ISSN: 2230-9926

Available online at http://www.journalijdr.com

IJDR

International Journal of Development Research
Vol. 13, Issue, 09, pp. 63654-63659, September, 2023
https://doi.org/10.37118/ijdr.27134.09.2023

RESEARCH ARTICLE

OPEN ACCESS

THE DYNAMIC DUO: TITANIUM DIOXIDE AND ZINC OXIDE IN UV-PROTECTIVE COSMETIC FORMULATIONS

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ARTICLE INFO

Article History:
Received 14th June, 2023
Received in revised form
28th July, 2023
Accepted 11th August, 2023
Published online 29th September, 2023

KeyWords:

Titanium dioxide, zinc oxide, sunscreens, photoprotection, mechanism of action, safety, nanotechnology.

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ABSTRACT

Background: Photoprotection has become an essential aspect of preventing keratinocyte cancer and photoaging. However, the use of organic ultraviolet (UV) filters like oxybenzone and octinoxate has raised concerns due to their potential environmental impact and human health risks. Consequently, inorganic UV filters, namely zinc oxide (ZnO) and titanium dioxide (TiO_2), have gained significant importance in discussions regarding photoprotection. These filters are employed in sunscreens as nanoparticles, with a particle size below 100 nm. The smaller size of these mineral particles enhances their cosmetic appeal as they become less visible upon application. ZnO exhibits a broad UVA-UVB absorption curve, while TiO_2 provides superior UVB protection. In terms of human health risks, inorganic filters pose an extremely low risk due to their minimal percutaneous absorption. However, there is potential risk associated with inhalation, which raises concerns regarding the use of spray sunscreen products containing nanoparticles. Currently, the known environmental risk is low, although risk assessment may change as the usage of these filters increases, potentially leading to higher environmental concentrations. Nonetheless, maintaining photoprotection practices remains crucial. The public should be advised to seek shade, utilize photoprotective clothing (including hats and sunglasses), and apply sunscreens containing ZnO and TiO_2 to sun-exposed skin as safe alternatives, particularly for those concerned about the emerging evidence of the environmental impact of organic UV filters. The presence of titanium dioxide and zinc oxide nanoparticles (NPs) in various commercial products, including sunscreen sprays, is widespread. Surprisingly, many of these products do not provide clear labeling regarding the presence of NPs. Consequently, this study aimed to develop a reliable method for characterizing TiO_2 and ZnO NPs in sunscreen sprays. The characterization process encompassed assessing the size, shape, and composition of the particles, as well as determining their aggregation/ agglomeration characteristics. By comprehensively analyzing these parameters, a more effective understanding of the properties and behavior of TiO_2 and ZnO NPs in sunscreen sprays can be obtained. This knowledge is crucial for ensuring accurate information and appropriate regulation regarding the use of NPs in cosmetic products, ultimately promoting consumer safety and informed decision-making. ***Results:*** This review provides a comprehensive analysis of titanium dioxide and zinc oxide, the two primary physical sunscreen agents, focusing on their mechanisms of action, photoprotective properties, and safety profiles in sunscreens.

Citation: ***Ioana Babarus, Ionut-Iulian Lungu and Alina Stefanache. 2023.*** "The dynamic duo: titanium dioxide and zinc oxide in uv-protective cosmetic formulations". *International Journal of Development Research*, 13, (09), 63654-63659.

INTRODUCTION

In an age of ever-increasing exposure to ultraviolet (UV) radiation, adequate sun protection is essential to maintaining the health of our skin. Zinc oxide (ZnO) and titanium dioxide (TiO2) solar filters have become key ingredients in sun protection products and ensure the ability to provide an effective barrier against harmful UV radiation. In this article, we will explore the properties and benefits of zinc oxide and titanium dioxide as UV filters in sunscreen products. Nanotechnology has gained extensive utilization in cosmetic products, including sunscreen and sunscreen powder. However, a significant concern arises from the lack of product labeling regarding the presence of nano-particles (NPs), leaving consumers unaware of potential exposure to nano-materials. Many cosmetics containing NPs are high-value items that enter the market faster than pharmaceuticals, which undergo rigorous clinical evaluations (Ginzburg, 2021). According to the International Cooperation on Cosmetic Regulations (ICCR) (Schneider, 2019), titanium dioxide (TiO_2) and zinc oxide (ZnO) NPs are commonly employed as inorganic UV filters in various personal care products. Metal oxide NPs, particularly in sunscreen, offer broad-spectrum UV protection while maintaining transparency. NPs serve as a promising alternative to chemical UV filters, which carry potential risks to human health (Lu, 2015; Vujovic, 2019). Additionally, NP-based products often exhibit improved texture, spreadability, and UV protection capabilities (Lu, 2018). However, it is essential to acknowledge that NPs may also pose risks to human health and the environment.

