Quercetin-loaded Hydrogels for Skin Ageing and Inflammation

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Nature has led to the discovery of interesting compounds, with noteworthy applications in nanotherapeutics. Particularly from the marine environment, sodium alginate (SA) is a marine polymer that demonstrated the ability to form hydrogels, an interesting property for the development of cutaneous nanoformulations [1]. SA is commonly combined with other polymers to attain specific hydrogel properties; such it is the case of poly(vinyl) alcohol (PVA). In fact, hydrogels have been gaining interest among research groups for cutaneous application instead of other conventional dosage forms (creams, lotions, ointments), and the main advantages are related with higher water content and non-greasy texture, better skin feel and cooling effect, better skin hydration and longer drug absorption, reduced transepidermal water loss, skin biocompatibility and better patient compliance [2, 3]. Quercetin, a natural polyphenolic flavonoid commonly found in fruits and vegetables, is widely known for its strong anti-inflammatory and antioxidant activity. Particularly in skin research, quercetin was reported as active against melanoma, inflammation, and skin ageing [4].
In this work, the potential of quercetin-loaded SA/ PVA hydrogels was explored as a non-invasive nanostrategy to overcome skin inflammatory diseases and skin ageing. To explore the combination of these two polymers, 3 different SA/ PVA blended hydrogel ratios were prepared (1:1, 2:1 and 1:2) and the same combinations were formulated to incorporate quercetin in its structure, proceeding to its physicochemical characterization and skin permeation profile.
The designed hydrogels were found to have pH around 6, which is adequate to for skin application, and revealed a quercetin entrapment efficiency of 60%. Complementary analysis of swelling assay was performed for 3 hours, concluding that the higher amount of sodium alginate in the hydrogel leaded to a higher swelling capacity. All hydrogels were analysed by Fourier-transformed Infrared Spectroscopy, morphological analysis was performed by Scanning Electron Microscopy, as well as elemental analysis by Energy-dispersive X-ray spectroscopy. Aiming the cutaneous application of the formulations, all unloaded and quercetin-loaded hydrogels were submitted to rheology studies. The main observations revealed pseudoplastic behaviour, no evidence of thixotropy, good resistance to deformation and profile maintenance with temperatures ranging from 20°C up to 40°C. Quercetin loaded SA/ PVA blended hydrogel exhibited antioxidant activity, confirmed by radical scavenging assays (ABTS and DPPH).
To evaluate the penetration/ permeation of quercetin through the skin, two different models were used: the Human *stratum corneum* Phospholipid Vesicle-based Permeation Assay and the isolated *stratum corneum* from pig ear skin. Both model barriers revealed high penetration and low permeation of the flavonoid at the end of 24 hours. This behaviour will allow a local and prolonged skin effect, making the use of these hydrogels a good solution to consider for the treatment of skin ageing and inflammation.

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