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Smart delivery of polyphenols: Alginate microencapsulation meets advanced skin models

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Abstract

Background: Polyphenols are promising cosmetic active ingredients due to their antioxidant and skin-protective properties. However, their instability and poor solubility limit their cosmetical application and effectiveness [1,2]. Microencapsulation in biocompatible polymers, such as alginate, arises as an excellent option to overcome these limitations by enhancing stability and enabling prolonged release [3]. **Objective:** This study aimed to evaluate the stability, bioactivity, and permeation of catechin, epicatechin, chlorogenic acid (CGA), neochlorogenic acid (NCGA), and their mixture in pure and encapsulated forms, using advanced 3D *in vitro* and *ex vivo* skin models, according to the European Regulation n.º 1223/2009. **Methods:** Polyphenols were encapsulated in sodium alginate by spray-drying (115/70 °C) and assessed by scanning electron microscopy (SEM), Differential scanning calorimetry (DSC), and Fourier transform infrared spectroscopy (FTIR). Antioxidant and antiradical activities were evaluated by Ferric Reducing Antioxidant Power (FRAP) and radical scavenging assays. Cytocompatibility was evaluated in keratinocytes (HaCaT) and fibroblasts (HDF). A 3D co-culture skin model was constructed and permeation results compared with *ex vivo* human explants coupled to Franz diffusion cells and a reconstructed human epidermis model (SkinEthic™). **Results:** Encapsulation yielded stable microparticles (37-53%) with improved thermal stability. Antioxidant/antiradical activities significantly increased, particularly for catechin, epicatechin, and CGA, demonstrating synergistic effects in the mixture. Encapsulated polyphenols presented higher cell viabilities (> 60% in HaCaT and > 80% in HDF), in comparison with the pure forms. Permeation studies revealed reduced compound diffusion and sustained release, particularly for catechin and epicatechin. *Ex vivo* human skin explants revealed minimal permeation of flavan-3-ols, while CGA, NCGA and the mixture surpassed 50% permeation after 24 hours of exposure. Furthermore, enhanced viability was observed following polyphenol applications in the constructed 3D and SkinEthic™ models, while tissue integrity was preserved (**Figure 1**). **Conclusions:** Alginate microencapsulation enhanced the stability, bioactivity, and safety of polyphenols, while enabling controlled skin delivery. The combined use of advanced 3D and *ex vivo* models provides relevant insight into polyphenols' permeation and supports their use as innovative cosmetic ingredients.

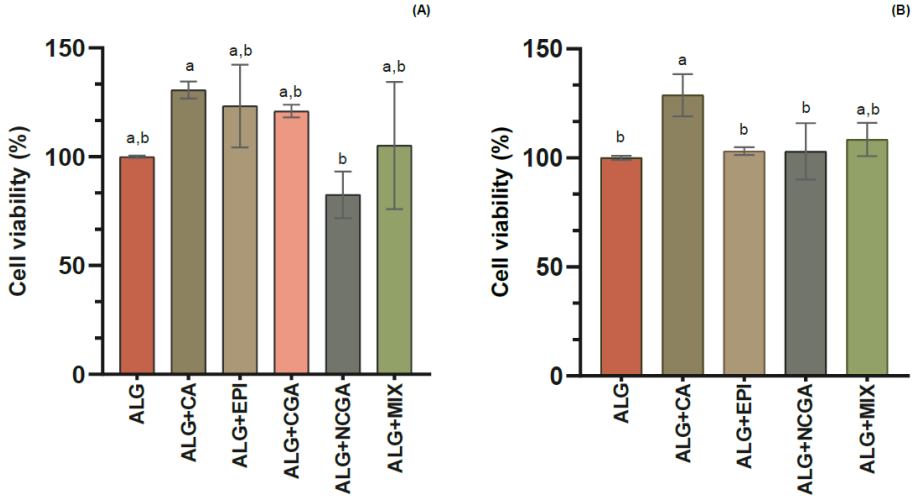

Figure 1. MTT assay with (A) 3D co-culture model and (B) SkinEthic™ RHE model after exposure to alginate microparticles. Results are expressed as mean ± standard deviation (SD) (n=3). Different letters (a,b) indicate significant differences between the compounds (p<0.05).

Keywords: 3D skin model; permeation studies; polyphenols

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