Water Diffusion in Methacrylate Based Copolymer Hydrogels of 2-Hydroxyethyl Methacrylate

David J.T. Hill, Mohammad Chowdhury, Phuong Y. Ghi, Naomi G. Moss, Andrew K. Whittaker*

Polymer Materials and Radiation Group, Department of Chemistry, University of Queensland, Brisbane, Australia 4072

Summary: The diffusion of water into cylinders of polyHEMA and copolymers of HEMA with THFMA, BMA and CHMA were studied over a range of copolymer compositions. The diffusion of water into the polymers was found to follow a Fickian, or case I mechanism. The diffusion coefficients of water were determined from mass measurements and NMR imaging studies. They were found to vary from $1.7 \pm 0.2 \times 10^{-11}$ $m^2 s^{-1}$ for polyHEMA at 37 °C to lower values for the copolymers. The mass of water absorbed at equilibrium relative to the mass of dry polymer varied from 52-58 wt% for polyHEMA to lower values for the copolymers.

Introduction

Poly(hydroxyethyl methacrylate), polyHEMA, and its copolymers with other methacrylate monomers have found numerous medical applications due to their well documented biocompatibility[1,2,3]. Applications of these copolymers include polymeric matrices for the controlled release of bioactive agents[4-6], intraocular and contact lenses[7] and soft cushioning materials for use in dentistry and surgery[8]. In controlled release systems, for example, the drug is initially incorporated within the core of a glassy polymer, and then, when body fluids migrate into the polymer plasticizing it, the trapped drug is allowed to diffuse out through the swollen hydrogel matrix. Thus the diffusion of water into the polymer is vital for release of the drug, and the water and drug diffusion kinetics are dependent on the nature of the polymer matrix.

The diffusion of water into a polymer matrix is influenced by: the polymer microstructure, the polarity of the copolymer segments, the glass transition temperature of the polymer, the flexibility of the polymer backbone, the molecular weight of the polymer, the crosslink density and interchain interactions, the degree of chain branching and the presence of bulky comonomer pendant groups. The kinetics of water sorption, as well as the equilibrium amount of water which can be absorbed by the matrix, are particularly dependent on the nature of the comonomers present, the comonomer

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composition and the crosslink density.

Herein we review some of our work[9-14] on water diffusion into polyHEMA and its copolymers with tetrahydrofurfuryl methacrylate, THFMA, n-butyl methacrylate, BMA, and cyclohexyl methacrylate, CHMA. These investigations have included mass uptake measurements and NMR imaging studies of the water profile during its diffusion into the polymers. We also compare the sorption of water by polyHEMA with that for polyHEMA crosslinked with diethyleneglycol-dimethacrylate (DEGDMA) and with tetraethyleneglycol-dimethacrylate (TEGDMA)[11].

Experimental

Stabilized BMA and CHMA (Aldrich Chemical Company), THFMA (DAJAC Laboratories) and HEMA (Ubichem Ltd) were purified by chromatography using anhydrous Al_2O_3 (neutral, Merck) and distillation at reduced pressures (. 10^2 Pa). Only the middle fractions were used experimentally[12,13]. DEGDMA and TEGDMA (Aldrich Chemical Company) were purified by chromatography using anhydrous Al_2O_3[11]. The purity of the monomers was confirmed by NMR analysis.

Cylindrical samples of the polymers were prepared in cylindrical teflon moulds for the diffusion studies[11-13]. For the HEMA copolymers with THFMA, BMA and CHMA, the monomers were weighed into a 25 mL pyrex glass flask in the required mole ratios and 0.08 weight % BPO was added, based on the mass of the monomers. The mixtures were shaken until the BPO had dissolved, and then they were poured into the teflon moulds (diameters in the range 3.0 - 10 mm and length 20 - 40 mm). The polymerizations were forced to complete conversion of monomer to polymer in a vacuum oven using various temperature/time protocols[12,13] over the temperature range 40 ^{0}C - 120 ^{0}C. After polymerization, the polymer cylinders were removed from the teflon moulds, the absence of residual monomer was confirmed by FT-NIR analysis, and the ends were ground to a smooth, flat finish prior to the diffusion measurements.

Some polyHEMA cylinders were prepared using using ^{60}Co (-radiolysis at 25 ^{o}C, as were polyHEMA cylinders which were crosslinked with DEGDMA and TEGDMA[11]. Again, the absence of residual monomer was confirmed by FT-NIR analysis, and the ends were also ground to a smooth, flat finish prior to the diffusion measurements.

