Soluble chain fractions in hydrophilic polymer networks: origin and effect on dynamic uptake overshoots

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The dynamic swelling behaviour of crosslinked poly(2-hydroxyethyl methacrylate) networks containing well characterized soluble fractions of poly(ethylene glycol) was studied. The mass uptake as a function of time exhibited a significant overshoot above the final equilibrium value. The magnitude and duration of the overshoot depended on the concentration and molecular weight of the soluble fraction, and was attributed to the presence of the soluble fraction. A statistical model was used to show that polymer networks formed by free-radical copolymerization and crosslinking reactions may contain a significant intrinsic soluble fraction made up of unreacted monomer and polymer chains that have not become incorporated into the gel. It is therefore suggested that this soluble fraction may contribute to swelling overshoot. The statistical model was used to relate the quantity and molecular weight of the intrinsic soluble fraction to the free-radial reaction parameters.

(Keywords: non-Fickian transport; diffusion; network polymers; penetrant overshoots)

INTRODUCTION

Hydrophilic polymer networks such as poly(2-hydroxyethyl methacrylate) (PHEMA) and poly(ethylene glycol) (PEG) have been studied extensively as materials for pharmaceutical and biomedical applications[1–3], including carriers for controlled drug delivery and materials for prosthetic devices. One mechanism for controlled drug release[1,4] involves the swelling of a dry polymer network by a biological fluid. The swelling of the polymer network allows the incorporated drug to diffuse out. Since the solute diffusivity and release characteristics depend on the degree of swelling of the polymer network, a thorough understanding of the mechanism of water uptake, including the role of the intrinsic polymer soluble fraction, is required to predict and explain the release behaviour. Diffusional characteristics of the soluble fraction must also be considered when applications require polymer contact with biological tissue. Indeed, if soluble chains were to leach out, they might cause tissue irritation[5].

Penetrant transport in polymers has been studied both theoretically and experimentally[6–8]. A number of authors[9–29] have observed anomalous transport phenomena in which penetrant uptake did not obey Fick's law of diffusion. One type of anomalous transport, known as two-stage sorption[7,19–21], is often exhibited by a penetrant uptake *versus* time curve that attains a quasi-equilibrium value (a plateau), then increases to true equilibrium value. A second anomalous transport behaviour that has been observed in recent years with a variety of systems[22–32] is known as overshoot sorption. Plots of penetrant uptake *versus* time exhibit an uptake that passes through a maximum M_m and then decreases to a final equilibrium uptake value M_e as shown in *Figure 1*.

Uptake overshoots have been reported by Franson and Peppas[22] for water uptake in poly(2-hydroxyethyl methacrylate-*co*-*N*-vinyl-2-pyrrolidone) copolymers. The phenomenon was further investigated by Peppas and collaborators for cyclohexane transport in polystyrene[23–25] and by Vrentas *et al.*[26] for ethylbenzene vapour sorption into poly(ethyl methacrylate). Studies by Smith and Peppas[23] and Peppas and Urdahl[24,25] indicated that the penetrant overshoot was greater for loosely crosslinked samples. Based on these results, the sorption overshoot was attributed to different timescales of penetrant transport and macromolecular relaxation[23–25]. Thus, rapid penetrant uptake is followed by a relaxation of the macromolecular chains leading to partial exudation of the penetrant[23–25].

Kambour *et al.*[27], Titow *et al.*[28] and Overbergh *et al.*[29] have also observed sorption overshoots for penetrant transport in isotactic polystyrene and polycarbonates. The sorption overshoots were attributed to penetrant-induced crystallization. Ordered regions were formed during the transport process, causing rejection of previously sorbed penetrant. Solvent-induced ionic aggregation, resulting in a variety of dynamic swelling behaviour cases including uptake overshoot, has been reported by Lyubimova and Frenkel[30].

Lee[31,32] and Wood *et al.*[33] have observed water uptake overshoot in polymer gels containing water-soluble salts in the form of either drugs[31,32] or residual initiator[33]. This behaviour was attributed to an initially large chemical potential or osmotic driving force for swelling due to the presence of excess solute within the gel. Subsequently, the solute diffused out of the gel, thereby reducing this driving force and leading to deswelling of

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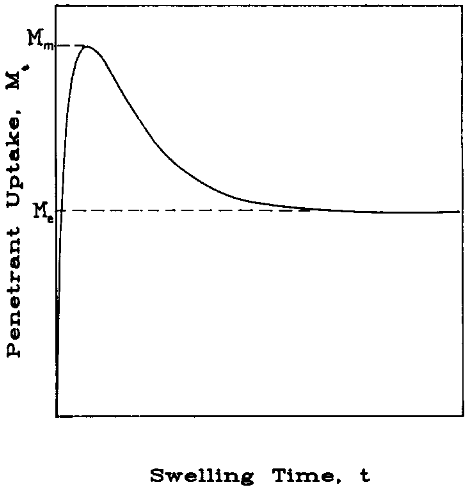

Figure 1 Penetrant uptake M_t as a function of time, illustrating sorption overshoot. Maximum uptake M_m and equilibrium uptake M_e are shown

the network. Eventually the concentrations inside and outside the network were equalized and the network reached its final equilibrium.

