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Nanotechnology-based cosmetics: regulation, claims, and cosmetovigilance

Cosméticos baseados em nanotecnologia: regulamentação, alegações e cosmetovigilância

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ABSTRACT

The rapid expansion of the cosmetics industry has been accompanied by an increasing demand for innovative and customized products based on scientific base. One of the innovative products is a nanotechnology-based product. This article discusses any potential risks associated with nanotechnology-based cosmetics use, how the government should regulate the product to protect the public and promote public understanding. The government should create effective regulations, but these regulations must not be detrimental to manufacturers. The government has an essential role in establishing effective regulations for both consumers and producers. In addition, the government should encourage manufacturers to provide rational claims and effective advertising.

Keywords: Cosmetics; Nanotechnology; Safety; Pharmacovigilance.

RESUMO

A rápida expansão da indústria cosmética foi acompanhada por uma crescente demanda por produtos inovadores e customizados. Um dos produtos inovadores é um produto baseado em nanotecnologia. Este artigo discute os riscos potenciais associados ao uso de cosméticos baseados em nanotecnologia e como o governo deve regulamentar o produto e promover a compreensão do público. O governo deve criar regulamentações eficazes, mas esses regulamentações não devem ser prejudiciais aos fabricantes. O governo tem um papel fundamental em estabelecer regulamentações eficazes, tanto para os consumidores quanto para os produtores. Além disso, o governo deve incentivar o fabricante a fornecer alegações racionais e publicidade eficaz.

Palavras-chave: *Indústria cosmética; Nanotecnologia; Segurança; Farmacovigilância.*

Review Article

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INTRODUCTION

Cosmetics encompass a vast array of products that are primarily intended for external use and are intended to cleanse, perfume, alter the appearance of, neutralize aromas emanating from, or more generally maintain the health of the body parts to which they are applied. As a result of globalization, the function of these products is swiftly transforming, and their use is increasingly regarded as essential to personal health. The rapid expansion of the cosmetics industry has been marked by a growing demand for innovative and customized products based on ever-increasing scientific knowledge. One of the innovative products is based on nanotechnology.[1]

Nanotechnology is a new field that has been intensively researched over the past several decades. According to an inventory compiled by an initiative on emerging nanotechnologies, the global market contains more than 1,800 nanotechnology-based consumer products manufactured by over 620 companies in 32 countries.[2] Nanotechnology is the study of nanostructures, which, by definition, are any material that is at least 100 nanometres in size or smaller. The optical, thermal, electrical, and magnetic properties of nanostructures are distinctive. In cosmetics, numerous nano-delivery systems, such as liposomes, nano-emulsions and nanocrystals, lipid nanoparticles (NPs), polymeric NPs, and microparticles, are utilized. The primary benefits of using nanocomponents in cosmetics are: improving the stability of some unstable cosmetic ingredients in formulations[1]; enhancing the permeability of some active ingredients[2]; enhancing the efficacy and tolerance of UV absorbers[3]; and making products more aesthetically pleasing[4], such as converting the active minerals in mineral sunscreens into smaller particles so they do not leave visible white patches on the face.[3] However, the use of very small particles in consumer products has raised safety and environmental concerns.[4] NP skin penetration and toxicological effects are unknown, but a variety of local, chronic, metabolic, and photoinduced toxicities are possible.[5]

Another concern is the public's comprehension of how a producer's claim can be affected by label and commercial branding. Government should also provide well-regulated rules for labelling and claims that give marketers opportunities to advertise and at the same time educate the public about the risks and benefits of using cosmetics containing nanotechnology. In addition, the government should educate the public more about nanotechnology in cosmetics that they may use on a daily basis.

Prior to being registered or marketed, cosmetics did not require any clinical tests to determine their safety for human use. The majority of novel cosmetics, including those containing active ingredients and nanotechnology, are created using only animal testing. Therefore, it is vitally essential for the government to closely monitor any reports of cosmetic use-related adverse effects. A competent cosmetovigilance system can encompass this monitoring.