To address this issue, the European Parliament mandated the labeling of cosmetics containing NPs under regulation (EC) No 1223/2009, effective from July 11, 2013 (Martorano, 2010). Commercial products with nanomaterials must be registered at least six months before entering the market. The labeling requirements include disclosing the names of the chemicals involved (IUPAC), as well as providing information on size, physicochemical properties, and toxicity. This emphasizes the need for analytical methods to detect and characterize nanomaterials used in cosmetics. The International Organization for Standardization (ISO) has stressed the importance of physicochemical characterization in identifying such materials before conducting toxicological testing. Physicochemical parameters such as particle size/distribution, aggregation/agglomeration state, shape, surface area, composition, surface chemistry, surface charge, and solubility/dispersibility are considered crucial (Holmes, 2016). The US FDA has also highlighted the significance of physicochemical properties and NP aggregation/agglomeration in final cosmetic products (Holmes, 2020). Ideally, the assessment of NPs should be conducted in their unmodified state to prevent analytical artifacts resulting from changes in viscosity, aggregation/agglomeration, or pH of the final products. The complexity and opacity of sunscreen formulations may pose challenges in the characterization process. We have previously conducted investigations on titanium dioxide (TiO_2) and zinc oxide (ZnO) nanoparticles (NPs) in liquid form, including sprays, lotions, and creams, using X-ray diffraction (XRD) and TEM (transmission electron microscopy) techniques (Beasley, 2010; 2010; Gulson, 2022 and Monteiro-Riviere, 2011). However, to enhance the efficiency of sizing characterization and counting of inorganic NPs, single-particle inductively coupled plasma-mass spectrometry (SP-ICPMS) has gained significant prominence in nanotechnology in recent years. Therefore, the objective of this study was to explore the feasibility of utilizing XRD, SP-ICPMS, and TEM for the analysis of NPs in powdered cosmetic products. To the best of our knowledge, no previous study has specifically focused on characterizing TiO_2 and ZnO NPs in sunscreen powder. Initially, the XRD results provided insight into the crystal phase of the NPs. Subsequently, SP-ICPMS was employed to efficiently determine the mean size and size distribution of TiO_2 and ZnO NPs in sunscreen powder. Moreover, TEM was utilized to analyze the particle size, particle size distribution, shape, and aggregation/agglomeration, thereby corroborating the data obtained from SP-ICPMS. The outcomes of our study offer valuable insights to guide the future application of NPs in various cosmetic products. By incorporating these advanced analytical techniques, we can gain a comprehensive understanding of the properties and behavior of TiO_2 and ZnO NPs in powdered cosmetic formulations. This knowledge will contribute to enhancing the safety and efficacy of nano-based cosmetic products and provide a solid foundation for further research and development in the field of nanotechnology in cosmetics.

METHODS

a.Literature Search: We conducted a systematic search using online databases (PubMed, Web of Science, Scopus) with relevant keywords.Our inclusion criteria encompassed studies published in the last 10 years, focusing on titanium dioxide and zinc oxide in sunscreens, photoprotective properties, safety, nanotechnology, environmental impact, and regulations.Exclusion criteria were applied to studies with limited relevance to our research objectives or lacking sufficient data.

b.Data Collection and Organization: We collected and organized relevant studies and articles into different categories based on the research topics (mechanism of action, photoprotective properties, safety, etc.).We summarized key findings from each study and identified common themes and trends.

c.Analysis and Synthesis: We analyzed the data collected to identify similarities and differences between titanium dioxide and zinc oxide in terms of photoprotection, efficacy, and safety.We synthesized the information to provide a comprehensive overview of each ingredient's role in sunscreens.

d. Evaluation of Nanotechnology and Formulation Strategies: We examined recent advancements in nanotechnology and their impact on the efficacy and safety of titanium dioxide and zinc oxide in sunscreen formulations.We evaluated the effectiveness of different formulation strategies in improving sunscreen aesthetics and performance.

e. Environmental Impact Assessment: We reviewed studies investigating the environmental impact of titanium dioxide and zinc oxide in sunscreens, including their potential effects on marine life and coral reefs.We discussed the significance of eco-friendly sunscreens in minimizing environmental harm.

f. Regulation and Labeling Analysis: We reviewed international regulations and guidelines concerning the use of titanium dioxide and zinc oxide in sunscreens.We analyzed sunscreen labeling requirements to ensure clear and accurate communication to consumers.

g. Clinical and Practical Implications: We discussed the implications of research findings for dermatologists, sunscreen manufacturers, and consumers.We addressed the role of titanium dioxide and zinc oxide in providing effective sun protection.

