Synthetic hydrogels: 1. Hydroxyalkyl acrylate and methacrylate copolymers – water binding studies

Philip H. Corkhill, Alan M. Jolly, Chiong O. Ng and Brian J. Tighe
Speciality Polymer Group, Department of Molecular Sciences, Aston University, Aston Triangle, Birmingham B4 7ET, UK

(*Received 29 September 1986; revised 10 March 1987; accepted 16 March 1987*)

Copolymers of hydroxyethyl acrylate (HEA), hydroxypropyl acrylate (HPA), hydroxyethyl methacrylate (HEMA) and hydroxypropyl methacrylate (HPMA) with styrene and with methyl methacrylate have been studied. Variations in nature and composition have been correlated, both with the total equilibrium water content of the resultant hydrogel and with the more detailed water binding behaviour as revealed by differential scanning calorimetry studies. Differential scanning calorimetry enables the relative proportions of non-freezing and freezing water to be determined and, in addition, enables the fine structure of the melting endotherm to be observed. Particular interest centres around the ability to produce hydrogels in which all freezing water has been eliminated by progressive incorporation of non-hydrophilic monomer or crosslinking agent (ethylene glycol dimethacrylate). Distinct differences are observed between hydrophilic acrylates and methacrylates in the relative effects of temperature on the equilibrium water contents of their respective copolymer series.

(Keywords: hydrogel; water binding; differential scanning calorimetry; hydroxyalkyl acrylates)

INTRODUCTION

Hydrogels may be conveniently described as hydrophilic polymers that are swollen by, but do not dissolve in, water. This is usually achieved by a low degree of crosslinking, as in the case of conventional elastomers, which means that hydrogels are effectively water-swollen polymer networks. Although many naturally occurring polymers may be used to produce this type of material, the structural versatility available in synthetic hydrogels has given them distinctive properties, which in turn have enhanced their practical utility. Although the constituent monomers had been known for some years, it was not until Wichterle and coworkers[1] drew attention to the unique properties of hydrogels based on poly(2-hydroxyethyl methacrylate), in the early 1960s, that interest in this class of materials was aroused. Another notable feature of this Czechoslovakian work was the demonstration that hydrogels of this type could be used for the fabrication of soft contact lenses[2], which has proved to be their most fruitful commercial application.

Although much work has been carried out on polyHEMA there have been relatively few studies of copolymers of HEMA with hydrophobic comonomers. Linear and block copolymers of HEMA with styrene have been examined to determine the effect of composition on the surface properties[3,4]. The reaction rates and reactivity ratios for the HEMA–St system and for the polymerization of HEMA with hydrophobic alkyl acrylates have also been determined[5,6]. Our interest in such systems has been associated principally with biomedical applications, such as contact lenses and artificial liver support systems. Some aspects of this work have been patented and the biomedical relevance of this type of material reviewed[7–11].

The underlying role of water in acting as a plasticizer, a transport medium in the polymer matrix for dissolved species (such as oxygen) and a 'bridge' between the very different surface energies of synthetic polymers and body fluids, is responsible for the unique position that hydrogels occupy in the field of biomaterials. The resultant interest in biomedical and other applications of hydrogels is reflected both in specific studies on, for example, thromboresistance[12,13] and in the substantial number of reviews of these areas[7,14–17].

The water absorbed by a hydrogel network is quantitatively represented by the equilibrium water content, *EWC*, the ratio of the weight of water in the hydrogel to the weight of the hydrogel at equilibrium hydration, expressed as a percentage:

$$EWC = \frac{\text{weight of water in the gel}}{\text{total weight of hydrated gel}} \times 100\% \quad (1)$$

The *EWC* is arguably the most important single property of a hydrogel, influencing as it does the permeability, mechanical, surface and other properties of the gel. There is a great deal of evidence to suggest that water in polymers can exist in more than one state[18–40] and that these states of water in the hydrogel will also affect its properties. This evidence will be amplified later in this paper. Thus the water present in a polymer network exists in a continuum of states between two extremes. These are, water strongly associated with the polymer network through hydrogen bonding, sometimes called 'bound' or non-freezing water, and water with a much greater degree of mobility, unaffected by the polymeric environment and sometimes referred to as 'free' or freezing water. The properties of a hydrogel are therefore strongly influenced

0032-3861/87/101758-09$03.00

both by the *EWC* of the hydrogel and by the ratio of freezing to non-freezing water.

Although of long standing interest in natural polymers, especially the cellulosics, water binding has only relatively recently attracted interest in synthetic systems of this type. Work on the water binding of cellulose and related materials has been in progress since 1933 and this early work, where there was much variation in the results, has been discussed by several authors[31,41]. There has also been interest in the water binding properties of cellulose acetate[20] for use in reverse osmosis membranes for desalination, where a low freezing water content promotes salt rejection.

A variety of techniques exists for the study of water binding in polymers. This may lead to confusion because the ratio of the various states of water present in the hydrogel will depend on the experimental technique used. Each technique can have some influence on the water structuring, together with the dynamic and thermodynamic properties of the water present in the hydrogel. Thus the technique used to study water binding will to some extent determine the number of states into which the water is classified and even the terms used to describe those states. A comparison of these descriptions has been assembled in *Table 1*.

When water binding is studied by differential scanning calorimetry (d.s.c., the technique favoured in the studies presented here) it is convenient to refer directly to the experimentally determined states (i.e. non-freezing and freezing water). This difference arises because the freezing behaviour of water in these polymers is anomalous, as even when cooled to very low temperatures only part of the available water in the polymer freezes. This enables a quantitative determination of the relative amounts of freezing and non-freezing water to be made and further information to be obtained from the fine structure of the melting endotherms.

In this paper the results of measurements of physical properties and water binding behaviour of various hydrophilic–hydrophobic copolymer hydrogels will be presented. These provide a useful insight into the effect of structure on water binding processes and the key to a range of applications for these materials, some of which have been outlined above.

EXPERIMENTAL

Monomers

Optical grade HEMA was supplied by Kelvin Lenses Ltd. 2-Hydroxypropyl methacrylate (BDH), hydroxyethyl acrylate (BDH), hydroxypropyl acrylate (BDH), methyl methacrylate (BDH) and styrene (BDH) were purified by reduced pressure distillation as described in the literature[42] and their purity monitored by gas–liquid chromatography (g.l.c.). Ethylene glycol dimethacrylate (BDH) and azo-bis-isobutyronitrile (Aldrich) were used as supplied.

