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Comparison of mercury levels in various tissues of albino and pigmented mice treated with two different brands of mercury skin-lightening creams

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Abstract

The use of mercury containing skin-lightening creams are becoming increasingly popular among dark-skinned women. The long term use of certain brands may cause serious health effects over the years. In the present study, we investigated the dermal absorption of mercury and its accumulation in the tissues of albino and pigmented mice treated with two brands of mercury containing skin-lightening creams for a period of one months at different intervals. The mean ± SD of mercury in the selected brands were: (1) Fair & Lovely (0.304 ± 0.316 μg/g); and (2) Rose (77513.0 ± 71063.0 μg/g). Mercury levels were measured in a total of 133 and 144 liver, kidney and brain tissue samples of albino and pigmented mice respectively by the Atomic Absorption Spectrophotometer coupled to Vapour Generator Accessory. In both strains, we found that the mercury concentration in the tissues of mice treated with Rose skin-lightening cream samples was significantly higher than those treated with Fair & Lovely skin lightening cream. Looking at the mercury concentration in the tissue samples with respect to the application of skin lightening creams at different intervals, the highest mercury concentrations were found in the tissues of albino and pigmented mice treated three times a day. On the other hand, the lowest mercury concentrations were found in the tissues of mice treated once a week. Despite the brand of skin-lightening cream that was applied, the study indicated that mercury was readily absorbed through the skin of both albino and pigmented mice as evidenced with its accumulation in the brain, kidney and liver tissues where the kidney had the highest mercury content and brain had the lowest (it $P<0.0001$). Significant differences in the mercury levels were observed between the albino and pigmented mice. This emphasizes the protective role of melanin against mercury toxicity. Results of this study stresses the potential harm of these mercury containing skin-lightening creams regardless of their mercury contents especially for women who apply these creams frequently or for extended periods. Permanent nephrological or/and neurological deficits may occur if the damage is severe and diagnosis and treatment are delayed.

Introduction

The application of mercurial preparations to the skin has been accepted for centuries (Cole *et al.* 1930; Turk & Baker 1968). Absorption and excretion of mercury following inunaction are directly dependent on the amount of metal in the base (Cole *et al.* 1930). Organic forms such as phenyl mercuric acetate are sometimes used as cosmetic preservatives, while inorganic forms; such as ammoniated mercury, are the active ingredients in skin bleach creams (Marzulli & Brown 1972). Skin lightening creams containing inorganic mercury are widely used by dark-skinned people to obtain a lighter skin tone (Gras & Mondain 1981; Scarpa & Guerci 1987; Mahe *et al.* 1993), probably due to the inhibition of pigment formation. Although, melanin has a major role in protection against ultraviolet ra-

diation, its function in modifying chemical damage in the skin is still controversial. Melanin is both a free radical scavenger and a sunscreen (Kaidbey *et al.* 1979; Corsaro *et al.* 1995; Moan 1998; Meyskens *et al.* 2001). It may also act to remove the mutagenic and carcinogenic toxic oxygens from the keratinocytes and Langerhans cells (Nordlund *et al.* 1989). Unlike, black or brown-skinned people who are relatively well protected from sun induced inflammation, aging and malignant melanogenesis, albinotic skins which are devoid of melanogenic activity are highly suscptible to sunburn and other phototoxic reactions (Zhang *et al.* 2000). Cases of facial dermatitis and other dermatological complications were also reported due to the use of mercury skin-lightening creams (Sun 1987; Aberer *et al.* 1990; Pitche *et al.* 1997). Mercury is absorbed through the skin (Marzulli & Brown 1972; Barr *et al.* 1973; Baranowska-Dutkiewicz 1982; Bourgeois *et al.* 1986). The skin is composed of three layers: epidermis, dermis and the hypodermis (Mongtagna & Parakkal 1974). The outermost part of the epidermis is the stratum corneum which is built of several layers of flattened, dehydrated, keratinised dead cells. The stratum corneum functions as the main barrier site in the skin for water, electrolytes and chemicals (Emmett 1986). A substance may use two routes to penetrate the skin. First, the appendageal route where a molecule can transport through the sweat glands, sebaceous glands and hair follicles. Second, the epidermal route where the substance can penentrate between the cells of stratum corneum followed by transport through the lowest tissues of the epidermis into the dermis where it reaches the blood vessls and is distributed into the systematic circulation (Rice & Cohen 1996). There have been reports of mercury poisoning occurring after the application of mercurous containing skin-lightening creams, soaps and ointments (Balluz *et al.* 1997; Weldon *et al.* 2000; McRill *et al.* 2000; Tlacuilo-Parra *et al.* 2001; Pelclova *et al*. 2002).

