



Mercury in skin-care products in India and consumer exposure risks

Supriti Pramanik, Mukesh Kumar, Asif Qureshi*

Department of Civil Engineering, Indian Institute of Technology (IIT) Hyderabad, Kandi, TS, 502285, India

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ABSTRACT

We report concentrations of mercury in skin-care products in India and the associated health risks. Mercury concentrations were 0.11 µg/kg (median; 5th percentile–95th percentile = 0.04–0.58 µg/kg; n = 24) in body lotions, 0.22 µg/kg (0.04–0.38 µg/kg, n = 10) in moisturizing lotions, 0.67 µg/kg (0.30–1.33 µg/kg, n = 8) in blemish balms, 0.16 µg/kg (0.06–7.43 µg/kg, n = 11) in bleaches, 0.13 µg/kg (0.04–0.98 µg/kg, n = 34) in skin lightning (fairness) creams manufactured within the country, and 9.24×10^6 µg/kg (2.92×10^6 – 3.17×10^7 µg/kg, n = 14) in imported skin lightning (fairness) creams, much higher than the 1 ppm (1 ppm = 10^3 µg/kg) regulatory limit. Probabilistic human health risk assessment for adult women (age > 21 y) revealed that computed hazard quotients from dermal exposure to the high-mercury fairness creams were >100 in all cases. The mass of mercury entering into the society via skin-care products is highly sensitive to the mass of high-mercury fairness creams that is imported to India; ten tonnes of import can introduce 29–317 kg of mercury every year. As such, analysis and labeling of mercury contents in skin-care products by manufacturers, and raising awareness among regulatory authorities to restrict the import of high-mercury fairness creams, is required.

1. Introduction

Indian skin-care industry is a billion-dollar industry. Skin lightning (or fairness) products have been estimate to account of almost 50% of this market, worth about \$US 0.45–0.53 billion (Shroff et al., 2018). Skin color is strongly tied to economic class, marital prospects, occupation status, caste and post-colonial hierarchy (Hall, 2003; Shroff et al., 2018).

Skin-lightning and other cosmetic products have also been reported to contain harmful chemical compounds, such as those of mercury (Borowska and Brzóska, 2015; Gbetoh and Amyot, 2016). These substances can adversely affect circulatory, urinary and neurological functions (Michalek et al., 2019). Mercury is used in skin lightning products as a skin-bleaching agent, as it inhibits melanin production (Engler, 2005), and as a preservative in other cosmetics such as hand and body creams and lotions, ‘bleaches’ and possibly others products, although there is no justification for this use (eCFR, 2020).

These products are applied regularly to various body parts from where they can be assimilated into the body. Concentrations of mercury in skin lightning creams (also sold as skin whitening or fairness creams) have been reported to be very variable, from order of 0.001 µg/g (µg mercury per g product) to order of 10000 µg/g (Agrawal and Mazhar,

2015; Agrawal and Sharma, 2017; Gbetoh and Amyot, 2016; Ho et al., 2017; Ricketts et al., 2020). Skin lightning creams from twenty-two countries were reported to contain mercury in the range 0.0002–22, 100 µg/g (ZMWG, 2018). Cases of mercury toxicity have been reported in humans who have used skin lightning creams containing mercury in excess of 12,000 µg/g [e.g. (Copan et al., 2015; Mudan et al., 2019)].

Here we report concentrations of mercury in body lotions, blemish balms, moisturizing lotions (essentially the same as body lotions but sold as such), skin lightning/fairness creams [six of which were in the twenty-two country high mercury content list (ZMWG, 2018)], and bleaches (a type of lotion that is applied to the face for 5 to 15 min and is subsequently washed off). We then estimate the human dermal exposure to mercury and evaluate whether this exposure may exceed a reference dermal dose [(Murphy et al., 2009) derived from the oral reference dose (ATSDR, 1999; USEPA, 1995)]. As the skin-care industry is a very large industry with potentially millions of population using their products, we also provide estimates of the quantity of mercury that may be introduced into the market and Indian society as part of skin-care products.

