Chapter

Heavy Metals in Cosmetics

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Abstract

This review provides a comprehensive insight into the content of five heavy metals found in cosmetics and their effects at the site of application and on several organs via the dermal route of administration. Regulation of these products is very limited with little information on limits of these metals at the disposition of manufacturers. Lead and arsenic are considered to be contaminants in cosmetics whereas cadmium may be present as a coloring agent besides being a contaminant. Nickel is notorious for its association with allergic chronic dermatitis. Though mercury is rarely present in cosmetics, it has been found in significant quantities in skin lightening creams. A multi-variate meta-analysis was conducted to determine the relationships between the five metals and any possible differences between the sixteen categories of formulations used for facial and body skin care and cosmetic purposes. In general, lipsticks, eye shadows, face paints, make-up foundation and skin lightening creams exhibited a high amount of heavy metals superior to the levels of these metals in other facial and body products. The outcome of this analysis urges regulators and manufacturers to consider routine monitoring for the presence of these metals in cosmetics.

Keywords: lead, cadmium, nickel, mercury, arsenic, metallokinetics, metallodynamics

1. Introduction

A cosmetic is any product that is intended to be applied superficially to the human body to keep the treated part in good health. In this process, the cosmetic should not alter the physiological functioning of the body [1]. The use of cosmetics has been practiced since antiquity as apart from cleansing, cosmetics also beautify and alter the appearance hence making the individual more appealing and attractive. There are a plethora of ingredients that were and are used in the formulation of cosmetics. The general intended purposes of cosmetics have not changed throughout centuries and millennia, the formulation of these cosmetics has undergone significant transformations, some of which include the processing and the ingredients used for their formulation. The processing has changed from a domestic/small scale production to cater for a small number of individuals to industrial/large scale production to cater for a wider consumer population with the use of worldwide advertising and social media. On the other hand, the constitution of cosmetics has also changed with time. With industrialization and the use of petrochemically-derived substances, the cosmetic formulation changed from one based on natural products to one which is mainly based on petrochemicals. However, during these past decades, there was a change in the constitution of cosmetics, to include more natural ingredients, due to the great interest and concern by consumers.

As a consequence, the massive production of cosmetic products with a wide range of ingredients, has raised several health and safety concerns. Nowadays, cosmetics are generally regulated [2]. One major concern is that cosmetics overlap in use and functionality with topical medicines. Several regulatory bodies attempted to devise a proper definition for cosmetic products with the intent to segregate cosmetic products from topical medicinal products. Within the European Union (EU), Council Directive 93/35/EEC [3] amending Council Directive 76/768/EEC, a definition for cosmetic products was laid down in article 1 of the directive. In the first part of the definition, the external body parts which may be treated with cosmetics are mentioned. Other body parts are excluded and this eludes to the understanding that cosmetic products should not be applied to these other body parts. The second part is related to the 'activities' which are allowed for a product to be considered as a cosmetic. These distinguish cosmetics from topical medicinal products which are intended for the control or treatment of conditions or else in making a medical diagnosis [4]. However, whereas topical medicinal products are meticulously scrutinized before their placement on the market, cosmetics do not undergo rigorous testing. Nevertheless, for cosmetic products, the manufacturers, distributors and importers are responsible for the safety of cosmetic products being placed on the market [5]. The latter regulation also states clearly what ingredients are prohibited for their presence in cosmetic products. Amongst the prohibited ingredients several heavy metals are also included. Whereas some metals and their salts are completely prohibited (e.g., tin, arsenic, cadmium, nickel and lead), other metals and their salts are either allowed with a specific limit or else only specific salts for such metals are allowed (e.g., cobalt, chromium, gold, mercury and selenium amongst others). Such additions may not be intentional as the addition of some minerals may originate from a natural source. Heavy metals, such as cadmium (Cd), lead (Pb), nickel (Ni), arsenic (As) and mercury (Hg) were also detected in numerous other raw materials which can be used for the production of cosmetics considered as natural products. These include honey [6], argan oil [7], and olive oil [8] as well as citrus essential oils [9].

Because of this, some authorities also impose limits on the presence of certain metals in cosmetics. For example, The Cosmetic Ingredient Review Expert Panel established by Food and Drug Administration (FDA) in the USA issued limits on As (5 ppm), Pb (5 ppm) and other heavy metals (20 ppm) [10]. The World Health Organisation (WHO) set limits for Pb (10 ppm), Cd (0.3 ppm) and Hg (1 ppm). The EU's limits for Pb, Cd and chromium are 0.5, 0.5 and 1.0 ppm, respectively, while the Canadian authorities set limits for Pb (10 ppm), Cd (3 ppm) and Hg (3 ppm) [11]. However, there tends to be inconsistency in the type of metals and the limits for the metals by different authorities. As a consequence, this lack of harmonization leads to confusion amongst authorities as regulators, several manufacturers as producers and the general population as consumers. Despite all this, several researchers investigated the potential presence of heavy metals in a wide range of products. This review aims at compiling a large number of studies related to the presence of heavy metals in cosmetics and their potential harm in human beings.

