

UNIVERSITI PUTRA MALAYSIA

CONTENT OF HEAVY METALS (Ni, Cd, Pb) IN SKIN LIGHTENING PRODUCTS AND DERMAL HEALTH RISK AMONG YOUNG ADULT WOMEN

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Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfilment of the Requirements for the Degree of Master of Science

June 2016

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Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfilment of the requirement for the degree of Master of Science

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By

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June 2016

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Background: Human exposure to heavy metals occurs on daily basis mainly via ingestion of contaminated food sources or inhalation of resuspended dust. Other less obvious sources of dermal exposure includes heavy metal from beauty products. Indeed, heavy metal can be detected in most of beauty products in the form of impurities. The issue of the heavy metals appears as impurities in beauty products was not widely discussed. As skin lightening is the most popular beauty products in certain countries, the presence of heavy metal impurities in it can lead to direct exposure to a large number of individuals. Objective: The aim of this study was to determine the heavy metals concentration in skin lightening product namely facial moisturizing cream and to assess the risk from dermal exposure of its continued application. Additionally, this study attempts to determine the practice, knowledge and perception toward the use of skin lightening among female universities students in Malaysia. Information on perceived skin problem caused by the use of skin lightening was collected. Methodology: This is a cross-sectional study that involved 198 female students which took place in Universiti Putra Malaysia (UPM) and International Islamic University Malaysia (IIUM) from November 2014 to April 2015. Questionnaire was used to determine students' practice, knowledge and perception on skin lightening. This study sampled 33 skin lightening creams (17 local brands and 16 non-local brands) available in the local market. Samples were digested and tested for heavy metals which are nickel (Ni), cadmium (Cd) and lead (Pb) by using Inductively Coupled Plasma Optical Emission Spectrometry (ICP-OES). The physicochemical properties including moisture content, pH, type of emulsion and spreadability were measured. The health risk assessment from continued application was assessed by using Margin of Safety (MoS) and Hazard Quotient (HQ). This study has obtained ethical approval from the Ethics Committee for Research involving Human Subjects of Universiti Putra Malaysia (JKEUPM) prior conducting the study. Result: A total of 117 (59.7%) respondents aged between 20 to 30 years are currently using skin lightening products. Most of the respondents aware that skin lightening might cause health effect (87.8%, N=172). Most of the respondents have the perception that lighter skin provides high self-esteem (54.6%, N=107). The most common skin problems experienced were skin peeling (54.5%, N=22). The concentration of Ni, Cd and Pb in

non-local samples was higher compared to local samples with average (standard deviation) of 0.207 ± 0.15 mg/kg, 0.018 ± 0.02 mg/kg and 0.107 ± 0.08 mg/kg respectively. The range MoS of heavy metals in this study was higher than 100 suggesting that the presence of heavy metals impurities in the skin lightening samples were within an acceptable risk to human health. The MoS for Ni was 4.0×10^7 to 1.1×10^8 , 1.8×10^5 to 4.1×10^5 for Cd and 1.8×10^4 to 8.4×10^4 for Pb. The HQ for Ni and Cd were less than 1, whereas HQ for Pb was greater than 1 indicating that a potential may exist for adverse health effects. **Conclusion:** Heavy metals impurities detected in the samples studied were at low concentration and within acceptable risk to human except for Pb. However, care should be taken as metals are able to accumulate in human body and the health effects from it remained concern.

