

## Levels of Toxic Metals in Skin Lightening Agents Marketed in Nigeria

DOI: <https://doi.org/10.24297/jac.v16i0.8317>

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### Abstract:

**Background:** Bleaching agents produced by registered companies in developed countries have regulated concentrations. But various local skin lightening agents produced in Africa, especially Nigeria have no identified active agent. This study determined the levels of potentially toxic heavy metals constituents of bleaching agents commonly used by Nigerians.

**Methods:** Twelve different types of skin lightening creams (Extra white, Make me white, Extract, Perfect white, UV lightening, Pure skin, Body treat, Dodo up, Bronze tone, White express, Peau Claire and Otentika) available Nigerian markets were randomly collected based on their usage and availability. Three non- lightening creams served as the controls for this study. Levels of mercury, lead, cadmium, chromium and arsenic were determined in both lightening and non- lightening creams (controls) using atomic absorption spectrophotometer (AAS).

**Results:** All lightening creams 12/12 (100%) contained significantly ( $p < 0.05$ ) higher levels of mercury compared with the control. 11/12 (91.7%) of the lightening creams contained significantly ( $p > 0.05$ ) higher levels of lead compared with the control. Levels of arsenic were significantly ( $p < 0.05$ ) higher in 11/12 (91.7%) of the lightening creams compared with control. Levels of cadmium increase significantly ( $p < 0.05$ ) in 4/12 (22.92%) of the lightening creams compared with the control. 4/12 (22.92%) of the lightening creams contained significantly ( $p < 0.05$ ) higher levels of chromium compared with control.

**Conclusion:** It may be concluded that mercury, cadmium, lead and arsenic are common constituents of lightening creams marketed in Nigeria. To avert the risk and consequences of metal toxicity in the use of the lightening agents, levels of toxic metals should be monitored officially in cosmetics (e.g. creams), while the manufacturers are educated about the potential risks associated with higher levels of these metals. This study could therefore provide valuable information for health researchers and policy makers.

**Keywords:** Toxic metals, skin lightening agents

### Introduction:

Skin bleaching is a purposeful lightening of the skin, pigment removal or body beautification by using chemicals [1]. It can lead to permanent or temporary alteration of the color of the outer layer (epidermis) of the skin [2]. This practice cuts across all ages, races, beliefs and ideologies. Even the white race that might claim advantage over others still engage in skin bleaching, probably as a method of maintaining their body color or for other purposes. African women are among the most widely represented users of skin-lightening products because of a belief that fair skin leads to beauty than dark skin [3]. A large fraction of the population, primarily women and young girls in Asia, Africa and Latin America use skin lighteners. Nevertheless, the young female adolescents have been identified as most prone to skin bleaching practice [4]. Survey reports these figures of users in specific countries; Senegal 27 %, Mali 25 %, Togo 59 %, South Africa 35 %, Nigeria 77 %, Hong Kong 45 %, Republic of Korea 28 %, Malaysia 41 %, Philippines 50 % and Taiwan 37 % . Reason given by 61 % of the respondents to the survey is that they felt younger with a fair complexion [5]. The users believe that the bleaching agents are meant

for cleansing, beautification, promoting attractiveness or altering the appearance of the users without affecting the body's structure and function [6].

