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Review Article

Review: Policy strategy of nano cosmetic testing in Indonesia

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Abstract

The implementation of nanotechnology in the cosmetic industry has developed promptly in recent decades. Among them are sunscreen, skincare, decorative makeup, and hair colorant. The cosmetics industry is a significant user of nanoscale raw materials in its manufacturing procedures. However, the supervision regarding the safety and quality of cosmetic products containing nanomaterials (NMs) in Indonesia conducted by the Indonesian FDA remains not fully optimized. This poses a challenge for the Indonesian FDA, particularly concerning the significance of employing appropriate characterization methods and the necessity for systematic evaluation. Hazard identification, exposure evaluation, microbiological testing, and NM characterization are some methods that can be conducted for monitoring nano cosmetics. Procuring instruments for nano-analysis will be a significant investment for the purpose of monitoring cosmetic products marketed in Indonesia.

Keywords

Characterization, nano cosmetic, policy, risk assessment, Indonesia

Introduction

In recent years, the development of nanotechnology has experienced a tremendous surge, especially in the cosmetic industries (Pastrana et al. 2018; Santos et al. 2019; Dubey et al. 2022; and Gupta et al. 2022). According to the Indonesian FDA website about the number of registered cosmetic notifications until January 2024, more than 402,419 cosmetic products have been notified in Indonesia, nineteen of which are claimed as nano products and about 5,058 products including the word 'gold' in its label (Indonesian FDA 2024). This happens because the scope of cosmetic products is on the finished product, thus the utilization of nanotechnology in cosmetic products is believed to increase the product's value for consumers.

Nanotechnology is defined as the imaging, modelling, measurement, design, characterization, production, and application of structures, devices, and systems controlled by the manipulation of size and shape at the scale of 1–100 nanometres (at the atomic, molecular, and macromolecular levels) that produce structures, devices, and systems with at least one superior characteristic. At the nanoscale, the physical, chemical, and biological levels matter are different at smaller scale, such as atoms, or at a larger scale than the compound. The advantages of nanomaterial (NM) including being stronger, more reactive, and having better conductivity than the same material at normal size. The manifestation of these advantages in cosmetic products is in the form of better UV protection, deeper skin penetration, longer lasting effects, increased color intensity, and better finish (Szczyglewska et al. 2023).

The three most widely implemented types of cosmetic product using nanotechnology which are include sunscreen, skincare, colorants, hair care, and dental care product. (Fig. 1). Skincare products enhance skin appearance and function by promoting collagen production and preventing free radical damage. Moisturizers contain nanostructured particles that create a moisture-retention layer, treating skin conditions like dermatitis and psoriasis. Sunscreen active ingredients also contain nanostructured particles for a less greasy, transparent, and odorless appearance. Lipsticks and lip glosses contain bioactive ingredients to moisturize and nourish lips. Nano cosmetic hair products target hair follicles and release active compounds for protective coatings and making hair look shiny (Sharma et al. 2023). Sunscreens mostly use single or combination between mineral-based materials and their performance is highly dependent on their particle size. However, nanosystems that are widely employed in the formulation of cosmetics must take some toxicological considerations for human health. Some studies have reviewed risk factors towards human health associated with using NMs, either contained in cosmetic products or not (Tetley 2007; and Shokri 2017). Gupta et al. (2013) reported that both TiO_2 and ZnO nanoparticles (NPs) caused (photo) cytotoxicity and genotoxicity, and occasional observations of these effects on live skin layers have been made, particularly in cases of long-term exposures with ZnO (Smijs and Pavel 2011). Besides that, based on research conducted in the U.S., NPs can seriously endanger soil life and marine life (Kaur et al. 2007). Not to mention the study conducted by Luanpitpong et al. (2014) which found that carbon nanotubes cause granulomas in the lungs of lab animals and are cytotoxic to cells.

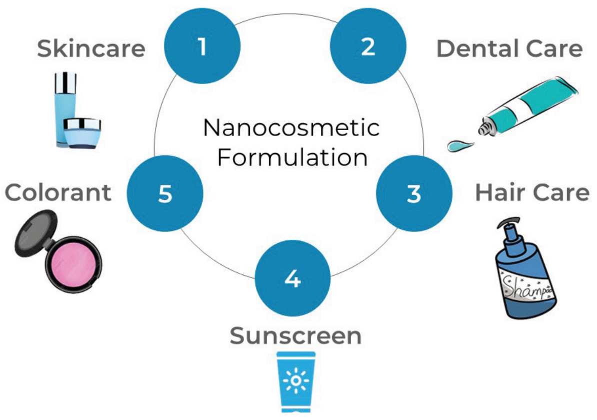

Figure 1. Scope of nano cosmetics.

