OCULAR RETENTION OF OPHTHALMIC VEHICLES EVALUATED IN THE RABBIT BY GAMMA SCINTIGRAPHY

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The preparation and in vitro evaluation of drug vehicle carriers are frequently undertaken with the objective of developing an ophthalmic product to maximize residence time in the precorneal area. A dependency upon in vitro data alone is considered limiting necessitating in vivo studies for correlation and reliable interpretation. In the present study, a non-invasive gamma scintigraphic technique was used (Wilson, et al., 1983) to determine the in vivo behaviour of ophthalmic vehicular bases after topical instillation into the eyes of New Zealand white rabbits. The radiolabelled compound, technetium-99m labelled diethylenetriaminepentaacetic acid (^{99m}Tc-DTPA) was incorporated into PVA 15 and 20% w/v, a paraffin base Modulan ("Modulan") and Plastibase. For each base, 15 mg of the preparation was instilled into the test eye (n=4) with scintigraphic images of 60 second duration taken at 0, 10, 30, 60 minutes and hourly thereafter, up to 480 minutes post-instillation. The activity of ^{99m}Tc-DTPA (initial activity 3.53± 0.27 ROI) was monitored to provide quantitative data of the retention capacity of the instilled vehicles. The resultant activity-time profiles, Figure 1, show that the precorneal clearance of each vehicle 60 minutes post-instillation approximated to 85% of the total dose instilled. Differences in the vehicular activity profiles became apparent with time. The order of increasing residence time was predicted to be PVA 15% < Plastibase < PVA 20% < "Modulan" which represented a function of viscosity. However, the sustained residence times were found not to comply with this ranking order. On the basis of statistical interpretation and grading the vehicles in sequence of greater ^{99m}Tc-DTPA remaining, the following descending order of contact times was determined; Plastibase > "Modulan" > PVA 15% > PVA 20%. The physicochemical nature of each vehicle in establishing a suitable precorneal film was considered to be more important than viscosity alone. A diminished film covering the ocular surface occurred with the PVA gels due to poor spreadibility and agrees with the findings that increasing vehicle viscosity does not necessarily prolong ocular contact time (Melis-Decerf and van Ooteghem, 1979). Plastibase, a predominantly hydrophobic base, was expected to provide an effective coating of the precorneal lipophilic surface. An hydrophobic film of this nature was less susceptible to the drainage process facilitated by the tear-blink response. The emollient properties of the "Modulan" offered an enhanced ocular lubrication compared to the Plastibase. This increase in hydrophilicity promoted precorneal clearance resulting in the lower ^{99m}Tc-DTPA activities. The radionuclide procedure generated useful information towards assessing the efficiency of possible ophthalmic vehicles. However, the final choice must be made in association with other biological and physicochemical factors.

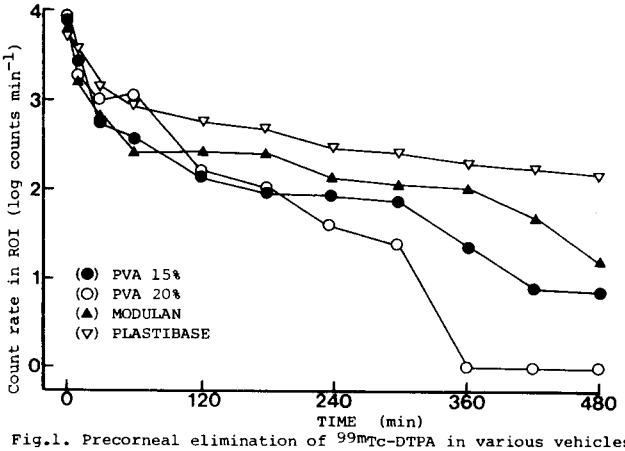

Fig.1. Precorneal elimination of ^{99m}Tc-DTPA in various vehicles

Melis-Decerf, C. and van Ooteghem, M.V. (1979), J. Pharm. Pharmac. 31:12-15.
Wilson, C.G., Olejnik, O. and Hardy, J. (1983), J. Pharm. Pharmac. 35:451-454.