Identified constituents of skin lightening creams include mercury, hydroquinone, kojic acid, azelaic acid, arbutin, vitamin C, magnesium ascorbyl phosphate, calcium ascorbate and ascorbyl glucoside [7, 8]. Other lightening products may have niacinamide (vitamin B), licorice extract, chromabright, azelaic acid aleossin from aloe vera plant, kojic acid, alpha arbutin, beta arbutin, ascorbyl glucoside or magnesium ascorbyl phosphate, mulberry extract, glycolic acid, licorine extract, niacinamide lactic acid, lemon juice extract, emlica, potato and turmeric. Such chemicals are capable of inhibiting the enzyme(s) in the tyrosine-melanin pathway, via different mechanisms [9,10,11]. In the past, the quickest way to lighten skin was with hydroquinone. But since this active ingredient has toxic effects, it has been banned in many countries across Africa and Europe [12]. A study by California medical officials on some facial lightening creams contained mercury levels of 20,000 to 56,000 ppm [13]. Claudia et al. [14] recorded levels of mercury between 878 and 36,000 ppm in six lightening creams studied in Mexico. In Saudi Arabia a study by Al-Ashban et al. [15] on skin lightening creams recorded levels of mercury between 2.46 to 23222 ppm; while Voegborio *et al.*, [16] in the same country recorded mercury levels between 1.18 to 5650 ppm in 17 skin lightening cream samples. In Kenya, a study by Maina [17] showed that levels of mercury in seven different brands of skin lightening creams significantly higher. Skin lightening is currently one of the most common forms of potentially harmful body modification practices causing metabolic dysfunctions and cancer in the users [18]. It was then recommended that the manufacturers should be informed about the hazards of high concentrations of mercury, since various local bleaching creams have no identified active agent [19]. Considering the toxic effects of the active chemical constituents of bleaching creams, levels above maximum permissible limits would be harmful to both skin and other organs. The allowable levels of active chemical constituents of bleaching creams are 2 % by weight for hydroquinone, 1 ppm for mercury, 3 % by weight for magnesium ascorbyl phosphate, 2 % by weight for ascorbyl glucoside, 2 % by weight for kojic acid and 7 % by weight for arbutin in skin care products [3, 20]. Mercury is a heavy metal that has higher than 3 g/cm<sup>3</sup> densities and has biological effects at low concentrations and is toxic when present in cells at higher than the tolerable physiological levels [21, 22]. There is limited information on the levels of heavy metals in ointments and creams used for skin bleaching in Nigeria. Therefore, this study was designed to determine the levels of mercury, lead, cadmium, chromium and arsenic in commonly used bleaching creams in Nigeria.

## **MATERIALS AND METHODS**

### **Materials:**

Twelve different types of skin lightening creams (Extra white, Make me white, Extract, Perfect white, UV lightening, Pure skin, Body treat, Dodo up, Bronze tone, White express, Peau Claire and Otentika) being used by young adult females in Lagos, Nigeria were randomly collected based on their usage and availability. Another three non-lightening creams such as Vaseline were purchased from a supermarket. Levels of mercury, lead, cadmium, chromium and arsenic were determined

### **Cleaning of apparatus**

All apparatus were soaked in detergent solution overnight, rinsed and soaked in 10 % analytical grade nitric acid overnight before being rinsed with distilled water. The glasswares were dried in an oven at 105°C.

### **Chemical, reagents and solvents for preparation of sample**

Analytical grade of concentrated nitric acid (HNO<sub>3</sub>), Hydrochloric acid, Distilled water.

### Sample preparation / digestion

A 20 mL of freshly prepared acid mixture of concentrated nitric and hydrochloric acid (ratio 3:1) was added to 1.0g of cream. The conical flask was covered and mixture heated at 200°C until there was no brown fume produced. The solution was cooled, made up to the mark using distilled water then filtered using Whatman paper (Number 1).

### Analysis of Sample:

Atomic absorption spectrophotometer with mercury vaporizer unit (model MVU-IA) was used to analyze the samples using the method of Kaneko et al [23].

### Statistical Analysis:

All statistical analyses were performed using Statistical Package for Social Sciences (SPSS), version 21.0. The data were expressed as Mean  $\pm$  SD. Student (t) test was used for comparison of analytes in lightening creams and controls. P-values less than 0.05 were considered significant.

### Results and Discussion

All lightening creams analyzed contained significantly higher levels of mercury compared with the non-lightening creams (controls) as shown in Table 1. Higher levels of mercury observed in all lightening creams might be due to inorganic mercury such as ammoniated mercury and mercuric iodide used as ingredients of the skin lightening creams [24]. Higher levels of mercury observed in our lightening creams despite the allowable level of 1 ppm for cosmetics approved by WHO [3, 20], could expose the users to toxic concentrations of mercury.