Several regulatory bodies in the world have made regulations related to nano cosmetics. These regulations have been ratified by the Indonesian FDA into the Indonesian FDA Regulation No. 17/2022 regarding Amendments to the Food and Drug Authority Regulation No. 23/2019 concerning Technical Requirements for Cosmetic Ingredients (Indonesian FDA 2022). The Indonesian FDA conducted premarket surveillance of nano cosmetics through the e- Notification System. For cosmetic ingredients that are suspected to be nano-sized or as cosmetic technology develops in the world and other new nano-sized compounds emerge, the notification applicants is required to complete Product Information Document (PID) when they submit the notification.

For post-market surveillance purposes of nano cosmetic products in the form of chemical testing, it is necessary to consider several obstacles that may arise. First, NPs naturally tend to bond with each other to form agglomerates and aggregates. With this behaviour change, NMs characterization are necessary to be done before and during production to obtain valid results. Consideration is needed in determining the appropriate test method to determine the level of NM. Thus, the test method for NM may consist of more than one parameter. For example, measuring the particle size distribution of NMs using images from transmission electron microscopy, TEM (Zhang and Wang 2023). Second, the unavailability of adequate instruments and test methods to characterize NMs. It would be a challenge for the Indonesian FDA to supervise the safety and quality of nano cosmetics. There are two policy issues on the proposed testing of nano cosmetics including up to now there is no regulation that clearly describes the characterization of NM analysis in cosmetic products and the urge for comprehensive testing of nano cosmetics increases as a form of monitoring of commercial cosmetic products in the market. Until now, experts in nanotechnology field in the world have not agreed to formulate the right characterization for NM analysis. However, based on several studies, NM characterization based on physicochemical properties which includes the following picture (Fig. 2). Moreover, due to the very small particle size and possible changes in physical, chemical, and biological properties, the analysis of NM-based cosmetic compounds cannot only be seen in one parameter. Comprehensive testing is needed, in addition to quantify the levels of analytes that have been regulated in the regulations, and to measure the correctness of the particle size as well according to the claims submitted by the company.

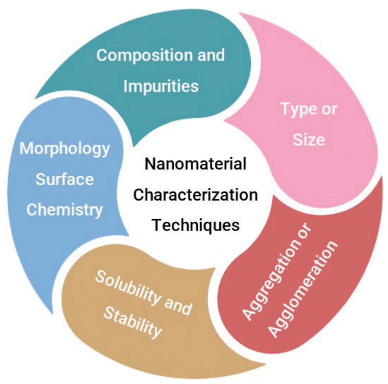

Figure 2. NM characterization techniques.

This article aims to offer alternative solutions for policymakers in Indonesia on the policy issue to formulate policy strategy of nano cosmetic testing in Indonesia. Moreover, the rapid screening testing of nano cosmetic is considered as a first step in monitoring nano cosmetic products commercially in the market.

Regulations governing NMs in cosmetic products

Since the introduction of nano cosmetics 20 years ago, non-governmental organizations (NGOs), political organizations, and government organizations around the world have been concerned about the potential risks of NM in consumer products. The implementation of regulations in the world related to nano cosmetics can be seen in Table 1. Since these regulations, there has been no appropriate method to characterize NMs in cosmetics until now.

NM definition

The European Union (EU) Commission (2022) set out updated recommendations in 2022 regarding the definition of NMs. NMs are materials in the form of solid particles, whether naturally occurring, incidental, or synthetic, which meet a size distribution of 50% or more and meet at least one of the following criteria:

a. One or more external dimensions of the particle are in the range of 1 to 100 nm.
b. The particle has an elongated shape such as a rod, fiber, or tube, where two external dimensions are smaller than 1 nm and the other dimension is larger than 100 nm.
c. particles have a plate-like shape, where one external dimension is smaller than 1 nm and the other dimension is larger than 100 nm.

In the determination of particle number-based size distributions, particles with at least two orthogonal external dimensions larger than 100 μm may not be considered. However, materials with a specific surface area by volume <6 m^2/cm^3 should not be considered as NMs.

Table 1. History of international regulations related to nano cosmetics.