Keywords: Heavy metals; skin lightening products; dermal health risk assessment; female student



Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Master Sains

KANDUNGAN LOGAM BERAT (Ni, Cd, Pb) DALAM PRODUK PEMUTIH KULIT DAN RISIKO KESIHATAN KULIT DALAM KALANGAN WANITA DEWASA AWAL

Oleh

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Pengerusi : Sharifah Norkhadijah Syed Ismail, PhD Fakulti : Perubatan dan Sains Kesihatan

Latarbelakang: Pendedahan manusia terhadap logam berat berlaku setiap hari terutamanya melalui proses pencernaan sumber makanan yang tercemar atau menghidu partikel habuk yang terbentuk dalam proses pernafasan. Sumber lain bagi pendedahan logam berat ke atas kulit adalah melalui penggunaan produk kecantikan. Logam berat sememangnya boleh dikesan dalam kebanyakan produk kecantikan dalam bentuk unsur surih. Isu kewujudan logam berat sebagai unsur surih tidak dibincangkan secara meluas. Oleh kerana produk pemutih kulit merupakan produk kecantikan yang popular di beberapa negara, kewujudan unsur surih logam berat didalamnya boleh menyebabkan pendedahan secara langsung kepada sebilangan besar individu. Objektif: Kajian ini bertujuan untuk menentukan kepekatan logam berat didalam produk pemutih kulit jaitu krim pelembap wajah dan untuk menilai risiko daripada pendedahan kulit hasil daripada penggunaan berterusan. Selain itu, kajian ini bertujuan untuk menentukan amalan, pengetahuan dan persepsi berkaitan produk pemutih kulit dalam kalangan pelajar perempuan universiti di Malaysia. Maklumat berkaitan masalah kulit yang disebabkan oleh produk pemutih juga dikumpulkan. Metodologi: Kajian ini merupakan kajian keratan rentas yang melibatkan 198 pelajar perempuan yang dilaksanakan di Universiti Putra Malaysia (UPM) dan Universiti Islam Antarabangsa Malaysia (UIAM) bermula daripada November 2014 sehingga April 2015. Soal-selidik digunakan untuk menentukan amalan, pengetahuan dan persepsi pelajar berkaitan pemutihan kulit. Maklumat berkaitan krim pemutih kulit yang digunakan responden dicatat. Sebanyak 33 krim pemutih kulit disampel (17 jenama tempatan dan 16 jenama bukan-tempatan) daripada pasaran. Sampel dicernakan dan diuji untuk kandungan logam berat iaitu nikel (Ni), kadmium (Cd) dan plumbum (Pb) dengan menggunakan Inductively Coupled Plasma Optical Emission Spectrometry (ICP-OES). Ciri-ciri fisikokemikal termasuk kandungan lembapan, pH, jenis emulsi dan penyebaran juga diukur. Risiko kesihatan melalui penggunaan berterusan dinilai menggunakan Margin Selamat (Margin of Safety, MOS) dan Quotient Bahaya (Hazard Quotient, HQ). Kajian ini telah mendapat kelulusan daripada Jawatankuasa Etika Universiti untuk Penyelidikan Melibatkan Manusia (JKEUPM) sebelum dijalankan. Hasil Kajian: Sejumlah 117 (59.7%) responden berumur antara 20 hingga 30 tahun merupakan pengguna produk pemutih kulit. Kebanyakan responden menyedari bahawa produk

pemutih kulit mungkin boleh menyebabkan masalah kesihatan (87.8%, N=172). Kebanyakan responden mempunyai persepsi bahawa kulit yang lebih putih meningkatkan keyakinan diri (54.6%, N=107). Masalah kulit yang biasa dialami adalah kulit menggelupas (54,5%, N=22). Kepekatan Ni, Cd dan Pb dalam sampel bukantempatan adalah lebih tinggi berbanding sampel tempatan dengan masing-masing memiliki purata (sisihan piawai) sebanyak 0.207±0.15 mg/kg, 0.018±0.02 mg/kg dan 0.107±0.08 mg/kg. Kisaran nilai MoS untuk logam berat dalam kajian ini adalah lebih tinggi daripada 100, menandakan bahawa kewujudan logam surih dalam sampel berada dalam risiko yang boleh diterima keatas kesihatan manusia. MoS untuk Ni adalah 4.0×10^7 hingga 1.1×10^8 , 1.8×10^5 hingga 4.1×10^5 untuk Cd dan 1.8×10^4 hingga 8.4×10^4 untuk Pb. HQ untuk Ni dan Cd adalah kurang daripada 1, manakala HQ untuk Pb lebih besar daripada 1 yang menunjukkan bahawa potensi yang mungkin wujud untuk kesan kesihatan yang tidak diingini. Kesimpulan: Unsur surih logam berat yang dikesan dalam sampel kajian berada pada tahap kepekatan yang rendah dan didalam had risiko yang boleh diterima oleh manusia kecuali untuk Pb. Walau bagaimanapun, penjagaan perlu diambil kerana logam berat boleh berkumpul didalam badan manusia dan kesan kesihatan daripadanya kekal sebagai satu kebimbangan. (490 patah perkataan)