Preparation of membranes

Membranes were produced by the polymerization of the monomer mixture in a glass mould. Two glass plates (15 cm × 10 cm) were each covered by a Melinex (polyethylene terephthalate) sheet to permit easy separation of the plates. The plates were placed together with two polyethylene gaskets (each 0.2 mm thick) separating the Melinex sheets. Spring clips were used to hold the mould together, leaving sufficient space for the insertion of a G22 syringe needle for the injection of the monomer mixture into the mould cavity.

Table 1 Comparison of terms used in water binding studies

Terms				Reference
Primary	Secondary			27, 28, 29
Bound	Free			21, 22, 23, 26
Non-freezing	Freezing			20, 21, 32
Primary bound	Secondary bound	Free	Bulk	30, 31
Bound water which rejects salts	Bound water which can contain salts	Free water weakly interacting with polymer	Completely free water	36
Bound	Interfacial	Bulk		18, 19
Bound	Interfacial	Free		33, 34, 35
Non-freezing	Freezable bound	Free		37, 38, 39, 40
X	Y	Z		18, 19, 33, 34
W_3	W_2	W_1		24, 25

In a typical copolymer composition the monomers were mixed together with ethylene glycol dimethacrylate crosslinker 1.0% (w/w) and azo-bis-isobutyronitrile 0.5% (w/w) until a homogeneous solution was obtained. The mixture was outgassed with nitrogen before injection into the mould. The mould was then placed in an oven at 60°C for three days followed by 2 h postcure at 90°C. The spring clips were removed and, after opening the mould, the membrane was separated from the Melinex sheets, then placed in distilled water to hydrate for at least a week. Studies with a variety of monomer combinations showed that, provided the hydration medium was changed daily, constant values of equilibrium water content were reached in four or five days. Our experience, with the systems described in this paper, is that the period of time was sufficient both to reach equilibrium hydration and to extract any of the water soluble residuals (as detected by the appropriate g.l.c. technique used in initial assessments of monomer purity).

Equilibrium water content

The *EWC* was measured by weight difference as follows. Samples were cut from a hydrated sheet of the hydrogel with a size seven cork borer. Any surface water was removed with filter paper before the samples were transferred to a pre-weighed sample bottle. The number of samples used (5–10) was varied according to the expected water content in order to give a reasonable total hydrated weight (*ca.* 0.2 g). Thus, even with lower (*ca.* 5%) water content polymers this produced a difference between hydrated and dehydrated weights of 0.01 g.

The samples were weighed, then dehydrated overnight under vacuum at 60°C to achieve constant weight. The *EWC* was calculated using equation (1), and the final value is an average of the results from at least three determinations. Some attempt to obtain an objective view of the precision of the measurement was made with the important hydrogel, polyHEMA. A statistical analysis on 100 samples of the hydrogel was found to give a mean *EWC* of 37.6% with $\Sigma_{n-1}=0.42$.

The accuracy of this technique depends on the assumption that the sample of constant weight, obtained by vacuum dehydration, contains no water. This has been a source of some debate in the field of hydrogel chemistry.

Our use of refractive index and density measurements provided a helpful means of support for this assumption. The densities and refractive indices of hydrated samples are affected by the water binding states (see 'Water binding studies', below) in the polymer. For this reason they are not useful as unambiguous techniques for *EWC* determination. However, no such problems arise with dehydrated samples. A more sensitive method for detecting water (independent of its binding state) in hydrogels is the Karl Fischer titration. This may be used as a rapid method of *EWC* determination. In this context, however, it is particularly valuable in confirming the validity of the vacuum dehydration technique for the removal of water. This confirms the validity of the assumption in the gravimetric method for *EWC* determination.

Refractive index

The refractive indices of hydrated copolymer sheets were measured with an Abbé refractometer, the temperature of the prisms being controlled by circulating water from a controlled temperature water bath.

Density measurements

The densities of hydrogel membranes were determined in both hydrated and dehydrated states by using a Davenport density gradient column apparatus. Columns were constructed following the procedure in the instruction manual[43], with a mixture of two miscible liquids to give a density range from 1.00 to 1.32 g cm^{-3}. The columns were calibrated using coloured marker floats of known densities, which were placed in the column and allowed to reach equilibrium. The positions of the floats at equilibrium were then measured with a cathetometer.

The densities of the hydrogels in the dehydrated state were measured as follows. A sample cut from a hydrated sheet was dehydrated under vacuum at 60°C to constant weight. The dehydrated sample was then moistened in carbon tetrachloride and introduced into the top of a suitable column of known density range. The position of the sample was monitored with time and the final height was recorded when equilibrium had been attained. To obtain the densities of hydrated samples the surface water was removed with a soft tissue paper and the sample was moistened with carbon tetrachloride before being introduced into the top of the density gradient column. The position of the sample was again monitored with time and the final height reading was taken when equilibrium had been reached.

For both hydrated and dehydrated samples height readings for several samples of the same composition were taken and the average was used, together with the calibration curve constructed from the cathetometer readings of the marker floats of known density, to determine the density of each composition.

Differential scanning calorimetry

Thermograms were obtained using a Perkin–Elmer differential scanning calorimeter, DSC-2, fitted with a liquid nitrogen sub-ambient accessory. From a hydrated sheet of the gel 1–4 mg samples were cut and the surface water was carefully removed with filter paper. The samples were sealed in pre-weighed aluminium sample pans and the weight of each sample noted. The samples were cooled to 223 K to ensure that any supercooled water was frozen and then allowed to reach equilibrium. The samples were then heated to 253 K and subsequently heated at the rate of 5 K min^{-1} to ambient temperature. The thermogram was recorded on a Servoscribe 1S 524-20 potentiometric recorder, fitted with a temperature event monitor and a DISC integrator.

A calibration graph was obtained by measuring areas under the peaks produced by weighed samples of distilled water under identical conditions. The area under the melting peaks of the hydrogel sample was measured and the amount of freezing water present in the hydrogel was calculated from the calibration graph.