The copolymer cylinders were placed in distilled water in a water bath for which the temperature was controlled to $\pm$ 1 ^{0}C. The polymers were removed periodically from the bath, the surface water was removed, they were weighed, and an NMR image of the water diffusion front was obtained. The experimental details associated with the NMR imaging process have been reported elsewhere[14].

Results and Discussion

The distinguishing features of the monomers are the hydrophilic polar hydroxy group of HEMA; the bulky hydrophobic side-chains of BMA and CHMA, the less hydrophobic side-chain of THFMA and the crosslinking ability of the DEGDMA and TEGDMA. Studies on these series of copolymers provide information about the influence of the side-chains and the introduction of crosslinks on the water diffusion and equilibrium water contents of the polymers.

The nature of the copolymerizations of HEMA with the comonomers have been studied in detail[12,15,16] and it has been shown that they are close to ideal polymerizations. This means that there is relatively little tapering of the feed composition with conversion, and hence of the instantaneous copolymer composition, as the polymerizations proceed to high conversions.

Water Sorption by PolyHEMA.

The diffusion of water into a series of polyHEMA cylinders has been studied at 25 ^{o}C, 37 ^{o}C and 45 ^{o}C for polymers prepared by a range of polymerization protocols. A series of typical mass uptake data are demonstrated in Figure 1 for sorption at 37 ^{o}C. From Figure 1, it is possible to identify a change in the trend of the mass uptake at the point at which the glassy core disappears at a relative mass uptake of $\approx$ 0.6, and there is evidence for an over-shoot in the mass uptake just prior to equilibrium being established. These effects are related respectively to the dimensional changes that occur in the cylinders when the glassy core disappears, and the system becomes totally rubbery, and the slow relaxation of the polymer chains as equilibrium is approached.

The mass uptake of a penetrant into an infinite cylinder of radius a can be represented by equation 1 for a Fickian diffusion model[9]

$$\frac{M_t}{M_\infty} = 1 - \sum_{n=1}^{\infty} \frac{4}{a^2 \alpha_n^2} \exp(-D\alpha_n^2 t) \qquad (1)$$

where t is the time for which penetrant diffusion has occurred, M_t and M_4 are the mass uptakes at time t and at equilibrium, respectively, D is the diffusion coefficient, and α_n are defined in terms of the roots of the zero order Bessel function, $J_0(a\alpha_n) = 0$.

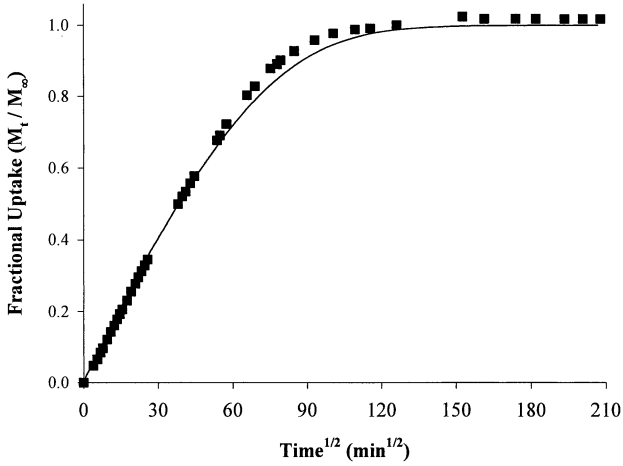

Figure 1. Water mass uptake data for a polyHEMA cylinder of diameter 1.0 cm measured at 37 °C. The solid line shows the fitted curve for equation 1 for data up to a relative mass uptake of 0.6, which is the point at which the glassy core disappeared.

The diffusion of water into polyHEMA cylinders has been found to be adequately represented by equation 1[12,13]. The best values of the diffusion coefficients for water, were determined by nonlinear least squares curve fits to equation 1 using only uptake data prior to the point of disappearance of the glassy core. A typical curve fit is shown in Figure 1. The diffusion coefficients obtained were found to be dependent on the details of the temperature/time protocols adopted during preparation of the cylinders. For example, for a range of polymerization protocols we have obtained values of D of

$1.7 \pm 0.2 \times 10^{-11}$ m^2 s^{-1} at 37 °C. The small variations in the values are believed to arise from the differences in the extent of chain entanglement and the crosslink density developed during polymerization. As expected, the mass uptake/time curves for cylinders varying in diameter from 3.0 to 10.0 mm prepared by the same polymerization protocols were found to be different. However, the values of D determined from the data fits to equation 1 were the same within the estimated experimental error of $\pm$ 0.2 x 10^{-11} m^2 s^{-1}.

