



Health risk assessment of heavy metals in cosmetic products sold in Iran: the Monte Carlo simulation

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Abstract

Cosmetics can contain harmful compounds such as heavy metals. Several metals have a cumulative effect on the body, especially fatty tissues, and may have different health effects on the human body over the long term. Therefore, the main objective of this study was to assess the health risks of heavy metals in cosmetics in Iran. Also, in this study, Monte Carlo simulation was used to investigate uncertainties. In this study, heavy metals data of cosmetics were extracted from studies carried out at intervals 2010–2018. International and Iranian databases such as Google Scholar, Web of Science, Springer, Science Direct, PubMed, Scopus, Irandoc, Magiran, Scientific Information Database (SID), and Information Institute for Scientific (ISC) were searched for this purpose. In this study, the index of the Margin of Safety was calculated to determine the risk of human contact with metallic impurities in cosmetic products used by humans. In the selected period, 11 studies were conducted on the measurement of heavy metals in cosmetics in Iran. In these studies, cosmetics such as eye shadow, eye pencil, powder, cream, and lipstick were studied. The Margin of Safety (MoS) values calculated for different metals were higher than the established safe standard by WHO. The highest and lowest amount of systemic exposure dosage in all types of cosmetic investigated (lipstick, cream, eye pencil, face powder, and eye shadow) was related to Fe and Hg. The mean hazardous quotient (HQ) for Cd, Cr, Ni, Cu, Mn, Zn, Pb, and Hg was 1.05E-03, 1.03E-01, 7.95E-03, 2.59E-03, 1.05E-03, 4.98E-03, 7.22E-04, 1.85E-01, and 1.35E-05, respectively. The highest HQ (6.10E-01) was found for Pb, which was observed in the cream.

Keywords Health risk assessment · Heavy metals · Cosmetic · Monte Carlo simulation

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Introduction

Several studies showed that some heavy metals can accumulate over time in the body of animal and human and so cause health problems (Mazzei et al. 2013; Saleh et al. 2019; Thyssen and Menne 2009; Fakhri et al. 2018). These metals, through binding to the cell's protein, inhibit normal cellular function and cause death, which can lead to many diseases (Asgari Rad et al. 2016; Ferrante and Conti 2017). One of the ways of human exposure to heavy metals is the use of cosmetics. The contamination of cosmetic products from the past to the twentieth century was normal to various heavy metals such as lead (Pb) and cadmium (Cd) (Berkowitz et al. 2006). Cosmetic products are widely used daily by many people in the world, especially by women. Cosmetics are used in direct contact with the skin. The skin structure, as the first defensive barrier, prevents the entry of some pollutants into the internal tissues to a large extent. But cosmetic products used in areas such as oral cavity, lips, eyes, or mucus can put the consumer at a more high exposure to metals (Loretz et al. 2008; Nohynek et al. 2010). According to published reports and available evidences, the use of cosmetics has increased in recent years. The excessive consumption of cosmetics and the lack of attention to their quality standard and the entry of these products into the country from frontier provinces, which are easily and inexpensively available to the public, can lead to various illnesses and diseases (Sharafi et al. 2017). More serious concerns about the use of cosmetics in our country are due to the young age of using cosmetics at the contrary of European (SccS, 2012) and developed countries (Mohammadi et al. 2014; Sharafi et al. 2017). Frequent use of cosmetics may increase the adsorption of heavy metals when eating lipstick or sweating the skin surface that is covered with creams, cosmetics, or makeup. Nnorom et al. (2005) conducted a study on the metals in cosmetics used in Nigeria and showed that the mean of Pb in three types of cosmetics (lipstick, eyeliner, and pencil eye) ranged by 78 to 123 µg/g (Nnorom et al. 2005). Some studies show that most cosmetics manufacturers and factories use heavy metals to extend the life of the products (Bocca et al. 2014; Lim et al. 2018). In recent years, various researches have shown that there is a direct relation between these cosmetic products and the incidence of types of cancer, especially breast cancer, skin sensitivities, respiratory disorders, fertility problems, multiple abortions, and genetic disorders (Lim et al. 2018; Gunduz and Akman 2013; Nourmoradi et al. 2013).

