.17 mg/kg). Measured levels of Pb in our samples were within regulatory limits set by Canada and USFDA, which are 10 mg/kg and 20 mg/kg, respectively (USFDA, 2013). In addition, range of Pb concentration in lotion samples was almost similar to the previously reported level (Borowska and Brzóška, 2015), but was lower than reported by Ababneh and Al-Momani (2018) in body lotions.

3.2. Heavy metals' content in hair dye

Measured levels of HMs in 6 brands of hair dyes (n = 18) are presented in Table 1. Comparatively wide variation of Cd was observed among the analyzed samples of hair dye. Wherein, D6 had highest Cd level (0.17 ± 0.02 mg/Kg), which was significantly different from other samples of hair dye ($p < 0.05$). However, Cd was below the detection limit in D1 and D3. Almost similar Cd concentrations were reported previously (0.01–2.47 mg/kg) by Brzóška et al. (2018) and Ozbek and Akman (2016) in different brands of hair dye. The Cr metal was highest D5 (0.13 ± 0.02 mg/Kg), while in other samples descending order of Cr was: D4 > D3 > D2 > D6. Whereas, in D1 Cr was below the detectable limit. Additionally, measured levels of Cr in our samples were much less than reported earlier (Borowska and Brzóška, 2015; Brzóška et al., 2018). Iron was detected in majority of the samples of hair dye except D6. Highest concentration of Fe was in D5 (0.42 ± 0.22 mg/Kg). Conversely, in D1, D2, D3, D4 and D5 there was no significant difference in Fe concentration ($p < 0.05$).

Likewise, there was no significant difference in Ni concentration calculated for D2, D3, D4 and D5 samples (3.79 ± 1.00, 3.06 ± 0.88, 3.82 ± 0.27 and 4.18 ± 0.23 mg/Kg, respectively). Whereas, measured level of Ni in D6 (Table 1) was lowest (0.08 ± 0.02 mg/Kg). These values were similar to previous reports in hair dyes (0.03–0.37 mg/Kg) by Ozbek and Akman (2016), but, less than reported by Brzóška et al. (2018). Sample D5 and D4 had highest concentration of Pb at 5.84 ± 0.19 and 5.67 ± 0.23 mg/Kg, respectively, whereas D6 contains least amount of Pb (0.40 ± 0.11 mg/Kg), which was significantly different at $p < 0.05$ than other brands of hair dyes. In addition, measured levels of Pb in hair dyes were less as compared to previously reported by Brzóška et al. (2018), but were slightly higher than reported by Ozbek and Akman (2016).

3.3. Measure levels of HMs in foundation

In nine different national and international brands (n = 27) of foundation, Cd concentration varied from 0.06 to 0.16 mg/Kg in F9 and F3 samples of foundation respectively (Table 1). In majority of the samples, there was no significant difference in Cd ($p < 0.05$). Relatively, measured levels of Cd in our samples were lower than reported previously i.e. 0.18–29.1 mg/Kg (Nnorom et al., 2005) and up to 5.09 mg/Kg (Ababneh and Al-Momani, 2018) in the foundation samples collected from the markets of Nigeria and Jordan, respectively. F9 contains highest Cr level (0.30 ± 0.02 mg/Kg), followed by F5, F8 and F7 (0.28 ± 0.02, 0.26 ± 0.02 and 0.26 ± 0.01 mg/Kg, respectively). And these values were comparable with previous report (Borowska and Brzóška, 2015). Fe content in foundation samples depicted wide variation from 45.4 ± 11.7 mg/Kg (F1) to 2.29 ± 1.00 mg/Kg (F6). However, these values were less than reported by Borowska and Brzóška (2015). Ni levels varied from 4.79 to 6.34 mg/Kg in F1 and F7, respectively ($p < 0.05$). Ni concentration in our samples were comparable with previously reported in foundation (Ababneh and Al-Momani, 2018), but were less than described by Borowska and Brzóška (2015). Concentration of Pb in the analysed samples ranged from 1.94 ± 0.16 to 3.95 ± 0.15 mg/Kg in F7 and F5, respectively ($p < 0.05$). However, these values were less than previous reports (Ababneh and Al-Momani, 2018; Borowska and Brzóška, 2015).

3.4. HMs' concentration in whitening cream

Among the different brands of whitening cream (n = 18), comparatively, W6 had highest concentration of Pb (4.02 ± 0.39 mg/Kg), followed by W5 (3.44 ± 0.24 mg/Kg) and W4 (3.43 ± 0.06 mg/Kg). However, these values were not significantly different at $p < 0.05$ (Table 1). Our findings were almost similar to previously reported levels of Pb in whitening creams from Pakistan (Ullah, 2017), but were much lower than reported in same product by Borowska and Brzóška (2015). No significant differences in the concentration range of Cr (0.27–0.32 mg/Kg), Fe (1.80–2.60 mg/Kg) and Cd (0.10–0.14 mg/Kg) were noted among different brands of whitening cream ($p < 0.05$). Highest concentration of Cr, Fe and Cd were detected in W4 W2 and W6 respectively (Table 1). Moreover, Cd, Cr and Fe levels in different brands of whitening creams were comparable with previous report (Borowska and Brzóška, 2015), but were relatively less than reported by Ullah (2017).