The form of mercury plays a role in how much is absorbed via dermal or oral routes. Organic (methyl) mercury is of greater concern than inorganic mercury; however, all forms of mercury are absorbed through the skin and mucosa, and dermal exposure can result in systematic toxicity. For the general population, the major route of mercury exposure is dietary intake. Mercury compounds may cause allergic reactions, skin irritation, or adverse effects on the nervous system. Clinical symptoms of overexposure to mercury include tremors, weakness, memory loss, dermatitis and impaired kidney function, with the form of mercury typically determining the specific symptoms.

Several studies have reported the possible pathological consequences of mercury toxicity in the exposed individuals. Bingol and Ackay [25], Al-Saleh [7] and Barrat *et al.* [26] reported that chronic exposure to either inorganic or organic mercury may damage the brain, kidneys, nervous system and developing foetus. A high concentration of mercury in pregnant women is known to considerably increase the risk of permanent brain damage and may lead to acrodymia (pink baby syndrome). Exposure of mercury to placental cells causes damage to the developing fetus [25, 27]. Chronic exposure to either inorganic or organic mercury may damage brain, kidneys, nervous system and developing foetus [26]. By inhibiting the production of melanin, the skin is more susceptible to skin cancer. Nephro-toxic effects have been attributed to application of inorganic mercury salts. Exposure of mercury to placental cells causes damage to the developing foetus [25,27]. In other studies [28, 29], observed that complications of mercurial toxicity include exogenous ochronosis, dermatitis, facial acnes, facial hypertrichosis, hyper and hypo-pigmentation, reduction in the skin resistance to bacterial and fungal infections, anxiety, depression, psychosis, impaired wound healing, the fish odour syndrome, nephropaty, steroid addition syndrome and predisposition to infections.

**Table 1: Levels of Mercury ( $\mu\text{g/g}$ ) in Bleaching Creams and Non-Bleaching Cream (Control)**

Name of Cream	Control	lightening Cream	t-test	p-values
Extra white	366.7 $\pm$ 57.7	1733.3 $\pm$ 115.5	18.3	<0.001(S)
Make me white	366.7 $\pm$ 57.7	1400 $\pm$ 200	8.6	0.01(S)
Extract	366.7 $\pm$ 57.7	1933 $\pm$ 115.5	21	<0.001(S)
Perfect white	366.7 $\pm$ 57.7	2200 $\pm$ 200	15.3	<0.001(S)
UV lightening	366.7 $\pm$ 57.7	1666.7 $\pm$ 305.5	7.2	0.002(S)
Pure skin	366.7 $\pm$ 57.7	1466.7 $\pm$ 115.5	4.0	0.016(S)
Body treat	366.7 $\pm$ 57.7	1733.3 $\pm$ 115.5	18.3	<0.001(S)
Dodo up	366.7 $\pm$ 57.7	2333.3 $\pm$ 305.5	11.0	<0.001(S)
Bronze tone	366.7 $\pm$ 57.7	2066.7 $\pm$ 115.5	22.8	<0.001(S)
White express	366.7 $\pm$ 57.7	1333.3 $\pm$ 230.9	7.0	0.002(S)
Peau Claire	366.7 $\pm$ 57.7	1333.3 $\pm$ 115.5	13	<0.001(S)
Otentika	366.7 $\pm$ 57.7	1133.3 $\pm$ 115.5	10	0.001(S)

The concentrations of lead in the creams showed that only Otentika did not contain significant ( $p > 0.05$ ) amount of lead (Table 2) compared with the controls. However, sufficient evidence shows that blood lead levels  $< 5 \mu\text{g/dL}$  are associated with decreased renal function and that blood lead levels  $< 10 \mu\text{g/dL}$  are associated with increased blood pressure and hypertension [30]. Other bleaching creams have significantly ( $p < 0.05$ ) higher levels of lead compared to the control cream. Although, inorganic lead in the creams crosses the skin less readily with a low permeability co-efficient of about 10-4 cm/hour, prolonged exposure to lead from cosmetics might lead to lead accumulation in the tissues. Previous studies show that lead exerts adverse effects on numerous organs and metabolic pathways including the central nervous system, kidneys and on the heme synthetic pathway. Other studies show that exposure to lead results in neurological disorders, infertility and hypertension [30].

