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Nanomaterials in Cosmetics: Safety Concerns and Approaches for Risk Reduction

Baihan Wang *

Faculty of Science, University of Waterloo, Waterloo, Canada

* Corresponding Author Email: b99wang@uwaterloo.ca

Abstract. Nanotechnology has become an important driver of innovation in the development of cosmetics industry, offering enhanced stability, improved skin penetration and absorption and increased efficacy of active ingredients. However, the safety of nanomaterials has raised widespread concerns, especially their ability to penetrate biological barriers and enter the human body system. This article reviews the major mechanisms through which nanoparticles (NPs) may cause damage to human health, focusing on oxidative stress, immune response and bioaccumulation. At the same time, the article explores several strategies to mitigate nanoparticle-induced hazards, including the use of biocompatible materials, surface modification techniques such as surface coatings and charge modification and doping techniques to balance biocompatibility and efficacy. Finally, the article looks at a future with a combination of technological advancement and regulatory recommendations. The article also emphasizes the significance of establishing harmonized regulatory frameworks with the aim to contribute to the safe and sustainable application of nanomaterials in cosmetics.

Keywords: Nanotechnology; cosmetics; health; toxicity.

1. Introduction

In recent eras, the application of nanotechnology in cosmetics has been on the increase due to the significant improvements in product performance it provides. Nanoscale materials can provide multiple benefits, including higher stability, improved skin penetration and absorption, and enhanced bioactivity of active ingredients. For example, titanium oxide and zinc oxide NPs are widely used in sunscreens to provide ultraviolet protection. Additionally, metal and polymer-based NPs are used in skin care products due to the antibacterial and antioxidant properties they preserve. Nanotechnology's potential to significantly impact or even alter the cosmetics industry is fully demonstrated by these examples [1].

Though NPs' unique physiochemical properties make NPs effective, they also pose great threat to human health. NPs' nanoscale dimension allows them to penetrate humans' biological barriers and enter the human body system. After entering the human body system, NPs can trigger multiple health-related problems, including mitochondrial dysfunction, chronic inflammation or long-term accumulation in multiple organs [2, 3]. Accordingly, serious toxicological evaluation of NPs has become an urgent and unavoidable demand to achieve NPs' safe application in cosmetics.

This review focuses on three major aspects of the safety concerns nanoparticles in cosmetics bring about, namely oxidative stress, immune response and bioaccumulation. It further introduces three strategies to address these safety concerns, such as material selection, surface modification and doping techniques. These strategies are designed to balance between efficacy, biocompatibility and sustainability. Additionally, the importance of aligning technological advancements with consumer health and regulatory frameworks is also stressed in the review.

2. Safety Risks

2.1. Oxidative Stress

Nanoparticles' ability to induce oxidative stress has emerged as a central mechanism of nanotoxicity. Oxidative stress is broadly defined as a state where the production of reactive oxygen species (ROS) and the neutralization capacity of antioxidant defense systems are imbalanced. Though ROS serve as signaling molecules under physiological conditions, an excess generation of ROS overwhelm cellular defenses and cause molecular damage. Due to the small size, large surface area-to-volume ratio and high surface reactivity of NPs, many engineered NPs generate excessive ROS either directly through electron transfer reactions or indirectly by releasing metal ions. For example, titanium oxide (TiO_2) NPs can catalyze ROS production under light exposure, whereas silver and zinc oxide NPs, which are both widely used in cosmetics, produce Ag^+ and Zn^{2+}, which disrupt redox homeostasis. Increased ROS levels result in multiple harmful consequences that further activate stress response pathways and may trigger apoptosis or inflammatory signaling, including lipid peroxidation, protein oxidation, mitochondrial dysfunction and DNA strand breaks. Additionally, endogenous antioxidant enzymes can be negatively affected by NPs. As an example, Ag NPs can alter the conformation of catalase, while TiO_2 NPs modify superoxide dismutase. These interactions weaken the cellular antioxidant capacity and amplify oxidative injury, making oxidative stress a major concern in evaluating the safety of NPs [4].

