CHARACTERIZATION OF POLY(2-HYDROXYETHYL METHACRYLATE) GELS

J.M. Wood, D. Attwood and J.H. Collett*
Department of Pharmacy, University of Manchester,
Manchester M13 9PL, U.K.

ABSTRACT

The crosslinking density and pore sizes of poly(2-hydroxyethyl methacrylate) (polyHEMA) hydrogels have been measured and correlated with the diffusion characteristics of a solute through the polymer. Studies indicated that diffusion is hindered both by obstruction by the polymer chains and by the immobility of the solvent within the gel. Values for the diffusion coefficient of a solute, D, and interaction parameters between the solvent and polymer suggest that as the concentration of crosslinking agent in the polymer network increases, the hydrophobicity of the polymer and the mobility of the solvent in the gel increase. Increased crosslinking however, increases the effectiveness of the obstruction effect, and the overall effect is a reduction in D.

INTRODUCTION

The control of the diffusion rate of a solute through a hydrogel network is of importance when the hydrogel has potential use in the fabrication of a drug delivery device. The diffusion

* correspondence

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rate of solutes through hydrogels is governed both by the physical structure of the polymer network, and the chemical nature of the polymer. It has been shown previously (1) that in polyHEMA hydrogels containing more than 31% water, diffusion occurs primarily through the pores in the gel network whereas in gels of lower hydration, the solute dissolves in the polymer and is transported between the chains. In this work, the effect of changes in polymer concentration and crosslinking density on the diffusion of a low molecular weight solute through polyHEMA gels has been examined. Pore sizes of the gels have been estimated and the polymer crosslinking density measured using stress-strain tests.

MATERIALS

The following materials were used:

2-Hydroxyethyl methacrylate and ethylene glycol dimethacrylate (EGDMA), purities 97% and 98% respectively, (Fluka); salicylic acid, 7-C^{14}, specific activity 57 $\mu Ci\ mmol^{-1}$, (New England Nuclear Corporation), salicylic acid, AnalaR, (BDH).

METHODS

Gels were prepared by Co^{60} γ irradiation of aqueous monomer solutions under nitrogen by the method described previously (2). Gels of thickness 0.3 cm and in the shape of dumbells were prepared for the tensile tests. Stress-strain tests were carried out using a J J Lloyd tensile tester type 22K. The gels were subjected to a fixed strain rate of 16 mm min^{-1} at a temperature of 24 ± 1°C. In order to prevent dehydration of the gel, samples

were held in a humidity cabinet, into which air saturated with water vapour was pumped.

Measurement of diffusion coefficients was carried out using the double disc method described previously (1).

The volume fraction of polymer in the gel was calculated from the gel hydration. Gel hydrations were measured by weighing the gel, drying to constant weight in a vacuum oven, then re-weighing. The volume fraction of polymer was then calculated from the hydration and the initial gel volume.

Gel volumes were measured on a Beckmann air pycnometer. These values were also used in density calculations.

RESULTS AND DISCUSSION

Crosslinking Densities and Molecular Weights Between Crosslinks.

The stress-strain equation thought by some workers (3) to be that most applicable to polyHEMA, is the Mooney-Rivlin equation:-

$$\sigma = 2(C_1 + C_2/\alpha)(\alpha - \alpha^{-2}) \qquad (I)$$

where σ is the applied force per unit area and α is the ratio of the extended to the initial length of the specimen. The constants C_1 and C_2 were derived graphically. The crosslinking density, v, was calculated from equation II (4,5):-

$$v = \frac{C_1 + C_2/\alpha}{RTv_2^{2/3}} \qquad (II)$$

where R is the gas constant, T is the temperature and v_2, the volume fraction of polymer in the gel.

Since the crosslinking molecule is difunctional, it creates a maximum of two crosslinks per molecule. Thus the theoretical

value of the crosslinking density, v_c, is given by $v_c = 2c$, where c is the concentration of the crosslinking agent (EGDMA).

A plot of the experimentally determined crosslinking density v, against v_c, is shown in Figure 1. The effective crosslinking density of 0.5×10^{-4} mol cm^{-3} in the absence of the crosslinking agent indicates that a high proportion of the crosslinks in the polyHEMA network are caused by physical chain entanglements and noncovalent molecular interactions between the chains. The slope of the graph is 0.82, indicating that the crosslinking reaction does not go to completion (slope = 1.0).

The molecular weight between crosslinks, M_c, is a parameter closely related to the crosslinking density. M_c has been calculated from equation III (6):-

$$M_c = \frac{\rho R T v_2^{1/3}}{G_s} \qquad \text{(III)}$$

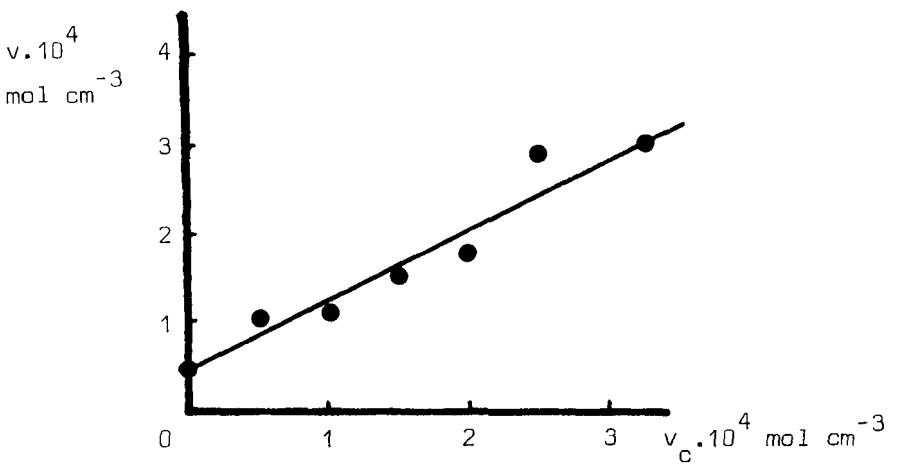

Fig. 1.
Relationship between theoretical crosslinking density, v_c and experimentally determined values, v.