No.	Organization	Country	Endorsement	Subject	Reference
1.	*Europe Commission* (EC) notified the rule from World Trade Organisation (WTO)	The European Union (EU)	11th February 2022	Cosmetic products are prohibited from containing NM from styrene/acrylate copolymer, sodium strilen/acrylate copolymer, copper, colloidal copper, hydroxyapatite, gold (nano), colloidal gold, gold tioethylamino hyaluronic acid, Acetyl heptapeptide-9 colloidal gold, platinum, colloidal platinum, acetyl tetrapeptide-17 colloidal platinum.	World Trade Organization 2023
2.	Indonesian Food and Drug Authority (FDA)	Indonesia	2022	Indonesian FDA Regulation No. 17/2022 regulated five nano ingredients in cosmetic products with certain restrictions, i.e Pigment Black 6 & 7 (CI 77266), tetramethyl butylphenol/MBBT, titanium dioxide, trisbiphenyl triazine, and zinc oxide.	Indonesian FDA 2022
3.	Indonesian Food and Drug Authority (FDA)	Indonesia	2019	The Head of Indonesian FDA Regulation No. 23/2019 regarding Technical Requirements for Cosmetic Ingredients regulated four nano ingredients in cosmetics, i.e Pigment Black 6 & 7 (CI 77266), titanium dioxide, tris-biphenyl triazine, and zinc oxide	Indonesian FDA 2019
4.	Indonesian Food and Drug Authority (FDA)	Indonesia	2015	The Head of Indonesian FDA Regulation No. 18/2015 regarding Technical Requirements for Cosmetic Ingredients contains one cosmetic nano ingredient, Tris-biphenyl triazine.	Indonesian FDA 2015
5.	U.S. Food and Drug Administration (FDA)	United States of America	2014	nano cosmetics	US Food and Drug Administration 2014; Pastrana et al. 2018
6.	EC Directive	The European Union (EU)	2013	nano labelling	Lohani et al. 2014
7.	EU published EC Directive 1223	The European Union (EU)	2009	Safety assessment of (nano) TiO_2, ZnO, MBBT, and tris-biphenyl triazine that commonly used as UV filters. It has also allowed carbon black (nano) for use as a colorant in cosmetic products	European Commission 2009; Pastrana et al. 2018
8.	U.S. Food and Drug Administration (FDA)	United States of America	2006	FDA Task Force	Pastrana et al. 2018
9.	Europe Commission (EC)	The European Union (EU)	1976	Cosmetic guidelines	Pastrana et al. 2018
10.	Pharmaceutical and Medical Safety Bureau (PMSB), Ministry of Health, Labor, and Welfare, MHLW)	Japan	1948	Regulation of cosmetics is set out in the Pharmaceutical Affairs Act	Sidebottom 2003
11.	U.S. Food and Drug Administration (FDA)	United States	1938	FDA Cosmetics Act	Pastrana et al. 2018

NMs in cosmetic products

Based on the technology, the types of the types of NMs commonly commonly used by the cosmetics industry are divided into three (3), namely inorganic NPs, nano liposomes, and nano emulsions (Shokri 2017; Santos 2019; and Sharma et al. 2023) as follows:

a. Inorganic NPs.
Inorganic NPs are non-toxic, hydrophilic, biocompatible, and very stable when compared to Organic NPs. For example, Au and Ag NPs. They act by altering cell wall permeability, increasing reactive oxygen species production, and inhibiting bacterial growth.

b. Nano liposomes.
Nano liposomes are used for cosmetic delivery applications, for example, to deliver vitamin A, vitamin E, and antioxidants into the skin. Nano liposomes function to increase skin permeability and moisturize the skin. In addition, nano liposomes are also used in deodorants and antiperspirants to carry fragrances.

c. Nano emulsion.
Nano Emulsions are colloidal dispersions that contain nano-scale droplets of varying sizes, ranging from a few nm to 200 nm. Examples: conditioners and body lotions.

According to these three types of NMs, the author's focus lies on the bio persistence properties of the NMs, as nanoliposomes, nano emulsions act as nanocarriers rather than as active substances (Fig. 3).

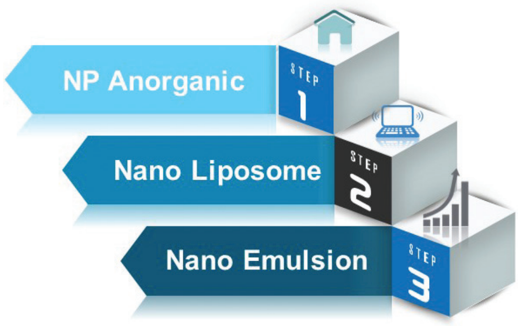

Figure 3. Types of NMs.

