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Original article

Investigation on the elemental profiles of lip cosmetic products: Concentrations, distribution and assessment of potential carcinogenic and non-carcinogenic human health risk for consumer safety

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ABSTRACT

Metal contamination of lip care products can cause potential adverse effects for consumers, hence assessment of human health risks associated with the consumption of these products is inevitable to ensure the consumers' safety. In the presented study, the profiles of 18 elements in 37 of the most popular lip cosmetic products, of various types and brands, sold in the Saudi Arabian markets, were investigated and their associated potential carcinogenic and non-carcinogenic human health risks were assessed. The metal concentrations were determined using inductively coupled plasma mass spectrometry preceded by microwave digestion for sample preparation. In general, the concentrations of the investigated metals were lower than the safe permissible limits with the exception of Cd, Pb and Hg. The results found that Cd was regarded as the primary metal contaminant present in the analyzed lip products contributing to 66.3% of the total determined carcinogenic health risk. Overall, however it was observed that there was no significant non-carcinogenic (hazard index < 1) or carcinogenic ($Risk_T < 10^{-4}$) health risks associated with the use of the investigated lip products. Although all the calculated values in this study were within the acceptable limits, special attention should be taken in order to prioritize minimizing the trace metals in lip products, especially for Cd, Pb, Ti and Hg. This study could provide vital data needed to ascertain the degree to which heavy metal exposure through cosmetics is prevalent.

1. Introduction

The proliferative use of cosmetics worldwide is reflected in the regular and monumental growth of the cosmetic industry, which is projected to be valued at nearly half a trillion US dollars within the next five years (Brandt et al., 2011, Ferreira et al., 2021). Widespread cosmetic use is observed universally in all countries, irrespective of economic standing, and is only bound to increase in the future (Arshad et al., 2020). Cosmetics encompass a wide array of products employed for personal use to enhance and promote physical appearance and as a recent trend have been marketed as 'self-care' items targeted to promote well-being (Ferreira et al., 2021; Shaaban et al., 2018). Cosmetic items may range from skin care products (such as creams and exfoliants), make-up products (lipsticks, blusher, eye shadow) to body care items (cleansers, lotions, antiperspirants) (Arshad et al., 2020; Malvandi and Sancholi, 2018).

There is growing concern over reports of heavy metal contamination in cosmetic products. Heavy metals such as lead, zinc, chromium, cadmium, aluminum and mercury have been reported to be found in trace amounts of several cosmetic products such as lipsticks, sunscreens, eyeshadows and antiperspirants (Bocca et al.,

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2014; Piccinini et al., 2013). Evidence has shown that heavy metal environmental exposure poses a significant threat to human health (Bocca et al., 2014). While the reported levels of heavy metals in the majority of cosmetic products appears to be in trace amounts, there remains great cause for concern owing to the pattern of cosmetic use. Most cosmetics are used multiple times daily over prolonged periods of time. One study revealed that an average of up to twelve cosmetic products are used by women on a daily basis (Shaaban and Alhajri, 2020) and up to six products are used by men daily (Ficheux et al., 2015; Meng et al., 2021). The cumulative impact of such chronic use must be taken into account when considering the actual exposure to heavy metal contaminants (Meng et al., 2021).

Heavy metals often become incorporated in cosmetics as a constitutive component of the pigments or preservatives used in compounding the product (Liu et al., 2013; Zakaria and Ho, 2015). Cosmetics that contain natural derivatives have been reported to contain even higher levels of heavy metal contaminants (Klaschka, 2016; Meng et al., 2021). Alternatively heavy metal contamination may be an inadvertent consequence of the manufacturing or packaging process (Klaschka, 2016; Meng et al., 2021). While there are strict guidelines and recommendations that are aimed to regulate the levels of heavy metals in individual cosmetic products, more is required to account for the cumulative nature of cosmetic use given the toxicity profile of the majority of heavy metals present in most products. It should be noted that national guidelines must also take into account the manufacture and sales of counterfeit products which are widespread in Asian countries (Malvandi & Sancholi, (2018). The circulation of unregulated items in the market represents a significant threat to consumer safety and health.

The health consequences of heavy metal exposure through cosmetic use are not limited to topical effects such as contact dermatitis, dermal irritation and skin allergies (Volpe et al., 2012), but may encompass a series of systemic consequences as well. Heavy metals are not subject to biodegradation or transformation have tendency to bioaccumulate (Li et al., 2015; Malvandi & Sancholi, (2018)). Transdermal absorption of heavy metals has been reported in a number of studies (Lim et al., 2018; Tartaglia et al., 2019), while some studies have shown the degree of heavy metal penetration through the stratum corneum is limited to trace amounts, they highlight the need to account for the pattern of use which offers continued and long-term exposure to the metals over time (Bocca et al., 2014; Lim et al., 2018). Heavy metal transdermal penetration into the circulatory system has been shown to occur especially in areas of damaged or sensitized skin or thinner corneal layers of the skin such as the eye or lip area. Studies have highlighted the risk of using lip cosmetics via multiple applications poses a significant ingestion hazard (Liu et al., 2013; Malvandi & Sancholi, (2018); Zakaria & Ho, 2015). Reported tissue damage that may be caused by heavy metals can include; inflammatory and oxidative cell damage, cellular death, DNA damage, neurotoxicity and carcinogenicity (Kim et al., 2015; Smith et al., 2016).

There is an abundance of evidence within the literature that describes the effects of specific metal toxicities. Lead is a highly - toxic metal that can cause serious health problems including neurological, teratogenic and carcinogenic effects.

(Lim et al., 2018; Zakaria & Ho, 2015).

Chromium exposure has been associated with liver and kidney damage (Gondal et al., 2010), while cadmium exposure is linked to cardiovascular toxicities (Angeli et al., 2013). Most heavy metals have been shown to have both carcinogenic and teratogenic effects upon prolonged exposure over long periods of time (Bocca et al., 2014; Lim et al., 2018). Mercury and lead for example have been shown, upon prolonged maternal exposure, to lead to increased incidence of fetal death (Brandt et al., 2011, Meng et al., 2021).

While a number of governmental authorities have drafted and implement strict guidelines to monitor and regulate the contamination levels and potential exposure of heavy metals in cosmetics, there remains a need for vital data to determine the prevalence and incidence of cosmetic use and the degree of potential exposure in the general population given both the current pattern of behavior as well as the nature of the products available for use. The aim of this study is to determine the elemental composition of lip cosmetic products widely consumed in Saudi Arabia using inductively coupled plasma mass spectrometry (ICP-MS). Also, to assess the carcinogenic and non-carcinogenic health risk associated with their consumption. This is a hallmark study of its nature within the region providing vital data needed to ascertain the degree to which heavy metal exposure through cosmetics is prevalent within the wider population.

2. Materials and methods

2.1. Chemicals and reagents

All the standard elements (Al, Mn, Fe, Cr, Co, Cu, Zn, As, Se, Sr, Ag, Cd, Sn, Sb, Ba, Hg, Ti, Pb) were purchased from Merck (Darmstadt, Germany). Ultrapure water was obtained from a Milli-Q water purification system (Millipore, Bedford, MA, USA). Trace metal grade nitric acid was purchased from Sigma–Aldrich (St. Louis, MO, USA).

Stock solutions of the individual and multi-elements standards were prepared at a concentration of 1000 mg/L. The desired range of dilutions were prepared by further dilution from the stock solution using nitric acid.

2.2. Instrumentation

The metals concentrations were determined using inductively coupled plasma mass spectrometry (ICP-MS) Agilent-7800 system (Agilent Technologies, Tokyo, Japan), equipped with a nebulizer, auto-sampler, re-circulating chiller and spray chamber. The ICP-MS system was operated under the following conditions: argon gas flow rate-15 L/min, nebulizer gas flow rate- 0.8 L/min, argon auxiliary gas flow rate- 0.7 L/min, integration time- 0.3 s, sample uptake rate- 400 μL/min and RF power-1400 W. The concentration of metal contaminants in each sample was determined in triplicate.

2.3. Sample collection

Due to the overwhelming abundance and variety of lip cosmetic products available in the current market a web-based questionnaire was developed before the initiation of the study to determine the most widely consumed types and brands of lip cosmetic products among females in Saudi Arabia. The questionnaire included several age groups (ranging from 18 to 60 + years) and was also designed to determine the varied consumption patterns across age. After excluding the incomplete responses, the final number of participants was 727. The first section of the survey focused on the demographic characteristics of the participants such as age, educational level, profession and living area (north, east, south, central and west province of Saudi Arabia). The second part of the survey included a set of questions related to the use frequency of lip cosmetics and the preferred consumer brands and types. The participants were asked to check the type and brand of lip cosmetic products they usually consume. For each product checked, respondents were asked to indicate the frequency of application and usage period on average.

