TOPICAL OCULAR MODEL

Development and Performance Evaluation of a semi-mechanistic PBPK Model for Topical Ocular Delivery of Pilocarpine and Timolol to Rabbit Eye

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Background

Eye drops and topical drug dosage forms are among the most convenient ocular drug administration routes, as they are non-invasive, self-administered and show high patient compliance. A predictive mechanistic model integrating eye anatomical and physiological parameters with the active pharmaceutical ingredient properties and formulation characteristics can assist with getting better insight into drug bioavailability and disposition in the interior eye which is currently lacking . *In vitro in vivo* extrapolation approaches linked with physiologically based pharmacokinetic (PBPK) modeling provides one powerful tool to serve this purpose. Such models can help reduce, refine and replace animal studies and inform and speed up ocular drug development.

Material and Methods

Figure 1: Flow chart of work stages

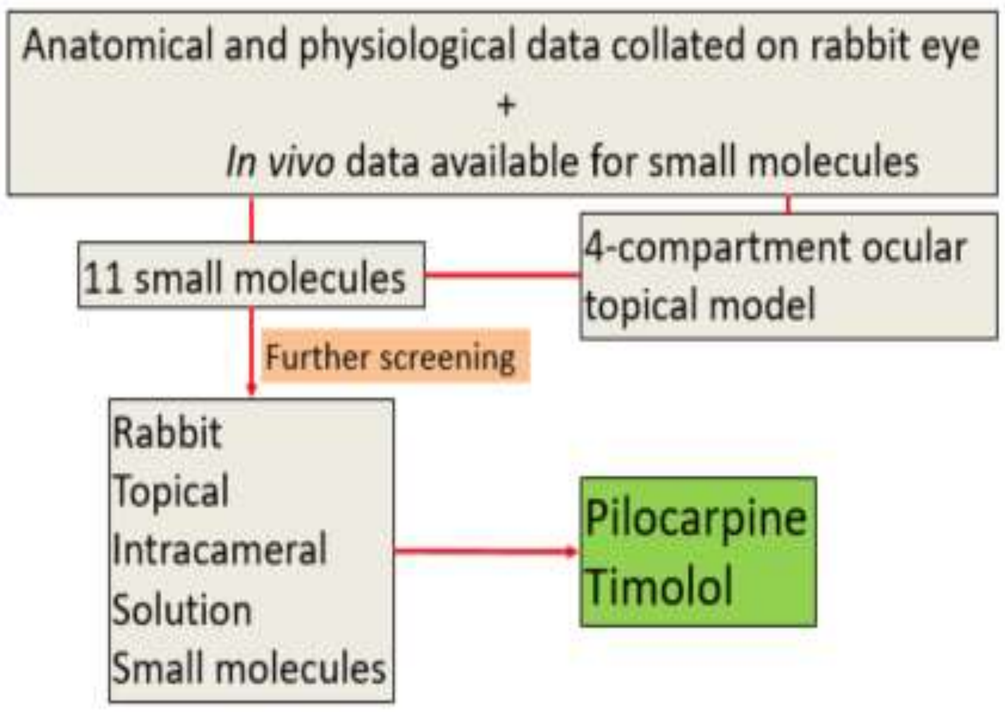

Table 1: The model parameters and their sources

Parameter	Timolol	Pilocarpine
Permeability from tear fluid to cornea	Estimated from corneal epithelial rabbit study	Fitted
Clearance from tear fluid to conjunctiva	Estimated from in-vivo precorneal clearance study	Estimated from in-vitro precorneal clearance study
Clearance from cornea to aqueous humor	Fitted	Fitted
Clearance from aqueous humor	Estimated from intracameral injection study	Estimated from intracameral injection study
Volume and flows in and out of the reservoir	Estimated from intracameral injection study	Estimated from intracameral injection study

