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Electrospun brinzolamide carrier – potential antiglaucoma drug delivery platform

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Introduction

Pharmacological treatment of glaucoma is based on aqueous solutions and suspensions. Their precorneal residence time is very short, which results in low drug bioavailability and makes frequent dosing obligatory. The drug spreading over the eye is partially absorbed to the bloodstream, which further reduces the drug rate absorbed at the destination site [1].

In the last few years attention has been drawn to the potential nanofibers in ophthalmology [2,3]. Nanofibers are well known for providing sustained and controlled delivery of active ingredients [4]. Non-woven of any shape can be put near the pupil. When made of proper materials, they can be less prone to clearance and provide more localized delivery than traditional formulations [3].

An electrospun delivery system of poorly soluble antiglaucoma drug brinzolamide (BRZ) based on mucoadhesive hydroxypropyl cellulose (HPC), polycaprolactone (PCL) and beta-cyclodextrin (β-CD) has been formed. Cyclodextrins improve water solubility of hydrophobic ingredients, increasing its permeability to target tissues [5]. In combination with hydrophilic and hydrophobic polymer, a sustained drug delivery is expected to be achieved. To evaluate the drug delivery system potential basic studies of the nanofibers, complexation ability between cyclodextrin and brinzolamide, and permeability of brinzolamide through lamb corneas were performed.

Experimental Methods

HPC/PCL/β-CD/BRZ nanofibers have been formed via electrospinning from hexafluoroisopropanol solutions. Their morphology was studied using scanning electron microscope (SEM).

Phase solubility study was performed on a series of aqueous solutions. Additional samples containing HPC beside BRZ and β-CD were prepared to evaluate HPC influence on complexation. After incubation in elevated temperature the samples were filtered and brinzolamide amount was measured using high performance liquid chromatography (HPLC).

Supramolecular structure study of the complex was performed using Fourier transform infrared spectroscopy with attenuated total reflection sampling technique (ATR FTIR) in search of changes in spectra compared to pure components indicating interaction between them.

Brinzolamide permeation from the nanofibers through lamb corneas was studied using Franz diffusion cells. Corneas with nanofibrous samples on top were mounted on acceptor chambers filled with phosphate buffered saline (PBS). Donor chambers were put on top and the cells were put in water baths on heated magnetic stirrers. At predetermined time points samples were collected and replaced with pure PBS. Commercial brinzolamide solution was tested for a reference; 15 repetitions were made for each delivery platform to obtain reliable data. Brinzolamide content in the samples was measured using HPLC.

Results and Discussion

Proper morphology fibers with a diameter from several dozen nm up to about 1 μm were obtained using selected processing/materials parameters.

Cyclodextrins increased brinzolamide solubility in PBS, although above a certain β-CD/BRZ ratio BRZ solubility started to decrease, probably due to complexes aggregation. HPC significantly increased brinzolamide solubility.
The complex spectrum was similar to the pure β-CD spectrum; among others the peak corresponding to OH stretching vibration was narrowed and shifted, which is interpreted as evidence of a successful complexation.
Permeation of BRZ from the nanofibers was slow and sustained. There was no burst release. Permeation profiles of BRZ from the nanofibers and commercial solution were similar. Considering large drug loss from the later and significantly reduced loss expected with the nanofibers, the system potential for a more effective prolonged delivery is very high.

Conclusion

Complexation takes place between β-CD and BRZ, favored by HPC. Effective gradual BRZ permeation from the nanofibers through animal corneas is achieved. In further study mucoadhesion of the nanofibers will be evaluated.

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