



## **Skin Bleaching Practices: Products, Mechanisms and Effects**

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. Author DA designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors DAA and BOO managed the analyses of the study. Author BOO managed the literature searches. All authors read and approved the final manuscript.*

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## **ABSTRACT**

Skin bleaching is the use of chemical substances to lighten the colour of the skin. Despite various publications and documentaries on the harmful effects of skin bleaching, it is still becoming increasingly common especially among the black skin coloured individuals. A lighter skin has been perceived to be synonymous with beauty. Most skin lightening products are known to act on different pathways of melanin biosynthesis. The major lightening products used include hydroquinone, mercury and topical steroids which come as soaps, body wash, gels and creams. Skin lightening can cause a myriad of cutaneous and systemic adverse effects and so continuous public health awareness to sensitize individuals on the dangers of skin bleaching and proper regulations by the Government and relevant authorities must be put in place.

**Keywords:** *Skin bleaching; skin lightening; melani; cutaneous; systemic; adverse effects; public health.*

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## 1. INTRODUCTION

Skin bleaching also known as lightening, whitening, brightening and depigmentation, is the use of chemical substances to lighten the colour of skin [1,2]. The World Health Organization(WHO) defines skin bleaching as the intentional alteration of one's natural skin to one relatively, if not substantially lighter in colour through the use of chemical skin lightening agents, either manufactured, homemade or the combination of the two [3,4]. Bleaching is an age-long practice which initially arose out of racial prejudice and the perception that white skin is superior or more attractive. The practice of bleaching is also believed to improve appearance, attractiveness and acceptability [3,5]. The bleaching culture was reported to have gained full acceptance in Nigeria in the sixties [3], and this practice is gaining momentum all over the world. Products applied to lighten the skin can act at different sites of the melanin synthesis pathway [6,7]. Most individuals who bleach have underlying issues with self-esteem and self-worth. Colorism and racism tend to play a major role in an individual's desire to be lighter [3,8] Females are disproportionately affected, though skin bleaching can be carried out by both sexes. Many agents for skin whitening are a significant risk to health [1,6,9,10].

The objective of this article is to discuss the cutaneous and systemic effects of bleaching and the mechanisms with which various lightening agents work.

## 2. MELANIN SYNTHESIS OVERVIEW

Melanin is the main substance responsible for the colour of the skin and hair. It is a class of dark polymers generated by the body during the synthesis of melanin through the process of "melanogenesis" and it involves a chain of enzyme-catalysed chemical reactions and non-enzyme-catalysed reactions [11-13].

The variation of skin colour among individuals is mostly caused by variation of the content of melanin in the skin. Other factors that influence skin colour includes the amount of blood in blood vessels, skin thickness, and the content of carotenoids in skin [11,12].

An overview of melanogenesis is important because most of the bleaching agents act on the pathway of melanogenesis.

Two major types of melanin can be distinguished based on its chemical composition and biological route of synthesis: the black and brown eumelanin and the red and yellow pheomelanin, other types identified are the neuromelanin and the mixed melanin pigment [11,14].

Melanin is synthesized in melanosomes which are organelles produced in melanocytes. Cells dedicated to this function are present in the body and determines the colour of the skin, hair, eyes, and other structures of the body(13). Melanocyte-stimulating hormone (MSH) is a group of peptide hormones produced by the skin, pituitary gland, and hypothalamus(11,15). MSH is produced from the same precursor molecule as Adrenocorticotrophic hormone (ACTH) called pro-opiomelanocortin (POMC) [11,13-15].

Melanogenesis is a complex process which begins from the hydroxylation of L-tyrosine, to L-dihydroxyphenylalanine (L-DOPA) and several oxidation, polymerization and conjugation to the final products, eumelanin and pheomelanin [11,13] (Fig. 1).

The transfer of melanosomes with the melanin it contains to keratinocytes is a necessary condition for the visible pigmentation of the skin [11,12].

