Simulation of Measurment of Corneal Permeability By Multi-Drop Method Using COMSOL Multiphysics®

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Abstract

Ocular drug delivery has always been a challenge due to the eye's unique physiology and anatomy. Barriers to drug delivery include static barriers such as corneal layers and dynamic barriers such as tear flow. Some of these effects are modeled and explained in this project. Here, the focus was to simulate the transport of a hydrophilic dye (drug analog), fluorescein after topical application on the ocular surface, in a novel multi-drop approach to estimate epithelial permeability (PE). PE is a clinically relevant maker to assess the health of the Cornea, especially its outermost layer epithelium. In the multi-drop method, first, one drop of 0.35% fluorescein was added on the ocular surface and the fluorescein clearance dynamics parameters were determined using a custom-built spot fluorometer of high depth resolution (~280 um) and high sensitivity. Next, two drops of 2% fluorescein were instilled 15 min apart, and fluorescence in the stroma was measured 15 min later. The penetration or transport of Fluorescein was simulated on COMSOL Multiphysics® software using the Transport of Diluted Species and the Mathematics modules in a one-dimensional model since the variation of concentration of fluorescein is only across the depth of cornea(in one direction). Fluorescein partitions into the epithelium from the tear film, where its concentration falls due to the presence of lipophilic membrane of the epithelium. Subsequently, Fluorescein is found to accumulate and diffuse in the epithelium, where the transport was modeled to be pseudo-steady state diffusion because of the presence of cytoplasm inside the cells. Fluorescein then partitions at the epithelial-stromal boundary into the stroma. Subsequently, fluorescein accumulates and diffuses in the stroma transiently (unsteady state). In summary, the transport of fluorescein was modeled after topical applications, and the concentration profiles obtained confer well with the previously established scientific findings. The simulation results facilitate the understanding of transport mechanisms and barriers for drug transport through the cornea and hence, may facilitate rational drug delivery strategies.

Figures used in the abstract

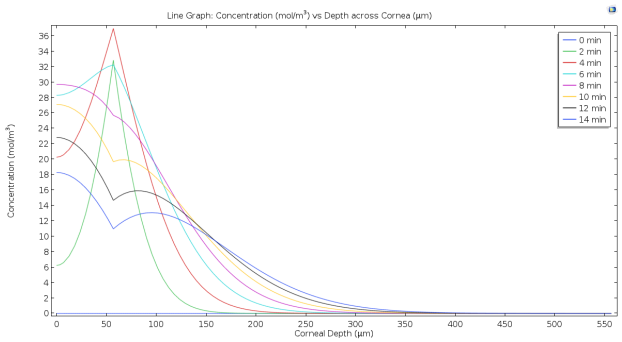

Figure 1: Spatial profile of Fluorescein concentration across Cornea after two loading drops