A NON-INVASIVE PERFUSION TECHNIQUE FOR MEASURING THE CORNEAL PERMEATION OF DRUGS

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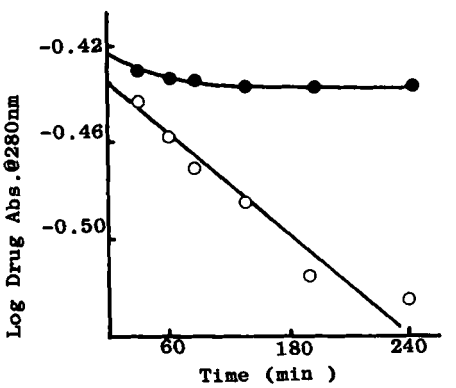
Numerous techniques have been used to study the factors influencing the penetration of topically applied drugs. Since the cornea acts as the principal barrier to the penetration of most ophthalmic drugs, in vitro models are frequently developed to study drug-corneal transport. The techniques may involve excising the cornea from the experimental animal, which requires elaborate apparatus and consideration of the problem of keeping the corneal cells alive and the question of corneal integrity cannot be ignored. Francoeur and Patton (1979) describe an in situ perfusion system which overcomes these problems. The fixing of the perfusion apparatus to the cornea involved the application of a chemical bonding agent which could be detrimental to the corneal epithelium. We have greatly improved this by incorporating onto the base of the perfusion unit, a hard contact lens with a central hole. Positioning the lens over the eye and applying a small positive pressure prevented leakage of the drug reservoir. The drug permeation for 2 x 10^{-3}M benzocaine in isotonic Sorensens buffer at pH 7.4 and ambient temperature was calculated by the mass flux equations (Francoeur and Patton 1979). Preliminary studies used the surgical adhesive technique, showed good correlation with the data by Francoeur and Patton (1979) (Table 1). It was observed that an increase in the uptake of benzocaine occured using the new lens-perfusion apparatus. This was predicted since the corneal perfusion area was greater. Benzocaine perfusion studies on the killed animal significantly reduced the uptake characteristics of benzocaine (Figure 1) since the termination of the flow of aqueous humour on death, sink conditions no longer apply and a benzocaine-cornea equilibrium is established after 2 hours. The combined results of the viable and cadaverous corneas clearly demonstrated that benzocaine not only partitions into the cornea but permeates into the underlying ocular tissues. This new technique can be applied to a quantitative permeability assessment of ophthalmic products with the minimum of physical trauma to the eye.

Table 1. The uptake of 2 x 10^{-3}M benzocaine into the cornea.

Technique	Benzocaine clearance $ml.min^{-1}$ $\pm s.e.m.$ $n=4$	Perfusion area mm^2	Clearance per mm^2
Francoeur + Patton (1979)	$1.23x10^{-3} \pm 4.71x10^{-5}$	28.3	$4.35x10^{-5}$
Surgical adhesive	$1.14x10^{-3} \pm 9.05x10^{-5}$	28.3	$4.03x10^{-5}$
Lens	$3.83x10^{-3} \pm 1.43x10^{-4}$	(90.3)	$4.24x10^{-5}$

Value in parenthesis is an apparent value, the corneal curvature has not been considered.

Fig.1. Benzocaine-corneal clearance for viable (○) and cadaverous (●) rabbit corneas.



Francoeur, M. and Patton, T.F. (1979) Int. Jnl. Pharm. 2:337.

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