Nanogels for Sustained Ocular Delivery of Brimonidine for Treatment of Glaucoma

Dileep R. Janagam.[1], Linfeng Wu.[1], Junjie Zhang [2], Tao L. Lowe[1]
[1]Department of Pharmaceutical Sciences, University of Tennessee Health Science Center,
[2] Department of Pharmaceutical Sciences, Henan Eye Institute

Statement of Purpose

Glaucoma is a group of eye conditions that can damage the eye's optic nerve due to increased intraocular pressure and result in vision loss and blindness. It is one of the main causes of blindness in the United States. Brimonidine is an effective drug for treating glaucoma, but its efficacy is hampered by the ocular barriers and tears film drainage occurring continuously in the precorneal area. In this study we have developed and evaluated a series of biodegradable polymeric nanogel systems that have potential to enhance brimonidine's permeability across ocular barriers, and sustain release of brimonidine after topical administration.

Methods

A series of hydrolytically degradable nanogels composed of N-isopropylacrylamide and 2-hydroxyethylmethacrylate-lactatedextran were synthesized with different crosslinking density, hydrophobicity, and charge density. The size and morphology of the nanogels were measured by DLS and AFM. The degradation of the nanogels was characterized using FTIR and AFM. Brimonidine was loaded into the nanogels during the synthesis process. The release of brimonidine from the nanogels was monitored by Q-TOF. Human microvessel endothelial cells and fetal human retinal pigmented epithelial cells grown on polyester Transwell filters are used as *in vitro* BRB models. Porcine sclera, choroid-RPE and sclera-choroid-RPE tissues are used as *ex vivo* sclera/BRB models. Porcine cornea tissues are used as an *ex vivo* cornea model. The permeability of the nanogels alone and the effects of the nanogels on the permeability of brimonidine across the *in vitro* and the *ex vivo* BRB, and the *ex vivo* cornea are investigated. The *in vivo* ocular distribution of the nanogels was studied post one day subconjunctival injection.

Results

FTIR results confirm the successful synthesis and hydrolytic degradation property of the nanogels. DLS and AFM measurement demonstrate that the sizes of the nanogels are around 40-50 nm at 37 °C. The nanogels can sustain brimonidine release, and increase the permeability of brimonidine across the *in vitro* and the *ex vivo* BRB, and *ex vivo* cornea. The nanogels can reach the cornea, iris-ciliary body, retina and vitreous after subconjunctival injection.

Conclusion

The developed degradable and non-toxic nanogels may have great potential to achieve sustained brimonidine across ocular barriers via both subconjunctival and topical administrations to treat glaucoma.