Mucoadhesion and biological evaluation of brinzolamide-loaded electrospun nanofibers – *in vitro* and *ex vivo* assessment

O. Cegielska[1*], P. Sajkiewicz[1], M. Sierakowski[2]

[1] Laboratory of Polymers and Biomaterials, Institute of Fundamental Technological Research, Polish Academy Of Sciences, Warsaw, Poland, [2] Institute of Biological Sciences, Cardinal Stefan Wyszynski University in Warsaw, Warsaw, Poland
*ocegiels@ippt.pan.pl

Traditional topical ophthalmic medications have a major disadvantage of very short precorneal residence time and systemic penetration, and thus low drug bioavailability, requiring frequent dosing. Hydrophobicity of ophthalmic active ingredients is an additional difficulty for their effective delivery [1]. To overcome these challenges, nanofibers loaded with poorly soluble antiglaucoma drug brinzolamide (BRZ) based on mucoadhesive hydroxypropyl cellulose (HPC), polycaprolactone (PCL) and beta-cyclodextrin (β-CD), varying in PCL:HPC ratio, have been formed via electrospinning. Preferentially, the fibers would be placed close to the pupil as a nonwoven piece, and held in place by HPC interactions with the mucus [2]. In the multicomponent system, cyclodextrins were responsible for drug complexation, increasing its permeability to target tissues, and PCL for increasing mechanical properties of the carrier, which has been confirmed and reported previously [3].
The nonwovens, formed using previously selected parameters from hexafluoroisopropanol solutions [3], underwent mucoadhesion and drug permeation studies *ex vivo* using a sheep model (Figure 1), drug release study, cytotoxicity evaluation on L929 fibroblasts, and a modified pharmacopeial sterility test including UV-treated samples, to evaluate the possibility of bioburden reduction with UV light.
Relatively high mucoadhesive properties, increasing with HPC:PCL ratio as expected, and sustained drug permeation of therapeutic concentrations *ex vivo* for all formulations were confirmed. No undesirable cell response was noted for any formulation, and UV was found effective in eliminating the bioburden. Although the classic release test has shown burst release, we presume it helped reaching a concentration gradient necessary for permeation through corneas, making drug complexation and mucoadhesion key-factors for obtaining successful local delivery to the internal parts of the eye. We believe that the proposed electrospun materials containing HPC in majority can be an attractive alternative for traditional antiglaucoma medications.
The authors acknowledge funding provided by the Polish National Science Centre (NCN), grant number 2019/35/N/ST5/03882.

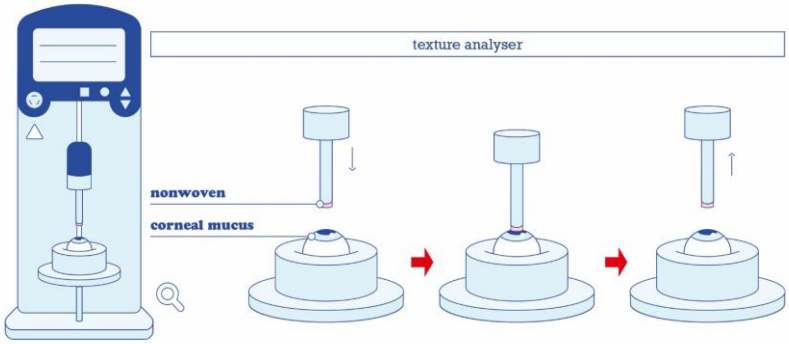

Figure 1. Experimental set-up for the evaluation of mucoadhesion of the nonwovens [3].

References

[1] V. Agrahari; A. Mandal; V. Agrahari; H.M. Trinh; M. Joseph; A. Ray; H. Hadji; R. Mitra; D. Pal; A.K. Mitra *Drug Delivery and Translational Research*, 2016, 6(6), 735-754.
[2] B. Chatterjee; N. Amalina; P. Sengupta; U.K. Mandal *Journal of Applied Pharmaceutical Science,* 2017, 7(05), 195-203.
[3] O. Cegielska; M. Sierakowski; P. Sajkiewicz; K. Lorenz; K. Kogermann *European Journal of Pharmaceutics and Biopharmaceutics*, 2022, 180, 48-62.