

# Use of Potentially Harmful Skin-Lightening Products among Immigrant Women in Rome, Italy: A Pilot Study

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## Key Words

Contact dermatitis · Topical corticosteroids · Mercury · Hydroquinone · Metals · Skin-lightening products

## Abstract

**Background:** Skin-lightening products are increasingly common in European cities. These products may contain substances that are banned under EU regulations as they can induce adverse effects, including cutaneous and systemic reactions (e.g., mercury, hydroquinone and topical corticosteroids). **Objectives:** To assess the knowledge, attitudes and practices of women regarding skin-lightening products and to quantify the potentially harmful substances in the products used. **Methods:** We performed a cross-sectional study among 82 non-Italian women visiting an outpatient facility in Rome, Italy. The women completed a questionnaire on product use, side effects and risk awareness. We performed patch tests among a subgroup of 48 women who presented with contact dermatitis. We also quantified the allergenic and toxic substances in the 14 products reported, using dynamic reaction cell inductively coupled plasma mass spectrometry for metals and high-performance liquid chroma-

tography for hydroquinone and topical corticosteroids. **Results:** Out of the 82 women, 33 used skin-lightening products; about one fourth of these women were aware of potential risks. Three cosmetic creams and two soaps contained high concentrations of metals (Cr, Ni and Pb); hydroquinone was found in three creams and one oil. The only topical corticosteroid detected was dexamethasone, in one product. More than half of the women in the clinical evaluation had irritant contact dermatitis (i.e., negative response to patch test). **Conclusions:** Among immigrant women in Rome, the use of skin-lightening products seems to be fairly common, and some of these products contain potentially hazardous substances. Consumers must be informed of the potential risks, and EU regulations must be more strictly enforced.

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## Introduction

The use of skin-lightening products has become increasingly common, especially in Asia, Latin America and Africa. In Europe, they are widely used among immigrants who live in cities, especially women. Most per-

sons apply these products, which are available as creams, milks, oils, ointments and soaps, all over the body, whereas others apply them only on the face, neck and arms. The lightening agents contained in these products consist mainly of mercury (Hg), hydroquinone (1,4-dihydroxybenzene) and topical corticosteroids (TCs), at different concentrations, together with other compounds (hydrogen peroxide, poly-hydroxy acids, azelaic acid, phenols, solvents and salicylic acid) [1–3]. These chemicals can induce adverse effects on human health, including cutaneous and systemic complications [4]. Skin-lightening products may also contain elements such as cadmium (Cd), cobalt (Co), chromium (Cr), nickel (Ni) and lead (Pb), which can be intentionally added by the manufacturers or be present as impurities.

One of the most effective skin-lightening substances is hydroquinone, whose mechanism of action is based on the inhibition of melanin formation; however, it may cause irritant contact dermatitis and hypopigmentation. TCs, particularly highly potent, which are anti-inflammatory agents used to treat skin disorders, are also commonly used as skin lighteners and can cause a number of complications, in particular acne, mycoses, striae, telangiectasia, hypertrichosis and diabetes mellitus. The toxic effects of Hg, which can be extremely effective in lightening dark spots and stubborn pigmentation, are subtle and cumulative, building up over time. Skin contact with Hg compounds can lead to irritation, including patches of inflammation and the appearance of tiny, close together bumps, which may burst and discharge matter and later crust over, leading to soreness and discomfort [1, 5–7].

In Europe, the Rapid Alert System for Non-Food Products (RAPEX) facilitates the rapid exchange of information between member states and the Commission on measures taken to prevent or restrict the marketing or use of products posing a serious risk to the health and safety of consumers. The RAPEX has reported that many illegal products marketed as cosmetics and containing banned substances are sold on the European market. In the European Union, skin-lightening products are considered as cosmetics, whose use, in terms of protecting human health, is governed by Regulation No. 1223/2009 [8, 9].

Hydroquinone is classified as carcinogenic and mutagenic [10], and since 1 December 2010 it has been banned from use in cosmetic products, as reported in Annex III of Regulation No. 1223/2009. TCs are also banned from use in cosmetics. As regards metals, Cd, Cr (chromic acid and its salts), Hg, Pb and their compounds, some compounds of Ni and Co are banned by the same regulation.