RESULTS AND DISCUSSION

General observations

A range of polymers and copolymers was prepared, containing varying proportions of styrene and methyl methacrylate on the one hand and hydroxy alkyl acrylates and methacrylates on the other. The copolymers prepared are essentially random copolymers, as the reactivity ratios of the monomers are similar. Thus in the HEMA–St copolymer the reactivity ratios are 0.56 and 0.41, respectively, and for the HEMA–MMA copolymer the values are 1.25 and 0.79, respectively. There is almost 100% conversion in the system, with only traces of hydroxyalkyl acrylates or methacrylates being eluted when the polymers are hydrated. The composition of the copolymers is substantially as predicted, this being confirmed by elemental analysis and density measurements on hydrated and dehydrated polymers. Departure from stoichiometry is comparatively unimportant here, but produces problems and marked deviation from random behaviour in, for example, hydrogels based on styrene–vinyl pyrrolidone copolymers where the reactivity ratios are 15.7 and 0.045, respectively.

All the copolymers investigated contained both a hydrophilic and a hydrophobic component. The HEMA–St, HEMA–MMA and HPMA–St copolymers were found to be rigid and brittle over the whole composition range, in the dehydrated state. However, the corresponding copolymers containing HEA or HPA were comparatively flexible, the flexibility increasing with increasing HPA or HEA content. When hydrated, the flexibility of the copolymers was dependent on the amount of water absorbed, which in turn depends upon the interaction between water molecules and the polar chains of the copolymers.

This varying interaction of water with the polymers can be monitored both in terms of mechanical properties and in terms of freezing and non-freezing water states by d.s.c. The nature of water binding has important consequences for the permeability and permselectivity of the polymers, which will be discussed in subsequent papers.

Copolymer structure and hydration properties

The effect of the hydrophilic component on the *EWC* of styrene copolymers, with each of the hydroxyalkyl acrylates and methacrylates studied, is shown in *Figure 1*. In all the copolymer series the *EWC* increases as the percentage of hydrophilic monomer in the copolymer increases. The *EWC* of the copolymers at a given composition depends upon the balance of contributing

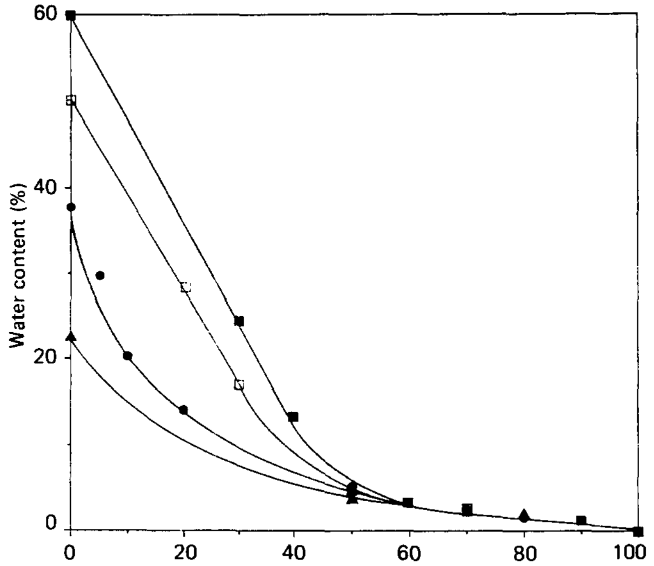

Figure 1 Variation in equilibrium water content with composition at 22°C for styrene copolymers with: (●) HEMA, (▲) HPMA, (■) HEA and (□) HPA

steric and polar effects. The polar contribution arises predominantly from the hydroxyl group and to a lesser extent from the ester group, whereas the steric effects arise from the combined contribution of the phenyl group, together with the α-methyl group and alkyl side chain component of the hydrophilic monomer. In copolymers where styrene is the major component, the *EWC*s of the hydrated copolymers are virtually independent of the nature of the hydrophilic monomer. In these compositions the bulky phenyl group is the dominant factor controlling the water absorption of the copolymer. These copolymers are rigid, as would be expected from materials with a low water content. When the hydrophilic monomer is the major component of the copolymer it controls the *EWC* and it can be seen that the hydrophilicities of the monomers decrease in the order HEA>HPA>HEMA>HPMA. It would be expected that because of the adidtional steric hindrance of the α-methyl group on the polymer backbone, HEA and HPA would be more hydrophilic than HEMA and HPMA respectively. The *EWC*s of the homopolymers show that HPA and HPMA are more hydrophobic than HEA and HEMA respectively, because of the extra CH_2 group in the sidechain.

It is interesting to compare the isomeric monomers HPA and HEMA. The greater water content of the HPA copolymers, throughout the composition range, illustrates that a greater reduction in water content is obtained by methylene insertion onto the backbone than methylene introduction in the sidechain.

The densities of the HEMA–St and HEMA–MMA copolymers were measured in both the hydrated and dehydrated states (*Figure 2*). In the dehydrated copolymers density increases linearly with increasing amounts of HEMA. This suggests that the copolymer composition varies linearly between the two extremes, as would be expected from a random amorphous copolymer. However, in the hydrated polymers the densities pass through a maximum. The composition of the copolymer at this maximum is consistent with the composition at which an obvious transition of the hydrated sample, from rigid to flexible, takes place. The copolymer composition at which this maximum occurs can be thought of as the composition separating hydrogels and non-hydrogels, for that copolymer series. As subsequent results and discussion will show, there is a compositional variation in the water structuring properties of these copolymers, a feature that may be conveniently observed by d.s.c. measurements. Initially (i.e. at low hydroxylalkyl acrylate or methacrylate compositions) the water absorbed is strongly hydrogen bonded to the polymer. At higher proportions of hydrophilic monomer and therefore higher *EWC*s, strongly bound water is present together with water in a more mobile form, sometimes called free or more correctly freezing water. Polymer combined with freezing water has a lower density than polymer combined with strongly bonded water. Therefore the densities of the hydrated copolymers start to reflect this.

Water binding will subsequently be discussed in more detail, but one further observation is appropriate at this point, namely that freezing water can also be regarded as plasticizing water in view of its greater relative effect on chain mobility. It is for this reason that the transition from rigid to flexible behaviour, referred to above, takes place at a point corresponding to the first appearance of freezing water in the copolymer series.

The refractive index of the dehydrated HEMA–St copolymer decreases linearly with increasing amounts of HEMA (*Figure 3*). With the hydrated copolymer, however, the refractive index decreases substantially, at the same copolymer composition at which the density started to reverse (*Figure 2*). This corresponds to the point where freezing water is first present in the hydrogel and would be expected since the refractive index of water (1.33) is much lower than that of dehydrated polyHEMA (1.50) or polystyrene (1.59). Both density and refractive index measurements may be used to predict the *EWC* of hydrogels. When the polymers contain substantial relative proportions of non-freezing water, however, abnormally low values are obtained for the water contents, unless a correction is made for the water binding phenomenon described above.