Based on the analyzed data, a total of 37 lip cosmetic products (10 lip gloss (LG), 3 lip balm (LB), 12 lip pencil (LP) and 12 lip stick (LS)) from four of the most popular brands in the market. The samples were classified according to their brands into brand A, brand B, brand C and brand D. (the authors preferred to keep the brands anonymous, but the identity of each brand is available upon request) were purchased from different stores in the Eastern province, Saudi Arabia. Detailed information about the samples of lip cosmetic products (samples codes, brands and types) is presented in Table S1.

2.4. Sample preparation

Microwave-induced digestion was employed for sample preparation using microwave digestion system CEM (model Mars, USA) equipped with closed vessel (EasyPrep) of Teflon reaction vessels. Briefly, 0.5 g of each sample was accurately weighed and transferred into a clean digestion vessel. Initially, the samples were digested with 5 mL of 65% nitric acid and the vessels were closed using glass funnels to allow nitric acid reflux during the digestion and kept in the microwave digester at 120 °C for 5 hr. Finally, the resulting digested samples solutions were diluted to 25 mL with ultrapure water and then filtered to remove insoluble materials such as waxy debris, glitter or colored particulates. All the digested samples were stored at 4 °C until further analysis. The concentrations of the studied metals were then determined using ICP-MS.

2.5. Quality control and validation

The quality control and verification of the method were performed according to (USEPA, 1996). The validation was ensured by the use of reference standard materials. Calibration curves were constructed for the studied elements at seven concentration levels. The linearity of the calibration curves were evaluated by the coefficient determination and was found to be $\geq$0.999 for all studied elements, indicating good linearity. The limit of detection (LOD) and limit of quantification (LOQ) were calculated from the slopes of the calibration curves for each individual element using the following equations:

$$LOD = 3.3 \times \frac{SD\ of\ the\ intercept}{Slope}$$

$$LOQ = 10 \times \frac{SD\ of\ the\ intercept}{Slope}$$

Where SD is the standard deviation. In this study, LODs and LOQs for the studied elements were in the range of 8.00×10^{-6} to 7.00×10^{-4} and 2.64×10^{-5} to 2.31×10^{-3} mg/kg, respectively. The LODs and LOQs values are presented in Table 1. The recovery of the analytical method was evaluated using spike recovery methods. The recovery was in the range of 98.0 % to 107.5%. Intra-day and inter-day precision were evaluated by analyzing the samples three times within the same day and on three consecutive days, respectively. Intra-day and inter-day precision were confirmed by the variation coefficients which were below 5 and 10%, respectively.

The uncertainty (u) was also calculated according to the following formula:

$U_{combined} = (U_1^2 + U_2^2 + U_3^2 + U_4^2...)^{1/2}$, where the experimental uncertainties in the 1st, 2nd, and 3rd measurements are referred to as U_1, U_2, and U_3, etc. The uncertainty percentage was calculated using the following equation: % uncertainty = absolute uncertainty/measurement × 100.

In this study, all values ranged between 0.2 and 0.5%. All values of the quality control, uncertainty and method validation are presented in Table 1.

2.6. Statistical analysis

The statistical analysis of the data was performed using Statistical Package for Social Science (SPSS version 22) (IBM Corp., Armonk, NY, USA) and Microsoft Excel (Office 365). For describing the concentrations of metals in the analyzed lip cosmetics samples, descriptive statistical parameters such as mean and standard deviation were used. Analysis of Variance (ANOVA) were performed using SPSS at a significance level of $p < 0.05$. Pearson's correlation test was used to determine the correlation between metals concentrations in the analyzed lip products.

2.7. Health risk assessment

Pollutants can enter the human body via three main pathways including inhalation, ingestion and dermal contact (Zhang et al., 2019). The major pathway of trace elements in lip cosmetics entering the human body is ingestion (Lim et al., 2018; Zakaria & Ho, 2015). Therefore, in this study the health risk assessment based on oral exposure was utilized to evaluate the risk associated with consuming lip products contaminated with trace metals (USEPA, 2005; Wu et al., 2020). The exposure dose was calculated using the following equation:

$$ADD_{ing} = \frac{C \times IR \times EF \times ED}{BW \times AT} \times CF \qquad (1)$$

(USEPA, 1997) ADD_{ing} is the average daily dose (ADD) of ingested metals in lip cosmetic products (mg/kg/ day); C is the mean concentration of the metals in the analyzed lip products (mg/kg); IR is the intake rate of the lip cosmetic products (mg/day). In this study, the intake rate for average and heavy lip products users was considered to be 25.78 and 149.02 mg/day, respectively (Koo, 2013). An absorption rate of 50% and 100% were utilized in the health risk assessment in the current study. Although the absorption rate of 100% is impossible because of bioavailability constraints (H. Li et al., 2019; Zhao et al., 2016), it has been utilized in this study from the safety perspective for lip products users; EF is the exposure frequency (365 day/year); ED is exposure duration (70 years, based on the maximum duration of the exposed population) (USEPA, 2011). BW is the body weight (kg). The average weight of Saudi adult females according to a national nutritional survey of Saudi population is 61.9 kg (Al Othaimeen et al., 2007); AT is the average time of exposure (25,550 days) (ED years × 365 days/year). CF is a conversion factor (10^{-3}).

Hazard quotient (HQ) was taken as a measure of non-carcinogenic risk assessment (F. Li et al., 2017) by dividing the daily exposure dose to the reference dose according to the following equation:

$$HQ = ADD_{ing}/RfD \qquad (2)$$

HQ is the hazard quotient of metals through ingestion; ADD_{ing} is the daily exposure dose of metals in lip products calculated from equation (1); RfD is the reference oral dose (mg/kg/day). The RfD of the studied metals in lip cosmetic products were 0.5, 1.5, 0.38 and 0.009 for Cr, As, Cd and Pb, respectively (Adamiec and Jarosz-Krzemińska, 2019; Lim et al., 2018; USEPA, 2018; Zhang et al., 2019).

HQ values lower than 1 indicates no adverse health effects while HQ values higher than 1 indicates possible adverse health effects. The non-carcinogenic risk of mix metals in lip products was measured by hazard index (HI) which was calculated by sum-

Table 1
QC parameters, LODs and LOQs of the investigated metals in lip products.

Element	Calibration slope	R^2 value	%Accuracy	%Repeatability	% Uncertainty	LOD	LOQ
Al	49,534	0.9988	103.52	1.06	0.2	1.20E−05	3.96E−05
Cr	6213	0.9999	101.09	1.03	0.3	8.00E−05	2.64E−04
Mn	5412	0.9996	104.85	1.92	0.5	7.00E−05	2.31E−04
Fe	690	0.9999	105.52	2.17	0.2	4.30E−04	1.42E−03
Co	561	0.9999	100.16	1.02	0.3	1.00E−05	3.30E−05
Cu	8595	0.9998	107.2	3.04	0.3	6.00E−05	1.98E−04
Zn	4089	0.9996	97.9	1.53	0.5	1.00E−04	3.30E−04
As	5246	1.0000	101.7	2.74	0.4	6.90E−04	2.28E−03
Se	3250	0.9999	99.81	1.71	0.2	1.00E−05	3.30E−05
Sr	1240	0.9999	99.25	3.95	0.2	9.00E−05	2.97E−04
Ag	680	0.9999	102.4	2.75	0.2	3.00E−05	9.90E−05
Cd	5977	1.0000	101.4	1.12	0.5	6.50E−04	2.15E−03
Sn	5249	0.9999	99.8	4.07	0.5	5.70E−04	1.88E−03
Sb	62,014	1.0000	107.5	1.34	0.4	5.00E−05	1.65E−04
Ba	50,243	0.9999	103.2	2.61	0.3	5.00E−05	1.65E−04
Hg	43,210	0.9999	99.7	3.08	0.2	7.00E−04	2.31E−03
Tl	580	1.0000	101.9	1.25	0.2	8.00E−06	2.64E−05
Pb	33,937	1.0000	102.1	2.21	0.2	4.00E−05	1.32E−04

ming up the HQ values for all metals according to the following equation:

$$\mathrm{HI} = \sum HQs \tag{3}$$

$Risk_i$ was taken as a measure of carcinogenic risk assessment (F. Li et al., 2017) by dividing the daily exposure dose to the reference dose according to the following equation:

$$Risk_i = ADD \times SF \tag{4}$$

$Risk_i$ is the carcinogenic risk of metals in lip products; SF is the carcinogenicity slope factor of metals (mg/kg/day). The reported SF values for Cd, Pb, Cr and As are 0.38, 0.0085, 0.5 and 1.5 (mg/kg/day), respectively (Lim et al., 2018; USEPA, 2018; Zhang et al., 2019). Similarly, the carcinogenic risk of mix trace metals was measured by $Risk_T$ which was calculated by summing up the $Risk_i$ values for all metals in lip products according to the following equation:

$$\mathrm{Risk}_T = \sum \mathrm{Risk}_i \tag{5}$$

$Risk_T$ represents the overall carcinogenic risks caused by trace metals in lip products: $Risk_i$ is the carcinogenic risk of each metal in lip products calculated from equation (4). The acceptable value of carcinogenic risk ranges from 10^{-6} to 10^{-4}. Therefore, any value higher than 10^{-4} indicates that there is a certain degree of carcinogenic risk on human health (Khandare et al., 2021).

