Unveiling the Risks: Endocrine Disrupting Effects of Components in Skin Lightening Creams

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Abstract

Skin lightening is a widespread cosmetic practice that involves the use of chemical compounds to alter skin tone, often with the aim of achieving a lighter complexion. Despite its popularity, there is growing concern about the potential health risks associated with skin bleaching products, particularly their effects on the endocrine system. This narrative article explores the complex relationship between skin bleaching components and their impact on endocrine function, shedding light on a critical yet often overlooked aspect of this controversial practice. The findings in this study suggest that the endocrine disrupting effects of skin lightening components extend beyond localized skin reactions to systemic disturbances in hormone regulation. Therefore, the use of skin lightening creams should be approached with caution. Regulatory measures are also urgently needed to restrict the use of harmful ingredients in cosmetic products and promote safer alternatives. Healthcare providers play a vital role in educating the public about the risks of skin lightening and advocating for stricter regulations to protect consumer health. Addressing the endocrine disrupting effects of skin bleaching components is crucial for safeguarding the wellbeing of individuals and communities worldwide.

Keywords: *Endocrine disruptors, Skin bleaching, Hydroquinone, corticosteroids, alpha hydroxyl acids*

1.0 Introduction

Skin lightening, a cosmetic practice aimed at altering skin color by lightening it, has a long history dating back to the slave trade era (Thant *et al*., 2023). This practice involves the topical application of cosmetics containing chemical agents such as hydroquinone, corticosteroids, mercury, among others to the skin. Despite stringent regulations in some countries, evidence suggests that skin lightening products containing mercury remain commonly used, particularly in African and Asian countries. (Thant *et al*., 2023)

In Africa, this is currently practiced by people irrespective of age, gender, level of education, social status and religious belief (Asumah *et al*., 2022). The prevalence of skin lightening in

Africa is 27.1% while a prevalence of 77% has been reported in Nigeria, thus, making the country the African country with the highest use of skin lightening cosmetics (Thant *et al*., 2023). A report showed that 72% women and 28% men used skin lightening cosmetics in Nigeria (Olumide *et al*., 2008). Prevalence of 30%, 50% and 60% were reported in Ghana, Mali and Senegal, respectively (Yayehrad *et al*., 2024).

A variety of skin lightening cosmetic brands are available in the Nigerian market, each with its unique composition. In a study conducted in Ago Iwoye, Ogun state, Nigeria, the hydroquinone levels in four commonly used skin lightening creams were assessed. The concentration of hydroquinone ranged from 2.58% to 4.17%, exceeding the minimum requirement of 2% set by the World Health Organization (WHO) (Osobamiro *et al*., 2023). The brands analyzed included Caro White, Paw Paw, Honey e, and White Essence (Osobamiro *et al*., 2023). Another study identified several brands containing hydroquinone, such as Carotone, Caro White, Looking Good, and Skin Light. Conversely, brands like Pure Skin, Clear Essence, Movate, and Perfect White were found to be non-hydroquinone containing skin lightening creams (Nwosu *et al*., 2019).

The widespread use of skin lightening products in Africa can be attributed to a complex interplay of economic, sociocultural, and psychosocial factors. These factors are deeply rooted in historical contexts, including the legacy of white supremacy beliefs and the enduring impact of colonialism (Egbi and Kasia, 2021, Thant *et al*., 2023).

The endocrine system plays a vital role in regulating various physiological processes by releasing hormones, which control metabolism, growth, development, reproduction etc. Endocrine disruption is the interference of the endocrine system with certain chemicals termed endocrine disrupting chemicals. They interfere with synthesis, transport, receptor binding and metabolism of hormones (Ahn and Jeung, 2023). The consequences of endocrine disruption can range from reproductive disorders to metabolic dysfunction and increased risk of certain cancers.

Several studies have been conducted on skin bleaching, there is however paucity of information on the interference of the components of skin bleaching cosmetics on the endocrine system. This review aims to explore the complex relationship between skin lightening components and their impact on endocrine function, shedding light on a critical yet often overlooked aspect of this controversial practice.