3.5. Measured levels of HMs' lipstick

In different brands of lipstick ($n = 18$), HMs' concentration vary significantly ($p < 0.05$) from one brand to another. As shown in Table 1, LS5 depicted highest concentration of Cd (0.20 ± 0.04 mg/Kg), while this metal was lowest in LS6 (0.05 ± 0.01 mg/Kg). Average value of Cd in different brands of lipsticks was comparable to previously reported level (El-Aziz et al., 2017). Cr concentration was ranged from 0.07 to 0.47 mg/Kg, with highest level in LS5 and lowest in LS6. These values were low than reported by El-Aziz et al. (2017), but were comparable to Al-Saleh and Al-Enazi (2011). A wide variation in the concentration of Fe from 2.53 mg/Kg to 29.7 mg/Kg was observed in different brands of lipstick. LS3 had highest Fe content, while it was below the detection limit in LS6. Moreover, Fe levels in our samples were relatively lower than previous reports (El-Aziz et al., 2017; Ullah, 2017). Average concentration of Ni was highest in LS5 (6.92 ± 0.02 mg/Kg), followed by LS4 > LS3 > LS1 > LS2, but were not significantly different at $p < 0.05$. Additionally, measured levels of Ni were less than reported previously (El-Aziz et al., 2017; Nnorom et al., 2005). Mean concentration of Pb ranged from 0.40 ± 0.02 mg/Kg (LS6) to 5.89 ± 0.23 mg/Kg (LS5) brand. However, measured levels of Pb in our samples were comparable to data provided by Hepp et al. (2009), but were very low than reported by El-Aziz et al. (2017) in different brands of lipstick.

3.6. Distribution of HMs' sunblock

Average level of Cr in sunblock samples ($n = 18$) varied from 0.31 to 0.48 mg/Kg, Fe from 2.30 to 2.77 mg/Kg and Cd from 0.12 to 0.16 mg/Kg, with no significant difference ($p < 0.05$). Highest Cr and Cd contents were detected in S6, while S3 had maximum level of Fe (Table 1). Comparative analysis revealed that measured levels of Fe and Cd were within the range as reported earlier (Ababneh and Al-Momani, 2018; Lim et al., 2018). However, sunblock samples from Korean market contain relatively lower levels of Ni, Pb, Fe, Cr and Cd i.e. 0.07, 0.36, 0.60, 0.12 and 0.002 mg/Kg respectively (Lim et al., 2018). Similarly, lower levels of Pb (0.46 mg/Kg) and Ni (1.77 mg/Kg) were reported by Ababneh and Al-Momani (2018) in Sunblock creams. Ni concentration was maximum in S4, followed by S1, S6 and S5. It was observed that Ni concentration in our samples was relatively higher than reported earlier (Ababneh and Al-Momani, 2018). The highest concentration of Pb was estimated in S6 and lowest was quantified in S1. These values were comparatively higher than previous reports (Ababneh and Al-Momani, 2018).

3.7. Comparative assessment of HMs' concentration in cosmetic products

Comparative assessment of average heavy metal contents in the cosmetic products is summarized in Table 2. Cadmium exposure leads to several injurious health effects, most prominent are heart failure, kidney, liver and brain damage (Agoramoorthy et al., 2008). In some cases severe eye keratitis had been observed on exposure to high Cd concentration present in kohl (Amry et al., 2011). Average concentration of Cd was ranged from 0.06 ± 0.01 to 0.26 ± 0.02 mg/kg in hair dyes and lotions, respectively. These values were within the safe limit (3 mg/kg) in cosmetic products set by USFDA (2016). Both, Cr (III) and Cr (VI) have potential adverse effects on skin and cause contact allergies and skin cancer (Bocca et al., 2014). Ascending order of mean concentration of Cr in the cosmetic products was: Sunblock > lipstick > whitening cream > lotion > foundation > hair dye. Average concentration of Cr from 0.43 ± 0.01 to 0.09 ± 0.01 mg/kg was lower than the maximum limit (50 mg/kg) set by USFDA (2016). Iron is considered as one

of the essential nutrient like Zn, but higher concentration of Fe in cosmetic products causes the death of body cells (Miyajima et al., 2002), thus leads to colorectal cancer (Senesse et al., 2004). In the present study, average concentration of Fe varied from 0.31 ± 0.01 to 12.0 ± 1.75 mg/kg in hair dyes and lipstick, respectively. In other products decreasing order of Fe was: foundation > sunblock > whitening cream > lotion.

Different brands of sunblock had exceptionally higher Ni concentration, followed by lipsticks, whitening creams, foundations, hair dyes and lotions (Table 2). And exposure to Ni contaminated cosmetics may cause skin allergies (Borowska and Brzóska, 2015). Lead exposure to human body may cause serious health effects including cellular death, DNA damage, and oxidative stress and can also cause neurotoxic, reproductive failure and carcinogenic health effects (Kim et al., 2015). Average concentration of Pb was highest in the sunblock at 6.37 ± 0.05 mg/kg, followed by lipsticks and hair dyes (4.49 ± 0.34 and 4.50 ± 0.34 mg/kg, respectively). The comparative evaluation revealed that on the whole sunblock creams exhibited the highest average concentrations of Cr, Ni and Pb, while Fe and Cd were dominant in the lipsticks and lotions, respectively.

Among different brands of lotions Pb was highest in concentration (2.81 ± 0.09 mg/kg), followed by Ni, Fe, and Cr (2.59 ± 0.08 , 2.14 ± 0.07 and 0.28 ± 0.01 mg/kg, respectively), whereas Cd had the lowest value (0.26 ± 0.02 mg/kg) as shown in Fig. 1a. However, none of the analysed metals exceeded their respective permissible limits. The average levels of Pb, Cd and Ni were found to be lower in the present study than the previously reported levels (Ababneh and Al-Momani, 2018; Lim et al., 2018). In the case of hair dyes (Fig. 1b), average Pb content (4.50 ± 0.34 mg/kg) was substantially higher than the other metals, while Cd was at lowest level. Average concentration of Pb in the present study was comparatively higher, while Fe and Cd were comparable to the reported levels (Hussein, 2015) in hair dyes. However, mean Cr content reported in another study (Iwegbue et al., 2016) was much higher in hair dyes while the same samples contained relatively lower level of Ni than the present study. In different brands of foundations (Fig. 1c), Fe was dominating with an average value of 9.64 ± 1.50 mg/kg, followed by and Pb, while Cr and Cd were lowest in concentrations.