3. Results and discussion

3.1. Profiles and distribution of metals in lip products

3.1.1. Descriptive statistics

Descriptive statistics were applied to extract the basic information and construct the significant relationship regarding each variable in the dataset. The major different characteristics of the data such as the mean, maximal concentrations as well as ranges for each element were explained in order to construct an ease-to-interpret orders for all the studied elements. The statistical analysis were applied in terms of descriptive statistics, PCA, Pearson correlation, and One-Way ANOVA.

The PCA and Pearson's correlation reduces the dataset in terms of general variability and significant correlations where the data is simplified for interpretation of the major variability, significance or coinciding point for the elements studied in different samples. Whereas, ANOVA reveals the differences for these elements within as well as among the different brands / groups of samples studied.

In this study, the occurrence of 18 metals has been investigated in the most widely consumed lip products from various types and brands in Saudi Arabia. The mean and maximum concentrations of metals in all analyzed lip cosmetic samples ranged between 1.38×10^{-5}-1.15 and 1.00×10^{-4}-4.91 (µg/g), respectively. The concentrations of elements differed between lip products from various brands. The mean elemental abundance and other descriptive statistics of sum, range, mean, and standard deviation for all the elements for each brand of cosmetics are presented in Table 2.

The concentration of elements were also widely varied among the four types of lip products (Fig. 1). It was observed that the highest concentration of Co and Pb were found in lip balm, followed by lip stick and lip gloss. The concentrations of Pb in this study were higher than those observed in China (Y. Li et al., 2021), Saudi Arabia (Al-Saleh and Al-Enazi, 2011), Iran (Malvandi & Sancholi, (2018), Nigeria (Sani et al., 2016) and USA (Liu et al., 2013), lower than those reported by Gondal et al. (Gondal et al., 2010) and similar to those observed in South Korea (Lim et al., 2018) and in Turkey (Gunduz and Akman, 2013). This variation may be attributed to the differences in the production country and the kinds of clays used for cosmetics manufacturing (Tateo and Summa, 2007; Viseras et al., 2007). It has been documented that natural clays vary considerably in mineral and chemical compositions. Consequently, the high adsorption capacity of clays can lead to accumulation of trace elements which results in human health risks (Mattioli et al., 2016; Roselli et al., 2015).

3.1.2. Principle component analysis (PCA)

PCA is considered a dimension reduction technique where the bulk of a huge-data is reduced to lesser dimension which allows the data with more variability to be presented in fewer dimension and an interpretable manner. Based on the variability (%variability), different components are constructed for each variable in the dataset where the more uncorrelated variables are separated based on the more nearer variability level. PCA is generally applied to visualize the significant correlations between the variables of a huge dataset. The concept is based on the Eigen-value where a more significant relationship is denoted if the Eigen value reaches more towards 1. The PCA was carried out on the data matrix of total metal concentrations (18 metals × 37 cases) of the lip products samples. The PCA analysis combined the data into seven various components with a cumulative variability of 78.211% and an individual variability of 14.453% (PC1), 13.683% (PC2), 11.899% (PC3), 10.033% (PC4), 9.814% (PC5), 9.657% (PC6), and 8.671% (PC7). For elements; Mn, Co, and Se were loaded in PC1 showing

Table 2
The descriptive statistics of sum, range, mean, and standard deviation for all the elements in the four brands of lip products.

Brand	Al	Cr	Mn	Fe	Co	Cu	Zn	As	Se	Sr	Ag	Cd	Sn	Sb	Ba	Hg	Ti	Pb
Brand A	N = 9																	
Sum	2.61	0.0002	6.82	1.61	0.002	0.24	0.36	0.37	0.036	0.028	0.149	0.56	0.0057	0.015	0.0094	0.195	0.038	7.5
Mean	*0.29*	*0.00002*	*0.75*	*0.17*	*0.0002*	*0.026*	*0.04*	*0.042*	*0.004*	*0.0031*	*0.016*	*0.062*	*0.0006*	*0.0016*	*0.001*	*0.021*	*0.0042*	*0.83*
Minimum	0.11	<LOD	<LOD	0.04	<LOD	0.002	<LOD	<LOD	<LOD	0.0002	0.004	0.008	0.0002	0.0007	<LOD	0.001	0.001	0.021
Maximum	1.04	0.0001	2.14	0.35	0.001	0.095	0.14	0.13	0.012	0.007	0.042	0.149	0.0021	0.0041	0.005	0.042	0.009	2.01
SD	0.3	0.00004	0.91	0.11	0.0004	0.03	0.056	0.059	0.0049	0.0026	0.014	0.052	0.0005	0.0011	0.0017	0.014	0.0034	0.63
Brand B	N = 8																	
Sum	5.63	0.00009	5.57	0.23	0.005	0.83	0.39	0.25	0.044	0.026	1.58	5.41	0.0013	0.017	0.002	0.11	0.021	5.63
Mean	*0.7*	*0.00001*	*0.69*	*0.02*	*0.0006*	*0.104*	*0.049*	*0.031*	*0.0055*	*0.0032*	*0.198*	*0.67*	*0.0001*	*0.0022*	*0.0002*	*0.013*	*0.0026*	*0.7*
Minimum	0.11	<LOD	0.004	<LOD	<LOD	0.012	<LOD	<LOD	<LOD	<LOD	0.003	0.015	<LOD	0.0003	<LOD	0.001	<LOD	0.021
Maximum	1.07	0.00005	2.1	0.08	0.004	0.51	0.19	0.11	0.017	0.008	0.54	1.063	0.0006	0.0075	0.0007	0.041	0.006	3.01
SD	0.38	0.00002	0.78	0.028	0.0014	0.16	0.072	0.048	0.007	0.0033	0.22	0.48	0.0002	0.0024	0.0003	0.012	0.0024	1.186
Brand C	N = 10																	
Sum	3.61	0.0001	5.62	2.76	0.006	1.56	0.32	0.47	0.14	0.0048	0.055	5.9	0.0032	0.013	0.0014	5.8	0.086	17.17
Mean	*0.36*	*0.00001*	*0.56*	*0.27*	*0.0006*	*0.15*	*0.032*	*0.047*	*0.014*	*0.0004*	*0.0055*	*0.59*	*0.00032*	*0.0013*	*0.00014*	*0.58*	*0.0086*	*1.717*
Minimum	<LOD	<LOD	0.005	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.004	<LOD	<LOD	<LOD	<LOD	<LOD	0.17
Maximum	1.07	0.00008	2.94	2.3	0.004	0.74	0.204	0.17	0.12	0.004	0.045	2.004	0.0015	0.0042	0.001	2.28	0.053	4.18
SD	0.36	0.00002	1.05	0.71	0.0012	0.21	0.067	0.061	0.037	0.0012	0.014	0.66	0.00048	0.0017	0.00032	0.75	0.016	1.32
Brand D	N = 10																	
Sum	3.42	0.00008	5.56	5.79	4.91	2.03	0.25	0.76	0.11	0.065	0.55	4.48	0.0037	0.054	0.069	0.78	0.06	12.1
Mean	*0.34*	*0.000008*	*0.55*	*0.57*	*0.49*	*0.203*	*0.025*	*0.076*	*0.011*	*0.0065*	*0.055*	*0.448*	*0.00037*	*0.0054*	*0.0069*	*0.078*	*0.006*	*1.21*
Minimum	<LOD	<LOD	<LOD	0.041	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.008	<LOD	<LOD	<LOD	<LOD	<LOD	0.021
Maximum	1.02	0.00006	3.11	1.34	4.91	0.71	0.1	0.19	0.07	0.042	0.42	2.004	0.0015	0.04	0.063	0.23	0.015	3.02
SD	0.35	0.00001	1.11	0.52	1.55	0.24	0.042	0.083	0.021	0.012	0.131	0.6	0.0005	0.0123	0.02	0.078	0.005	0.77
Grand total	N = 37																	
Sum	15.28	0.0005	23.59	10.41	4.92	4.66	1.34	1.86	0.33	0.12	2.34	16.36	0.013	0.1002	0.081	6.89	0.205	42.41
Mean	0.41	0.00001	0.63	0.28	0.13	0.12	0.036	0.05	0.0091	0.0033	0.063	0.44	0.0003	0.0027	0.0022	0.186	0.005	1.146
Minimum	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	0.004	<LOD	<LOD	<LOD	<LOD	<LOD	0.021
Maximum	*1.07*	*0.0001*	*3.11*	*2.3*	*4.91*	*0.74*	*0.204*	*0.19*	*0.12*	*0.042*	*0.54*	*2.004*	*0.0021*	*0.04*	*0.063*	*2.28*	*0.053*	*4.18*
SD	0.37	0.00002	0.95	0.49	0.8	0.19	0.058	0.065	0.022	0.0071	0.141	0.55	0.0004	0.0065	0.0104	0.45	0.009	1.052

SD: Standard deviation, LOD: Limit of detection.