In Italy, few studies have been conducted on the prevalence of use of skin-lightening products or their side effects. In 2011, the San Gallicano Dermatological Institute in Rome, Italy and the Istituto Superiore di Sanità (Italy's National Institute of Public Health, Rome) developed the project 'Prevention of Skin Diseases Caused by Skin-Lightening Cosmetics among the Immigrant Population', which is funded by the National Institute for Health, Migration, and Poverty (NIHMP). The objectives of the project are to estimate the prevalence of use of skin-lightening cosmetics and to evaluate the clinical side effects and possible risks associated with these products among immigrant women living in Rome.

## Subjects and Methods

### *Study Population and Questionnaire*

The study population consisted of 82 non-Italian women who visited the outpatient and diagnostic facilities of the NIHMP in the period from January to June 2011. The women were asked to participate in the survey by filling in a self-completed questionnaire that consisted of 33 items. The questionnaire included personal data (age, marital status, nationality, educational level and employment status) and information on the use of skin-lightening products. It aimed in particular at whether or not the individual used such products, the type of product, the brand, where the product was purchased, the dosage, the duration and frequency of use, use during pregnancy and lactation, and estimated monthly expenses for the products. The participants were also asked to report any possible side effects. The questionnaire also included items for evaluating the level of knowledge and awareness of risks posed by the use of the potentially dangerous chemicals contained in these products.

### *Physical Examination*

In a subgroup of 48 women who presented with contact dermatitis suspected to be caused by a cosmetic product (including products not used for skin lightening), we identified the chemical substance responsible for the contact dermatitis. To this end, we used standard and specific series patch tests, which were performed and read in accordance with the guidelines of the International Contact Dermatitis Research Group [11]. The allergens tested were chosen based on the products that the women had used (reported in the questionnaire) and on the chemical composition of these products.

### *Statistical Analysis*

Statistical analysis of the results of the questionnaires was carried out using the SPSS software (IBM, USA). The associations among variables were evaluated by  $\chi^2$  test; the associations were considered to be statistically significant when the p value was <0.05. The associations between the use of skin-lightening products and sociodemographic variables were evaluated using multiple logistic regression.

### Biochemical Analysis

Based on the results of the questionnaires, the most commonly reported skin-lightening cosmetics were identified. Samples of these products ( $n = 14$ ) were either provided by the women themselves or purchased in Rome for the purpose of this study. The products consisted of bath soaps ( $n = 2$ ), creams ( $n = 6$ ), oils ( $n = 2$ ) and beauty care milks ( $n = 4$ ). The cosmetics were produced in Bolivia, Colombia, the Ivory Coast, France, India, Switzerland, Taiwan, the United Kingdom and the United States (the manufacturing country remained unknown for two body creams; for one of these creams, the brand was not available).

Trace elements were quantified with dynamic reaction cell inductively coupled plasma mass spectrometry (Elan DRC II, Perkin Elmer SCIEX, Norwalk, Conn., USA) in samples previously digested in a microwave oven (Ethos Plus, Milestone, FKV, Sorisole, Bergamo, Italy) with Suprapur concentrated nitric acid and hydrogen peroxide (Romil, Cambridge, UK). To evaluate the performance of the method, some standard parameters were evaluated: limit of detection and quantification (LoD, LoQ), recovery (%) and repeatability (as a percent variation coefficient).

Hydroquinone and TCs, extracted from the sample by methanol (Panreac Química, Barcelona, Spain) were quantified by high-performance liquid chromatography (Alliance Waters 2695, Waters, Milford, Mass., USA), which is suitable for identifying and quantifying hydroquinone in cosmetics. The same method was also used to detect TCs. Thin layer chromatography was used to confirm the identity of the analyzed compounds.

## Results

### Sociodemographic Data

The 82 women who completed the questionnaires originated from Africa ( $n = 57$ ; 69.5%), Latin America ( $n = 16$ ; 19.5%), Asia ( $n = 3$ ; 3.7%) and other/unknown area ( $n = 6$ ; 7.3%). The median age was 35 years (range 18–60).

### Cosmetic Data

The results of the questionnaires showed that 33 (40.2%) of the 82 women were using skin-lightening products at the time or had used them in the past, for a mean duration of 3 years (range 8 months to 20 years). The women reported that they spent an average of EUR 20 per month on these products. The age at first use ranged from 15 to 40 years. No significant association was found between demographic variables and product use, although use was more common among women <35 years of age (43.9%) compared to older women (35.9%), and women with a university degree (53.8%) compared to women who had completed middle school (36.7%) and high school (37.1%).