2.0 Components of Skin Lightening Cosmetics

Skin lightening products contain a variety of chemical compounds that inhibit melanin production, the pigment responsible for skin coloration. Some of the most commonly used skin lightening components include hydroquinone, corticosteroids, mercury, alpha hydroxy acids (AHAs), arbutin kojic acid and azelaic acid (Gillbro and Olsson, 2011, Owolabi *et al*., 2020, Egbi and Kasia, 2021).While these compounds are intended to lighten the skin, their potential endocrine disrupting effects raise significant concerns about their safety.

Hydroquinone has been a prominent ingredient in cosmetics utilized for hyperpigmentation treatment for more than four decades (Gilbro and Olsson, 2011). It acts by binding to histidine molecules located at the active site of tyrosinase. This interaction inhibits the oxidation of tyrosine to L-dihydroxylphenylalanine (L-DOPA), consequently disrupting melanin synthesis. This mechanism of action is well-documented as the depigmentation mechanism of hydroquinone.(Juliano, 2022). Hydroquinone is also implicated in the generation of free radicals, which contributes to the oxidative damage of biological membrane components. It is hypothesized that hydroquinone reduces glutathione levels, resulting in decreased nucleic acid synthesis and the degradation of melanosome (Gilbro and Olsson, 2011).The most prevalent complication associated with hydroquinone usage is ochronosis. This condition is thought to occur due to the inhibition of dermal homogentisate oxidase activity by hydroquinone, leading to the accumulation of homogentisate. Subsequently, homogentisate undergoes polymerization, resulting in the formation of ochronotic pigment (Juliano, 2022). Trimethylaminuria, characterized by a fishy odor in body fluids, is another recognized complication associated with hydroquinone use. It is postulated that hydroquinone inhibits the oxidation of trimethylamine to trimethylamine N-oxide, contributing to the manifestation of this condition (Juliano, 2022).

Arbutin, a derivative of hydroquinone, exhibits melanogenesis inhibition by competitively and reversibly binding to tyrosinase. Notably, it achieves this without disrupting tyrosinase mRNA transcription, distinguishing its effects as milder compared to hydroquinone (Gillbro and Olsson, 2011, Juliano, 2022)

Kojic acid functions as a tyrosinase inhibitor by chelating copper atoms located within the active site of tyrosinase (Liu *et al*., 2022). Additionally, it inhibits dopachrome tautomerization to 5,6-

dihydroxyindole-2-carboxylic acid, further contributing to its melanogenesis inhibition effects.(Owolabi *et al*., 2020, Phasha *et al*., 2022).

Azelaic acid operates as a competitive inhibitor of tyrosinase, thereby exerting its melanogenesis inhibitory effects. Additionally, its anti-proliferative and cytotoxic properties are linked to its ability to inhibit thioredoxin reductase.(Gillbro and Olsson, 2011).

3.0 Endocrine disrupting Effects of Some Skin Bleaching Components

Evidence suggests that certain components of skin lightening products have the capacity to disrupt the endocrine system, potentially leading to both local and systemic disorders. This aspect will be explored in the following section

Hydroquinone

In spite of the various studies conducted on hydroquinone, reports on its hormone disrupting potentials have not been adequately studied. Hydroquinone has been implicated in thyroid disorders. This is via interference with thyroid hormone synthesis and function (Owolabi *et al*., 2020). Thyroid hormones play a crucial role in the metabolism, growth and development, and disruptions in thyroid function can have far-reaching consequences for overall health.

A study revealed that the application of hydroquinone-containing cream led to a significant overestimation of capillary glucose levels, persisting for approximately one hour after cosmetic use (Omengue *et al*., 2018). A similar finding was reported in another study (Choukem *et al*., 2018). Additionally, participants using a 1% hydroquinone-containing cosmetic displayed elevated capillary glucose levels, despite insulin adjustments in a separate report (Bouche *et al*., 2015). The exact mechanism behind this phenomenon remains unclear, but it may impact the pancreatic beta cells responsible for insulin production. Elevated blood glucose levels typically trigger insulin release to facilitate cellular glucose uptake, implying that prolonged use of hydroquinone-based creams could potentially accelerate pancreatic beta cell aging and death.