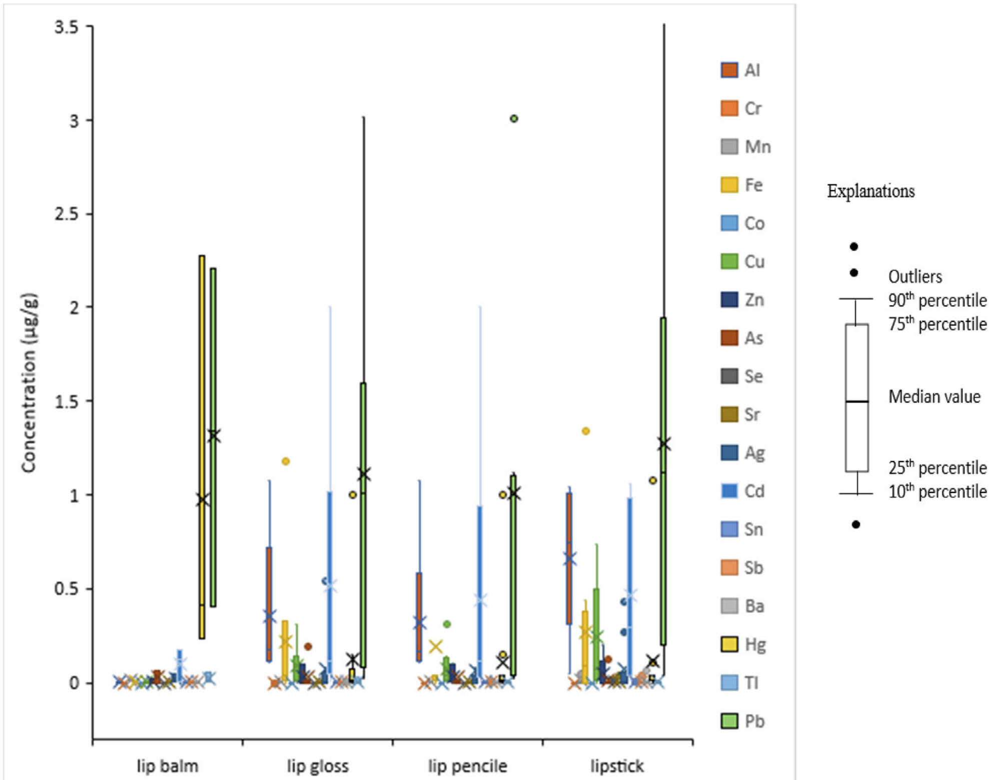

Fig. 1. Box plot showing the distribution of the investigated metals in four types of lip products. The mean concentrations are given as (x) and the median is the line within the box. The dots are outliers.

the highest variability followed by Sr, Ag, and Sb (PC2), Cd and Pb (PC3), Cu and As (PC4), Hg and Ti (PC5), Al and Zn (PC6) whereas, Cr and Ba in (PC7). Fe was distributed both in PC1 and PC4 whereas, Sn was loaded in PC7 with a negative variability. The PCA loading is shown in Table 3 and Fig. 2. The validity of PCA-analysis is confirmed by KMO and Bartlett's test of sphericity with a high chi-square value of 371.910 at significance of $P = 0.000$.

3.1.3. Pearson's correlation

Pearson's correlation was used to describe the linear relationship among the two bivariate data i.e. how much the two variables correlate in terms of similarity or significance in a dataset. Pearson's correlation was applied herein to further confirm the correlations observed in the PCA. A value > 0.50 was considered to correlate the two bivariate data points, irrespective of the correlation whether it was positive or a negative value. Any value approaching "0" was declared a poor correlation. The metal-to-metal correlation data in terms of linear correlation coefficient values that are significant at the 0.01and 0.05 levels were examined. The pairs with positive correlation observed were (Fe: Mn), (Co: Mn), (As: Fe and As: Zn), (Se: Mn, Se: Fe, and Se: Co), (Ag: Al, Ag: Sr), (Sb: Al, Sb: Sr, and Sb: Ag), (Ti: Hg), and (Pb: Cd) whereas,

Table 3
Principle Component Analysis (PCA) for the analyzed lip products (n = 37).

PCA analysis for lip cosmetic products										
Components	PC1	PC2	PC3	PC4	PC5	PC6	PC7	KMO and Bartlett's Test		
Al	−0.171	0.328	0.312	−0.056	−0.099	**0.721**	0.192	Kaiser-Meyer-Olkin Measure of Sampling Adequacy		0.290
Cr	−0.025	−0.119	0.213	−0.188	0.388	−0.028	**0.687**	Bartlett's Test of Sphericity	Approx. Chi-Square	**371.910**
Mn	**0.819**	−0.002	−0.114	−0.070	−0.058	0.149	0.116		df	153
Fe	**0.621**	0.019	−0.013	**0.630**	−0.084	−0.333	−0.070		Sig.	**0.000**
Co	**0.635**	0.134	0.067	−0.228	0.169	−0.135	−0.164			
Cu	−0.301	0.236	0.207	**0.767**	0.054	0.117	−0.067			
Zn	−0.027	−0.052	−0.447	0.235	0.031	**0.746**	−0.200			
As	0.261	−0.165	−0.435	**0.699**	0.031	0.192	−0.204			
Se	**0.890**	0.037	0.007	0.164	0.004	−0.092	0.000			
Sr	0.085	**0.942**	−0.087	0.101	−0.032	−0.008	−0.048			
Ag	−0.007	**0.644**	−0.399	−0.036	−0.206	0.318	0.117			
Cd	−0.161	0.032	**0.760**	0.031	−0.154	0.186	−0.123			
Sn	0.254	−0.220	0.127	−0.351	0.078	0.271	−**0.611**			
Sb	0.065	**0.931**	0.170	0.024	0.010	0.028	−0.023			
Ba	0.079	−0.021	0.001	−0.128	−0.058	0.092	**0.689**			
Hg	−0.116	−0.051	−0.170	0.021	**0.787**	−0.403	0.084			
Tl	0.142	−0.061	−0.133	0.024	**0.925**	0.203	−0.005			
Pb	0.136	−0.107	**0.845**	−0.031	−0.104	−0.165	0.181			
Individual %variance	14.453	13.683	11.899	10.033	9.814	9.657	8.671			
Cumulative %variance	14.453	28.136	40.035	50.068	59.882	69.540	78.211			

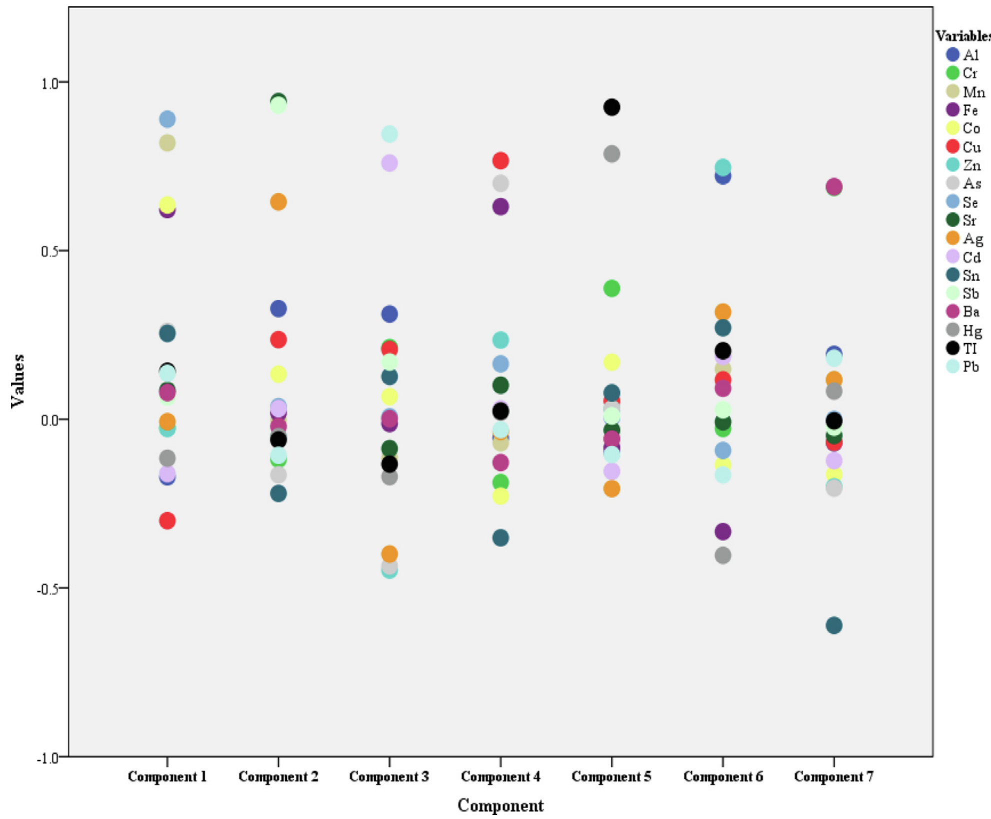

Fig. 2. The PCA presentation for components loading for the investigated elements.

