DIFFUSION OF SMALL MOLECULES IN POLY-N-ALKYL CYANOACRYLATES

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

In a recent study diffusion coefficients of low molecular weight compounds in poly-methyl methacrylate and poly-vinyl acetate were determined by desorption from polymer films (Vezin & Florence, 1977). Although preparation of intact films of the poly-alkyl cyanoacrylates suitable for permeation and desorption experiments of the type previously described, is impossible due to the extreme fragility and lack of tensile strength of these polymers in bulk, (Loew & others, 1967) films suitable for determination of diffusion coefficient have been prepared by adhesion of cast films to nylon blocks.

Diffusion coefficients (D) of some of the substances studied previously have been measured by desorption in situ from cast films of solid solutions of the diffusing material in a range of poly-n-alkyl cyanoacrylates, and from desorption experiments with comminuted polymer particle samples. Diffusion coefficients at zero concentration (D_o) have been found to be invariant with polymer molecular weight, over the range $\sim 10^3 < M_n < 10^7$, as with other polymers, such as the polystyrenes, (Bezrukov & others, 1971).

Table 1: Diffusion coefficients at zero concentration (D_o) in two poly-n-alkyl cyanoacrylates

	$\log_{10} D_o$, $m^2 s^{-1}$	
Compound	poly-alkyl cyanoacrylate, at 37°C	
	n-Hexyl-	n-Butyl-
Salicylic acid	-11.57	-13.47
p-nitroaniline	-12.24	-13.72
Trinitrophenol	-13.43	-14.66
Procaine	-13.29	- -
Fluphenazine	-14.40	-15.72

The increase in diffusivity with increase in the length of the polymer side chain reflects differential thermal oscillation of the side chain. In any amorphous polymer series such as the cyanoacrylates, the diffusion coefficient of small solute depends upon the nature of the side chain alone.

Diffusion of drugs in these polymers is more rapid than in poly-vinyl acetate, and much slower in poly-ethyl cyanoacrylate, (Vezin & Florence, 1977). The general shape of the plot of log D vs log diffusant molecular weight is similar to those in the non-biodegradable polymers, suggesting a superficial approximation to the predictive model for diffusion coefficient of Chalykh & Vasenin (1966). Accurate prediction of D can only be made by interpolating between compounds of similar structure. However as extrapolation, e.g. from trinitrophenol to fluphenazine is inaccurate, ($\sim$ 1 log D unit) this suggests a very complex dependence of D upon diffusant molecular weight characterising the structure of each separate polymer.

Bezrukov, O.F., Budtov, V.P. & others (1971). Vysokomol. soyed A,13 (4), 876-83.
Chalykh, A. Ye. & Vasenin, R.M. (1966). Ibid., 8 (11), 1908 - 16.
Loew, F., Herrman, H.D. & Pulleske, H. (1967). Med. Mitt. (Melsungen), 41, 49.
Vezin, W.R. & Florence, A.T. (1977). J. Pharm. Pharmac., 29, 11P.