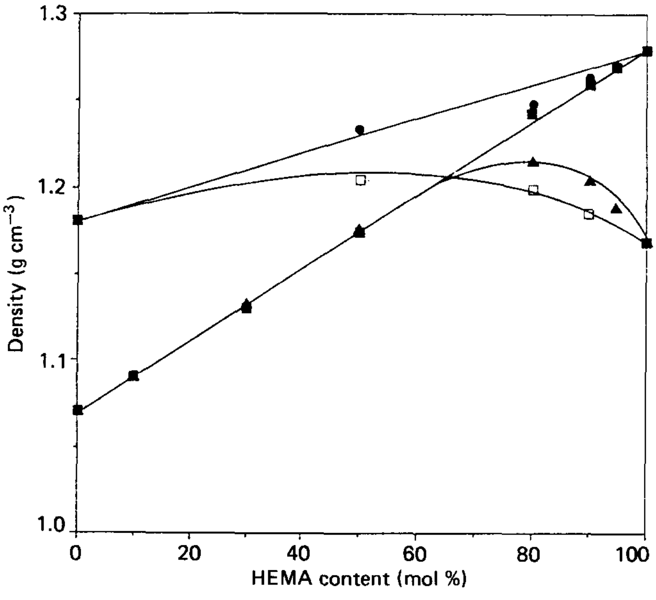

Figure 2 Densities of (▲) hydrated and (■) dehydrated HEMA–St copolymers, (□) hydrated and (●) dehydrated HEMA–MMA copolymers at 22°C

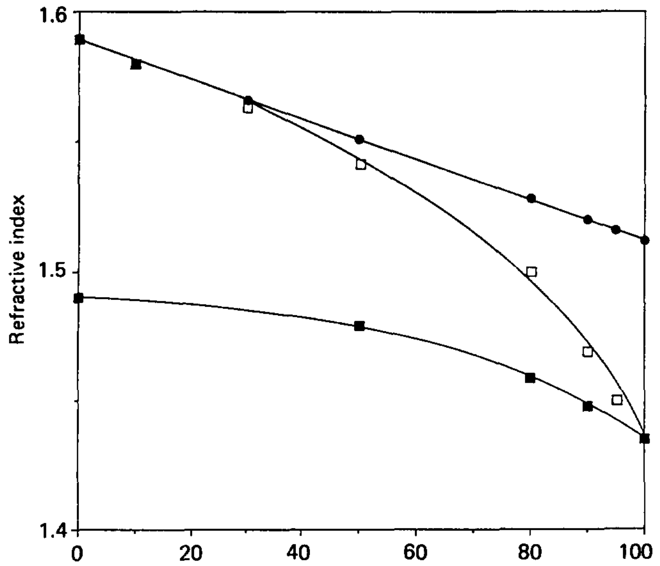

Figure 3 Refractive indices of (□) hydrated and (●) dehydrated HEMA–St copolymers and (■) hydrated HEMA–MMA copolymer at 22°C

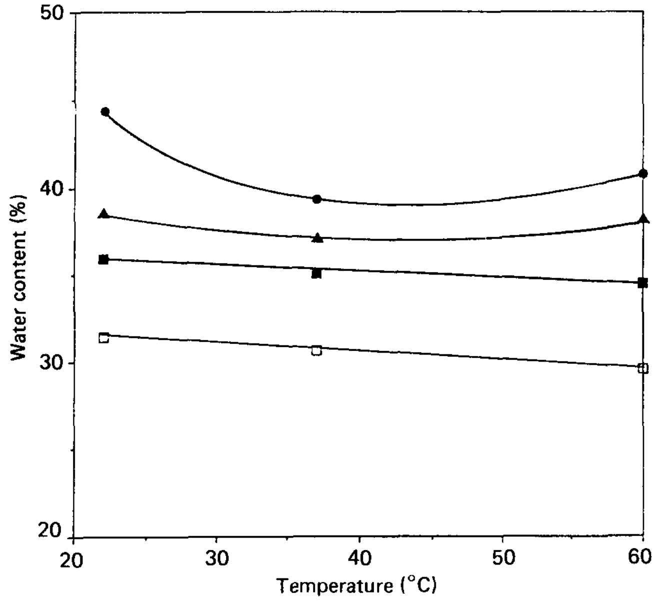

Figure 4 Effect of hydration temperature on equilibrium water content of polyHEMA containing (●) no added crosslinker, and (▲) 0.5%, (■) 2.0% and (□) 5.0% ethylene glycol dimethacrylate crosslinking agent

The effect of temperature on the water binding properties of hydrogels is important, principally because of the wide range of biomedical applications for which these materials have been used[7,14–17]. It is necessary to know how the water contents, and therefore the dimensions, of the hydrogels vary from room temperature to body temperature and also at the higher temperatures that are often involved in sterilization procedures. The effect of temperature on *EWC* has been examined for polyHEMA with varying levels of ethylene glycol dimethacrylate crosslinking agent (*Figure 4*). These results together with those for HEMA–St copolymers, HEMA–MMA copolymers and HPA–St copolymers, all at a nominal crosslink density of 1%, are presented. The results for polyHEMA and HEMA copolymers with St and MMA, shown in *Figure 5*, indicate that the *EWC* is fairly insensitive to temperature, in the region 22–70°C. There is in fact a slight difference between the effect of increasing the crosslink density and the effect of introduction of hydrophobic styrene monomer. Starting at similar *EWC*s, as the temperature is increased, the *EWC* of the more highly crosslinked HEMA decreases at a greater rate than the *EWC* of any of the HEMA–St copolymers. The increased retractive force in polyHEMA with the higher crosslink density acts to reduce the *EWC* more rapidly than in the HEMA–St copolymer, where only the hydrophobic group concentration is a factor.