### 2.1 Literature Review

Today, the global skin lightening industry is estimated to be in the multibillion dollar range [16]. In Africa, Nigeria is the largest consumer of skin lightening products. While there is no substantial data on the use of skin lightening products around the world, a WHO report claims that 77% of Nigerian women use them on a regular basis while countries like Togo, South Africa, and Senegal are not lagging far behind [3,8,17]. Around the second half of the 20<sup>th</sup> century, there was an increase in the use of skin lightening products while the practice was said to have formally begun in Nigeria in the 1940s [3,18]. The total amount spent in Nigeria in one year was estimated to be about \$28 million [3].

Skin lightening, however, is not limited to Africa. In 2017, Asia-Pacific made up more than half of the global market for skin lightening products, with China accounting for about 40% of sales, Japan 21%, and Korea 18% [3]. In India, the sales of skin lightening creams in 2013 was about US \$300 million [4]. As of 2013, the global

market for skin lighteners was projected to reach \$19.8 billion by 2018 based on sales growth primarily in Africa, Indian-Asia, Caribbean and the Middle [4,9].

In the United states and United Kingdom, many skin whiteners are illegal. Mercury was banned by US FDA in 1973 and by EU in 1976 while hydroquinone have been banned in South Africa, Japan and EU [17]. Studies done on the concentration of mercury and hydroquinone in various soaps and creams showed a high concentration and such products are frequently still sold even after shops have been prosecuted [4,5,19,20]. Most users of these skin whitening products are unaware of the dangers they come with, also, manufacturers and promoters of these products tend to downplay the risks [3,10]. Millions of dollars are spent yearly worldwide on various bleaching products [16,121]. This practice is unregulated in many developing nations; in developed countries, enforcement of regulation is often unsatisfactory due to multiple sources of procurement, herbal extracts, off-label use of medications to mention a few [3,9].

There are legitimate reasons to bleach the skin. Some zones of hyperpigmentation may be depigmented to match the surrounding skin in some skin conditions like moles and melasma [2,4,8]. In extensive vitiligo, areas with normal skin colour may be depigmented to give a more uniform appearance [22]. However, unregulated skin bleaching can cause multiple health

problems, both local and systemic [5,9,17,23] Such problems range from striae, increased susceptibility to infections, ochronosis, poor wound healing, nephrotic syndrome, chronic kidney disease and malignancies [5,9,17,23]. Skin bleaching also affects psychological aspect of patients life as it affects the self-esteem of individuals that desire to bleach to improve attractiveness or those that are now dependent of its use and have come down with adverse effects [3,24].

## 2.2 Skin Lightening Mechanisms

Skin whitening agents work by reducing the presence of melanin in the skin and can do so by acting on any of the pathways of melanogenesis. Some of the lightening agents are known to have more than one mechanism of action [7,8,16].

## 2.3 Common Lightening Agents

### 2.3.1 Hydroquinone

Hydroquinone (1,4-dihydroxybenzene) is considered the primary topical ingredient for inhibiting melanin production [7]. It has various modes of action with which it causes skin lightening some of which are the inhibition of tyrosinase synthesis, the destruction of melanocytes, depletion of glutathione with concomitant melanosome degradation and melanocyte damage [1,7,17,25].

