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DOI: <https://doi.org/10.18621/eurj.1314329> *Medicinal Chemistry* **Evaluation of mercury in skin lightening creams commonly used in Trinidad and Tobago and their associated health risk**

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# ABSTRACT

**Objectives:** This study investigated the presence of mercury in commonly used over the counter skin-lightening creams available in Trinidad and Tobago. The objective of this study was to evaluate if skin-lightening creams commonly used in Trinidad and Tobago contained Mercury, and establish the health risks presented by these products.

**Methods:** Nineteen skin-lightening creams were analysed using Cold Capor Atomic Absorption Spectrophotometry (CV-AAS). Margin of Safety (MoS) and Hazard Quotient (HQ) calculations were used to assess risk to users.

**Results:** Of the nineteen creams assessed, sixteen contained high concentrations of mercury (0.294-14414.5 µg/g), only three creams had no mercury detected. 9 of the 19 samples contained levels of mercury that exceed the Minamata convention’s accepted limit of 1µg/g, with 3 samples exceeding 3800.000 µg/g. Risk assessments using MoS and HQ showed that 3 of the samples were unsafe for use and are considered hazardous. The study also revealed that many creams do contain mercury even if it did not constitute part of the product formulation. **Conclusion:** The data infers that some manufacturers do add mercury to their formulations while others are the victims of contaminated raw materials. MoS and HQ show that 21% of the samples were unsafe and 16% can be considered hazardous for human use. It is possible that with such levels of mercury in these products and the popularity of these products within the Caribbean Community and its diaspora, that there exists a significant amount of members with higher than acceptable mercury levels, with undiagnosed clinical symptoms. **Keywords:** Mercury, mercury toxicity, skin lightening, skin whitening, skin brightening, bleaching, consumer

safety, risk assessment, spectrophotometry

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he population of Trinidad and Tobago consists mostly of African and East Indian descendants, and skin lightening practices such as the use of skin lightening or bleaching creams have been commonly used by individuals with darker skin tones from the African [1] and East Indian [2] populations. In these populations and among many others, a lighter complexion is deemed more beautiful, signifies a higher social status [3] and enhanced economic mobility [4]. Studies show that skin bleaching is on the

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rise and is more prevalent among females [5] and research have also found that skin bleaching is more prevalent among women with higher academic achievement [4] who are more prone to seek professional employment. This is further supported by studies in hiring practices where lightly colored individuals have a statistically higher chance of being hired than darker colored persons [6]. There is evidence that the existence of pigmentocracy, particularly in Jamaica and Trinidad and Tobago, is a driver for skin bleaching in the region [7].

 The use of skin bleaching creams in the Caribbean is not restricted to women only but also to men who are seeking a lighter skin complexion. In 2011, a famous regional singer launched his own line of skin whitening products to add to the already popular men's line of skin whitening creams, and his wife launched a similar line in 2021 [8]. Lighter skin not only enhances the perception of greater attraction but also enhances the appearance of tattoos on skin as the darker colored tattoos contrast better with light skin than dark skin.

 Mercury exists in inorganic, elemental, and organic forms. Ammoniated mercury ointments were commonly used for the treatment of psoriasis, but cases of nephrotic syndrome from use of these ointments have been reported since 1962 [9]. The adverse effects of alkyl mercury on the central nervous system have been reported since 1949 [10]. The adverse effects of mercury on the skin and eyes of Iranian dentists have been reported since 1949 [11]. Ammoniated mercury was first studied as a skin lightening agent when it was found in 1952 that the ions reduced melanin production and resulted in a 15% reduction in skin tone [12]. More recently, methylmercury is currently used in some skin-lightening products [13]. Mercury inhibits production of the skin pigment melanin in epidermal melanocytes by inactivating sulfhydryl mercaptan enzymes, which leads to the subsequent inactivation of tyrosinase, which is critical in melanin production [14]. The forms of mercury commonly used in skin-lightening products include; ammoniated mercury, mercury iodide, mercurous chloride, mercurous oxide, or mercuric chloride [15]. Mercury absorption can occur through inhalation, dermal absorption or orally, as advised in some products [16]. The main factors influencing dermal absorption are the amount and the frequency of application and the skin layer hydration [13]. Other factors affecting the rate of mercury absorption are external temperature and skin thickness.

 Long-term exposure to mercury caused by repeated applications can lead to damaging impacts to skin [17], nervous system [18] and kidneys [19]. Dermal effects following mercury-related skin-lightening products include scarring, skin discoloration, and rashes [17]. Additionally, mercury may cause skin-related diseases such as contact dermatitis, pink disease (acrodynia), and mercury exanthema [18].