In whitening creams Figure (1d), Ni had highest mean concentration of 6.24 ± 0.04 mg/kg, followed by Pb and Fe (3.25 ± 0.09 , 2.15 ± 0.06 mg/kg, respectively), while Cd was relatively lower. Measured levels of Ni were comparatively higher than the previously reported levels in whitening cream from Nigeria, but Cr, Fe and Cd levels were considerably lower than those from Nigeria (Iwegbue et al., 2015; Ababneh and Al-Momani, 2018). In lipsticks, Fe was leading with average concentration of 12.0 ± 1.75 mg/kg (Fig. 1e), followed by Ni and Pb (6.64 ± 0.03 and 4.49 ± 0.34 mg/kg, respectively). These values were within the permissible limits. In addition, mean Pb and Fe concentrations were comparable (Lim et al., 2018), but Cd, Cr and Ni were higher than reported earlier (Ababneh and Al-Momani, 2018; Lim et al., 2018), while, Cd concentration was more or less same as reported by Ababneh and Al-Momani (2018). In the sunblock samples Figure (1f), average concentration of Ni (7.99 ± 0.36 mg/kg) was highest, followed by Pb and Fe (6.37 ± 0.05 , 2.52 ± 0.04 mg/kg, respectively), whereas Cd had lowest level (0.132 ± 0.002 mg/kg).

3.8. Multivariate analysis

Different multivariate analysis viz. Pearson's correlation coefficient, hierarchical cluster analysis (HCA) and principal component analysis (PCA) were performed to identify the natural and anthropogenic sources of HMs' contamination in cosmetic products. Results of correlation analysis in Table 3, demonstrating there were highly significant ($p < 0.01$) positive associations between Cr-Pb

Table 2
Average concentration (\pm SE) of HMs in cosmetic products.

Cosmetic products	No. of samples	Cd	Cr	Fe	Ni	Pb
Lotion	90	0.26 \pm 0.02	0.28 \pm 0.01	2.14 \pm 0.07	3.0 \pm 0.1	2.81 \pm 0.09
Hair dyes	18	0.06 \pm 0.01	0.09 \pm 0.01	0.31 \pm 0.01	2.9 \pm 0.3	4.50 \pm 0.34
Foundations	27	0.115 \pm 0.003	0.24 \pm 0.004	9.6 \pm 1.5	6.0 \pm 0.1	3.05 \pm 0.09
Whitening creams	18	0.123 \pm 0.002	0.297 \pm 0.003	2.2 \pm 0.1	6.23 \pm 0.04	3.25 \pm 0.09
Lipsticks	18	0.15 \pm 0.01	0.34 \pm 0.02	12.0 \pm 1.8	6.64 \pm 0.03	4.49 \pm 0.34
Sunblock	18	0.132 \pm 0.002	0.43 \pm 0.01	2.52 \pm 0.04	8.0 \pm 0.4	6.4 \pm 0.1

