



Active Compound and Heavy Metals in Bleaching Creams and Their Health Effects: A Review

Faten M. Ali Zainy^{1*}

¹Chemistry Department, Faculty of Science, University of Jeddah, P.O. Box 80327, Jeddah 21585, Saudi Arabia.

Author's contribution

The sole author designed, analysed, interpreted and prepared the manuscript.

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ABSTRACT

For a long time, it could be found that appearance enhancement products fell into the cosmetic category. Therefore, more people want to appear beautiful, thus the desire to appear beautiful has been urgent since the early days. Skincare products, hair, perfumes, oral care, and nail products are used by women despite their containment of toxic chemicals harmful to health in a society that wants to look its best because it is a beauty freak. Different toxic components and dangerous chemicals utilized in cosmetics are integrated beyond acceptable limits. These heavy metals may reason dangerous sick influences on the skin causing carcinogenicity. Therefore, it begins to be a requirement for people to turn out having knowledge of the different dangers of heavy metals utilized in cosmetics.

Keywords: Heavy metals; bleaching creams; biological effects; active ingredients.

1. INTRODUCTION

Definition of Skin-lightening is the various options for increasing the skin's surface appearance, and

skin bleaching practices. Skin-whitening creams base beauty on relating to race hierarchy, therefore, may be caused serious social danger [1].

*Corresponding author: E-mail: fmzainy@uj.edu.sa;

When the public's increasing attention in skin whitening, lightening components utilized to newly regularly integrate. The factors which make light skin which had contained natural or artificial materials and it contained different doses of melanogenesis. It could be utilized to therapy skin to get as whiter skin may be equivalent to beauty in various cultures [2].

Women have used many cosmetics as a daily product and do not have sufficient knowledge of the cosmetics contain. When cosmetics contain very few heavy metals, this is a health hazard because cosmetics are used for a long time[3].

Skin bleaching products, which have been in utilized Asian countries, are now greatly valued by Western populations, who develop skin spots consequence to exposure to the sun [4].

Skin bleaching indicates the practice, deeply embedded for women which utilizing natural or synthetic materials to whiten the skin by decreasing the melanin concentration in the skin [5]. Natural antioxidants are chemical materials that have proved as effective in skin bleaching, and also, it showed the useful side influences [6], and proliferative [7], safeguard macromolecules like collagen versus sun radiation [8]. Natural lightening constitutes useful and it has begun to be more prevalent at the present time. Cosmetic

formulations may be caused to consumers' worry about artificial constitute components and dangers which appear for human health [9].

1.1 Definition of Whitening Cream

Skin bleaching is an expression utilized for whitening skin with artificial means. Thus, melanins are produced by specialist cells, which describe by melanocytes. Melanin has contained two kinds: eumelanin and pheomelanin and it could be mixtures of both types Fig. 1. The increased production of accumulation melanin caused a number of skin diseases, which include hyperpigmentation [10,11]

1.2 Active Ingredients Acting on the Melanin Formation Process Vitamin C

Ascorbic acid (vitamin C) is easily analyzed in aqueous media; therefore, may be utilized their derivatives due to their stable which act transforming tyrosine into melanin [12]. Moreover, the association of vitamin C with coppers an absolutely necessary in tyrosinase activity. Furthermore, it does not have the dangerous influences of hydroquinone [13]. This active component is not utilized alone but it was always utilized in combination with another component.

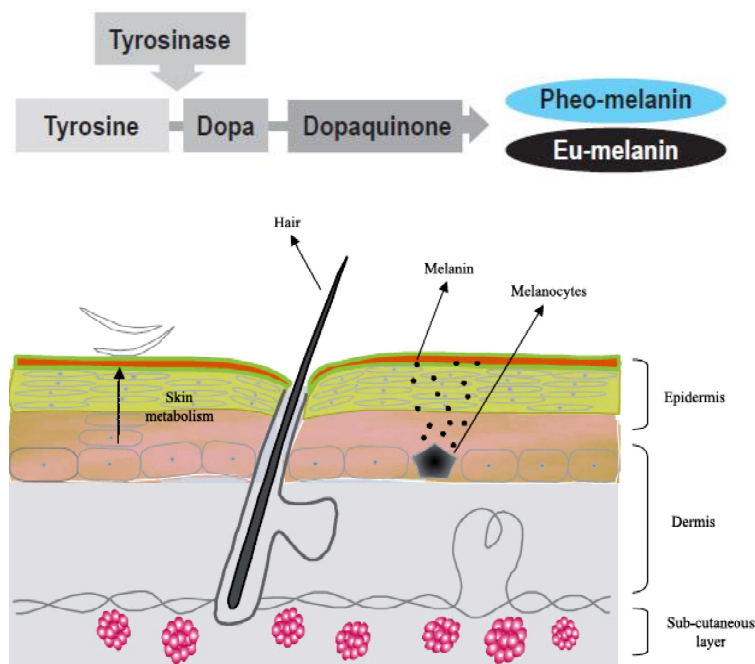


Fig. 1. Production of melanin

1.3 Hydroquinone (HQ)

HQ is a depigmenting factor and it could be decreased the transformation of DOPA to melanin. The reactive oxygen species (ROS) lead to participates in whitening action [14].