2. Heavy metals

Heavy metals are elements that are primarily found in the d and p-blocks of the periodic table showing a metallic character and an ability to form salts. Some sources specify that heavy metal should have a high density [12]. Such metals include lead, cadmium, nickel, mercury and arsenic amongst others.

The main concern is that heavy metals are ubiquitous and are present in several matrices both living and non-living. Particularly in living matrices, heavy metals may interfere with beneficial metals some of the latter being replaced by heavy metals that would result in the erratic physiological functioning of bodily systems. This is not an issue related only to mammals and humans, but such erratic behavior, in terms of morbidity and mortality has been observed in other animals, such as insects [13], and also in plants. Some of these heavy metals accumulate in biological systems and one source for such accumulation is the daily and/or repeated use of cosmetic products such as face powders, lipsticks and eye shadows [2]. Some heavy metals are commonly found in cosmetics [14–20].

3. Metallokinetics and metallodynamics within the body

The absorption, distribution, metabolism, excretion and interaction of heavy metals with bodily systems are complex processes that are not yet fully understood. This is even more complex when considering that some cosmetics are applied and rinsed shortly after (such as toothpastes, shampoos and conditioners and cleansers), others are applied and allowed for a few minutes to hours (such as body creams, lotions and facial makeup) and those that are applied and remain in contact with the skin for several hours (such as nail polish and hair dyes). The kinetics and dynamics of metals present in these cosmetic products, vary significantly in their fate and their extent of effects [21].

With the application of cosmetic products, the mode of entry of heavy metals in the body is via dermal or topical application. These metals may have either topical and/or systemic effects in humans [22]. At the site of application, heavy metals may accumulate in the stratum corneum causing local effects, that may be exhibited as allergic contact dermatitis associated with an excess of a metal (such as Ni, cobalt and chromium) at the site [23, 24] because of their binding to keratin [22]. In the case of Ni, this metal has a high affinity to the histidine component of the filaggrin in the stratum corneum [25]. Although, the mechanism by which heavy metals damage the skin is not yet fully understood, it is believed that this may be provoked by the formation of free radicals and/or by an inflammatory effect [26]. It was discovered that metals may accumulate with repeated application of contaminated cosmetics. Consequently, such areas would serve as reservoirs and hence lead to long-term exposure of the individual to the metal, even when such cosmetics are no longer applied [27]. The exposure of the skin to heavy metals may extend the dermal inflammation to the systemic system [26]. Ni can only penetrate and reach the general circulation, when damage is provoked by other metals [28]. Other metals such as Hg, Pb and Cd may enter the general circulation through the skin layers and transported to various organs within the body [29, 30]. This permeation can occur via sweat glands and hair follicles. Besides direct contact, oral ingestion of heavy metals may occur by the application of cosmetic products either to the lips (e.g., lipstick, lip gloss and lip balms) or within the buccal cavity (toothpastes, mouthwashes and breathe sprays) or by hand to mouth transfer of any cosmetic applied to any body part [31]. Thinner facial skin is more permeable than skin elsewhere [32]. Several studies show that certain heavy metals (such as Pb, Hg and Cd) found in topical cosmetics are found in high concentrations in the blood, urine and internal organs of individuals who use cosmetics when compared to individuals who do not [33–40]. Cosmetics that are applied directly to the skin may contain moisturizing agents that increase skin

permeation that may allow the entry of xenobiotics, to which some heavy metals may be bound, into the general circulation [41]. Apart from the binding of heavy metals to exogenous substances [42], these may also bind to endogenous biological molecules, hence replacing the beneficial metals. These metals may bind to several functional groups such as the amine, carboxylic and thiol function groups present in several proteins, some of which have functional roles (such as enzymes), while others have structural roles (such as collagen, keratin, actin and myosin). These metals can also bind to nucleic acids which may lead to defective DNA and RNA synthesis that may result in carcinogenesis. The application of underarm products has been hypothetically associated with the possibility of breast cancer [43]. Therefore, heavy metals provoke several toxic effects at the cellular and molecular levels [44, 45].

Several authors reported the presence of heavy metals in cosmetic products. This review gives an insight into the presence and effects of the most notorious and underestimated heavy metals in cosmetics products. The metals under discussion are lead, cadmium, nickel, mercury and arsenic.