Kata kunci: Logam berat; produk pemutihan kulit; penilaian risiko kesihatan kulit; pelajar perempuan

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LIST OF ABBREVIATIONS

| 1.00 | |
|---------|--|
| ACD | Allergic Contact Dermatitis |
| ADI | Average Daily Intake |
| AOAC | Association of Official Analytical Chemists |
| ATSDR | Agency for Toxic Substances and Disease Registry |
| BfR | Bundesinstitut für Risikobewertung, |
| Cd | Cadmium |
| ECHA | European Chemical Agency |
| EWG | Environmental Working Group |
| GMP | Good Manufacturing Practice |
| HC-SC | Health Canada-Santé Canada |
| HQ | Hazard Quotient |
| ICP-OES | Inductively Coupled Plasma Optical Emission Spectrometry |
| MoS | Margin of Safety |
| Ni | Nickel |
| NOAEL | No Observed Adverse Effect Level |
| Pb | Lead |
| RfD | Reference Dose |
| SED | Systemic Exposure Dosage |
| SCCS | Scientific Committee on Consumer Safety |
| TPCH | The Toxics in Packaging Clearinghouse, |
| US EPA | Unites State Environmental Protection Agency |
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CHAPTER 1

INTRODUCTION

1.1 Background study

Skin lightening is a beauty practice where it involved with the use of various type of skin lightening agent or chemical substance with a purpose to lighten the skin tone or provide a fair skin complexion by reducing the concentration of melanin (Mire, 2005). It is a popular practice throughout the world as people try to acquire lighter skin and also the social advantage and economic benefit that comes with it (Hunter, 2011). It is often to associates fair skin with status, wealth and desirability and it also represent the elegance and nobility (Leong, 2006).

The obsession and practice to have white and pale skin can be traced back from the ancient times. In ancient Japan, Geisha were known for their painted white skin practice, as it symbolized the beauty, grace, and high social status (Amponsah, 2010). From the West in 17th and 18th centuries, in order to differentiate themselves from the common laborers, aristocrats and rich citizens applying lead oxide powder to their faces (Leong, 2006). Pure hydroquinone was used by farmers and civil workers to keep their skin clear and soft during Achaemenid dynasty. Besides, the white skin with a matte shine was considered to be an attribute of a high origin and status during the epoch of the middle Ages and down to the middle of the 19th century (Amponsah, 2010; Dahl et al., 2004). It was reported that the first archaeological evidence of skin lightening substance was found in Ancient Egypt around 4000 BC (Durosaro et al., 2012). Study done by Andrew (2007) has reported that the skin lightening practice by using Kohl and Henna have long ago been recorded in North Africa (Durosaro et al., 2012). In traditional Chinese myth, it was claimed that pearls can lighten the skin tone and enhance the radiance of the skin by taking pearl powder mixed together with hot water on daily basis (Leong, 2006).