Of the women who used skin-lightening products, only 1 used the product because it was prescribed by a

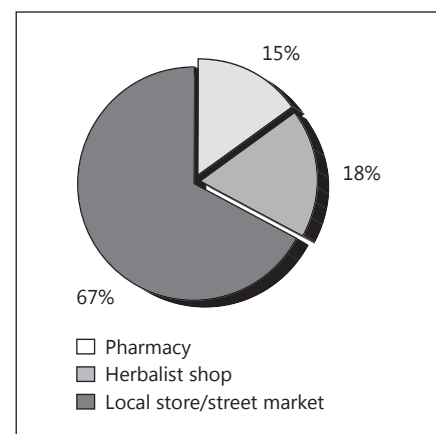


**Fig. 1.** Type of vendor from which skin-lightening products were purchased.

physician for a specific medical treatment; 12 women used the product because they had seen an advertisement (especially on the Internet); the other 13 women had heard about the product from other sources, such as shop keepers and friends; this information was not available for 7 women. The products had been purchased most often in local stores or street markets, followed by herbalist shops and pharmacies (fig. 1).

Of the 82 participants, 34 (41.5%) were aware of the risks associated with the use of skin-lightening products; of these women, 23 (67.6%) recognized Hg as the most dangerous chemical component. Of the women who used skin-lightening products for whom this information was available (30 women), 12 were aware of the risks and 18 were not.

### Clinical Evaluation

For the 48 women who participated in the clinical evaluation, the most commonly affected sites of reaction were the face, hands and feet; the reactions were classic contact dermatitis ( $n = 31$ ), leukoderma ( $n = 5$ ), pigmented dermatitis ( $n = 6$ ) and other ( $n = 6$ ). For 24 of these women, the suspected contact dermatitis had appeared after the use of a skin-lightening product.

Of the 48 women, 22 (46%) were positive to at least one allergen of the patch test: 16 (33%) were positive to  $\text{NiSO}_4$ , 5 (10%) to fragrance mix, 5 (10%) to *p*-phenylenediamine, 3 (6%) to  $\text{CoCl}_2$ , 3 (6%) to Balsam of Peru, 1 (2%) to a corticosteroid mix and 1 (2%) to hydroquinone. 12 of the 22 women were positive to more than one allergen.

**Table 1.** Method performance for Cd, Co, Cr, Hg, Ni and Pb

| Element | LoQ, ng/g |      |     |      | Recovery, % |      |     |      | Repeatability, CV% |      |     |      |
|---------|-----------|------|-----|------|-------------|------|-----|------|--------------------|------|-----|------|
|         | cream     | milk | oil | soap | cream       | milk | oil | soap | cream              | milk | oil | soap |
| Cd      | 5.3       | 1.7  | 0.6 | 2.0  | 102         | 97   | 93  | 97   | 3                  | 4    | 3   | 8    |
| Co      | 1.5       | 0.6  | 0.3 | 1.2  | 99          | 99   | 104 | 101  | 4                  | 5    | 2   | 3    |
| Cr      | 6.5       | 2.4  | 1.0 | 11.0 | 97          | 102  | 118 | 106  | 7                  | 14   | 14  | 8    |
| Hg      | 2.6       | 1.4  | 0.6 | 4.2  | 114         | 107  | 106 | 109  | 6                  | 2    | 1   | 8    |
| Ni      | 12.1      | 4.1  | 2.3 | 7.8  | 81          | 83   | 96  | 87   | 11                 | 12   | 3   | 11   |
| Pb      | 9.7       | 5.7  | 4.5 | 7.1  | 100         | 100  | 94  | 98   | 6                  | 4    | 2   | 2    |

