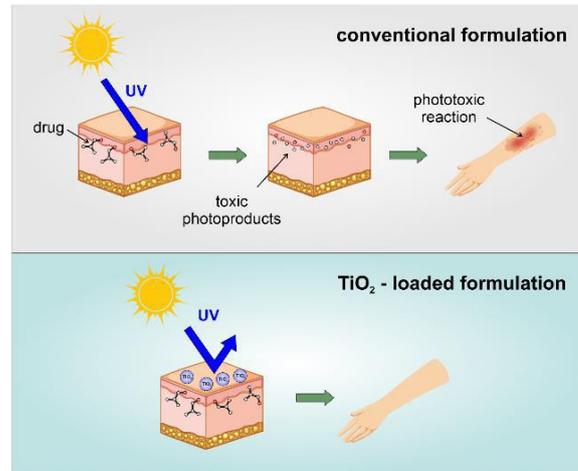


## Titanium Dioxide in a New Light: Reducing Toxicity and Improving the Photoprotective Properties of TiO<sub>2</sub> Through Nanoparticle Modification

Sunlight has been used for centuries in the treatment of various ailments, but it also has a darker side – it can lead to drug degradation and the formation of toxic photoproducts. This can result in skin reactions, both phototoxic and photoallergic. With nearly 400 medicinal substances capable of triggering such effects, the issue is of global concern. Analyzing the photochemical properties of drugs and developing protective strategies is crucial, as phototoxicity increases the risk of skin cancer and can significantly complicate therapy.

**One way to reduce the impact of light on drugs applied to the skin (e.g., in ointments, creams, or gels) is by using photoprotective ingredients. Titanium dioxide (TiO<sub>2</sub>) is commonly used for this purpose, as it can scatter light and help protect active substances.**

However, a European Commission regulation from January 14, 2022, withdrew the approval of TiO<sub>2</sub> labeled E171 in food due to its toxic effects. Concerns about the genotoxicity of TiO<sub>2</sub> nanoparticles, or their potential to damage genetic material, have spread across Europe (Regulation 2022/63). Consequently, the European Medicines Agency (EMA) mandated the pharmaceutical industry to seek alternatives to TiO<sub>2</sub> in medicinal products. This situation presents an opportunity to research modifications of TiO<sub>2</sub> nanoparticles to reduce their genotoxicity, particularly focusing on their interaction with light and the generation of harmful free oxygen radicals.



In April 2025, the World Health Organization (WHO) called for urgent action to improve the diagnosis and treatment of fungal infections, emphasizing the need for investment in research and the development of new antifungal drugs. Fungal infections, affecting 10–20% of the population, are common skin conditions. Deep fungal infections of the skin are particularly serious and often require prolonged treatment with oral antifungal medications, which can cause significant side effects. Therefore, topical treatment of dermatophytosis is considered a preferred alternative. However, the WHO report highlighted the growing issue of drug-resistant fungal infections, pointing to the urgent need for more effective and safer antifungal therapies. Unfortunately, many antifungal drugs also suffer from the previously mentioned problem of photosensitivity.

**This project aims to address these concerns by synthesizing new titanium(IV) oxide nanoparticles with an enhanced safety profile and improved photoprotective properties and developing a new semi-solid formulation for the antifungal drug voriconazole topical delivery. Voriconazole was chosen due to its high association with phototoxic reactions.**

As part of the preliminary research for the project, modified TiO<sub>2</sub>@CeO<sub>2</sub> nanoparticles were developed, demonstrating a significantly reduced potential for generating reactive oxygen species and enhanced effectiveness in protecting photolabile drugs from UV radiation. Additionally, a hydrogel formulation containing voriconazole was prepared, utilizing microemulsions as drug carriers. The proposed project will focus on a comprehensive assessment of the new material's toxicity, including studies on skin irritation, sensitization, acute toxicity, and skin permeation, as well as on the development and thorough characterization of a hydrogel incorporating the newly synthesized TiO<sub>2</sub>@CeO<sub>2</sub> nanoparticles.

**This innovative project aligns with global trends in developing new drug formulations with enhanced safety and efficacy. The results will provide crucial insights into the feasibility of using modified TiO<sub>2</sub> nanoparticles in skin drug technology and offer a new perspective on treating dermatophytosis.**