MATTEK
A BICO COMPANY

Corneal Drug Delivery | Application Note

PERMEATION ASSESSMENT OF EYE DROP FORMULATIONS USING EPICORNEAL

Objective

To evaluate drug permeability of topically applied eye drop formulations and monitor the effects on tissue viability with the EpiCorneal in vitro human tissue model.

Methods

Upon receipt, tissues were equilibrated overnight as per MatTek's EpiCorneal Drug Delivery Protocol. 50 µl of Xalatan® (Pfizer) or Monopost® (Thea Pharmaceuticals), both containing 50 µg/ml of latanoprost* prodrug, were topically applied to the tissues (n=3) and incubated at 37˚C, 5% CO_2 (Figure 1). Receiver solution samples were collected over a 12 hour period and analyzed for latanoprost acid using an HPLC-PDA method.

The apparent permeability (Papp) was calculated by the following equation:

$$Papp\ (cm/s) = J/(3600 \times C_{Don})$$

Where: J – the steady state flux ($nmol \cdot cm^{-2} \cdot h^{-1}$), C_{Don} - the initial donor compartment concentration of latanoprost acid ($nmol/cm^3$).

*Latanoprost acid is an effective agent in treating glaucoma. Latanoprost isopropyl ester prodrug is more lipophilic and better absorbed through the cornea.

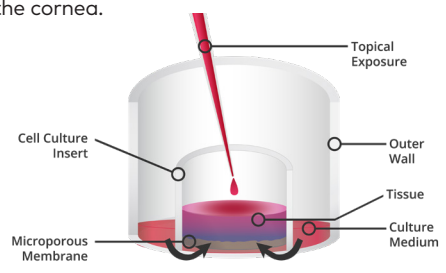

Figure 1. Schematic of EpiCorneal™ tissue model in cell culture inserts at air liquid interface. Test articles are topically applied and culture medium is replaced by receptor medium (assay medium or Krebs Ringer Buffer).

Results

Xalatan® eye drops (containing 0.02% BAC solution as a preservative) had a high permeation rate, Papp = 5.3 $x10^{-5}$ compared to Monopost® (a preservative-free formulation), Papp = 6.9 $x10^{-6}$ (Figure 2). Xalatan® eye drops had a significant effect on tissue viability (60.5% of negative control) and reduced the barrier property (Table 1).

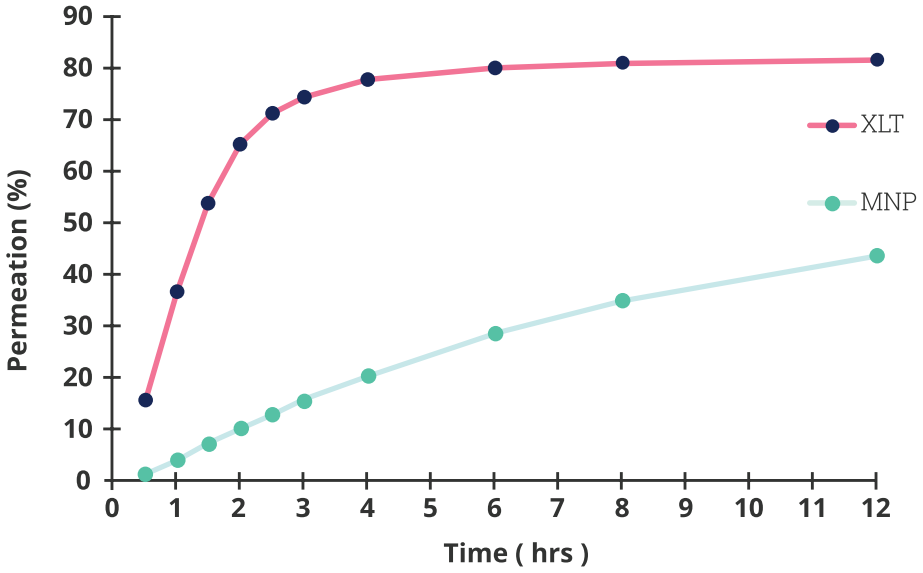

Figure 2. Latanoprost acid cumulative permeation profile in Xalatan® and Monpost® eye drops. - XLT, Xalatan; - MNP, Monopost.

Table 1. Summarized results of the Latanoprost Acid permeation

		Tissue permeability			Viability and barrier integrity[a]	
Formulation	Abbr.	Steady state period (h)	Steady state Flux ($nmol \cdot cm^{-2} \cdot h^{-1}$)	$P_{app.}$ ($cm \cdot s^{-1}$)	% Viability (MTT assay)#	% Permeability (LY assay)*
Xalatan®	XLT	0.5-1.5 (r=0.998)	3.67 (±0.20)	5.3 $x10^{-5}$	60.5 (±0.37)	2.32 (±0.30)
Monopost®	MNP	0.5-6 (r=0.996)	0.480 (±0.016)	6.9 $x10^{-6}$	83.8 (±7.40)	1.44 (±0.18)

LY, Lucifer yellow; MTT, MTT (3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) tissue viability assay
[a] Viability and barrier integrity were assessed at the completion of the permeability experiment; #, relative to the Negative Control; *, relative to the initial concentration (C_0)

Conclusion

Permeation assessment of topically-applied ophthalmic formulations withthe EpiCorneal in vitro human tissue model is suitable and comparable to an intact human cornea for ocular drug delivery studies.