The link between endocrine disruption and oxidative stress has been suggested (Kim *et al*., 2022). Hydroquinone has been documented to trigger oxidative stress within retinal pigment epithelium

(RPE) cells (Bhattarai *et al*., 2021). The heightened production of reactive oxygen species (ROS) is recognized as a catalyst for activating the Nucleotide-binding domain, Leucine-rich repeat, and Pyrin domain 3 (NLRP3) inflammasome, leading to the cleavage and subsequent release of interleukin-1 beta (IL-1β), which is implicated in inflammatory disease pathogenesis (Bhattarai *et al*., 2021). Additionally, in another investigation, hydroquinone was found to elevate oxidative stress in retinal pigment epithelium (RPE) cells through the activity of NADPH oxidase (Bhattarai *et al*., 2020). Further studies have corroborated these findings, demonstrating hydroquinone's ability to induce ROS production in ARPE-19 cells (Kauppinen *et al*., 2012; Piippo *et al*., 2018 Bhattarai *et al*., 2020).

The carcinogenicity of hydroquinone remains a topic of debate; nevertheless, numerous reports suggest its potential carcinogenic and genotoxic effects. Hydroquinone has been linked to DNA damage, evidenced by reduced intracellular poly(ADP-ribose) polymerase (PARP) levels. Additionally, it has been implicated in the induction of NLRP3-independent secretion of interleukin-18 (IL-18) in human RPE cells (Bhattarai *et al*., 2021).

Hydroquinone has been associated with an elevated occurrence of renal tubule adenomas in male F344 rats (O' Donoghue *et al*., 2021). Moreover, increased rates of liver adenomas and thyroid gland follicular cell hyperplasia have been documented in both male and female B6C3F1 mice following exposure to hydroquinone (Kari, 1989, Shibata *et al*., 1991). Additionally, hydroquinone has been linked to leukemia, hepatic carcinoma, and renal tubular carcinomas (Kari *et al*., 1992). In vitro studies have indicated the genotoxic potential of hydroquinone in cell cultures, demonstrating chromosomal alterations such as increased frequencies of DNA gaps, DNA breaks, and sister chromatid exchanges (Tsutsui *et al*., 1997). One hypothesis posited that the genotoxic effect of hydroquinone may stem from the cellular production of peroxide, leading to DNA fragmentation and eventual apoptosis (Hiraku and Kawanishi, 1996). However, contrasting findings were reported in a study where no evidence of DNA damage was observed in certain cells exposed to hydroquinone at doses up to 420 mg/kg/day (O'Donoghue *et al*., 2021).

Hydroquinone's detrimental impact on immune functions has been documented. One study revealed its capacity to heighten immunologic allergic reactions by promoting the production of

immunoglobulin E and interleukin-4 (Lee *et al*., 2002). Similarly, another study demonstrated that hydroquinone disrupted innate host defenses against bacteria by inducing oxidative stress and modifying membrane receptors in circulating neutrophils (Ribeiro *et al*., 2011). Hydroquinone also disrupts immune responses by inhibiting lymphocyte proliferation through the suppression of DNA synthesis (Li *et al*., 1996). Its cytotoxic effects on immune system cells, including eosinophils, neutrophils, and lymphocytes, occur via the caspase 9/3 pathway (Yang *et al*., 2011; Lee *et al*., 2012).

Corticosteroids

Corticosteroids, when absorbed into the bloodstream through topical application, can suppress the Hypothalamus-Pituitary- Adrenal (HPA) axis and impair adrenal function (Maguire and Hoff, 2011). This can result in adrenal insufficiency, characterized by fatigue, weakness, and immune dysfunction. In severe cases, adrenal crisis may occur, posing a life-threatening emergency (AlQadri *et al*., 2022)**.**

Prolonged use of corticosteroid-containing skin bleaching products can lead to persistent hyperglycemia. This is attributed to the corticosteroids' capacity to stimulate glucose production in the liver and promote lipolysis in adipose tissue. Consequently, these actions contribute to insulin resistance and disturbances in insulin production, both of which are implicated in the development of diabetes mellitus.(Li and Cummins, 2022).

Corticosteroids have been found to decrease peripheral glucose uptake in muscle and adipose tissues (Sakoda *et al*., 2000, van Raalte *et al*., 2009). Prolonged use of glucocorticoids can lead to changes in body composition, including an increase in adipose tissue deposition in the trunk region (Suh and Park, 2017). Furthermore, corticosteroids promote endogenous glucose production by activating various genes involved in hepatic carbohydrate metabolism, thereby stimulating gluconeogenesis (Vegiopoulos and Herzig, 2007, van Raalte *et al*., 2009).