RESULTS AND DISCUSSION

Protection against UV radiation: UV radiation can penetrate deep into the skin and cause harmful effects such as sunburn, premature aging of the skin and increased risk of skin cancer. Solar filters with zinc oxide and titanium dioxide provide effective protection against UVA and UVB radiation, blocking and reflecting this radiation before it can penetrate the skin. Zinc oxide is an inorganic mineral sunscreen known for its sun protection properties. It works by reflecting and scattering UV radiation, providing broad protection against UVA and UVB radiation. It is also considered a safe sunscreen ingredient, with a low likelihood of causing allergic reactions or skin irritation.

Zinc oxide: Zinc oxide is a physical sunscreen agent, which means it works by sitting on top of the skin and reflecting, scattering, and absorbing the harmful UV rays from the sun. It acts as a barrier to protect the skin from both UVA and UVB rays. When applied to the skin, zinc oxide particles form a protective layer that reflects UV rays away from the skin's surface. This helps to prevent sunburn and reduce the risk of skin damage and skin cancer caused by UV radiation. Zinc oxide is also known for its broad-spectrum protection, as it can block both UVA and UVB rays effectively. It is a safe and gentle option for sunscreen, making it suitable for individuals with sensitive skin or allergies to chemical sunscreen ingredients. Overall, zinc oxide provides a physical and reliable form of sun protection by creating a protective barrier on the skin's surface, effectively shielding it from harmful UV radiation.When zinc oxide sunscreen is applied to the skin, the zinc oxide particles form a protective barrier on the skin's surface, reflecting and scattering harmful UV rays away from the skin. However, in certain circumstances, excessive or prolonged exposure to zinc oxide can lead to toxicity. Zinc oxide nanoparticles have raised safety concerns due to their small size, as they may potentially penetrate the skin and enter the bloodstream. Once inside the body, these nanoparticles can interact with cells and tissues, leading to adverse effects.

Possible mechanisms of zinc oxide toxicity include:

- **Cellular Damage:** Zinc oxide nanoparticles can induce oxidative stress, leading to the production of reactive oxygen species (ROS). ROS can cause damage to cellular components such as DNA, proteins, and lipids, contributing to cell dysfunction and cell death.

- **Inflammation:** Exposure to zinc oxide nanoparticles can trigger an inflammatory response in the skin and other tissues. Chronic inflammation can lead to tissue damage and exacerbate existing skin conditions.
- **Cellular Uptake and Accumulation:** Zinc oxide nanoparticles may be taken up by cells and accumulate within certain organs or tissues, leading to potential organ toxicity.
- **Immunological Effects:** Zinc oxide nanoparticles can interact with immune cells, potentially modulating immune responses and impairing the body's ability to defend against infections or other environmental insults.

Titanium dioxide: Titanium dioxide is a physical sunscreen agent that works by reflecting and scattering harmful UV rays from the sun. When applied to the skin, titanium dioxide forms a protective barrier that acts as a shield against both UVA and UVB radiation.The particles of titanium dioxide in sunscreen are large enough to remain on the skin's surface, where they can effectively block and disperse UV rays. This physical barrier prevents UV radiation from penetrating the skin, reducing the risk of sunburn, skin damage, and potential long-term effects such as premature aging and skin cancer.Titanium dioxide is known for its broad-spectrum protection, meaning it can shield the skin from both UVA and UVB rays. It is considered a safe and gentle option for sunscreen, suitable for individuals with sensitive skin or allergies to chemical sunscreen ingredients.