Brynda *et al.*[34] and Cifkova *et al.*[5] have recently discussed the presence of a soluble fraction consisting of oligomers and a small amount of high-molecular-weight chains in poly(2-hydroxyethyl methacrylate) (PHEMA) gels formed by free-radical copolymerization of 2-hydroxyethyl methacrylate (HEMA) with a small amount of the crosslinking agent ethylene glycol dimethacrylate (EGDMA). Although the authors did not consider the effect of this intrinsic soluble fraction on the dynamic swelling behaviour of the polymer gels, the oligomers and polymer chains could lead to a sorption overshoot in a manner similar to residual drugs or initiator.

In this paper, the effect of a soluble chain fraction (henceforth referred to as the sol fraction) on the dynamic swelling behaviour of the polymer network is examined. Well characterized sol fractions of known concentration and molecular weight are produced by polymerizing HEMA with inert poly(ethylene glycol) (PEG) chains of various lengths. The dynamic swelling behaviour is characterized as the quantity and molecular weight of the sol fraction are increased. A statistical model for the reaction system is used to illustrate that a significant fraction of the polymer may not be incorporated into the three-dimensional network, and therefore exists as a soluble and extractable fraction. The effect of this intrinsic sol fraction on the dynamic swelling behaviour is also examined. It is found that a soluble fraction may lead to overshoot sorption behaviour in a manner similar to soluble salts or residual initiator.

EXPERIMENTAL

Sample preparation

The monomer 2-hydroxyethyl methacrylate (HEMA; Aldrich Chemical Co., Milwaukee, WI) was purified by extraction[35] and was stored at a temperature of 5°C until use. Ethylene glycol dimethacrylate (EGDMA; Aldrich Chemical Co.) was used as received as the crosslinking agent. Poly(ethylene glycol) samples (PEG; Aldrich Chemical Co.) with number-average molecular weights of 194, 350, 1000, 1500 and 3400 were used to produce well characterized sol fractions.

The polymerizable monomer mixture contained 99 mol% HEMA and 1 mol% EGDMA. Inert uncrosslinked PEG was used to produce a well characterized sol fraction with mass fractions of 0, 0.05, 0.10 and 0.20. The free-radical polymerization was initiated with 0.4 wt% 2,2′-azobis(2-methylpropionitrile) (AIBN; Aldrich Chemical Co.) and was allowed to react at a temperature of 60°C for 15 h in 5 ml polyethylene vials under nitrogen. At the end of the reaction, the polymer cylinders were cut into discs with a diameter of 14.0 mm and a thickness of 1.0 mm. The variation in sample thickness was less than 5%.

Swelling studies

Dynamic swelling experiments were conducted in 500 ml of distilled deionized water at 25 ± 1°C. The PHEMA discs were weighed periodically and the sample weight was recorded along with total swelling time. After the samples reached an equilibrium degree of swelling, they were dried in air at 60°C for 7 days, then dried under vacuum over calcium sulphate to constant weight. The final dried weights of the samples were recorded.

MATHEMATICAL MODELLING

Sol fraction in three-dimensional networks

A three-dimensional polymer network may be formed by a polymerization reaction if at least one of the comonomers has a functionality greater than 2. In the copolymerization of HEMA and EGDMA, the former has a functionality of 2, while the latter has a functionality of 4. As the reaction proceeds, the reacting mixture contains linear chains and chains linked by crosslinks. At the gel point, there are enough crosslinks to produce a macromolecular network, which extends throughout the reaction mixture. Subsequently, the mixture contains a gel fraction, consisting of the polymer network, and a sol fraction, which contains unreacted monomer and polymer chains that have not become incorporated into the network. A sol fraction of polymer chains may exist even at complete conversion.