**Table 2.** Mean concentrations and standard deviations of Cd, Co, Cr, Hg, Ni and Pb in skin-lightening products

| Sample      | Concentration, ng/g |         |        |       |        |       |
|-------------|---------------------|---------|--------|-------|--------|-------|
|             | Cd                  | Co      | Cr     | Hg    | Ni     | Pb    |
| Soap 1      | <LoQ                | 3.2±2.4 | 101±7  | <LoQ  | 31±1   | 55±2  |
| Soap 2      | <LoQ                | 3.0±1.8 | 42±15  | <LoQ  | <LoQ   | <LoQ  |
| Body milk 1 | <LoQ                | 3.1±1.8 | <LoQ   | <LoQ  | <LoQ   | <LoQ  |
| Body milk 2 | <LoQ                | <LoQ    | <LoQ   | <LoQ  | <LoQ   | <LoQ  |
| Body milk 3 | <LoQ                | <LoQ    | <LoQ   | <LoQ  | <LoQ   | <LoQ  |
| Body milk 4 | <LoQ                | <LoQ    | <LoQ   | <LoQ  | <LoQ   | <LoQ  |
| Cream 1     | <LoQ                | <LoQ    | <LoQ   | <LoQ  | <LoQ   | <LoQ  |
| Cream 2     | 17±1                | 2.4±0.1 | 137±12 | <LoQ  | 20±4   | <LoQ  |
| Cream 3     | <LoQ                | 2.1±0.1 | 188±18 | <LoQ  | 97±4   | <LoQ  |
| Cream 4     | <LoQ                | <LoQ    | <LoQ   | <LoQ  | <LoQ   | <LoQ  |
| Cream 5     | 14±1                | 117±3   | 720±53 | 39±21 | 408±15 | 202±2 |
| Cream 6     | <LoQ                | <LoQ    | <LoQ   | <LoQ  | <LoQ   | <LoQ  |
| Oil 1       | <LoQ                | <LoQ    | <LoQ   | <LoQ  | <LoQ   | <LoQ  |
| Oil 2       | <LoQ                | <LoQ    | <LoQ   | <LoQ  | <LoQ   | <LoQ  |

### *Chemical Characterization of the Skin-Lightening Products*

*Determination of Cd, Co, Cr, Hg, Ni and Pb.* The elements can be classified according to the type of action: topical and allergenic action (Co, Cr and Ni) and topical and systemic action (Cd, Hg and Pb). By law, none of these elements should be present in cosmetics. The performance of the method for detecting metals in the cosmetics is summarized in table 1. Overall recovery and repeatability were quite satisfactory, except with regard to Ni for cream and milk. The limits of quantification are suitable for the purposes of this analysis. The mean concentrations of metals present in the samples of skin-lightening products are shown in table 2 (the results are the means of 5 replicates). A quantifiable level of Hg was

found in only one sample (cream 5). The same product also contained very high concentrations of Co, Cr, Ni, Cd and Pb (20 times the LoQ). The concentrations of the elements in cream samples varied: creams 1, 4 and 6 had concentrations below the limits of quantification (except for Co for cream 6), whereas creams 2 and 3 had high concentrations of Cr and Ni. All of the body milks were compliant with EU standards, except for body milk 1, which was not compliant for Co. The oils were also compliant with European standards. With regard to the soaps, they were compliant in terms of Cd and Hg, yet were not compliant for Co, Cr, Ni and Pb. In particular, the concentration of Cr was well above the LoQ in both samples, and Ni was high in soap 1.

**Table 3.** Hydroquinone content in 100 g of product

| Sample  | Label claim (quantity) | Hydroquinone, g |
|---------|------------------------|-----------------|
| Oil 2   | yes (not specified)    | 7.7             |
| Cream 1 | yes (3 g)              | 1.5             |
| Cream 3 | no                     | 5.7             |
| Cream 6 | yes (5 g)              | 4.3             |

*Determination of Hydroquinone and TCs.* Hydroquinone, which is banned from use in cosmetics, was detected in 4 of the 14 samples (creams 1, 3 and 6 and oil 2). The quantity found in these products is shown in table 3, together with the declaration of the manufacturer on the labels. In one of these products (cream 3) the label did not indicate the presence of hydroquinone. The only TC detected was dexamethasone, and only in one product (cream 6); the quantity found was the same as that reported on the label (5 g per 100 g). Kojic acid was identified in three samples (milks 1 and 2 and oil 1, as reported on the labels) [12, 13].

## Discussion

In our study, the results of the questionnaire showed that a high proportion (40.2%) of immigrant women used skin-lightening products, that their use tended to be more common among younger women and those with a higher level of education (although the associations were not significant), that the products were most frequently purchased at local street markets, and that a high proportion of women had heard of the product from Internet advertising. The importance of our findings on the frequency of use of skin-lightening products lies in the fact that some of the substances contained in these products can produce allergic reactions and that the presence of these substances is not always reported on the package label or controlled by the manufacturers.