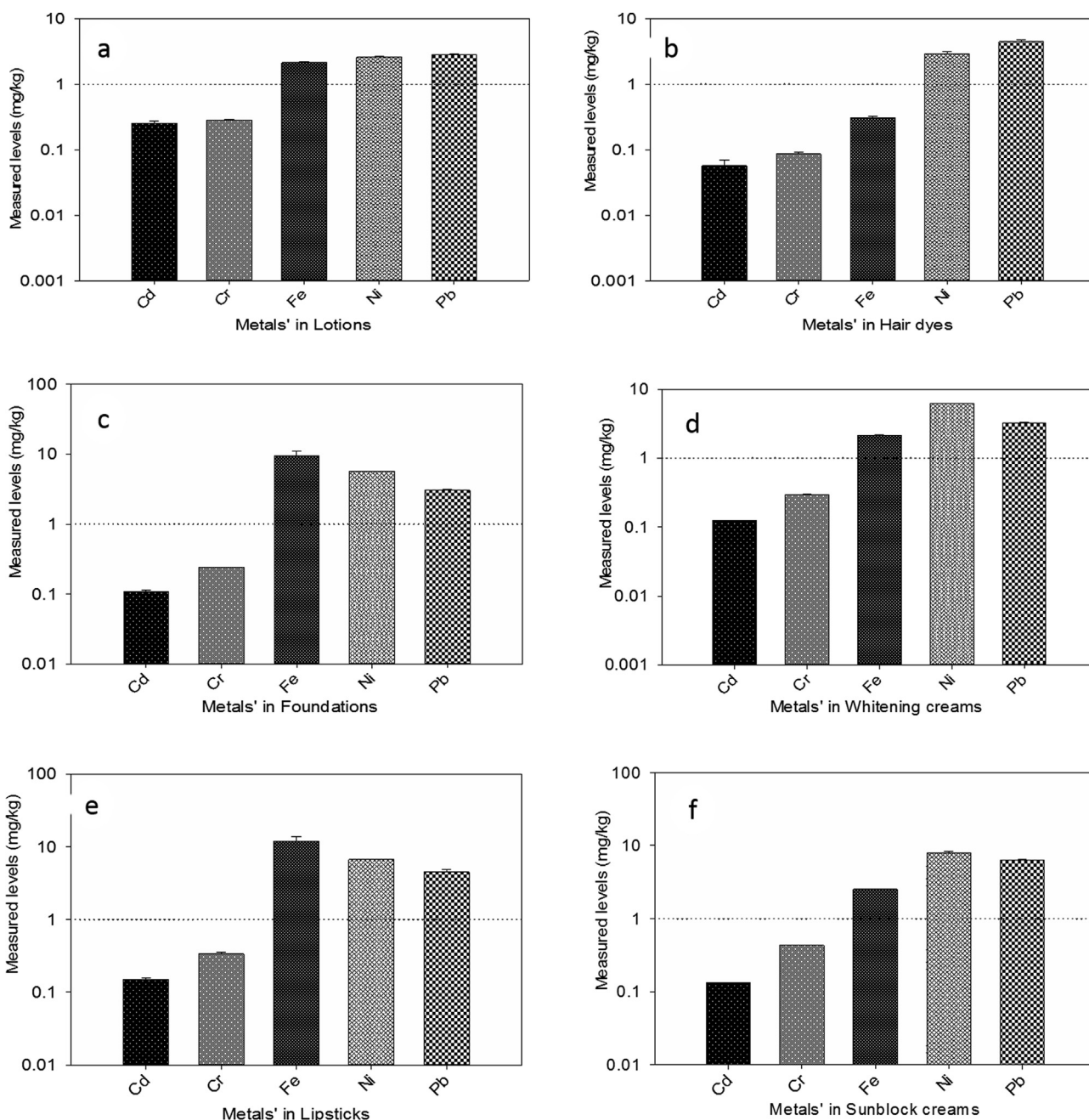


Fig. 1. (a-f). Average concentration of HMs (mg/Kg) in cosmetic products.

($r = 0.946$), Ni-Pb ($r = 0.932$) and Cr-Ni ($r = 0.916$) in different brands of lotion. However, Fe showed negative correlations with all metals. In hair dyes Ni was significantly correlated at $p < 0.01$ with Pb ($r = 0.960$), while Cd showed strong negative associations with Ni and Pb ($r = -0.972$, $r = -0.953$, respectively) at $p < 0.05$. In

foundation samples there were no significant positive or negative relationships except Fe and Ni ($r = -0.702$). Pb metal depicted highly significant ($p < 0.01$), positive interactions with Cd ($r = 0.938$) in whitening creams and with Cr, Ni and Cd ($r = 0.943$, $r = 0.935$ and $r = 0.911$, respectively) in lipstick samples.

Table 3
correlation coefficient matrixes of HMs' concentration (mg/Kg) in cosmetic products.

Lotions						Hair Dyes					
Variables	Cd	Cr	Fe	Ni	Pb	Variables	Cd	Cr	Fe	Ni	Pb
Cd	1.000					Cd	1.000				
Cr	-0.079	1.000				Cr	-0.356	1.000			
Fe	-0.056	-0.319	1.000			Fe	0.209	0.401	1.000		
Ni	0.137	0.913**	-0.346	1.000		Ni	-0.972*	0.547	0.721	1.000	
Pb	0.196	0.946**	-0.212	0.932**	1.000	Pb	-0.953*	0.565	0.535	0.960**	1.000
Foundations						Whitening creams					
Variables	Cd	Cr	Fe	Ni	Pb	Variables	Cd	Cr	Fe	Ni	Pb
Cd	1.000					Cd	1.000				
Cr	-0.263	1.000				Cr	0.403	1.000			
Fe	-0.539	-0.440	1.000			Fe	-0.036	0.367	1.000		
Ni	0.405	0.476	-0.702*	1.000		Ni	0.115	0.265	-0.234	1.000	
Pb	0.326	-0.409	0.122	-0.321	1.000	Pb	0.938**	0.416	-0.243	0.405	1.000
Lipstick						Sunblock					
Variables	Cd	Cr	Fe	Ni	Pb	Variables	Cd	Cr	Fe	Ni	Pb
Cd	1.000					Cd	1.000				
Cr	0.887*	1.000				Cr	0.164	1.000			
Fe	-0.111	0.530	1.000			Fe	0.011	-0.544	1.000		
Ni	0.416	0.710	-0.121	1.000		Ni	0.317	-0.003	-0.515	1.000	
Pb	0.911*	0.943**	0.113	0.935*	1.000	Pb	0.697	0.696	-0.251	0.060	1.000

** Correlation is significant at the 0.01 level (2-tailed), * Correlation is significant at the 0.05 level (2-tailed).

Likewise, Pb also had strong positive correlation with Cd and Cr in sunblock samples (Table 3).

Hierarchical cluster analysis (HCA) was done using BioVinci 1.15 (Fig. 2). Based on the mean concentration of HMs, different categories of cosmetics products were divided into two main clusters. Foundations and lipstick were in first cluster, whereas whitening creams and sunblock were placed together in second cluster along with close associations of lotions and hair dyes. Color scheme on heat map also compare precisely the HMs concentration in different categories of cosmetic products. Pb and Ni were in same group with highest average concentration in different brands of sunblock, hair dyes, whitening creams and lipstick (Fig. 2). Fe was highest in lipstick and foundation brands, while Cd and Cr were high in different varieties of lotions, lipstick and sunblock.

Three principle components viz. PCA1, PCA2 and PCA3 were extracted based on eigenvalue (>1) and percentage variance more than 81% in PCA analysis executed using Varimax rotation with Kaiser Normalization (Fig. 3). PC1 had 45.15% variation with maximum loading of Ni, Pb and Cr metals with percentage variance of 0.872, 0.842 and 0.789, respectively. The percentage contribution of these metals in PC1 indicating similarity in their sources of contamination. The percentage variation of PC2 and PC3 was 28.87 and 20.34, respectively. Cd metal exhibited highest loading value (0.981) in PC2, while Fe was dominating in PC3 with percentage variance of 0.970 (Table S3).

