

In Vitro and Ex Vivo Permeation studies of Polyphenols: assessing the Safety of these ingredients for Topical Application

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The study of permeation of natural cosmetic active ingredients is essential to ensure product safety and compliance with European Regulation (EC) No. 1223/2009 [1]. Phenolic compounds are highly valued in cosmetics for their potent antioxidant properties and their role in supporting extracellular matrix integrity, which contributes to improved skin appearance and function [2]. This work aimed to evaluate the effects of catechin, epicatechin, chlorogenic acid, neochlorogenic acid, and their combination on the viability of keratinocytes (HaCaT) using the MTT assay, after exposure to various concentrations (15.625–500 µg/mL). Moreover, a permeation study using Franz diffusion cells coupled to human skin over a 24-hour period was performed. The compounds permeation was quantified by LC-MS. In terms of cell viability, exposure to lower concentrations (15.625–125 µg/mL) significantly enhanced cell viability. Conversely, the combination of the four compounds resulted in lower overall viability, suggesting potential antagonistic interactions. At the highest tested concentration (500 µg/mL), most compounds exhibited cytotoxic effects, except for epicatechin, which maintained cell viability at levels comparable to the control. The *ex vivo* permeation results showed a time-dependent increase in the permeation of all tested phenolic compounds, with the highest concentrations observed at the final time points. Future perspectives of this work include optimizing phenolic compound formulations to enhance skin permeation through encapsulation.

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References:

- [1] Union, P. Regulation (EC) No 1223/2009 of the European Parliament and of the Council. *Off. J. Eur. Union* **2009**, L342, 59.
- [2] Wu, W.; Mi, Y.; Meng, Q.; Li, N.; Li, W.; Wang, P.; et al. Progress in Research on Plant-Derived Polysaccharide Microparticles for Skin Applications. *Chin. Herb. Med.* **2025**, *17*, 279–291.