Refojo[44] has postulated that hydrophobic bonding is important in polyHEMA and that the formation of these bonds is an endothermic process. Similar views of the balance of hydrophobic bonding and macromolecular hydration have been applied to the behaviour of natural polymers for many years. In principle this broad rationale can be applied to any hydrogel system. Okano *et al.*[45] have used fluorimetric analysis to detect hydrophobic interactions between the α-methyl groups of oligo-HEMA in a mixed water–dioxane solvent, containing more than 70% water by volume. Hydrophobic bonds are van der Waals interactions between non-polar groups. These result from the driving force that the solubility of a non-polar group in water, hydrophobic hydration, is entropically unfavourable because the water is capable of structuring in the vicinity of a non-polar compound. These hydrophobic bonds act as crosslinks and reduce the *EWC* of the hydrogel. An increase in the temperature reduces the hydrophobic hydration and increases the formation of hydrophobic bonds. On the other hand, water forms hydrogen bonds with the polar groups of the polymer and this hydrophilic hydration will increase with increasing temperature. The polymer network should also expand entropically with increasing temperature, causing an increase in the capacity for water absorbtion.

The competition between these processes will determine the shape of the equilibrium water content–hydration temperature curve. Both the magnitude and position of occurrence of any minimum, in the hydration–temperature profile, will be determined by the nature of the constituent monomers. In the case of crosslinked

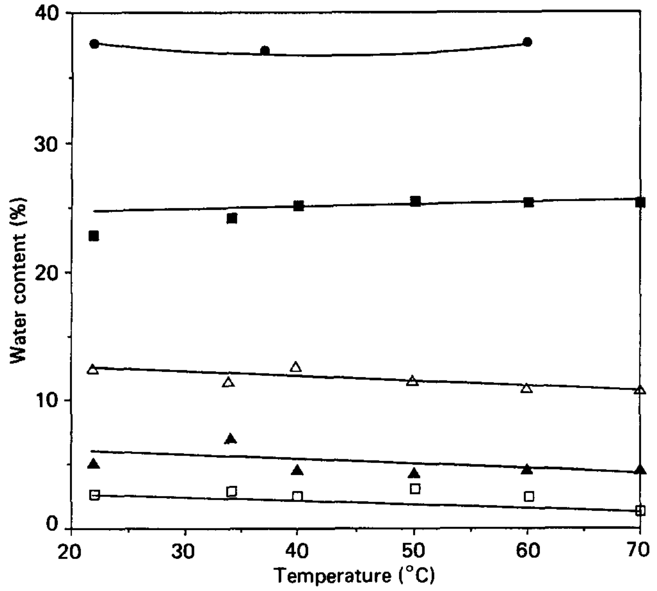

Figure 5 Equilibrium water contents of (●) polyHEMA, (■) HEMA–St 90/10, (△) HEMA–MMA 50/50, (▲) HEMA–St 50/50 and (□) HEMA–St 30/70 at various hydration temperatures

polyHEMA and HEMA copolymers with styrene and methyl methacrylate (*Figures 4* and *5*) virtually no deviation from linearity is observed. Previous work[46,47] has indicated that minima do occur for these compositions in the region from 50 to 80°C. However, these minima are indistinct and although the primary experimental data points of the various workers may be successfully overlaid the major disagreement lies in the extent to which minima can be successfully discerned. This is in part due to the difficulty in obtaining accurate and reproducible measurements of *EWC*s at high temperatures. Warren and Prins[48], however, have calculated the partial molar heat of dilution, $\overline{\Delta H}_{\mathrm{dil}}$, for polyHEMA and found it to be negative below 55°C. This is indicative of a hydrophobic interaction leading to increased water structuring. Above 55°C, $\overline{\Delta H}_{\mathrm{dil}}$ is positive, as the normal dispersion forces overcome the water structuring effect. Therefore a minimum might be expected in the hydration–temperature profile at this temperature.

The influence of monomer structure on the hydration temperature curve is shown in *Figure 6*, which presents results for HPA–St copolymers shown in comparison to the HEMA–St results presented previously. The slow decrease in *EWC* for HEMA–MMA copolymers is also explained by an increase in hydrophobic bonding as the temperature is increased, a factor that appears to dominate *EWC* in the methacrylate polymers and copolymers. With the HPA–St copolymers there is more effective competition, with hydrophobic bonding dominating at temperatures up to 40°C and hydrophilic hydration being the dominant factor at temperatures above this. The *EWC*s seem to indicate that acrylates are more hydrophilic than methacrylates. This is confirmed when the effect of temperature on *EWC* is examined, with hydrophilic bonding playing a much greater role in determining the *EWC*s of acrylates. The greater hydrophilicity of the acrylates is due to the presence of a hydrogen, rather than a methyl group, on the main chain, as discussed previously.

The HPA–St 50/50 copolymer at temperatures of 50°C and above becomes opaque. This indicates that the hydrogel is heterogeneous and contains water clusters whose dimensions are greater than the wavelength of light. In this series, water clustering of this type is only a problem in copolymers containing similar proportions of a hydrophilic and hydrophobic monomer, as the water absorbed cannot be distributed evenly throughout the network. In copolymers containing a high percentage of styrene there is no uptake of water as the temperature rises and in copolymers containing a high percentage of HPA monomer, there is sufficient space in the network for the water to be absorbed homogeneously. One exception to this is the HPA–St 70/30 copolymer at 70°C, which is translucent, indicating that large water clusters are beginning to form.

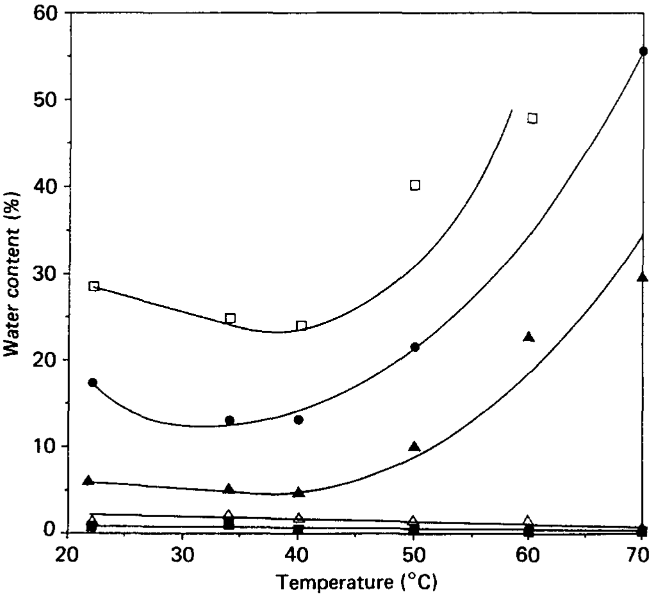

Figure 6 Variation in equilibrium water content with hydration temperature for (□) HPA–St 80/20, (●) HPA–St 70/30, (▲) HPA–St 50/50, (△) HPA–St 30/70 and (■) HPA–St 10/90 copolymers

Water binding studies

Although the *EWC* of a polymer and the way it varies with temperature give some degree of insight into the competitive bonding processes at work in hydration, analytical techniques are available which enable water binding states to be further probed.