2.2. Immune Response

Nanoparticles can interact with the immune system in various ways, often acting as both stimulators and regulators depending on their physiological properties. NPs are first recognized by innate immune cells such as macrophages, dendritic cells and neutrophiles after entering the body. These immune cells attempt to engulf and eliminate the NPs, which in term causes them to release cytokines that initiate inflammatory signaling. Certain metal-based NPs such as silver, cobalt and nickel are likely to cause local inflammatory reactions, including skin redness, itching, or irritation. This is because those metal-based NPs can stimulate the secretion of some pro-inflammatory mediators, such as TNFa. Nanoparticles' characteristics such as size, surface charge and surface properties are essentially responsible for these immune responses. For example, severe immune responses are more likely to be triggered by smaller or positively charged NPs, since they are more likely to be taken in by immune cells. However, certain NPs such as gold or super-paramagnetic iron oxide can suppress excessive immune responses, showing their potential as immune modulatory agents. In conclusion, NP-induced immune responses depend highly on the context and require careful evaluation when producing NPs [1, 5].

2.3. Accumulation

The bioaccumulation of NPs caused by long-term exposures is also an important safety concern in nanotechnology's applications in cosmetics. NPs can easily penetrate human's biological barriers and enter the human body system through pathways like respiration, digestive tract and skin contact thanks to their nanoscale dimensions. After entering human's systemic circulation, NPs can be transported to and accumulate in distal organs and tissues such as liver, spleen, heart, and bone marrow [6]. Such accumulation of NPs is related to problems that can result in fibrosis or organ failure, such as sustained inflammation, mitochondrial dysfunction and progressive tissue damage [7]. Moreover, the accumulation can lead to DNA damage and cell mutation, which potentially increase the risk of getting cancer [8]. A recent in-vitro and in-silico research looked at the accumulation of silver nanoparticles (AgNPs) in human lungs. As shown in the result, annual bioaccumulation of AgNPs can reach 0.46-64mg in blood. Whereas the safe level for an male adult is 25mg [9]. In conclusion, the long-term exposure and bioaccumulation of NPs are important factors to consider when applying NPs to cosmetics.

3. Approaches

3.1. Material Selection

Selecting safe materials that combine biocompatibility and potency to build NPs is a promising way to make low-risk NPs. For example, “next-generation lipids” combines biodegradability, efficacy and absorption efficiency. It serves as a promising material to manufacture lipid-based NPs. Quinn et al. (2021) developed biodegradable lipid nanoparticles by applying Michael addition combinatorial chemistry to incorporate biocleavable disulfide and acetal linkages into the hydrophobic tails. These bonds make NPs stable in circulation while ensuring rapid intercellular degradation, leading to efficient substance release, reduced systemic toxicity and improved biodegradability in human body [10]. Similarly, Akram et al. (2021) studied the formulation of water-in-oil nano-emulsions. They used pharmaceutically approved oils and food-grade surfactants such as polyglycerol polyricinoleate (PGPR) to achieve spontaneous emulsification. They showed that stable nano-emulsion can be produced with safe and biocompatible components by adjusting surfactant type, mixing order and dispersed phase ratio. Their results provide a way to encapsulate both hydrophilic and hydrophobic agents with minimal toxicity [11].

3.2. Surface Modification

The risks of NPs can also be decreased by modifying the surface of NPs. Surface modification can be achieved by surface coating, altering surface charge density, or changing surface hydrophobicity. NPs can be coated with various substances such as single- or multi-layer polymers. For example, Guido te al. (2024) developed a surface coating method of using glutathione monoethyl ester (GHS_{zwt}), which is a zwitterionic derivative of glutathione, to effectively mitigate gold NPs’ biological risks. Gold NPs coated by such material obtain several upgrades, including strong resistance to protein corona formation, improved colloidal stability under physiological conditions, and smaller risks of triggering immune response. In conclusion, the GHS_{zwt} coating serves as a simple and biocompatible coating material for compromising NPs’ efficacy and safety [12].

Applying surface modification to reduce risks of NPs can also be achieved by modifying NP’s surface charge density.Recent work by Motezakker et al. (2024) highlights the critical role of surface charge density in determining nanoparticle diffusion behavior within biological-like polymer networks. They demonstrated that relative surface charge density is as significant as network concentration in controlling nanoparticle transport by combining coarse-grained molecular dynamics simulations with experimental diffusion studies. During their research process, nanoparticles demonstrate distinct moving patterns depending on relative surface charge density-sticking, sliding, or bouncing. These discoveries suggest that fine-tuning nanoparticle charge density serves as a promising factor to optimize substance delivery efficiency and minimize potential adverse effects such as oxidative stress, immune activation, or unintended accumulation in tissues or organs [13].