Neurological effects relating to mercury in skin-lightening products are headaches, tremors, ataxia, irritability, numbness, paranoid delusions, depression, and insomnia. Renal effects include nephrotic syndrome – a non-specific kidney disorder characterized by oedema, proteinuria, albumin, and globulins [19]. AlSaleh [20] argues that mercury toxicity affects unborn children when their mothers use mercury-related creams on their bodies. Ricketts *et al*. [13] confirmed that pregnant women using creams with mercury can transfer mercury to the child; a case in Belgium indicated that high levels of mercury in a pregnant woman’s urine and blood were also traced to her infant. Furthermore, in November 2022, as reported in CNN Edition, a mother lost her peripheral vision from clear exposure to mercury in beauty creams and the toxic levels in her home placed her entire family at risk [21].

 Although there have not been any reported cases of mercury poisoning due to skin creams in Trinidad and Tobago, this does not mean that they do not exists. Literature has discussed at length the adverse health effects of skin-lightening creams. One study found that repeated applications of skin-lightening products with high mercury content were associated with kidney damage [20]. A recent systematic review using 832 individuals from Kenya, the United States (US), Jamaica, and Hong Kong found that nine individuals from Kenya experienced tremors, lassitude, vertigo, and neurasthenia [22]. In Jamaica, 139 individuals reported itchiness, irritability, and other effects such as headaches, depression, and in the US and Hong Kong, the most frequently reported outcomes include fatigue, nervousness/irritability, severe headaches, depression and anxiety, weakness, insomnia, memory loss, tremors, and body/joint pain [22].

## Regulations

 The effects of Mercury on the human body are well known, and it has been well established that the use of Mercury and Mercury Compounds in skin lightening creams and products constitutes a hazard to users of these products [23]. As such, many nations have instituted regulations governing the use of mercury in cosmetic products either as a component or contaminant. The regulatory limits set by various nations varied from 0 µg/g to 3µg/g [24] in the few countries that implemented such regulations; however, signatories to the Minamata Convention have adopted the limit of 1µg/g of inorganic mercury. The convention does not cover eye cosmetics that may use thimerosal (an organic form of Mercury) as a preservative.

 The United States Food and Drug Administration (US FDA) sets a limit of 65 µg/g of total mercury in eye cosmetics where no alternatives are present [25]. Trinidad and Tobago is not a signatory to the Minamata Convention and currently has no regulatory limits for mercury in products. However, the islands of the Caribbean who are signatories of the Minamata Convention have adopted the 1 µg/g limit, but there appears to be little enforcement.

## METHODS Sample Collection

Samples of skin lightening creams were purchased over the counter at various pharmacies and cosmetic stores throughout Trinidad and Tobago in April 2022 and analysed during the period May-June 2022. One sample of each of the available skin lightening creams was purchased. Nineteen samples were collected and represent at least one sample of all of the available brands on the market at the time. Only over - the - counter commercially available products were used in this study.

## Equipment and Reagent

 Ultrapure water having a resistivity of <18 mΩ.cm was used to prepare all reagents, standards and samples. All chemicals used were of the American Chemical Society (ACS) grade or better.

1. Nitric Acid, ACS Grade 70% (Sigma-Aldrich,

USA)

1. Hydrogen Peroxide, ACS Grade 30% (Sigma-

Aldrich, USA)

1. Triton-X 100, ACS Grade (Sigma-Aldrich,

USA)

1. 50 mL Boiling Tubes (Pyrex, USA)
2. Whatman No.541 Hardened Ashless Filter Paper (Sigma-Aldrich, USA)
3. Class A 50 mL and 25 mL Volumetric Flasks (Pyrex, USA)
4. 1000 μg/mL Stock Solution Hg (Accustandard, USA)
5. Tin (II) chloride, ACS Grade (Sigma-Aldrich,

USA)

1. VWR Dry Heating Block (VWR)
2. Varian SpectrAA-800 Atomic Absorption Spectrophotometer with Deuterium Background Correction (Agilent)
3. Varian VGA77 Hydride Generator (Agilent)
4. The quartz Mercury flow cell (Agilent)
5. P100 Micropipette (Gilson Pipetman)

## Glassware Preparation

 All glassware were washed with anionic detergent and rinsed with tap water followed by deionized water. They were then soaked for a minimum of 24 hours in a diluted nitric acid bath, after which they were rinsed with deionized water. The glassware was then dried in an oven at 60 °C overnight and allowed to cool to room temperature before being used.