* Corresponding author.

E-mail address: asif@ce.iith.ac.in (A. Qureshi).

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2. Materials and methods

2.1. Mercury in skin-care products

Skin-care products were obtained from supermarkets, stand-alone brick and mortar shops and online platforms. Fifteen brands of body lotions, five of blemish balms, five of moisturizing lotions (essentially the same as body lotions but sold as moisturizers), twenty-six of fairness creams [six of which were in the high mercury content list in the twenty-two country summary of (ZMWG, 2018)], and eight of bleaches were procured. None of the products had mercury content reported in their labels.

Mercury content of the skin-care product was determined using a direct mercury analyzer, DMA-80 (Milestone Srl., Italy). The instrument uses the principle of thermal decomposition and atomic absorption spectroscopy to detect the mass of mercury in the analyzed samples. The limit of detection, determined as three times the standard deviation of method blanks, was 0.01 ng and the limit of quantitation, defined as ten times the standard deviation of method blanks, was 0.033 ng. All analyzed samples yielded results above the limit of quantitation. For further quality assurance and control, some samples were spiked with known mass of mercury standard (0.125 ng, 0.25 ng, or 0.5 ng) and recoveries were $102 \pm 8\%$ ($n = 31$). For all products, except the six suspected high-mercury products, samples were directly put in sample boats and analyzed. When the mercury recovery from analysis of a single sample boat was low, samples in multiple boats were thermally treated,

cream market) to calculate the extent to which they may add mercury to the society.

2.3. Human health risk assessment

A risk assessment for mercury uptake via dermal absorption from skin-care products by adult females (age > 21 y) was conducted. Skin-care products body + moisturizing lotions, blemish balm, fairness cream, and bleach were considered separately to assess their individual contributions to risk. A reference dose for dermal absorption (RfD_{DER}) was calculated as (Ho et al., 2017; Murphy et al., 2009):

$$RfD_{DER} = RfD_{ORAL} \times GI_{ABS} \quad (1)$$

where RfD_{ORAL} is the reference oral dose for mercury chloride [0.3 µg/kg-bw/d (micrograms of mercury per kilogram of body weight per day)] (ATSDR, 1999; USEPA, 1995). GI_{ABS} is the efficiency of gastrointestinal absorption, 7%–15% (Park and Zheng, 2012) (Table 1).

Loretz et al. (2005) have reported the use of body lotions and face creams in three hundred and sixty women aged 19–65 years in the United States. They have reported the mass of skin-care product applied to each body part, hands, arms, legs, feet, neck, back, throat and other body areas in terms of applications per day, and the mass of product applied per day. Accordingly, dermal uptake of mercury from skin creams applied to any body part can be calculated as a daily absorbed dose (DAD , µg/kg-bw/d) (USEPA, 2007):

$$DAD \cdot (\mu\text{g}/\text{kg} - \text{bw}/\text{d}) = \frac{DA_{EVENT} \left(\frac{\mu\text{g}}{\text{cm}^2 \cdot \text{event}} \right) \times SA \text{ (cm}^2\text{)} \times EF \left(\frac{365 \text{ d}}{\text{y}} \right) \times ED(\text{y}) \times EV \left(\frac{\text{events}}{\text{d}} \right)}{BW(\text{kg}) \times AT(\text{d})} \quad (2)$$

the released mercury was allowed to amalgamate on the gold traps, and mercury detection was done after amalgamation of sufficient amount of mercury (the “integration” function in DMA-80). The suspected high-mercury samples were diluted with type-1 water in beakers pre-cleaned with soap and distilled water, filled with 10% HCl for 24 h and rinsed with copious amount of type-1 water. No cross-contamination was observed.

