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# Mercury, hydroquinone and clobetasol propionate in skin lightening products in West Africa and Canada

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ABSTRACT

Skin lightening products are types of cosmetics (creams, gels, lotions and soaps) applied voluntarily on skin. Several of these products contain a variety of active ingredients that are highly toxic. Among those toxic agents, the present study focuses on mercury, hydroquinone, and clobetasol propionate. Out of the 93 lightening soaps and 98 creams purchased in large city markets in sub-Saharan West Africa and in small ethnic shops in Canada, 68–84% of all creams and 7.5–65% of all soaps exceeded regulatory guidelines for at least one active ingredient when considering different regulations. Mercury was found in high concentrations mainly in soaps, while hydroquinone and clobetasol propionate concentrations exceeded US FDA standards in some creams for all countries included in our study. Concentrations of the three compounds declared on labels of soaps and creams usually did not correspond to concentrations actually measured, particularly for mercury and hydroquinone. Overall, our results indicate that most studied skin-lightening products are potentially toxic and that product labels are frequently inaccurate with respect to the presence of toxic agents.



## 1. Introduction

Skin lightening products are types of cosmetics sold as creams, gels, lotions and soaps that are applied voluntarily on skin. In many African and Asian countries, and in many large cities worldwide where communities from these countries reside, the use of skin lightening products is becoming increasingly popular (Lewis et al., 2012; Uram et al., 2010; Mahe et al., 2007; Petit et al., 2006). Previous studies conducted in major cities of some West African countries have shown that a significant proportion (between 26% and 67%) of adult females used these products daily to lighten their skin (Dadzie and Petit, 2009). Several of these products claim to contain a variety of active ingredients that are highly toxic (Bocca et al., 2014; Al-Saleh et al., 2012; Mahe et al., 2007). Among those toxic agents, the present study focuses on mercury, hydroquinone, and clobetasol propionate. We selected these three ingredients amongst others because they are amongst the most toxic and most used agents in lightening products, and they are often subject to regulations (Groupe Thématique 'Peau Noire' de la Société Française de Dermatologie, 2011; Dadzie and Petit, 2009; Del Giudice et al., 2003).

Inorganic mercury (e.g. mercurous chloride, ammoniated mercury, mercurous oxides or mercuric chloride) is the form of mercury commonly found in skin lightening products (Olumide et al., 2008; Palmer et al., 2000). It is a very toxic element that can inhibit melanin production by competing with copper in tyrosinase, resulting in the appearance of paler skin (Engler, 2005; Denton et al., 1952). Its cutaneous absorption is carried out either through the epidermis or through sweat glands, sebaceous glands or hair follicles, and significant dermal absorption can occur depending on different factors such as hydration of the stratum corneum and the frequency of application of these products on the skin. Urinary excretion is the major route of elimination (Chan, 2011; Copan et al., 2015; Sin and Tsang, 2003). Inorganic Hg concentrates mainly in the kidney, in particular in the tubular region where lesions have been observed after acute oral intake of $Hg^{2+}$ salts (Al-Saleh et al., 2005). With repeated applications, the cumulative effect of prolonged low-dose exposure may lead to nephrotoxic effects, proteinuria and nephritis (Al-Saleh et al., 2005; Engler, 2005). The central nervous system can also be affected by inorganic Hg under certain conditions. In fact, although penetration of the blood-brain barrier by inorganic mercury is poor, prolonged exposure can result in central nervous system accumulation and neurotoxicity (Copan et al., 2015; Chan, 2011).

Hydroquinone is a major benzene metabolite widely used in skin lightening products. It is a well-known hepatotoxic and carcinogenic agent (Enguita and Leitao, 2013). In contact with skin, hydroquinone acts as an alternate substrate of tyrosinase. In the place of tyrosine, which should be transformed into melanin, hydroquinone metabolizes into quinones and free radicals.

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These radicals can then attack melanocyte membranes exerting a cytotoxic effect (Gillbro and Olsson, 2011).

Creams containing clobetasol propionate are drug products that are normally sold in several countries to treat various skin conditions. These products are unfortunately diverted from their normal use and used by women for skin whitening. They have anti-inflammatory, antipruritic, and vasoconstrictive properties and are known to reduce production of the arachidonic acid and of prostaglandin (Hammarstrom et al., 1977). The mechanism by which the topical steroids lighten the skin, in general, is unclear (Dadzie and Petit, 2009). However, it seems that these molecules have a strong affinity for the specific receptors for the keratinocytes and the melanocytes causing a depigmenting effect (Roguedas-Contios and Garcia-Le Gal, 2005). They may have many adverse effects on user health (Fanny et al., 2014; Sene et al., 2008; Mahe et al., 2007).

Several safety standards have been established for these toxic agents by international and national organizations. In the case of hydroquinone products, they are officially banned in Canada and the European Union (EU, 2009; Hc-sc.gc.ca, 2015) but are still allowed in the United States and several countries of West Africa at a concentration up to 1.5–2% (US FDA, 2016; Ivory Coast, 2015). However, mercury is banned in lightening products sold in the European Union and of Ivory Coast but allowed in cosmetics sold in Canada and the United States in concentrations up to 1 μg/g (Hc-sc.gc.ca, 2016; US FDA, 2016). Finally, most regulations consider that the standard limit of clobetasol propionate in dermatological preparations is 0.05% (US FDA, w/w) when it is sold with prescription.