4. The presence of typical heavy metals in cosmetics and their effects

4.1 Lead

One of the most studied heavy metals is lead. Lead is not normally used for its potential properties but it is rather considered as a contaminant with serious effects on human health. When a lead comes in contact with vital organs, it is neurotoxic, nephrotoxic and hepatotoxic [46, 47] and may provoke effects also on the reproductive system [48]. Lead can also affect fetal development through its passage via the placenta [49, 50]. Some studies have shown that it is considered a potential carcinogen to humans [51]. It has been reported that the level of Pb in the blood of consumers who use eye cosmetics was threefold higher than that of non-consumers [52]. Lead is acquired from industrial dust and fumes, car emissions, industrial chemicals such as old paints and pesticides, and a burning of fossil fuels. Food contamination may occur from some of these sources. Authorities worldwide are in a continuous struggle to establish permissible limits for Pb. The World Health Organization established a limit of 10 ppm [53]. The permissible level according to [54] is 0.1 mg/l. The FDA established a maximum permissible content of 10 ppm for Pb in color additives for the manufacture of cosmetics using Good Manufacturing Practices [10]. However, in color additives, the Pb content should not exceed 20 ppm [55]. Lead and its salts are prohibited in any cosmetic product within the EU [5]. Health Canada established a limit of 10 ppm for lead in cosmetic products [11].

As shown in **Tables 1**–**3**, several researchers investigated the presence of lead in several cosmetic products. The lipstick group is one of the most widely investigated groups with over fifteen citations. Only one study reported the absence of Pb in lipsticks [67, 70] whereas three other studies reported negligible Pb content in lipsticks [56–58] as their lower limit. Four studies showed a significantly high lead content (73.1–3760 ppm) [14, 16, 18, 57]. Most studies reported a Pb content that is within the 20 ppm permissible limit established by the FDA [59]. Some studies also tried to establish any differences between the high- and low-priced lipsticks (0.06–0.106 ppm) [60]. Eyeshadows ranks second in terms of investigated groups for Pb content. Four studies reported negligible Pb content in eyeshadows [31, 71–73] as their lower end. Whereas some studies have reported low Pb content as their lower end, the

	Pb	Cd	Ni	Hg	As
Lipsticks	<DL-252.4 [14, 18, 45, 56–66] 0.27–3760 [16]	ND-60.20 [14, 18, 45, 56, 58, 60–69]	ND-22.8 [18, 45, 56, 60–62, 64, 66, 70]	<DL to 80.00 [58, 61–63]	0.01–6.931 [58, 62, 63]
Eye-shadows	<DL-81.5 [16, 19, 31, 58, 61, 62, 65, 71–74]	<DL-55.59 [19, 58, 61, 62, 65, 71, 72, 74]	< 0.5–359.4 [19, 31, 61, 62, 71, 72, 74]	<DL-181.00 [58, 62]	<DL-1630 [58, 62, 75]
Eyebrow pencils and eye liners	0.109–61.22 [58, 59, 62, 63]	ND-1.12 [58, 62, 63]	2.1–10.52 [62]	ND-67.42 [58, 62, 63]	ND-2.071 [58, 62, 63]
Mascaras	ND-12.51 [58, 59, 73]	ND-0.034 [58]	ND-0.028 [76, 77]	ND-0.002 [58]	0.050–1.656 [58]
Make-up foundation	<DL to 190 [60, 61, 63, 64, 78]	<DL to 17 [45, 60, 61, 63, 64]	<DL to 13.1 [60, 61, 64]	48.99–60.77 [63]	0.12–1.0 [63]
Face paints	0.02–370 [79]	0.01–19.2 [79]	7.6 ppm [79]	ND-0.004 [69]	0.125.0 [79]
Face cream	ND-1.9 [62]	ND-0.37 [14, 62]	ND [70]	ND-1.27 [62]	ND-0.171 [62]
Toothpaste	ND-18.092 [21, 80, 81]	ND-2.490 [80–82]	0.025–18.535 [80–82]	ND-13.14 [81, 83]	0.06–26.94 [83]

Table 1.
The content of heavy metals in face products; cosmetics and face care products.