Some research has been held to discuss the assessment and mitigation of risk related to nanotechnology and cosmetic, such as that done by Lohani et al., Nohynek et al., Ferraris et al., Singh & Nanda, and Gupta et al.[6–9] However, they did not mention that public awareness itself plays a crucial role in identifying risks and the need for cosmetovigilance to monitor the cosmetics' long-term safety. This article discusses any potential risks associated with the use of nanotechnology-based cosmetics, how the government should regulate the product to safeguard the public, and how the government should increase public understanding and awareness of nanotechnology-based cosmetics on the market. As well as pharmacovigilance, the government should collect and manage all reports related to cosmetic use in a coordinated system.

The "nano" term

Because the definition of what constitutes a nanomaterial is presently evolving, it is difficult to determine how many nanomaterials are used in cosmetic products. The use of the prefix "nano" in cosmetic advertising and labelling may differ from how regulatory authorities use the term.[10] According to the Indonesian Food and Drug Agency (Indonesian FDA) statute, nanomaterials are materials that are insoluble or bio-persistent and are intentionally made with one or more external dimensions, or internal structures, with a scale of 1 to 100 nm, or with a scale of more than 100 nm but has very different characteristics from the starting material.[11]

The European Union (EU) regulation define the same scope. According to EC Regulation 1223/2009, nanomaterial is a material that is insoluble or bio-persistent and intentionally manufactured with one or more external dimensions, or an internal structure, on the scale from 1 to 100 nm.[12,13] By that description of nanomaterial, the Cosmetics Regulation in EU primarily provides guidelines for the incorporation of compounds, such as nanomaterials that are deliberately manufactured and insoluble/partially soluble or bio-persistent (e.g., metals, metal oxides, etc.). Conversely, nanoscale materials that are soluble, degradable, and/or non-persistent in biological systems (e.g., liposomes, emulsions, plant-derived vesicles, etc.) are not nanomaterials and, as such, are not governed by this regulation.[13,14]

In the other hand, the FDA does not presently have a definition of a nanomaterial, but in June 2014 it issued final guidance to help provide regulatory clarity in FDA's regulation of nanotechnology-containing products.[10] The use of nanomaterials in cosmetics is governed by the Indonesian FDA statute number 21/2022 regarding cosmetic notification. It is stated that cosmetics containing nanomaterials are classified as having an uncertain safety profile, necessitating additional data and a review of their safety.

Marketed products

Almost every category of personal care products on the market contains engineered NPs, from sunscreens and anti-aging creams to toothpastes.[8] An environmental working group issued a report in May 2006: "Nanomaterials, sunscreens and cosmetics:

small ingredients – big risks." The report included deodorants, soaps, toothpastes, shampoos, hair conditioners, sunscreens, anti-wrinkle creams, moisturizers, foundations, face powders, lipstick, blush, eye shadow, nail polish, fragrances, and aftershave lotions. Involved materials include various metal oxides and various lipid formulations with nanoscale particles.[15]

In 2006, Estée Lauder introduced a variety of NP-containing products to the nano-market. According to Singh & Nanda,[8] formulations containing NPs allow products, such as anti-wrinkle creams, to penetrate the epidermis more deeply. The largest cosmetics company in the world, L'Oréal, has patented the use of numerous nanosome particulates as nutrient delivery systems. They created RevitaLift Anti-Wrinkle Cream and RevitaLift Double Lifting, both of which contain nanosomes of Pro-Retinol-A.[6] Nano Emulsion Multi-Peptide Moisturizer is manufactured by Hanacure and contains a high concentration of peptides.[16] Tiande has also marketed the microcapsule collagen-based Nano Corrector lifting.[17] Lancome introduced Soleil Instant Cooling Sun Spritz SPF 15, containing vitamin nanocapsules, and Primordiale Optimum Lip, containing vitamin E nanocapsules.[6]

Christian Dior of France, Procter & Gamble, Shiseido, and Estée Lauder are also incorporating NPs into their cosmetics. The other major leaders in this field are Colorescience, Revlon, Pureology, La Prairie, Neutrogena, Johnson & Johnson, Caudalie, Chanel, Beyond Skin Science LLC, SkinCeuticals, The Body Shop, Dr Brandt, Prestige, Sircuit, Dermazone Solutions, Crown Laboratories, Birch Trees, Nucelle, Skin Ceuticals, Rosacea Care, Image skincare, Almay, Barneys New York, Bellapelle Skin Studio, AmerElite Solutions, AmorePacific, Cell Rx, and Avon. Moreover, many boutique lines sell nanotechnology-based cosmetics.[8]