the pairs with negative correlations observed were (Fe: Al), (Hg: Al), (Pb: Zn), (Pb: As) and (Pb: Ag). The Pearson's correlation confirms the PCA-loading for the elements. The positive correlation of Fe with Mn, Co, Se were seen in PC1 with major variability. Likewise, the positive pairs correlations for Ag with Sb, and Sr etc. were observed in PC2, Pb and Cd in PC3, Ti and Hg in PC5. The analysis confirms the major variability and correlation of these elements in the list of thirty seven samples (Table 4).

3.1.4. One way ANOVA

The statistical model of ANOVA is applied when there are more than 2 or 3 groups. ANOVA usually reveals significant differences between and within different groups of samples. In this a number of brands with different formulations were analyzed hence, one way ANOVA was applied to express the significant correlations between and within the groups of different brands for the level of different metals studied. One way ANOVA was performed for significant differences of elemental abundances within and between different brands of the samples. The ANOVA results suggested non-significant ($P > 0.05$) group (brands) differences for Al ($F_{3, 33} = 2.374$, $P = 0.088$), Cr ($F_{3, 33} = 0.397$, $P = 0.756$), Mn ($F_{3, 33} = 0.096$, $P = 0.962$), Fe ($F_{3, 33} = 2.271$, $P = 0.099$), Co ($F_{3, 33} = 0.892$, $P = 0.456$), Cu ($F_{3, 33} = 1.538$, $P = 0.223$), Zn ($F_{3, 33} = 0.252$, $P = 0.859$), As ($F_{3, 33} = 0.784$, $P = 0.512$), Se ($F_{3, 33} = 0.418$, $P = 0.741$), Sr ($F_{3, 33} = 1.231$, $P = 0.314$), Cd ($F_{3, 33} = 2.384$, $P = 0.087$), Sn ($F_{3, 33} = 1.418$, $P = 0.255$), Sb ($F_{3, 33} = 0.810$, $P = 0.497$), Ba ($F_{3, 33} = 0.926$, $P = 0.439$), Ti ($F_{3, 33} = 0.712$, $P = 0.552$), and Pb ($F_{3, 33} = 1.847$, $P = 0.158$) whereas, Ag ($F_{3, 33} = 4.211$, $P = 0.013$) and Hg ($F_{3, 33} = 4.526$, $P = 0.009$) were observed with significant group differences.

For individual differences between the groups Tukey's Post Hoc test was applied. The test revealed no significant differences ($P > 0.05$) for all the elements in the four different brands, except Ag and Hg. For Ag, significant differences were observed between brand A & brand B ($P = 0.02$) and, brand C & brand D ($P = 0.01$). For Hg the significant differences were observed between brand A and brand C ($P = 0.02$), brand B and brand C ($P = 0.02$), and brand C and brand D ($P = 0.03$) (Table 5). Ag was observed to be higher in brand B ($N = 8$, $M = 0.198$, $SD = 0.227$) and brand D ($N = 10$, $M = 0.055$, $SD = 0.131$) as compared to brand A ($N = 9$, $M = 0.016$, $SD = 0.014$) and brand C ($N = 10$, $M = 0.005$, $SD = 0.014$). Hg levels were observed to be higher in brand C ($N = 10$, $M = 0.580$, $SD = 0.757$) and D ($N = 10$, $M = 0.078$, $SD = 0.078$) when compared to brand A ($N = 9$, $M = 0.021$, $SD = 0.014$) and brand B ($N = 8$, $M = 0.013$, $SD = 0.012$).

3.1.5. Elemental occurrence and allowed limits

A widespread elemental abundance was observed in all samples and corresponding brands. The LB3 sample (brand D) showed the highest amount of Co among the 37 samples, followed by Se, Fe, Ti, Zn, Sr, Sb, and Pb in considerable amount. The LS11 (brand D) sample was observed with the highest amount of Sb and Sr compared to other samples, with significant amounts of Ag, Cu, Al, and Fe. The LS8 sample (brand C) contained the highest amount of Cu and Zn among the samples, with Cd, As, Al, and Ti in acceptable concentrations. The LB2 (brand C) showed the highest abundance for Se and Fe as compared to any other sample in the list, with small amounts of Pb, Hg, Sb, Sn, and Sr. The LS12 sample (brand D) showed the highest amount of Ba in the list along with a considerable amount of Cr, Al, Pb, Ti, and Se. The LB1 (brand C) consisted of the highest amount of Pb and Ti, and with second highest amount of Cr among the samples. LS1 (brand A), LP8 (brand C), and LG8 (brand D) showed the highest amount of Sn, with small amount of Al, Ag, Sn, and Pb. The samples of LG10, LP10, and LS10 (brand D) revealed an intermediate amount of Fe, Cu, and Zn only whereas, LG5, LP5, and LS5 (brand B) were observed with highest

Table 4
Pearson's correlation among concentrations of the detected metals in the analyzed lip products.

	Al	Cr	Mn	Fe	Co	Cu	Zn	As	Se	Sr	Ag	Cd	Sn	Sb	Ba	Hg	TI	Pb
Al	1																	
Cr	0.025	1																
	0.881																	
Mn	−0.063	0.093	1															
	0.709	0.586																
Fe	**−0.352**	−0.203	**0.334**	1														
	0.033	0.227	**0.043**															
Co	−0.187	−0.081	**0.439**	0.236	1													
	0.268	0.634	**0.007**	0.159														
Cu	0.220	−0.141	−0.314	0.205	−0.112	1												
	0.190	0.407	0.059	0.223	0.511													
Zn	0.254	−0.283	0.142	−0.134	−0.105	0.216	1											
	0.129	0.090	0.402	0.429	0.535	0.200												
As	−0.195	−0.313	0.192	**0.571**	−0.132	0.265	**0.459**	1										
	0.248	0.059	0.256	**0.000**	0.437	0.113	**0.004**											
Se	−0.174	−0.097	**0.630**	**0.672**	**0.459**	−0.154	−0.061	0.278	1									
	0.304	0.567	**0.000**	**0.000**	**0.004**	0.362	0.722	0.095										
Sr	0.164	−0.126	0.071	0.153	0.086	0.242	0.025	0.024	0.088	1								
	0.331	0.457	0.674	0.365	0.612	0.150	0.882	0.889	0.603									
Ag	**0.373**	−0.187	0.102	−0.103	−0.051	0.004	0.301	0.096	0.025	**0.579**	1							
	0.023	0.269	0.547	0.544	0.765	0.983	0.070	0.572	0.883	**0.000**								
Cd	0.250	0.023	−0.145	−0.168	−0.082	0.165	−0.130	−0.269	−0.131	−0.025	−0.107	1						
	0.135	0.894	0.393	0.320	0.630	0.328	0.444	0.107	0.441	0.882	0.527							
Sn	0.015	−0.236	0.028	−0.041	0.146	−0.300	0.104	0.063	0.153	−0.122	−0.240	0.022	1					
	0.929	0.159	0.868	0.811	0.389	0.071	0.542	0.710	0.366	0.472	0.153	0.898						
Sb	**0.361**	−0.078	0.016	0.086	0.077	0.209	−0.096	−0.145	0.090	**0.904**	**0.416**	0.112	−0.086	1				
	0.028	0.647	0.925	0.614	0.651	0.214	0.573	0.393	0.597	**0.000**	**0.010**	0.511	0.613					
Ba	0.153	0.289	−0.085	−0.053	0.013	−0.130	−0.121	−0.152	0.051	−0.005	−0.001	−0.104	−0.121	0.025	1			
	0.364	0.082	0.615	0.756	0.941	0.444	0.477	0.369	0.765	0.978	0.997	0.540	0.475	0.884				
Hg	**−0.333**	0.215	−0.136	−0.020	0.019	−0.045	−0.189	−0.029	0.017	−0.124	−0.159	−0.293	−0.204	−0.121	−0.065	1		
	0.044	0.201	0.422	0.905	0.913	0.793	0.262	0.864	0.921	0.463	0.348	0.078	0.226	0.476	0.702			
TI	−0.053	0.293	0.064	−0.009	0.176	−0.046	0.214	0.231	0.090	−0.053	−0.087	−0.195	0.167	−0.052	0.021	**0.621**	1	
	0.755	0.078	0.708	0.958	0.297	0.788	0.203	0.169	0.596	0.753	0.607	0.248	0.322	0.761	0.901	**0.000**		
Pb	0.171	0.214	0.034	0.110	0.032	−0.009	**−0.536**	**−0.380**	0.119	−0.177	**−0.325**	**0.494**	0.019	0.026	0.094	−0.080	−0.207	1
	0.311	0.203	0.840	0.517	0.851	0.956	**0.001**	**0.020**	0.484	0.294	**0.050**	**0.002**	0.910	0.878	0.578	0.639	0.218	

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

Table 5
One way ANOVA table for the different brands of the analyzed lip products.