From Malaysia, the historic white colonial presence predominantly comes from the British occupancy. Therefore, the desire for whiteness possibly contains an element of a residual cultural nostalgia for a time before the racial pressure from the post-war era. It was concluded that, the whitening practice among Asian people were addressed to this hyphothesis; some form of atonement or repayment or some kind erasure of visible difference among them (Goon and Craven, 2003). Within Malaysia, all three of the main ethnic groups associate fair skin with beauty. Malays for instance, associate light skin with high status, believing that laborers and villagers are darker than blue-blooded Malays (Willford, 2007). Additionally, in a 2002 survey, 74% of men in Malaysia said women with fair complexion are more attractive compared to the darker-skinned counterparts (Solomon et al., 2012).

The fascination with lighter skin tone has been passed from one generation to another, explaining the unending popularity of the skin lightening practices. This popularity were then translated into the economic growth of skin lightening products in the beauty industry. Franklin (2013) report that the global skin lightening industry is expected to reach USD10 billion by the end of the year 2015. The largest market for skin lightening consumer are from Asia, followed by African and Latin American countries who are also the consumers of skin lightening products (Franklin, 2013). Asia continent shows strong hold in skin lightening industry where it can be seen in the domination of skin lightening products in Asia skin-care market with 60 percent of sales in 2003 (Leong, 2006). By 2018, the global market of skin lighteners is projected to reach USD19.8 billion, increasing from USD10 billion in 2015. This phenomenon was driven by the increasing desire for light-coloured skin among both men and women especially from the Asian, African and Middle East region. The skin lightening market is emerging from its traditional stronghold of women's into the men's segment. The demand for male skin lightening products is on steady rise, especially in Asia as the personal grooming gaining significance interest among men (King, 2013).

Skin lightening products contains an active ingredient or a combination of several ingredients that help to lessen the amount of melanin production in the skin where it is applied. Skin lightening products involves the use of lightening agents such as tritenoin, ascorbic acid, azelaic acid and kojic acid (Katsambas and Stratigos, 2001). Skin lightening process also known as skin bleaching, skin lightening, skin brightening and skin toning (Blay, 2007). Skin lightening agents generally work by targeting naturally produced melanin, and many of the commonly used agents are known as competitive inhibitors to tyrosinase. Tyrosinease is one of the key enzymes in melanogenesis process. It is a glycoprotein located in the membrane of the melanosome, a minifactorial vesicle inside the melanocyte. Tyrosinase involve in catalyzing the first two steps of melanin production: the hydroxylation of L-tyrosine to L-dihydroxyphenylalanine (L-DOPA) and the subsequent oxidation of this o-diphenol to the corresponding quinone, L-dopaquinone (Gillbro and Olsson, 2011). By suppressing the formation of tyrosinase, the action of tyrosinase will be stopped thus prevent the melanin production.

Aside from skin lightening agent, other additive such as preservatives are added as to prevent the growth of microorganism in consumer products, which if not prevented can cause spoilage or contamination of the finished products and also fragrance which is added to impart pleasant odor to the cosmetics products (Roden, 2010; SCCS, 2011). The incorporation of various types of skin lightening agents along with other ingredients has actually introduced different type of impurities or contaminant in it. Impurity is an unintentionally added substance to a product, which forms either as a by-product of the manufacturing process, formed by the breakdown of ingredients or comes as environmental contaminant from raw ingredients (Sahu et al., 2014). Heavy metal is among the impurities of concern that is often present in beauty products. It is an environmental contaminant of raw ingredient. Canada has banned mercury (Hg), arsenic (As), lead (Pb), cadmium (Cd), beryllium (Be), selenium (Se), and thallium (Tl) as intentional ingredients in cosmetics (Environmental Defence Canada, 2011).

Skin lightening products has always been associated with health problem. This is due to the fact that variety of chemicals used to impede melanin production (i.e. glycolic acid, mequinol, corticosteroids and azelaic acid) that can cause redness, thinness, and fine wrinkling of the skin, as well as the increase towards skin infections (Franklin, 2013). Other well-described complications of the practice are nephrotic syndromes which caused by mercury and exogenous ochronosis, a localized paradoxical hyperpigmentation of skin related to long-term use of hydroquinone (Mahe et al., 2003; Gandhi et al., 2012).