## Sample Preparation

 A 0.5 ± 0.1 g of each skin lightening cream sample was weighed in triplicate into clean, dried labelled boiling tubes. 5 mL of a mixture of 70% Nitric and 30% Hydrogen peroxide were added along with 1mL of a 5% TritonX-100 solution to each of the boiling tubes, mixed, and allowed to pre-digest at room temperature for 24 h. The boiling tubes were then placed in a heating block set to 95 °C and allowed to digest for 3 h as per the method of Maharaj *et al*. [26]. The digested samples were cooled to room temperature and filtered through a Whatman No. 541 hardened ash less filter paper into a 50 mL class ‘A’ volumetric flask. The contents were made to volume and homogenized by inverting several times. These samples were analysed for Mercury by Cold Capor Atomic Absorption Spectrophotometry (CV-AAS).

## Sample Analysis

Samples were analysed using CV-AAS method as de scribed by Mohammed *et al*. [27]. The VGA77 Hydride Generation Accessory was coupled with Varian SpectrAA800 AAS. The reductant used was Tin (II) Chloride (25%) made up in 20% HCl. The flow rate of the reduction was kept at 1.0 mL/min, the sample was 6.71 mL/min, argon was 2.0 L/min and a delay time of 70 seconds was used in this analysis.

 Calibration was performed using working mercury standards of 5 µg/L, 10 µg/L, 20 µg/L, 30 µg/L, 40 µg/L, and 50 µg/L prepared by serial dilution from a 10 µg/mL NIST Traceable Mercury Standard Solution. Quality was assured by the use of spiked samples. Samples were spiked by adding 50 µL of a 10 µg/mL of the stock standard to a 50 mL volumetric flask using a P100 micropipette, and made up to volume with the sample solution. This gave a 10 µg/mL addition of Mercury, and this was analysed in triplicate. The recoveries determined were between 96-102% [28].

## Risk Assessment

 The assessment of health risks of mercury-containing skin lightening creams was evaluated using the noncancerous risk approach as defined by the Scientific Committee on Consumer Safety (SCCS) safety evaluation model for dermal risk [29], and the US Environmental Protection Agency (USEPA) risk assessment guidelines for dermal risk [30].

### Margin of Safety (MoS)

 The margin of Safety (MoS) is used to evaluate the risk characterization and is calculated with equation (1) for dermal exposure. A MoS above 100 is considered safe, while values below 100 are considered

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The exposure where no adverse effect is observable is referred to as No Observed Adverse Effect Level (NOAEL) and is calculated using equation (2). This is used to evaluate the relationship between exposure and toxic response [29].

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 RfDdermal (mg/kg.day) is the dermal reference dose for a specific metal, UF is an uncertainty factor, and MF are a modulating factor [29]. The default values for UF and MF are 100 and 1, respectively [29, 31]. RfDdermal for calculating risk assessment via dermal uptake has not been established by regulatory bodies [32].

 RfDdermal is calculated from the established RfDoral using the fraction of metal Absorbed in the Gastrointestinal Tract (ABSGI) [33]. The RfDdermal for Inorganic Mercury is established at 0.0003mg/kg.day [30], and the ABSGI for Inorganic Mercury is 1.0. [30] RfDdermal was calculated using equation (3).

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 RfDdermal Hg = 0.0003 x 1.0 = 0.0003 mg/kg.day The U.S. EPA 2021 outlined non-cancer hazard concern levels for the NOAEL as follows [34];

▪ NOAEL > 1000 mg/kg.day minor clinical

signs of toxicity

▪ NOAEL < 1000 mg/kg.day, moderate clinical chemistry and organ weight

▪ NOAEL ≤ 10 mg/kg.day is high evidence of adverse health effects in humans.

SEDdermal is the systemic exposure dose for dermal exposure (mg/kg.day) and is calculated using equation (4).

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 SSA is the skin surface area in cm2 and is calculated as 0.165 [35] fraction of the total body surface area of 18,000 cm2 as defined by the USEPA [36] and constitutes the face, neck and arms. The SSA can be calculated to be 2,970 cm2. DAevent is the absorbed dose per event (mg/cm2), The Scientific Committee on Consumer Safety (SCCS) recognizes that in many conventional calculations of MoS, oral bioavailability of an element is assumed to be 100% if oral absorption data are not available. The standard fingertip unit for a female is 0.4 g [37], and application to hand, arm and face + neck is 1, 3 and 2.5 fingertip units respectively [37], 6.5 fingertip units or 2.6g of cream can be used to cover 2,970 cm2. DAevent can be calculated to be 0.875 mg/cm2. “f “ is the frequency of application of the final product (day-1) [29]. Application frequency of 2 day-1 was used [13] and average body weight of 60 kg for adult [30].