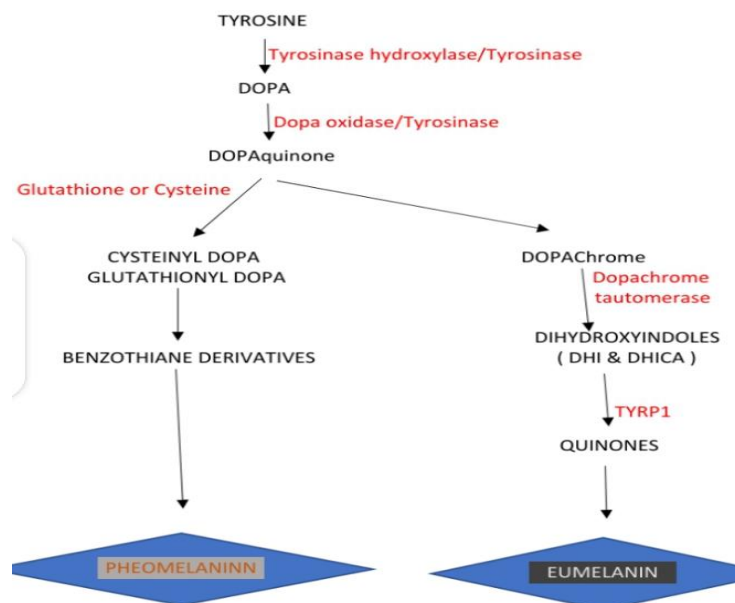


Fig. 1. Melanin biosynthesis pathway (Original: designed by author)

**Table 1. Skin lightening agents and their mechanisms of action**

<b>Skin lightening mechanisms</b>	<b>Lightening agent</b>
Tyrosinase activity inhibition	Hydroquinone, mequinol, arbutin, azelaic acid, kojic acid, resveratrol
Inhibition of tyrosinase transcription	Tretinoin, glucosamine, retinol, retinaldehyde, N-acetylglucosamine
Acceleration of epidermal turnover	Retinoids, lactic acid, vitamin C, vitamin E, glycolic acid, salicylic acid
Inhibition of melanosome transfer	Linoleic acid, Niacinamide (Vitamin B3), serine protease inhibitors, lecithin
Destroying melanocytes	Hydroquinone
Anti-inflammatory	Niacinamide, soymilk
Antioxidants	Vitamin C, vitamin E, glutathione

Topical hydroquinone comes in 2% -4% or greater as the percentage constitution in most western countries have been set to that limit [7]. With topical use, it is known to cause several adverse effects like permanent depigmentation, exogenous ochronosis, nail discolouration and contact dermatitis while its metabolite has been implicated in bone marrow toxicity [10,11,25].

### 2.3.2 Corticosteroids

Topical corticosteroids (TCs) can be effective by the suppression of cytokines such as endothelin-1 and GM-CSF, which mediate UV-induced pigmentation [23]. TCs inhibit pro-opiomelanocortin (POMC), the precursor protein for  $\alpha$ -melanocyte stimulating hormone ( $\alpha$ -MSH), which is produced in the intermediate lobe of the pituitary to stimulate epidermal melanin production thus causing bleaching of the skin [1,10,17,26]. They are also known to cause initial blanching due to vasoconstriction and slowing down skin cell turnover by decreasing the number and activity of melanocytes [24].

### 2.3.3 Glutathione

Glutathione is a tripeptide molecule and an antioxidant that plays an important role in preventing oxidative damage to the skin [27]. Amongst the many mechanisms postulated to contribute to its anti-melanogenic properties are inhibition of tyrosinase enzyme, skewing of melanogenesis from the darker eumelanin to the lighter pheomelanin and scavenging of free radicals [6].

### 2.3.4 Mercury

Many skin whiteners contain a form of toxic mercury as the active ingredient.

Mercury in cosmetics exists in two forms: inorganic and organic [5,10] Inorganic

mercury (e.g. ammoniated mercury) is used in skin lightening soaps and creams while organic mercury compounds [ethyl mercury] and phenyl mercuric salts) are used as cosmetic preservatives in eye makeup, cleansing products and mascara [1,6]. Mercury has been banned in most countries for use in skin whitening. According to the World Health Organization (WHO), a product contains mercury if you see one of more of these ingredients: calomel, cinnabaris, hydrargyri oxydum rubrum and quicksilver [4,7].

Adverse effects of the inorganic mercury contained in skin lightening soaps and creams include kidney damage, skin rashes, reduction in skin resistance to infections, peripheral neuropathy and psychosis [1,5,9,10,19].

### 2.3.5 Arbutin

Some alternative skin lighteners are derived from natural sources of hydroquinone. It is a naturally occurring beta-D-glucopyranoside of hydroquinone [7,28].

