DIFFUSION OF SMALL MOLECULES IN AMORPHOUS POLYMERS

W.R. Vezin, A.T. Florence, Department of Pharmaceutical Technology, University of Strathclyde, Glasgow, G1 1XW

Although much work has been carried out on the diffusion of steroids in polymers in relation to the design of sustained action dosage forms, there is little information to allow prediction of the diffusion coefficients of drugs in polymeric matrices. Diffusion coefficients of solutes of molecular weight ranging from 110 to 550 dissolved in two polymers, polymethylmethacrylate (PMMA) and polyvinylacetate (PVA) have been obtained from desorption rates into aqueous buffers and from sorption measurements into virgin polymer. The polymers were cast into films on plate glass levelled on mercury or in some cases directly on to triple distilled mercury surfaces. Films were annealed after evaporation of the solvent for periods of up to 96 h. The annealing process does not affect the results obtained. Analysis of the solute concentration in the bathing solutions into which portions of the films were placed was carried out spectrophotometrically. Diffusion coefficients were calculated using standard equations (Crank, 1975). No dependence of diffusion coefficient on the molecular weight fractions of the PMMA and PVA was detected; organic buffer components do affect the measured values of diffusion in PVA, probably by a plasticizing mechanism.

Table 1. Diffusion coefficients of small solutes in two polymer films at 37°C.

Solute	Mol. Wt.	PMMA $-\log D_o^a$	PVA $-\log D_o^a$
Hydroquinone	110.1	18.24	-
Salicylic Acid	138.1	18.02	14.36
4-Nitro-aniline	138.1	18.52	14.52
Trinitrophenol	229.1	19.45	15.12
Procaine	236.3	18.87	14.84
Promethazine	284.4	20.85	15.84
Fluphenazine	438.5	20.76	15.98
Fluphenazine enanthate	549.7	20.95	15.74

a) D_o is the diffusion coefficient at zero concentration ($m^2 s^{-1}$)

Predictive empirical equations determining D as a function of molecular weight have been given (Tanquary & Lacey, 1974; Lieb & Stein, 1969) but shape factors intervene to make these generally inapplicable. From our results, it is obvious that alteration of the drug molecule (e.g. esterification) to control diffusion is less useful than choice of alternative polymer. It is likely that the smallest dimension of the diffusant molecules is the rate-controlling parameter.

We thank E.R. Squibb for their support of W.R.V.

Crank, J. (1975). Mathematics of Diffusion. Oxford, Clarendon Press.
Lieb, W.R., Stein, W.D. (1969). Nature, 224, 240-243.
Tanquary, A.C. & Lacey, R.E. (Eds.) (1974) in Controlled Release of Biologically Active Agents (Adv. Exp. Med. Biol.) Vol. 47. New York, Plenum Press.