	Pb	Cd	Ni	Hg	As
Body lotions	<DL to 47.5 [61, 62]	ND [62]	ND-0.003 [62]	<DL to 47.5 [61, 62]	ND-0.007 [62]
Hair shampoos and conditioners	0.66–54.56 [14, 62]	ND [14, 62]	0.01–0.06 [62]	ND-21.08 [62, 83]	0.002–0.2 [62, 84]
Cleansers	0.04–22.14 [14, 62]	ND [14]	ND-0.08 [62]	ND-0.72 [62]	ND-0.009 [62]
Lotions	0.068–8.29 [64]	0.007–2.13 [64]	0.012–6.29 [64]	18.98–19.02 [83]	1.537–1.543 [83]
Hair dyes and creams	0.402–17.70 [17, 63, 64]	0.001–1.11 [63, 64]	0.081–4.167 [64]	53.74–90.32 [63]	0.16–0.71 [63]
Tonic creams	0.35–0.55 [85]	0.35–0.55 [85]	3.40–4.70 [85]	—	—
Beauty cream	14.38–50.39 [14, 86]	2.40–6.27 [86]	0.0175–5.09 [87, 88]	47.17–124.8 [83]	5.08–10.74 [83]

Table 2.
The content of heavy metals in body products.

higher end exceeded the 20 ppm limit established by FDA [16, 19, 61, 71, 74]. Other eye products include eyebrow pencils (0.109–18.60 ppm) [58, 62, 63] and mascaras (ND-12.51 ppm) [58, 59, 73], all within the 20 ppm limit established by the FDA.

	Pb	Cd	Ni	Hg	As
Skin lightening creams	<DL-143 [21, 60, 61, 64, 89]	0.1–1.276 [60, 64, 89]	2.59–11.17 [60, 64]	<DL-126,000 [15, 53, 61, 70, 89–94]	0.7–12.30 [53, 89]
Sunblock cream	ND-6.889 [62, 64]	ND-0.155 [62, 64]	ND-12.37 [62, 64]	ND-1.62 [62]	ND-0.01 [62]

Table 3.
The content of heavy metals in face and body products.

There is only one study that reported Pb levels of 61.218 ppm in mascaras [59]. Face products vary significantly in their Pb content. Make-up foundation and face powders contain negligible Pb content up to 190 ppm as reported by [61]. Other studies did not exceed a content of 22.57 ppm [60, 63, 64], although one study reported a maximum of 41 ppm [78]. Face washes exceed the FDA limit (24.06–40.61 ppm) [14] and face creams contain minimal content of Pb (0.77 ± 1.13 ppm) [62]. Cosmetic face paint is a potential threat to frequent consumers as reported levels go up to 16.6 ppm [79]. Most hair products do not pose a potential problem as reported for hair shampoos, conditioners and dyes [17, 62–64]. Only one study reported a level of 54.56 ppm in hair products [14]. Several studies investigated body products that are applied over a larger surface area than those mentioned previously. Beauty creams contain a considerable amount of Pb with levels reaching 50.39 ppm [14, 86]. Although, somebody lotions contain low Pb levels [62], one study shows also high Pb content in such products [61]. This same study also reports a high Pb level in skin-lightening creams (up to 43.04 ppm) alongside another study showing a maximum level of 143 ppm [89]. On the other hand, two studies show low Pb contents (<4.015 ppm) [60, 64]. Cleansers and lotions also contain low Pb levels (< 22.14 ppm) [14, 62, 64]. Products that are applied to the buccal cavity include toothpaste. These may pose a problem in addition to mucosal absorption, Pb can be also ingested and absorbed via the gastrointestinal tract. In some studies, the level of Pb in toothpaste is minimal (0.036 ppm) [80], however, in other studies, the highest levels were 12.04 ppm [81] and 18.092 ppm [21].

Lead is considered as a contaminant that is present to different extents in various cosmetic preparations. Several authorities recognize Pb as a toxic metal by setting up limits for its presence in cosmetics.

4.2 Cadmium

Cadmium is one of the metals that has been used in cosmetics for its colored salts, ranging from deep yellow to orange [2]. It has been associated with several toxicities in humans, mainly attributed to its absorption after topical application of several cosmetics [49, 86, 95] though this is very low (0.5%). Topically, it may cause irritant dermatitis [96]. The main concern with Cd is that it tends to accumulate in human tissues and then release slowly into the general circulation. However, it normally binds to the keratin. Systemically, it mainly affects the skeletal, reproductive, metabolic [88], respiratory and renal systems [97, 98]. It has been associated with osteoporosis, diabetes, lung cancer and kidney damage [99]. It contributes also to skin ageing as it may provoke oxidative stress [25]. Despite of its presence in cosmetics, it may be found in several sources such as industrial wastes, agrochemicals (pesticides and fertilizers) and batteries. According to the WHO, the permissible limit for cadmium

is 0.3 ppm [53]. The permissible level according to [54] is 0.06 mg/l. The oral limit for Cd is 0.09 μg/kg to 3 ppm as given by USP for nutritional supplements. Cadmium and its salts are prohibited in any cosmetic product within the EU [5]. Health Canada established a limit of 3 ppm for Cd in cosmetic products [11].

