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Nanotechnology in cosmetics

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ABSTRACT

Nanomaterials are being used in cosmetic products for various effects. However, their use also raises potential safety concerns. Some of these concerns can be addressed by determining the type of nanomaterials used, as well as stability, potential for skin absorption, route of exposure, and how they are formulated in cosmetic products. There has been considerable effort internationally to harmonize approaches in order to address definitional issues and safety concerns related to the use of nanomaterials in cosmetic products.

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1. Introduction

Nanomaterials are currently being used in cosmetic products; however, the actual number of nanomaterials being used depends on how these materials are defined. Some nanomaterials may have increased bioavailability or toxicity; therefore, the potential skin absorption of these nanoparticles is an important consideration in the determination of whether safety concerns exist. Issues about the safety of a nanosized ingredient may also depend on its stability, since unstable nanomaterials will likely not be readily absorbed. Regulation of nanomaterials used in cosmetics in the United States is based on FDA's post-market authority over cosmetics. Cosmetic regulation of nanomaterials as well as the International Cooperation on Cosmetic Regulation (ICCR) process will be described.

2. Use and safety of nanomaterials

2.1. Definition of nanomaterials in cosmetics

It is difficult to determine the number of nanomaterials used in cosmetic products because the definition of what constitutes a nanomaterial is currently evolving. The use of the prefix “nano” in cosmetic advertising and labeling may not coincide with how the term is used by regulatory authorities.

The FDA does not currently have a definition of a nanomaterial but issued final guidance in June of 2014 to help provide regulatory clarity in FDA's regulation of products containing nanotechnology (Guidance for Industry Con, June 2014). FDA has developed certain points to consider when attempting to identify applications of nanotechnology in FDA regulated products: (1) whether a material or end product is engineered to have at least one external dimension, or an internal or surface structure, in the nanoscale range (approximately 1 nm to 100 nm) or (2) whether an engineered material or end product exhibits properties or phenomena including physical or chemical properties or biological effects that are attributable to its dimension(s), even if these dimensions fall outside the nanoscale range, up to one micrometer.

The European Union (EU) cosmetic regulation states that a nanomaterial is an “insoluble or biopersistant and intentionally manufactured material with one or more external dimensions, or an internal structure, on the scale of from 1 to 100 nm” (Regulation (EC) No 1223/2 and 9). Therefore, if stability and solubility are considered, certain unstable classes of nanomaterials (liposomes, solid lipid nanoparticles, and nanostructured lipid carriers) may not be considered nanoparticles under this regulation.

Many of the nanomaterials found in cosmetic products that claim to promote enhanced skin absorption may in fact be unstable when applied to the skin and, therefore, unable to carry ingredients beneath the surface layer of the skin. However, they may facilitate skin absorption by promoting increased diffusion from the cosmetic vehicle into the surface layer of skin (Schafer-Korting et al., 2007). Only insoluble, stable nanoparticles, such as

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titanium dioxide, nanogold, nanosilver and polymers, are clearly identified as nanoparticles that might enter into the body and possibly cause safety issues directly.

2.2. Use of nanomaterials in cosmetics

Probably the most common claim for the use of nanomaterials in cosmetics is to enhance the delivery of cosmetic ingredients into the skin. The small size of lipid vesicles may enable these materials to be absorbed more readily into skin (Cevc and Blume, 1992). Scientific studies to substantiate these claims have provided differing results. These may be due to study conditions such as nanoparticle size and stability that make it difficult to achieve consistent results even within the same laboratories. Differing physicochemical properties of vesicles can likely affect their interactions with skin (Honeywell-Nguyen et al., 2002). Some vesicles may not penetrate the skin but may simply release their ingredients onto the surface of the skin in a manner that facilitates uptake and penetration into the surface layers of skin (Schafer-Korting et al., 2007).

Nanomaterials also may be used to impart stability to formulations that contain ingredients that may decompose due to oxidation and other causes (Ourique et al., 2008). However, carrier nanoparticles may have stability problems upon application to the skin.

Nanoparticles of titanium dioxide and zinc oxide are used predominantly in sunscreen non-prescription drug products; however, they may also be used in cosmetic products (where the resulting product may be both a drug and a cosmetic depending on product claims). These nanomaterials remain effective blockers of UV radiation but also result in a transparent formulation that is pleasing to the consumer.

Nanoparticles of silver are used in consumer products as antibacterial or preservative agents. Cosmetic products in the US cannot make antibacterial claims, since this claim is associated with a physiological function, and, thus, its use is limited to drug products. Of note, nanosilver is not currently listed by the EU in Annex 5 of the Cosmetic Directive, which is the approved list for preservatives allowed to be used in cosmetic products.

2.3. Skin absorption of nanomaterials

The potential skin absorption of nanomaterials is an issue that must be addressed in order to help understand the safety and usefulness of these materials in cosmetic products.