A network-forming reaction may be analysed using a statistical model in which structural information about the reaction system is obtained by considering the ensemble of tree-like structures built from the monomer units based on rules for bond formation[26]. Expressions for a variety of structural averages can be obtained most efficiently using link probability generating functions, which describe the distribution of bonded states between consecutive generations. Expressions for many structural averages have been derived in terms of the link probability generating functions[36–38], including pre-gel molecular weights, post-gel number of elastically active network chains, and gel and sol fractions. After the gel point, molecular weights of the sol fraction may be calculated independent of the gel[38].

Probability generating functions

The link probability generating functions for the free-radical copolymerization and crosslinking reaction have been formulated[39] and are shown below. The link probability generating functions for the zeroth generation are:

$$F_{01}(s_1, s_2) = 1-a+a\{(1-p)+p[(1-r)s_1+r(1-c)s_2+rc]\}^2 \quad (1)$$

$$F_{02}(s_1, s_2) = F_{01}^2 \quad (2)$$

The link probability generating functions for all generations higher than the zeroth are:

$$F_1(s_1, s_2) = 1-p+p[(1-r)s_1+r(1-c)s_2+rc] \quad (3)$$

$$F_2(s_1, s_2) = \{1-p+p[(1-r)s_1+r(1-c)s_2+rc]\}F_{01} \quad (4)$$

Here, the subscript 0 refers to the zeroth generation while the subscripts 1 and 2 refer to HEMA and EGDMA respectively. The parameter p is the probability of propagation, and is equal to the rate of propagation divided by the sum of the rates of propagation, termination and chain transfer. The parameter r is equal to the fraction of double bonds belonging to molecules of the crosslinking agent, and may be calculated from the composition of the initial monomer mixture. Finally the parameter c is equal to the fraction of the reacted crosslinking agent that is incorporated in intramolecular cycles. Here, s_1 and s_2 are dummy variables corresponding to HEMA and EGDMA, respectively. In this model, cyclization is accounted for in a simple and approximate manner. The analysis is discussed in more detail elsewhere[39].

The probability of propagation p is affected by any variable that changes the rate of propagation relative to the rates of termination and chain transfer. Therefore, p depends on the concentrations of reacting species such as monomers, chain transfer agents and growing radicals as well as factors such as viscosity and temperature. The value of p for a typical free-radical polymerization is around 0.996, with lower values in the presence of chain transfer agents. In general, the value of p will change during the course of the reaction due to the effects of monomer drift and diffusion-controlled termination; however, qualitative information about the reaction system can be obtained by assuming p remains constant. The values of p and c during the course of the reaction of HEMA with EGDMA are presently being measured. Here, we will show simulation results using representative values of these parameters to demonstrate their effect on the quantity and molecular weight of the intrinsic sol fraction.

The number-average primary chain length may be expressed in terms of the probability of propagation p. The primary chains are the linear polymer chains that would be left if all crosslinks were cut. The average primary chain length L_p is given by the following equation:

$$L_p = (1-p)^{-1} \quad (5)$$

The soluble weight fraction f_s may be expressed in terms of the link probability generating function[36–39] as shown below:

$$f_s = m_1 F_{01}(v_1, v_2) + m_2 F_{02}(v_1, v_2) \quad (6)$$

Here, m_1 and m_2 are the mass fractions of HEMA and EGDMA respectively, and v_1 and v_2 are the corresponding extinction probabilities, given by the lowest roots of the following simultaneous equations:

$$v_1 = F_1(v_1, v_2) \quad (7)$$

$$v_2 = F_2(v_1, v_2) \quad (8)$$

The average molecular weight of the soluble fraction may be calculated by writing probability generating functions that consider only the soluble fraction[38]. Quantities restricted to the soluble fraction will be distinguished by a circumflex (ˆ). The link probability generating functions for the soluble fraction can be written in terms of the overall generating functions as shown below:

$$\hat{F}_{01}(s_1, s_2) = \frac{F_{01}(v_1 s_1, v_2 s_2)}{F_{01}(v_1, v_2)} \quad (9)$$

$$\hat{F}_{02}(s_1, s_2) = \frac{F_{02}(v_1 s_1, v_2 s_2)}{F_{02}(v_1, v_2)} \quad (10)$$

The mole fractions $\hat{n}_1$ and $\hat{n}_2$ may be related to n_1 and n_2 as shown below:

$$\hat{n}_1 = \frac{n_1 F_{01}(v_1, v_2)}{n_1 F_{01}(v_1, v_2) + n_2 F_{02}(v_1, v_2)} \quad (11)$$

$$\hat{n}_2 = \frac{n_2 F_{02}(v_1, v_2)}{n_1 F_{01}(v_1, v_2) + n_2 F_{02}(v_1, v_2)} \quad (12)$$

