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*Report*

# Thermal Behavior of Poly Hydroxy Ethyl Methacrylate (pHEMA) Hydrogels

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The freezing and melting behavior of water in poly hydroxy ethyl methacrylate (pHEMA) hydrogels of different cross-linker and water contents was investigated in relation to the glass transition temperature ($T_g$) of the gels. After prolonged cooling at −15°C a constant amount of 1.7 mol water per monomeric unit did not freeze, regardless of both the cross-linker and the water content of the gels. At this water content and temperature, pHEMA gels were below their $T_g$, and the water molecules were prevented from diffusing to the ice crystals formed in the gel. Therefore, the inability of part of the water in pHEMA gels to freeze is not a thermodynamic phenomenon but is caused by kinetic factors.

KEY WORDS: pHEMA; hydrogels; thermal analysis; melting enthalpy; glass transition; elastic solution.

## INTRODUCTION

Hydrogels have been widely studied as materials for controlled-release drug dosage forms (1). The structure of these gels has been described as a more or less rigid polymer framework with water-filled channels that are available for transport (2,3). It has been reported that different types of water are present in these gels, with different thermodynamical properties, namely, bound, interfacial, and bulk water (4). Based on thermoanalytical experiments, it has been concluded that the ratio of the different types of water was determined to a large extent by the cross-linker content of the gels (5,6).

We have recently demonstrated that the abnormal thermal behavior of water in poly(hydroxy ethyl methacrylate) gels is caused by the extremely slow crystallization upon cooling (7,8), and not by thermodynamic binding of water to the polymer. Specifically, the melting enthalpy of the water in the gels was strongly dependent on the cooling time below 0°C, and it reached a maximum when the gels were kept at −15°C for 20 hr (8).

Experiments with an isoperibolic calorimeter showed that during absorption of water by an initially dry pHEMA gel, only the first 20% of all the water that enters the gel has an enthalpic interaction with the polymer, a quantity that corresponds to 1 mol water/mol monomeric unit pHEMA (monomol pHEMA) (9). In the study presented here we have investigated if this amount corresponds to the amount of nonfreezing water after prolonged cooling of the gels with different water and cross-linker contents. An important parameter for the mobility of molecules in an amorphous polymeric system is the glass transition temperature, $T_g$. Therefore, the $T_g$'s of the gels were determined in relation to their water and cross-linker contents.

## METHODS

The gels were based on poly-hydroxy-ethyl-methacrylate (pHEMA) cross-linked with ethyl dimethacrylate (EDMA), as described earlier (10). Systems were made containing 0, 1, 2, and 5% (w/w) cross-linker and were designated 0XL, 1XL, 2XL, and 5XL. Gels with lower water contents than those in equilibrium with pure liquid water were prepared by equilibration over different saturated aqueous salt solutions.

The water content of the gels was determined as the weight difference before and after drying at 140°C and at ±10 mm Hg for 18 hr. Further drying did not result in a measurable increase in weight loss.

The thermoanalytical experiments were carried out in a Mettler DSC 30, using hydrogel disks of about 1-mm thickness and 3- to 4-mm diameter.

To determine the maximum melting enthalpies the gels were cooled to −25°C at a rate of 1°C/min to induce crystallization and were subsequently kept at −15°C for 20 hr. Finally, their melting enthalpies were measured by heating from −15°C to 10°C at a rate of 1°C/min. The temperature of −15°C was chosen as a compromise between the high temperature, desirable to maintain as much mobility in the water as possible in order for the molecules to arrange themselves in ice crystals, and the low temperature necessary to avoid melting phenomena.