According to the results of our clinical evaluation, which was conducted among 48 women who presented with contact dermatitis suspected to be caused by a cosmetic product, the most frequent clinical picture was irritant contact dermatitis, with a negative response to patch test, whereas only a minority of the individuals had allergic contact dermatitis. For 24 of the women, the suspected contact dermatitis had appeared after the use of a skin-lightening product. The highest percentage of women were allergic to Ni (33%). However, in most cases the re-

action was due to jewelry that contained Ni, and it remains to be determined whether the quantity of Ni in the products tested is sufficient for producing contact dermatitis.

Regarding the composition of skin-lightening products, few published studies exist. In a study conducted in Kisumu (Kenya, Africa), very high levels of Hg iodide were found in eight types of EU-produced toilet soaps collected at a market, whereas lower concentrations were found in locally produced soaps [14]. In Mexico, Hg in skin-lightening facial creams from a local market was quantified by cold vapor atomic absorption spectrometry: 6 of the 16 creams contained dangerous amounts of Hg, from 878 to 35,824 ppm, whereas the quantity of Hg in the remaining samples was below the limit of detection (<5 ppb) [15].

In our study, we analyzed 14 skin-lightening products for the presence of metals, hydroquinone and TCs, most of which are banned from use in cosmetic products by EU regulatory agencies, in that their presence may pose a health threat. According to our results, 7 out of the 14 products contained at least one metal; of these, 5 contained metals at concentrations that did not comply with EU standards. In our study, hydroquinone was detected in 4 products. In studies conducted on cosmetic creams in Taiwan, the United Kingdom, the United States, China, Sudan and Thailand, no hydroquinone was detected [3, 16], whereas a hydroquinone content of 2.0 and 4.0% (declared on the label) was confirmed in gels and creams purchased from a Brazilian compounding pharmacy [17]. A TC (dexamethasone) was detected in only one product. Generally, TCs are used as anti-inflammatory agents in treating several skin diseases [18], yet they are also commonly used as depigmenting agents among dark-skinned African women [19]. In Europe, corticosteroid creams are considered as pharmaceutical products and can be sold only by authorized dealers [20]. We also detected kojic acid in three samples. Kojic acid is produced by many species of fungus, including *Penicillium*, *Acetobacter* and *Aspergillus*; like hydroquinone, it is a tyrosinase inhibitor and is used in the cosmetics industry as an anti-pigmenting agent, yet it is not considered to be toxic [21, 22].

Thus, of the products tested, 9 can be considered to be potentially harmful to human health. One product (cream 5) may constitute a particularly high risk, in that it contained Hg and very high concentrations of Co, Cr, Ni, Cd and Pb (20 times the LoQ). Moreover, not all of the products that contained these substances reported this information on the package label, nor was the quantity reported accurate. According to EU legislation, the non-intend-

ed presence of a small quantity of a prohibited substance (technically unavoidable in good manufacturing practice) is permitted, provided that such presence is in conformity with EU regulations. In soaps 1 and 2, body milk 1 and creams 2, 3 and 6, the concentration of Co was quite low yet nonetheless higher than the limits established by legislation. In these cases, although Co was probably present as a contaminant, the concentration was not measured by the manufacturer.

In interpreting the results of this study, some potential limitations should be taken into consideration. First of all, as the results are based on relatively few women, it is possible that they cannot be generalized to the population of immigrant women in Italy. However, these analyses were conducted as part of a pilot study, and there are currently plans to expand the study to a larger geographic area. With regard to the methods used to detect the substances in cosmetic products, the overall recovery was quite satisfactory, except for Ni for creams and milks. In fact, the quantification of Ni was very challenging, probably because of the variety of unknown components of the cosmetics. The limits of quantification seemed to be slightly high, but they were calculated taking into account the final dilution and weight.

Despite these limitations, our results are important in that they show that the use of skin-lightening products is fairly common among immigrant women in Rome

and that some of these products contain potentially hazardous substances. For these reasons, it is essential for consumers to be informed of the potential harm associated with their use. In light of these considerations, the San Gallicano Dermatological Institute has produced and distributed a pamphlet on the potential hazards of using these products. However, even if consumers are made aware of which substances are harmful, not all manufacturers report the presence of the substances on the product label, or they report that the substance is present in concentrations that are lower than the actual concentration. For these reasons, it is necessary for the regulations on cosmetics to be more strictly enforced.

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### Disclosure Statement

The authors declare that there is no conflict of interest with any financial organization regarding the material discussed in this paper.

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