Of the techniques available for the study of water binding, nuclear magnetic resonance (n.m.r.) spectroscopy, d.s.c., dilatometry and specific conductivity, all of which have been examined in connection with our own work, d.s.c. is in many ways the most convenient. The reasons for this include the ease of preparation of the small samples, which are sealed in aluminium sample pans to minimize any loss of water from the sample. Additionally, the ease with which measurements on the sample can be made enables the water binding data to be elucidated far more quickly than would be possible, for example, by using n.m.r. relaxation measurements. Furthermore, melt/freeze recycling can be carried out rapidly and easily, enabling more detailed crystallization and water structuring information to be obtained[49].

Although discrepancies between values for freezing and non-freezing water arise due to differences in techniques, further experimental variation can result from the well known difficulty of purifying HEMA, which contains as major impurities ethylene glycol dimethacrylate (EGDM) and methacrylic acid. In addition to this, polymerization conditions can lead to disproportionation of monomer and generation of further EGDM. As a result two extreme situations may be envisaged, one resulting from the influence of excess crosslinking agent and the other from the influence of adventitious carboxyl groups in the polymer chain. At physiological and slightly acidic pH the influence of the carboxyl group is small, but at high pH the influence of the carboxylate anion has a dramatic effect, leading to a marked increase in the ratio of freezing to non-freezing water. Unless the hydrating solution is deliberately buffered, adventitious carbon dioxide normally results in acidic hydration conditions and the effect of addition of crosslinking agent dominates that of the carboxyl groups.

The results of the water binding studies carried out on polyHEMA and the HEMA copolymers are presented in *Figures 7* and *8*. The effect of crosslink density on the *EWC* and freezing water content of polyHEMA (*Figure 7*) generally follows the expected trend, showing a decrease in both *EWC* and freezing water content as the crosslink density increases. The trend in non-freezing water content may be determined by inspection, since it is

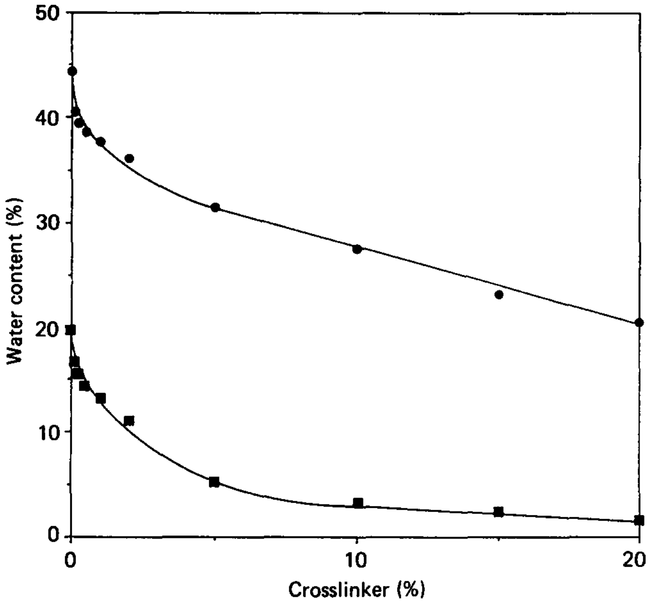

Figure 7 The equilibrium (●) and (■) free water contents of polyHEMA with increase in cross-linker concentration at 22°C

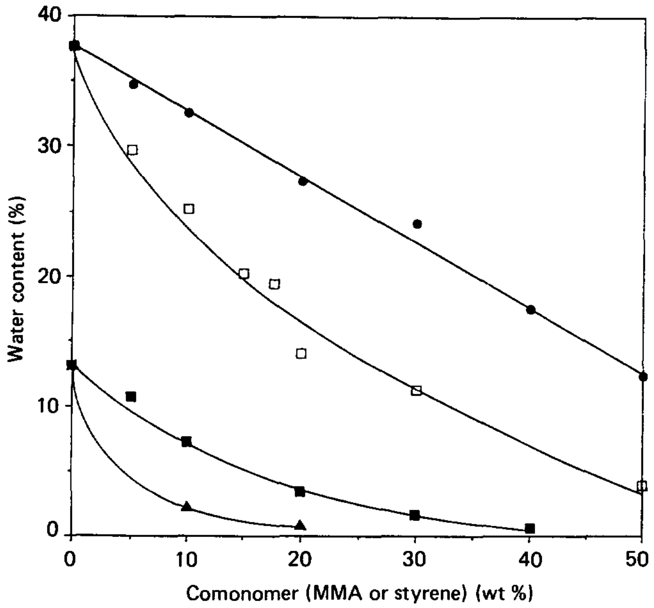

Figure 8 Effect of composition on the water contents of HEMA–MMA ((●) *EWC*, (■) free water) and HEMA–St ((□) *EWC*, (▲) free water) copolymers at 22°C

simply the difference between these values. An increase in the crosslink concentration causes a slight decrease in the non-freezing water content, but a large decrease in the freezing water content, since increasing the crosslink density decreases both mobility and hydrophilicity within the network. The percentage of non-freezing water in the polymer appears to remain fairly constant at around 24% (slightly higher than the value of 20% reported for polyHEMA with 1% crosslinker by Lee *et al.*[19]). However, because the total water content of the system decreases, the number of moles of non-freezing water per mole of HEMA repeat unit in the polymer decreases (from 3.2 for polyHEMA with no crosslinker to 2.8 for polyHEMA with 5% crosslinker). This small change in non-freezing water is a result of the decreasing availability of hydrophilic binding sites, due to increased steric occlusion.

A simplistic view of the water binding process suggests that in non-freezing water the water molecules are hydrogen bonded to hydrophilic groups on the polymer chain, while freezing water molecules are hydrogen bound to both freezing and non-freezing water molecules. Using the concept of hydration shells, it is possible to envisage the non-freezing water hydrogen bonded to the hydrophilic sites (in this case hydroxyl groups) on the polymer chain, with other hydration shells of freezing water molecules surrounding the inner hydration shell. As the number of monomer units between crosslinks decreases, the network becomes more tightly bound and there is a marked decrease in freezing water content with increasing crosslink concentration, together with a small decrease in the number of moles of non-freezing water per mole of hydrophilic repeat unit.

