Chitosan/SBE-β-CD NPs with external coating of thiolated hyaluronic acid for ophthalmic delivery of Indomethacin

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Indomethacin is topically administered for the treatment of conjunctivitis, uveitis and inflammation of posterior segment. It is currently available as 0.1% 2-Hydroxypropyl-beta-cyclodextrin (HP- β-CD) eye drop, however subjected to the major drawbacks that hamper its bioavailability: nasolacrimal duct draining, reflex blinking and low volume of conjunctival sack. Aim for the project was the creation of nanoparticulate system to improve residential time of Indomethacin in the conjunctival sack, enhancing the solubility, stability and permeability of the drug. The nanoparticles (NPs) were obtained through ionotropic gelation technique, exploiting interaction between positively charged amino group of chitosan and negatively charged sulphate group of Sulfobutylether-β-Cyclodextrin (SBE-β-CD). Chitosan was used for its biosimilar properties and the cyclodextrin for its well-known advantages derived from host-guest complexation. The NPs were external coated with Thiolated Hyaluronic acid to improve their mucoadhesive properties. The free thiol groups of cysteamine derivatives are able to form disulphide bonds with cysteine rich domains of mucin, hence enhancing the residential time of the delivery system in the conjunctival sack. The NPs were morphologically characterized through Size (340 ± 7 nm), Z-potential (+18,3 ± 0,4 mV), NMR, IR, DSC. The mucoadhesive properties of the NPs were evaluated using texture analyser with ex-vivo studies on chicken's trachea and oesophagus. Further studies were conducted with Curcumin loaded NPs for fluorescence studies after artificial tear wash-off. The irritability and toxicity effects of NPs were disclaimed with HECAM and ICE tests. NPs improved drug permeability, while maintaining a similar release profile, sustained over time, to the commercially available cyclodextrin based eye drop. The developed NPs show increased residential time in conjunctival sack, drug stability and permeability, no irritancy and toxicity for local administration, making them an optimal and innovative drug delivery system for ocular release.