Glucocorticoids are known to induce appetite and augment caloric food consumption, thereby heightening susceptibility to obesity and diabetes mellitus. These effects are mediated in part through the stimulation of neuropeptide Y in the hypothalamus, leading to enhanced leptin resistance. Additionally, glucocorticoids stimulate gluconeogenic enzymes and promote insulin resistance in the liver, ultimately resulting in hyperglycemia (Li and Cummins, 2022).

Glucocorticoids stimulate the beta cells of the pancreas, resulting in increased insulin secretion (hyperinsulinemia) and hyperplasia of the beta cells as a compensatory mechanism to counteract glucocorticoid-induced insulin resistance. However, continuous exposure to glucocorticoids can lead to apoptosis of pancreatic beta cells. Furthermore, glucocorticoids inhibit the secretion of osteocalcin, which indirectly affects insulin secretion.(Li and Cummins, 2022).

Glucocorticoid-induced diabetes mellitus (GIDM) has been recognized as a complication of glucocorticoid therapy for over six decades (Suh and Park, 2017). Its prevalence is estimated to be around 12%, although, the exact prevalence of hyperglycemia resulting from glucocorticoid therapy remains uncertain, posing a challenge for healthcare providers and endocrinologists. Glucocorticoids exacerbate hyperglycemia in diabetic patients, reveal previously undiagnosed diabetes mellitus, or may trigger the onset of GIDM, which represents an independent risk factor for other complications associated with glucocorticoid use (Perez *et al*., 2014). Other mechanisms underlying GIDM include inhibited glyceroneogenesis, pancreatic beta cell destruction, and increased fatty acid synthesis (Suh and Park, 2017).

Continued elevation of blood sugar levels resulting from glucocorticoid use heightens the susceptibility to infections (Suh and Park, 2017). Both diabetic and non-diabetic hospitalized patients with hyperglycemia have shown poorer outcomes, regardless of the underlying condition (Brady *et al*., 2014). Adequate management of blood sugar levels has been linked to reduced complications and lower mortality rates (ADA, 2017, Umpierrez *et al*., 2012, Baldwin and Apel, 2013). Moreover, prolonged use of glucocorticoids raises the risk of cardiovascular diseases (Kwon and Hermayer, 2013). This could be via mechanism involving the up-regulation of plasma endothelin-1 by corticosteroids (Börcsök *et al*., 1998). Endothelin-1 is a vasoconstrictor linked with cardiovascular disease. (Deng *et al*., 2023)

A research study revealed a link between the administration of glucocorticoids and hypertension among patients diagnosed with rheumatoid arthritis (Costello *et al*., 2021). While the investigation concentrated on individuals who orally consumed glucocorticoids at a dosage of ≥7.5 mg, it implies that those with rheumatoid arthritis who utilize cosmetics containing corticosteroids may face an elevated likelihood of developing hypertension.

Prolonged and excessive glucocorticoid therapy leads to an augmentation in body fat accumulation, characterized by a greater distribution of visceral abdominal fat compared to peripheral subcutaneous fat (Rafacho *et al*., 2014, Geer *et al*., 2014).

Mercury

Mercury-containing cosmetics induce skin whitening by competing with copper ions in tyrosinase, binding to the histidine residue in the enzyme's catalytic center, thus inhibiting melanin synthesis (Chen *et al*., 2020). Mercury salts in creams and cosmetics are readily absorbed by the skin, penetrating the epidermis and entering through the sweat glands and hair follicles (Park and Zheng, 2012). Skin absorption of mercury is influenced by various factors including the frequency of topical application, the lipophilic nature of the cosmetic vehicle, mercury concentration, skin integrity, and the hydration level of the stratum corneum (Juliano, 2022).

Reported signs of mercury poisoning from the use of skin whitening cosmetics include both organ-specific and systemic symptoms. Gastrointestinal disturbances such as nausea, hypersalivation, metallic taste in the mouth, and gingivostomatitis have been documented (Juliano, 2022). Neuropsychiatric symptoms, including muscular weakness, depression, anxiety, peripheral neuropathy, and psychosis, are commonly observed (Engler, 2005, Mohammed *et al*., 2017). Acute renal tubular necrosis and chronic renal glomerular injury are indicative of acute and chronic mercury poisoning, respectively (Ladizinski *et al*., 2011). The ability of mercury to pass from the mother to the fetus via the placenta underscores the potential harm of using skin lightening cosmetics containing mercury during pregnancy (Engler, 2005, Juliano, 2022). Additionally, hypertension has been reported in children exposed to mercury-containing skin whitening creams (Copan *et al*., 2015).