Elements		Al		Cr		Mn		Fe		Co		Cu		Zn		As		Se	
(I) Brand	(J) Brand	(I-J)	Sig.	(I-J)	Sig.	(I-J)	Sig.	(I-J)	Sig.	(I-J)	Sig.	(I-J)	Sig.	(I-J)	Sig.	(I-J)	Sig.	(I-J)	Sig.
Brand A	N.Y.X	−0.413	0.09	0.00001	0.86	0.061	0.99	0.149	0.91	−0.0004	1	−0.077	0.83	−0.0089	0.99	0.0101	0.98	−0.002	0.99
	SIPHORA	−0.07	0.97	0.000008	0.92	0.196	0.97	−0.097	0.96	−0.0003	1	−0.129	0.44	0.0076	0.99	−0.005	0.99	−0.01	0.76
	N.A.R.S	−0.051	0.98	0.00001	0.71	0.201	0.97	−0.4	0.26	−0.491	0.55	−0.176	0.19	0.0146	0.95	−0.034	0.67	−0.008	0.88
Brand B	M.A.C	0.413	0.09	−0.00001	0.86	−0.0618	0.99	−0.149	0.91	0.0004	1	0.077	0.83	0.0089	0.99	−0.01	0.98	0.0015	0.99
	SIPHORA	0.342	0.19	−0.000002	0.99	0.134	0.99	−0.246	0.68	0.00002	1	−0.052	0.93	0.0166	0.93	−0.016	0.95	−0.009	0.85
	N.A.R.S	0.362	0.15	0.000003	0.99	0.139	0.99	−0.549	0.08	−0.49	0.58	−0.099	0.68	0.0235	0.84	−0.044	0.49	−0.006	0.94
Brand C	M.A.C	0.07	0.97	−0.000008	0.92	−0.196	0.97	0.097	0.96	0.0003	1	0.129	0.44	−0.0076	0.99	0.0054	0.998	0.0102	0.76
	N.Y.X	−0.342	0.19	0.000002	0.99	−0.134	0.99	0.246	0.68	−0.00002	1	0.052	0.93	−0.0166	0.93	0.0155	0.95	0.0087	0.85
	N.A.R.S	0.019	0.99	0.000006	0.96	0.0057	1	−0.302	0.47	−0.49	0.53	−0.046	0.94	0.0069	0.99	−0.029	0.76	0.0025	0.99
Brand D	M.A.C	0.051	0.98	−0.00001	0.71	−0.201	0.97	0.4	0.26	0.491	0.55	0.176	0.19	−0.0146	0.95	0.0342	0.67	0.0076	0.88
	N.Y.X	−0.362	0.15	−0.000003	0.99	−0.139	0.99	0.549	0.08	0.49	0.58	0.099	0.68	−0.0235	0.84	0.0443	0.49	0.0061	0.94
	SIPHORA	−0.019	0.99	−0.000006	0.96	−0.0057	1	0.302	0.47	0.49	0.53	0.046	0.94	−0.0069	0.99	0.0288	0.76	−0.003	0.99

Elements		Sr		Ag		Cd		Sn		Sb		Ba		Hg		Ti		Pb	
(I) Brand	(J) Brand	(I-J)	Sig.	(I-J)	Sig.	(I-J)	Sig.	(I-J)	Sig.	(I-J)	Sig.	(I-J)	Sig.	(I-J)	Sig.	(I-J)	Sig.	(I-J)	Sig.
Brand A	N.Y.X	−0.00017	1	−0.181	0.02	−0.614	0.09	0.0004	0.2	−0.0005	0.99	0.0007	0.99	0.0077	1	0.0015	0.98	0.1297	0.99
	SIPHORA	0.0026	0.84	0.0109	0.99	−0.528	0.14	0.0003	0.5	0.0003	0.99	0.0009	0.99	−0.5587	0.02	−0.004	0.72	−0.883	0.25
	N.A.R.S	−0.0034	0.72	−0.039	0.9	−0.385	0.39	0.0002	0.63	−0.0037	0.6	−0.0058	0.62	−0.0569	0.98	−0.002	0.97	−0.376	0.85
Brand B	M.A.C	0.00017	1	0.181	0.02	0.614	0.09	−0.0004	0.2	0.0005	0.99	−0.0007	0.99	−0.0077	1	−0.002	0.98	−0.13	0.99
	SIPHORA	0.0028	0.83	0.192	0.01	0.086	0.98	−0.0001	0.9	0.0008	0.99	0.0001	1	−0.5664	0.02	−0.006	0.52	−1.012	0.17
	N.A.R.S	−0.0032	0.76	0.142	0.09	0.228	0.79	−0.0002	0.8	−0.0032	0.73	−0.006	0.54	−0.0646	0.98	−0.003	0.86	−0.505	0.72
Brand C	M.A.C	−0.0026	0.84	−0.0109	0.99	0.528	0.14	−0.0003	0.5	−0.0003	0.99	−0.0009	0.99	0.5587	0.02	0.0043	0.72	0.8827	0.25
	N.Y.X	−0.0028	0.83	−0.192	0.01	−0.086	0.98	0.0001	0.9	−0.0008	0.99	−0.0001	1	0.5664	0.02	0.0059	0.52	1.0124	0.17
	N.A.R.S	−0.006	0.24	−0.05	0.81	0.142	0.92	−0.00005	0.99	−0.0041	0.5	−0.0067	0.48	0.5018	0.03	0.0026	0.92	0.5071	0.68
Brand D	M.A.C	0.0034	0.72	0.039	0.9	0.385	0.39	−0.0002	0.63	0.0037	0.6	0.0058	0.62	0.0569	0.98	0.0017	0.97	0.3756	0.85
	N.Y.X	0.0032	0.76	−0.142	0.09	−0.228	0.79	0.0002	0.8	0.0032	0.73	0.0066	0.54	0.0646	0.98	0.0033	0.86	0.5053	0.72
	SIPHORA	0.006	0.24	0.05	0.81	−0.142	0.92	0.00005	0.99	0.0041	0.5	0.0067	0.48	−0.5018	0.03	−0.003	0.92	−0.507	0.68

Table 6
Estimated non-carcinogenic health risks of the investigated metals in lip products (n = 37).

Metal	(ADDing)		HQ		(ADDing)		HQ	
	50% bio-accessability				100% bio-accessability			
	Average users	Heavy users	Average users	Heavy users	Average users	Heavy users	Average users	Heavy users
Al	8.6E−06	4.97E−05	8.60E−06	4.97E−05	1.7E−05	9.94E−05	1.72E−05	9.94E−05
Mn	1.2E−05	7.19E−05	8.88E−05	5.13E−04	2.5E−05	1.44E−04	1.78E−04	1.03E−03
Fe	5.9E−06	3.39E−05	8.38E−06	4.84E−05	1.2E−05	6.78E−05	1.68E−05	9.68E−05
Cr	1.2E−09	6.77E−09	3.90E−07	2.26E−06	2.3E−09	1.35E−08	7.81E−07	4.51E−06
Co	2.8E−06	1.60E−05	9.24E−04	5.34E−03	5.5E−06	3.21E−05	1.85E−03	1.07E−02
Cu	2.6E−06	1.52E−05	6.57E−05	3.80E−04	5.3E−06	3.04E−05	1.31E−04	7.60E−04
Zn	7.5E−07	4.36E−06	2.51E−06	1.45E−05	1.5E−06	8.72E−06	5.03E−06	2.91E−05
As	1.1E−06	6.08E−06	3.51E−03	2.03E−02	2.1E−06	1.22E−05	7.01E−03	4.05E−02
Se	1.9E−07	1.10E−06	3.81E−05	2.20E−04	3.8E−07	2.20E−06	7.61E−05	4.40E−04
Sr	7.0E−08	4.04E−07	1.17E−07	6.74E−07	1.4E−07	8.09E−07	2.33E−07	1.35E−06
Ag	1.3E−06	7.64E−06	2.64E−04	1.53E−03	2.6E−06	1.53E−05	5.29E−04	3.06E−03
Cd	9.2E−06	5.32E−05	9.21E−03	5.32E−02	1.8E−05	1.06E−04	1.84E−02	1.06E−01
Sn	7.8E−09	4.52E−08	1.30E−08	7.54E−08	1.6E−08	9.04E−08	2.61E−08	1.51E−07
Sb	5.6E−08	3.26E−07	1.41E−04	8.15E−04	1.1E−07	6.52E−07	2.82E−04	1.63E−03
Ba	4.6E−08	2.66E−07	2.30E−07	1.33E−06	9.2E−08	5.32E−07	4.60E−07	2.66E−06
Hg	3.9E−06	2.24E−05	2.43E−02	1.40E−01	7.8E−06	4.49E−05	4.85E−02	2.80E−01
Tl	1.2E−07	6.67E−07	3.85E−02	2.22E−01	2.3E−07	1.33E−06	7.69E−02	4.45E−01
Pb	2.4E−05	1.38E−04	6.82E−03	3.94E−02	4.8E−05	2.76E−04	1.36E−02	7.89E−02
	HI	8.38E−02	4.84E−01	HI	1.68E−01	9.69E−01		