Chronic exposure to either inorganic or organic mercury can permanently damage the brain, kidneys, and developing fetus (Gale 1981; Vahter *et al.* 2000; Warfvinge 1995; Silverberg *et al.* 1967; Oliveira *et al.* 1987).The chemical and physical forms of mercury determine its absorption, metabolism, distribution and excretion pathways (ASTDR 1992).

Skin-lightening creams are widely available in Saudi markets. Results from previous study (Al-Saleh & El-Doush 1997) revealed that about 45% of the tested skin lightening cream samples that are commonly used in Saudi Arabia had mercury in the range of 1.18 to 5260 ppm well above the FDA's permissible limit 1 ppm. Under conditions of good manufacturing practice, trace amount of mercury in cosmetics is unavoidable. Therefore, the U.S.A., Food and Drug Administration (FDA) has established that mercury in cosmetics should be less than 1 ppm (FDA 1992). The association between the use of skin lightening creams and urinary mercury in young healthy women that had no occupational exposure to mercury was investigated (Al-Saleh & Shinwari 1997), 23% women had mercury levels above the reference value proposed by the WHO in 1991 for non-exposed population (WHO 1991). The wide popularity and availablity of mercury containing skin-lightening creams in Saudi markets has urged us to examine its safety. In this study, we aimed to determine the levels of mercury in the brain, liver and kidney tissues of female mice treated with two different brands of mercury containing skin-lightening creams for a month. Although, it is generally accepted that one of the main functions of melanin is to protect the skin against ultraviolet radiation, its function in modifying chemical damage in the skin is still controversial. Therefore, we were also interested to evaluate if quatitative differences in the mercury levels would be found between pigmented and albino mice.

Materials and methods

Reagents

Chemicals were as follows: concentrated nitric acid and hydrochloric acid, trace metal grade; 30% hydrogen peroxide, $H_2O_2$and mercury (1000 μg/ml) were all purchased from Fisher Scientific, Co. Spring Field USA. Stannous chloride ($Sncl_2$) was bought from BDH Chemical Ltd. Poole.UK.

Animal treatment

A total of 75 female CD1 (Albino) and 70 female C57 BL (Pigmented) mice, 8 and 6 weeks age at the onset of the experiment, respectively were obtained from animal care facilities in KFSH&RC. The albino mice had a weight of 34.447 $\pm$ 3.725 g and the pigmented mice weighed 18.888 $\pm$ 1.413 g. The animals were housed individually in Makrolen cages M1, M2, M3 sizes (Kral Kolb, U.S.A.) and were fed standard dry pellet diet and water ad libitum. Both food and water were examined for mercury and found to be free. The experimental animals were classified into two groups

according to the type of the skin-lightening cream used. Each group was subdivided into five sub-groups. Animals in sub-group I served as control. Animals in subgroup II, III, IV and V were treated once per week, one per day, twice per day and three times a day with skin-lightening cream respectively. The treatments in all the groups were continued for one month. This research project was evaluated and approved by both the Research basic Committee and the Animal Care and Use Committee of King Faisal Specialist Hospital and Research Centre.

