

# PHYSIOLOGICALLY RELEVANT MULTICOMPARTMENT MODELS TO PREDICT OCULAR DRUG DELIVERY FOLLOWING TOPICAL, SUBCONJUNCTIVAL, SUBRETINAL, AND INTRAVITREAL DELIVERY

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## ABSTRACT

This study aims to model the penetration pathways of low, medium, and high molecular weight ocular therapeutics as they enter the posterior segment of the eye following either bolus injection or sustained release delivery to the subconjunctival space, the subretina, intravitreally, or topically. Four compartmental models were developed and simulated for each of the delivery modalities using MATLAB (v R2022a). For the bolus injection simulations, subretinal, topical, subconjunctival, and intravitreal administration took the most to least amount of time to reach peak concentrations in the vitreous, respectively for the low molecular weight molecule simulation. Due to the inability of high molecular weight molecules to penetrate the eye topically, no concentration following topical administration was simulated for the medium and high molecular weight molecules; however, the other three curves follow the same trends. In all cases, the time to peak concentration was instantaneous for the bolus injection into the vitreous. The times to peak concentration are increasingly slower for the other routes as molecular weight increases. The numerical values of the peaks following sustained release simulations revealed that they were all less than those following bolus injections but had shallower drop-offs. All administration routes achieved the minimum threshold.

**Keywords:** targeted drug delivery; ocular drug delivery; compartmental modeling; pharmacokinetic modeling; bolus injections; sustained release drug delivery

## INTRODUCTION

### *General eye anatomy*

The eye is a complex organ with many specialized tissues. The anterior portion of the eye consists of the cornea, aqueous chamber and humor, lens, iris and ciliary body, and conjunctiva. The posterior portion consists of the vitreous body and humor, and retina (Figure 1). [1] This study focuses on the flow of ocular drugs from one of these tissues to the next as they diffuse towards the vitreous.

### *Importance and usage of ocular drug delivery*

The specific method of drug delivery is an important factor when choosing treatment options for various conditions of the eye. Systemic drug delivery, while sometimes effective, is difficult owing to potential side effects and poor penetration into the ocular tissues due to the blood retinal barrier. While diseases that affect the anterior portion of the eye are easier to treat as they are more readily accessible, it can be difficult to achieve adequate dosing to the posterior portion. Several