



Permeation Assessment of Model Compounds and Ophthalmic Drugs Using the EpiCorneal Drug Delivery Assay

Objectives

To evaluate the corneal permeability of model compounds with a wide range of hydrophobicity, molecular weight, and excipients using the EpiCorneal in vitro human 3D tissue model.

Methods

Upon receipt, tissues were equilibrated overnight as per MatTek's EpiCorneal Drug Delivery Protocol. 400 µl of each formulation were topically applied to the tissues (n=3) and incubated at 37°C, 5% CO₂. The following parameters were used during tissue permeability analysis: permeation area - 0.6 cm², donor volume - 400 µl, acceptor volume - 300 µl, exposure time -180 min.

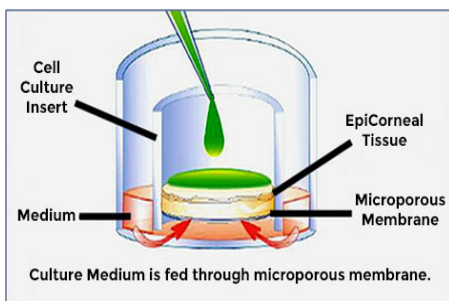


Figure 1: Schematic of EpiCorneal™ tissue model in cell culture inserts at air liquid interface. Test articles are topically applied and culture medium is replaced by receptor medium (assay medium or Krebs Ringer Buffer).

Results

The correlation of permeation coefficients to excised animal corneas for model drugs was r²=0.84.

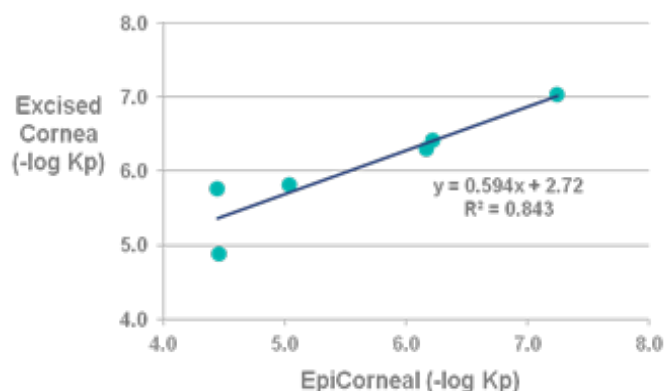


Figure 2. EpiCorneal tissue model displays excellent correlation with excised animal corneas.

Conclusion

Tissue permeability of model formulations with different properties was similar to that of the excised cornea. EpiCorneal tissue model is suitable for eye permeation studies.

Table 1. Permeation of model compounds and ophthalmic drugs through EpiCorneal tissue model

Substance	Abbr.	MW	Properties/ Use	Donor Conc. (µg/ml)	λ (nm)	COR-100 Papp (cm/s) ⁵	Excised corneas Papp (cm/s)
Sodium fluorescein	Na-Fl	332	hydrophilic dye, marker of tissue damage	250	490/528	6.1±0.1x10 ⁻⁷	3.8±1.1x10 ⁻⁷ #
Fluorescein isothiocyanate-dextran	FD-4	4,000	macromolecule	2500	490/528	5.7±3.8x10 ⁻⁸	9.1±4.9x10 ⁻⁸ #
Lucifer yellow	LY	444	hydrophilic dye, marker of tissue damage	100	450/528	6.8±0.7x10 ⁻⁷	5.0±0.03x10 ⁻⁷ *
Rhodamine B	RhB	479	lipophilic dye	50	550/645	3.5±0.4x10 ⁻⁵	1.3±0.2x10 ⁻⁵ #
Ofloxacin	OFL	361	synthetic antibiotic, fluoroquinolone	1500	288	9.2±2.1x10 ⁻⁶	1.5±0.1x10 ⁻⁶ @
Voriconazole	VOR	349	tiazole antifungal	500	256	3.6±0.3x10 ⁻⁵	1.7±0.1x10 ⁻⁶ &

⁵ Values represent mean ± SD (n=3); # excised rabbit cornea ¹; * excised rabbit cornea ²; @ excised rabbit cornea ³; & excised goat cornea ⁴

¹ Hahne M, et al. *Int.J.Pharm* 2011;416:268-279; ² Guerra FB, et al. *AAPS Annual Meeting and Exposition. New Orleans, Louisiana, 2010*; ³ Hosny KM. *AAPS PharmSciTech* 2009;10:1336-1342; ⁴ Malhotra S, et al. *Journal of pharmaceuticals* 2014;2014:490595.