



embrane permeable low molecular weight drugs

- Drugs that are membrane permeable tend to be low molecular weight, e.g. steroids. Such drugs can clear both by aqueous outflow through the front of the eye (anterior pathway) and permeation through the back of the eye (RCS pathway).
- Low molecular weight drugs diffuse more quickly in the vitreous than biologics, such as antibodies, which are much larger. Once a low molecular weight drug is dissolved in the vitreous it will tend to clear within hours.
- Implants and suspensions are used to increase the duration of action of low molecular weight drugs.
- The PK-Eye can be used to evaluate dissolution and release profiles of permeable drugs that are formulated to increase their duration of action.

Use of the PK-EyeTM to determine the $t_{1/2}$ of permeable drugs

- To prolong the time of a permeable drug in the vitreous body requires a two-step strategy: (i) dissolution from a suspension or release of the drug from an implant into the vitreous and (ii) clearance of the drug through BOTH the front and back of the eye.
- Drug permeability can be calculated and then used to form *in vitro-in vivo* correlations (IVIVCs) to account for drug clearance from the back of the eye.

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PK-Eye + IVIVCs = ocular clearance of a permeable drug from a novel formulation

- Triamcinolone acetonide (TA, Kenalog[®]) is poorly soluble (~25 µg/mL) and is used clinically as suspension which slowly dissolves to extend its duration of action.
- TA is injected as a suspension (4.0 mg) into the PK-Eye. The extended clearance profile is due to the time needed for dissolution.



OPTCEUTICS

	data	human	clearand		
Parameters	In vit	ro	In vivo		
Dose of TA (mg)	4.0		4.0		
t _{1/2} (days)	28		15.6		
Value for 1 t _{1/2} (hours)	674		374		
Concentration of TA in the PK-Eye (µg/mL)	~ 25		-		
Amount of drug eliminated after 1 t _{1/2} (mg)	1.1		2.0		
Difference between in vitro and in vivo clearance: 0.878 mg					

TA half life measured in humans is 15.4-18.6 days.

IVIVC for TA

Email: admin@optceutics.com Website: www.optceutics.com

PK-Eye

Estimated