This study was conducted on cosmetic produced in Iran. Iran is a country located in Southwest Asia and in the Middle East area with an area of 1,648,195 km². Comparison of the per capita consumption of cosmetics in Iran and European countries shows that Iranians spend on average about 4.5% of their annual income for cosmetics while the Germans only 1.5% and the French and English also 1.7%. The income from

cosmetics sales in Iran is very high (about 2 billion and 400 million dollars), which after Saudi Arabia, Iran is the largest consumer of cosmetics in the Middle East (Ziarati et al. 2012). Some researchers have indicated that there is no direct relation between the concentration of heavy metals and the cost of cosmetics (Sani et al., 2016); however, results obtained through Sharafi study showed that Pb concentrations were lower in brands (Sharafi et al. 2017). Another study revealed that the Pb concentration in cheaper brands was higher compared to the expensive brands (Malakootian et al. 2012). On average, women eat about 1.8 kg of lipstick over their lifetime, and the harmful effect of this cosmetic product, especially those with longer shelf life, is higher (Nnorom et al. 2005; Gondal et al. 2010). Several researches have already been carried out to measure the concentration of heavy metals in cosmetics (Malakootian et al. 2012; Ziarati et al. 2012; Nourmoradi et al. 2013; Mohammadi et al. 2014; Karimi and Ziarati 2015; Asgari Rad et al. 2016; Naalbandi et al. 2016; Sharafi et al. 2017; Balarastaghi et al. 2018; Mansouri et al. 2018). Since families are less careful about the materials and the types and quality of cosmetics, the risk of causing lead-induced complications is very serious. However, in none of these studies, the health risk assessment of heavy metals as impurities of cosmetics has not been evaluated. So, the main objective of this study was to assess the health risks of heavy metals in cosmetics available in Iran. Also, in this study, the Monte Carlo simulation was used to investigate uncertainties.

Materials and methods

Data collection and analysis

In this study, heavy metals concentrations as impurities into cosmetics were extracted from studies carried out by 2010 to 2018. The metals studied were cadmium (Cd), chromium (Cr), nickel (Ni), copper (Cu), manganese (Mn), iron (Fe), zinc (Zn), lead (Pb), and mercury (Hg). International and Iranian databases such as Google Scholar, Web of Science, Springer, Science Direct, PubMed, Scopus, Irandoc, Magiran, Scientific Information Database (SID), and Information Institute for Scientific (ISC) were investigated for this purpose. Finally, 11 studies were found eligible. Table 1 displays the data of these studies.

Health risk assessment of cosmetic products

Non-cancer risk, safety evaluation of facial cosmetic products, and Margin of Safety

In this study, the Margin of Safety (MoS) index was used to assess the risk of contact with heavy metals in cosmetic products. MoS is an uncertainty factor (El-Aziz et al. 2017). The

Table 1 Heavy metals measured in various cosmetics

	Concentration (µg/g)								
	Cd	Cr	Ni	Cu	Mn	Fe	Zn	Pb	Hg
Eye shadow	0.4–2.18	30.8–43.97	19.88–32.05	6.68–56.77	42.2–165.57	1008.5–1332.2	32.01–258.26	81.02–140.57	ND*–0.075
Eye pencil	0.07–1.93	34.36–47	30.73–40.86	3.49–73.37	232.41–401.13	1254–1271.5	7.98–82.29	96.37–120.45	ND–0.0017
Powder	ND–0.22	32.51–51.98	22.99–43.81	2.4–58.88	21.5–157.43	963.49–1325	16.12–242.13	88.32–280.9	ND–0.0025
Cream	ND–0.08	29–65.27	9.63–37.94	2.36–28.54	3.51–8.12	157.71–534.78	3.62–10.22	11.54–129.26	ND
Lipstick	ND–403	27.78–110.72	9.16–74.46	1.86–21.72	8.93–32	804.3–1382	3.64–216.53	109.66–198.49	0.0077–0.022

*ND, not detected

(Malakootian et al. 2012; Ziarati et al. 2012; Nourmoradi et al. 2013; Mohammadi et al. 2014; Karimi and Ziarati 2015; Asgari Rad et al. 2016; Naalbandi et al. 2016; Sharafi et al. 2017; Balarastaghi et al. 2018; Mansouri et al. 2018)

formula for calculating the MoS is shown in Eq. 1. In this equation, NOAEL is the *Lowest No Observed Adverse Effect Level*. Also, SED is the systemic exposure dosage (in µg/kg BW. Day). In other words, the MoS index is the ratio of NOAEL to SED day. According to the World Health Organization (WHO) proposal, the lowest amount of the MoS is 100. So, if the MoS content of a cosmetic product is 100 or higher, its use is safe.