Although increased crosslink density in polyHEMA hydrogels produces marked changes in water binding behaviour, similar effects arise from the introduction of hydrophobic and especially sterically hindering monomers such as methyl methacrylate and styrene. The effect of composition on the equilibrium and free water contents of HEMA–MMA and HEMA–St copolymers is shown in *Figure 8*. As the percentage of hydrophobic monomer increases the *EWC* falls and the copolymers become more rigid. This decrease in flexibility can be attributed to the reduction of freezing water in the copolymer (13.2% in polyHEMA but only 0.5% in the 60/40 HEMA–St copolymer) and is a demonstration of the plasticizing effect of freezing water. The freezing water content of a polymer also has a marked effect on other mechanical properties, together with permeability and permselectivity. The interaction of non-freezing water with the hydrophilic sites on the polymer chain decreases its ability to solvate any ions, thus dramatically depressing salt permeation in polymers where only non-freezing water is present.

The number of moles of non-freezing water per repeat unit in the methacrylate copolymer series decreases from 2.8 for polyHEMA to 1.4 for the HEMA–MMA 60/40 copolymer. Comparing the 80/20 HEMA–MMA and HEMA–St copolymers, the numbers of moles of non-freezing water per repeat unit are 2.2 and 1.6, respectively, reflecting the greater hydrophobicity of styrene than methyl methacrylate.

This behaviour, which is an extension of that discussed for the effect of the somewhat smaller levels of crosslinking agent in polyHEMA, reflects not only the decreasing hydrophilicity but also the importance of steric effects and resultant restricted mobility and availability of water binding sites within the polymer.

The total amount of non-freezing water in the polymer is obtained from the area under the d.s.c. melting endotherm but it is possible to derive more information from the fine structure of the d.s.c. curves. The melting endotherm of polyHEMA with 1% crosslinker shows a fairly sharp peak at 272.5 K running into a slightly broader peak at 274 K. Temperature cycling leads to a slight increase in the area under the peaks with an increase in size of the 274 K peak while the size of the peak at lower temperature decreases. The melting endotherm for polyHEMA containing only 0.25% crosslinking agent is markedly different, with two distinct peaks at 270 and 274 K. Temperature cycling increases the size of the 274 K peak while the size of the 270 K peak is reduced.

Pedley and Tighe[49] have explained this increase in terms of a move to more ideal crystallization behaviour.

The melting endotherms for HEMA copolymers with hydrophobic monomers are similar to those for polyHEMA. Thus HEMA–MMA 90/10 has a peak at 274.5 K with a shoulder at 273 K. As the percentage of hydrophobic monomer increases the peak width decreases and the peak moves to a lower temperature. HEMA–MMA 60/40, for example, shows a narrow peak at 272 K with a shoulder at 271.5 K. The peak shapes are again changed by temperature cycling, indicating that this causes a redistribution of the freezing water in the hydrogel. Marked deviation from monolithic melting peaks is produced by strongly hydrogen bonding monomers, such as acrylamide or *N*-vinyl pyrrolidone, a point which will be more fully discussed in a later paper.

These results suggest that not all the freezing water is completely unaffected by the polymeric environment. A portion of the freezing water crystallizes and remelts at a different temperature from that of pure water. This supports the idea that the water present in a hydrogel exists in a continuum of states between the extreme non-freezing and freezing forms.

CONCLUSIONS

In this work we have examined the general physical and water binding characteristics of a range of copolymers of hydroxyalkyl acrylates and methacrylates with non-hydrophilic monomers. The observations relating to the total amount of water in the hydrogel are clearly related to the balance of hydrophilicity and hydrophobicity in the copolymer and, in particular, the steric and polar contributions of backbone substituents.

The hydroxyalkyl acrylates and methacrylates themselves show a smooth and systematic increase in hydrophilicity from hydroxypropyl methacrylate through hydroxyethyl methacrylate and hydroxypropyl acrylate to hydroxyethyl acrylate, the most hydrophilic monomer examined here. More interesting effects arise when the monomers are copolymerized with such comonomers as styrene, methyl methacrylate and ethylene glycol dimethacrylate. It is apparent in all these cases (*Figures 1, 7, 8*) that there is a distinct non-linearity in the compositon *versus* equilibrium water content graphs, an effect that is more marked with styrene than with methyl methacrylate.

The case of EGDM is slightly unusual in that it behaves not only as a non-hydrophilic monomer, but also as a crosslinking agent. The effect of its role as a crosslinking agent is especially marked at low extents of EGDM incorporation, when the linear crosslinked polymer suffers a more dramatic *pro rata* decrease in network expansibility than is the case at progressively higher crosslink densities. At higher crosslink densities the *EWC*s of the EGDM–HEMA copolymers show similar *EWC*-composition profiles, but with lower *EWC*s than the MMA–HEMA copolymers. The explanation for the lack of linearity in these cases lies in the different water binding states that are encountered in synthetic hydrogels. As *Figure 8* shows, incorporation of increasing quantities of St or MMA in copolymers with HEMA has the effect of 'titrating out' freezing water. In contrast, the non-freezing water in the hydrogels decreases regularly as the amount of St of MMA in the copolymer increases. It is interesting that density and refractive index measurements provide a useful method of predicting water content, provided that these variations in water binding behaviour are taken into account.

The effect of temperature on water binding has been discussed in terms of the balance between hydrophobic bonding between substituent groups in the polymer chain and the hydrophilic interactions, which are normally dominant. Interesting differences between acrylate and methacrylate copolymers have been observed in this respect (*Figure 6*). These can be rationalized in terms of the effect of the hydrophilic/hydrophobic balance in the backbone on the ease of phase separation within the hydrated gel. It is one of the potential values of the types of polymer described here that the water binding properties (which, as our subsequent papers will show, have such a marked effect on the permselectivity and permeability of the materials) can be modulated to produce a range of hydrogels which show a remarkable temperature independence of water binding behaviour.

ACKNOWLEDGEMENTS

We would like to thank C. J. Hamilton for the statistical study on the *EWC* of polyHEMA, the SERC for financial support (A.M.J.) and the University of Aston for financial support (P.H.C. and C.O.N.).

