Permeation Assessment of Latanoprost Eye Drop Formulations Using the EpiCorneal Tissue Model

Objectives

Latanoprost acid is an effective agent in treating glaucoma. Latanoprost isopropyl ester prodrug is more lipophilic and better absorbed through the cornea. Two commercial formulations of latanoprost eye drops were tested using the EpiCorneal in vitro human 3D tissue model to study corneal drug permeability and to monitor effects on tissue viability.

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. Receiver solution samples were collected over a 12 hr 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 ($nmol/cm^3$).

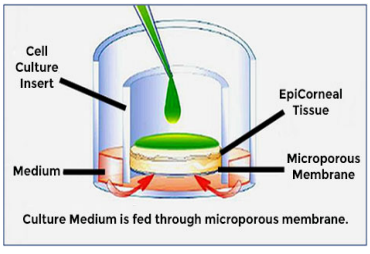

Figure 1: Schematic of EpiCorneal™ tissue model in cell culture inserts at air liquid interface. Test articles are topically applied and culture medium is replaced by receptor medium (assay medium or Krebs Ringer Buffer).

Results

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

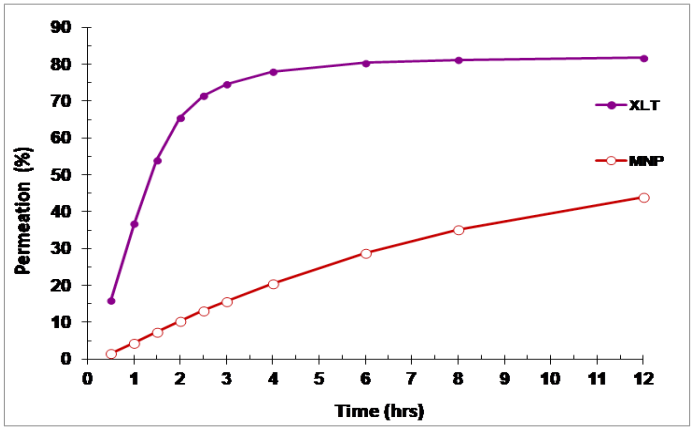

Figure 2. Latanoprost acid cumulative permeation profile in Xalatan® and Monpost® eye drops.
● - XLT, Xalatan; ○ - MNP, Monopost.

Conclusion

Tissue permeability of ophthalmic formulations with different properties was similar to that of the intact cornea. The EpiCorneal tissue model is suitable for eye permeation and biocompatibility studies.

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)	5.3×10^{-5}	60.5 (±0.37)	2.32 (±0.30)
Monopost®	MNP	0.5-6 (r=0.996)	0.480 (±0.016)	6.9×10^{-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)