The formula for calculating the NOAEL is shown in Eq. 2. In this equation, the RfD, UF, and MF are the oral reference doses, the uncertainty factor, and the modifying factor, respectively. The RfD is the oral reference doses for various heavy metals. The RfD is an estimate of a daily dermal exposure with the cosmetic product in the human population, which does not cause harmful effects during a lifetime (El-Aziz et al. 2017). Based on United States Environmental Protection Agency (USEPA), the RfDs for Cd, Cr, Ni, Cu, Mn, Fe, Zn, Pb, and Hg are 0.001, 0.001, 0.02, 0.04, 0.14, 0.7, 0.3, 0.04, and 0.0003, respectively (El-Aziz et al. 2017). In Eq. 2, the amount of UF and MF as the default values is 100 and 1, respectively (El-Aziz et al. 2017). After calculating the amount of the NOAEL, the SED content should be obtained. The formula for calculating the SED is shown in Eq. 3. In this equation, the Cs and SSA are the heavy metals concentration in the cosmetic product (mg/kg) and the skin surface area (cm²) onto which the products are applied, respectively. When, the SSA varies depending on the type of cosmetic studied. The SSA for face powder, eye shadow, lipsticks, eye pencil, and cream is 563, 24, 4.8, 3.2, and 565, respectively. The AA is the daily amount of used cosmetic. The AA for face powder, eye shadow, lipsticks, eye pencil, and cream is 0.51, 0.02, 0.057, 0.005, and 1.54 g, respectively. RF and F are the retention factor and the frequency of daily use of cosmetics, respectively. The amount of RF leave-on cosmetics is considered 1. The F for face powder, eye shadow, lipsticks, eye pencil, and cream is 2, 2, 2, 2, and 2.4, respectively. BF and BW are the bioaccessibility factor and body weight (kg), respectively. The BW value used in this research was 60 kg.

The proposed values of SSA, AA, and RF used in this research were the standard values established by the Scientific Committee on Consumer Safety (SCCS 2012). After calculating the amount of the NOAEL, we obtained the SED, MoS, and hazardous quotient (HQ).

The HQ (Eq. 4) used to calculate the risk level in the risk assessment for the exposure level of a pollutant is the ratio of the concentration which is expected not to cause any side effects when the subject is exposed to a chemical to the exposure level. If the HQ is 1 or less, no harmful effect on health due to exposure is expected, and if the HQ value is greater than 1, it is considered not safe for human health (EPA 1997b; El-Aziz et al. 2017; Ghaderpoori et al. 2018a, b; Keramati, Miri et al. 2018). To estimate the total potential health effects of noncarcinogenic caused by exposure to a mixture of metals in cosmetic products, the hazardous index (HI) was calculated. HI is the sum of the HQ values calculated for all heavy metals, for example, nine metals in this study, which was calculated by Eq. 5. In other words, the HI is the total HQ (or THQ). If the HI value < 1, the exposed local population (consumers) is said to be safe; if the HI value ≥ 1, it is considered as not safe for human health (Guerra et al. 2012). After calculating the HQ and the HI, cancer risk (CR) should be calculated. The formula for calculating the CR is shown in Eq. 6. The CR is obtained by multiplying the SED and the SF. SF is the slope factor, and it is defined as the risk generated by a lifetime average amount of 1 mg/kg/day of carcinogenic heavy metals. The permissible or tolerable limits are considered to be 0.0001 to 0.000001 (or 10⁻⁴–10⁻⁶) for a carcinogenic element (Copat et al. 2018). The slope factor for Pb was 0.0085.

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

$$\text{NOAEL} = \text{RFD} \times \text{UF} \times \text{MF} \quad (2)$$

$$\text{SED} = \frac{\text{Cs} \times \text{AA} \times \text{SSA} \times \text{F} \times \text{RF} \times \text{BF}}{\text{BW}} \times 10^{-3} \quad (3)$$

$$\text{HQ} = \frac{\text{SED}}{\text{RFD}} \quad (4)$$

$$\text{HI} = \sum \text{HQ} = \text{HQ}_{\text{Cd}} + \text{HQ}_{\text{Cr}} + \text{HQ}_{\text{Ni}} + \text{HQ}_{\text{Cu}} + \text{HQ}_{\text{Mn}} + \text{HQ}_{\text{Fe}} + \text{HQ}_{\text{Zn}} + \text{HQ}_{\text{Pb}} + \text{HQ}_{\text{Hg}} \quad (5)$$

$$\text{Cancer Risk} = \text{SED} \times \text{SF} \quad (6)$$

Monte Carlo simulation (MCS)

