Preparation, in vitro and in vivo evaluation of solid-in-oil dispersion-based formulation the anti-glaucoma drug, timolol maleate

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ABSTRACT

Lowering Intraocular pressure (IOP) is a main therapeutic objective in glaucoma patients because IOP is an important risk factor for glaucoma progression. The objective of this work was to formulate and evaluate, in vitro and in vivo, a stable and effective Solid in Oil (S/O) topical formulation of the antiglaucoma drug, timolol maleate (TM). S/O dispersions were prepared by emulsification of aqueous TM solutions in cyclohexane using different amount of the span 85 then lyophilizing the emulsion to produce TM – Span 85 complexes. The complexes were then dispersed in castor oil using tip sonicator to produce S/O nanodispersions. S/O nanodispersions were evaluated in terms of particle size, polydispersity index, encapsulation efficiency, morphology, physical stability, as well as transcorneal permeation and accumulation of TM. In addition, the in vivo tolerability and efficacy of the prepared formulation in lowering intraocular pressure were evaluated in rabbits.

Spherical nanoparticles of TM with a particle size of about 134-155 nm were successfully prepared and found to be physically stable. The encapsulation efficiency was high and was found to be dependent on the level of Span 85 used.

In comparison to TM solution, S/O nanodispersion enhanced TM permeation and decreased accumulation in transcorneal diffusion studies. In addition, application TM S/O nanodispersion onto rabbit eyes resulted in a significant reduction in IOP in comparison to TM aqueous solution.