Two mercury containing skin-lightening creams were chosen according to their mercury contents. Fair & lovely comes from India (100 g per package); and Rose manufactured in Lebanon (25 g per package). In order to apply 1 mg per cm^2skin-lightening creams to the back neck of experimental mice, we needed 4 and 10 packages of Fair & Lovely and Rose respectively. Therefore, random sampling was done to ensure that the mercury content is uniformed in all purchased creams. Results of the mercury content (Mean $\pm$ SD) in the selected skin-lightening creams are listed below:

Fair & Lovely: 0.304 ± 0.316 μg/g (number of tested packages $= 4$); and
Rose: 77513.0 ± 71063.0 μg/g (number of tested packages $= 8$).

The above creams were applied on mice for a month.

Tissue dissection

At the end of one month, mice in both experiments were scarified by cervical dislocation and the brain, liver and kidney were removed, retained in a -70 °C freezer until analysis.

Tissue samples were thawed at room temperature and approximately 0.5 g of wet tissues were digested in Teflon vessels with 4 ml concentrated nitric acid for 3–4 hours at room temperature, then placed in the oven overnight at 85 °C. After digestion, the samples were allowed to cool to room temperature and 1 ml of H_2O_2 was added. Samples were heated again in the oven for 1 hr at 85 °C. The clear supernatant was transferred to polypropylene tubes and diluted to 10 ml with deionised water. Mercury contents were expressed as μg/g wet weight.

Analytical procedure

Mercury analysis was performed using a Varian Atomic Absorption 880 with Zeeman background correction (AA-880Z), coupled to a Vapour Generation Accessory VGA-76 (Varian Techtron Pty. Ltd. Australia) as described by (Rothery 1989). The gas used was argon. In this study, flow rates were about 8 ml per minute for the sample, 1.4 ml per minute for the stannous chloride solution, and 1.5 ml per minute for the hydrochloric acid. The reductant channel of the VGA-76 contained 25% stannous chloride in 20% hydrochloric acid. The acid channel contained 5 M hydrochloric acid.

Calibration standards for tissues samples were prepared each day using a manual standard addition procedure in the range of 0.5–8 μg/L for mercury. Quadruplicate determinations were made on all samples.

The accuracy of the method was determined by measuring the recovery of mercury added to tissue samples. These spiked tissue samples were run with the test samples using the same analytical procedure. The analytical recovery for tissue samples spiked with 14 to 60 μg/g mercury ranged from 96% to 101.8% which thought to be satisfactory.

Statistical analyses

As the distribution of mercury data was markedly skewed, logarithmic transformations of the data were applied. The groups were compared statistically using Student's t-test or one way-analysis of variance followed by Tukey's multiple comparison procedure. A propability less than 0.05 was considered as significant. This was carried out with Statgraphics Software (1999) statistical program.

Results

Type of mercury containing skin-lightening creams

One-way analyses of variance provided evidence for statistically significant differences in mercury levels among the different types of skin-lightening creams (Albino mice: F-ratio $= 250.92$, $P = 0$; pigmented mice: F $= 205.62$, $P = 0$) as shown in Table 1. In order to determine which means are significantly different from others, we used Tukey's multiple comparison procedure. For albino mice, the results of this method showed that no significant differences in the mercury levels were found between the non-treated mice and treated mice with Fair & Lovely skin-lightening cream compared to mice treated with Rose. The highest mercury concentrations were found in the

Table 1. The Mean ± SD and ranges of mercury (μg/g) in all tested tissues of albino mice and pigmented mice as classified by the application of skin-lightening creams. Statistical evaluation for each animal strain was done using one way analysis of variance.

Skin-lightening creams	Mean ± SD	
	Albino mice	Pigmented mice
Fair & Lovely	0.193 ± 0.319 (0.014–1.391) $n = 60$	0.05 ± 0.041 (0.0–0.139) $n = 57$
Rose	67.472 ± 70.181 (0.391–288.759) $n = 58$	33.989 ± 36.447 (0.183–123.117) $n = 57$
None	0.041 ± 0.041 (0.004–0.106) $n = 15$	0.032 ± 0.044 (0.0–0.139) $n = 30$
Level of significance	F = 250.92, $P = 0$	F = 205.62, $P = 0$

Values between paranthesis are the ranges.

tissues of mice treated with Rose. Tissues from pigmented mice treated with Rose skin-lightening creams tended to have the highest mercury concentrations, whereas, those non-treated and mice treated with Fair & Lovely tended to have lower mercury concentrations. No significant differences were found in the mercury concentrations between the non-treated pigmented mice and those treated with Fair & Lovely. But both were significantly lower than pigmented mice treated with Rose skin lightening cream.