Arbutin is derived from the leaves of bearberry, cranberry, mulberry, or blueberry shrubs, and is also present in most types of pears. Its depigmenting mechanism is thought to act by reversibly suppressing melanosomal tyrosinase activity [14,28].

Arbutin and other plant extracts are considered safe alternatives to commonly used depigmenting agents to make the skin fairer. It is reported to be less cytotoxic to melanocytes compared to hydroquinone [14,25,18]. A major setback in its use is that it causes paradoxical hyperpigmentation [28].

### 2.3.6 Kojic acid

Kojic acid (5-hydroxy-2 hydroxymethyl-4-pyrone) is a by-product in the fermentation process of malting rice for use in the manufacturing of sake, the Japanese rice wine [7].

Kojic acid inhibits catecholase activity of tyrosinase [14] Kojic acid is an unstable ingredient in cosmetic formulations so kojic dipalmitate is used as an alternative [1,19].

### 2.3.7 Vitamin C

Vitamin C and its various forms, including ascorbic acid and magnesium ascorbyl phosphate (MAP), are considered an effective antioxidant for the skin and help to lighten skin [8,19]. It acts by raising glutathione levels in the body [6,4]. It also interacts with copper ions at the tyrosinase active site and acts as a reducing agent at various oxidative steps of melanin formation, hence inhibiting melanogenesis [8].

## 2.4 Other or Ungrouped Treatment

### 2.4.1 Complications of bleaching

Long-term use of skin lightening compounds can cause both systemic and cutaneous adverse

effects [1,9,10,23,26,18]. Some of these effects can be detrimental to health therefore, mass enlightenment is required to create awareness of the dangers of these products. Most effects are cutaneous (local) however, systemic effects which are mostly due to suppression of the hypothalamic-pituitary-adrenal axis and transdermal absorption of hazardous substances can also be seen [1,9,10,24,18].

### 2.4.2 Exogenous ochronosis

This condition was first reported by pick in 1906 [10]. It presents as blue-black macules on sun exposed area like the malar area, temple, inferior cheek, and neck [10,20,29] (Fig. 2) .The lightening agent implicated is hydroquinone, though, phenol or resorcinol have also been reported to be associated with exogenous ochronosis [6,8,29] Histologically, yellow-brown banana shaped fibres are seen in the papillary dermis [10]. Homogenization and swelling of the collagen bundles with moderate histiocyte infiltration is also noted [10].

### 2.4.3 Steroid complications

Skin lightening products that contain corticosteroids can cause steroid acne,

**Table 2. Other skin lightening agents**

Lightening agent	Effect
Monobenzene	Cause destruction of melanocytes and permanent depigmentation [20].
Mequinol	It is a melanocytotoxic agent and UV inhibitor [7,8].
Azelaic acid	It is a component of grains, such as wheat, rye, and barley. It acts by reducing the production of keratin [14].
Alpha Hydroxy acid (AHA)	are a class of chemical compounds that consist of a carboxylic acid substituted with a hydroxyl group on the adjacent carbon [7,8].

**Table 3. Effects of skin lightening agents**

Cutaneous Effects	Systemic Effects	Others
<ul style="list-style-type: none"> <li>• Exogenous ochronosis</li> <li>• Acne and hypertrichosis</li> <li>• Prominent striae</li> <li>• Telangiectasia</li> <li>• Skin atrophy</li> <li>• Dermatophyte infections</li> <li>• Bacterial infections like pyoderma, erysipelas</li> <li>• Scabies</li> <li>• Contact dermatitis</li> <li>• Folliculitis</li> <li>• Impaired wound healing and wound dehiscence,</li> <li>• Fish odor syndrome</li> </ul>	<ul style="list-style-type: none"> <li>• Hypertension,</li> <li>• Hyperglycaemia</li> <li>• Hypercorticism or adrenal deficiency</li> <li>• Mercurial nephropathy.</li> <li>• Peripheral neuropathy</li> <li>• Neuropsychiatric symptoms</li> </ul>	<ul style="list-style-type: none"> <li>• Glaucoma</li> <li>• Cataract</li> <li>• Osteoporosis</li> <li>• Menstrual irregularities</li> <li>• Steroid addiction syndrome</li> </ul>

