Thiolated hydroxypropyl- β-cyclodextrin as a promising mucoadhesive tool to prolong poorly soluble drugs ocular residence time

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Abstract

Therapeutic efficacy of powerful active ingredients is limited by poor eye bioavailability mostly due to blinking reflex and nasolacrimal drainage (1). The purpose of this study was to synthesize a mucoadhesive thiolated hydroxy-propyl-β-cyclodextrin (HPβCD) able to prolong the ocular residence time of the non-soluble model drug dexamethasone (Dex).
A microwave-assisted method with thiourea in acid conditions led to HPβCD thiolation. HPβCD-SH was then purified via size exclusion chromatography and characterized via ^{1}H NMR spectroscopy.
The modified β-CD was evaluated for thiol content, drug inclusion properties, viscoelastic and mucoadhesive behavior. In the end, an Irritation test and the elimination kinetics test from tear fluid, have been performed on New Zeland albino rabbits.
HPβCD-SH oligomer displayed 150 ± 50 µmol thiol groups per gram. The thiolated product did not show any cytotoxicity to Caco-2 cells at a concentration of 0.5% (m/v) within 24 h. The dynamic viscosity was increased up to 2.2-fold within 60 minutes at 37 °C, as confirmed by microrheological tests. Moreover, HPβCD-SH displayed long mucoadhesion in *ex-vivo* assays, with more than 80% of product retained on the ocular surface after 2 h 30 min. *In vivo* tests in rabbits confirmed *in vitro* results as mean residence time (MRT) and maximum residence time (RT max) were increased 4- and 6-fold, respectively, compared to pristine HPβCD.
According to these results, thiolated HPβCD might be a promising tool to provide prolonged ocular residence time of poorly soluble drugs like Dex. *In vivo* evaluations of drug corneal permeation are in progress.

Biography

[1] Grassiri, Brunella, Zambito, Ylenia and Bernkop-Schnürch, Andreas. Strategies to prolong the residence time of drug delivery systems on ocular surface. Advances in Colloid and Interface Science 2021, Vol. 288, 102342.