The number-average molecular weight of the soluble fraction may be calculated using the following equation[38]:

$$\hat{M}_n = (2\hat{n}_1 M_1 + 2\hat{n}_2 M_2)/D$$

with

$$D = 2 - \hat{n}_1\left(\frac{\partial \hat{F}_{01}(s_1, s_2)}{\partial s_1} + \frac{\partial \hat{F}_{01}(s_1, s_2)}{\partial s_2}\right)_{s_1=s_2=1} - \hat{n}_2\left(\frac{\partial \hat{F}_{02}(s_1, s_2)}{\partial s_1} + \frac{\partial \hat{F}_{02}(s_1, s_2)}{\partial s_2}\right)_{s_1=s_2=1} \quad (13)$$

RESULTS AND DISCUSSION

Sol fraction simulations

Simulation results for the quantity and molecular weight of the sol fraction at complete conversion demonstrate the effect of the parameter p. *Figure 2* shows simulation results for the sol fraction as a function of conversion for a system in which $p = 0.996$, $r = 0.0198$ and $c = 0.04$. A value of $r = 0.0198$ corresponds to an EGDMA fraction of 1 mol%. Before the gel point, the reaction mixture is 100% sol fraction. After the gel point the sol

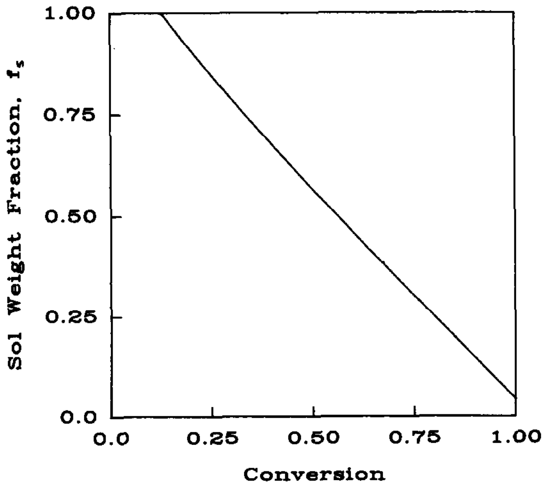

Figure 2 Simulation results for sol weight fraction f_s as a function of conversion with $p = 0.996$, $r = 0.0198$, $c = 0.04$

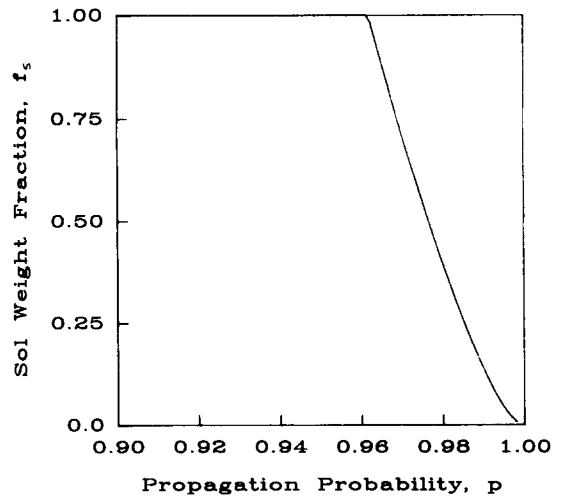

Figure 3 Simulation results for sol weight fraction at complete conversion f_s as a function of propagation probability p, with $r = 0.0198$, $c = 0.04$

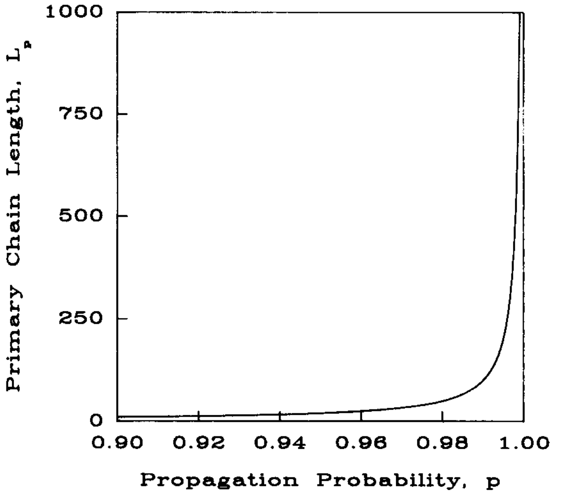

Figure 4 Simulation results for primary chain length L_p as a function of propagation probability p

fraction decreases monotonically as material is incorporated in the network. At 100% conversion, most of the polymer is incorporated into the gel; however, a small fraction remains in the sol.