1.2 Problem statement

All cosmetic products marketed in Malaysia must first be notified to the National Pharmaceutical Control Bureau (NPCB), an agency under the Ministry of Health (MOH), prior the product can be manufactured, imported or sold in Malaysia. All notified cosmetic products must comply with the requirements specified in the Guidelines for Control of Cosmetic Products in Malaysia. Sufficient and reliable documentation must be submitted by manufacturer prior receiving notification by NPCB. The company who notifies the product (notification holder) must ensure that they are responsible for all matters related to the product marketed in Malaysia. The notification holder also accountable for ensuring the safety, quality and the claimed benefits of the products (Ministry of Health Malaysia, 2015).

In Malaysia, under the Guidelines for Control of Cosmetic Products in Malaysia, Annex II listed the substances which must not form part of the composition of cosmetic products. According to this Annex, metals including Cd, Pb, Ni, Hg and also its compound are prohibited to be used as ingredients in cosmetics because they are considered unsafe (CTWG, 2009). Additionally, the more controversial cosmetic ingredients such as hydroquinone also prohibited to be used in cosmetic products. Hydroquinone is a scheduled poison substance and cosmetic products containing hydroquinone are classified as pharmaceutical products that require registration with the Drug Control Authority (DCA) (Ministry of Health Malaysia, 2014). Given that the issue of some harmful substance namely heavy metals used as intentional cosmetic ingredients has been addressed accordingly, attention turns to the presence of these substances as traces or impurities. In the Malaysian guideline, it has been indicated that the presence of traces of substances listed in Annex II shall be allowed provided that such presence is technically unavoidable in good manufacturing practice and that it comply with the Article 3 of the ASEAN Cosmetic Directive (CTWG, 2009).

However, concern arises over the 'technically unavoidable traces'. Several publication has pointed out that, the 'technically unavoidable traces' of heavy metals is rather ambiguous, subject to different interpretation and largely dependent on the technology used during the cosmetic production (Marinovich et al., 2014). There are currently no international standards for heavy metal impurities in cosmetics. However, some countries, namely Germany and Canada provide limits for impurities in beauty products as a protection for consumers (HC-SC, 2012; BfR, 2006).

Heavy metals can be frequently and easily detected in beauty products due to the persistent nature of these substances and it cause them to be present in the manufacture of pigments and other raw ingredients used in beauty industry in the form of impurities (HC-SC, 2012). Heavy metals are not biodegradable and therefore can accumulate in human vital organs. Even though some of the heavy metal appear as impurities or in trace amount, according to Tchounwou et al. (2010), certain type of metals such as Ni, Cd, Co, Cr, Cu and Se can be harmful to humans even at low concentrations (Demirezen and Aksoy, 2005). Considering the risk associated with metal contamination in beauty products, an appropriate management and well-defined limit of 'traces of metals' in beauty products is required.

Ni, Cd and Pb are the concern in this study as they were the most common contaminant detected in variety of beauty products (Chauhan et al., 2010). Ni was commonly known to cause allergic dermatitis to sensitive people (Duda-chodak and Blaszczyk, 2008). There were reported case by five Ni-sensitive women that develop facial eczema due to the used of foundation products containing traces of Ni (Foulds, 2006). Kidney damage, bone deformity, and the ability of bones to break was the health problems related to long-term exposure to lower levels of Cd (ATSDR, 2012). Meanwhile, Pb has been known to be able to cross the placenta during pregnancy and has been associated with intrauterine fetal death, premature delivery and low birth weight (Papanikolaou et al., 2005).

In cosmetic industry, skin lightening products account for 60% of sales of skin-care items (Leong, 2006). In addition, 80% of Asian consumers consider skin lightening to be the most important property of skincare cosmetics (Lopaciuk and Loboda, 2013). As the skin lightening products were the most widely used beauty products, the presence of harmful metal, even at low concentration can cause exposure to large number of individuals.

