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Molecular Mechanisms of Melanogenesis in Hyperpigmentation: From Signaling Pathways to Nanocarrier-Based Therapeutic Strategies

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Abstract

Hyperpigmentation remains a complex dermatological challenge, often resistant to conventional topical therapies due to the skin's inherent barrier function and the chemical instability of active depigmenting agents. Traditional formulations of depigmentation agents frequently suffer from poor dermal penetration and dose-dependent toxicity, leading to localized irritation and high relapse rates. This review highlights the transformative role of cosmeceutical nanotechnology in overcoming these limitations through advanced delivery systems, including lipid-based nanocarriers, polymeric nanoparticles, and microbiota-derived metabolite platforms. These nanosystems enhance the stability, controlled release, and targeted delivery of active compounds to melanocytes within the basal epidermis while modulating key molecular pathways involved in

melanogenesis. Their mechanisms include inhibition of tyrosinase activity through active-site copper chelation, suppression of microphthalmia-associated transcription factor (MITF) signaling, and disruption of melanosome transport and transfer to keratinocytes. Emerging microbiota-based approaches further contribute by regulating oxidative stress, inflammation, and pigmentation while helping maintain skin homeostasis. Experimental and clinical evidence demonstrates that nanocosmeceutical formulations significantly improve depigmenting efficacy. Despite these advantages, challenges remain regarding nanotoxicity, long-term safety, large-scale manufacturing, and the lack of harmonized regulatory frameworks governing nanocosmeceuticals. As demand for effective and minimally invasive skincare continues to grow, nanotechnology provides a promising strategy for developing safer, more stable, and highly bioavailable therapies for hyperpigmentation. Continued research, standardized safety evaluation, and clearer regulatory guidelines are essential to facilitate the successful clinical translation and commercialization of nanotechnology-based depigmenting formulations. © 2026, HH Publisher. All rights reserved.

Author keywords

Melanogenesis; MITF pathway; Molecular targeting; Nanotechnology; Tyrosinase inhibition

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