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Corneal and conjunctival drug permeability: systematic comparison and pharmacokinetic impact in the eye

Eva Ramsay[a,b,*], Eva M. del Amo[a], Elisa Toropainen[a], Unni Tengvall-Unadike[a], Veli-Pekka Ranta[a], Arto Urtti[a,b], Marika Ruponen[a]

[a] School of Pharmacy, Faculty of Health Sciences, University of Eastern Finland, 70211 Kuopio, Finland
[b] Centre for Drug Research, Division of Pharmaceutical Biosciences, Faculty of Pharmacy, University of Helsinki, P.O. Box 56, FI-00014 Helsinki, Finland

*** Correspondence to**: Eva Ramsay (Telephone: +358 29 4159636; Fax: +358 29 4159138). E-mail address: eva.ramsay@uef.fi (E. Ramsay).

Abstract

On the surface of the eye, both the cornea and conjunctiva are restricting ocular absorption of topically applied drugs, but barrier contributions of these two membranes have not been systemically compared. Herein, we studied permeability of 32 small molecular drug compounds across an isolated porcine cornea and built a quantitative structure-property relationship (QSPR) model for the permeability. Corneal drug permeability (data obtained for 25 drug molecules) showed a 52-fold range in permeability (0.09-4.70 x 10^{-6} cm/s) and the most important molecular descriptors in predicting the permeability were hydrogen bond donor, polar surface area and halogen ratio. Corneal permeability values were compared to their conjunctival drug permeability values. Ocular drug bioavailability and systemic absorption via conjunctiva were predicted for this drug set with pharmacokinetic simulations. Drug bioavailability in the aqueous humour was simulated to be less than 5% and trans-conjunctival systemic absorption was 34-79% of the dose. Loss of drug across the conjunctiva to the blood circulation restricts significantly ocular drug bioavailability and, therefore, ocular absorption does not increase proportionally with the increasing corneal drug permeability.

Key-words

Corneal permeability
Conjunctival permeability
Ocular drug delivery
Eye drops
Ocular absorption
Porcine
QSPR

Abbreviations

QSPR (quantitative structure-property relationship)
$LogD_{7.4}$ (the logarithm of the octanol-water distribution coefficient at pH 7.4)
$P_{app, CJ}$ (conjunctival permeability)
$P_{app, CO}$ (corneal permeability)
PSA (polar surface area)
HBD (hydrogen bond donor)