1.4 Retinol and Retinaldehyde

Retinoids are which production of cytokines that happen pro-inflammatory and are thus exciting molecules [15]. Finally, the "photomutagenicity" of retinol needs that certain reservation when exposed to the sun [16]. Even however the outcomes got decreases of could be positive, this kind of product appears lower than ideal. The best level of protection for the full day may be due to skincare cosmetics are used at an average of 2 mg/cm² and reapplied every 2 h [17].

1.5 Tyrosinase Inhibitors

Arbutin Fig. 2 is obtained from various plants.

More research observed that the arbutin is influential as hydroquinone but lower toxic [18]. This factor is photostable readily degraded by heat, which could be a necessity to incorporate at cold temperatures into the selection excipient [19]. Aloesin in Fig. 3 is a

glycoprotein extracted from the plant of Aloe and which it had contained up to 25% aloesin [20].

Glabridin is having the ability to lower the activity of tyrosinase [21]. Kojic acid is shown in Fig. 4 was utilized protect the natural color of foods, and it is a popular component in de-pigmentation preparations [22].

1.6 Mechanism

De-pigmentation can be carried out as following (i) adjusting the tyrosinase, (ii) adjusting the absorption of melanosomes (iii) participation with melanosomes maturation [23]. Moreover, biosynthesis melanin is by tyrosinase, great lightening factor action particularly in lowering the role of the enzyme by different mechanisms [24]. Thus, tyrosinase inhibitors have more and more significance in the protection of hyperpigmentation and skin lightening [25].

The color of the skin and hair is the responsibility of melanin and also it is a light-absorbing pigment [26]. Melanin biosynthesis plays an important role in protecting the skin from the harmful rays of the sun in addition to eliminating the free radicals of oxygen [27]. Oxidative stress is an immediate result of changes in the climate and human group lives and causes a change in connective tissues and most important to accelerated aging [28]. Melanogenesis is adjusted by more enzymes as shown in Fig. 5 [29].