2.2. Mass of mercury entering the Indian society via skin-care products

India’s skin-care market was about \$US 0.9–1.07 billion in 2018 and half of it was occupied by the skin lightning (fairness cream) industry (Shroff et al., 2018; WHO, 2019). A body lotion can cost anywhere between Rs. 0.5 to Rs. 4 per gram or \$US 6700–53600 per tonne (1 \$US = Rs. 74.63) and fairness creams between \$US 13,400–2.68 million per tonne (Rs. 1 to 200 per g) [estimated using data from our own purchases, and browsing, through brick and mortar shops and online e-commerce portals]. A \$US 500 million skin-care industry (excluding fairness creams) would thus mean sales of 74626–9328 tonnes of creams (excluding fairness creams) by mass per year and a \$US 500 million fairness cream industry would mean sales of 37,300–186.6 tonnes of fairness creams (including domestic and imported) by mass per year. Obtaining sales of each advertised brand was not possible in this work. Therefore, we multiplied our approximately estimated sales mass with the determined concentrations of mercury in skin-care products excluding fairness creams, and fairness creams, respectively, to estimate the mass of mercury entering the Indian society every year. It was not possible to find the market share (either on monetary, or mass, basis) of the imported fairness creams analyzed by us. We thus evaluated scenarios (1% of total fairness cream market or 10% of the total fairness

where DA_{EVENT} (µg/cm²/event) is the absorbed dose per event, SA is the skin surface area of the body part available for contact, EF is the exposure frequency, ED is the exposure duration (adult lifetime), EV is the event frequency, BW is the body weight (Table 1) (USEPA, 2011), and AT is the averaging time (considered to be the same as ED in days, $ED \times 365$). Body lotions and moisturizing lotions will be applied to all reported body parts (Loretz et al., 2005). Blemish balms, fairness creams and bleaches are applied to the face only. It is assumed that a person applies the skin-care product every day, resulting in an EF of 365 d/y. Bleaches are a special case of skin-care products in that they are applied for 5 to 15 min and washed off. They are used once every few days. Therefore, we assume bleach is applied for only 5 min and is applied to the face once every three days. Mass of bleach applied is accordingly assumed to be the same as the mass of face cream applied in a day divided by three to account for the once-in-three-days frequency of application.

DA_{EVENT} (µg/cm²/event) is calculated as (Murphy et al., 2009).

$$DA_{EVENT} = C_{CREAM} \times Abs \times AdF \quad (3)$$

Table 1

Parameters used for exposure calculations (DF = dispersion factor; 95% of model values lie between median $\times DF$ and median $\div DF$).

Parameter	Median	DF
Efficiency of gastrointestinal absorption, GI_{ABS} (%) ^a	10.2	1.46
Body weight (kg) ^b (females, > 21 y)	75.2	1.57
Mercury concentrations in skin-care products	From this study	

^a (Park and Zheng, 2012).

^b (USEPA, 2011).

where C_{CREAM} is the concentration of mercury in the skin-care product ($\mu\text{g/g}$) obtained from this study (modeled probabilistically as described later). Abs is the absorbance factor (0.001 or 0.03) (Murphy et al., 2009), fraction of applied mercury in creams that is absorbed in the body, with 0.001 corresponding to a conservative estimate and 0.03 considering that some skin-care products may contain compounds that facilitate percutaneous absorption (Murphy et al., 2009), and AdF is the adherence factor (mass of cream applied to the body part divided by the surface area of the body part per event, $\text{g}/\text{cm}^2\text{-event}$) (Murphy et al., 2009). Volatilization of mercury from the skin surface is assumed to be negligible as a simplification and a worst-case scenario, since mercury in skin-care products is probably in the form of mercuric or mercurous chlorides, mercurous oxide or ammoniated mercury (Chan, 2011); and although while volatilization has been reported after application of high mercury content creams (concentration 2.8×10^7 – $2.1 \times 10^8 \mu\text{g}/\text{kg}$), it is unclear what percent of mercury applied on skin is volatilized after application (Copan et al., 2015).