The production, distribution and sale of these products normally regulated in several countries is nevertheless carried by informal channels making difficult the compliance with recommended standards (Bocca et al., 2014; Glenn, 2008). Many of these products are readily available on streets, markets, and in non-pharmaceutical shops in West Africa and North American cities with West African communities where control of these products by local health authorities remains difficult (Hamann et al., 2014; Adepoju-Bello et al., 2012; Peregrino et al., 2011; Glenn, 2008; Voegborlo et al., 2008). Because these products are popular and can pose many problems on user's health, it is important to establish if these standard limits are respected in skin lightening products sold in countries around the world, especially in West Africa where there are several cases of adverse effects associated with topical application of these products such as nephropathy and exogenous ochronose (Levitt, 2007; US FDA, 2009).

In this study, we focused on two geographical regions where females use these products and we determined mercury, hydroquinone, and clobetasol propionate in a wide variety of skin lightening creams and soaps. Specifically, we collected products from various local markets in West Africa and in Montreal (Canada), a large North American city with an important West African population. In Africa, we focused on Benin, Ivory Coast, Mali and Senegal. Our main objective was to determine the concentrations of different active ingredients commonly found in skin lightening products in West Africa and Canada, and to compare them with regulatory guidelines. We further tested if concentrations of active ingredients stated on product labels are accurate and therefore correctly inform the consumers on the risk associated with the product.

## 2. Materials and methods

### 2.1. Sampling of skin lightening personal care products

A total of 191 skin-lightening creams and soaps (98 creams and 93 soaps) commonly used by women were purchased from the local markets of West Africa and Canada. In West Africa, we collected the products in the largest markets of the cities of Cotonou (Benin) in August 2013, and Bamako (Mali), Dakar (Senegal) and Abidjan (Ivory Coast) in August-September 2014. In Canada, we bought imported products in June 2013 in a dozen of small ethnic beauty shops located in the city of Montreal. Most of the products analyzed were imported from different countries of Asia (Malaysia, Thailand and India), EU (France, Italy, UK and Germany), and of North America (USA, Dominican Republic), whereas some were locally imported from Africa (Democratic Republic of the Congo, Ivory Coast).

We analyzed mercury in all soaps and creams of all countries, notably in 6 soaps and 18 creams purchased in Benin, in 27 soaps and 25 creams purchased in Ivory Coast, in 20 soaps and 12 creams purchased in Mali, in 23 soaps and 25 creams purchased in Senegal and in 17 soaps and 18 creams purchased in Montreal, Canada (Fig. 2a).

We measured hydroquinone in all creams of all countries. Similarly, we measured clobetasol propionate in all creams except in those containing hydroquinone exceeding 2% because we did not expect the simultaneous presence of hydroquinone and clobetasol propionate in the same cream at high concentrations. We did not measure hydroquinone or clobetasol propionate in soaps because these ingredients are not expected in lightening soaps (Groupe Thématique 'Peau Noire' de la Société Française de Dermatologie, 2011).

### 2.2. Mercury analyses

Cream and soap samples were analyzed using an automatic MERCURY SP-3D analyzer (Nippon Instruments, Osaka, Japan) in accordance with USEPA method 7473. After combustion at 700 °C, mercury was converted catalytically to elemental mercury. Following dual gold amalgamation, the quantity of mercury was measured by cold vapor atomic absorption at a wavelength of 253.7 nm. Between 10 and 100 mg of soap and cream samples were placed on a layer of an additive (mixture of sodium carbonate and calcium hydroxide; EMD Chemicals, NJ, USA) in a ceramic boat as suggested by the supplier. The sample was then covered with a layer of the same additive. A layer of aluminum oxide ($Al_2O_3$; Acros Organics) was placed over the sodium carbonate–calcium hydroxide layer. The aluminum oxide layer was covered with another layer of the additive. The boat was then transferred manually into the ceramic thermal decomposition tube. After feeding the samples, all operations from the sample decomposition to the mercury detection were automatically carried out with SP-3D mercury analyzer system. Reference materials (Tort-2, $270 \pm 60$ ng/g; Dorm-4, $410 \pm 55$ ng/g; National Research Council of Canada, Ottawa, Canada) were analyzed every 10 samples to ensure reproducibility and to assess analytical quality. The analyses were accepted when measurements of certified reference materials were in the certified range. Mean concentrations of certified materials were $284 \pm 1$ ($n=5$) and $383 \pm 2$ ($n=9$) for Tort-2 and Dorm-4, respectively. The instrument detection limit (IDL) is 0.01 ng/g.

### 2.3. Hydroquinone analyses

To extract hydroquinone, we accurately weighed 0.050 g of skin lightening cream and added 10 mL of ethanol. Samples were incubated in a water bath for 20 min at 50 °C, and let to cool down before analysis (Al-Saleh et al., 2012). We determined hydroquinone by a high-performance liquid chromatography (HPLC) method slightly modified from Al-Saleh et al. (2012) (HPLC with a UV-DAD detector, Agilent 1200, Santa Clara, US). Briefly, 1 mL of each sample was filtered through a 0.45 μm syringe filter and