Cadmium is another metal, which is banned by several authorities but still found in several cosmetics, as reported by several researchers (**Tables 1**–**3**). One of the studies that reports the absence of Cd in lipsticks was conducted by [67]. Several other studies reported levels that were lower than 0.002 ppm and levels that reached content of 60.20 ppm. Despite this, only two studies showed levels of Cd higher than 5 ppm [65, 68]. Due to possible ingestion, lipstick use may be linked to systemic toxicity. A study established a difference between high-priced (0.34 ± 0.20 ppm) and low-priced (0.89 ± 0.58 ppm) lipsticks [60]. Although, eye shadows may contain the deep yellow to orange pigments more than lipsticks, the Cd content of eye shadows as reported by several researchers did not exceed 3 ppm [19, 58, 62, 63, 71, 72, 74]. However, levels of 8.89 ppm [71] and 55.59 ppm [65] were reported for eye shadows. Another eye make-up was reported to contain low Cd content by three studies. For eyebrow pencils, the maximum content of Cd was 1.12 ppm [63], whereas the content of Cd in mascaras was reported to be lower, i.e., 0.034 ppm [58]. Other facial cosmetics were also reported to contain a low amount of Cd, with levels less than 0.96 ppm [45, 60, 63, 64]. The highest level was expressed to be that of 17 ppm [61] in the make-up foundation. Similarly, Cd levels did not exceed 0.67 ppm and 0.37 ppm in face washes and face creams, respectively [14]. Tonic creams did not exceed a level of 0.55 ppm [85]. In face paints, the average level reported was 0.6 ppm [79]. Cadmium was also absent in hair shampoos and conditions, with levels being below the detection limit [14, 62]. Negligible Cd content was also present in hair dyes with levels not exceeding 1.11 ppm [63, 64]. Body cosmetics are also generally low in Cd with levels not exceeding 0.92 ppm in skin lightening creams [60, 64, 89], 0.121 ppm in sunblock creams [62, 64] and 2.13 ppm in lotions [64]. No cadmium was detected in body lotions [62] and cleansers [14]. The level of Cd in most toothpastes did not exceed 0.058 ppm [80, 81] but a maximum of 2.49 ppm was reported [82].

Although, Cd is considered one of the most common and noxious heavy metals, it seems that its use in cosmetics is very limited. It may be concluded that Cd presence in cosmetics is considered to be a contaminant rather than an ingredient, as a coloring agent.

4.3 Nickel

Nickel is one of the metal impurities which is inevitably found in several natural ingredients used in cosmetic products. Most of the salts containing nickel are green in color, hence also its potential use as a colorant. However, nickel is considered to be a contact allergen that may provoke dermal sensitization, allergies, and dermatitis [100] by direct and often prolonged exposure. Persons have been diagnosed with Ni allergy due to its presence in topical cosmetic products and jewelry [101]. Nickel may also affect the respiratory system which may result in nasal and lung cancer [98]. Despite of the potential use of cosmetics to maintain the skin in a rejuvenating state, Ni in such products may lead to oxidative stress and hence promote skin aging [25]. This may be due to the overexpression of collagenases in the skin leading to the weakening of the skin matrix and a subsequent loss in elasticity [102]. The International Agency for Research on Cancer (IARC) has classified metallic Ni as a potential

carcinogen to humans (Group 2B) and its compounds as carcinogenic (Group 1) [103]. Nickel may be found occurring naturally in soil and volcanic dust. This may be acquired from industrial dust and fumes. Due to the potential skin sensitization, limits for Ni presence in products have been proposed. Limits of 5 ppm [88] and 1 ppm [104] were suggested for certain household products and detergents, respectively. Likewise, in cosmetics, a Ni limit was also proposed particularly aimed for sensitized persons. Most "nickel-free" products on the market, contain less than 1 ppm of Ni [31, 105, 106]. The permissible level is 0.20 ppm according to [107] for oral consumption. Nickel and a number of its salts are prohibited in any cosmetic product within the EU [5]. These include nickel monoxide, dinickel trioxide, nickel dioxide, trinickel disulphide, tetracarbonynickel, nickel sulphide, nickel dihydroxide, nickel carbonate and nickel sulphate.