Pastrana et al. 2018; and Sharma et al. 2023 listed some examples of commonly used NMs in cosmetic products as follows:

a. Titanium dioxide → serves to increase skin protection against UV A and UV B rays in sunscreen products without leaving a white residue on the skin surface (white cast).
b. Silicon dioxide (SiO_2) → increases the effectiveness of the coated surface.
c. Gold NP → acts as a conductor to facilitate skin penetration.
d. Carbon black → as an active colorant in lipstick, thus the lipstick sticks strongly to the lips, so that it can be long-lasting.

Identification of nano cosmetic products marketed in Indonesia and globally

Tracking of nano cosmetic products marketed in Indonesia, both domestic and imported origin, could be done through three (3) approaches. Nationally, it is done by searching the cosmetics notification database through the Indonesian FDA's e-Notification of Cosmetics page (Indonesian FDA 2024). Table 2 shows a few nano cosmetic products sold in Indonesia. The criteria used in data selection as follows:

1. The presence of „nano" claim or nano ingredients is explicitly mentioned in the package of the product.
2. The product has an Indonesia registration number.
3. The data was collected in January 2024 by accessing https://cekbpom.pom.go.id/kosmetika.

Based on the nano cosmetic products that have been registered in the Indonesian FDA, it shows that the potential

Table 2. Some nano cosmetic products marketed in Indonesia.

No.	Trademark	Industry	Indonesian FDA Notification	Claim
1	Supreme Bionanoceramide Barrier Moisturizer	Aroma Prima Livindo	NA18230103407	Anti-Aging
2	Exclusive Cosmetics (Exco) Day Cream	Nanotech Natura Indonesia	NA18210111796	Sunscreen
3	Feeling My Skin Salicylic Acid Nanosome Acne Spot	Pesona Bintang Utama	NA18220105853	Anti-Acne
4	Systema Nano Advanced Oral Care System (Spring Fresh)	Lion Wings	NA18211400070	Dental Care
5	Systema Nano Advanced Oral Care System (Menthol Breeze)	Lion Wings	NA18131400012	Nano Calcium in Dental Care Products
6	Wrinkles And Lines Defense Biolift Nanotech Advance Lifting Serum	Mustika Ratu	NA18162000146	Anti-Aging
7	Aishaderm Premium Anti Aging-Nano Essence	Dion Farma Abadi	NA18172000176	Anti-Aging
8	Day Cream, Face Glow with Nano 3 Glow	Pesona Amaranthine Cosmetiques	NA18230106053	Anti-Aging
9	Liquid Facial Wash, Face Glow with Nano 3 Glow	Pesona Amaranthine Cosmetiques	NA18230106053	Anti-Aging
10	Refreshing Facial Toner, Face Glow with Nano 3 Glow	Pesona Amaranthine Cosmetiques	NA18231203615	Anti-Aging
11	Nigh Cream, Face Glow with Nano 3 Glow	Pesona Amaranthine Cosmetiques	NA18231901212	Anti-Aging
12	Salicylic Acid Nanosome Acne Spot	Pesona Bintang Utama	NA18220105853	Anti-Aging

market for nano cosmetics in Indonesia is huge. Skincare products dominated the types of nano cosmetic productssold on the market today.

Meanwhile, Table 3 illustrates the summary of globally sold cosmetic products, based on data obtained from Gupta et al. 2013; Lohani et al. 2014; Pastrana et al. 2018; Abdulazeem et al. 2022; and Sharma et al. 2023. According to it, we can infer that skincare products dominated the cosmetics market using nanotechnology, followed by lip and hair products.

Table 3. Nanosystems-based cosmetic products sold globally.