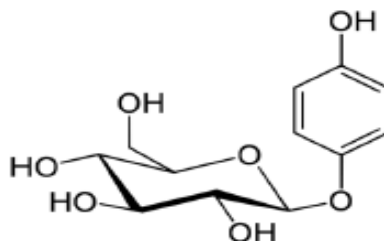


Fig. 2. Arbutin formula

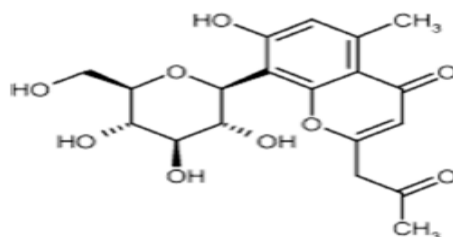


Fig.3. Aloesin formula

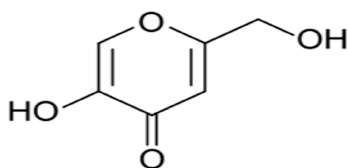


Fig. 4. Kojic acid formula

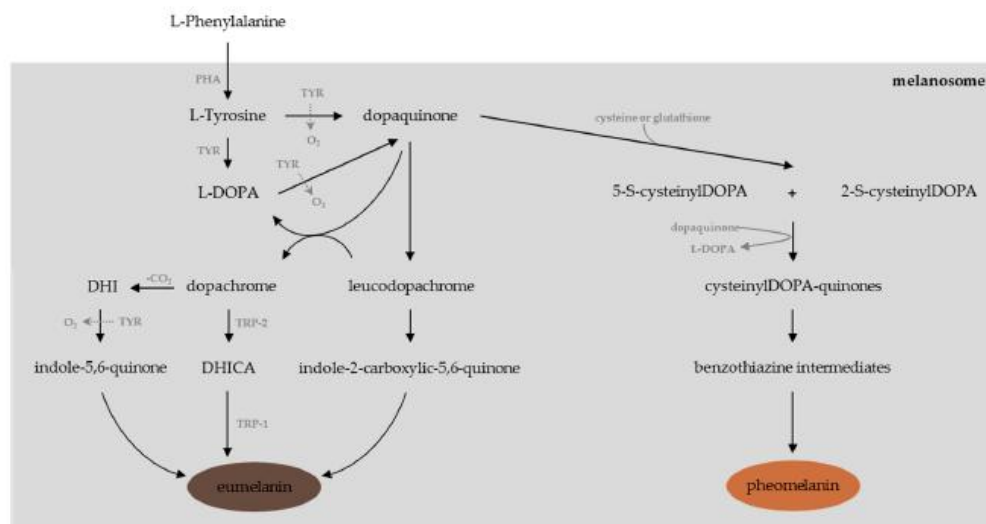


Fig. 5. The melanogenesis pathway (adapted after [29,30])

1.7 Health Risk

Skincare products may reason allergic and skin harmful it can stay on the body for a long duration [31]. Skin whitening factor as hydroquinone (HQ) is dangerous chemicals and potential mutagenicity. Ochronosis is described by a gradually darkening of the region to which the cream which contained a great dose of HQ is used for many years [32].

The allergic reactions correlated with deodorant and fragrances are great may be due to the aroma or other components. Aromas can enter the body byway the skin (adsorption), and it can be caused by more symptoms. Chemicals carcinogens were found as coumarin, phethleugenol, while phthalates are suspected hormone disrupters [33].

Skin lightening creams - usually sold illegally had contained serious components that could put your health in danger. Dermatologists told that they are seeing more women from complications concerning the utilize of skin-lightening creams [21].

The side influences of skin lightening applications are Dermatitis with severe drying, cracking of the skin, cancer, and more other symptoms. The hypopigmentation for the skin prone to UV damage can be caused by skin cancers like melanoma [34]. The applications of Kojic acid (KA) are antimicrobial and antiviral, antitumor, antidiabetic, anticancer, and anti-speck. As well as KA and its derivatives are utilized to an antioxidant, anti-proliferative, anti-inflammatory, cardioprotective, and skin-lightening agent products it could be due to tyrosinase inhibitory activity [35].

1.8 Heavy Metals

1.8.1 Heavy metals that used as bleaching agent

1.8.1.1 Lead

Skin contact with Lead happens daily, and also it could be having been found to be absorbed during the skin [36]. The utilization of leaded eye powders has been connected with elevated blood-Lead levels in children and women [37]. In addition, it can also be transferred to infants

during breastfeeding [38] and stored in bones [39]. Lead compounds have been classified as suspected carcinogenic to humans [36].

1.8.1.2 Nickel

Lead metal in nature, therefore, everyone is exposed to small amounts, including cosmetics [36]. Great levels of exposure can lead to health influences be controlled on the way and the type kind of nickel exposed to [36]. Meanwhile, confirmed kinds of Nickel are considered to be "toxic" for the reason that it's carcinogenic to humans [36]. Allergy to Nickel is also popular it could be caused to severe contact dermatitis [36]. Nickel allergy due to eye shadow was found; even as 1 ppm of it may trigger an allergy [40].

1.8.1.3 Mercury

Mercury metal is established in cosmetics. Skin-bleaching soaps and creams are mostly used between dark-skinned peoples in the world [41].

Mercury salts inhibit the melanin, resulting in lighter skin and it could be found in cosmetics exists in two forms: inorganic and organic. Inorganic mercury is utilized in skin-whitening soaps and creams. Organic mercury compounds are utilized as preservatives materials for cosmetics. The major harmful influence of inorganic mercury is kidney damage [41].

Mercury causes skin rashes, skin discoloration, and a lowering in the skin's resistance to bacterial and fungal infections. Mercury in cosmetic products is finally discharged into sewage and enters through the environment, and converted to highly toxic methyl mercury in fish. Pregnant women transfer the mercury to their fetus when consumed with these fish, which can later outcomes in neurodevelopmental deficits in the children [41].

1.8.1.4 Zinc

Zinc is one of the important elements for humans and problems may occur due to not eating this element. Excessive exposure to this ingredient causes toxic effects through the mouth or the skin and causes gastrointestinal pain. So far, there is no evidence proving that zinc is a carcinogen, but it is known that the high density of this mineral is toxic to living cells [42]. Moreover, it was found that toothpaste contains high levels of zinc (1842 and 2417 ppm). These

ratios were higher than reported by Odukudu et al. [43] for toothpaste formulations (0.743 ppm). On the other hand, children's toothpaste does not contain the element zinc. Meanwhile, zinc is found in plaque, saliva, and tooth enamel. However, zinc has been incorporated into toothpaste to keep the teeth clean. Furthermore, a study by Lynch [20], it was observed that elevated zinc levels persist for hours after using toothpaste for oral hygiene.