Modifying nanoparticles’ physiological properties such as hydrophobicity is another critical method of reducing risks of NPs through modification of surface properties. For lipid nanoparticles (LNPs), hydrophobicity is an essential factor in its interaction with biological systems. Highly hydrophobic surfaces strongly absorb plasma proteins, resulting in the formation of a protein corona, which alters biodistribution and immune recognition. Additionally, hydrophobic NPs exhibit improved affinity for lipid bilayers, which can negatively affect membrane integrity and trigger cytotoxicity for inflammatory responses. Several strategies can be taken to reduce these risks. For example, PEGylation can be applied to create a hydrophilic shield. Zwitterionic surface coatings can also be used to balance charge and reduce nonspecific interactions. Additionally, hydrophilic polymers or polysaccharides such as chitosan and hyaluronic acid can be incorporated [2]. These strategies provide improved colloidal stability, minimized immune response, and enhanced biocompatibility to LNPs.

3.3. Doping

Doping is a widely used, effective approach to reduce safety risks of inorganic NPs. Doping refers to changing NPs' crystal structures by adding impurities to improve NPs' chemical and physical properties. Doping is especially useful in manufacturing safe zinc oxide nanoparticles (ZnO NPs). ZnO NPs are widely used in medical or cosmetics industry. However, the generation of reactive oxygen species (ROS) and the release of zinc ions led by ZnO NPs can cause oxidative stress. A recent study by Yin et al. (2024) proves doping as an effective strategy to balance ZnO NPs' efficacy and safety. By systematically comparing ZnO NPs that are doped with three dopants (e.g. Fe, Mn, Co), they demonstrated that the selection of dopant element essentially determines the cytotoxicity. The result shows that whileelementsssing increased $cytotoxcytotoxicity$dative stress, which lead to elevated toxicity, Fe doped ZnO NPs exhibited a suppressed dissolution and a reduction in ROS generation. Most notably, Co-doped ZnO NPs, particularly at a doping concentration of 2%, achieved the most favorable compromise between efficacy and harm [14].

Flame spray pyrolysis (FSP) is a widely used, highly versatile and scalable technique for NP doping. Unlike conventional wet-chemical or vapor-fed methods, FSP operates by atomizing a liquid precursor solution into fine droplets, which are then combusted into a high-temperature, self-sustaining flame. The precursor then undergoes evaporation, decomposition, nucleation, particle growth and rapid quenching within milliseconds. FSP has the advantage of incorporating dopant elements directly into the crystal structure during synthesis, ensuring precise control over particle size, morphology and electronic properties [15].

4. Outlook

The application of nanomaterials in cosmetics will not only depend on scientific development in the future, but also on robust regulatory and governance frameworks. The European Union has established a comprehensive legal framework, demanding clear definitions, standardized testing methods and transparent safety assessments to address uncertainties surrounding NP's behavior. In the future, progress of nanomaterial application in cosmetics should focus on improving the notification process, communicating with users using digital technologies and harmonizing international definitions of nanomaterials. Additionally, it is essential to align innovation with consumer safety and environmental sustainability, which requires comprehensive sustainability considerations, such as replacing synthetic substances with natural nanomaterials and applying greener formulation methods.

5. Conclusion

Nanotechnology has provided cosmetics with significant advantages, including improved stability, enhanced skin penetration and absorption, and increased efficacy. However, NP's special physiological properties also bring about significant safety concerns. As shown above, oxidative stress, immune response and long-term accumulation are key safety risks nanoparticles in cosmetics bring to human health. To ensure safe and sustainable use of NPs, approaches that balance efficacy and safety and lower potential hazards such as surface coating, doping and using biocompatible and degradable materials can be used. In the future, combining toxicological insights with harmonized regulatory frameworks will also be essential to developing nanotechnology and advancing its application in cosmetics while ensuring safety.

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