No	Form	Exposure Area	Function	Nano Active Ingredients/Type	Trademark	Manufacturer	Country	Reference
1	Cream	Skin/Eye	Moisturizer	Nano Capsule	Hydra Flash	Lancôme	USA	Pastrana et al. 2018
2	Cream	Skin/Eye	Moisturizer	Nano Capsule	Hydra Zen Cream	Lancôme	USA	Sharma et al. 2023
3	Cream	Skin/Eye	Anti-wrinkle	colloidal silica and soy protein nanoparticles	Lancôme Renergie Microlift	Lancôme	USA	Ferraris et al. 2021
4	Cream	Skin/Eye	Anti-wrinkle sunscreen	colloidal silica and soy protein nanoparticles	Soleil Soft-Touch Anti-Wrinkle Sun Cream SPF 15	Lancôme	USA	Sharma et al. 2023
5	Cream	Skin/Eye	Anti-Aging	Nano Capsule	RevitaLift Anti-Wrinkle and Firming Face and Neck Contour Cream	L'Oreal	France	Pastrana et al. 2018
6	Cream	Skin/Eye	Anti-Aging	Nano Liposome	Revitalift Double Lifting	L'Oreal	France	Ajazzuddin et al. 2015
7	Cream	Skin/Eye	Anti-cellulite	Nano Liposome	Lipoduction	Osmotic Cosmetics	USA	Pastrana et al. 2018
8	Cream	Skin/Eye	Sunscreen	Titanium dioxide	Nivea Moisturising Sun Lotion	Nivea	EU	Pastrana et al. 2018
9	Cream	Skin/Eye	Sunscreen	Zinc Oxide	ZinClear-IM™	Antaria	North America and Europe (EMEA)	Ferraris et al. 2021
10	Cream	Skin/Eye	Moisturizer	Zinc Oxide	Nano-in Deep Cleaning	Nanotech Co	Taiwan	Ajazzuddin et al. 2015
11	Cream	Skin/Eye	Concealer	ZnO/Ti_xO_y	Sunforgettable™	Colore Science	USA	Ferraris et al. 2021
12	Cream	Skin/Eye	Whitening	Arbutin	Nano Bright™	Biospectrum	Korea	
13	Cream	Skin/Eye	Anti-wrinkle	Nanosphere	Eye Tender	Kara Vita	USA	Ajazzuddin et al. 2015
14	Cream	Skin/Eye	Anti-wrinkle, Anti aging	Nano Capsule	Eye Contour NanoLift	Euoko	Canada	Ferraris et al. 2021
15	Cream	Skin/Eye		Hyaluronic Acid Nano Capsule	Power Moist™ Nano Hyaluronic Acid	-	-	Ferraris et al. 2021
16	Cream	Skin/Eye	Sunscreen	TixOy	Soltan	Boots	UK	Ferraris et al. 2021
17	Cream	Skin/Eye	Anti-aging	Fullerene C-60	Zelens Fullerene C-60 Night Cream	Zelens	UK	Pastrana et al. 2018
18	Cream	Skin/Eye	Sunscreen	Methylene Bis-Benzotriazolyl Tetramethylbutylphenol	DiorSnow Pure UV Base SPF 50	Dior	France	Ferraris et al. 2021
19	Lotion	Skin/Eye	Moisturizer	Nanosphere	Fresh As A Daisy Body Lotion	Kara Vita	USA	Sharma et al. 2023
20	Liquid	Skin/Eye/ Gastrointestinal Tract	Moisturizer	Nano Gold (Au)	Nano Gold Energizing Treatment	Chantecaille	Denmark	Ferraris et al. 2021
21	Liquid	Skin/Eye	Anti-acne	Nanosphere	Clearly It! Complex Mist	Kara Vita	USA	Ferraris et al. 2021
22	Solid (Powder)	Skin/Eye/ Gastrointestinal Tract	Moisturizer/ anti-aging	Nano-stretch	DiorSkin Forever	Dior	France	Pastrana et al. 2018
23	Soap	Skin	Anti bacteria	Nano Silver (Ag)	Cor Silver	Cor	USA	Pastrana et al. 2018
24	Toothpaste	Mouth	Anti-bacteria	Nano Silver (Ag)	Nano Phytoncide	SH Pharma	USA	Pastrana et al. 2018
25	Toothpaste	Mouth	Anti-bacteria	Nano Gold (Au)	Nanorama—Nano Gold Mask Pack	LEXON NanoTech	USA	Ferraris et al. 2021
26	Toothpaste	Mouth	Dental desensitizer and teeth remineralization	Nano Hydroxyapatite	Kinder Karex Hydroxyapatite	Dr. Kurt Wolff GMBH & Co. KG	Germany	Abdulazeem et al. 2022
27	Serum	n.a.	Anti-aging	Nanosphere	Nanosphere Plus	DermaSwiss	Swiss	Sharma et al. 2023
28	Face mask	Skin	Anti bacteria	Nano colloidal silver (Ag)	Cosil Whitening Mask	Natural Korea Company	Korea	Ferraris et al. 2021
29	Lip moisturizer	Lip	Moisturizer	Nano capsule	Primordiale Optimum Lip	Lancôme	USA	Sharma et al. 2023
30	Lip moisturizer	Lip	Anti-bacteria	Nano Silver (Ag)	Lip Tender	Kara Vita	USA	Sharma et al. 2023
31	Foam	Hair	Hair repair	n.a.	Seskavel Mulberry Anti-Hair Loss Foam	Sesderma	USA	Ferraris et al. 2021

Nanocosmetics assessment

Nanotechnology affects not only human health, but also the environment, in both beneficial and harmful ways. The possible advantages and disadvantages for the environment and human health must be urgently considered. This can be explained in the following paragraphs:

a. Potential health hazards of NPs.