Disparity in HMs concentration among different categories of cosmetic products and their distribution patterns in HCA and PCA is possibly associated with the type of raw material and the sources from where the raw material is collected. For instance, compounds of Fe such as, iron carbonates, ferric hydroxide, iron oxides (iron oxide black, iron oxide red, and iron oxide yellow) and the Cr compounds including Chromium (III) oxide, chromium (III) hydroxide are added intentionally as colour pigments in cosmetic products. Likewise, Cd is used in cosmetics as it has ability to produce different colours when combines with other components (Godt et al., 2006). For instance, the use of cadmium sulphide is because of its yellow colour, also it can develop range of colours from orange to black in combination with increased amount of selenium. Similarly cadmium yellow is added with viridian (Cr (III) oxide) to develop a light green mixture called cadmium green (Bocca et al., 2014). The amount added is dependent on the regula-

tory limits (EU, 2009), but the same metal may be present an impurity or added intentionally (Bocca et al., 2014). Other metals including Pb, Cd and Ni can be accumulated as impurities at various stages of cosmetic production, predominantly the addition of additives and colour minerals. Moreover, use of solvents, water and different machinery in cosmetic industries during sorting and manufacturing processes may also cause HMs contamination (Łodyga-Chruścińska et al., 2018).

3.9. Health risk assessment

3.9.1. Non-carcinogenic risk

The systemic exposure to cosmetic product predicts the amount of chemicals that enter human body through various exposure routes. The calculated values of systemic exposure dosage (SED) at 50% and 100% bio-accessibility for selected HMs in different cosmetic products are displayed in Table 4. It was noted that at 50% bio-accessibility, SED values for Cd and Cr ranged from $5.85 \cdot 10^{-7}$ to $2.21 \cdot 10^{-2}$ and $1.31 \cdot 10^{-6}$ to $3.22 \cdot 10^{-2}$ mg/kg/d respectively. However, Fe, Ni and Pb lay between $4.67 \cdot 10^{-5}$ to $1.90 \cdot 10^{-1}$, $2.59 \cdot 10^{-5}$ to $6.02 \cdot 10^{-1}$ and $1.75 \cdot 10^{-5}$ to $4.80 \cdot 10^{-1}$ mg/kg/d, respectively. Likewise, SED levels at 100% bio-accessibility for Cd, Cr and Fe ranged from $1.17 \cdot 10^{-6}$ to $4.41 \cdot 10^{-2}$, $2.62 \cdot 10^{-6}$ to $6.44 \cdot 10^{-2}$ and $9.34 \cdot 10^{-5}$ to $3.80 \cdot 10^{-1}$ mg/kg/d, respectively. The respective SED levels of Ni and Pb lay in the range of $5.19 \cdot 10^{-5}$ to $1.20 \cdot 10^0$ and $3.51 \cdot 10^{-5}$ to $9.60 \cdot 10^{-1}$ mg/kg/d at 100% bio-accessibility. The calculated values of SED were higher than the reported values by El-Aziz et al. (2017) in different facial cosmetic products. In the case of lipsticks, more or less similar SED levels were observed in the previous study (El-Aziz et al., 2017). Additionally, the SED values of HMs in the cosmetic products were almost comparable to those reported by Iwegbue et al. (2016) except for sunblock samples in which comparatively higher levels were recorded in the present study.

Risk to human health on exposure to metallic impurities present in the cosmetic products was evaluated by applying Margin of Safety (MoS). The estimated levels of MoS for the HMs in the cosmetic products at 50% and 100% bio-accessibility are presented in Table 5. In the samples of hair dye, foundation, whitening cream and lipstick MoS was greater than 100, which revealed that the evaluated samples were safe for use. However, in lotions and sun-