TABLE 1

Effect of Volume Fraction of Polymer, v_2, and Concentration of Crosslinking Agent on the Structure of polyHEMA Hydrogels

v_2	EGDMA conc. /10^4 mol cm^{-3}	M_c kg mol^{-1}	$D/10^7$ cm^2 s^{-1}	χ	r_p nm
0.62	0	36.47	1.26	0.9044	0.591
0.68	0	28.80	0.71	0.9927	-
0.70	0	28.52	0.63	1.0276	-
0.72	0	22.19	0.62	1.0656	-
0.74	0	21.28	0.62	1.1076	-
0.63	0.27	15.54	1.04	0.9157	0.576
0.63	0.53	10.63	0.90	0.9148	0.566
0.63	0.80	6.89	0.89	0.9132	0.565
0.63	1.06	5.04	0.85	0.9115	0.562
0.63	1.33	4.22	0.73	0.9103	0.552
0.63	1.59	2.94	0.72	0.9071	0.551

where ρ is the density of the dry polymer, and G_s is the elastic constant (6), calculated from:-

$$\sigma = G_s(\alpha - \alpha^{-2}) \qquad \text{(IV)}$$

Values of M_c shown in Table 1 decrease with increases in v_c and v, as expected.

Pore Sizes

The crosslinking density and molecular weight between cross-links govern the size of the pores within a polymer network, and hence control diffusion rates of solutes through the polymer.

The pore radius, r_p, was estimated from the ratio of the diffusion coefficient of a solute within the gel, D_p, to that in free solution, D_f. Equation V has been used (7) to relate D_f and D_p, on the assumption that the pores in a gel are cylindrical, and that all the solute is transported through the pores:-

$$\frac{D_p}{D_f} = 1 - \left(\frac{r_s}{r_p}\right)^2 \left[1 - 2.104 \frac{r_s}{r_p} + 2.09 \left(\frac{r_s}{r_p}\right)^3 - 0.95 \left(\frac{r_s}{r_p}\right)^5\right] \quad (V)$$

where r_s is the solute radius.

A value for D_f of 8.2×10^{-6} cm^2 s^{-1} for salicylic acid (the solute used) was taken from data of Edwards (8). Assuming the molecule to be spherical, the solute radius was determined from the partial molal volume, as calculated from the appropriate atomic volumes (9). Calculated values of the pore radius shown in Table 1 agree well with values quoted by Haldon and Lee (10) and Migliaresi et al (11) for polyHEMA gels. The values, which are subject to errors of ± 10% in the solute radius and ± 8% in D_p, decrease with decreasing values of M_c, although the decrease is less than expected.

It is assumed in the calculation of the pore radius that there is no immobilised water lining the walls of the pores. However, Andrade (12) has shown that in polyHEMA gels of high polymer concentration all or most of the water is immobilised, and consequently the values of r_p quoted in Table 1 are regarded as effective pore radii, i.e. the radii of the cross-sectional areas of the pores which contain freely diffusing water and are therefore available for diffusion. The diffusion of water-soluble

solutes occurs only through the bulk (freely-diffusing) water, and so the actual pore size of the polymer network is likely to be much larger than the quoted values, and can be calculated from the proportions of bound and normal water in the gel from the data of Andrade (12). Values of r_p for polymer concentrations of 68% and above are not quoted, since previous results (1) indicated that diffusion through these gels occurs mainly between the polymer chains and not through the pores.

Diffusion Coefficients

Values for the diffusion coefficient decrease with increases in volume fraction of polymer and crosslinker concentration, as expected. Values for M_c indicate that the crosslinking density increases much more rapidly with increasing crosslinker concentration than with increases in v_2. On this basis, D might be expected to decrease much more rapidly with increasing crosslinker concentration than for increasing polymer concentration. As seen from Table 1, this is not the case, and it is suggested that this may be a consequence of an increased hydrophobicity of the polymer network as the concentration of EGDMA is increased. The higher mobility of solvent in these more hydrophobic gels would increase the available diffusion volume and hence increase the diffusion coefficient of the solute. An increase in the diffusion coefficient of water though polyHEMA with increase in EGDMA concentration, has been reported (10). However, the tendency for D to increase is counteracted by the increased effectiveness of the obstruction effect at high crosslinking densities, tending to reduce the diffusivity. Haldon and Lee

(10) suggest that there is an optimum crosslinking density to give a minimum pore size (or diffusivity).

Interaction Between Polymer and Solvent

The interaction between the polymer and the solvent can be estimated in terms of Flory-Huggins interaction parameters, χ. Values of χ have been calculated from equation VI (6):-

$$\chi v_2^2 = -(\rho V_1/M_c)(v_2^{1/3} - v_2/2) - v_2 - \ln(1 - v_2) \qquad \text{(VI)}$$

where V_1 is the molar volume of water.

Table 1 shows χ increases with polymer concentration, due to a greater interaction between polymer and solvent, and decreases with increasing crosslinker constant, supporting the view that gels of high crosslinker content contain a higher proportion of freely diffusing solvent.

It can be concluded that the pore size, crosslinking density, and solvent mobility in the gel, govern the diffusion rate of solutes through polyHEMA gels. Characterization of both the polymer network and the nature of the water in the gel is important before attempting to formulate a controlled-release drug delivery device.

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