DRUG RELEASE FROM PLURONIC GELS

J Hadgraft and J R Howard, Department of Pharmacy, University of Nottingham, University Park, Nottingham NG7 2RD.

As part of an investigation into the potential use of Pluronic F127 gels as sustained release depot preparations, we have studied the in vitro release characteristics of model compounds from various gel formulations. Barbitone, butabarbital and amylobarbitone were chosen as model compounds. Pluronic gels were produced using the cold method described by Schmolka (1972). Drug was added after full hydration of the Pluronic had occurred. Dissolution of the drug was promoted by incubation of the mixture at 30°C. Release rates were measured by using apparatus similar to that developed by Billups and Patel (1970). The gel donor phase and aqueous receptor phase were separated by Celgard microporous polypropylene engineering film, previously impregnated with isopropyl myristate. This membrane acted as a hydrophobic barrier preventing problems of osmotic flux between aqueous gel and aqueous receptor phase. Borate buffer, pH 10, was used as receptor phase in all experiments. Barbiturate concentration in the receptor phase was measured spectrophotometrically. Linear relationships between the amount of barbiturate released and $(\text{time})^{\frac{1}{2}}$ existed, and for these the gradient gave values for the apparent diffusion coefficient of the barbiturate in the gel (Table 1). Apparent diffusion coefficients were also measured at 25°C and 37°C. The apparent diffusion coefficients when plotted as a function of temperature on an Arrhenius plot gave good linear relationships from which the energy for diffusion (E) can be calculated (Table 1).

Table 1. In vitro release of barbiturates from Pluronic F127 gels at 30°C. (Initial gel pH 7.4, initial concentration of barbiturate 0.2% w/v).

Gel Conc. % w/v	Compound	Diff. Coeff./$cm^2 sec^{-1}$	E/$kJmol^{-1}$
30	Barbitone	1.31×10^{-6}	27.0
30	Butabarbital	0.97×10^{-6}	25.1
30	Amylobarbitone	0.57×10^{-6}	26.2
25	Butabarbital	1.22×10^{-6}	22.4
20	Butabarbital	1.69×10^{-6}	26.7

At 30% w/v Pluronic concentration the apparent diffusion coefficient of the barbiturates increases in order of decreasing molecular weight; amylobarbitone (mwt 226), butabarbital (mwt 212), barbitone (mwt 184), but by a greater amount than one would expect in bulk water. This indicates differences in the solubility and distribution of the barbiturates between Pluronic F127 micelles and the accompanying free water channels. With increasing concentration of Pluronic F127 in the vehicle a corresponding decrease in apparent diffusion coefficient of butabarbital occurred. The mechanism for a reduced release rate may be due to the reduction of the size and number of water channels within the gel matrix and the increased solubilisation of barbiturate resulting in a reduced free water concentration. The energy for diffusion values are higher than those reported for lidocaine release from gels (Chen-Chow and Frank 1981) but are not high enough to indicate any major physical interaction between drug and matrix.

Billups, N.F., Patel, N.K. (1970) Am. J. Pharm. Ed. 34:190-196
Chen-Chow, P.C., Frank, S.G. (1981) Int. J. Pharm. 8:89-99
Schmolka, I.R. (1972) J. Biomed. Mater. Res. 6:571-582

0022-3573/82/120003P-01$02.50/0