The values of D obtained for a range of temperatures are shown in Figure 2, along with data reported by Gehrke et al.[17] for water sorption into flat sheets. The agreement between the data is good. The activation energy determined from the diffusion coefficients obtained herein was 12.9 $\pm$ 1.0 kJ mol^{-1}, which agrees well with the value of 11.9 kJ mol^{-1} reported by Gehrke and coworkers.

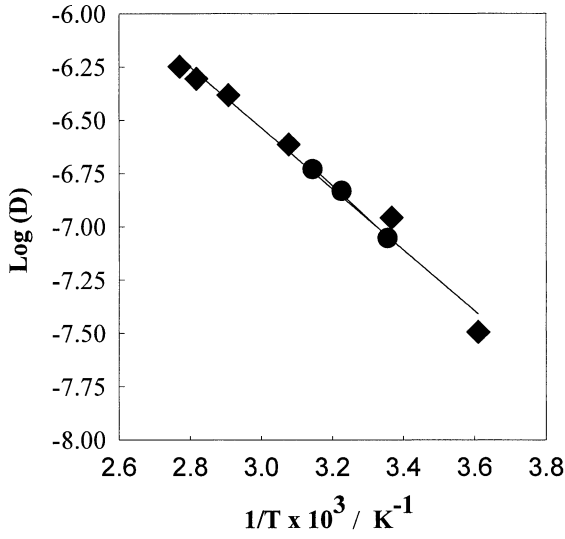

Figure 2. Plot of the logarithm of the diffusion coefficient versus reciprocal temperature for diffusion of water into polyHEMA. ♦ Gehrke et al.[17], ● This work.

The water uptake at equilibrium, S_4, expressed as a percentage of the original mass of the polymer, is:

$$S_4 = [(M_4 - M_0) / M_0] \times 100 \quad (2)$$

where M_0 is the mass of the dry polymer cylinder at time zero and M_4 is the mass of the polymer cylinder plus water at time infinity.

The equilibrium water uptake by polyHEMA cylinders was also found to be dependent on the polymerization protocol adopted in their preparation, and values of S_∞ in the range 52 - 59 % have been obtained at 37 °C for cylinders prepared by thermal initiation using BPO[12,13]. The equilibrium water uptakes for the polyHEMA cylinders prepared by (-irradiation, 58 %, agree with these values within experimental error[11]. The studies on polyHEMA cylinders prepared by γ-radiolysis also showed that incorporation of the crosslinking monomers DEGDMA and TEGDMA at concentrations up to 0.5 wt % resulted in a decrease in the equilibrium water contents over that for polyHEMA, as demonstrated in Figure 3. This observation reflects the reduced swelling capability of polyHEMA matrices containing added crosslinker.

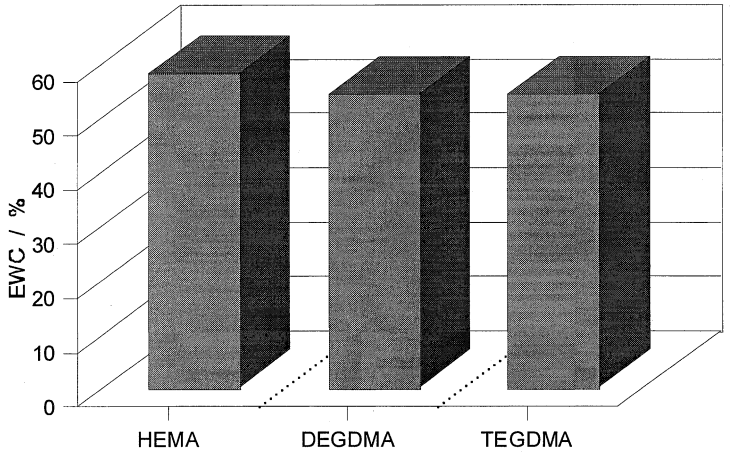

Figure 3. Equilibrium water contents (EWC) for polyHEMA and polyHEMA crosslinked with DEGDMA and TEGDMA (0.5 wt%) for water sorption at 37 °C.

Mass Uptake and Diffusion Coefficients for Copolymers.