Evidence suggests that even low levels of mercury exposure can disrupt the endocrine system, affecting organs such as the pituitary, thyroid, adrenal glands, and pancreas (Minoia *et al*., 2009).

Mercury exerts its endocrine-disrupting effects through various mechanisms, including reducing hormone-receptor binding and inhibiting important steroidogenic enzymes such as 21 α hydroxylase (Iavicoli *et al*., 2009). Insulin, adrenaline, testosterone, and estrogen are among the primary hormonal targets of mercury (Rice *et al*., 2014).

The inhibition of catecholamine breakdown due to the inactivation of S-adenosyl-methionine by mercury can lead to the systemic accumulation of epinephrine, resulting in symptoms such as ptyalism, tachycardia, hypertension, and hyperhidrosis (Clifton, 2007). Individuals exposed to mercury have been reported to exhibit reduced plasma levels of corticosterone (Iavicoli *et al*., 2009). Additionally, mercury exposure may induce adrenal hyperplasia, leading to stress on the adrenal gland and potentially contributing to adrenal atrophy, which could be a contributing factor in the pathogenesis of Addison's disease (Wada *et al*., 2009).

Mercury has also been associated with decreased pituitary function, which has been linked to symptoms of depression and suicidal thoughts in susceptible individuals, particularly teenagers (Rice *et al*., 2014). Furthermore, mercury exposure has been implicated in symptoms such as frequent urination and high blood pressure (McGregor and Mason, 1991).

Autopsy reports have revealed that the thyroid and pituitary glands have the potential to accumulate inorganic mercury to a greater extent than the kidneys (Tan *et al*., 2009). In a study, mercury levels in the pituitary gland were found to range from 6.3 to 77 ppb (Nylander and Weiner, 1991).

The detrimental impact of mercury on male and female fertility has been extensively documented (Sukhn *et al*., 2018, Maeda *et al*., 2019). Studies in experimental animals have revealed the accumulation of mercury in the ovaries, where it interferes with the secretion patterns of gonadotropins, disrupts ovarian cyclicity, and induces apoptosis of follicular cells and follicular atresia (McClam *et al*., 2023). Mercury-induced female infertility is associated with increased prolactin secretion, which negatively affects galactopoiesis (Bjørklund *et al*., 2019). Women exposed to mercury have reported conditions such as polycystic ovarian syndrome, amenorrhea, dysmenorrhea, galactorrhea, early menopause, and endometriosis, all of which are linked to infertility (Yang *et al*., 2002, Jones *et al*., 2007, Pan *et al*., 2007).

In individuals exposed to low levels of mercury, diminished semen quality and alterations in sex hormone levels have been observed (Li *et al*., 2022). Studies have shown that mercury accumulation in the testicles can disrupt testicular steroidogenic and spermatogenic functions (Rao and Gangadharan, 2008). Additionally, pre and postnatal exposure to mercury has been associated with reduced testosterone levels and Tanner stage >1 in children (Sarzo *et al*., 2022,

Liu *et al*., 2023). Co-exposure to mercury with other toxic metals like arsenic and cadmium may result in genetic polymorphism (Wirth and Mijal, 2010).

Mercury has been found to interfere with thyroid function by inhibiting thyroid hormone synthesis. This inhibition occurs through mechanisms that involve blocking iodine-binding sites, leading to disruptions in thyroid hormone production. Consequently, individuals exposed to mercury may experience dysregulation of body temperature, thyroid gland hyperplasia, and ultimately develop hypothyroidism (McGregor and Mason, 1991, Wada *et al*., 2009, Rice *et al*., 2014).

Research indicates that the pancreas may also be susceptible to the effects of mercury exposure. Mercury has been shown to bind to the sulfur-binding sites of insulin, leading to alterations in insulin production. This disruption in insulin production can result in dysglycemia, contributing to disturbances in blood sugar levels. (Chen *et al*., 2006, Rice *et al*., 2014).

