ASSESSMENT OF PRECORNEAL DRAINAGE OF OPHTHALMIC PRODUCTS BY LACRIMAL SCINTIGRAPHY

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In the development of an ophthalmic product, the major factors influencing drug bioavailability should be quantified. An important consideration is the continuous drug removal arising from tear production and drainage. Formulation to minimise the precorneal loss of an instilled preparation, has been based on the premise that viscous solutions prolong contact time with the eye thus increasing bioavailability to the ocular tissues and minimising systemic absorption. Both tear sampling and non-contact probe techniques have been used to follow precorneal dynamics (Lee & Robinson 1979), Chrai et al (1973)). However, previously described techniques have not permitted local variations in deposition to be followed simultaneously. A method of quantification of the precorneal drainage of ophthalmic preparations has been developed, adapted from the established clinical technique of gamma scintigraphy. Radionuclide labelled solutions of varying viscosities were prepared by mixing ^{99m}Tc-sodium pertechnetate with polyvinyl alcohol (PVA) at 1, 3.5 and 5% concentrations in saline. Groups of NZW strain rabbits, n=4 per group, received the formulations in random sequence. 50 ul volumes of the solutions were placed into an eye of each rabbit and the eye blinked manually three times. The rabbit was then placed beside a gamma camera fitted with a pinhole collimator and a series of images of 15 s duration collected for up to 10 minutes after instillation. Data were recorded by the computer for later analysis. From the images obtained, the distributions of the label on the corneal surface and in the inner canthus were quantified. The results are shown in Table 1. For the range of concentrations of PVA investigated, gamma scintigraphy was effective in quantifying the change in both corneal and canthal concentrations of the radiolabelled marker. The technique is simple, non-invasive and has general application for the optimisation of ophthalmic drug products.

Table 1. Clearance of ^{99m}Tc-Pertechnetate in PVA vehicles (Mean ±S.E.)

Region	PVA conc	0.75 min	1.50 min	3.50 min	7.00 min	10.00 min
		Count Rates in Regions of Interest (c.p.m./pixel)				
Cornea	0%	0.36±0.07	0.18±0.03	0.09±0.03	0.06±0.04	0.04±0.05
	1%	0.74±0.14	0.29±0.18	0.21±0.13	0.08±0.05	0.05±0.05
	3.5%	1.00±0.41	0.70±0.35	0.31±0.18	0.22±0.11	0.10±0.12
	5%	0.83±0.22	0.60±0.11	0.29±0.04	0.25±0.05	0.13±0.09
Inn.C.	0%	1.32±0.30	1.07±0.32	0.54±0.28	0.25±0.12	0.17±0.13
	1%	2.07±0.19	1.46±0.16	1.13±0.40	0.34±0.09	0.21±0.14
	3.5%	1.15±0.26	1.14±0.29	1.06±0.35	0.76±0.50	0.54±0.71
	5%	1.10±0.39	1.32±0.23	0.96±0.18	0.53±0.23	0.30±0.18

Key: Inn.C. = Inner canthus

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