amount of Ag, followed by Al, Zn, As, and Sr. The abundance for Pb and Cd was observed the highest levels in LP6, LS6 (brand B), LG6, LP9, LS9 (brand C), and LG9 (brand D). The remaining samples of LG3 and LP3 (brand A) contained Cr only whereas, LG1, LP1, LS3 (brand A), LP4, LS4 (brand B), LG7, LP7, LS7 (brand C), LP11 (brand D) showed a very small amount of Hg only. The number of samples of each brand containing the highest level of elements in descending order were found to be: brand C (10) > brand D (9) > brand B (7) > brand A (6). In terms of sample nature (LP, LS, LG, LB) the highest elemental abundance was observed in LS samples at the following order: LS (11) > LP (10) > LG (8) > LB (3).

In view of permissible limits, most of the elements were observed within the permissible ranges set by SASO (Saudi standards metrology and quality organization) (SASO, 2008), Canadian health regulations (Canadian health), European Union (European Union, 2009), (German federal government) and USFDA (USFDA, 2019). The main elements of concern with potential health risks in cosmetics products are usually Pb, Cd, As, Cu, Co, and Hg. Herein, the elements with abundance higher than the permissible limits were Cd, Hg and Pb.

For Cd, the range observed was 0.004–2.004 μg/g with mean and sum of 0.44 (±0.55) and 16.36 μg/g, respectively as shown in Table 2. Though the maximum value for Cd (2.004 μg/g) was within the permissible range of 5 ppm set by European Union (European Union, 2009). The samples observed with values exceeding 1 μg/g were; brand A (LP9, 2.004) > brand D (LG9, 2.004) > brand B (LS6, 1.063) > brand B (LP6, 1.047) > brand A (LG6, 1.047) > brand B (LS4, 1.027) > brand B (LG4, 1.008) > brand B (LP4, 1.008) > brand A (LS9, 1.001).

The elemental abundance for Hg showed a range of 0.00–2.28 μg/g with a mean and sum of 0.186 (±0.45) and 6.89 μg/g, respectively. The highest value observed for Hg (2.228 μg/g) was beyond the permissible limits of 0.1 μg/g (German federal government). The samples from respective brands showing the value above the defined range were; brand A (LB1, 2.280) > brand A (LG7, 1.004) > brand A (LS7, 1.074) > brand A (LP7, 1.00) > brand A (LB2, 0.412) > brand B (LB3, 0.237) > brand B (LG10, 0.15) > brand B (LP10, 0.15) > brand B (LS10, 0.106).

The element of Pb was observed in the range of 0.021–4.18 μg/g with a mean and sum of 1.146 (±1.052) and 42.41 μg/g, respectively. Most of the samples showed the values within the permissible range, however these values were beyond the German health regulations limit of 2 μg/g. The samples with values exceeding 2 μg/g were; brand C (LS9, 4.182) > brand D (LG9, 3.02) > brand D (LP9, 3.02) > brand C (LG6, 3.01) > brand B (LP6, 3.01) > brand C (LB2, 2.21) > brand B (LS6, 2.17) > brand A (LS1, 2.015).

The analyzed lip products samples with metal concentrations higher than the permissible limits are shown in Table 4. The values observed herein for Cd, Hg, and Pb were in concordance with the previous reports e.g. (Ullah et al., 2017) where most of the cosmetics products were observed with a high elemental abundance of Cd, Hg, Pb, Cu, and Co. For example, Gondal et al. reported high concentrations of Pb and Cd in lipsticks ranged from 6.4 to 9.9 and, 5.4 to 10.6 μg/g, respectively (Gondal et al., 2010). Also, Zakaria & Ho reported a high mean concentration of Pb in lipsticks ranged from 0.77 to 15.44 μg/g (Zakaria & Ho, 2015). It is noteworthy to mention that the remaining elements were also observed beyond the allowed limits in such reports whereas, our study found all these elements well within the specified ranges of European Union, Canadian and German health regulations (with the exception of Cd, Hg, and Pb).

3.2. Health risk assessment of exposure to metals in lip products

Detection of different metals in lip cosmetic products necessitates the evaluation of their health risk to ensure consumer safety. The non-carcinogenic risk of eighteen metals and carcinogenic risk of four trace metals were calculated for both average and heavy users of lip cosmetic products using the equations described in Section 2.7.

3.2.1. Non-carcinogenic risk assessment of metals in lip products

The calculated values of the exposure dose for the studied metals in different lip cosmetic products at 50% and 100% bio-accessibility are presented in Table 6. It was noted that at 50% bio-accessibility, ADDing values ranged from 1.17×10^{-9} to2.39×10^{-5} and from 6.77×10^{-9} to1.38×10^{-4} (mg/kg/day) for average and heavy users, respectively. Likewise, ADDing levels at 100% bio-accessibility for average and heavy users ranged from 2.34×10^{-9} to 4.77×10^{-5} and from 1.35×10^{-8} to 2.76×10^{-4} (mg/kg/day), respectively. Among the detected metals, Pb showed the highest exposure dosage ranged from 2.39×10^{-5} to 1.38×10^{-4} (mg/kg/day) for average users and from 4.77×10^{-5}