**Table 2: Levels of lead ( $\mu\text{g/g}$ ) in Bleaching Creams and Non-Bleaching Cream (Control)**

Name of Cream	Control	lightening Cream	t-test	p-values
Extra white	466.7 $\pm$ 115.5	1000 $\pm$ 200	4.0	0.016(S)
Make me white	466.7 $\pm$ 115.5	733.3 $\pm$ 115.5	2.8	0.047(S)
Extract	466.7 $\pm$ 115.5	1333.3 $\pm$ 115.5	4.6	0.010(S)
Perfect white	466.7 $\pm$ 115.5	1133.3 $\pm$ 115.5	7.1	0.002(S)
UV lightening	466.7 $\pm$ 115.5	1200 $\pm$ 200	5.5	0.005(S)
Pure skin	466.7 $\pm$ 115.5	1000 $\pm$ 200	4.0	0.016(S)
Body treat	466.7 $\pm$ 115.5	1133.3 $\pm$ 115.5	7.1	0.002 (S)
Dodo up	466.7 $\pm$ 115.5	1266.7 $\pm$ 115	8.5	0.001(S)
Bronze tone	466.7 $\pm$ 115.5	1666.7 $\pm$ 115.5	12.7	<0.001(S)
White express	466.7 $\pm$ 115.5	1066.7 $\pm$ 115.5	6.4	0.003(S)

Peau Claire	466.7±115.5	733.3±115.5	2.8	0.047(S)
Otentika	466.7±115.5	800±200	2.5	0.067(NS)

Levels of cadmium did not increase significantly in eight of the creams (Make me white, Extract, Perfect white, UV lightening, Pure skin, Body treat, White express and Otentika) compared with the controls. Meanwhile, four bleaching creams (Extra white, Perfect white, Dodo up and Peau Claire) demonstrated significantly ( $p < 0.05$ ) higher level of cadmium compared with the controls (Table 3). Although, absorption of cadmium through the skin is low (0.5%) and would be of concern only in situations where concentrated solution is in contact with the skin for several hours or longer. Cadmium binds to epidermal keratin when applied topically, thus explaining the limited dermal absorption observed *in vitro*. Several studies have implicated cadmium in many metabolic disorders and organ dysfunctions. Cadmium is classified as a human carcinogen by the National institute for Occupational Safety and Health [31].

**Table 3: Levels of cadmium ( $\mu\text{g/g}$ ) in Bleaching Creams and Non-Bleaching Cream (Control)**

Name of Cream	Control	lightening Cream	t-test	p-values
Extra white	100±20	400±25.0	3.7	0.002(S)
Make me white	100±20	266.7±15.5	2.5	0.007(S)
Extract	100±20	200±15.6	2.4	0.008(S)
Perfect white	100±20	333.3±115.5	3.5	0.025(S)
UV lightening	100±20	266.7±35.5	2.5	0.067(S)
Pure skin	100±20	90.0±40.0	0.16	1.20(NS)
Body treat	100±20	266.7±25.5	2.5	0.017(S)
Dodo up	100±20	333.3±115.5	3.5	0.025(S)
Bronze tone	100±20	466.7±115.5	5.5	0.005(S)
White express	100±20	78.0±37.7	0.20	1.37(NS)
Peau Claire	100±20	333.3±50.5	3.5	0.025(S)
Otentika	100±20	266.7±15.8	2.5	0.67(S)

As shown in Table 4, one of the bleaching creams (Peau Claire) did not have detectable level of arsenic. But significantly ( $p < 0.05$ ) higher levels of arsenic were observed in eleven bleaching creams compared with controls. Previous studies show that exposure through water, industrial sources, toxic waste sites and traditional medicines predispose people to arsenic. Since arsenic has pronounced affinity for skin and keratinizing structures including the hair and nails, the present study could implicate the use of skin bleaching creams as another route of exposure to arsenic. Available information show that arsenite inhibits the formation of acetyl-CoA, and succinic dehydrogenase. Many reports show that arsenate can replace phosphate in many reactions to form glucose-6-arsenate *in vitro*. It has been hypothesized that hexokinase could be inhibited in the glycolytic pathway [32, 33].