Figure 3 shows the effect of the parameter p on the sol fraction at complete conversion. The sol fraction increases as p decreases due to a reduction in the primary chain length, as shown in *Figure 4*, as the rate of propagation is reduced relative to the competing reactions. For $p < 0.96$, a value corresponding to a primary chain length of less than 25 repeating units, the sol fraction at complete conversion is 100% for a system containing 1% crosslinking agent. In this regime, the primary chain length is too short to allow the formation of a network structure since a significant number of chains will not contain any crosslinker units.

Figure 5 shows the effect of the parameter p on the number-average molecular weight of the sol fraction at complete conversion. For $p \leqslant 0.96$, the value corresponding to 100% sol fraction at complete conversion, an increase in p results in an increase in the molecular weight of the sol fraction due to the increase in the primary chain length. For $p > 0.96$, a network structure is formed before complete conversion, and the molecular weight of the sol fraction decreases as p increases because the longest chains have become incorporated into the gel.

Dynamic swelling results

In *Figures 6–10*, experimental data points are denoted by circles, squares, diamonds or triangles while the full curves represent cubic spline fits to the data. *Figure 6* shows the dynamic swelling profile of a crosslinked PHEMA sample containing 0.10 soluble fraction of PEG with molecular weight 196, as well as a small amount of intrinsic soluble fraction. The normalized mass uptake behaviour exhibits a pronounced maximum followed by a deswelling to a final equilibrium degree of swelling. The effect of the PEG mass fraction on the magnitude of the overshoot is shown in *Figure 7*. Clearly the magnitude of the overshoot increases as the PEG concentration increases from 0 to 0.20.

The effects of the molecular weight of the soluble fraction on the magnitude and duration of the uptake overshoot are shown in *Figure 8*. The largest overshoot

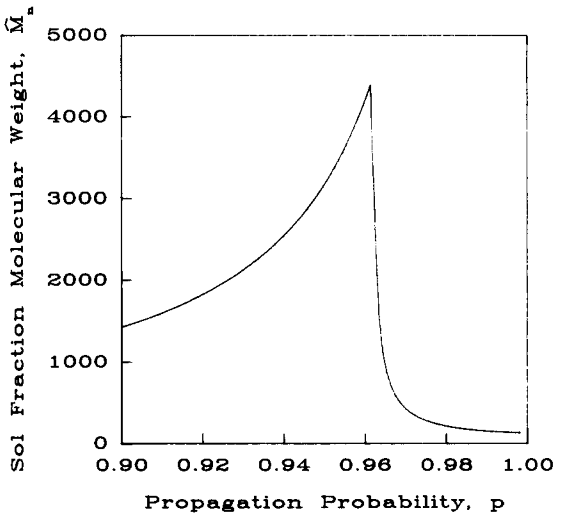

Figure 5 Simulation results for the sol fraction number-average molecular weight at complete conversion $\bar{M}_n$ as a function of probability p, with $r = 0.0198$, $c = 0.04$

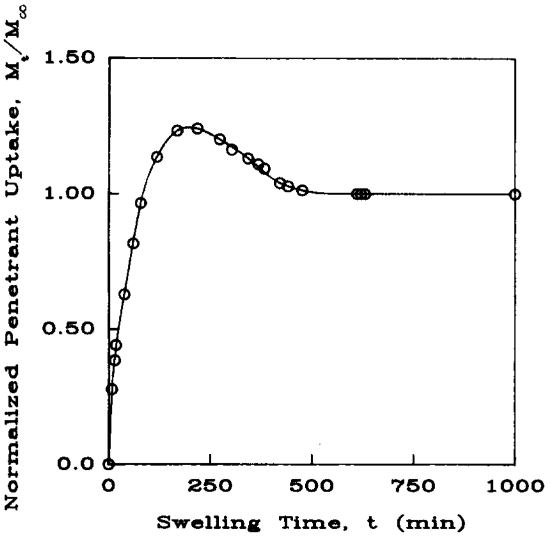

Figure 6 Dynamic swelling profile for a crosslinked PHEMA network containing 10 wt% PEG of molecular weight 196