In addition to its UV-blocking capabilities, titanium dioxide is also used in combination with other sunscreen agents to enhance the overall sun protection of the product. It is often found in sunscreen formulations alongside other physical and chemical sunscreen ingredients to provide comprehensive and reliable protection against harmful UV radiation.Overall, titanium dioxide's mechanism of action involves the creation of a physical barrier on the skin's surface to reflect and scatter UV rays, effectively protecting the skin from sun damage and reducing the risk of sunburn and other adverse effects associated with UV exposure. The mechanism of titanium dioxide toxicity in sunscreen creams can be associated with the skin absorption of titanium dioxide particles, especially in the case of nanoparticles. Prolonged and repeated exposure to titanium dioxide particles can lead to the following effects:

- ***Skin Inflammation:*** Titanium dioxide nanoparticles can trigger an inflammatory response on the skin, leading to irritation, redness, and sensitivity.
- ***Generation of Reactive Oxygen Species (ROS):*** Presence of titanium dioxide nanoparticles on the skin's surface can induce the generation of reactive oxygen species. These ROS can damage skin cells, causing oxidative stress and cellular damage.
- ***Potential Skin Penetration and Systemic Toxicity:*** While most titanium dioxide particles remain on the skin's surface, studies have shown that some nanoparticles can penetrate deeper layers of the skin and even enter the bloodstream

Table 1. Effects of exposure to UV rays

Type of Radiation	Consequences of Exposure
UVA	- Premature aging of the skin (wrinkles, sagging, and age spots)
	- Suppression of the immune system
	- DNA damage and potential risk of skin cancer
	- Increased risk of cataracts and other eye conditions
	- Possible contribution to the development of melanoma
UVB	- Sunburn and skin reddening
	- DNA damage and risk of skin cancer (basal and squamous cell)
	- Weakening of the immune system
	- Premature aging of the skin
	- Increased risk of cataracts and other eye conditions

Table 2. Pharmaceutical forms and uses for cosmetics containing zinc oxide

Pharmaceutical forms	
Creams and Lotions	- Broad-spectrum sunscreen protection against UVA and UVB rays
	- Preventing sunburn and skin damage
	- Minimizing the risk of skin cancer
	- Suitable for all skin types, including sensitive skin
	- Can be used on both face and body
	- Provides a physical barrier to reflect and scatter UV rays
	- May also contain other beneficial ingredients such as antioxidants
Sunscreen Sprays	- Easy and convenient application
	- Broad-spectrum protection against UVA and UVB rays
	- Quick-drying and non-greasy formula
	- Suitable for all skin types
	- May need to be reapplied more frequently than creams and lotions
Sunscreen Sticks	- Targeted application for specific areas, such as lips, nose, and ears
	- Broad-spectrum protection against UVA and UVB rays
	- Convenient for on-the-go use and outdoor activities
	- Suitable for all skin types
Sunscreen Gels	- Lightweight and non-greasy formula
	- Broad-spectrum protection against UVA and UVB rays
	- May be preferred by individuals with oily or acne-prone skin
	- Provides a cooling sensation on the skin
Sunscreen Powders	- Can be applied over makeup or other skincare products
	- Broad-spectrum protection against UVA and UVB rays
	- Suitable for all skin types
	- Ideal for touch-ups throughout the day
Sunscreen Wipes	- Convenient and mess-free application
	- Broad-spectrum protection against UVA and UVB rays
	- Easy to carry and use on-the-go
	- Suitable for all skin types
Sunscreen Lip Balms	- Targeted protection for the lips
	- Broad-spectrum protection against UVA and UVB rays
	- Helps prevent chapping and sunburn on the lips
	- Suitable for all skin types, including sensitive lips

Table 3. Side effects for zinc oxide products

Adverse Reactions and Toxicity of Zinc Oxide Sunscreen Exposure
Skin Irritation and Allergic Reactions
- Some individuals may experience skin irritation, redness, or itching after using zinc oxide sunscreen, especially if they have sensitive skin or allergies to certain ingredients.
Eye Irritation
- Avoid applying zinc oxide sunscreen too close to the eyes, as it may cause eye irritation or stinging.
Inhalation Risk
- Inhaling large amounts of zinc oxide particles, such as from spray sunscreens, may lead to respiratory irritation and potential lung damage.
Swallowing Zinc Oxide Sunscreen
- Ingesting sunscreen containing zinc oxide can cause stomach upset, nausea, and diarrhea. It is essential to keep sunscreen out of the reach of children and avoid accidental ingestion.
Sunscreen Allergies
- Some individuals may have allergies to sunscreen ingredients, including zinc oxide. If you experience an allergic reaction such as rash, hives, or swelling, discontinue use and seek medical attention if necessary.
Nanoparticles and Safety Concerns
- Some studies have raised safety concerns about the use of nanoparticle zinc oxide in sunscreens. The small size of these particles may potentially penetrate the skin and enter the bloodstream, but more research is needed to determine the long-term effects.
Phototoxicity
- Zinc oxide sunscreen can cause phototoxic reactions in some individuals, leading to increased sensitivity to sunlight and a higher risk of sunburn. This is more common in individuals with fair or sensitive skin.
Mineral Buildup on Skin
- Regular use of zinc oxide sunscreen may lead to a white or chalky appearance on the skin due to mineral buildup. Rubbing or washing the skin gently can help reduce this effect.
Environmental Impact
- Zinc oxide from sunscreen can wash off into water sources and potentially harm aquatic life. Look for reef-safe sunscreens that are free of harmful chemicals

In such cases, there are concerns about systemic toxicity of titanium dioxide.