**Table 4: Levels of arsenic ( $\mu\text{g/g}$ ) in Bleaching Creams and Non-Bleaching Cream (Control)**

Name of Cream	Control	lightening Cream	t-test	p-values
Extra white	0.00	333.3 $\pm$ 115	5.0	0.007(S)
Make me white	0.00	266.7 $\pm$ 115.5	4.0	0.016(S)
Extract	0.00	466.7 $\pm$ 115.5	7.0	0.002(S)
Perfect white	0.00	333.3 $\pm$ 115.5	5.0	0.007(S)
UV lightening	0.00	466.7 $\pm$ 115.5	7.0	0.002(S)
Pure skin	0.00	400.0 $\pm$ 58.0	6.8	0.002(S)
Body treat	0.00	400 $\pm$ 200.0	3.5	0.026(S)
Dodo up	0.00	266.7 $\pm$ 115.5	4.0	0.016(S)
Bronze tone	0.00	200.0 $\pm$ 31.0	4.0	0.016(S)
White express	0.00	333.3 $\pm$ 115.5	5.0	0.007(S)
Peau Claire	0.00	0.00	....	....
Otentika	0.00	200.0 $\pm$ 27.00	4.0	0.016(S)

Chromium has been implicated in the generation of free radicals, including DNA damage [34] and formation of stable DNA-chromium complexes, DNA strand breaks, DNA-DNA cross links, and DNA-protein cross links [35]. Reports show that dermatitis, allergic and eczematous skin reactions, skin and mucous membrane ulcerations, perforation of the nasal septum, allergic asthmatic reactions, bronchial carcinomas, gastro-enteritis and hepatocellular dysfunction occur after contact, inhalation, or ingestion of hexavalent chromium compounds [36]. In this study, Significantly ( $p < 0.05$ ) higher levels of chromium were observed in four bleaching creams; UV lightening, Body treat, Dodo up and Bronze tone when compared with the control cream (Table 5). Chromium was not detectable in eight of the bleaching creams (White express, Peau Claire, Otentika, Pure skin, Perfect white, Extract, Make me white and Extra white). In this study, chromium may not be considered as a major constituent of bleaching creams.

**Table 5: Levels of chromium ( $\mu\text{g/g}$ ) in Bleaching Creams and Non-Bleaching Cream (Control)**

Name of Cream	Control	lightening Cream	t-test	p-values
Extra white	0.00	0.00	0.00	(NS)
Make me white	0.00	0.00	0.00	(NS)
Extract	0.00	0.00	0.00	(NS)
Perfect white	0.00	0.00	0.00	(NS)
UV lightening	0.00	200.0 $\pm$ 65	7.0	0.007(S)
Pure skin	0.00	0.00	0.00	(NS)
Body treat	0.00	266.7 $\pm$ 115.5	4.0	0.016(S)

Dodo up	0.00	266.7±115.5	4.0	0.016(S)
Bronze tone	0.00	333.3±115.5	5.0	0.007(S)
White express	0.00	0.00	0.00	(NS)
Peau Claire	0.00	0.00	0.00	(NS)
Otentika	0.00	0.00	0.00	(NS)

It could be concluded that mercury, cadmium, lead and arsenic are common constituents of lightening creams marketed in Nigeria. To avert the risk and consequences of metal toxicity in the users of the lightening agents, levels of toxic metals should be monitored officially in creams and cosmetics. The manufacturers should be educated about the potential risks associated with higher levels of these metals. This study could therefore provide valuable information for health researchers and policy makers.

#### **Authors' contributions:**

MOA, OBS, LEA and SOA designed the research, MOA and LEA did the analysis and all authors contributed and approved the final manuscript.

**Conflict of interests:** The authors declared that they have no competing interests.

**Funding statement:** The study was self sponsored.

**Acknowledgement:** The authors appreciate Mr. J. Abegunde of the Department of Chemistry and Biochemistry, Caleb University Lagos for the technical and material supports.

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