Many factors should take into account in the health risk assessment. Usually, the risk is estimated as spot estimation (SE) (Qu et al. 2012). The SE provides little information about the degree of uncertainty surrounding the risk point in health risk assessment (Mesdaghinia et al. 2016). If uncertainty factors (parameter uncertainty, model uncertainty, and scenario uncertainty) are not taken into account, the information obtained will not be accurate (Koupaie and Eskicioglu 2015, Shahrababki et al. 2018). To overcome this defect, the USEPA (the United States Environmental Protection Agency) recommends using the MCS method (Kumar and Xagorarakis 2010, Rajasekhar et al. 2018). So, the MCS deals with uncertainties. To specify the uncertainty of each effective parameter, in this way, the probabilistic statistics are used. Therefore, MCS can present better health risk identification and exposure assessment (Mesdaghinia et al. 2016, Miri et al. 2018). In this technique, each value of parameter distribution is inserted into the exposure equation randomly, and this process completed many times until the distributions of predicted results, which indicate overall uncertainty of input parameters, are obtained (Jiang et al. 2015, Saha et al. 2017, Miri et al. 2018). All calculations of the MCS were performed using MS Excel.

Results and discussion

In the selected period in Iran, 11 studies were conducted on the measurement of heavy metals in cosmetics. In these studies, cosmetics such as eye shadow, eye pencil, powder, cream, and lipstick were studied. A summary of the heavy metals measured in cosmetic products is shown in Table 1. The metals studied were Cd, Cr, Ni, Mn, Fe, Zn, Pb, and Hg. Cd concentrations ranged from 0.4 to 2.18 µg/g in eye shadow, 0.07 to 1.93 µg/g in eye pencil samples, not detected (ND) to 0.22 µg/g in powder samples, ND to 0.08 µg/g in cream, and ND to 403 µg/g in lipstick samples. Order of Cd mean concentration in the samples was lipstick > eye shadow > eye pencil >

cream > powder. Canada and Germany have set the maximum amount allowed (MAA) for Cd as an impurity in cosmetic products at 3 and 5 µg/g, respectively (Iwegbue et al. 2016). Among all types of cosmetic products, the only concentration of Cd in lipstick was higher compared to Germany and Canada guidelines. In the cosmetics industry, Cd (cadmium sulfide, cadmium selenide) is used as a color pigment in many cases (e.g., cadmium green, cadmium yellow, etc.) and its ability to produce various colors in combination with other elements (Godt et al. 2006; Corazza et al. 2009). Cr concentrations ranged from 30.8 to 43.97 µg/g in eye shadow, 34.36 to 47 µg/g in eye pencil samples, 32.51 to 51.98 µg/g in powder samples, 29.15 to 65.27 µg/g in cream, and 27.78 to 110.72 µg/g in lipstick samples. Order of Cr mean concentration in the samples was lipstick > powder > cream > eye pencil > eye shadow. In the study of Iwegbue et al., the highest concentration of Cr was observed in eye shadows. In the cosmetics industry, Cr₂O₃·2H₂O (chromium oxide green) and Cr(OH)₃ (chromium hydroxide green) are used as coloring agents (Iwegbue et al. 2016; El-Aziz et al. 2017). Ni concentrations ranged from 19.88 to 32.05 µg/g in eye shadow, 30.73 to 41.4 µg/g in eye pencil samples, 22.99 to 43.81 µg/g in powder samples, 9.63 to 37.94 µg/g in cream, and 9.1 to 74.46 µg/g in lipstick samples. Order of Ni mean concentration in the samples was eye pencil > powder > lipstick > eye shadow > cream. Eye cosmetics like eye shadows and eye pencil are composed of many compounds like amorphous carbon, zincite (ZnO), galena (PbS), minimum (Pb₃O₄), sassolite (H₃BO₃), magnetite (Fe₃O₄), goethite cuprite (Cu₂O), (FeO(OH)), and talc (Mg₃Si₄O₁₀(OH)₂). The concentration of Cd, Cr, Pb, Ni, Zn, and Cu was 2350 ± 20, 2270 ± 240, 61,900 ± 1900, 3380 ± 210, 16,190 ± 120, and 36,240 ± 250 ng/g, respectively. Cu concentrations ranged from 6.68 to 56.77 µg/g in eye shadow, 3.49 to 73.37 µg/g in eye pencil samples, 3.5 to 58.88 µg/g in powder samples, 2.3 to 28.54 µg/g in cream, and 6.7 to 5.42 µg/g in lips stick samples. Order of Cu mean concentration in the samples was eye pencil > eye shadow > powder > cream > lipstick. Mn concentrations ranged from 42.2 to 165.57 µg/g in eye shadow, 232.41 to 401.13 µg/g in eye pencil samples, 21.5 to 157.43 µg/g in powder samples, 3.51 to 3.71 µg/g in cream, and 8.93 to 24.84 µg/g in lipstick samples. Order of Mn mean concentration in the samples was eye pencil > eye shadow > powder > lipstick > cream. Studies have shown that there are no international standards for the presence of metals such as Ni, Cr, and Co nitrate in cosmetics (Iwegbue et al. 2016). The findings of Iwegbue et al. showed that there is a high concentration of Mn (2100 µg/g) in some cosmetics such as a brand of eyeliner. The health effects (as cumulative effects) of contact with Mn are menstrual blood loss and pain (Iwegbue et al. 2016; El-Aziz et al. 2017). Fe concentrations ranged from 1008 to 1332.2 µg/g in eye shadow, 1254 to 1281.5 µg/g in eye pencil samples, 963.49 to 1320 µg/g in powder samples,

