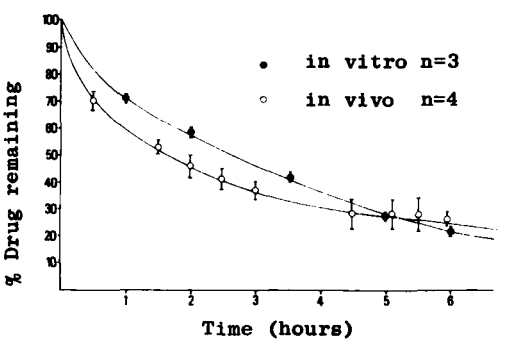
IN VITRO-IN VIVO EVALUATION OF A SUSTAINED RELEASE MATRIX TABLET

P.B. Daly, S.S. Davis, M. Frier, J. Hardy, J. Kennerley and C.G. Wilson, Department of Pharmacy and Medical School, University of Nottingham, Nottingham NG7 2RD.

Sustained release formulations of drugs can offer several advantages over existing preparations such as prolongation of activity, increased patient compliance and reduction of side effects. It is possible to study the release characteristics of such systems using in vitro dissolution tests, however, often it is difficult to correlate the results obtained with pharmacokinetic parameters. A method whereby it was possible to follow drug release in vivo would have considerable advantages and therefore we have studied the applicability of the non-invasive technique of gamma scintigraphy. A polymer matrix system (a specially treated form of hydroxypropylmethyl cellulose) was chosen as the release system. This material can be added directly to a formulation as an excipient and it achieves its effect by swelling to a gel-line consistency and allowing drug release by a combination of diffusion and surface erosion. A model, non-absorbed tracer compound, ^{99m}Tc-labelled diethylenetriaminepentaacetic acid (DTPA) was chosen for its physicochemical similarity to medicinal agents. It was incorporated in the base and tablets of approximately 120 μCi activity were prepared using a single punch tablet machine (Manesty Model F3) at 165 MNm^{-2}. The rate of dissolution of the tracer in vitro was monitored using the standard USP rotating basket apparatus with different pH solutions. The release profile could be defined by the matrix-release equation of Higuchi and it was little affected by the pH of the dissolution medium or the agitation condition.

In vivo release of drug was monitored in four healthy volunteers standing in front of a maxi camera II having a 40 cm field of view and fitted with a medium energy (400 Kev) parallel hole collimator. Anterior and posterior views of the abdominal region were obtained. From the images, regions of interest were drawn around the tablet. The geometric mean of the anterior and posterior counts was taken to allow for movement perpendicular to the plane of the camera. The activity remaining on the tablet was plotted against time (Figure). The in vitro and in vivo release characteristics can be seen to correlate well. At various times during the study each volunteer received two drinks of 200 ml water, containing 50 μCi ^{113}In-DTPA. This outlined the stomach and the intestines and thereby indicated the location of the tablet. The residence time of the tablet in the stomach ranged from 1 - 2 hours. The results indicate that gamma scintigraphy could be the method of choice for the in vivo evaluation of sustained release formulations in human volunteers.

In vitro and in vivo release of ^{99m}Tc-DTPA



0022-3573/81/120047P-01$02.50/0
© 1981 J. Pharm. Pharmacol.