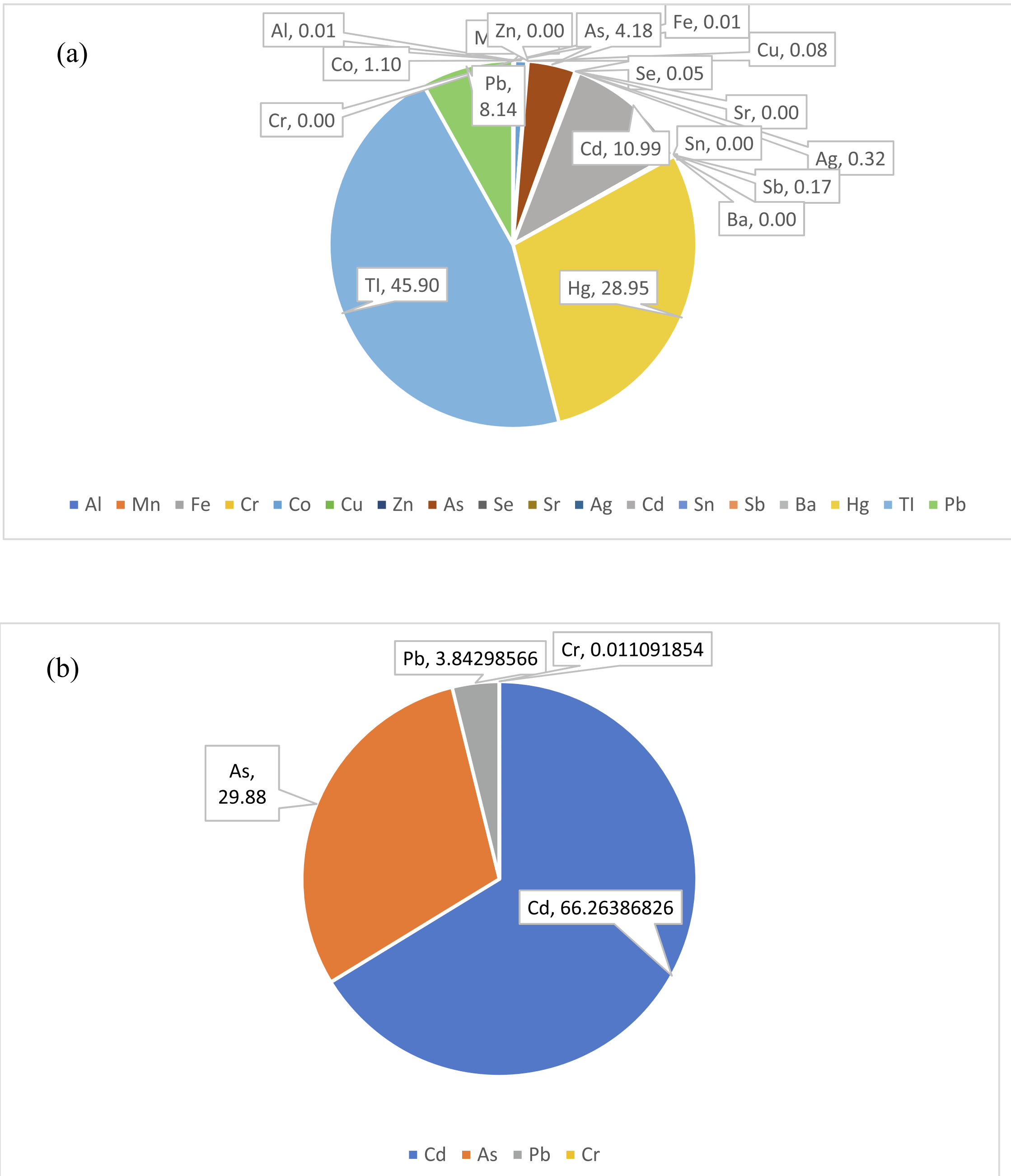

Fig. 3. (a) The relative contribution of each metal to the total non-carcinogenic health risk and (b) the relative contribution of selected metals to the total carcinogenic health risk (calculated at 100% bio-accessibility).

Table 7
Estimated carcinogenic health risks of selected metals in lip products (n = 37).

Metal	SF	Riski		Riski	
		50 % bio-accessability		100 % bio-accessability	
		Average users	Heavy users	Average users	Heavy users
Cr	0.5	5.86E−10	3.39E−09	1.17E−09	6.77E−09
As	1.5	1.58E−06	9.12E−06	3.16E−06	1.82E−05
Cd	0.38	3.50E−06	2.02E−05	7.00E−06	4.05E−05
Pb	0.009	2.03E−07	1.17E−06	4.06E−07	2.35E−06
RiskT		5.28E−06	3.05E−05	1.06E−05	6.10E−05

to 2.76×10^{-4} (mg/kg/day) for heavy users at 50% bio-accessibility and 100% bio-accessibility, respectively (Table 6).

The non-carcinogenic risk levels (HQ) for heavy users were higher compared to those for average users. As for heavy users, the non-carcinogenic risks for the studied metals ranged from 7.54×10^{-8} to 2.22×10^{-1} at 50% bio-accessibility and from 1.51×10^{-7} to 4.45×10^{-1} at 100% bio-accessibility. The relative contributions of each metal to the total non-carcinogenic risk (HI) calculated at 100% bio-accessibility are also shown in Fig. 3a. It was observed that Ti contributed to nearly half of the total non-carcinogenic risk (45.90%), followed by Hg (28.95%), Cd (10.99%), Pb (8.14%) and As (4.18%). Generally, the current findings signify that the values of HQ for each element were far below 1, indicating that there was no significant non-carcinogenic health risk for lip products users. The calculated values of HQ were lower than the reported values by Zakaria & Ho (Zakaria & Ho, 2015) and were almost comparable to the values reported in other studies e.g. (Arshad et al., 2020; Li et al., 2021).

3.2.2. Carcinogenic risk assessment of heavy metals in lip products

The carcinogenic risk to human health due to the consumption of lip products contaminated with trace metals was evaluated by calculating the carcinogenic risk ($Risk_i$). The estimated levels of $Risk_i$ for the metals in the analyzed lip cosmetic products at 50% and 100% bio-accessibility are presented in Table 7. Apparently, the carcinogenic risk levels for heavy users were higher than those for average users. It was observed that at 50% bio-accessibility, the carcinogenic risk levels ranged from 5.86×10^{-10} to 3.50×10^{-6} and from 3.39×10^{-9} to 2.02×10^{-5} for average and heavy users, respectively. Likewise, $Risk_T$ levels at 100% bio-accessibility for average and heavy users ranged from 1.17×10^{-9} to 7.00×10^{-6} and from 6.77×10^{-9} to 4.05×10^{-5}, respectively. Among the carcinogenic metals, cadmium showed the highest risk level ranged from 3.50×10^{-6} to 2.02×10^{-5} at 50% bio-accessibility and ranged from 7.00×10^{-6} to 4.05×10^{-5} at 100% bio-accessibility (Table 7). Cd was regarded as the primary contributor to carcinogenic risks in the analyzed lip products. It was found that Cd contributed to about two-third of the total carcinogenic risk (66.26%), followed by As (22.88%) and Pb (3.84%). The relative contributions of heavy metals to the total carcinogenic risk ($Risk_T$) calculated at 100% bio-accessibility are also shown in Fig. 3b. According to USEPA, acceptable range for carcinogenic risk is in the range from 1×10^{-6} to 1×10^{-4}. In this study, all carcinogenic risk levels were below the acceptable range, indicating that the cancer risks posed by trace metals in the analyzed lip products were acceptable. The calculated values of carcinogenic risk were more or less similar to those reported in previous studies e.g. (Arshad et al., 2020; Lim et al., 2018) and lower than those reported by Li et al. (Li et al., 2021). However all values calculated in this study were within the acceptable limit, special attention should be taken in order to prioritize minimizing the trace metals in lip products, especially for Cd, Pb, Ti and Hg, as these metals are non-biodegradable and can be accumulated into the body for long period of time resulting in alteration of the cell functions and disruption of internal cellular mechanisms as well (Stavrides, 2006).

Heavy metals can cause acute and chronic health effects including vascular damage, gastrointestinal and kidney dysfunction, skin lesions, nervous system disorder (Balali-Mood et al., 2021). Additionally, incidence of cancer could be enhanced by such impurities which can cause oxidative stress and DNA damage (Kim et al., 2015). Simultaneous exposure to two or more metals may have cumulative effects (Gazwi et al., 2020). Also, exposure to high-dose of heavy metals, particularly mercury and lead, may induce severe consequences such as bloody diarrhea, abdominal pain and kidney failure (Tsai et al., 2017). On the other hand, continual exposure to low-dose of heavy metals is considered a hidden threat that may cause neuropsychiatric complications such as anxiety, fatigue and detrimental impacts on the intellectual function, especially in children (Mazumdar et al., 2011). Humans are exposed to heavy metals from different sources such as environmental pollution, food contamination, industrial and agricultural operations (Balali-Mood et al., 2021).

Danger concerns with things that cannot be controlled by the individual (no ability to choose or exercise control), on the other hand risk is related to decision and choice (Green et al., 2010). Risk caused by harmful substances is dependent on exposure. For example, continuous use of cosmetics on a daily basis such as lip products over long period of time may adversely affect the health of heavy consumers on long term. However, exposure to heavy metals is inevitable in most cases, people are required to make safety decision and to indicate the measures they use to reduce the personal risks. People can keep the personal risk as small as possible by reducing potential exposure to harmful chemicals via minimizing the amounts of these chemicals in consumer products or via reducing their overall consumption. Consumers should be aware that aggregate and cumulative exposure to harmful ingredients contained in cosmetics may cause negative health impacts. Enhancing people's awareness regarding the substances contained in cosmetic products and their associated health risk may significantly enhance the consumers' choices and affect their decision regarding the consumption of cosmetics.

4. Conclusion

The concentrations of 18 elements in different types of lip products collected from the local markets in Saudi Arabia were determined using ICP-MS. The results of the presented study showed that the levels of metals varied in the different types and brands of the analyzed lip products. It was found that the concentrations of Cd, Hg and Pb were higher than the permissible limits. The HQ, HI, $Risk_i$ and $Risk_T$ values for the investigated metals were found to be below 1, therefore, there was no significant non-carcinogenic and carcinogenic health risks due to the exposure to metals contained in the analyzed lip products. However, periodic monitoring of the elemental composition of lip products and other cosmetics is of a paramount importance in order to ensure consumer safety. Also, minimizing the metals content in lip products especially for Cd, Pb, Ti and Hg should be considered to avoid the potential health effects that may occur due to the use of lip cosmetics over a long period of time especially for heavy users.

CRediT authorship contribution statement

Heba Shaaban: Conceptualization, Methodology, Writing – original draft, Funding acquisition, Project administration, Visualization, Supervision. **Sahar Y. Issa:** Formal analysis, Validation. **Rizwan Ahmad:** Writing – original draft. **Ahmed Mostafa:** Conceptualization. **Sara Refai:** . **Nooran Alkharraa:** Formal analysis. **Batool T. Albaqshi:** Formal analysis. **Dania Hussien:** Writing – review & editing. **Abdulmalik M. Alqarni:** Writing – review & editing.

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.jsps.2022.03.014.

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