

# Hydroxypropyl methylcellulose hydrogel of berberine chloride-loaded escinosomes: dermal absorption and biocompatibility

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Aim of this work was to prepare and characterize new nanocarrier-loaded hydrogel formulations for topical application, using hydroxypropyl methylcellulose (HPMC) and special nanovesicles, the escinosomes [1]. The combination of the two technological strategies, nanocarriers and hydrogels, was selected to circumvent some drawbacks of nanovesicles and develop stable and efficient skin-delivery systems [2]. HPMC is a derivative of cellulose with a wide range of physical and chemical properties, forming suitable hydrogel for dermatological applications. Escinosomes are a new vesicular carrier made of escin (ESN), a natural bioactive saponin clinically used for the anti-edematous and anti-inflammatory effects, plus phosphatidylcholine. Escinosomes are able to maintain the hyaluronidase inhibition activity of ESN, and load other active molecules such as berberine chloride (BRB), a natural quaternary isoquinoline alkaloid traditionally used for various therapeutic effects. BRB-loaded escinosomes were then entrapped in the polymeric matrix of HPMC and they were studied for drug release, dermal permeation, viscosity and biocompatibility properties. BRB did not affect ESN release and the low ESN release from the escinosome hydrogels confirmed the strong ESN interaction with the vesicular bilayer. Permeation profiles of aqueous ESN/BRB dispersions and escinosomes were compared with the corresponding hydrogels, showing a higher residence time of the HPMC-hydrogel. Moreover, the viscosity measurements evidenced their suitability for topical applications. Thus, the new escinosome HPMC-hydrogel formulations combine the advantages of a modified release and an increased transdermal permeability (escinosome components), with better viscosity properties (polysaccharide matrix). In addition, the developed escinosome HPMC-hydrogels were very stable with a very good safety profile, since biocompatibility studies showed no potentially hazardous skin irritation.

[1] Vanti, G., Bani, D., Salvatici, M. C., Bergonzi, M. C., & Bilia, A. R. (2019). Development and Percutaneous Permeation Study of Escinosomes, Escin-Based Nanovesicles Loaded with Berberine Chloride. *Pharmaceutics*, 11(12), 682.

[2] Elnaggar, Y. S., El-Refaie, W. M., El-Massik, M. A., & Abdallah, O. Y. (2014). Lecithin-based nanostructured gels for skin delivery: an update on state of art and recent applications. *Journal of controlled release*, 180, 10-24.

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