Further, if a person wears a piece of clothing above a body part after application of cream, for example a body lotion, we assumed that this clothing will remove only a negligible part of cream from the skin surface.

Combining (2) and (3) and rearranging gives, for any body part,

$$DAD \text{ (}\mu\text{g}/\text{kg} - \text{bw}/\text{d}) = \frac{C_{\text{CREAM}} \left(\frac{\mu\text{g}}{\text{g}} \right) \times Abs \times AdF \left(\frac{\text{g}}{\text{cm}^2\text{-event}} \right) \times SA \text{ (cm}^2\text{)} \times EV \left(\frac{\text{events}}{\text{d}} \right) \times EF \left(365 \frac{\text{d}}{\text{y}} \right) \times ED(y)}{BW(\text{kg}) \times AT(\text{d})} \quad (4)$$

$AdF \times SA \times EV$ is numerically equal to the mass (g) of skin-care product applied to the body part i per day (A_i , g/d). Introducing superscript i and cancelling out equal terms, we obtain the daily absorbed dose for body part i as

$$DAD_i \text{ (}\mu\text{g}/\text{kg} - \text{bw}/\text{d}) = \frac{C_{\text{CREAM}} \left(\frac{\mu\text{g}}{\text{g}} \right) \times A_i \left(\frac{\text{g}}{\text{d}} \right) \times Abs}{BW(\text{kg})} \quad (5)$$

The total mass of skin-care product applied per day (M) was considered to be 7.63 g/d (95% confidence range of 3.30–16.83 g/d) for body lotions and 1.39 g/d (95% confidence range of 0.45–3.99 g/d) for face creams (Loretz et al., 2005). We apportioned this mass to each body part in proportion to the number of applications per day to that body part and the body part's surface area. That is, mass of skin-care product applied per unit actual surface area per day (A , $\text{g}/\text{cm}^2\text{-d}$) can be given as,

$$M = A \times \sum_i (SA_i \times EV_i) \quad (6)$$

Where $\sum_i (SA_i \times EV_i)$ is the actual effective surface area to which mass M is applied any day.

$$\text{Thus, } A = M / \sum_i (SA_i \times EV_i) \quad (7)$$

$$\text{And, } A_i = A \times SA_i \times EV_i \quad (8)$$

That is, if a cream is applied to 100 cm^2 of a body part 0.5 times a day, it is effectively applied to 50 cm^2 per day, and if it is applied to 100 cm^2 for 2 times a day, it is effectively applied to 200 cm^2 per day. Introducing equation (8) in equation (5) and summing over all body parts results in a much simplified equation in terms of concentration of mercury in the

cream, mass of cream applied and the absorption factor, and body weight:

$$DAD_{\text{TOTAL}} \text{ (}\mu\text{g}/\text{kg} - \text{bw}/\text{d}) = \frac{C_{\text{CREAM}} \left(\frac{\mu\text{g}}{\text{g}} \right) \times M \left(\frac{\text{g}}{\text{d}} \right) \times Abs}{BW(\text{kg})} \quad (9)$$

Finally, hazard quotients (HQs) for exposure from each type of skin-care product were calculated as $HQ_{\text{PRODUCT}} = DAD_{\text{PRODUCT}}/RfD_{\text{DER}}$. DAD_{PRODUCT} , RfD_{DER} and HQ_{PRODUCT} are calculated probabilistically. All input parameters followed a lognormal distribution. 100,000 simulations were made in MATLAB® to obtain the output DAD and HQ distributions.

3. Results and discussions

3.1. Mercury in skin-care products

The Minamata Convention on Mercury stipulates that manufacturing, import and export of cosmetics containing more than $10^3 \mu\text{g}/\text{kg}$ (1 ppm) of mercury will not be allowed after the year 2020, except for eye lashes (UNEP, 2019). The United States Food and Drug Administration (US FDA) stipulates a limit of $10^3 \mu\text{g}/\text{kg}$ of mercury in any cosmetic product (except eye area products), only if the presence of levels lower than $10^3 \mu\text{g}/\text{kg}$ was unavoidable under 'good

manufacturing practice' (USFDA, 2020).