2.3.1. Insoluble nanomaterials

Quantum dots (QD) have been used by a number of investigators as model compounds to study the skin absorption of nanomaterials. They are stable particles and are highly fluorescent which enables tracking of any skin permeation that occurs by using instruments that measure this fluorescence.

Initial studies by Jessica Ryman-Rassmussen and coworkers (Ryman-Rasmussen et al., 2006) were conducted with pig skin assembled in diffusion cells. QDs with two different sizes and three different surface charges were selected to determine the effect of particle size and surface charge on skin penetration. Application to skin was made in a pH 8.3 or pH 9.0 buffer supplied by the manufacturer. Absorption into the skin was assessed by measuring fluorescence of the particles using confocal microscopy. Spherical QDs with each surface coating were found to penetrate through the stratum corneum into the viable epidermis and dermis within 8 h. The ellipsoidal QD with a glycol-amine coating was observed in the epidermis within 8 h; whereas a carboxylic acid coating resulted in a delay of epidermal penetration until 24 h. Recent additional studies (Prow et al., 2011) on the same QDs have shown that there is generally no penetration of QDs through intact human stratum corneum into the viable tissue below. The authors demonstrated that the manufacturer's alkaline buffer (pH 8.3) facilitated increased penetration of the uncharged PEG coated QDs into the viable epidermis of human skin in diffusion cell studies (Prow et al., 2011).

Titanium dioxide (TiO_2) and zinc oxide (ZnO) nanoparticles tend to agglomerate into particles larger than 100 nm and have been generally found in various studies to remain on or near the surface of the skin. Initially, in vitro studies were conducted to separately examine the skin penetration of both TiO_2 and ZnO (Gamer et al., 2006). Two TiO_2 formulations and one ZnO formulation were applied to triplicate samples of skin in diffusion cells and studies were run for 24 h. Stratum corneum layers were then removed by cellophane tape stripping, and viable skin and receptor fluid were analyzed for TiO_2 and ZnO. Results showed that neither nanoparticle used in the sunscreen formulations was able to penetrate porcine stratum corneum into the viable skin or receptor fluid.

The skin penetration of TiO_2 formulations has been evaluated, in vivo, in minipigs (Sadrieh et al., 2010). Three TiO_2 particles were used with the following sizes as measured by scanning electron microscopy (SEM): uncoated submicron sized, 300–500 nm; uncoated nanosized, 30–50 nm; and dimethicone/methacone copolymer coated nanosized, 20–30 nm diameter and 50–150 in length. Particles were applied at 5% by weight in a sunscreen formulation at a concentration of 2 mg/cm^2. At the end of the studies, the most concentrated amounts of all three types of particles were found in the surface layer of skin – the stratum corneum. Only isolated TiO_2 particles were found in lower layers of the skin. The authors concluded that the TiO_2 particles studied did not penetrate intact pig skin epidermis in a significant amount and, therefore, they are unlikely to penetrate human skin.

The skin absorption of zinc oxide nanoparticles in a transparent sunscreen formulation was examined using excised human skin in diffusion cells (Cross et al., 2007). Less than 0.03% of the applied zinc penetrated into the receptor fluid beneath the skin. No ZnO nanoparticles were found in the stratum corneum or viable epidermis as determined by electron microscopy. Further evidence of a lack of significant ZnO nanoparticle skin penetration was obtained in vivo with human volunteers (Zvyagin et al., 2008). A commercially available sunscreen formulation containing ZnO nanoparticles (about 15–30 nm in size) was applied in amounts to simulate exposure conditions. Multiphoton microscopy imaging of the surface of the skin and below was conducted immediately after application and at 4 h and 24 h later. ZnO nanoparticles were observed on the surface of the skin following application to the skin and at 4 h. ZnO appeared to localize in skin folds and at the top of hair follicle shafts without spreading to neighboring cells. None of the nanoparticles were observed on the skin surface at 24 h, presumably due to bathing. No evidence of ZnO penetrating past the stratum corneum into the viable epidermis was observed.

The skin absorption of both TiO_2 and ZnO nanoparticles in topical formulations was evaluated by in vivo and in vitro techniques using skin from weanling Yorkshire pigs (Monteiro-Riviere et al., 2011). The main purpose of this study was to determine if mild skin damage from UV irradiation that might be seen with sun exposure resulted in enhanced skin penetration of the nanoparticles. The skin for both in vivo and in vitro studies was pretreated with UV light prior to dosing with the nanoparticle formulations. At the end of the in vitro absorption studies, TiO_2 was found in deeper layers of the stratum corneum in the damaged skin, compared to normal skin, using transmission electron microscopy (TEM). No penetration into the stratum corneum was observed for ZnO nanoparticles with either normal or damaged skin. At the end