157.71 to 534.78 $\mu\text{g/g}$ in cream, and 804.3 to 1382 $\mu\text{g/g}$ in lipstick samples. Order of Fe mean concentration in the samples was eye pencil > lipstick > powder > eye shadow > cream. In other studies, also, high concentrations of Fe in cosmetic products have been reported. Ajayi et al. reported high Fe concentrations in graphite-based Kwali (0.98–1.2%) and Pb-based Kwali (more than 4300 $\mu\text{g/g}$) (Funtua and Oyewale 1997). High concentrations of Fe can reflect the use of natural resources in the provision of cosmetics (Iwegbue et al. 2016). Dalmazio and Menezes reported high concentrations of Fe in compact face powder (13.77 to 36 mg/g), Brazilian eye shadow (11.63 to 103.4 mg/g), and facial concealer/lipstick (4.259 to 24.26 mg/g) (Miyajima et al. 2002). The health effects (as cumulative effects) of contact with high concentrations of Fe are colorectal cancer and finally cellular death (Senesse et al. 2004; El-Aziz et al. 2017). Zn concentrations ranged from 32.1 to 318.76 $\mu\text{g/g}$ in eye shadow, 7.98 to 82.29 $\mu\text{g/g}$ in eye pencil samples, 16.12 to 242.13 $\mu\text{g/g}$ in powder samples, 3.62 to 10.22 $\mu\text{g/g}$ in cream, and 3.64 to 216.53 $\mu\text{g/g}$ in lips stick samples. Order of Zn mean concentration in the samples was eye shadow > powder > lipstick > eye pencil > cream. In most studies on cosmetics in different countries, a significant concentration of Mn has been detected (Sainio et al. 2000; Al-Dayel et al. 2011; Al-Qutob et al. 2013; Omenka and Adeyi 2016). In the study of Iwegbue et al., the highest and lowest concentrations of Zn were observed in face powder (3300 $\mu\text{g/g}$) and eyeliner (29.9 $\mu\text{g/g}$), respectively (Iwegbue et al. 2016). The Zn used in anti-dandruff shampoos has been shown to cause allergic contact dermatitis (Salvador et al. 2000; El-Aziz et al. 2017). The high concentrations of Fe, Zn, Mn, and Cu in some cosmetics are due to the use of the pigments of natural or inorganic like iron oxides, mica, carmine, aluminum powder, titanium dioxide, and manganese violet (Al-Saleh et al. 2009; Iwegbue et al. 2016). Pb concentrations ranged from 81.02 to 140.57 $\mu\text{g/g}$ in eye shadow, 96.37 to 218.35 $\mu\text{g/g}$ in eye pencil samples, 88.32 to 280.9 $\mu\text{g/g}$ in powder samples, 11.54 to 129.26 $\mu\text{g/g}$ in cream, and 109.66 to 198.49 $\mu\text{g/g}$ in lips stick samples. Order of Pb mean concentration in the samples was eye pencil > powder > lipstick > eye shadow > cream. United State Food and Drug Administration (USFDA) and Health Canada's National Health Products Directorate (NHPD) selected the limit for Pb in cosmetic applied to the human skin as 10 and 20 $\mu\text{g/g}$, respectively (USFDA 2007; Iwegbue et al. 2016). Tsankov et al. reported high concentrations of Pb (41.1 $\mu\text{g/g}$) in the samples in cosmetics (cleansing milk, cream, lipsticks, shampoo, hair dyes, rouge, eye shadow, powder, toothpaste, and fond de tient), which was higher than the recommended values (Tsankov et al. 1982). In some local cosmetics (a local eyeliner, Tiro), high concentrations of Pb (323 $\mu\text{g/g}$) are also reported (Iwegbue et al. 2016; El-Aziz et al. 2017). Hg (or mercury) concentrations ranged from ND to 0.0017 $\mu\text{g/g}$ in eye shadow, ND to 0.0017 $\mu\text{g/g}$ in