Number of mercury containing skin-lightening creams applications

Looking at the mercury concentration in tissue samples of albino and pigmented mice with respect to the number of skin-lightening creams treatment, the highest mercury concentrations were found in the tissues of mice treated three times per day with skin lightening creams (albino mice: 56.454 ± 82.058 μg/g, ranges 0.014 to 288.759 μg/g; pigmented mice: 26.082 ± 39.261 μg/g, ranges 0.0035 to 123.117 μg/g). On the other hand, the lowest mercury concentrations were found in the tissues of mice treated once per week with skin lightening cream (albino mice: 8.019 ± 19.664 μg/g, ranges 0.016 to 95.642 μg/g; pigmented mice: 1.760 ± 2.944 μg/g, ranges 0.002 to 10.329 μg/g). One-way analysis of variance showed signifcant differences among the number of treatments (albino mice: F-ratio = 5.77, $P = 0.0003$; pigmented mice: F-ratio = 5.04, $P = 0.0008$) as illustrated in Table 2. For albino mice, mercury concentrations decreased in the order of Three times a day (56.454 μg/g) > Twice a day (37.368 μg/g) > Once a day (31.14 μg/g) > Once a week (8.019 μg/g) > Non-treated (0.041 μg/g). When Tukey's multiple comparisons procedure was applied to the data. At 95% confidence level, the results of this method showed that no significant differences were found between the mercury levels in mice treated once a week, once a day, twice a day and three a days. But they were all statistically different from non-treated mice. Similar pattern was observed for pigmented mice, where mercury concentrations decreased in the order of Three times a day (26.082 μg/g) > Twice a day (25.871 μg/g) > Once a day (16.136 μg/g) > Once a week (1.760 μg/g) > Non-treated (0.032μg/g). Mercury levels in non-treated mice and mice treated once a week were not statistically significant, but their mercury levels were statistically lesss than those in mice treated once a day, twice a day and three times a day.

Type of tissues

In each of the tested skin lightening creams, mercury was the highest in kidney tissues and the lowest in brain tissues. The same distribution pattern was noted in the tissues of non treated mice. One-way analysis of variance showed statistically significant differences in the mecury concentrations for treated mice (albino mice: F-ratio = 10.99, $P = 0$; pigmented mice: F-

Table 2. The Mean ± SD, ranges of mercury (μg/g) in all tested tissues of albino mice and pigmented mice as classified by the number of skin-lightening creams applications. Statistical evaluation for each animal strain was done using one way analysis of variance.

Number of applications of skin-lightening creams	Mean ± SD	
	Albino mice	Pigmented mice
Once a week	8.019 ± 19.664 (0.016–95.642) $n = 29$	1.760 ± 2.944 (0.002–10.329) $n = 30$
Once a day	3.14 ± 51.032 (0.015–183.764) $n = 30$	16.136 ± 23.615 (0.0–63.913) $n = 30$
Twice a day	37.368 ± 60.068 (0.024–185.862) $n = 30$	25.871 ± 38.863 (0.006–105.648) $n = 24$
Three times a day	56.454 ± 82.058 (0.014–288.759) $n = 29$	26.082 ± 39.261 (0.004–123.117) $n = 30$
None	0.041 ± 0.041 (0.004–0.106) $n = 15$	0.032 ± 0.044 (0.0–0.139) $n = 30$
Level of significance	F = 5.77, $P = 0.0003$	F = 5.04, $P = 0.0008$

Values between paranthesis are the ranges.

ratio = 96.93, $P = 0$). Similar pattern was observed for the non-treated mice. The results are presented in Table 3.