There appears to be a combined impact of mercury and hydroquinone in individuals using hydroquinone-containing creams. According to a study conducted in Nigeria, pregnant women who used hydroquinone-containing creams showed significantly higher levels of serum mercury compared to those who did not use such creams. This was attributed to the aggravation of environmental dermal absorption of mercury by hydroquinone present in the skin lightening creams (Nwosu *et al*., 2019).

Persistent exposure to mercury, particularly through the application of skin lightening creams, can increase the susceptibility of users to both localized and systemic infections (Arinola *et al.*, 2011; Diousse *et al*., 2017).

The heightened susceptibility to infections in individuals using skin lightening products could result in an upsurge of phagocytes in response to infections, causing the generation of free radicals and depletion of antioxidants, consequently diminishing antioxidant capacity. This cascade of events may trigger oxidative stress (Taylor, 2002, Olumide *et al*., 2008, Arinola *et al*., 2011).

Alpha Hydoxyl Acids (AHA)

Hydroxyl acids are organic compounds characterized by the presence of one or more hydroxyl groups linked to a carboxylic acid. They are commonly found in nature, occurring naturally in

certain fruits, sugarcane, honey, and other sources (Barote *et al*., 2022). Hydroxy acids are broadly categorized into alpha and beta hydroxy acids. Alpha hydroxy acids include malic acid, glycolic acid, lactic acid, citric acid, and tartaric acid (Tang and Yang, 2018). These compounds are utilized in the treatment of keratinization disorders such as photoaged skin and acne, primarily due to their exfoliating potentials (Werth, 2012).

While hydroxyl acids are naturally occurring compounds, recent studies have highlighted their potential adverse effects. Reports have documented various skin reactions associated with their use, including swelling, rashes, itching, and changes in skin pigmentation, among others (CFSAN, 2024; Barote *et al*., 2022). The safety profile of AHAs is influenced by factors such as pH, concentration, the presence of free acid, and duration of exposure (Tang and Yang, 2018). Additionally, research has suggested that excessive sunlight exposure following the topical application of AHAs may increase the risk of photosensitivity to ultraviolet radiation and contribute to uneven skin pigmentation (Tang and Yang, 2018).

According to the report, individuals subjected to glycolic acid treatment at concentrations ranging from 20-50% for keratin layer removal experienced notable ultraviolet damage (Tang and Yang, 2018). Another study indicated that AHAs modified both the epidermal and dermal layers of the skin, with 1% AHA affecting the pH of the outer stratum corneum (Antoniou *et al*., 2010). Clinical tests have identified malic acid as an irritant, with reduced irritation noted as the pH of the applied substance rises. The concerns may arise from their interactions with the skin, particularly the epidermis (Tang and Yang, 2018).

Cancer, potentially stemming from disruptions in endocrine function, is characterized by the excessive production and buildup of lactate (Lee *et al*., 2021). During carcinogenesis, glycolysis is activated to produce energy (Lee, 2021). Changes in the genetic and epigenetic makeup that affect Krebs cycle enzymes facilitate the transition of cancer cells from oxidative phosphorylation to anaerobic glycolysis (Sajnani *et al*., 2017). This shift occurs because ATP generation through glycolysis is easier compared to oxidative phosphorylation, thereby promoting the proliferation of cancer cells. Approximately 60% of the required ATP is derived from glycolysis (DeBerardinis and Chandel, 2020).

Alpha hydroxyl acids, although, primarily used for their exfoliating properties, may also exert endocrine disrupting effects (Kornhauser *et al*., 2010). Limited research suggests that AHAs may interfere with hormone signaling pathways, potentially disrupting the delicate balance of endocrine regulation. Further studies are needed to elucidate the full extent of AHAs' impact on endocrine function.

4.0 Skin Pigmentation and Skin Lightening Practices in Pregnancy

During pregnancy, about 90% of expectant mothers frequently experience various changes in their skin, which include physiological alterations caused by hormonal changes, worsening of pre-existing skin conditions, and specific dermatoses unique to pregnancy, all requiring specialized care and treatment (Putra *et al*., 2022). Hormonal flunctuations, such as increase in oestrogen, progesterone, prolactin, and β-HCG are associated with skin pigmentation during pregnancy. Furthermore, alterations in protein, lipid, and carbohydrate metabolism, and adaptations in immune responses have also been implicated in skin pigmentation in pregnancy (Urasaki, 2010, Maluf *et al*., 2017). One notable physiological change observed during pregnancy involves elevated levels of androgens, which can exacerbate or accelerate the development of acne vulgaris and promote increased hair growth in various body areas (Bozzo *et al*., 2011). While these changes usually improve after delivery, they may persist, posing challenges for treatment (Karen and Pomeranz, 2012).