eye pencil samples, ND to 0.0025 $\mu\text{g/g}$ in powder samples, and ND and 0.0149 to 198.49 $\mu\text{g/g}$ in lipstick samples. In Abd El-Aziz et al. study, the maximum mercury concentration in eye shadow (0.075 $\mu\text{g/g}$) was determined (El-Aziz et al. 2017). In the study of Zhang et al., the maximum mercury concentration in cream (250 $\mu\text{g/g}$) was determined (Zhang et al. 2011). Murphy et al. in Cambodia measured the concentration of mercury in 19 skin creams. In nine types, the concentration of mercury was reported to be 19 to 12,590 $\mu\text{g/g}$. In ten types, also, the concentration of mercury was less than 0.5 $\mu\text{g/g}$ (Murphy et al. 2009). All the cosmetics in this research had a Hg concentration below the international guidelines of the USFDA (1 ppm) and Health Canada (3 ppm). The health effects (as cumulative effects) of skin contact with Hg are long-lasting neurological and kidney impairment (El-Aziz et al. 2017). Order of Hg mean concentration in the samples was lipstick > eye pencil > eye shadow.

Because of its composition (e.g., heavy metals), kohl as a cosmetic is considered by the US FDA as unsafe cosmetics for use and as an illegal substance to be imported or sold in the USA. While in some countries such as Pakistan, Iran, and Egypt, it is still largely sold in markets without any legal control (El-Aziz et al. 2017). In a study by Asgari Rad et al., in Iran, high concentrations of these compounds in Khol were reported (Asgari Rad et al. 2016).

As previously mentioned, the MoS index was calculated to determine the risk of human contact with metallic impurities in cosmetic products used by humans (based on Eq. 1). Table 2 shows the results of calculations SED and MoS. According to Table 2, the highest and lowest amount of SED in all types of investigated cosmetic (lipstick, cream, eye pencil, face powder, and eye shadow) are related to Fe and Hg. Only a few studies have reported mercury concentration, based on studied samples. If Hg was not considered, the lowest SED content ($\mu\text{g/kg}$. BW. Day) of heavy metals in lipstick, cream, eye pencil, face powder, and eye shadow was Cu (7.00E-08), Cd (2.39E-06), Cd (2.77E-10), Cd (1.80E-06), and Cd (1.88E-08), respectively. The highest SED of heavy metals Cd, Cr, Ni, Cu, Mn, Zn, Pb, and Hg was observed in cream, cream, cream, cream, face powder, face powder, face powder, cream, and face powder, respectively (Table 2). The provisional tolerable daily intake (PTDI) and the provisional tolerable weekly intake (PTWI) of Cd are set at 1 and 2 $\mu\text{g/kg}$. BW. day, respectively (Iwegbue et al. 2016). Therefore, the mean of SED of Cd (1.05E-06 $\mu\text{g/kg}$. BW. Day) in the cosmetics sold in Iran is much lower than the values of PTDI and PTWI. The PTDI of Pb is set at 3.6 $\mu\text{g/kg}$. BW. Day. Therefore, the mean of SED of Pb (7.04E-04 $\mu\text{g/kg}$. BW. Day) in the cosmetics sold in Iran is below the PTDI (Iwegbue et al. 2016). The tolerable daily intakes (TDI) of Ni and Cr are 720 and 200 $\mu\text{g/kg}$, respectively (Organization 2004). The estimated SEDs for Ni (1.59E-04 $\mu\text{g/kg}$. BW. Day) and Cr (3.09E-04 $\mu\text{g/kg}$. BW. Day)