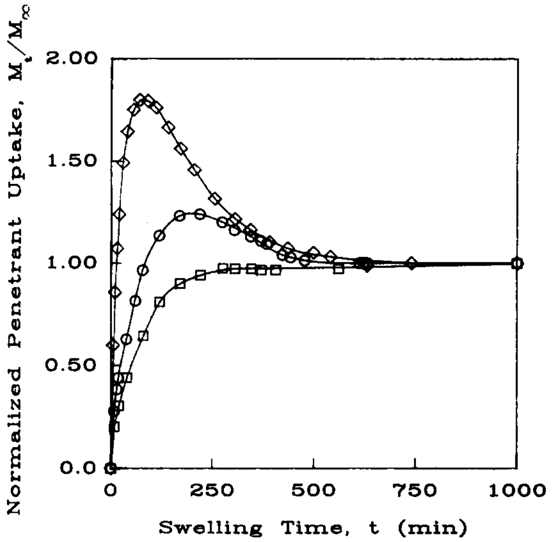

Figure 7 Dynamic swelling profiles for crosslinked PHEMA networks containing PEG of molecular weight 196: (□) 0 wt% PEG; (○) 10 wt% PEG; (◇) 20 wt% PEG

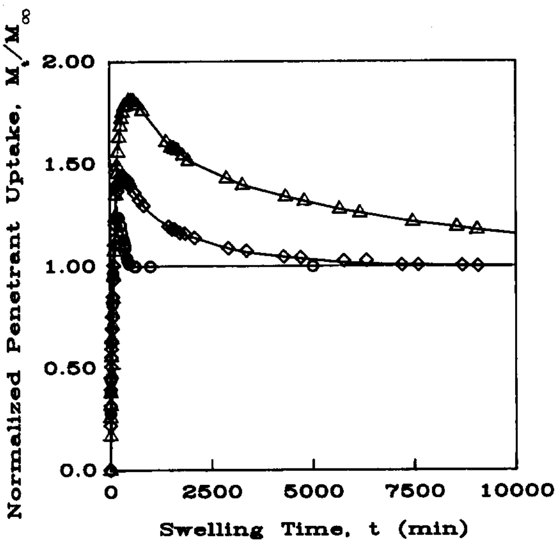

Figure 8 Dynamic swelling profiles for crosslinked PHEMA networks containing 10 wt% PEG of various molecular weights M_p: (○) $M_p=196$; (◇) $M_p=1500$; (△) $M_p=3400$

Water uptake overshoot and sol fraction

The uptake overshoots observed for this system, shown in *Figures 6–9*, may be attributed to the presence of a soluble PEG fraction in the crosslinked PHEMA network. The initially high degree of swelling is due to the enhanced affinity of the network for water arising from the free energy of mixing of water with the PHEMA gel and the PEG sol. Initially the system absorbs water to a maximum level; simultaneously the PEG sol fraction starts to diffuse out of the network. The diffusion of sol fraction out of the gel results in a decrease in the chemical potential (osmotic) driving force for swelling and the sample begins to deswell. Eventually, the PEG concentration reaches an equilibrium value inside and outside the network, and the sample reaches its equilibrium swelling value.

The dependence of the magnitude of the sorption overshoot on the fraction of the incorporated sol shown in *Figure 7* supports these conclusions. Higher overshoots corresponds to the sample with the largest PEG molecular weight. Furthermore, the length of time required for the uptake to attain its final equilibrium value increases as the PEG molecular weight is increased.

Finally, *Figures 9* and *10* illustrate the effects of extraction of the soluble chain fraction on subsequent dynamic swelling profiles. *Figure 9* shows the dynamic swelling profiles for a sample that originally contained 0.10 sol fraction of PEG 196. The initial dynamic swelling profile exhibits a pronounced overshoot. The sample was subsequently dried and a second mass uptake profile was obtained. Although the initial mass uptake profile exhibits overshoot behaviour, the second swelling reveals no overshoot. *Figure 10* shows the mass uptake profile for a sample containing only the intrinsic sol fraction (5.5 wt%), along with a profile obtained after the sol fraction was extracted. Although neither profile exhibits a pronounced swelling overshoot, the sample containing the intrinsic sol fraction exhibits a more rapid initial swelling rate.

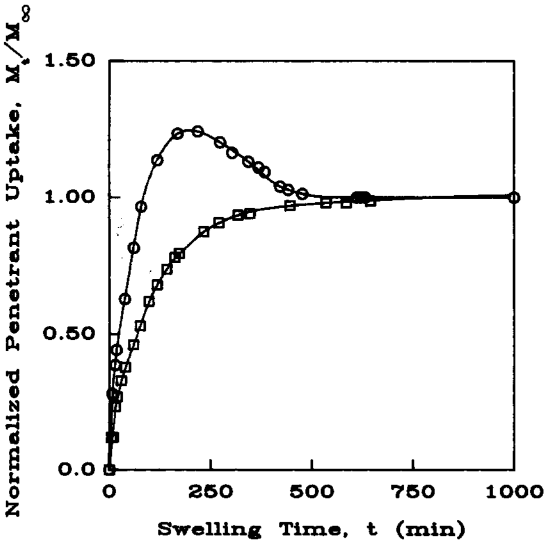

Figure 9 Dynamic swelling profiles for a crosslinked PHEMA network containing 10 wt% PEG of molecular weight 196: (○) before extraction of sol fraction; (□) after extraction of sol fraction