REFERENCES

1 Wichterle, O. and Lim, D. *Nature* 1960, **185**, 117

2 Wichterle, O. and Lim, D. US Patents 2 976 576, 1961; 3 220 960, 1965

3 Okano, T., Katayama, M. and Shinohara, I. *Nippon Kagakukaishi* 1976, (12), 1908

4 Okano, T., Katayama, M. and Shinohara, I. *J. Appl. Polym. Sci.* 1978, **22**, 369

5 Varma, I. K. and Patnaik, S. *Eur. Polym. J.* 1976, **12**, 259

6 Lebduska, J., Snuparek, J. Jr., Kaspar, K. and Cermak, V. *J. Polym. Sci.* 1986, **A24**, 777

7 Pedley, D. G., Skelly, P. J. and Tighe, B. J. *Br. Polym. J.* 1980, **12**, 99

8 Tighe, B. J. in 'Contact Lenses', Vol. 2, 2nd Edn., (Eds. A. J. Phillips and J. Stone), Butterworth, London, 1980, p. 377

9 Larke, J. R. and Tighe, B. J. (to National Research Development Corporation), British Patent 1 395 501, 1975

10 Larke, J. R., Pedley, D. G. and Tighe, B. J. (to National Research Development Corporation), British Patent 1 478 455, 1977

11 Larke, J. R., Pedley, D. G. and Tighe, B. J. (to National Research Development Corporation), British Patent 1 500 692, 1978

12 Hoffman, A. S., Horbett, T. A. and Ratner, B. D. *Ann. N.Y. Acad. Sci.* 1977, **283**, 372

13 Nakashima, T., Takakura, K. and Komoto, Y. *J. Biomed. Mater. Res.* 1977, **11**, 787

14 Andrade, J. D. (Ed.) 'Hydrogels for Medical and Related Applications', *ACS Symp. Ser.* 31, 1976

15 Tighe, B. J. in 'Macromolecular Chemistry', (Eds. A. D. Jenkins and J. F. Kennedy), Specialist Periodical Reports, No. 17, Vol. 1, The Chemical Society, London, 1980, p. 416

16 Tighe, B. J. in 'Macromolecular Chemistry', (Eds. A. D. Jenkins and J. F. Kennedy), Specialist Periodical Reports, No. 17, Vol. 2, The Chemical Society, London, 1982, p. 347

17 Heitz, W., Krappitz, W., Stutzel-Bilbao, C. and Neumann, B. *Angew. Makromol. Chem.* 1984, **123/124**, 147

18 Jhon, M. S. and Andrade, J. D. *J. Biomed. Mater. Res.* 1973, **7**, 509

19 Lee, H. B., Jhon, M. S. and Andrade, J. D. *J. Colloid. Interface Sci.* 1975, **51**, 225

20 Frommer, M. and Lancet, D. *J. Appl. Polym. Sci.* 1972, **16**, 1295

21 Frommer, M., Shporer, M. and Messalem, R. *J. Appl. Polym. Sci.* 1973, **17**, 2263

22 Shporer, M. and Frommer, M. *J. Macromol. Sci., Phys.* 1974, **B10**, 529

23 Yasuda, H., Olf, H. G., Crist, B., Lamaze, C. E. and Peterlin, A. in 'Water Structure at the Water–Polymer Interface', (Ed. H. H. G. Jellinek), Plenum Press, New York, 1975, p. 39
24 Aizawa, M. and Suzuki, S. *Bull. Chem. Soc. Japan* 1971, **44**, 2967
25 Aizawa, M., Mizuguchi, J., Suzuki, S., Hayashi, S., Suzuki, T., Mitomo, N. and Toyama, H. *Bull. Chem. Soc. Japan* 1972, **45**, 3031
26 Krishnamurthy, S., McIntyre, D., Santee, E. R. and Wilson, C. W. *J. Polym. Sci., Polym. Phys. Edn.* 1973, **11**, 427
27 Hoffman, A. S., Modell, M. and Pan, P. *J. Appl. Polym. Sci.* 1969, **13**, 2223
28 Jadwin, T. A., Hoffman, A. S. and Vieth, W. R. *J. Appl. Polym. Sci.* 1970, **14**, 1339
29 Sarbolouki, M. N. *J. Appl. Polym. Sci.* 1973, **17**, 2407
30 Nelson, R. A. *J. Appl. Polym. Sci.* 1977, **21**, 645
31 Froix, M. and Nelson, R. A. *Macromolecules* 1975, **8**, 726
32 Dehl, R. E. *Science* 1970, **170**, 738
33 Kim, E. H., Jeon, S. I., Yoon, S. C. and Jhon, M. S. *Bull. Korean Chem. Soc.* 1981, **2**, 60
34 Kim, E. H., Moon, B. Y., Jeon, S. I. and Jhon, M. S. *Bull. Korean Chem. Soc.* 1983, **4**, 251
35 Sung, Y. K., Gregonis, D. E., Jhon, M. S. and Andrade, J. D. *J. Appl. Polym. Sci.* 1981, **26**, 3719
36 Taniguchi, Y. and Horigome, S. *J. Appl. Polym. Sci.* 1975, **19**, 706
37 Nakamura, K., Hatakeyama, T. and Hatakeyama, H. *Textile Res. J.* 1981, **51**, 607
38 Nakamura, K., Hatakeyama, T. and Hatakeyama, H. *Polymer* 1983, **24**, 871
39 Hatakeyama, T., Yamauchi, A. and Hatakeyama, H. *Eur. Polym. J.* 1984, **20**, 61
40 Higuchi, A. and Iijima, T. *Polymer* 1985, **26**, 1833
41 Boesen, C. E. *Cellul. Chem. Technol.* 1970, **4**, 149
42 Yocum, R. H. and Nyquist, E. B. (Eds.) 'Functional Monomers', Vols. 1 and 2, Marcel Dekker, New York, 1973
43 'Davenport Density Gradient Column Instruction Manual', Davenport (London) Ltd
44 Refojo, M. F. *J. Polym. Sci.* 1967, **A5**, 3103
45 Okano, T., Ikemi, M. and Shinohara, I. *Nippon Kagakukaishi* 1977, (1), 93
46 Refojo, M. J. and Yasuda, H. *J. Appl. Polym. Sci.* 1965, **9**, 2425
47 Kuriaki, M. and Harata, T. *Maku* 1983, **8**, 39
48 Warren, T. C. and Prins, W. *Macromolecules* 1972, **5**, 506
49 Pedley, D. G. and Tighe, B. J. *Br. Polym. J.* 1979, **11**, 130