Non-woven Electrospun Micro/Nanofibers Inserts for Sustained Topical Ocular Drug Delivery

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Background: Ocular inserts are a promising strategy to achieve sustained drug delivery to the anterior segment of the eye. Common challenges with ocular inserts include corneal abrasion, accidental loss or sticking out due to poor muco-adhesiveness, allergic reaction and inflammation. However, electrospun patches have a high potential to overcome some of these issues due to their softness, strong mucoadhesiveness and improved biocompatibility. Moreover, their ability to achieve high drug loading and tailored thickness make them versatile in both the engineering and medical field. The aim of this research is to develop a small and effective ocular insert in the *cul-de-sac* which can achieve sustained drug delivery for one week in treating anterior segment ocular diseases.

Methods: PVA and PCL nano/microfibers were fabricated to deliver hydrophilic and hydrophobic anti-inflammatory agents such as triamcinolone acetonide and bromfenac sodium. Non-woven inserts were fabricated via the electrospinning process. PVA fibers were further crosslinked by glutaraldehyde after fabrication to avoid the rapid swelling and breakdown. Co-axial fibers were fabricated for further optimization to achieve pre-defined physiochemical properties. TEM and SEM were used to identify the micro-structure of the inserts. Thermal analysis was carried out to check possible solvent residue and polymorph. Thickness was recorded before and after swelling. Content analysis and in-*vitro* release were carried out and analyzed by HPLC. A procine-gastric model was used for the muco-adhesive test.

Results: PCL fibers tends to be several micrometers thick while PVA fibers are just 200-500 nanometers. Inserts with homogeneous nano-fibers were produced with a drug loading up to 40% by weight for both drugs. All inserts were highly hydrophilic according to the contact angle test despite the hydrophobicity of materials themselves, indicating the abundant capillary-like structures which act as potential tunnels for oxygen and water exchange. Inserts consisted of co-axial fibers and crosslinked fibers could remain a similar dimension after swelling for a week, while inserts made by uncrosslinked uni-axial fibers showed a thickness increase of around 50%. The inserts loaded with triamcinolone acetonide showed a sustained drug release for a week – with a 20-40% burst release followed by a 10-20% release per day. Inserts loaded with bromfenac sodium, on the other hand, showed a burst release higher than 60% with extremely slow follow release less than 0.1% per day. Electrospun inserts showed an average 73% higher rupture force compared with casting films in all cases, illustrating a better mucoadhesive property.

Conclusions: In this study, we developed coaxial electrospun nano/microfibers with predefined physicochemical properties to treat inflammation on the anterior ocular chamber. We demonstrated that co-axial fibers had better swelling properties and drug release pattern compared with normal nano-fibers.