Hierarchical clustering analysis

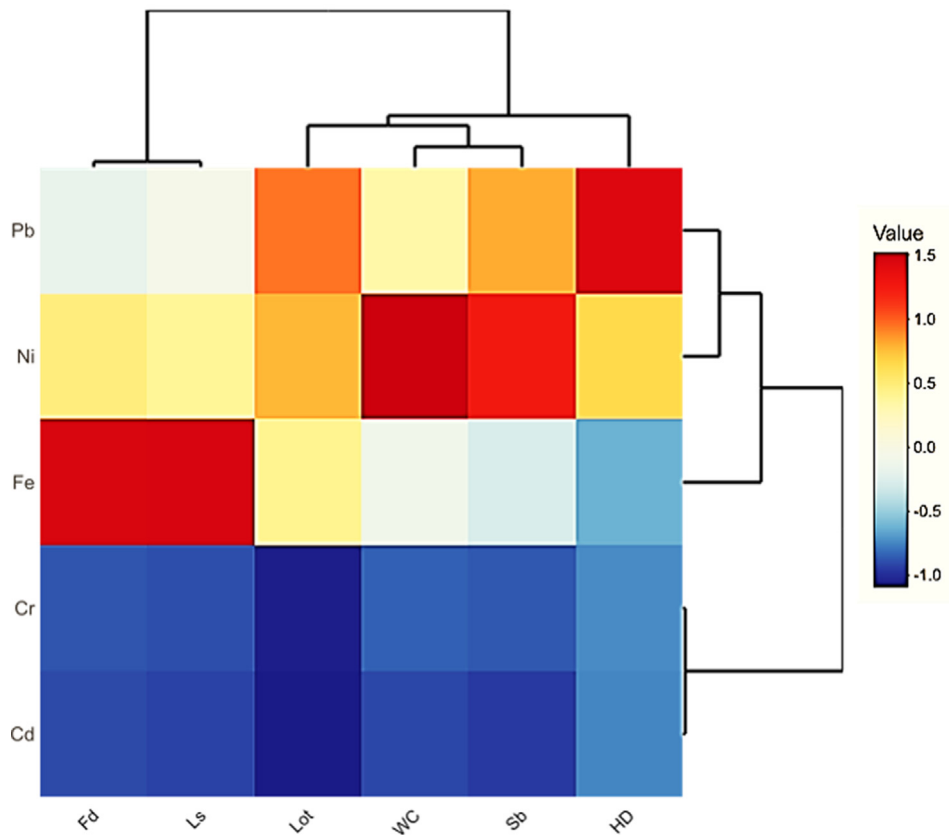


Fig. 2. Hierarchical cluster analysis of HMs in different categories of cosmetic products.

Component Plot in Rotated Space

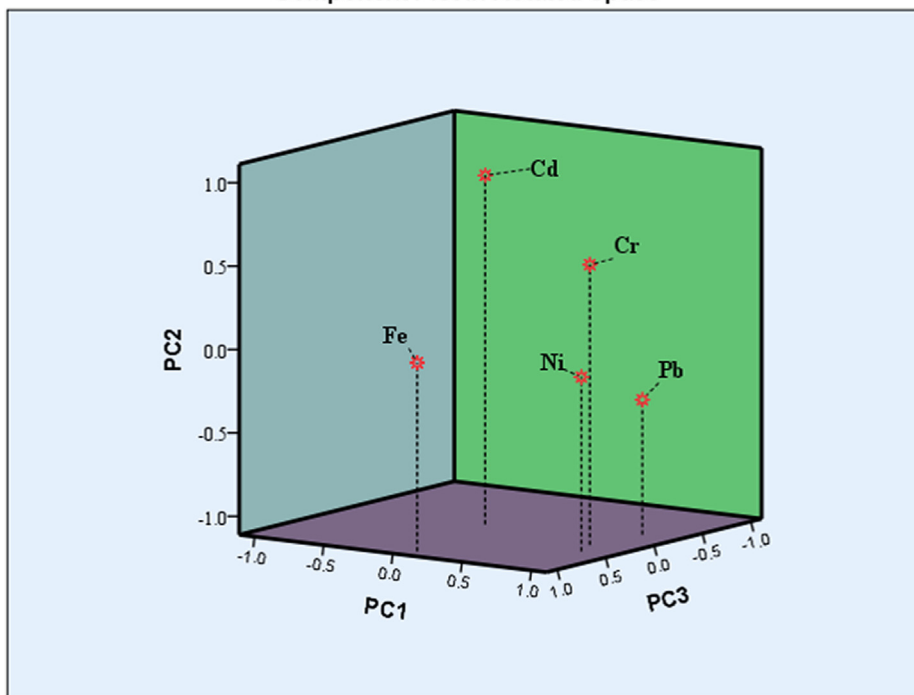


Fig. 3. Principle component analysis of HMs in cosmetic products.

Table 4
SED values (mg/kg/d) of HMs in the cosmetic products.

Sample	Cd	Cr	Fe	Ni	Pb
50% bio-accessibility					
Lotion	$2.21 \cdot 10^{-2}$	$2.43 \cdot 10^{-2}$	$1.84 \cdot 10^{-1}$	$2.23 \cdot 10^{-1}$	$2.41 \cdot 10^{-1}$
Hair dye	$1.15 \cdot 10^{-4}$	$2.00 \cdot 10^{-4}$	$6.28 \cdot 10^{-4}$	$5.89 \cdot 10^{-3}$	$9.13 \cdot 10^{-3}$
Foundation	$2.25 \cdot 10^{-4}$	$4.90 \cdot 10^{-4}$	$1.98 \cdot 10^{-2}$	$1.17 \cdot 10^{-2}$	$6.27 \cdot 10^{-3}$
Whitening cream	$1.64 \cdot 10^{-3}$	$3.95 \cdot 10^{-3}$	$2.86 \cdot 10^{-2}$	$8.30 \cdot 10^{-2}$	$4.32 \cdot 10^{-2}$
Lipstick	$5.85 \cdot 10^{-7}$	$1.31 \cdot 10^{-6}$	$4.67 \cdot 10^{-5}$	$2.59 \cdot 10^{-5}$	$1.75 \cdot 10^{-5}$
Sunblock	$9.97 \cdot 10^{-3}$	$3.22 \cdot 10^{-2}$	$1.90 \cdot 10^{-1}$	$6.02 \cdot 10^{-1}$	$4.80 \cdot 10^{-1}$
100% bio-accessibility					
Lotion	$4.41 \cdot 10^{-2}$	$4.86 \cdot 10^{-2}$	$3.67 \cdot 10^{-1}$	$4.45 \cdot 10^{-1}$	$4.82 \cdot 10^{-1}$
Hair dye	$2.31 \cdot 10^{-4}$	$2.90 \cdot 10^{-4}$	$1.26 \cdot 10^{-3}$	$1.18 \cdot 10^{-2}$	$1.83 \cdot 10^{-2}$
Foundation	$4.50 \cdot 10^{-4}$	$9.80 \cdot 10^{-4}$	$3.97 \cdot 10^{-2}$	$2.34 \cdot 10^{-2}$	$1.25 \cdot 10^{-2}$
Whitening cream	$3.06 \cdot 10^{-3}$	$7.38 \cdot 10^{-3}$	$5.35 \cdot 10^{-2}$	$1.55 \cdot 10^{-1}$	$8.08 \cdot 10^{-2}$
Lipstick	$1.17 \cdot 10^{-6}$	$2.62 \cdot 10^{-6}$	$9.34 \cdot 10^{-5}$	$5.19 \cdot 10^{-5}$	$3.51 \cdot 10^{-5}$
Sunblock	$1.99 \cdot 10^{-2}$	$6.44 \cdot 10^{-2}$	$3.80 \cdot 10^{-1}$	$1.20 \cdot 10^0$	$9.60 \cdot 10^{-1}$

Table 5
Margin of Safety (MoS) for selected HMs in the cosmetic products.