Cosmetic products with a micro size or more are considered low risk to consumers due to their topical use, not intended as medicinal products. Therefore, the approval process is not as stringent as for medicinal products, but this is different for nano cosmetics. Potential exposure pathways for NPs include the skin, lungs, and gastrointestinal tract as depicted in Fig. 4 (Riasat et al. 2016). Either purposefully or unintentionally, the ingestion of NMs can occur when they are transferred from the hands to the mouth. After consumption, a small quantity of the NPs may enter key organs and tissues and be absorbed by the body, leading to adverse effects (Gupta et al. 2022). NP, which has higher chemical reactivity, can cause toxicity through inhalation, ingestion, and skin contact. Not only that, but NPs may also cause harm to pregnant women and babies. Inhalation is the most common route of exposure, as workers and customers may breathe in NMs during manufacturing processes. Ingestion, either accidental or intentional, can also lead to harmful effects. After ingestion, the body may absorb the NPs, affecting vital organs and tissues. Topical use of NMs can also cause harmful effects. NPs can damage DNA and lead to malignancy due to their small size, making it difficult to separate them from the environment and their impact on human health (Gupta et al. 2022; and Sharma et al. 2023). Further, neonatal toxicity, a potential risk, can occur due to exposure to NPs in the placenta, endometrium, yolk sac, or fetus, leading to discomfort, oxidative stress, toxicity, and reproductive dysfunction in young children (Tetley 2007; and Gupta et al. 2022). Numerous NPs, including quantum dots, gold NPs, and silicon dioxide, can pass through the placental barrier, allowing them to concentrate in the fetus and induce embryo-fetal toxicity (Tang et al. 2015). All these health risks due to nano cosmetic exposure are illustrated in Fig. 4.

b. NPs' environmental risks.

NPs' capacity to build up in organisms and cause harm to them is connected to their impact after they are released into the environment. Although NPs are found in living things by nature, under certain circumstances, they may even be quite harmful. Furthermore, generated NPs tend to last longer due to the employment of stabilizers and surfactants, even if spontaneously formed NPs tend to join with time to build more extensive materials. Thus, it is necessary to evaluate how to use these materials might affect the ecosystem. Soil and water also may contain heavy metals like lead, cadmium, arsenic, and mercury, as well as microbiological pollutants and chemical poisons like herbicides, insecticides, phenols, and hydrocarbons. Furthermore, several of these toxicants—such as heavy metals and persistent organic pollutants (POPs)—occur in food chains and pose serious risks to both humans and wildlife through bioaccumulation in fish and other sea creatures. This might disrupt the ecological balance in underwater life. Plants are crucial for examining the environmental effects, as they interact with various environments and transfer NPs to humans and animals. They absorb NPs through flower surfaces, roots, leaves, or damaged regions. Plant toxicity investigations often focus on parameters like seed development rate, root development rate, or nitrogen fixation. Soil NP levels are higher than in water or air, making plants the main source of NPs at different trophic levels in the food chain. Studies have shown that TiO_2 -NPs have a more significant effect at lower concentrations due to the precipita-

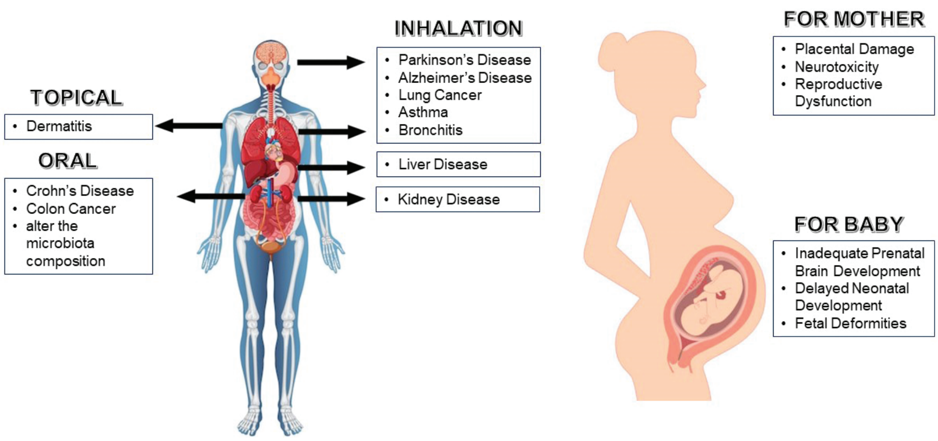

Figure 4. Illnesses linked to exposure to NPs. Source: iStockphoto.com and Freepik.com (Tetley 2007; Tang et al. 2015; Riasat et al. 2016; and Gupta et al. 2022).

tion of NPs, leading to DNA folding, chromosome abnormalities, and the generation of reactive oxygen species (ROS). Two independent research studies have investigated ZnO-NPs, showing growth inhibition, cell damage, NP-dependent gene expression decrease, poor photosynthesis, and delayed growth in plants exposed to different concentrations (Gupta et al. 2022).