Mean mercury concentrations in body lotions analyzed in this work ranged from 0.01 to 0.64 $\mu\text{g}/\text{kg}$ and in moisturizing lotions from 0.04 to 0.41 $\mu\text{g}/\text{kg}$ (Table 2). Concentrations in bleaches were 0.03–8.67 $\mu\text{g}/\text{kg}$. Mean concentrations in blemish balms, whose reported purpose is also to aid in 'fairness' and 'healthy glow', were, 0.22–1.54 $\mu\text{g}/\text{kg}$. Mean mercury concentrations in twenty brands of fairness creams [Fairness Creams (A); manufactured domestically] were 0.03–1.45 $\mu\text{g}/\text{kg}$, but in six brands [Fairness Creams (B)] were $2.50 \times 10^6 \mu\text{g}/\text{kg}$ to $4.02 \times 10^7 \mu\text{g}/\text{kg}$, 10^3 to 10^4 times higher than the regulatory limit. These six skin-lightening [Fairness Creams (B)] creams were manufactured outside India, and were found on and procured from online platforms. The same

Table 2
Summary of obtained concentrations ($\mu\text{g}/\text{kg}$) of mercury in skin-care products^a.

Product	N	Median	Percentile				DF ^b for Table 1
			5th	25th	75th	95th	
Body Lotions	24	0.11	0.04	0.07	0.16	0.58	5.9
Moisturizing Lotions	10	0.22	0.04	0.13	0.30	0.38	5.1
Body + Moisturizing lotions	34	0.12	0.04	0.07	0.23	0.48	5.1
Blemish Balms	8	0.67	0.30	0.57	0.82	1.33	2.6
Bleach	11	0.16	0.06	0.10	1.04	7.43	50
Fairness creams (A)	34	0.13	0.04	0.07	0.30	0.98	8.5
Fairness creams (B)	14	9.24×10^6	2.92 $\times 10^6$	6.20 $\times 10^6$	1.85 $\times 10^7$	3.17 $\times 10^7$	3.9

^a Estimated from raw data (Table S1) for the purpose of risk assessment. N includes analysis of multiple packs from same brand.

^b DF = dispersion factor; 95% of model values lie between median $\times DF$ and median $\div DF$

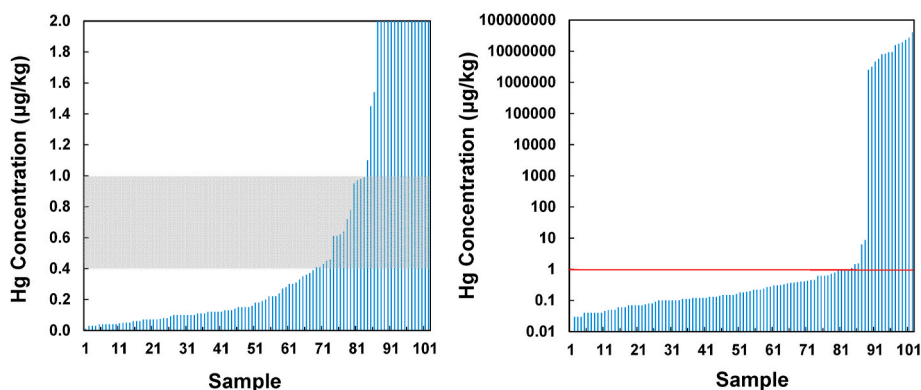


Fig. 1. Possible thresholds of mercury levels in skin-care products that are a result of impurities present in raw materials.

six brands have been reported to contain similar concentrations of mercury in an earlier study (ZMWG, 2018). Obtained concentrations for each skin-care product can largely be approximated using a log-normal distribution (Fig. S1).