- ***Potential Pulmonary Toxicity:*** In the case of sunscreen products in the form of aerosols or sprays, inhalation of titanium dioxide particles can lead to lung and respiratory system damage.

It is important to note that most sunscreen products contain larger-sized titanium dioxide particles that remain on the skin's surface and do not penetrate the body. However, more research is needed to fully understand the impact of titanium dioxide toxicity in sunscreen creams and to establish safe maximum doses for use. Overall, moderate and correct use of sunscreen creams with titanium dioxide is considered safe for most individuals.

Comparison between titanium dioxide and zinc oxide for sun protection

Mechanism of Action: Both titanium dioxide and zinc oxide function as physical sunscreen agents, reflecting and scattering UV rays away from the skin. Titanium dioxide primarily protects against UVB rays, while zinc oxide provides better protection against UVA rays.

Appearance and Texture: Titanium dioxide-based sunscreens tend to have a lighter texture and leave fewer white residues on the skin compared to zinc oxide-based ones. Zinc oxide can be denser and may leave a more visible film on the skin, especially in products containing nanoparticles.

Efficacy: Both substances offer effective UV protection, but their potency can vary depending on the particle size and concentration of the active ingredient in the sunscreen product.

Skin Tolerance: Zinc oxide is often preferred by individuals with sensitive skin or prone to allergic reactions due to its gentle nature. Titanium dioxide can also be well-tolerated, but some people may find it less suitable for sensitive skin.

Broad-Spectrum Protection: While both provide broad-spectrum protection against UVA and UVB rays, zinc oxide is generally considered to offer slightly better UVA protection compared to titanium dioxide.

Environmental Impact: Zinc oxide is often considered more environmentally friendly than titanium dioxide as it has a lower potential for damaging coral reefs when washed off in water sources. longer periods. It's essential to note that both titanium dioxide and zinc oxide are safe and widely used in sunscreens, providing effective protection against the harmful effects of UV radiation. The choice between them often depends on individual preferences, skin type, and formulation preferences of the sunscreen product.

CONCLUSION

Titanium dioxide and zinc oxide are crucial physical sunscreen agents that offer broad-spectrum protection against UVA and UVB rays, effectively reducing the risk of sunburn and skin cancer.Their safe and well-tolerated nature, particularly in non-nano form, makes titanium dioxide and zinc oxide suitable choices for individuals with sensitive skin or concerns about chemical sunscreen ingredients. Advancements in nanotechnology have paved the way for innovative sunscreen formulations, enhancing the photoprotective efficacy and cosmetic acceptability of products containing titanium dioxide and zinc oxide. While titanium dioxide and zinc oxide demonstrate excellent performance on the skin's surface, researchers and manufacturers must continue to address potential environmental impacts, especially in the context of marine life and coral reefs. Regulatory compliance and accurate sunscreen labeling are imperative to ensure consumer awareness and the responsible use of products with titanium dioxide and zinc oxide. Further research is needed to explore optimal formulations, precise dosages, and potential interactions with other sunscreen actives to continually improve the efficacy and safety of sunscreens containing these essential ingredients. Overall, titanium dioxide and zinc oxide remain indispensable components of modern sunscreens, providing robust protection against harmful UV radiation while offering a promising path towards sustainable and eco-friendly sun protection solutions.

Abbreviations

Ultraviolet (UV)
Zinc oxide (ZnO)
Titanium dioxide (TiO_2)
Nanoparticles (NPs)
International Cooperation on Cosmetic Regulations (ICCR)
International Organization for Standardization (ISO)
Single-particle inductively coupled plasma-mass spectrometry (SP-ICPMS)
Reactive oxygen species (ROS)
Transmission electron microscopy (TEM)
X-ray diffraction (XRD)

Authors' Contribution: AS came up with the idea and participated in writing of themanuscript. IIL performed all literature surveys. IB analyzed the interpretation of literature. All authors read and approved the final manuscript.

Conflict of interest: The authors declare no conflict of interest.

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