Diffusion coefficients have been obtained from mass uptake data for THFMA/HEMA[13], BMA/HEMA[12] and CHMA/HEMA[12] copolymers. Again, the

mass uptake data were fitted to equation 1, using a least squares curve fitting procedure, in order to determine the best values for the diffusion coefficients. The results are shown in Figure 4 relative to the diffusion coefficient for polyHEMA.

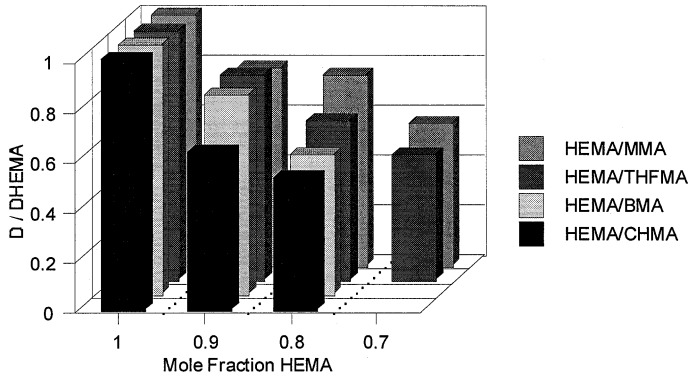

Figure 4. Diffusion Coefficients for HEMA copolymers relative to that for polyHEMA at 37 °C. The data for HEMA/MMA were calculated from the work of Franson and Peppas[18].

With increasing proportions of the comonomers, the diffusion coefficients decreased, reflecting the influence of the compositional microstructure on the diffusion of water into the cylinders. As the mole fraction of HEMA in the copolymers decreases, the fraction of HEMA units with two HEMA neighbours also decreases, and hence so do the average lengths of the HEMA sequences. These changes in the HEMA microstructure have the effect of inhibiting the diffusion of the polar water molecules through the copolymer matrices. The incorporation of small amounts of the non-polar side-chains of CHMA and BMA into polyHEMA were found to have a greater effect on the diffusion coefficient for water than does the incorporation of small amounts of the somewhat more polar side-chain of THFMA.

Franson and Peppas[18] have studied the diffusion of water into poly(hydroxyethyl methacrylate-co-methyl methacrylate), HEMA/MMA, at 37±0.5 °C. We have calculated the relative diffusion coefficients for these copolymers, using the data of Franson and Peppas, and they are also included in Figure 4. The diffusion coefficients for the MMA copolymers are larger than those for the other three copolymers at

corresponding comonomer mole fractions. This presumably reflects the balance between the hydrophobic and hydrophylic natures of the groups in the side-chains of the various methacrylate comonomers.

Mass Uptake of Water at Equilibrium.

The equilibrium mass uptakes for the copolymer cylinders at 37 °C were found to decrease with increasing comonomer mole fraction, as demonstrated in Figure 5. Again, the data for the various comonomers reflect the changing hydrophobicity of the comonomer side-chains, as was observed for the diffusion coefficients.

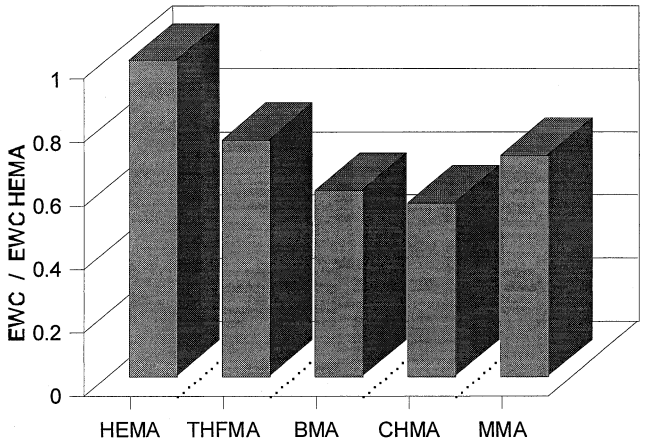

Figure 5. Equilibrium water contents, EWC, for a range of HEMA copolymer cylinders, F_{HEMA}= 0.8, of 10.0 mm diameter at 37 °C. The data for MMA/HEMA was taken from Franson and Peppas[18].

NMR Imaging of Water Diffusion.