Comparative analyses (Albino mice versus Pigmented mice)

Comparing the mercury contents in the tissues of albino mice to pigmented mice, Student's test indicated that the mercury contents in the tissues of albino mice were not signifcantly different (33.262 ± 59.503 μg/g) from those in pigmented mice (17.019 ± 30.803 μg/g). differences between the accumulation of mercury in albino mice compared to pigmented mice. When the comparison was done between the albino and pigmented mice taking into the consideration the type of the mercury containing skin lightening creams, the type of tissues and the number of applications. Table 4 presents the significance of the differences in the levels of mercury for each of brain, kidney and liver tissues of the albino and pigmented mice treated either with Fair & Lovely or Rose skin lightening creams. A part from the liver tissues of pigmented mice treated with Rose skin-lightening creams, significant differencences in the mercury levels between the albino and pigmented mice were noted. The brain, kidney and liver tissues of albino mice had higher mercury levels than those in pigmented mice. For the number of skin-lightening creams applications of either Fair & Lovely or Rose, Table 5 examines the differences in the mercury levels between the albino and pigmented mice. Mercury levels tended to be higher for the albino mice than the pigmented ones, but the differences were not significant for each category. However, it was significant only for those mice who were treated with Fair & Lovely skin-lightening creams twice a day. Finally, looking at the overall differences between the albino and pigmented mice treated with either Fair & Lovely or Rose skin-lightening creams, it seems albino mice had significantly higher mercury levels than pigmented mice.

The average body weight of albino mice before the application of skin-lightening creams was 34.447 ± 3.725 g which reduced significantly to 30.373 ± 3.495 g at the end of the experiment (t-statistics = 4.845, $P = 0.000007$). In contrast, the average body weight of pigmented mice increased signifcantly from 18.888 ± 1.413 g before the application of skin lightening creams to 20.91 ± 1.376 g at the end of the experiment (t-statistics = -6.546, $P = 5.684 \times 10^{-9}$.

Table 3. The Mean ± SD and ranges of mercury (μg/g) in the tissues of albino mice and pigmented mice as classified by the type of tissue. Statistical evaluation for each animal strain was done using one way analysis of variance.

Tissue	Albino mice		Pigmented mice	
	Treated	Control	Treated	Control
Brain	2.599 ± 3.867 (0.015–14.568) ($n = 38$)	0.007 ± 0.002 (0.004–0.009) ($n = 5$)	0.904 ± 1.260 (0.0–3.633) ($n = 38$)	0.00008 ± 0.0002 (0.004–0.0008) ($n = 10$)
Kidney	64.533 ± 79.404 (0.128–288.759) ($n = 40$)	0.096 ± 0.01 (0.081–0.106) ($n = 5$)	28.426 ± 37.624 (0.058–103.958) ($n = 38$)	0.081 ± 0.043 (0.032–0.139) ($n = 10$)
Liver	31.122 ± 48.773 (0.014–177.193) ($n = 40$)	0.021 ± 0.008 (0.011–0.029) ($n = 5$)	21.729 ± 32.518 (0.026–123.117) ($n = 38$)	0.015 ± 0.016 (0.0–0.039) ($n = 10$)
Level of significance	F-Ratio = 10.99, $P = 0$	F-Ratio = 96.93, $P = 0$	F = 10.69, $P = 0.0001$	F = 14.85, $P = 0.0002$

Values between paranthesis are the ranges.