This research was also focus on local and non-local product for relative comparison. Previous studies from other countries such as Jordan, Nigeria, Mexico, Saudi Arabia and India have able to detect heavy metal impurities including As, Bi, Cd, Pb, Ni, Hg, Fe, Mn, Zn, Se and Ti in the skin lightening products (Alqadami et al., 2013; Ababneh et al., 2013; Ayenimo et al., 2010; Peregrino et al., 2011; Sahu et al., 2014). In addition, the compliance towards the handling of heavy metal impurities in cosmetic products has been practiced extensively in country such as Canada, Germany, United States, Brazil and Korea (Marinovich et al., 2014; Bocca et al., 2014). However, there are limited available information on the current situation of heavy metal impurities in skin lightening products in Malaysia. Lightening products were broadly marketed and routinely used by 40% of Malaysian women (Frith and Mueller, 2010; Vera and Feagin, 2007). Despite of how widely used skin lightening products in Malaysia, there were very little study done to determine the presence of heavy metal impurities in products available in Malaysian market.

From our literature work, many study has been done among young adult women in Malaysia to understand the used of cosmetic and beauty products in general (Norudin et al., 2010; Lim et al., 2012). However, there were limited studies being carried out

focusing on skin lightening products, especially on the aspect of practice, general knowledge, awareness and also factors that motivates the practice among young adult women specifically university student in Malaysia. In marketing perspective, college or university students were always the targeted group as the long run customers of beauty products and they are exoected to have an ample contribution in the disposable income of society. They are also spend a lot on skin care and cosmetics that lighten the skin tones (Ali et al., 2011; Ramaswamy, 2013).

Besides on knowing the concentration of metal in skin lightening products, what more important is to assess the health risk due to exposure from skin lightening products used. Most skin lightening products are applied topically. Therefore the health risk should be evaluated dermally (Marinovich et al, 2014).

1.3 Study Justification

In beauty industry, the presence of heavy metal as ingredient is well regulated and monitored by authorities. Whereas in the case of heavy metal impurities, it is poorly regulated. Manufacturers are required to take care to remove these impurities, however only very few manufacturers remove these heavy metals from the final product due to unavailability of guideline for heavy metal impurities (Environmental Defence Canada, 2011).

Additionally, in spite of high interest that Malaysian have toward the used of skin lightening, there were very limited study on understanding the practice, general knowledge, awareness and also factors that motivates the practice in Malaysia, specifically among young adult women. Young adult women (16 to 25 years old) are found to be very sensitive about beauty and appearance to others. Due to the factors of peer pressure, the hype of crowd and others, it is common for them to lighten their skin when they reach a certain age (Bachan, 2009).

In order to assess the health risk among young adult women in Malaysia, it is crucial to determine the presence of heavy metal impurities in skin lightening products available in local market. With the increasing interest toward the used of skin lightening products and the lack of published report on the detection of heavy metal impurities in skin lightening product available in Malaysian market together with the limited information about the extent of this practice drive the need for this study to be done.