Mass uptake measurements on cylinders which have imbibed water are bulk measurements, and, in order to obtain information about the processes controlling diffusion of the water into the polymer matrix, it is necessary to make assumptions about the diffusion mechanism, and then to assess the goodness of fit of each model to the uptake data, as outlined above. In addition, mass uptake measurements, being bulk data, are influenced by diffusion through the flat ends as well as through the curved cylinder walls. This introduces uncertainty, and in order to carry out an analysis of these

data, it must be assumed that these end effects are negligible.

An alternative approach is to image the profile of the water diffusion front directly. This can be conveniently done in real time using NMR imaging of the water protons. Such an NMR profile is shown below in Figure 6 for water diffusion into a cylinder of BMA/ HEMA, with a mole fraction HEMA of 0.8.

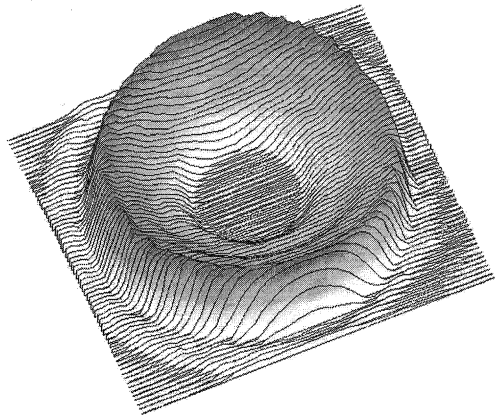

Figure 6. NMR image of the water diffusion front for a BMA/HEMA cylinder, F_{HEMA} = 0.8, at 37 °C. The diameter of the cylinder is 10 mm.

This image was obtained from a 3 mm slice through the centre of the cylinder, so it is uneffected by end effects. A cross section of this image profile is shown in Figure 7. The image and the cross section show that the maximum concentration of water in the cylinder is at the outer wall and that some of the central glassy core remains. The shape of the underlying profile appears to be Fickian-like, but there are clearly additional features on the walls of the profile. A similar cross section of a profile for a polyHEMA cylinder, see Figure 8, shows these additional features more clearly. We have assigned these features to water molecules located in cracks which are formed due to the tensile stresses generated in the glassy core at the interface between the glassy core and the surrounding, swelling rubbery region.

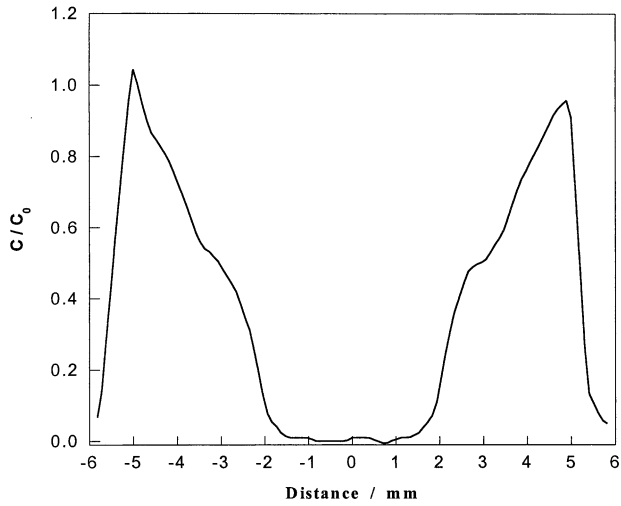

Figure 7. The cross section of an NMR image for water diffusion into a BMA/HEMA cylinder, $F_{HEMA} = 0.8$, at 37 °C. The profile was taken from the image shown in Figure 6. The symbol C represents the concentration of the water in the polymer matrix and C_0 the concentration of water at the surface of the cylinder.

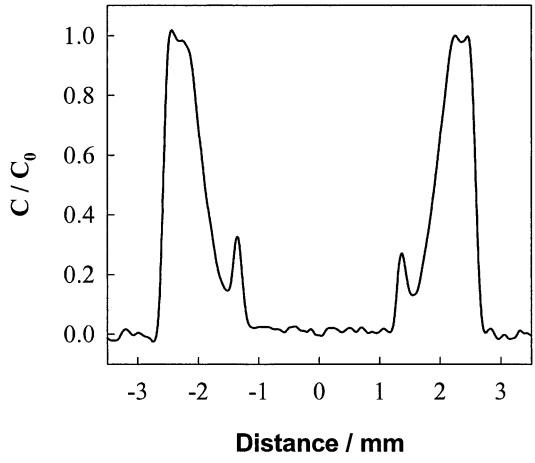

Figure 8. The cross section of an NMR image for water diffusion into a polyHEMA cylinder, diameter 5 mm, at 37 °C showing additional features at the edge of the glassy core. Fractional mass uptake 0.4. The symbol C represents the concentration of the water in the polymer matrix and C_0 the concentration of water at the surface of the cylinder.