Table 2 The systemic exposure dosage (SED) ($\mu\text{g/kg}$. BW. day) and the Margin of Safety (MoS) calculated for cosmetic products in Iran

		Cd	Cr	Ni	Cu	Mn	Fe	Zn	Pb	Hg
SED	Lipsticks	1.05E-06	5.26E-07	2.60E-07	7.00E-08	1.61E-07	9.04E-06	4.46E-07	1.15E-06	1.16E-10
	Cream	2.39E-06	1.19E-03	5.20E-04	3.73E-04	1.41E-04	7.63E-03	1.71E-04	2.44E-03	ND
	Eye pencil	2.77E-10	1.80E-08	1.90E-08	1.47E-08	1.44E-07	5.79E-07	2.27E-08	7.27E-08	7.77E-13
	Face powder	1.80E-06	3.52E-04	2.75E-04	1.44E-04	5.90E-04	9.78E-03	9.09E-04	1.26E-03	2.05E-08
	Eye shadow	1.88E-08	5.34E-07	3.64E-07	3.30E-07	1.23E-06	1.54E-05	2.78E-06	1.48E-06	1.03E-09
MoS	Lipsticks	1.54E+07	7.05E+05	1.19E+07	1.05E+08	1.05E+08	8.11E+06	3.46E+08	3.73E+05	4.49E+08
	Cream	4.19E+04	2.80E+02	5.21E+03	2.34E+04	1.13E+05	1.19E+04	2.08E+05	3.91E+02	ND
	Eye pencil	1.58E+09	1.69E+07	1.09E+08	8.26E+08	1.01E+08	1.21E+08	2.86E+09	6.18E+06	5.15E+10
	Face powder	5.54E+04	8.85E+02	8.01E+03	1.10E+05	4.31E+04	7.28E+03	8.41E+04	4.08E+02	1.95E+06
	Eye shadow	8.78E+06	5.76E+05	5.71E+06	2.74E+07	1.56E+07	4.61E+06	2.79E+07	2.84E+05	3.89E+07
USEPA - RfD		0.10E-02	0.10E-02	0.20E-01	0.40E-01	1.40E-01	7.00E-01	3.00E-01	0.40E-01	0.30E-03

ND, not detected

RfD, reference oral dose

constituted less than 1% of their respective TDI values. The selected PTDI for Cu is 5000 $\mu\text{g/kg}$. BW. Day (Organization 2004). The intake of Cu ($1.04\text{E-}04$ $\mu\text{g/kg}$. BW. day) from the use of the cosmetics products sold in Iran is less than 1% of the tolerable intake value of Cu. The recommended daily intakes (RDI) of Zn and Fe are set at 12 and 12.5 mg/day, respectively (National Research Council 1989). Also, the recommended dietary allowance (RDA) value for Mn is 10 to 18 mg/day. The estimated SEDs of Mn ($1.47\text{E-}04$ $\mu\text{g/kg}$. BW. day), Fe ($3.49\text{E-}03$ $\mu\text{g/kg}$. BW. day), and Zn ($2.16\text{E-}04$ $\mu\text{g/kg}$. BW. day) in the cosmetics sold in Iran are below their respective recommended intake values. Based on Table 2, the MoS values calculated for different metals were higher than the established standard by World Health Organization. Therefore, this cosmetic can be used safely. Of course, the use of cosmetics for a long time can lead to the accumulation of heavy metals and to relative harmful health effects. According to the WHO proposal, in order to safely use cosmetics, the MoS index should be more than 100 (SCCS 2012; Iwegbue et al. 2016). In Egypt, Abd El-Aziz et al. examined the MoS index in cosmetics used in this country. The results