Discussion

The presence of mercury in brain, kidney and liver tissues due to the application of mercury containing skin-lightening creams on mice is an indication that mercury can be absorbed through the skin. This confirms previous studies in human and animals (Palmer *et al.* 2000; Friberg *et al.* 1961; Skog & Wahlberg 1964; Daian *et al.* 1995). In this study, we measured the mercury levels from two areas of the skin. The mercury levels in treated skin area of 1 cm^2 from the back were 132.725 ± 163.793 μg/g (n = 37) compared to those in the abdomen area of 8.566 ± 11.804 μg/g (n = 39). The differences were not statistically significant ($P = 0.081$). According to previous human studies, anatomical site differences in the barrier function of the skin might exist (Rougier *et al.* 1988; Lotte *et al.* 1987; Palmer *et al.* 2000). Dermal absorption depends largely on the chemical and physical properties of the cream itself such as degree of ionization, molecular size, water and lipid solubility. In contrast to hydrophilic substances, the lipophilic substances penetrate the skin barrier (starum corneum) quite readily. Enhancers are commonly added to dermatological formulations to increase their permeability through the skin barrier such as glycerol (Barry 1983). Also, physical methods such as iontophoresis and sonophoresis are used to increase dermal penetration. Monteiro-Riviere *et al.* (1994) found that mercury can penetrate the skin through transappendageal and transepidermal routes using iontophoretic drug delivery method. In this study, both tested mercury containing skin-lightening creams are lipid/water based formulations where it is clear that mercury was able to penetrate the outer surface of the skin through stratum corneum, epidermis and dermis reaching the blood circulation and accumlating in the various tissues of the mouse. Results of this study revealed that mercury in each brand of the tested skin lightening cream had significant effect on various tissues of mice where kidney had the highest mercury content and brain had the lowest ($P < 0.0001$). In spite of the low mercury content in Fair & Lovely (less than the FDA perimissible of 1 ppm), mercury was found in the brain, kidney and liver after one month of exposure. Therefore, the repeated applications of Fair & Lovely Fair & Lovely skin-lightening cream over a longer period of time might have toxic effects on various organs. For example, a number of studies reported nephrotic syndrome due to the use of mercury containing skin-lightening creams (Brown *et al.* 1977; Giunta *et al.* 1983; Rosenman *et al.* 1986; Enwonwu 1987; Soo *et al.* 2003). On the other hand, the high mercury tissue levels in mice treated with Rose skin-lightening cream indicate a significant exposure even with once a week application. Recent study by Afonne *et al* (2002) revealed that low dose mercury exposure (i.e. 4 ppm) in mice produced necrosis and widening of the golmeruli. This level is far below the mercury content in Rose skin-lightening cream of 77513.0 μg/g. If the results of the study extrapolated to humans, they suggest that exposure to mercury after repeated application of mercury containing skin-lightening creams even below FDA perimissible limit (1 ppm) could lead

Table 4. Statistical differences in the mercury concentrations between albino mice and pigmented treated with different mercury containing skin-lightening creams as classified by the type of tissue.

Tissue	Fair & Lovely			Rose		
	Albino mice	Pigmented mice	t-statistics (P-value)	Albino mice	Pigmented mice	t-statistics (P-value)
Brain	0.021 ± 0.005 (0.015–0.028) $n = 20$	0.005 ± 0.036 (0.0–0.017) $n = 19$	10.799 (0)	5.464 ± 4.004 (0.391–14.568) $n = 18$	1.802 ± 1.248 (0.183–3.633) $n = 19$	2.965 (0.005)
Kidney	0.527 ± 0.373 (0.128–1.391) $n = 20$	0.096 ± 0.022 (0.058–0.143) $n = 19$	8.887 (1.032×10^{-10})	128.538 ± 65.703 (14.495–288.759) $n = 20$	56.755 ± 34.864 (4.341–103.958) $n = 19$	3.307 (0.002)
Liver	0.031 ± 0.018 (0.014–0.086) $n = 20$	0.0497 ± 0.018 (0.026–0.090) $n = 19$	−4.066 (0.0002)	62.214 ± 53.364 (1.937–177.193) $n = 20$	43.408 ± 34.372 (1.701–123.117) $n = 19$	0.728 (0.471)
Overall	0.193 ± 0.319 (0.014–1.391) $n = 60$	0.050 ± 0.041 (0–0.143) $n = 57$	2.922 (0.004)	67.472 ± 70.181 (0.391–288.759) $n = 58$	33.989 ± 36.447 (0.183–123.117) $n = 57$	2.497 (0.014)

Values between paranthesis are the ranges.

Table 5. Mercury concentrations in albino and pigmented mice treated with different mercury skin-lightening creams as classified by the number of applications of each of the studied skin-lightening creams.