**Table 4. Complications of use of the three major lightening agents**

<b>Hydroquinone</b>	<b>Steroid</b>	<b>Mercury</b>
Exogenous ochronosis	Steroid addiction syndrome	Renal damage
Allergic contact dermatitis	Striae	Neuropsychiatric symptoms
Irritant contact dermatitis	Steroid acne	Limb tremors
Nail discoloration	Folliculitis	Gingivitis
Conjunctival melanosis	Hypertrichosis	Erythroderma
Post inflammatory hypo or hyperpigmentation	Skin atrophy	Peripheral neuropathy
Carcinogenic effect	Telangiectasia	
	Cataract and glaucoma	
	Cutaneous infections (Tinea, Erysipelas)	
	Hypertension	
	Hyperglycaemia and DM	
	Cushingoid syndrome	
	Osteoporosis	

skin atrophy, striae, hypertrichosis and folliculitis as cutaneous effects [9,10,23]. Steroid acne lesions are usually papular, pustular or nodulocystic with comedones (Fig. 3). They can be found on the face, back, neck. Some patients may develop malassezia folliculitis also, following steroid use. Steroids can also cause vellus hair growth leading to hypertrichosis, though commoner with systemic steroids [23]. Skin atrophy and striae are also known to be caused by topical steroid use (Fig. 4).

#### 2.4.4 Infections and infestations

Dermatophytes are fungi that require keratin for growth and can cause superficial infections of the skin, hair, and nails. Fungal infections of the skin can be as a result of skin bleaching [9,10]. Tinea corporis and Tinea versicolor are among the common dermatophyte infections reported in several studies [2,9,23]. The use of topical steroids makes the fungal skin infection lose its characteristic feature presenting as Tinea incognito [10] (Fig. 5). Some may present with bacterial infections like pyoderma and erysipelas (Fig. 6), and infestations with scabies are also quite common [9,18,23].

#### 2.4.5 Systemic complications

Several systemic complications have been reported to associated with chronic use of skin lightening products [1,10] These complications are usually due to suppression of the hypothalamic-pituitary-adrenal axis from corticosteroid use which can cause hypertension, diabetes and Cushing's disease [1,9,10,29]. Other systemic complications can arise as a result of transdermal absorption and subsequent toxicity of the kidneys and the brain [17,18].



**Fig. 2. Exogenous ochronosis (photo credit-authors)**



**Fig. 3. Steroid acne (photo credit-authors)**

#### 2.4.6 Renal damage

Chronic exposure of the body to bleaching preparations can cause severe toxicity leading to



renal damage [4,6,19]. The product is usually absorbed through the skin and accumulates in body organs. Mercury and hydroquinone have been implicated as causative agents causing renal damage, however, mercury causes significant nephrotoxicity compared to other skin bleaching agents [2,9]. The type of mercury, the duration and the route of exposure will determine the degree of severity the patient comes down with and the type of toxicity [4,5]. Organic and metallic mercury are lipophilic and typically cause neurotoxicity, whereas inorganic mercury typically causes nephrotoxicity [1,5].



**Fig. 4. Striae (photo credit-authors)**



**Fig. 5. Tinea incognito (photo credit-authors)**

### 3. CONCLUSION

Colorism is a complex and loaded notion that requires re-examining our cultural norms about beauty. Skin bleaching practices are highly valued and practised majorly amongst black skin coloured individuals. This can cause mild to

debilitating effects and should be discouraged. Long-term educational approach will take a lot of time and effort.

Education and awareness campaigns with a deliberate attempt to broaden the spectrum of the skin tones that we see on our TV screens, billboards and cinemas will help the needle on colorism to eventually shift.

Strict regulations to ensure the safety of skin products being sold in stores across the continent as well as stiffer reprimand against offenders of these regulations would send a signal that the government means business.

### COMPETING INTERESTS

Authors have declared that no competing interests exist.

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