Current regulation

The majority of manufacturers comply with EU legislation, commercializing nanomaterials that are already authorized and for which Scientific Committee on Consumer Safety has conducted a comprehensive risk assessment. Several industries have recently shifted their focus towards nano-spectrum materials that are soluble, biodegradable, and/or non-persistent in biological systems in order to avoid all regulatory concerns. Due to their origin, these substances (such as nanoliposomes) are not considered nanomaterials.[13,14]

Cosmetics in the United States do not require premarket approval. However, manufacturers must ensure that their products are not mislabeled or tampered with (FDA, 2014c). In June 2014, the FDA published new guidance titled "Considering Whether an FDA-Regulated Product Involves the Application of Nanotechnology".[18] It applies to all pharmaceuticals, medical devices, culinary products, and cosmetics and provides a broad definition of 'engineered nanomaterials' between 1 and 100 nm in size. In addition, it suggests taking into account whether a material or final product exhibits size-related properties, even if its dimensions lie outside the nanoscale range (up to 1 μm). Similar to European regulations, the terms "engineered nanomaterials" and "intentionally manufactured material" have been implemented. They refer to objects that have been manipulated intentionally using nanotechnology, excluding naturally occurring nanostructures.[18] The aforementioned document is supplemented by the FDA's guidance on the safety of nanomaterials in cosmetic products",[19] which cites a number of other documents, such as the International Cooperation on Cosmetic Regulation (ICCP) report.[20] The ICCP report provides a summary of the analytical methodologies used to evaluate nanomaterials. Since there is no requirement for FDA approval, all liability for cosmetics rests with the manufacturer.[21]

Risk to consider

NPs are able to cross membranes and access cells, tissues, and organs that are inaccessible to larger particles because of their small size and structure. They can enter cells, causing additional injury or cell death.[22,23] Indonesian-FDA statute number 17/2022 establishes the item and concentration limits for nanomaterial use in cosmetics. All possibilities of these nanomaterials entering the nasal cavity are ruled out.[11] NPs typically enter the body via three distinct routes: inhalation, ingestion, and dermal absorption. Inhalation is the most widely recognized route of exposure to airborne NPs. Consumers may inhale nanomaterials when using products containing them. For instance, nanoscale titanium dioxide (TiO2) sunscreen sprays may cause the inhalation of nanomaterials, which may travel through the nasal nerves to the cerebrum (brain) and penetrate the blood and various organs, causing serious side effects.[24,25] Depending on their aerodynamic dimensions, inhaled nanomaterials can deposit anywhere along the respiratory tract, not just in the alveoli. Due to their minute size, only a fraction of nanometric particles can reach extrapulmonary organs. This entails migration of some solid particles, translocation to the blood and lymphatic systems through the pulmonary epithelial layers, and translocation to the central nervous system, through the nerve endings of the olfactory nerves, along the neuronal axons.[25]

However, there are additional toxicology risks, such as a mild risk of skin surface effect for any excipient that can damage skin layers and the possibility of the substance entering the bloodstream via transdermal activity, particularly with regard to cosmeceuticals, which refer to preparations that contain therapeutically active ingredients that have specific remedial effects upon topical application, in contrast to conventional cosmetics.[9,26] The term "cosmeceutical" derives from the combination of cosmetics and pharmaceutical information.[27] When cosmeceuticals are combined with nanotechnology, they become nano-cosmeceuticals, which are cosmetic formulations incorporating nano-drug delivery systems to transport cosmetic active molecules to the appropriate skin tissues, which could induce more undesirable side effect, since some penetration enhancers or carrier systems have been demonstrated to facilitate epidermal absorption of an active constituent to enter the bloodstream,[28]

as shown in a study conducted by Cevc et al. demonstrating the ability of transfersome vesicles to disrupt and destabilize stratum corneum, then confirmed the presence of intact vesicles in the bloodstream.[29] Several studies executed by other researchers on various types of ultra-deformable vesicles have yielded comparable results, including Niu et al. and Manconi et al.[30,31] Therefore, one must be concerned about the prospect of a substance that enters the bloodstream causing an undesirable systemic effect.