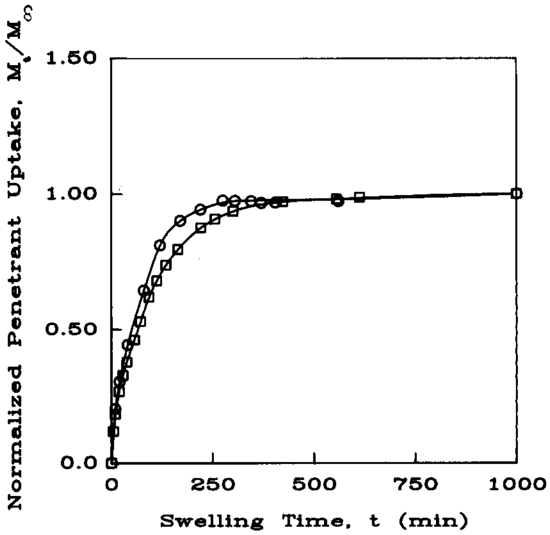

Figure 10 Dynamic swelling profiles for a crosslinked PHEMA network containing 5.5 wt% intrinsic soluble chains: (○) before extraction of sol fraction; (□) after extraction of sol fraction

are observed as the sol fraction is increased, and no appreciable overshoot is observed for samples containing no added soluble fraction. Furthermore, if the sol fraction is removed from the sample by extraction, subsequent dynamic swelling experiments do not exhibit overshoot, as shown in *Figure 9*. Since PHEMA does not crystallize, especially in the presence of water, the observed overshoot cannot be attributed to solvent-induced crystallization.

The dependence of the magnitude and duration of the sorption overshoot on the sol fraction molecular weight is also consistent with this picture. As the molecular weight of the sol fraction increases, the rate at which it diffuses through the network decreases, thus increasing the duration of the overshoot, as shown in *Figure 8*. Furthermore, the reduced rate of diffusion for large-molecular-weight sol fractions allows the overshoot degree of swelling to develop fully while a large fraction of the sol is still trapped inside the network. For this reason, the overshoot degree of swelling becomes more pronounced as the molecular weight of the PEG sol fraction increases.

The effect of the intrinsic sol fraction on the dynamic swelling behaviour is shown in *Figure 10*. The dried samples after the sol fraction had been extracted indicated that the sample originally contained 5.5 wt% intrinsic soluble fraction. This result is in good agreement with the simulation results for a sample polymerized to high conversion if chain transfer is not excessive. Although the intrinsic sol fraction did not result in a pronounced overshoot, it did lead to an enhanced swelling rate, as shown in *Figure 10*. The soluble fraction lowers the gel-phase chemical potential of water, and hence increases the overall driving force for swelling. A sol fraction containing PEG leads to more a dramatic uptake overshoot than the intrinsic HEMA sol fraction due to the greater thermodynamic compatibility of PEG with water. If chain transfer were extensive during the network-forming reaction, the intrinsic sol fraction would probably cause an appreciable overshoot.

Simulation results using the previously developed model indicate that a significant fraction of the polymer chains at complete conversion may not be incorporated in the three-dimensional network, and therefore exists as a soluble fraction. The simulations demonstrate that the quantity and molecular weight of the soluble fraction depend on the value of the parameter p, and therefore depend upon the reaction conditions. For example, the presence of a chain transfer agent would lead to a lower value of p and would increase the quantity of the intrinsic sol fraction. The simulation results for the quantity of the intrinsic sol fraction were in good agreement with our experimental results, while simulation results for the sol fraction molecular weight are consistent with the experimental results reported by Brynda *et al.*[34].

CONCLUSIONS

Sorption overshoots of water in crosslinked poly(2-hydroxyethyl methacrylate) networks may result from the presence of a soluble polymer fraction. This conclusion is supported by the dependence of the magnitude and duration of the uptake overshoot on the concentration and molecular weight of the sol fraction. Simulations using a statistical model for network formation by the free-radical copolymerization and crosslinking reaction indicate that a significant amount of sol fraction may exist at complete conversion. The possible presence of a soluble fraction in a network polymer should be considered when analysing dynamic swelling behaviour.