The assessment for nano cosmetics should meet the requirements as follows:

a. Hazard identification.
Hazard identification of an ingredient in a cosmetic product is the first step in the risk assessment of a product. This identification is based on previous safety studies conducted by the manufacturer, literature, and reports from consumers when the product is on the market. Parameters used to determine the relative hazard of ingredient in the cosmetic products, include information on the physicochemical properties of an ingredient such as molecular weight, purity, solubility, partition coefficient, and chemical interactions with other ingredients (Pastrana et al. 2018).
b. Exposure evaluation.
Toxicity profile analysis is conducted to identify the adverse effects of an ingredient on living organisms, either through *in vitro* or *in vivo* testing. However, *in vivo* animal testing is currently prohibited in Europe and the U.S., so data related to cosmetic adverse effects can be found at the post-marketing stage only. The purpose of exposure evaluation is to establish the value of the Lowest Observed Adverse Effect Level (LOAEL) and No Observed Adverse Effect Level (NOAEL) of the dose-response relationship of cosmetic products and their ingredients. Both LOAEL and NOAEL are reported in terms of drug mass rather than subject mass, so it is considered less relevant to identify NM characteristics, such as surface area, particle size, surface charge, shape, agglomeration, aggregation, and coatings that modify the hazard level of an ingredient at the nanoscale. For example, micro-sized or more materials such as copper do not show toxicity at a dose of 5 mg/kg but the same material at the same concentration can cause kidney damage if the copper used is nanoscale copper (Pastrana et al. 2018).
c. Microbiological testing.
The purpose of microbiological testing is to ensure that no microorganisms (e.g. colonies of *Staphylococcus*, *Clostridium tetani*, *Pseudomonas aeruginosa*, molds, yeasts, and fungi) can infect the skin or mucosa. This stage is the last test of the evaluation before the cosmetic product is released to the market.
d. NM characterization.
The selection of measurement techniques to characterize NMs depends on the intrinsic properties of the particles and their behavior under specific environmental conditions. Predispersed, low-concentration and single dispersed particles require different treatment from the characterization of powders or aggregated compounds and agglomerates. In addition to the technique selection, sample preparation is a key parameter to consider in the establishment of standard operating analytical procedures for routine testing. These standards include detailed information on the stages of sample preparation and the instrument conditions used for analysis. To date, no single analytical technique has been found that can characterize all the required parameters (Ferreira et al. (2023), Hartman et al. (2018), and Pastrana et al. (2018)). Ferreira et al. (2023), Hartman et al. (2018), ICCR (2011, 2012), and Pastrana et al. (2018) have defined several NM characterization techniques as illustrated in Table 4.

Table 4. Characterization of NMs in cosmetic products.

Parameter	Instrumental Analysis
Chemical Composition	Mass Spectrometry, EDX, NMR
Size, and Size Distribution	Electron Microscopy (AFM, cryogenic-TEM, SEM) Chromatography (Field Flow Fractionation FFF, Hydrodynamic Chromatography, size exclusion), Centrifugation (ultracentrifugation), Mass Spectrometry (SPMS, ICP-MS for metal), XRD (crystal size)
Agglomeration/ aggregation	Dynamic Light Scattering (DLS) is suitable for materials >100 nm in size, but TEM can show the allomeric results of aggregates.
Mass Concentration	Analytical Electron Microscopy, AEM (Combination of spectroscopy and electron microscopy for compositional analysis), CFM, gravimetry method, centrifugal sedimentation
Particle Size	Particle counters
Shape	Scanning electron microscopy (SEM)
Surface Morfology	Atomic force microscopy (AFM)
	AEM, CFM, UV/Visible spectrometry, XPS, IR, Raman
Surface Weight	Chromatography (e.g. : Capillary Electrophoresis), Zeta Potential
Specific Surface Area	Brunauer-Emmett-Teller (BET)
Stability	Nanosystems must be monitored periodically over a period of time to ensure that the particles do not change into a state of aggregation/agglomeration. For example, the stability of particles in the dispersed state can be assessed every 2–3 years using UV-Vis spectroscopy to ensure dispersion stability.

