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Permeability Studies on the Ocular Absorbance of Nanostructured Materials Across the Cornea

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Introduction: The eye provides a variety of defense mechanisms, which protect the organ against numerous different substances. These mechanisms include the bony orbit, the eyelids and cilia, the tear film and nasolacrimal drainage, corneal and conjunctival epithelium, and a submucosal secretory immune defense. In order to overcome the strong physiological barriers, new drug delivery systems have been established, including the development of nano-carriers. However, it is known that nanostructured materials are able to invade cellular structures and trigger toxic reactions. **Methods:** For the establishment of an *in vitro* system, fluorescence-labelled carboxyl polystyrene particles (CPP 20 nm and 200 nm) were characterized in terms of their physico-chemical properties (size, distribution, agglomeration, surface charge) in different biological media (i. e. MQ-water, 0.9% NaCl and tear fluid) using a ZetaSizer Nano-ZS (Malvern). **Ex vivo** permeability studies were performed with static Franz diffusion cells. Donor and receiver compartment were separated by insertion of three weeks cultured excised human corneae. CPP (20 nm) were suspended in physiological NaCl, applied in concentrations of 100 µg/ml and 250 µg/ml and incubated for 6 hours. Samples were withdrawn from the sampling port of each cell and fluorimetrically analyzed. After 6 hours the tissue was fixed, frozen, sliced into 10 µm thin slides and observed with a fluorescence microscope. **Results:** Size and surface charge of the particles differed according to the medium. Particles suspended in tear fluid showed reduced surface charges and diameters three times higher, compared to those, suspended in MQ-water and 0.9% NaCl. This increase in particle size can not only be explained by partial aggregation of the particles but also by the fact that in biological fluids, proteins attach to the nanoparticle surface, which leads to the so called 'protein corona'. Histopathological Analysis showed that corneal epithelium and endothelium detached during prolonged storage and incubation. Fluorescent particles were seen in the entire corneal stroma. **Conclusion:** 20 nm CPP can penetrate through Bowman's and Descemet membrane and the entire corneal stroma. Corneae with shorter culturing times will be used for the assessment of the epithelial barrier function.

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