Values obtain in fairness creams in this study, with the exception of the six creams with $> 2.50 \times 10^6$ µg/kg mercury, were in general lower than reported in previous studies from India, and from other countries. Two previous studies from India have reported concentrations of mercury in fairness creams between 140 and 360 µg/kg in 2017 (Agrawal and Sharma, 2017) and between 5 and 9 µg/kg in 2015 (Agrawal and Mazhar, 2015), with creams from four same brands analyzed in both the studies measuring 20 to 60 times higher in 2017 than in 2015. Mercury in fairness creams in Jamaica had mercury concentrations in the range 50 µg/kg to 1.75×10^7 µg/kg, six out of sixty products had mercury concentrations more than 1000 µg/kg (Ricketts et al., 2020), and in Malaysia between < 0.5 µg/kg (detection limit) to 1130 µg/kg on average (Ho et al., 2017). Mercury in fairness creams in Benin, Ivory Coast, Mali, Senegal and Montreal, Canada, were determined to be in the range 0.05–914 µg/kg (Gbetoh and Amyot, 2016).

Our assessment suggests that a concentration of up to 0.4–1.0 µg/kg can be attributed to impurities present in raw materials. Gbetoh and Amyot (2016) have plotted the concentrations of mercury in all sampled products in an increasing order and, noting the location of an abrupt increase in concentration, determined that about 0.6 µg/kg of mercury in creams were attributable to natural impurities in raw materials. Using a similar approach in our work, we find that raw material impurities could lead to mercury concentrations between 0.4 and 1.0 µg/kg

(Fig. 1). Any concentration higher than that may suggest addition of mercury compounds.

3.2. Mass of mercury entering the Indian society via skin-care products

Concentrations of mercury in skin-care products excluding fairness creams was in the range 0.04–1.33 µg/kg. Thus, production of 9328–74626 tonnes per year of these products would mean an addition of 0.3 g–99 g of mercury per year into the Indian society. In a hypothetical scenario, where mercury content of these products is 999 µg/kg (i.e. just lower than the 1000 µg/kg regulatory limit), mercury addition to the society would be 9–75 kg per year from these products.

The analyzed domestic fairness creams also had mercury in the range 0.04–0.98 µg/kg. If all the market share of 186.6–37300 tonnes per year is taken by these, the quantity of mercury introduced into the market would be less than approximately 36.5 g. However, the concentration of mercury in imported fairness creams was 2.92×10^6 – 3.17×10^7 µg/kg (equivalent to 2.9–31.7 kg Hg per tonne). Therefore, 54–118300 kg of mercury will be introduced into the Indian society if these imported fairness creams occupied even 10% of the total fairness cream market (similarly, 5.4–11830 kg mercury will be introduced if they occupied 1% of the fairness cream market).

While at present there are uncertainties in these estimates, they show the potential for introduction of substantial amounts of mercury into skin-care products. These estimates can be better constrained by a better availability of data on mass of skin-care products produced and the concentrations on mercury in those product. As such, reporting of