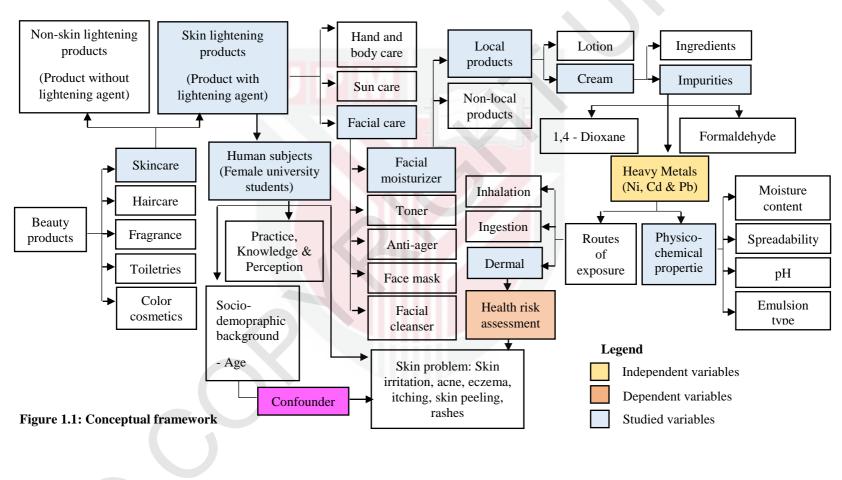
1.4 Conceptual frameworks

Figure 1.1 presents the conceptual framework of this study. Beauty market in general were divided into five major segments, which is skincare, hair care, color (make-up), fragrances and toiletries (Łopaciuk and Łoboda, 2013). Skincare was the most significant segment in beauty market, which consists of 27% of the market share in 2012 and the expansion was driven primarily from Asian market (Yun, 2014). The

skincare products can be classified either as skin lightening products if there were any skin lightening agents (azelaic acid, tretinoin, niacinamide and others) added in it or as non-skin lightening products. It was then divided into facial care, hand and body care and sun care. Facial care were further sub grouped according to the function of the products which are toner, anti-ager, moisturizer, mask and cleanser (Euromonitor International, 2006).

In the manufacturing of cosmetic products, there are two things that need to be address; the ingredients and impurities. Ingredients are materials added purposely because of its function such as humectant, emollient, preservatives, colorant etc.). While impurities are the unwanted compounds that presence as the residuals from manufacturing process, breakdown substance from product ingredients, environmental contaminants in the case of plant-derived ingredients, or what are called "unreacted monomers", the small building blocks of the large polymer ingredients common in cosmetics (EWG, 2007).

Despite heavy metals appearing as impurities, it have the ability to accumulate in the body from time to time. It is build up in fat cells, bones, glands and hair, and undoubtedly will lead to various health diseases such as cancer, allergic reaction, mutations, respiratory problems as well as development and reproductive problems (Ullah et al., 2013; HC-SC, 2012). The concentration of heavy metals in skin lightening products could be considered harmful or safe based on the health risk assessment (HRA). Heavy metal exposure on human occurs on daily basis mainly via ingestion of contaminated food sources or inhalation of resuspended dust. However, as most cosmetic products are intended for topical application, the health risk assessment in this study was focused on dermal exposure (SCCS, 2012).



1.5 Objectives

1.5.1 General objectives

The aim of this study was to determine selected heavy metals concentration (Ni, Cd, Pb) in skin lightening products available in the Malaysian market and to assess non carcinogenic health risk from dermal exposure of continued application to the skin

1.5.2 Specific objectives

- 1. To determine the skin lightening practice, knowledge and perception toward the use of skin lightening products among female universities students in Malaysia.
- 2. To analyse and compare the physico-chemical properties (moisture content, pH, spreadability, emulsion type) of local and non-local skin lightening products.
- 3. To analyse and compare the heavy metals concentration (Pb, Cd and Ni) in local and non-local skin lightening products.
- 4. To evaluate the relationship between physico-chemical properties and heavy metal concentration in the skin lightening products.
- 5. To determine the perceived skin problems caused by the use of skin lightening
- 6. To assess the health risk from dermal exposure of heavy metals through skin lightening product.

1.6 Hypothesis

- 1. There is a significant difference of physico-chemical properties (moisture content, pH, spreadability, emulsion type) between local and non-local skin lightening creams.
- 2. There is a significant difference of the heavy metals concentration (Pb, Cd and Ni) between local and non-local skin lightening creams.
- 3. There is significant relationship between physico-chemical properties and heavy metal concentration in skin lightening creams.
- 4. There is significant health risk of the heavy metal detected in skin lightening creams.

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