Samples	Cd	Cr	Fe	Ni	Pb
50% bio-accessibility					
Lotion	$2.27 \cdot 10^1$	$6.18 \cdot 10^1$	$7.62 \cdot 10^4$	$2.43 \cdot 10^3$	$1.74 \cdot 10^2$
Hair dye	$4.33 \cdot 10^3$	$1.03 \cdot 10^4$	$2.23 \cdot 10^7$	$9.17 \cdot 10^4$	$4.60 \cdot 10^3$
Foundation	$2.22 \cdot 10^3$	$3.06 \cdot 10^3$	$7.06 \cdot 10^5$	$4.62 \cdot 10^4$	$6.70 \cdot 10^3$
Whitening cream	$3.05 \cdot 10^2$	$3.80 \cdot 10^2$	$4.89 \cdot 10^5$	$6.51 \cdot 10^3$	$9.72 \cdot 10^2$
Lipstick	$8.55 \cdot 10^5$	$1.15 \cdot 10^6$	$3.00 \cdot 10^8$	$2.08 \cdot 10^7$	$2.39 \cdot 10^6$
Sunblock	$5.01 \cdot 10^1$	$4.66 \cdot 10^1$	$7.37 \cdot 10^4$	$8.97 \cdot 10^2$	$8.75 \cdot 10^1$
100% bio-accessibility					
Lotion	$1.13 \cdot 10^1$	$3.09 \cdot 10^1$	$3.81 \cdot 10^4$	$1.21 \cdot 10^3$	$8.71 \cdot 10^1$
Hair dye	$2.17 \cdot 10^3$	$5.17 \cdot 10^3$	$1.11 \cdot 10^7$	$4.59 \cdot 10^4$	$2.30 \cdot 10^3$
Foundation	$1.11 \cdot 10^3$	$1.53 \cdot 10^3$	$3.53 \cdot 10^5$	$2.31 \cdot 10^4$	$3.35 \cdot 10^3$
Whitening cream	$1.63 \cdot 10^2$	$2.03 \cdot 10^2$	$2.61 \cdot 10^5$	$3.48 \cdot 10^3$	$5.20 \cdot 10^2$
Lipstick	$4.27 \cdot 10^5$	$5.73 \cdot 10^5$	$1.50 \cdot 10^8$	$1.04 \cdot 10^7$	$1.20 \cdot 10^6$
Sunblock	$2.51 \cdot 10^1$	$2.33 \cdot 10^1$	$3.69 \cdot 10^4$	$4.49 \cdot 10^2$	$4.38 \cdot 10^1$

block the MoS values for Cd, Cr and Pb were below 100, which indicated that these products are not safe for use, particularly with reference to HMs contamination. In different cosmetic products analyzed by El-Aziz et al. (2017) and Iwegbue et al., (2016) levels of MoS were found higher than 100 while MoS for lipsticks was almost similar to the present study.

The HQ and HI values of the cosmetic products at 50% and 100% bio-accessibility levels are presented in Fig. 4. At 50% bio-accessibility, HQ values were found relatively higher in the lotion and sunblock samples wherein the values were greater than unity (1) for Cd, Cr and Pb, illustrating threat to human health, while in the samples of hair dye, foundation, whitening cream and lipsticks HQ values were considerably <1 elucidating that the samples were safe for human health.

Similarly, HI levels for the lotion and sunblock were greater than 1 at both 50% and 100% bio-accessibility, which demonstrated that excessive use of these products may cause health risk to consumer. In the case of hair dye, foundation, whitening cream and lipstick, HI levels were much <1, interpreting that the samples were safe for human health. HQ and HI values reported by El-Aziz et al. (2017) were also <1 for different facial cosmetics which are more or less closer to the values obtained in the present study.

3.9.2. Lifetime cancer risk (LCR)

Chromium (Cr), lead (Pb), nickel (Ni) and cadmium (Cd) are listed as carcinogenic HMs by International agency for Research on Cancer (IARC, 2012). Two major routes through which HMs can enter into the body are either by ingestion or through dermal absorption. HMs are non-biodegradable so they remain accumulated into the body for long time period. As a result, they not only alter the cell functions but also cause disruption of intra-

cellular mechanisms (Stavrides, 2006). Therefore, cancer related diseases are enhanced by such impurities that cause oxidative stress, DNA damage and cell death (Kim et al, 2015). Lifetime cancer risk (LCR) is the estimation of potential cancer risk to the users on exposure to HMs present in the cosmetic products. According to USEPA acceptable range for LCR is from 1×10^{-6} to 1×10^{-4} (Loh et al., 2007). The LCR was calculated for cancer causing metals (Pb, Ni, Cr and Cd) at 50% and 100% bio-accessibility (Fig. 5).

Among all the analysed HMs, lifetime cancer risk was estimated higher than the permissible limit and the cosmetic products may possess life time cancer risk except lipsticks. Most probable reason is that the lipstick is applied on comparatively small area in relatively less amount. Though, the condition is alarming and continuous use of these products over long time period may cause cancer to the users. It has been reported in previous study that LCR for different facial cosmetic products was below 10^{-6} including lipstick (Lim et al., 2018).

