

## Accepted Manuscript

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PII: S0928-0987(18)30155-6

DOI: doi:[10.1016/j.ejps.2018.03.034](https://doi.org/10.1016/j.ejps.2018.03.034)

Reference: PHASCI 4463

To appear in: *European Journal of Pharmaceutical Sciences*

Received date: 8 January 2018

Accepted date: 31 March 2018

Please cite this article as: Eva Ramsay, Eva M. del Amo, Elisa Toropainen, Unni Tengvall-Unadike, Veli-Pekka Ranta, Arto Urtti, Marika Ruponen, Corneal and conjunctival drug permeability: Systematic comparison and pharmacokinetic impact in the eye. The address for the corresponding author was captured as affiliation for all authors. Please check if appropriate. Phasci(2017), doi:[10.1016/j.ejps.2018.03.034](https://doi.org/10.1016/j.ejps.2018.03.034)

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

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### 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 ( $0.09\text{-}4.70 \times 10^{-6}$  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<sub>7.4</sub> (the logarithm of the octanol-water distribution coefficient at pH 7.4)

P<sub>app, CJ</sub> (conjunctival permeability)

P<sub>app, CO</sub> (corneal permeability)

PSA (polar surface area)

HBD (hydrogen bond donor)

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