As the diffusion front progresses through the cylinder, so too does the annulus of cracks. However, in the rubbery region behind the diffusion front the additional features are invisible because the plasticizing water molecules lower the Tg of the local matrix to below the measurement temparature. The greater mobility of the polymer chains therefore allow a repair process that can remove the remnants of the cracks. In the case of the BMA/HEMA cylinder, the presence of water in cracks is less evident than in polyHEMA cylinders, because of the inherently lower Tg of the matrix due to the presence of the bulky non-polar BMA side chains.

The diffusion coefficient for water can be determined by a curve fit of the profile of the diffusion front, such as those shown in Figures 7 and 8. For a Fickian model the variation of the water concentration with distance and time is given by:

$$\frac{C_{r,t}}{C_{0,\infty}} = 1 - \frac{2}{a}\sum_{n=1}^{\infty} \exp(-D\alpha_n^2 t)\frac{J_0(r\alpha_n)}{J_1(a\alpha_n)} \qquad (3)$$

where t is the time for which penetrant diffusion has occurred, $C_{r,t}$ is the concentration of the penetrant at distance r at time t, C_0 is the constant surface concentration, α_n and $J_0(x)$ are defined as above, and $J_1(x)$ is the Bessel function of the first order.

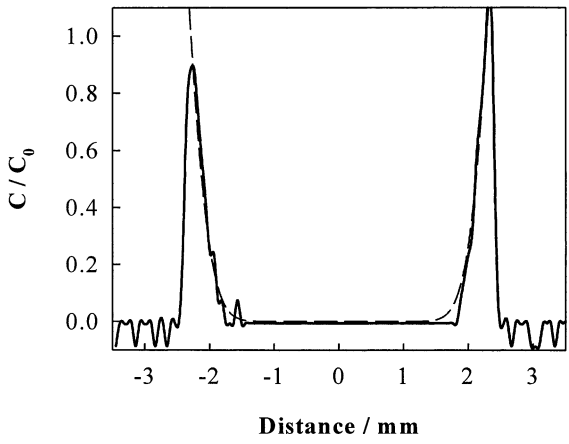

Figure 9. Concentration profile for diffusion of water into a polyHEMA cylinder, diameter 5 mm, at 37 °C showing a curve fit (----) to the profile based on equation 3. Fractional mass uptake 0.2. The symbol C represents the concentration of the water in the polymer matrix and C_0 the concentration of water at the surface of the cylinder.

Curve fits of the underlying water concentration profiles to equation 3 yielded values for the diffusion coefficients in agreement with those found from the mass uptake measurements within the experimental error. A typical curve fit to the profile of a polyHEMA cylinder is shown in Figure 9. For polyHEMA the best value of the diffusion coefficient, which fitted all of the profiles for fractional water uptakes from 0 to ≈0.95, was $1.5x10^{-11}$ m^2 s^{-1} [14]. This value compares well with the value of $1.7\pm0.2x10^{-11}$ m^2 s^{-1} obtained from the mass uptake study.

Conclusions

The diffusion of water into HEMA based polymers has been studied by mass uptake and NMR imaging. The value of the diffusion coefficient for water sorption into HEMA copolymers is lowered by the presence of a non-polar comonomer. By decreasing the proportion of HEMA in a copolymer, the average HEMA sequence length in the copolymer decreases, and so does the diffusion coefficient and equilibrium water content of the copolymer. For example the diffusion coefficient decreased significantly from $1.7\pm0.1x10^{-11}$ m^2s^{-1} for polyHEMA to $.9.1\pm0.1x10^{-12}$ m^2s^{-1} for CHMA/HEMA, $9.7\pm0.1x10^{-12}$ m^2s^{-1} for a BMA/HEMA and $1.3\pm0.1x10^{-11}$ m^2s^{-1} for a THFMA/ HEMA copolymer at compositions F_{HEMA}=0.8. The equilibrium water contents for the copolymers followed similar trends. The diffusion behaviour for water was found to be Fickian for the HEMA based copolymer systems. However, for polyHEMA and some of its copolymers with BMA, CHMA and THFMA, cracks were observed to appear in the glassy core adjacent to the diffusion front during water sorption, which allowed the formation of small water pools adjacent to the diffusion front.

Acknowledgements

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