Concerns have been raised regarding the potential dangers associated with the skin penetration of a number of cosmetic products containing chemical active ingredients or bioactive NPs (known as cosmeceuticals) .[6] Active Compounds such as alpha hydroxy acid (AHA), an exfoliant that can remove the top layer of skin to cure scars, wrinkles, acne, and to lighten the skin. As eliminating skin could be viewed as affecting body structure, AHA could be considered a drug by the FDA, despite being advertised in cosmetics. Therefore, AHA is classified as a cosmeceutical because it possesses both cosmetic and pharmaceutical properties.[32] Tranexamic acid,[33-36] retinoids,[37] hydroxycinnamic acid,[38] and some bioactive ingredients such as phlorotannin[39] have been also formulated and marketed as cosmetic products. Other compounds that function as moisturizers, antioxidants, anti-wrinkles, depigmenting agents, anti-cellulite agents, and sunscreens, are frequently used to formulate into some carrier system and become nano-cosmeceuticals.[37] However, many of these chemical additives are toxic to the human body, posing health risks ranging from moderate hypersensitivity to life-threatening anaphylaxis or fatal intoxication.[40] Therefore, any cosmetic containing an active ingredient, particularly one whose safety is unclear, should be given careful consideration.

Registration

Some points need to be considered in product registration or notification, such as: what is the exposure, is it assimilated, and if so, how much reaches the viable cells, and is it intrinsically toxic? The following are examples of more specific concerns regarding the safety of nanotechnology or NPs in cosmetic products:

Do cosmetic formulations containing nano-sized components (vesicles or droplets) entail additional risks compared to conventional cosmetics?

Does the increased skin penetration of nano-sized cosmetic formulations increase the risk of skin sensitization or systemic exposure?

Are insoluble NPs in sunscreens intrinsically more dangerous than microparticles or bulk material?

Do topically administered insoluble NPs remain on the skin surface or are they capable of penetrating the skin barrier of normal or compromised skin to reach systemic compartments of the organism?[5]

Nanomaterial penetration is an issue of concern in scientific discourse for at least two primary reasons: the toxicological consequences associated with nanotechnology and the need to reveal the function of nanomaterials as carriers that improve the bioactive agent's penetration.[1] Numerous beauty products claim to be based on sophisticated scientific research, giving consumers the impression that they are as effective and thoroughly tested as pharmaceuticals. In contrast, the cosmetics industry does not want its products to be regulated similarly to pharmaceuticals, as this would necessitate extensive, time-consuming, and expensive clinical trials to determine efficacy. It is therefore the responsibility of regulatory agencies to determine whether a product, despite its claims, is a cosmetic or should be classified as a drug due to its therapeutic effect.[41]

Regarding any risk calculated, several tests and documents must be completed by applicant during registration, such as: physicochemical laboratory tests, since properties of a product affect the body cumulatively, and safety in vivo or in vitro tests.

Claim and advertising

The informational value of a cosmetic advertising claim is the most significant factor in determining whether consumers try the advertised product.[42] The Indonesian-FDA regulation governing cosmetic labeling and claims is Indonesian-FDA statute number 3/2022, which established the prohibited and permitted claims for cosmetics and mentioned any permissible details and prohibited cosmetic claims. In fact, it is more of a broad guideline that does not specify in detail the permissible claims for each product category. In essence, it is up to the producer to construct a persuasive line to convince consumers to use their product. In Indonesia, producers are not required to obtain approval for labeling. They just release it to the market, and the Indonesian FDA conducts a post-market surveillance. The government, through the Indonesian FDA, perpetually educates cosmetic manufacturers on how to advertise and market their products in compliance with the law.

