In Vitro-In Vivo Correlation And CFD Modeling Of Solution Permeation In A PermeaPad® 96-well Plates

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Abstract

Problem Statement
Topical ophthalmic formulations must achieve sufficient drug uptake across the corneal barrier. We investigated dexamethasone sodium phosphate (DSP) permeation from Newtonian vehicles in an in vitro PermeaPad® 96-well plate and established an in vitro-in vivo correlation (IVIVC) against rabbit aqueous humor data.
COMSOL Multiphysics® Use
We employed the CFD Module in COMSOL Multiphysics® v5.6 to simulate mass-transfer within the PermeaPad® plate geometry under no-shaking and continuous-shaking conditions (350, 500, 850 rpm). The Laminar Flow and Transport of Diluted Species interfaces were coupled to capture diffusive and convective transport. Simulations ran on a 3D axisymmetric model imported from CAD geometry; no Application Library models or LiveLink™ products were used, nor was the Application Builder invoked.
Experimental Setup
Two Newtonian donor vehicles were prepared:
• PBS (μ = 1 cP)
• TheraTears® (0.25 % NaCMC, μ = 10 cP)
Each contained 5 mg/mL DSP at pH 7.4 and 300 mOsm. PermeaPad® wells were used (n=6), under either no shaking or continuous shaking (Eppendorf ThermoMixer C). Aliquots were sampled over 120 min and analyzed by UV-Vis plate reader. Rabbit in vivo data (Rosenblum et al., 1967) provided aqueous-humor concentrations for IVIVC.
Results
• IVIVC: DSP permeation without shaking (Papp =7.1 $\times 10^{-6}$ cm/s) correlated linearly (R^2 = 0.9972) with rabbit in vivo levels (Figure 1).
• CFD Simulations: Under no shaking, simulated profiles (Figure 2a) matched experimental valuse ($\leq \pm 0.02$ % error). Incorporating induced orbital shaking convective flows (Figure 2b) generated nearly identical permeation curves across 350, 500, and 850 rpm, explaining why experimental shaking rates showed no significant differences (ANOVA, $p > 0.05$).
Conclusions & Implications
1. PermeaPad® no-shake experiments reliably predicts in vivo rabbit absorption of DSP.
2. CFD modeling with the CFD Module captures both diffusion-controlled and convection-enhanced mass transfer, revealing that under our conditions shear has minimal impact once transport is boundary-layer limited.
3. These results support the use of PermeaPad® in formulation screening and highlight the power of COMSOL Multiphysics® for in silico optimization of ocular drug delivery.

Reference

[1] Charles Rosenblum, Laboratory sciences, 1967, 234-237.