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REFERENCES

1 Peppas, N. A. 'Hydrogels in Medicine and Pharmacy', CRC Press, Boca Raton, FL, 1987, Vols II and III
2 Langer, R. S. and Peppas, N. A. *Biomaterials* 1981, **2**, 201
3 Andrade, J. D. 'Hydrogels for Medical Related Applications', ACS Symp. Ser. No. 31, American Chemical Society, Washington, DC, 1976
4 Langer, R. S. and Peppas, N. A. *J. Macromol. Sci. Rev. Macromol. Chem. Phys. (C)* 1983, **23**, 61
5 Cifkova, I., Brynda, E., Mandys, V. and Stol, M. *Biomaterials* 1988, **9**, 372
6 Windle, A. H. in 'Polymer Permeability' (Ed. J. Comyn), Elsevier Applied Science, New York, 1985, p. 75
7 Astarita, G. and Nicolais, L. *Pure Appl. Chem.* 1983, **55**, 727
8 Lustig, S. R., Caruthers, J. M. and Peppas, N. A. *Polym. Prep.* 1989, **30** (1), 7
9 Alfrey, T., Gurnee, E. F. and Lloyd, W. G. *J. Polym. Sci.* 1966, **12**, 249
10 Peterlin, A. *Makromol. Chem.* 1969, **124**, 136
11 Kwei, T. K. and Zupko, H. M. *J. Polym. Sci. (A2)* 1969, **7**, 867
12 Wang, T. T., Kwei, T. K. and Frisch, H. L. *J. Polym. Sci. (A2)* 1969, **7**, 2019
13 Astarita, G. and Sarti, G. C. *Polym. Eng. Sci.* 1978, **18**, 388
14 Thomas, N. L. and Windle, A. H. *Polymer* 1980, **21**, 60
15 Petropoulos, J. H. and Roussis, P. R. *J. Membr. Sci.* 1978, **3**, 343
16 Peppas, N. A. and Sinclair, J. L. *Colloid. Polym. Sci.* 1983, **261**, 404
17 Berens, A. R. and Hopfenberg, H. B. *Polymer* 1978, **18**, 489
18 Vrentas, J. S. and Duda, J. L. *J. Polym. Sci., Polym. Phys. Edn* 1977, **15**, 403
19 Vieth, W. R., Howell, J. M. and Hsieh, J. H. *J. Membr. Sci.* 1976, **1**, 177
20 Bagley, E. and Long, F. A. *J. Am. Chem. Soc.* 1955, **23**, 2172
21 Joshi, S. and Astarita, G. *Polymer* 1979, **20**, 455
22 Franson, N. M. and Peppas, N. A. *J. Appl. Polym. Sci.* 1983, **28**, 1299
23 Smith, M. J. and Peppas, N. A. *Polymer* 1985, **26**, 569
24 Peppas, N. A. and Urdahl, K. F. *Eur. Polym. J.* 1988, **24**, 13
25 Peppas, N. A. and Urdahl, K. G. *Polym Bull.* 1986, **16**, 201
26 Vrentas, J. S., Duda, J. L. and Hou, A. C. *J. Appl. Polym. Sci.* 1984, **29**, 399
27 Kambour, R. P., Karasz, F. E. and Daane, J. H. *J. Polym. Sci.* 1966, **4**, 327
28 Titow, W. V., Braden, M., Currell, B. R. and Loneragan, R. J. *J. Appl. Polym. Sci.* 1974, **18**, 867
29 Overbergh, N., Berghmans, H. and Smets, G. *Polymer* 1975, **16**, 703
30 Lyubimova, V. A. and Frenkel, S. *Polym. Bull.* 1984, **12**, 229
31 Lee, P. I. *Polym. Commun.* 1983, **24**, 45
32 Lee, P. I. *J. Controlled Release* 1985, **2**, 277
33 Wood, J. M., Attwood, D. and Collett, J. H. *Int. J. Pharm.* 1981, **7**, 189
34 Brynda, E., Stol, M., Chytry, V. and Cifkova, I. *J. Biomed. Mater. Res.* 1985, **19**, 1169
35 Horsley, L. H. and Sheetz, D. P. US Patent 3162677, 1964
36 Gordon, M. *Proc. R. Soc. Lond. (A)* 1962, **268**, 240
37 Dobson, G. R. and Gordon, M. *J. Chem. Phys.* 1965, **43**, 705
38 Gordon, M. and Malcolm, G. N. *Proc. R. Soc. Lond. (A)* 1966, **295**, 29
39 Scranton, A. P. and Peppas, N. A. *J. Polym. Sci., Polym. Chem. Edn* 1990, **28**, 39