Enzyme-Activated Polymeric Composite Hydrogels for Enhanced Transdermal Delivery of Encapsulated Phycocyanin

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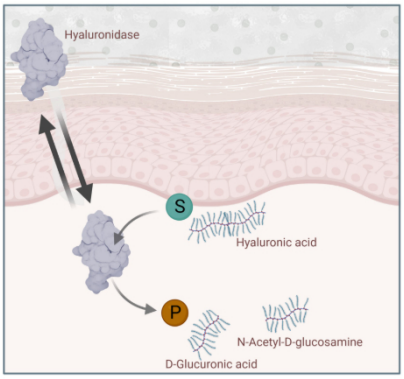
Skin disorders affect nearly 900 million people worldwide and remain a major unmet clinical need due to the limited efficacy of conventional topical therapies. Natural bioactive compounds (NBCs), such as phycocyanin (C-PC), exhibit potent antioxidant and anti-inflammatory activity [1], however, their clinical translation is hindered by poor physicochemical stability and limited transdermal penetration [2].

Herein, we report a multifunctional composite hydrogel platform that integrates polymeric microcapsule encapsulation, tunable poly(vinyl alcohol) (PVA)-based hydrogel networks, and enzymatic surface functionalization to enhance dermal delivery. C-PC was encapsulated into polymeric microcapsules with an encapsulation efficiency of 47%, enabling improved stability and controlled release. The microcapsules were incorporated into hydrogels based on PVA and its modified systems, including PVA–sulfobetaine methacrylate (PVA–SBMA) and PVA–propylene glycol (PVA–PG), allowing systematic tuning of hydration, mechanical properties, and handling behavior.

To overcome the barrier function of the skin, hyaluronidase was immobilized within the hydrogel system, providing localized enzymatic activity at the hydrogel and skin interface. This enzymatic functionality selectively modulates extracellular matrix components, facilitating enhanced permeation without compromising material integrity. The resulting hydrogels were characterized in terms of swelling behavior, structural integrity and enzyme activity demonstrating cohesive, transferable matrices suitable for topical application. The performance of the platform was evaluated using Franz diffusion cell studies. The aimed enhancement is based on the synergistic combination of microcapsule-mediated stabilization, a highly hydrated hydrogel environment, and enzyme-assisted modulation of the skin barrier.

Overall, this work introduces a modular and multifunctional dermal delivery platform that combines encapsulation, hydrogel design, and enzymatic activation, offering a promising strategy for the effective transdermal delivery of sensitive NBCs.

Keywords:
composite hydrogels, transdermal delivery, natural bioactive compounds, enzyme functionalization, phycocyanin, Hyaluronidase



Schematic illustration of the reaction of hyaluronidase which catalyses the hydrolysis of hyaluronic acid (S: substrate) through cleave linkages between N-acetylglucosamine and glucuronate (P: products), as well as enzyme association/dissociation equilibrium between the HG and the skin.

References:

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