show that in the examined samples, the value of this index was higher than the standard (El-Aziz et al. 2017). The findings of Iwegbue et al. in Nigeria showed that the MoS value was higher than the standard values (Iwegbue et al. 2016). In addition, face powder had lower MoS values compared with facial cosmetic products studied (Table 2). The MoS values showed that there is little risk associated with the heavy metals in these cosmetics except for face powder. Iwegbue et al. reported that the values of MoS in cosmetic samples was higher than other types (Iwegbue et al. 2016). It is possible that health risks increase in three different paths: dermal contact, oral, and inhalation. Cosmetic materials from the two main paths dermal contact and oral can be related to the human body. But the oral seems to be the main and most important route (El-Aziz et al. 2017). Eq. 4 (HQ) and Eq. 5 (HI) were used to calculate the noncarcinogenicity risk of contact with cosmetic products. Table 3 presents the results for the HQ and HI calculated. According to Table 3, the amount of HQ in the cosmetic samples examined for various metals is below 1. The mean HQ for Cd, Cr, Ni, Cu, Mn, Zn, Pb, and Hg was $1.05\text{E-}03$, $1.03\text{E-}01$, $7.95\text{E-}03$, $2.59\text{E-}03$, $1.05\text{E-}03$, $4.98\text{E-}03$, $7.22\text{E-}04$, 1.85E-

Table 3 The hazardous quotient (HQ) and hazardous index (HI) calculated for cosmetic products in Iran

	HQ									Total HQ or HI
	Cd	Cr	Ni	Cu	Mn	Fe	Zn	Pb	Hg	
Lipsticks	1.05E-03	1.75E-04	1.30E-05	1.75E-06	1.15E-06	1.29E-05	1.49E-06	2.88E-04	2.90E-07	1.55E-03
Cream	2.39E-03	3.98E-01	2.60E-02	9.33E-03	1.01E-03	1.09E-02	5.69E-04	6.10E-01	ND*	1.06E+00
Eye pencil	2.77E-07	6.01E-06	9.51E-07	3.67E-07	1.03E-06	8.28E-07	7.56E-08	1.82E-05	1.94E-09	2.77E-05
Face powder	1.80E-03	1.17E-01	1.37E-02	3.60E-03	4.22E-03	1.40E-02	3.03E-03	3.14E-01	5.13E-05	4.72E-01
Eye shadow	1.88E-05	1.78E-04	1.82E-05	8.25E-06	8.80E-06	2.20E-05	9.28E-06	3.71E-04	2.57E-06	6.37E-04

*ND, not detected

01, and $1.35\text{E-}05$, respectively. The highest amount of HQ ($6.10\text{E-}01$) was found in Pb, which was observed in the cream. The HI or THQ to lipstick, cream, eye pencil, face powder, and eye shadow were $1.55\text{E-}03$, $1.06\text{E+}00$, $2.77\text{E-}05$, $4.72\text{E-}01$, and $6.37\text{E-}04$, respectively. As shown in Table 3, the amount of HI in cream is higher than 1. The findings of this work are in agreement with those reported by El-Aziz et al. and Iwegbue et al. (Iwegbue et al. 2016; El-Aziz et al. 2017). In the case of continuous use cosmetics, some heavy metals can potentially improve the cancer risk in humans. Eq. 6 (risk) was used to calculate the oral cancer risk of contact with cosmetic products (oral pathway). The oral cancer risk of Pb to lipstick, cream, eye pencil, face powder, and eye shadow was $1.32\text{E-}12$, $5.95\text{E-}06$, $5.29\text{E-}15$, $1.58\text{E-}06$, and $2.20\text{E-}12$, respectively. The maximum value of oral cancer risk was $5.95\text{E-}06$ in cream, and the minimum value was $5.29\text{E-}15$ in eye pencils. The results of this section were concordant with Abd El-Aziz et al. study (Iwegbue et al. 2016).

Conclusion

This study was conducted on cosmetic products in Iran. The main objective of our study was to assess the health risks of heavy metals as impurities in Iranian cosmetics. A Monte Carlo simulation was used to investigate uncertainties also. Heavy metals data of cosmetics were extracted from studies carried out at intervals 2010–2018. After primary searching, 11 studies were found. The index of the MoS was used to assess the risk of contact with heavy metals in cosmetic products. The health risks carcinogenic (CR) and noncarcinogenic (HQ and HI or THQ) were calculated. Also, to specify the uncertainty of each effective parameter, in this way, the probabilistic statistics are used. The metals studied were Cd, Cr, Ni, Mn, Fe, Zn, Pb, and Hg.

Human beings are always exposed to various products and chemicals. By increasing demand of the population and increasing the number of used substances, humans are ever more exposed of unskilled materials. The results of this study indicate that more attention should be paid to materials or products that are used directly in contact with humans skin. So, a constant monitoring by health authorities on various products represents both the principal consumers health maintaining modality or control of safety of the same products.

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