Glass-transition temperatures ($T_g$'s) were determined by heating the gels to a temperature at least 20°C above their $T_g$ and subsequently cooling them at a rate of 2.5°C/min to a

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Table I. Nonfreezing Water Fractions of Gels with Different Water and Cross-Linker Contents

| Cross-linker content (%, w/w) | Water content: % (w/w) water per total gel weight (Δ ± 0.1) | Water content: mol $H_2O$ per monomol HEMA (Δ = ±0.01) | Maximum melting enthalpy (J/g gel) | Nonfreezing water content: % (w/w) water per total amount of water present | Nonfreezing water content: % (w/w) water per total gel weight (Δ = ±0.2) | Nonfreezing water content: mol $H_2O$ per monomol HEMA (Δ = ±0.1) |
|---|---|---|---|---|---|---|
| 0 | 41.2 | 5.1 | 88 ± 2 | 33 ± 2 | 13.6 | 1.7 |
| 0 | 27.6 | 2.8 | 32.5 ± 2 | 63 ± 1 | 17.4 | 1.8 |
| 0 | 21.0 | 1.9 | 9.5 ± 1 | 85 ± 1 | 17.8 | 1.6 |
| 0 | 14.9 | 1.3 | — | 100 | 14.9 | 1.3 |
| 1 | 40.0 | 4.8 | 82 ± 2 | 36 ± 2 | 14.4 | 1.7 |
| 2 | 38.3 | 4.5 | 76 ± 2 | 38 ± 2 | 14.6 | 1.7 |
| 5 | 34.3 | 3.8 | 62 ± 2 | 44 ± 2 | 15.1 | 1.7 |

temperature at least 40°C below the glass transition region, after which the glass transition was recorded in a heating run at a rate of 10°C/min. In all cases the gels were weighed before and after the analysis, to assure that no weight loss due to evaporation had occurred.

## RESULTS AND DISCUSSION

The results as obtained from the melting experiments are given in Table I. Clearly the melting enthalpies decreased with decreasing water content. A typical example of a melting curve is given in Fig. 1. As has been shown before by our group (7,8), the double character of the melting peak does not originate from the presence of different types of water, but from the development of a metastable nonequilibrium situation upon cooling the gel. This double character largely disappears after the coooling procedure described above.

From the position of the curve it is clear that the whole melting process takes place near 0°C, which means that no large corrections in the melting enthalpy have to be made, due to a difference in specific heat between water and ice. Also, there are no enthalpic interactions between the freezing water and the polymer, as can be concluded from the experiments with the isoperibolic calorimeter (8,9). Therefore it may be concluded that the melting enthalpy of pure ice (320 J/g) can be used as a good approximation for the melting of ice in the hydrogels (8).

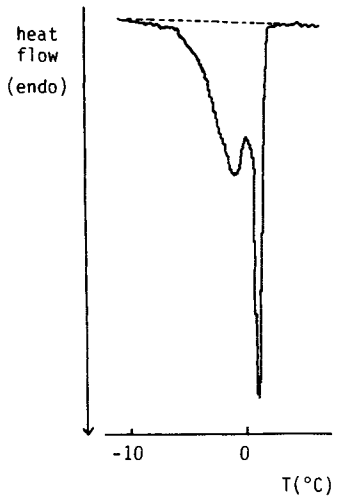


Fig. 1. Melting curve of a pHEMA gel without cross-linker and a water content of 5.1 mol $H_2O$ per mol pHEMA monomer.

With this value of 320 J/g and from the results given in Table I, it is possible to calculate the fractions of the water in the gels that do not freeze upon cooling. These fractions are given in Table I. A common way to express the water contents of hydrogels is to use weight percentages: grams of water per gram of total gel weight, multiplied by 100. However, it may be more informative to express the water content on a stoichiometric basis, for instance, as moles of water per mol of pHEMA monomer, especially in the case when the amount of nonfreezing water is calculated. As can be seen in Table I (last column), this amount comes to a remarkably constant value of about 1.7 mol of water per mol of pHEMA monomer, regardless of either the cross-linker or the water content of the gel. Gels that contain less than 1.7 mol of water per mol of pHEMA monomer did not exhibit melting phenomena.

This finding contradicts earlier publications, where the amount of nonfreezing water was assumed to be highly dependent on the cross-linker content (5,6). As shown by the isoperibolic measurements, only 1 mol of water per mol of pHEMA monomer has an enthalpic interaction with the polymer. There is a discrepancy, between this value and the value of 1.7 found in the present study. Several factors could account for the discrepancy including temperature differences. The isoperibolic experiment was carried out at 25°C, while the melting studies necessarily took place around 0°C. Probably more important, however, are kinetic factors, which was the reason for including the $T_g$ measurements in this study.

