Formulation and In Vitro Characterization of Ketorolac Tromethamine—Loaded Nanoparticles for Sustained Ocular Delivery

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Purpose
Formulation and characterization of ocular ketorolac tromethamine (KT)-loaded nanoparticles for sustained drug delivery and improved transcorneal permeation.

Methods
Bioadhesive KT-loaded nanoparticles for ocular delivery were formulated with different polymers using different formulation techniques. Chitosan (CS) nanoparticles were prepared by ionic gelation method using tripolyphosphate (TPP) as an anionic cross linking agent. Alginate (ALG)/CS nanoparticles were prepared by the ionotropic pre-gelation of alginate with CaCl2 and polycationic crosslinking with chitosan. Eudragit RL100 nanoparticles were prepared by nanoprecipitation technique. KT-loaded nanoparticles were evaluated for particle size, zeta potential, entrapment efficiency and in-vitro release of KT. The formulae with optimum physicochemical characteristics were tested for ex-vivo transcorneal permeation and compared with the marketed eye drops (Acular®).

Results
CS/TPP nanoparticles formulation prepared with 0.45mg/ml CS and 0.6mg/ml TPP was selected for further studies due to optimum particle size (565.1 nm), zeta potential (+10.5 mV) and entrapment efficiency of 41.75%. ALG/CS nanoparticles formulation prepared with 0.2% ALG, 0.2% CS and 0.5% CaCl2 showed the smallest particle size (334.7 nm) with positively charged zeta potential (+21.4 mV) and entrapment efficiency of 32.81%. KT-loaded Eudragit RL100 nanoparticles prepared with acid buffer (pH 3) as aqueous phase and ethanol as organic phase in ratio of 1:2 and a drug to polymer ratio of 1:1 showed the maximum entrapment efficiency (91.61%) and optimum particle size (252.8nm) with positive zeta potential (+16.8 mV). All nanoparticles formulations showed a sustained release of KT. A transcorneal permeation study was carried out for nanoparticles formulae with optimum physicochemical characteristics. All tested formulae exhibited higher transcorneal permeation through the excised goat cornea as compared with KT-marketed eye drops (Acular®).

Conclusion
The KT-loaded nanoparticles prepared with different types of polymers demonstrated high efficacy in sustaining the KT release profile and improving its ex-vivo transcorneal permeation.