Results and Discussion

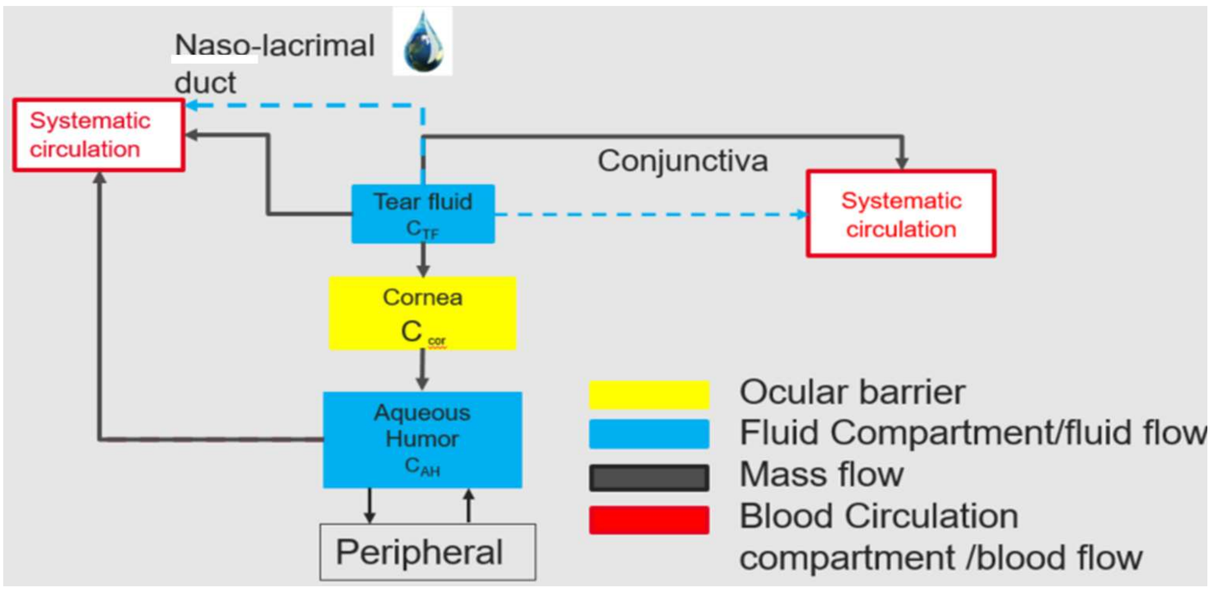

Figure 2: Topical anterior eye model for rabbit

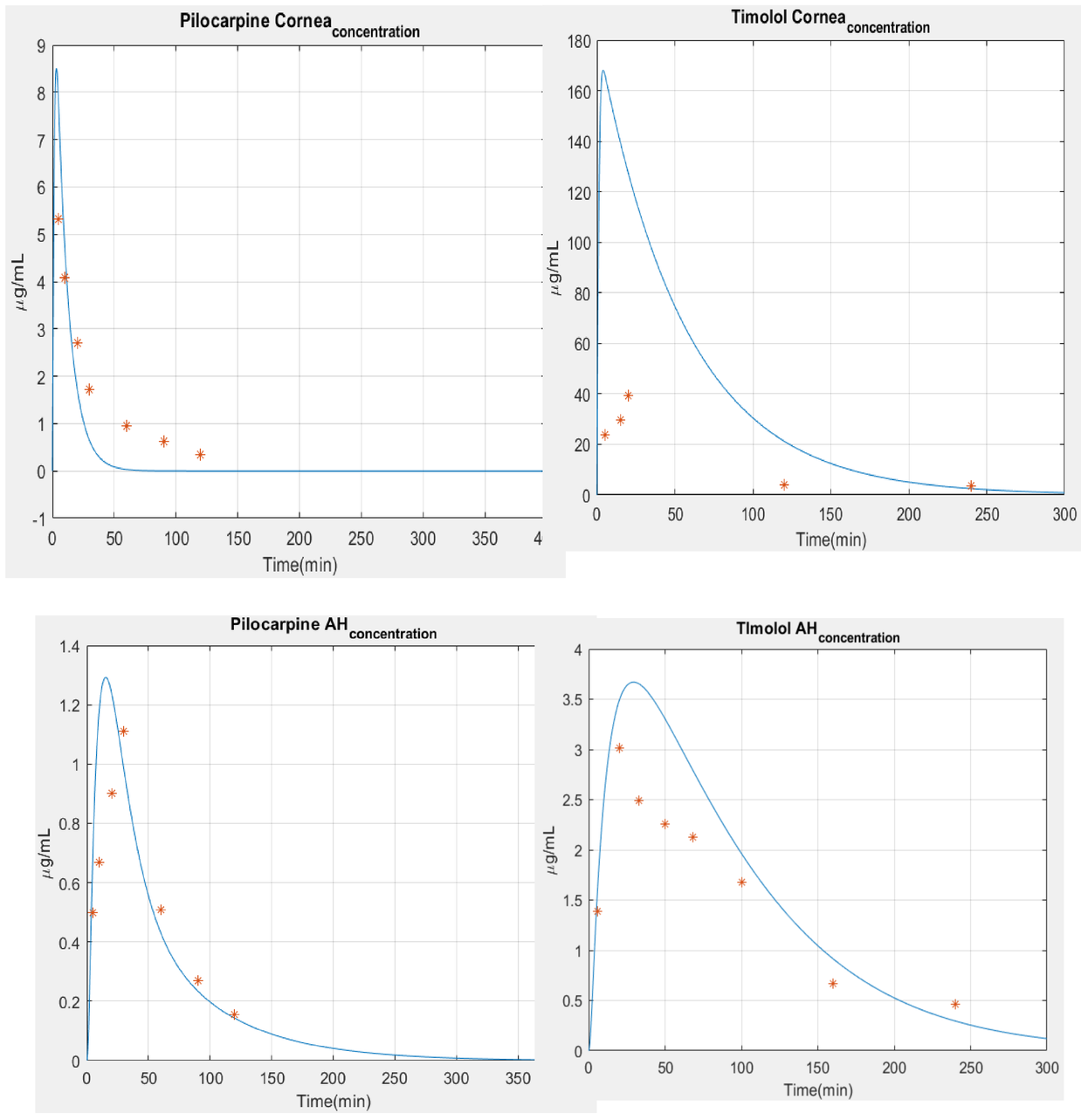

Figure 3: Cornea and Aqueous humor Concentration time profiles for Pilocarpine and Timolol

Conclusion

A semi-mechanistic PBPK model for topical ocular drug delivery of small molecules to rabbit eyes was developed. We aim to develop predictive models/algorithms to determine the rest of the model parameters and assess its performance for a wider range of drugs. In future work the model will be extended to make predictions in the human eye.

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