A typical example of a curve representing the glass transition region in pHEMA gels is represented in Fig. 2. All three points A, B, and C, can be chosen to denote the glass transition temperature, but since in this study C was the most reproducible point, it was chosen for the comparison of the $T_g$'s of the gels in question. The $T_g$'s for the different gels are given in Table II. Two 5XL gels, containing relatively large amounts of water, did not produce glass transitions that could be meaningfully extrapolated but showed a very gradual change in their specific heat over a wide temperature range. They are marked with a superscript *a* in Table II.

The decrease in the glass transition temperature with increasing water content of the gel is very clearly visible in

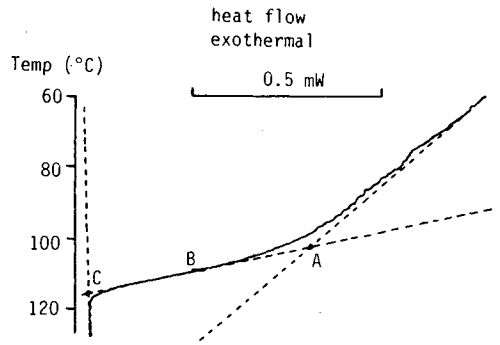


Fig. 2. Glass transition curve of a dry pHEMA gel containing 1% cross-linker.

the other gels (Fig. 3). The $T_g$ of gels containing 1.9 mol of water per mol of pHEMA monomer is 14°C, and in fact the whole glass transition region of these gels covers a range from −6° to +14°C, measured from point A to point C. This means that gels with a higher water content than this value theoretically have a $T_g$ below 0°C, but this glass transition is completely obscured in the DTA measurements by the freezing and melting behavior of the water in the gel.

The occurrence of a glass transition, by itself, offers a logical explanation for the freezing and melting behavior of pHEMA gels: at temperatures below 0°C the water in the gels starts to crystallize, and a phase separation occurs between ice and the polymer–water system. The ice crystals formed do not contribute to the plasticizing effect of water in pHEMA. At a water content of 1.7 mol water per mol

Table II. $T_g$'s of Gels with Different Water and Cross-Linker Contents

| Cross-linker content (%, w/w) | Water content (mol $H_2O$ per monomol HEMA) | $T_g$ (°C) ($\Delta = \pm 1$) |
|---|---|---|
| 0 | 0 | 115 |
| 1 | 0 | 117 |
| 2 | 0 | 119 |
| 5 | 0 | 126 |
| 0 | ≈0.1 | 100 |
| 1 | ≈0.1 | 104 |
| 2 | ≈0.1 | 106 |
| 5 | ≈0.1 | 113 |
| 0 | 0.4 ± 0.05 | 76 |
| 1 | 0.4 ± 0.05 | 78 |
| 2 | 0.4 ± 0.05 | 79 |
| 5 | 0.4 ± 0.05 | 87 |
| 0 | 0.76 ± 0.05 | 57 |
| 1 | 0.76 ± 0.05 | 59 |
| 2 | 0.76 ± 0.05 | 59 |
| 5 | 0.76 ± 0.05 | 63 |
| 0 | 1.2 ± 0.05 | 36 |
| 1 | 1.2 ± 0.05 | 36 |
| 2 | 1.2 ± 0.05 | 36 |
| 5 | 1.2 ± 0.05 | —[a] |
| 0 | 1.9 ± 0.05 | 14 |
| 1 | 1.9 ± 0.05 | 14 |
| 2 | 1.9 ± 0.05 | 14 |
| 5 | 1.9 ± 0.05 | —[a] |

