HYALURONIC ACID DERIVATIVE MICELLES AS OCULAR PLATFORMS TO DRUG RELEASE AND CORNEAL PERMEATION

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In traditional ocular formulations, only small amount of the administered drug penetrates the cornea to reach the intraocular tissue. One approach to improve the drug ocular bioavailability was to develop colloidal drug delivery systems. Polymeric micelles seem to be very promising for their capacity to dissolve a variety of hydrophobic drugs by enhancing their water solubility and so their bioavailability. They are able to increase ocular drug permeability due to interact with the complex corneal structure.

Considering the advantages to use mucoadhesive polymer to increase drug residence time on the ocular surface, the aim of this work was to prepare hyaluronic acid-based micelles as a platform to release corticosteroids on the ocular surface. Three amphiphilic derivatives of hyaluronic acid (HA), bearing different amount of hexadecylamine chains (C_{16}), were synthesised and characterized. These are able to form micelles by using the co-solvent evaporation method. All HAC_{16} derivatives have shown the ability of durable mucoadhesive interactions and resulted potentially useful for corticosteroids encapsulation. Drug-loaded micelles were prepared and characterized in term of drug loading amount and particle size. Moreover, the *in vitro* drug release studies from micellar systems were carried out in comparison with the dissolution profile of the free drug suspension. Cytocompatibility studies also were performed with HCEpiC cells.

HAC_{16}b (DD_{C16}mol%=12%) micelles are selected as the best nanosystems, and their capacity to improve the drugs permeability across corneal barrier are evaluated. Thus, the *ex vivo* permeation studies were conducted using bovine corneas and Franz type diffusion cells.