1.8.2 Health hazards of heavy metals in bleaching creams

Skin remains the main important source of heavy metal toxicity in humans. Thus, different cosmetics had contained heavy metals. The levels of Cr, lead, and cadmium in cosmetics products was higher than the limits levels as follows: 1.0, 10.0, and 0.3 ppm, respectively, according to the EPA and the World Health Organization. Long time use of cosmetics is a potential source of heavy metal toxicity [44].

The health risk was estimated in skin-lightening products using the Margin of Safety (MoS) and Hazard Quotient (HQ). The results showed that the MoS value of the metal was higher; this means that the being of metal impurities was within the ability to be agreed risk. The HQ value of the metal was higher, which points out the potential for adverse health influence. Therefore, the heavy metals are able to accumulate and influences on human health also remain a concern [45].

The heavy metals were determined in bleaching creams from the local market of Saudi Arabia. The results reported that the creams and cream mixtures containing heavy metals above the permissible limit could be influences on human health [46].

ZainyFaten [47] evaluated the toxic and nontoxic metals in cheaper blusher and eye shadow cosmetic brands. The results reported that the Fe was present with a high concentration in most blusher samples reaching 14311.63 ppm, while Al reached 1378.50 ppm only. Pb, Ag, Au, and Ni were absent in most samples. On eye shadow samples, iron was present strongly with a concentration reaching 9930.95 ppm on green samples but absent in violet- and white-colored eye shadow samples. Al was present in most of the samples with a level reaching 2484.38 ppm. The gold-colored eye shadow samples were rich in Fe and Al levels reaching 1943.87 and

1745.27 ppm, respectively. Mn concentration reached 2033.33 ppm in blue-colored eye shadow samples, while Cu concentration reached 3134.35 ppm in violet-colored eye shadow samples. Ti was present in all samples with low concentration. Conclusion: Women must avoid using cheaper brands to prevent exposure to the high concentrations of toxic materials which cause a negative effect on human health.

Topical absorption and toxicity of heavy metals toxicity of metal and its cure are well documented [48]. Exposure to metals may happen during the diet [49] and utilize of cosmetics. Utilize of underarm cosmetics has been studied as a maybe reason for breast cancer [50]. It is due to that they utilize heavy metals, as impurities in the preparation of cosmetics [51].

Maximum limits permissible of heavy metals according to SASO (the Saudi standards metrology and quality organization), FDA, Health Canada, and German showed in Table 1.

Arsenic can cause acute toxicity, genetic toxicity, reproductive and developmental toxicity, biochemical toxicity, and chronic toxicity [52].

Mercury can cause anxiety, autoimmune diseases, and difficulty with balance, fatigue, hair loss, irritability, memory loss, restlessness, recurrent infections, tremors, damage to the brain, lungs, and kidney [53].

Lead toxicity is a general problem; it is a substantial critical disease in children. Exposure to low levels of lead has been dangerous to pregnant women.

Antimony Chronic exposure may intensively cause the irritation of the eyes, skin, and lungs [54].

1.8.3 Evaluation of bleaching cream according to SASO and FDA specification

1.8.3.1 Measurements of physical parameters

In physical parameters were measurements according to the standard methods by Sturm et al. [59].

1.8.3.2 Determination of thermal stability

Phase separation investigator of skin lightening cream was examined by thermal stability according to the standard methods by Sturm et al [59].

1.8.3.3 Determination content of total fat and water

The fatty matter is extracted using petroleum ether then evaporation and weighed. Water content was carried out by Karl Fischer method according to the standard methods by Kamakshi [60].

1.8.3.4 Measurement of viscosity

The viscosity creams were measured by Brookfield viscometer apparatus according to in the standard methods by Sturm et al [59].

1.8.3.5 Determination of microbial Contamination

The microbial content was estimated by utilizing the pour plate method and serial dilution technique according to the standard methods by Sturm et al.[59].

1.8.3.6 Study of the stability

The products were kept at the room temperature 45° C and it was checked for every week according to in the standard methods by Sturm et al. [59].