The above methods can be summarized into several methods based on their order of priority, including the following:

a. Sample preparation stage.
Separation/extraction processes can alter NMs and can subject particles to aggregation, deaggregation, etc.
b. Chemical composition analysis of NMs using Inductively Coupled Plasma - Atomic Emission Spectroscopy (ICP-AES), Inductively Coupled Plasma Mass Spectrometry (ICP-MS).

Based on Fig. 5 above, NM analysis can use AUC, TEM, SEM, DLS, XDC, and FFF instruments.

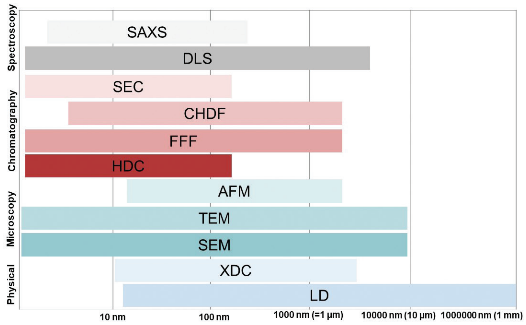

Figure 5. NM Measurement techniques based on particle size range.

Exploration of rapid detection of NMs in cosmetic products

Until now, there is no rapid detection method for NM analysis in cosmetic products. The currently available heavy metal screening method is the Reinsch Test (New York City Government undated). It needs to be proven whether this method can be used for screening some NM compounds, such as gold, titanium dioxide, zinc oxide and silver.

Challenges

As the backbone of monitoring marketed cosmetics in Indonesia, the National Quality Control Laboratory of Drug and Food (NQCLDF), as part of the Indonesian FDA, has the main responsibility to conduct testing of various analytes and to produce tens to hundreds of valid analytical methods up to now which are then implemented by the Indonesian FDA provincial offices all over Indonesia by doing routine analysis. These analytical methods include quantitative, qualitative, and contaminant analysis methods on various cosmetic products using various instruments such as High-Performance Liquid Chromatography (HPLC), Liquid Chromatography tandem Mass Spectrometry (LCMS/MS), Gas Chromatography (GC), Gas Chromatography-Mass Spectrometry (GCMS), High Performance Ion Chromatography (HPIC), and Atomic Absorption Spectroscopy (AAS). Furthermore, the increasing trend of nano cosmetics at the global level in recent years has made the Indonesian FDA need to prepare for the invasion of imported cosmetic products with nano size claims come to Indonesian territory. In addition, the current ease of technology transfer also makes it easier for the domestic cosmetic industry to adopt this technology to increase the value of its products. Therefore, the Indonesian FDA needs to conduct a stricter supervision of nano cosmetic products marketed in Indonesia. On the other hand, until now NQCLDF has not yet fully evaluated any NM compound found in cosmetics. The Indonesian FDA currently does not hold the instruments that are frequently used for NM characterisation due to its uncompetitive price, and its utilization in laboratories is still uncommon. Thus, the Indonesian FDA would have to make a significant upfront financial commitment in order to acquire the tools needed for NM characterisation.

Policy recommendations

Based on the above policy issues, there are several policies that can be recommended, including the following:

a. For the purpose of screening (rapid detection), alternative testing can be used by the Reinsch Test. The Reinsch Test was discovered by Hugo Reinsch in 1841 (New York City Government undated). Though the Reinsch Test can only analyse antimony, arsenic, bismuth and mercury, this technique may also be used for the analysis of zinc oxide and titanium dioxide. It needs further study to prove that this method can be used for qualitative analysis of organometallic nanoparticle compounds.
b. The necessity for clear and easily legible labelling indicating the presence of nanomaterials (NM) in cosmetic products is evident. This is following the ISO/TS 13830:2013 standard. The provision of this information can help consumers increase their confidence in deciding which cosmetic products to buy or to use. The types of cosmetics that need to be nano-labeled are divided into two, namely:
   - Cosmetic products which are main ingredients made in NP size.
   - Nano-sized by-products produced during the production process. This may affect the technical properties of the product or pose a risk to health or the environment.

The writing of active ingredients and carriers in the form of NM must be written in the form of "[nano]" (European Commission 2009; Hartmann et al. 2019; and Santana et al. 2019).

c. The analytical method of NM characterization in cosmetics is urgent considering that several products have been notified to contain NM. In addition, with the entry into force of the Free Trade Area (FTA), including in ASEAN (named ASEAN Free Trade Area, AFTA), imported cosmetic products can reach markets in Indonesia.

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