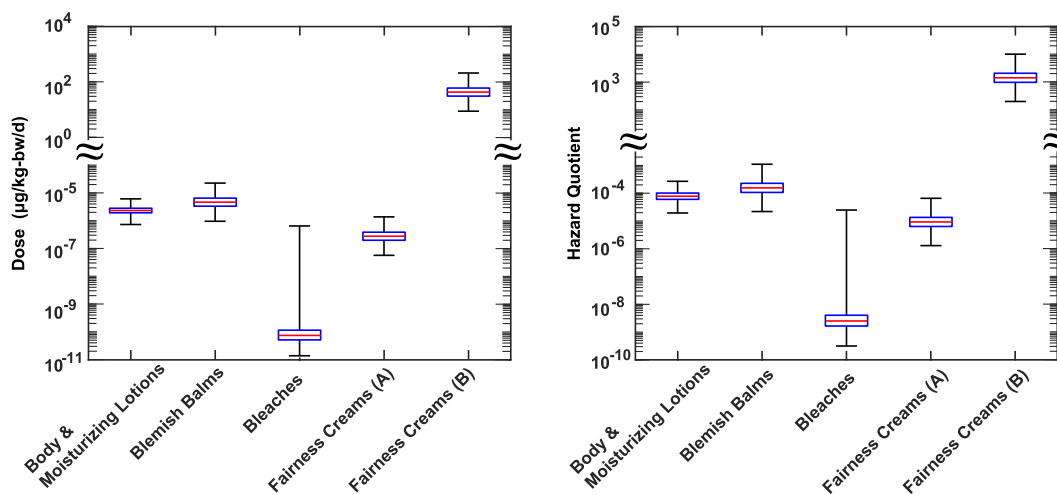


Fig. 2. Daily absorbed doses, and hazard quotients for dermal exposure to mercury in skin-care products when 0.1% of applied mercury is absorbed in the skin. Values shown are the simulated median (the middle red line), 25th and 75th percentiles (edges of the blue boxes), and minimum and maximum values (bars). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

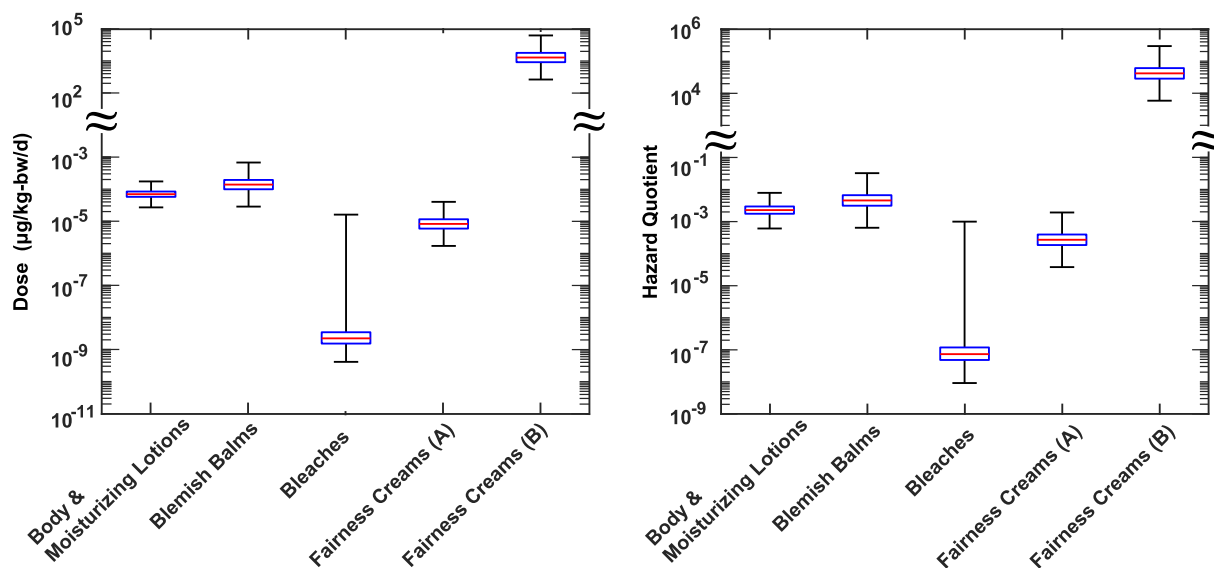


Fig. 3. Daily absorbed doses, and hazard quotients for dermal exposure to mercury in skin-care products when 3% of applied mercury is absorbed in the skin. Values shown are the simulated median (the middle red line), 25th and 75th percentiles (edges of the blue boxes), and minimum and maximum values (bars). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

mercury contents in creams by manufacturers would be important.