### Hazard Quotient (HQ)

Hazard quotient (HQ) is a common tool for estimating health risk in cosmetics[38-40], and is the ratio of sys temic exposure dose (SED) of a substance as compared to the dermal reference dose (RfD) of the heavy metal [41]. HQ values more than 1 indicate that potential non-carcinogenic health effects are present. While HQ<1 are considered safe for human health. The Hazard Index was not determined in this study since only one hazard was evaluated.

 HQ is calculated as shown in equations (5).

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## Statistical Analysis

 Statistical analysis of mercury concentrations in skin-lightening creams was determined by Pearson correlation analysis, with a P<0.05 value being considered significan

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## RESULTS

*Mercury Content of Skin Lightening Creams* The 19 samples of the skin-lightening creams were analysed for their total Mercury content by CV-AAS (Table 1). These creams originated from Jamaica, Pakistan, India, China, U.K, Singapore, Philippines, the EU, the United States and Trinidad and Tobago. None of which were registered by the Food and Drug Administration of Trinidad and Tobago. Only one sample identified “Ammoniated Mercury” as a component. Three samples contained no detectable mercury (Nu

Brite Plus Cream, Fade Off Serum and KAVI Advance Melanin Repair Serum), whereas 16 samples contained measurable levels of mercury (0.294-14414.5 µg/g of Hg).

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 Significant levels of mercury were found in

Deluxe Silken (14.414 µg/g), 7 Days Magic Brighten ing Cream (4005.548 µg/g), and Sandal Beauty Cream (3855.478 µg/g).

### Health Risk Assessment

 The Margin of Safety (MoS) and Hazard Quotient (HQ) are calculated in Table 2.

## DISCUSSION

There is currently no standard for the recommended

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concentration of mercury in skin care products by the Food and Drug Administration (FDA) of Trinidad and Tobago as this country is not yet a signatory of the Minamata Convention.

 Significant levels of mercury can have severe health effects and permanent irreparable damage to organs, sight, and hearing. The rate of dermal absorption of mercury compounds increases with the concentration of mercury and prior hydration of the skin [42]. At such high levels, the rate of dermal absorption can be rapid. The degree of dermal absorption can also vary with the skin integrity and lipid solubility of cos-

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metic products. Other avenues for entry of mercury from such creams may be from ingestion of the product after topical application around the mouth and hand-to-mouth contact, including intimate partner contact. The use of mercury-containing cosmetic products such as these can also contaminate the home and its occupants, resulting in secondary mercury poisoning [43].

 The levels obtained from these three products suggest that mercury compounds are added as part of the formulation either as an active ingredient or as a preservative, yet only one sample (Deluxe Silken) shows Ammoniated Mercury on its label. The labeling of cosmetics globally is very relaxed and varies from country to country. Most countries do not require detailed listing of ingredients and except for colour additives, the United States FDA does not require cosmetic products and ingredients for premarket approval [44].

 Six other samples contained mercury levels exceeding the 1µg/g limit adopted by most countries. These values varied from 1.223 µg/g to 2.223 ug/g and may be attributed to contamination from machinery or from contaminated raw material such as vegetable based oils[45] or naturally sourced emulsifiers. In all cases, mercury absorption through the skin, frequency of use and the bioaccumulation of the metal can result in all the creams containing even traces of mercury to be potentially hazardous to human health. Chronic exposure to mercury can lead to tremors, insomnia, memory loss, neuromuscular effects, headaches, and cognitive and motor dysfunction. Mild subclinical symptoms of central nervous system and cardiovascular toxicity can be seen at exposure levels as low as 0.070 µg/kg/day [46]. This dismisses the notion of safe level for Mercury.

 The results of this study correspond well with previous studies. Mohammed *et al*. [16] in 2017 found similar levels of mercury in skin lightening creams sold in Trinidad and Tobago with values ranging from a low of 0.473 µg/g to a high of 14.507.741 µg/g for a sample of Deluxe Silken cream. Rickets *et al*. [13] in 2020 found in Jamaica Mercury ranging from 0.050 µg/g to 17345.000 µg/g. Hamann *et al*. [14] in 2014 found in the US Mercury ranging from 1729.000µg/g to 45,622.000µg/g. Peregrino *et al*. [47] found in 2011 mercury levels ranging from 878.000µg/g to 36,000.000µg/g and Prevodnik *et al*. [48] in 2018 found mercury levels in skin lightening creams ranging from 93.000 µg/g to 16,353.000 µg/g from 338 samples taken from 22 countries. Majeed *et al*. [49] in 2021 found levels ranging from 3.600 µg/g to 240.000 µg/g, Sin and Tsang [50] in 2003 found levels ranging from 660.000 µg/g to 57,000.000 µg/g, Pramanik *et al*. [39] in 2021 found levels ranging from 0.004 µg/g to 31,700.000 µg/g and Dwijayanti and Susanti [51] in 2018 found levels ranging from 47.180 µg/g to 4,554.000 µg/g of mercury in creams.