Table 1. Comparison the permissible limits of heavy metals on cosmetics in different specification

Metal organization	Lead	Arsenic	Cadmium	Mercury	Antimony	References
German Federal Government	20.0 ppm	5.0 ppm	5.0 ppm	1.0 ppm	10.0 ppm	[55]
Health Canada	10.0 ppm	3.0 ppm	3.0 ppm	1.0 ppm	5.0 ppm	[56]
FDA	20.0 ppm	3.0 ppm	0.0	1.0 ppm	0.0	[57]
SASO	10.0 ppm	2.5 ppm	1.0 ppm	0.5 ppm	2.0 ppm	[58]

Table 2. Methods reported in the literature for elemental determination in bleaching creams

Country	Metals	Technique	Sample preparation	Concentration ppm	References
Saudi	Cd, As, Pb, Tl and Ti	ICP-OES	microwave digestion	0.4 to 0.5	[61]
Nigeria	Pb, Cd, Hg and As	AAS	HNO ₃ and HCl 3:1 ratio	10, 0.3, 1 and 10	[62]
Nigeria	Pb, Cd, Fe and Co	atomic absorption spectrophotometer	HNO ₃ and HCl 3:1 ratio	0.4 to 0.5	[63]
Iraq.	Hg	atomic absorption spectrophotometer	HNO ₃ and HCl 3:1 ratio	0.482 to 29.54	[64]
Baghdad/Iraq	Ni, Pb, Cd	AAS	HNO ₃ and HCl 3:1 ratio	0.4 to 0.5	[65]
Kenya	Hg,Pb, Cd, Zn, Mn, Ce	AAS	HNO ₃ and HCl 3:1 ratio	0.4 to 0.5	[66]
Malta and other European countries	Ag, Cd, Cr, Cu, Fe, Hg, Mn, Ni, Pb, Sn and Zn	Microwave Plasma-Atomic Emission Spectrometer	HNO ₃ and H ₂ O ₂	0.001 to 029	[67]
EU	Pb, Cd, Hg, Ni and Cr	Microwave Plasma-Atomic Emission Spectrometer	HNO ₃ and H ₂ O ₂	0.1,0.05,0,0,0	[68]
WHO	Pb, Cd, Hg, Ni and Cr	Microwave Plasma-Atomic Emission Spectrometer	HNO ₃ and H ₂ O ₂	2, 2 0,0 0	[69]
Canada	Pb, Cd, Hg, Ni and Cr	Microwave Plasma-Atomic Emission Spectrometer	HNO ₃ and H ₂ O ₂	10,3,3,0,0	[70]
Germany	Pb, Cd, Hg, Ni and Cr	Microwave Plasma-Atomic Emission Spectrometer	HNO ₃ and H ₂ O ₂	0.5,0.1, 0.1, 0, 0	[71]
US FDA	Pb, Cd, Hg, Ni and Cr	Microwave Plasma-Atomic Emission Spectrometer	HNO ₃ and H ₂ O ₂	10,0,0,0,0,50	[72]

Table 3. Biological effect reported in the literature for using bleaching creams

Country	Product	No of populations	Biological effect	Reference
Ghana	Bleaching creams	100 women	can damage the skin	[73]
Rwanda	Bleaching creams	80 rats	Hydroquinone reduced skin thickness and caused epidermis disruption	[74]
India	Cream	86.7%	not be safe to human health	[75]
Germany	Cream	73.3%	not be safe to human health	[75]
S. Africa	Bodylotions	66.7%	not be safe to human health	[75]
S. Africa	Cream	60%	not be safe to human health	[75]
India	Cream	53.3%	not be safe to human health	[75]
India	Cream	53.3%	not be safe to human health	[75]
Germany	Lotions	53.3%	not be safe to human health	[75]
Germany	Lotions	53.3%	not be safe to human health	[75]
Chain	Lotions	40%	not be safe to human health	[75]
Indonesia	Lotions	40%	not be safe to human health	[75]
Ethiopia	Lotions	20%	not be safe to human health	[75]
Ethiopia	Make-up	33.3%	not be safe to human health	[75]

1.8.4 Determination of heavy metals in bleaching creams using different methods

From the literature in different countries were determined heavy metals using different methods in bleaching creams and the findings are reported in Table 2.

1.8.5 The biological effect for bleaching cream on human health

Bleaching cream and cosmetics products of skin have risk of toxicity and deleterious effects to the human because of their multiplicative contamination with heavy metals and uncertain mixing of different components.

2. CONCLUSION

Heavy metal impurities in cosmetics are common, so they should be reduced to the minimum permissible level. Because most women use cosmetics daily human systemic exposure to their ingredients can rarely be completely excluded. To encourage improvements in the manufacture, marketing, and use of cosmetic products by the population, it is necessary to apply a unified cosmetic-vigilance around the world. This public health strategy is a genuine means of obtaining information on the safety of cosmetic products and their ingredients, preventing the risks associated with the use of cosmetics to become a serious public health problem.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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