3.3. Human health risk assessment

Using the concentrations of mercury obtained in the skin-care products in this work (Table 2 and Supplementary Material Table S1) we find that the daily absorbed doses of mercury from application of body and moisturizing lotions, blemish balms, bleaches, or fairness creams (A) were lower than 10^{-4} µg/kg-bw/d for an absorption factor of 0.001. However, doses were as high as 9–210 µg/kg-bw/d for Fairness Creams (B) (Fig. 2). Consequently, HQ for exposure from Fairness Creams (B) was always greater than 100. Doses were even higher when considering an absorption factor of 0.03 (Fig. 3). The minimum HQ for exposure from Fairness Creams (B) was 600 and the maximum HQ was 305,000. These are extremely high numbers. In contrast, HQ for all other products was lower than 0.1, individually or summated. Occurrence of high concentrations of mercury in Fairness Creams (B) and the estimation of high hazard quotients call for an urgent regulatory assessment and action, in analysis and control of mercury in fairness creams. As mercury toxicity in humans has been observed when fairness creams with mercury concentrations 1.20×10^7 µg/kg to 2.80×10^7 µg/kg, similar to those found in Fairness Creams (B), have been used by consumers (Copan et al., 2015; Mudan et al., 2019), there are potential toxicological risks to users who may be regularly using Fairness Creams (B).

Finally, we note that the information on mass of skin-care products used per day by consumers, that was used in this work, was obtained from a survey conducted in the United States (Loretz et al., 2005). As such, primary data on product use in India would be needed to improve the health risk estimates for Indian populations. Also, the calculated value of hazard quotient depends on the estimated daily absorbed dose. This in turn is dependent on the concentration of mercury in cream, and the used absorbance factor which is related to the skin permeability coefficient (Murphy et al., 2009). A skin permeability coefficient of 10^{-3} cm/h has been suggested for inorganics in aqueous suspensions (USEPA, 2007) and the same value is reviewed for mercuric chloride (USEPA, 1992; Wahlberg, 1965). Drawing parallels between permeability of mercury and cadmium, Murphy et al. (2009) suggested a ‘scoping’ dermal absorption factor of 0.001, scoping meaning 0.001 cm^3 of cream applied per cm^2 of skin will be absorbed per hour. But considering that such skin-care products may be designed to enhance

bioavailability and percutaneous absorption, they also suggested using a higher absorption factor of 0.03, consistent with absorption of mercury chloride on Guinea Pig skin (2%–4.5%) (Skog and Wahlberg, 1964). But the results from experiments on Guinea Pig skin were limited to solutions of mercury chloride compounds of molarity greater than 0.04 M, equivalent to 8000 µg-mercury/g-water (0.04×200 g-mercury/L-water). Therefore, more research is also required to obtain better estimates of mercury absorption from skin-care products containing very low to very high concentrations of mercury or its compounds.

4. Conclusions

Majority of the skin-care products analyzed in this work had mercury concentrations much lower than the stipulated limit of 10^3 µg/kg. Exceptions were some imported fairness cream products which had mercury concentrations in excess of 2.50×10^6 µg/kg. Use of these products could result in toxicity and regulatory monitoring and control may be required for them. Labeling of mercury contents in skin-care products by manufacturers, and monitoring of imported fairness cream (and other skin-care products) by regulatory authorities to prohibit the entry of products high in mercury contents, will help in the alleviation of health risk concerns for consumers, a better accounting of mercury flows in the country, and the overall implementation of the Minamata Convention on Mercury.

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Supplemental Material

One supplementary table (Table S1) and one supplementary figure (Fig. S1).

CRedit authorship contribution statement

Supriti Pramanik: Conceptualization, Methodology, Formal

analysis. **Mukesh Kumar:** Formal analysis. **Asif Qureshi:** Supervision, Conceptualization, Methodology, Formal analysis.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.yrtph.2021.104870>.

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