

## Abstract

### Nanomedicines on Multidrug Treatment Strategies for Vitiligo.

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Vitiligo is a skin pigmentary disorder caused by selective destruction of melanocytes and characterized by progressive patchy loss of skin pigmentation. It affects 0.5%-2% of adults and children worldwide. Current topical and systemic drugs used to treat vitiligo are ineffective and have low local accumulation due to skin barrier properties and drug metabolism/inactivation. Therefore, topical use of ultradeformable nanomedicines may provide a clinically relevant approach. The objective of this study was to prepare ultradeformable nanocarriers for percutaneous co-administration of khellin and idebenone. The nanocarriers were characterized physicochemically. The mean size, size distribution, zeta potential, long-term stability and entrapment efficiency were determined. Ethosomes and transferomes that exhibited better physicochemical properties and stability for topical skin application were used for further in vitro experiments. Percutaneous permeation studies, using human stratum corneum and epidermis (SCE) membranes, showed that transferomes had the best percutaneous permeation profiles and improved the distribution of Khellin and Idebenone through the skin. Furthermore, ultradeformable vesicular nanocarriers loaded with Khellin/idebenone stimulated melanin production and recovery of normal skin pigmentation. In vivo studies in human volunteers demonstrated adequate safety of transferomes, confirming their relevance for potential clinical use. Overall, our data showed that the investigated vesicular nanomedicine is able to effectively co-deliver two drugs, idebenone (an antioxidant) and khellin (a furanochromone drug). Therefore, this dual delivery system could be a novel clinical approach for the treatment of vitiligo.