 The World Health Organization (WHO) identifies Bangladesh, China, Dominican Republic, Hong Kong, Jamaica, Lebanon, Malaysia, Mexico, Pakistan, Philippines, Republic of Korea, Thailand, and the United States of America as the main producers of mercury-containing skin lightening products [23]. However, this study shows that 31% of skin-lightening products tested in this study were produced in the EU and contain some levels of mercury. Mohammed *et al*. [16] found that 60% of the skin lightening products available in the Trinidad and Tobago Market in 2017 were manufactured in the EU, and Rickets et.al found 19% of the skin lightening products available in Jamaica were produced in the EU.

 The Margin of Safety (MoS) levels determined in this study show that Deluxe Silken, 7 Days Magic Brightening Cream, and Sandal Beauty Cream, exceeded the USEPA guidelines for MoS having values that fell below 100. These samples are considered unsafe for usage and hazardous to human health. The extremely low MoS obtained for Deluxe Silken, 7 Days Magic and Sandal Beauty Cream are of particular concern as these can lead to severe medical conditions even from short term usage and could be considered proximal hazards as mercury from these products can affect persons in close proximity to the user.

 Ravima’s Beauty Discoloration Defense can also be considered unsafe for use. This sample had a MoS of 106.007 and fell above the USEPA guidelines of 100 MoS but may be within the margin of error of this study and could easily fall below 100 MoS.

 The results of MoS correlate very strongly with the Hazard Quotient (HQ) calculation with the same samples being determined to be hazardous. Deluxe Silken, 7 Days Magic Brightening Cream and Sandal Beauty Cream did not only exceed the HQ limit of 1 but did so by a margin of several thousands, further highlighting the severe health hazard these three products pose to the users and their immediate surroundings. Ravima’s Beauty Discoloration Defense also showed similar behavior where its HQ value was marginal at 0.943 and should be considered unsafe for use by users.

 In this study, four of the samples analyzed can be considered hazardous; this represents 21% of the skin lightening products available on the Trinidad and Tobago market. Furthermore, three of the samples or 16% can be considered extreme hazards. As these are popular brands easily available and commonly used in Trinidad and Tobago, the health risks of exposure to mercury both acute and chronic are extremely high. This risk can easily be extended to close members of the household, including children and intimate partners. It should be noted that this risk assessment assumes that the products are used exclusively on the face, neck, and arms. It did not consider the use of these skin-lightening products on intimate areas where the skin is thinner and blood flow is greater. Bleaching of intimate areas has been growing in popularity among both gay and heterosexual populations [52] and introduces an even greater risk since these areas show increased absorption.

## CONCLUSION

In this study, 84% of samples contained mercury and 47% exceeded the Minamata limit of 1µg/g. From the health risk, three samples are unsafe and one marginal. This study indicates that for some products, manufacturers deliberately add Mercury compounds without appropriately representing the components on the labels and shows the need for more appropriate labeling regulation and enforcement in the cosmetic industry. This study also revealed the potential risks posed using manufacturing processes and raw material selection. Since Trinidad and Tobago is not a signatory to the Minamata convention, manufacturers and distributors are not mandated to enforce the 1ppm limit set by the convention for cosmetic products; however, the obvious health risks to the population pose by these products must be considered. The popularity of skin whitening products in Trinidad and Tobago places the population at significant risk of chronic mercury poisoning with implications to the cost of healthcare, reduced productivity, and quality of life. This study only considered over the counter readily available commercial skin lightening creams and did not consider “under the counter” products which can pose significant hazards to its users.

*Authors’ Contribution*

 Study Conception: TM; Study Design: TM; Supervision: MT; Funding: The University of the West Indices; Materials: NR; Data Collection and/or Processing: SB; Statistical Analysis and/or Data Interpretation: TM; Literature Review: NR, TM; Manuscript Preparation: TM, NR and Critical Review: YK.

*Conflict of interest*

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