Biodegradable nanospheres containing Sulfobutyl-ether-β-cyclodextrin for levofloxacin ocular delivery

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Levofloxacin (LVF) is an antibacterial drug approved for the treatment of ocular infections. However, due to the low ocular bioavailability, high doses are needed causing so bacterial resistence. Polymeric nanospheres (NPs) loading antibiotic drugs represent the most promising approach to eradicate ocular infections and to treat pathogen resistance. In this study, we have developed chitosan NPs based on sulfobutyl-ether-β-cyclodextrin (CH/SBE-β-CD NPs) for ocular delivery of LVF. CH/SBE-β-CD NPs loading LVF were characterized in terms of encapsulation parameters, morphology, and sizes, in comparison to NPs produced by CH gelation with tripolyphosphate (CH/TPP NPs). The interaction between LVF and SBE-*β*-CD was investigated in solution by nuclear magnetic resonance (NMR) and UV-vis spectroscopy. They evidenced the formation of LVF/SBE-*β*-CD inclusion complex in 1:1 molar ratio, that significantly influenced the encapsulation parameters of NPs, producing a consistent increase of encapsulation efficiency and drug loading compared to CH/TPP NPs. NPs were homogenous in sizes with a hydrodynamic radius between 80-170 nm and polydispersity index of less than 20% which make them suitable for ocular administration. Positive zeta potential (ζ) values of all prepared NPs (about +26 mV and +24 mV for CH/SBE-*β*-CD NPs and CH/TPP NPs, respectively) could promote their interaction with the negatively charged ocular tissue, increasing their residence time and consequently LVF efficacy. *In vitro*, antibacterial activity against Gram-positive and Gram-negative bacteria showed a double higher activity of CH/SBE-β-CD NPs loading LVF compared to the free drug, suggesting that chitosan NPs based on SBE-β-CD could be a useful system for the treatment of ocular infections.