4. Conclusion

In general, Cr, Ni and Pb were higher in the sunblock samples, while Cd and Fe were maximum in different brands of lotions and lipsticks respectively. Increase in the concentrations of HMs in the cosmetic products was mainly due to the type and source of raw materials used, processing techniques, storage and mode of transportation.

Close association of Cr, Ni and Pd and disparity in Cd and Fe assessed by multivariate analysis revealed similarity and variation in their sources of contamination in cosmetic products. Health risk assessment exposed that generally MoS, HQ and HI values were within the permissible limit for hair dyes, foundations, whitening

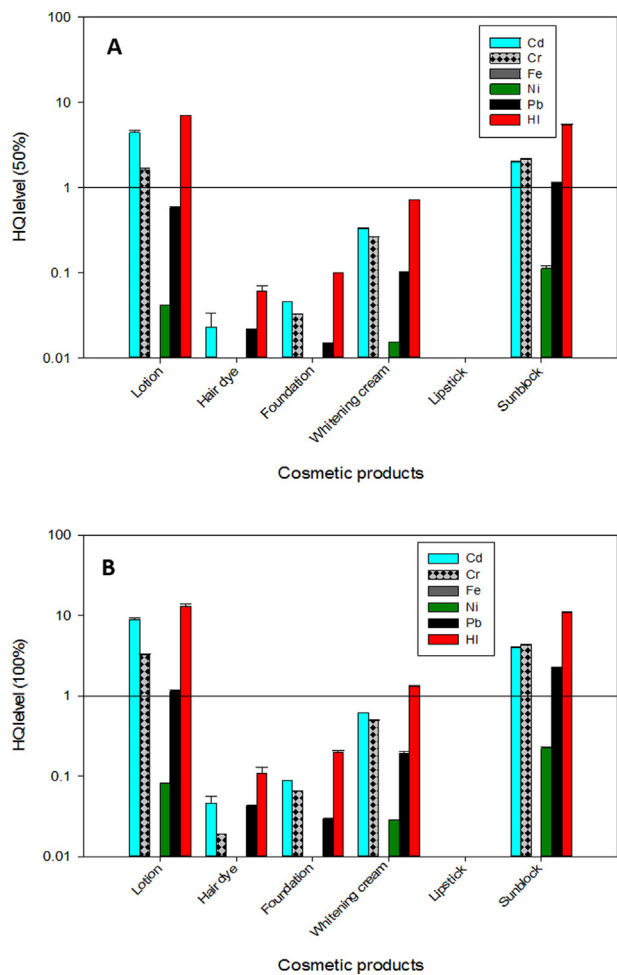


Fig. 4. HQ and HI values of cosmetic products at 50% (A) and 100% (B) bio-accessibility levels.

creams and lipsticks, but were outside the acceptable range for lotions and sunblock creams. The LCR value was higher than the permissible limit in all cosmetic products except lipsticks. Irrespective of the fact that in studied samples HMs concentration were within the regulatory limits, daily exposure to these products may cause cumulative effects such as high risk of skin cancer and other chronic health disorders. Therefore, safer limits for HMs along with their quality control should be obligatory. Additionally, continuous monitoring programmes for the cosmetic products, particularly with reference to HMs adulteration, should be adopted to ensure the human safety and security.

Declarations

Ethics approval and consent to participate
No ethical approval was required to conduct this research work

Consent for publication

Prior consent was taken from all authors to publish findings mentioned in this paper

Availability of data and material

We have already provided all data of research work in this article in tables, figures and supplementary tables

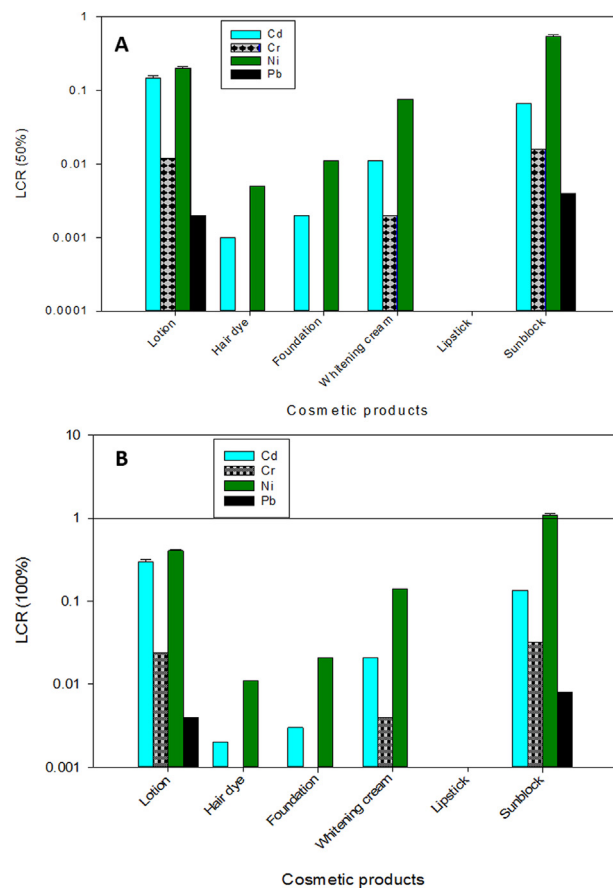


Fig. 5. LCR of cosmetic products at 50% (A) and 100% (B) bio-accessibility levels.

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Authors' contribution

HA proposed and conducted research, and prepared first draft, MZ involved in experimental work and data compilation, MHS analyse data and revised article, AMA supervised project, involved in data analysis and finalization of article.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jpsps.2020.05.006>.

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