Due to its possible implications in allergenic reactions, the content of Ni in a number of cosmetic products was reported by a number of research groups (**Tables 1–3**). The risks associated with Ni intoxication is more possible with cosmetics that are potentially ingested. Lipsticks and lip products are amongst these candidates. Most lipstick products investigated by research groups rarely contained less than 0.20 ppm of Ni for oral consumption. Due to the short-term duration of lipstick on the lips, these products are applied frequently by consumers. This may pose a further exacerbation if ingested. The maximum levels in most studies range from 1.61 to 22.8 ppm of Ni in lipsticks [18, 45, 56, 61, 64, 66, 70]. However, in one study it was reported that the mean Ni content was 0.10 ± 0.14 ppm [62]. It was demonstrated that the price has no impact on Ni content of lipsticks (high-priced 8.24 ± 3.29 ppm and low-priced 5.15 ± 4.19 ppm) [60]. Oral consumption may be due to the accidental swallowing of toothpaste. Studies have shown the range of Ni content in most toothpaste is between 0.02 and 2.54 ppm [80, 81] but another study reported maximum levels of 18.535 ppm [82]. Dermal sensitization has been associated with eye cosmetic products. In this situation the 1 ppm threshold is applicable. Several studies have reported levels of Ni which exceed 1 ppm. Only two studies show that the minimum level of Ni in eye-shadows was less than 1 ppm [19, 31]. In several studies, maxima for Ni levels ranged between 4.133 and 359.4 ppm [61, 62, 71, 72, 74]. Nickel has been found in a green eye liner which provoked a form of contact dermatitis in a 47-year-old woman [76] whereas another study reported contact allergy to a Ni-containing mascara [77]. A study reported a mean Ni content of 6.31 ± 4.21 ppm in eyebrow pencils [62]. Most make-up foundation products seem to contain high amounts of Ni, quoting the minimum values above 3 ppm and the maximum values to 13.01 ppm [60, 64]. Only one study reported values being less than the detection limit [61]. In a study on face paints, the average Ni content was 7.6 ppm [79]. However, in other facial formulations such as face washes and creams, the content was reported to be very low with a mean of 0.04 ± 0.11 ppm [14] or not detectable [70] for these formulations respectively. Hair products are of no major concern, as the levels in shampoos and conditions do not exceed 0.06 ppm whereas the highest content of Ni in hair dyes is 4.167 ppm [64]. Body products vary in Ni content. In general, Ni does not exceed 12.37 ppm, but the 1 ppm of Ni is exceeded for most products that include skin lightening creams, sun blocks, tonic creams and body creams [60, 64, 85, 87, 88]. Body lotions and cleansers seem to contain very low Ni contents (<0.08 ppm) [62].

Whereas Ni in mascaras and eye shadows has been implicated in its involvement in allergic chronic dermatitis, several studies have reported that Ni allergy cannot be considered as the main risk factor in patients reporting eye-lid dermatitis [108].

4.4 Mercury

Mercury is one of the heavy metals that is widely used in cosmetic formulations. Although, mercury is known as a shiny, silvery, dense liquid, it may occur in various inorganic and organic compounds. In the inorganic form, such as ammoniated Hg, it is used for its skin lightening properties, whereas in the organic form, such as phenyl mercuric and ethyl mercuric salts, it is used as a preservative in mascaras and eye makeup cleansing products [90, 109]. After dermal application, Hg penetrates through the skin via the hair follicles and sweat glands [29, 96]. During this process, part of the Hg is reduced to the metallic form that accumulates in the skin tissue. Hg blocks tyrosinase in situ, inhibiting the melanin-forming enzyme [110], hence its use in skin-lightening creams [22]. Only one study mentioned that cream had the abbreviation 'precip blanc' on the label, which should suggest that this product contains Hg [36]. Systemically, Hg may exhibit a range of signs which include vomiting, nausea and kidney damage, central nervous sytstem effect which include irritability, tremors, weakness, nervousness, fatigue and memory loss. It may affect also the sensorial systems, that is, loss in hearing, taste and vision. Finally, high Hg content may lead to death [111, 112]. In some instances, following dermal absorption and systemic uptake, Hg may induce autoimmune glomerulonephritis. Studies reveal significant accumulation of mercury in several organs and body fluids, such as hair (22.5 ppm, twice that in non-cosmetic users), blood (up to 233 nmol/l, more than four times than that in non-cosmetic users] and urine (up to 2531 nmol/day, fifty times more than that in non-cosmetic users) [39, 91, 113, 114].

Mercury is a metallic element that is naturally occurring in the environment and its compounds are the most common form that exists naturally in the environment. Due to its ubiquity, several authorities issued limitations for Hg use. For instance, the FDA restricts its use and is regulated in cosmetic products. The FDA allows a maximum level of 1 ppm of Hg in mercury-contaminated lead acetate when used as a colour in cosmetics [10]. Within the European Union, mercury and its compounds are not allowed in cosmetics, whereas phenyl mercuric salts are only allowed as preservatives in eye care products at a maximum allowable level of 70 ppm [5] whereas in the US it is allowed up to a level of 65 ppm by weight [10]. Health Canada allows a maximum Hg content of 1 ppm in cosmetics [11].