[a] No sharp $T_g$ measurable

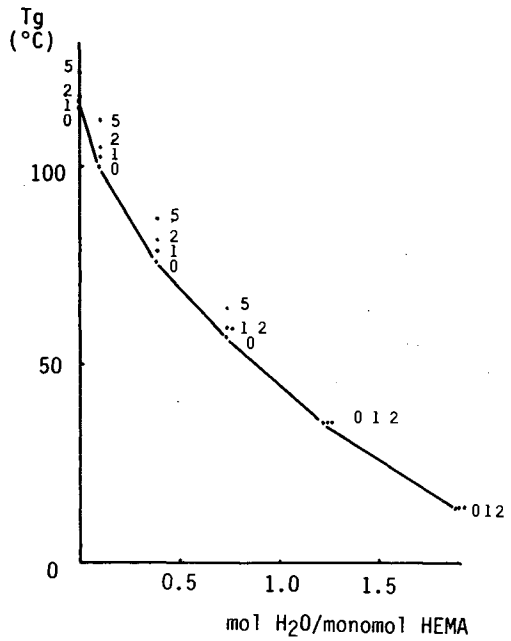


Fig. 3. Plot of the $T_g$ of pHEMA gels of different cross-linker contents vs water content.

pHEMA monomer and at a temperature of −15°C, the polymer–water phase has turned from a rubbery into a glassy system. As a consequence, the diffusion coefficient of water in the system drops by several orders of magnitude, thus preventing the water molecules to arrange themselves in the ice crystals formed.

These data strongly support earlier observations by our group, from which it was concluded that the nonfreezing behavior of a part of the water in pHEMA gels is due not to thermodynamical causes but mainly to kinetic factors (7,8). They also confirm the conclusion that in cases like these, DSC or DTA experiments cannot be used in the way described here to investigate the existence of a separate class of "bound" water in hydrogels.

The data presented here do not provide information on the structure of the glassy state. The isoperibolic experiments have shown that 1 mol of water in pHEMA shows an enthalpic interaction with the polymer upon absorption (9). The extremely slow diffusion in glassy polymer systems, however, makes it impossible to discriminate between this 1 mol and the remaining 0.7 mol that does not freeze. Further, the results do not contain evidence for the existence of different types of water in a hydrogel, nor do they demonstrate fundamental differences between gels with different cross-linker contents, in contradiction to conclusions reported in earlier publications on pHEMA (4,5). In this work (4,5) differences in thermal behavior and specific conductivity of pHEMA gels of varying water contents were explained in terms of thermodynamically different classes of water. Sharp changes in the properties of those gels around a water content of 20% of the dry polymer weight were ascribed to the bound character of this water. This quantity, however, equals an amount of ~1.7 mol of $H_2O$ per mol of pHEMA monomer, and in view of what is reported here and in our earlier studies (7), a rubber-to-glass transition probably is the real cause for the change in the properties. The reported

dependence of the character of the water on the cross-linker content (5,6) is contradicted by our work as well, and therefore it seems justified to conclude that the abnormal thermal behavior of water in pHEMA gels is not due to the presence of thermodynamically different types of water, but to kinetic factors in which a glass transition in the polymers plays a decisive role.

Similar results for purely organic systems were reported by Arnouts and Berghmans (11), who have shown that cooling a polystyrene–decaline system leads to a phase separation, which is followed by a vitrification process.

Our conclusion is also in agreement with earlier thermal (7), isoperibolic (8), and nuclear magnetic relaxation (7,12) studies by our group, from which it was concluded that hydrogels may be considered as elastic solutions of polymer in water, in which the majority of the water is not divided over thermodynamically different states but behaves as one type of water, the average mobility of which is strongly reduced by the presence of the polymer.

## CONCLUSIONS

(1) Upon cooling a pHEMA gel below 0°C a metastable, nonequilibrium situation develops, in which 1.7 mol of water per mol of pHEMA monomer does not crystallize, regardless of either the initial water or the initial cross-linker content.

(2) The development of this metastable situation is caused by a phase separation process. Water separates as ice crystals from the polymer–water phase, which at a temperature below 0°C and at a water content of about 1.7 mol per mol of pHEMA monomer, goes through a rubber-to-glass transition. The diffusion coefficient of the water molecules then drops by several orders of magnitude, which prevents their transport to the crystalline phase.

(3) The abnormal behavior of water is observed in pHEMA gels upon cooling them below 0°C and subsequent heating and in pHEMA gels with a relatively low water content is caused by this nonequilibrium situation, and not by the presence of thermodynamically different types of water.

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