Oxidative stress has been reported in newly delivered mothers that used skin lightening creams and their babies. In a report, levels of hydrogen peroxide were notably elevated in the serum of mothers who used skin lightening cream and in the cord blood of their infants compared to those who did not use such creams, both in maternal serum and cord blood samples (Adeyera *et al*., 2020). Moreover, the total antioxidant capacity in the cord blood of infants born to mothers using skin lightening cream was significantly lower compared to infants born to non-users (Adeyera *et al*., 2020). Evidence suggests that pregnant women who use skin lightening products containing teroids may face an increased likelihood of delivering babies with smaller placentas and potentially lower birth weights (Sendrasoa *et al*., 2017).

Table 1: Endocrine Disrupting Mechanisms of Certain Components of Skin Lightening Creams

Endocrine disrupting Component	Mechanism(s) of action	Refs
Hydroquinone	Interference with thyroid hormones metabolism	Owolabi *et al*., 2020
Hydroquinone	Overestimation of glucose level	Omengue *et al*., 2018, Choukem *et al*., 2018
Hydroquinone	Induction of oxidative stress	Bhattarai *et al*., 2020, 2021
Corticosteroid	Suppression of hypothalamus-pituitary-adrenal axis	Maguire and Hoff, 2011
Corticosteroid	Elicitation of persistent hyperglycaemia	Li and Cummins, 2022
Corticosteroid	Elicitation of hyperinsulinaemia	Li and Cummins, 2022
Mercury	Reduction of hormone-receptor binding Inhibition of key steroidogenic enzymes. Example: 21 α hydroxylase	Iavicoli *et al*., 2009
Mercury	Inhibits catecholamine breakdown due to the inactivation of S-adenosyl-methionine	Clifton, 2007
Mercury	Interferes with corticosterone synthesis	Iavicoli *et al*., 2009
Mercury	Induces adrenal hyperplasia	Wada et al, 2009
Mercury	Disrupts sex hormone synthesis	McClam *et al*., 2023, Bjørklund *et al*., 2019, Li *et al*., 2022, Liu et al., 2023
Mercury	Interferes with thyroidal function	McGregor and Mason, 1991, Wada *et al*., 2009, Rice *et al*., 2014
Mercury	Interferes with insulin production	Chen *et al*., 2006, Rice *et al*., 2014
Mercury	Increases susceptibility to infections	Arinola *et al*., 2011, Diousse *at al*., 2017

Previous reports have shown a link between oxidative stress and various female reproductive disorders, such as abnormalities in ovaries, fallopian tubes, and embryos (Hussain *et al*., 2021). Additionally, several studies have connected oxidative stress to pregnancy complications and adverse outcomes, such as recurrent spontaneous abortion and intrauterine growth restriction. These complications may arise from inadequate oxygen and nutrient supply to the developing foetus, potentially leading to placental dysfunction and hypoplasia (Duhig *et al*., 2016, Sultana *et al*., 2017).

According to a study involving Nigerian pregnant women, those who used skin lightening creams for over five years showed significantly higher levels of immunoglobulins G and M in maternal serum, cord blood, and breast milk compared to non-users who served as controls. This heightened presence of maternal and neonatal IgG and IgM may potentially elevate their risk for autoimmune diseases in the future (Nwosu *et al*., 2019).

5.0 Conclusion

In conclusion, the practice of skin lightening poses significant risks to endocrine health, largely due to the presence of potent chemical compounds with known or suspected endocrine disrupting effects. Hydroquinone, corticosteroids, mercury, and alpha hydroxy acids are among the key culprits implicated in endocrine disruption associated with skin bleaching products. As awareness of these risks grows, there is an urgent need for regulatory measures to restrict the use of harmful ingredients in cosmetic products and promote safer alternatives. Additionally, healthcare providers play a crucial role in educating the public about the potential health hazards of skin bleaching and advocating for more stringent regulations to protect consumer health. By addressing the endocrine disrupting effects of skin bleaching components, we can safeguard the wellbeing of individuals and communities worldwide.

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