The main emphasis of analysis by researchers was conducted on skin-lightening creams due to their interaction with melanin metabolism. Very few studies report levels below the 3 ppm threshold [15, 53, 70] (**Tables 1**–**3**). Other studies reveal values up to 126,000 ppm [61, 89–93]. Although, in some lipstick products, the Hg content was below the detection limit [58, 61, 62], some of these same studies and others reveal contents up to 80 ppm [63]. The status of Hg contamination in eye cosmetic products varies significantly with levels of up to 181 pm in eye shadows [58, 62], 67.42 ppm in eyebrow pencils [58, 62, 63] but levels of up to 0.002 ppm in mascaras [58]. Apart from the make-up foundation where levels of Hg reach a maximum level of 60.77 ppm [63], other face products contain minimal amounts of Hg, such as face creams (0.09 ± 0.37 ppm [62]), sunblock creams (0.41 ± 1.21 ppm [62]) and face paints (<0.004 ppm [69]). In some studies, it was reported that the content of Hg in hair products is below the detection limit [62] whereas in other studies, it reached a maximum of 90.32 ppm [63, 83]. Body care products such as body lotions and cleansers contain varied amounts of Hg [62], with products from the first group with contents up to 47.5 ppm [61]. In some beauty creams, the Hg level reached a

maximum of 124.8 ppm [83]. The presence of mercury in toothpaste has not been widely investigated, but in two studies, the Hg level was reported to reach a maximum of 13.14 ppm [81, 83].

As can be concluded from these studies, Hg is one of the least detected heavy metals in most cosmetics [22], but not in skin-lightening products. Mercury is found intentionally in face and skin care products rather than in products for purely cosmetic use. Apart from skin-lightening properties, Hg compounds are claimed to reduce and remove freckles, treat acne, and prevent and remove wrinkles [22].

4.5 Arsenic

Arsenic is a metalloid that is present ubiquitously as a major contaminant in the environment. Although, it is redox inactive, its target functional groups are sulfydryl groups on proteins which may lead to the depletion of glutathione [115], an essential antioxidant of an amino acid origin, which prevents damage of cellular components caused by radicals and heavy metals. On long-term dermal exposure, As can cause hyperpigmentation and keratosis *in situ*, but systemically it may lead to carcinogenesis and vascular diseases [115, 116]. Though considered as a less significant contaminant in cosmetics than other heavy metals, authorities sought to establish limits for its presence in cosmetic products due to long-term exposure. The problem with As contamination goes beyond the legal cosmetic products placed on the market. It has been found in high quantities in cosmetic products from the underground market [58]. As with Hg, the FDA established a limit for As (up to 3 ppm) for lead acetate, as a colorant, contaminated with this metalloid [10]. This acceptable maximum limit goes also under the general limits set by Health Canada for all cosmetics [11]. Arsenic and its salts are prohibited in any cosmetic product within the EU [5].

In general, several studies reveal that As is not a significant contaminant and levels of this metalloid rarely exceed the 3 ppm limit (**Tables 1**–**3**). In lipsticks, although most studies report a level of up to 0.34 ppm [62, 63], a study reported a maximum level of 6.931 ppm of As [58]. In eye cosmetics, the maximum permissible limit is rarely exceeded. In general, eye shadows, eyebrow pencils and mascaras do not contain As levels more than 3.704, 2.071 and 1.656 ppm, respectively [58, 62, 63]. However, in a study, it was reported that in kohl, there was an alarming presence of As (810–1630 ppm). Kohl is an ancient eye cosmetic still used nowadays [75]. The danger with kohl is not solely because of its use as a cosmetic but there are claims that falsely indicating its use for the treatment of eye conditions. Apart from the presence of As in kohl, other face cosmetics, such as foundations and creams contain minimal quantities of As, reported as up to 1.0 and 0.171 ppm, respectively [62, 63]. Less commonly used products include face paints particularly used by opera actors in China. Levels of As reach a maximum of 25 ppm [79]. Shampoos, conditioners and dyes used on the hair contain low As concentrations (<0.71 ppm) [62, 63, 94]. Likewise, in a study, the As content for cleansers and sunblocks does not exceed 0.010 ppm [62] but higher levels were reported for body lotions (1.543 ppm) [83]. There are some concerns with skin-lightening creams as some exceed the 3 ppm threshold [53, 89] and other creams with levels up to 10.74 ppm [83]. In some toothpaste, the As content was 26.94 ppm [83]. Most likely, As is present as a contaminant with other heavy metals used for this purpose. In spite of these findings, As is one of those elements that is rarely found in cosmetics [22]. However, its presence may raise concerns particularly in legal products that are used on a long-term basis and in illegal cosmetic products on the underground market.