Number of applications	Fair & Lovely			Rose		
	Albino mice	Pigmented mice	t-statistics (P-value)	Albino mice	Pigmented mice	t-statistics (P-value)
Once a week	0.150 ± 0.289 (0.016–1.107) $n = 15$	0.047 ± 0.039 (0.002–0.115) $n = 15$	1.525 (0.138)	16.450 ± 26.168 (0.391–95.642) $n = 14$	3.473 ± 3.415 (0.183–10.329) $n = 15$	1.704 (0.099)
Once a day	0.137 ± 0.174 (0.015–0.582) $n = 15$	0.066 ± 0.049 (0.0–0.143) $n = 15$	0.684 (0.499)	62.143 ± 57.748 (3.077–183.764) $n = 15$	32.206 ± 24.531 (1.082–63.913) $n = 15$	1.257 (0.219)
Twice a day	0.358 ± 0.497 (0.024–1.391) $n = 15$	0.042 ± 0.036 (0.006–0.095) $n = 12$	2.286 (0.031)	74.378 ± 67.37 (4.247–185.862) $n = 15$	51.699 ± 41.262 (1.929–105.648) $n = 12$	0.777 (0.445)
Three times a day	0.126 ± 10.168 (0.014–0.534) $n = 15$	0.045 ± 0.036 (0.004–0.110) $n = 15$	1.122 (0.271)	116.806 ± 83.182 (5.990–288.759) $n = 14$	52.119 ± 41.716 (2.538–123.117) $n = 15$	1.898 (0.068)
Overall	0.193 ± 0.319 (0.014–1.391) $n = 60$	0.050 ± 0.041 (0–0.143) $n = 57$	2.922 (0.004)	67.472 ± 70.181 (0.391–288.759) $n = 58$	33.989 ± 36.447 (0.183–123.117) n = 57	2.497 (0.014)

Values between paranthesis are the ranges.

to nephrotic syndrome. Women during pregnancy and lactation could be also at risk since a previous study by Lauwerys *et al.* (1987), reported a case of a woman who had recently given birth and who had used during pregnancy and lactation a soap containing 1% mercury as mercuric iodide and a mercury containing cream. Cutaneous absorption of mercury by the mother was confirmed by the finding of high levels of mercury in blood and in urine 4 months after delivery at a time when she was still using the soap and cream. Although no mercury containing cream or soap was used on her baby's skin and the lactation period lasted only one month, high mercury levels were still found in the baby's blood and urine 3 months after delivery.

Another interesting finding in this study is the significant difference in mercury content between the

albino and pigmented mice. This suggests that melanin in pigmented mice exerts a protective effect against mercury. The production of melanin pigment which is a complex of polymers dervided from the amino acid tyrosine requires the interaction of at least three malanogenic enzymes, which regulate the type and amount of melanins produced (Furumura *et al.* 1998). In 1952, Lerner described the antipigmentation property of mercury as a result of the displacement of copper ions from the active site of the melanin formation enzyme, tryosinase, rendering it inactive. Therefore, mercury containing skin-lightening creams could be potentially dangerous since stripping melanin leaves the skin more susceptible to sun damage increase the risk of developing malignant melanoma (Hill *et al.* 1997; Gilchrest *et al.* 1999). Despite the fact that albino mice accumulates higher mercury in their tissues than pigmented mice, the mercury levels in the tissues of pigmented mice treated with Rose skin lightening cream were high enough to induce various pathological conditions such as renal dysfunction.

This animal study emphasizes the potential toxicity of these creams regardless of the type of cream including the one (Fair and Lovely) which contains <1 μg/g and highlights the need to the importance of regulating their sell. Women who are using mercury containing skin-lightening creams are at risk of permanent nephrological or/and neurological deficits because early exposure have no clinical manifestations. Others are also at risk for mercury toxicity including developing fetus, infants and men. Recently, Adebajo (2002) has reported that the use of skin-lightening creams has become a socially acceptable phenomenon that is widly practiced by both men and women in Nigeria. Therefore, dermatologists should be aware of adverse effects of mercury containing skin-lightening creams and ask their patients about the use of such creams.

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