With the accelerated development of nanotechnology and pharmaceutical ingredients in cosmetics, the industry is becoming increasingly competitive. Because cosmeceuticals claim to contain properties of both cosmetics and pharmaceuticals, they may constitute a "grey area" because they cannot be classified as either cosmetics or pharmaceuticals.[32] As a result, consumers may be required to ingest these products with little guidance and a heightened level of caution.[42] In the other hand, consumers cannot presume the veracity of cosmeceutical claims or the efficacy of these products.[27] Furthermore, Indonesian FDA should renew their regulation on labeling and claim that put a special part of cosmetic with nanotechnology more especially on cosmeceutical.

Advertising's purpose is to induce immediate action, to create liking and preference for a product, to generate product awareness,[43] and to educate the customers about the functionality of the product. It brings the existence of certain products to the attention of the intended consumers and informs the consumer and influences their purchasing behavior in various ways.[44] In other words, good advertising can increase public aware-

ness of nanotechnology-based cosmetics, allowing consumers to comprehend the risks and benefits of using these products. Additionally, they can safeguard themselves against the use of high-risk products. Government should encourage producers to create enlightening advertising in order to foster a positive advertising environment. As mentioned by Protopapa & Plangger, educating marketing practitioners is a crucial component of this transition toward more diverse and inclusive marketing.[43]

These days, advertising communication activities are compelled to use multiple media, traditional and new media. New media is a novel form of communication founded on digital technology and network technology, with smart terminals as the target of communication. Diversified and personalized interaction forms create a rich brand experience, allowing consumers to receive brand-delivered information more directly and become secondary communicators more independently, thereby creating a virtuous circle of joint image communication.[45] Therefore, government should exert greater effort to regulate advertising in all media.

Cosmetovigilance

With high development of cosmetics with nanotechnology, negative effects of cosmetics continue to exist in the consumer population.[40] In occupational hygiene, one must bear in mind that the direct human health risk posed by a nanomaterial depends on exposure probability and, if applicable, exposure concentration and duration. Second, it depends on whether these materials, once inside the body, manifest specific nanostructure-related behaviour.[25] Similar to other maladies, cosmetic-related disorders also result in pharmacoeconomic loss.[46]

The concept of pharmacovigilance is relatively new and distinct from industry surveillance, whose primary purpose is to use safety information for commercial gain. Cosmetovigilance is the public health surveillance of cosmetic products with the goal of protecting public health. For the purposes of cosmetovigilance, causality is defined as the examination of the relationship between a cause (cosmetic product) and an effect (manifestation). There are numerous techniques for determining causality, the majority of which are founded on the evolution of semiological and chronological elements.[46]

Although a study conducted in Sweden between 1989 and 1994 on the utility of implementing a cosmetovigilance system received a small number of adverse effect notifications and thus concluded that cosmetovigilance was of little value, the study did find that cosmetovigilance was necessary.[47]

Future perspective

Prior to marketing a cosmetic product in Indonesia, the producer is required to notify the Indonesian FDA, through the Cosmetic Notification System. The procedure is so expedient, requiring no more than 14 days to evaluate the document before releasing the approval letter. Unless the product contains nanomaterials, additional time is required to assess its safety.[48]

The Indonesian FDA encourage the producer to disclose whether or not their products contain nanomaterials or materials modified by nanotechnology.

However, according to Singh & Nanda, the cosmetics industry has been reluctant to disclose the use of nanoscale synthetic materials.[8] Therefore, the registration officer should have extensive knowledge of nanotechnology in order to conduct screening prior to receiving the registration document. If there is any chance that the product is related to nanotechnology, the industry must be consulted. In addition, the cosmetics industry and other stakeholders should be able to identify potential nanomaterial safety concerns and to discuss various regulations and recommendations imposed by various regulatory agencies.[9]

People need more information and education about the potential benefits and risks of nanotechnology. The Indonesian FDA may utilize any method to disseminate information, including social media and collaboration with public influencers. People can protect themselves and comprehend what to do with their product if they have adequate knowledge. ●

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Approval of the final version of the manuscript; study design and planning; preparation and writing of the manuscript; data collection, analysis and interpretation; active participation in research orientation; intellectual participation in propaedeutic and/or therapeutic conduct of the studied cases; critical literature review; critical revision of the manuscript.

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Preparation and writing of the manuscript.