5. General considerations

The studies discussed in the previous sections highlight the importance of specific metals as contaminants and additives in cosmetic products. To determine any particular relationships between formulations, a multi-variate meta-analysis was carried out using Spearman correlation and Principal Component Analysis, taking into account the maximum levels obtained for the various cosmetic formulations. Pearson correlation statistics (**Table 4**) reveal a relationship between all five metals ($r > 0.466$). Two latent factors had an eigenvalue greater than 1, which together explained 80.54% of the total variance. The factor loadings demonstrated the different groups of variables (**Figure 1**). Factor 1, displayed on the horizontal axis, weighed heavily on Pb, Cd, Ni and As with lipsticks, eye shadows, face paints, make-up foundation and skin

Variables	Cd	Ni	Hg	As
Pb	0.538	0.495	0.527	0.579
Cd		0.779	0.334	0.750
Ni			0.446	0.641
Hg				0.465

Table 4.
Spearman correlation matrix for the five metals.

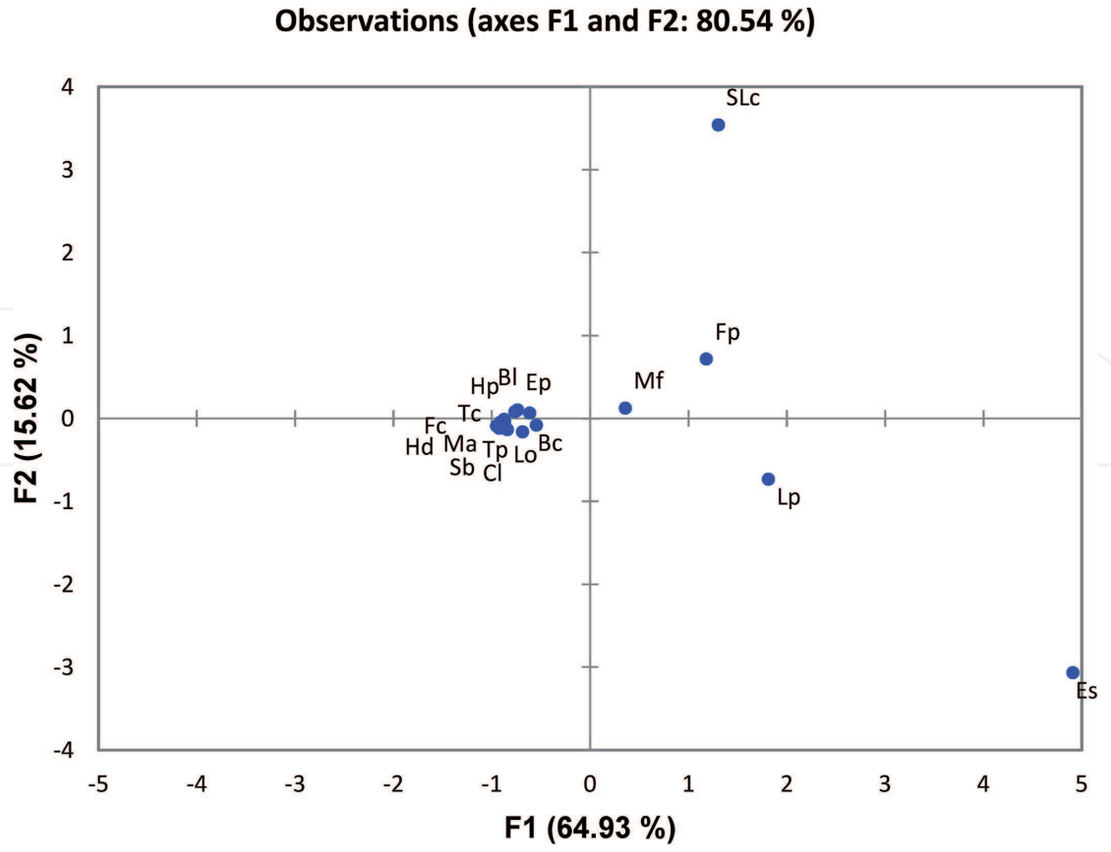

Figure 1.
Observations plot for the formulations. Legend: Lp = lipsticks; Es = eye shadows; Ep = eyepencils; Ma = mascaras; Mf = foundation; Fp = face paint; Fc = face cream; Tp = toothpaste; SLc = skin-lightening creams; Sb = sunblock; Hp = hair products; Hd = hair dyes; Bl = body lotion; Cl = cleansers; Lo = lotions; and Tc = tonic creams.

lightening creams exhibiting high levels of these metals. These formulations were discriminately different from the rest. On the other hand, F2, displayed on the vertical axis, weighed heavily on Hg with skin lightening creams having superior quantities of this metal for the other formulations. This multi-variate analysis consolidates the findings from previous studies. The findings of such research works are at the disposition of authorities and policy makers for the formulation of high-quality cosmetic products.

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