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Polymer-water interactions in cross-linked gels determined by calorimetric measurements

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ABSTRACT

Calorimetric measurements have been carried out to determine to which extent water interacts with p-HEMA gels and with p-(HEMA+MAA) gels. It appeared, that 0.14 g water/g dry p-HEMA and 0.23 g water/g dry p-(HEMA+MAA) show strong negative enthalpy changes on sorption in the polymer, the enthalpy changes being -180 J/g and -360 J/g water respectively.

INTRODUCTION

Hydrogels, which have a number of pharmaceutical applications, are hydrophilic, crosslinked polymers that swell in water. In our laboratory we are investigating this kind of polymers as they can be used as carriers for drugs (1).

One of the major goals in our field of research is to manipulate the physical properties of hydrogels in order to affect the transport of drugs and to control the release of drugs from hydrogels. The mobility of drugs in "pure" hydrogels, which means without additional chemicals, is affected by at least two parameters: the flexibility of the polymeric chains and the mobility of water in the hydrogel. Both the flexibility of the chains and the mobility of water are influenced by polymer-water interactions.

The temperature at which the rigid polymeric chains change into more mobile chains is referred to as the glass transition temperature. We already measured the glass transition temperature of copolymers of p-(hydroxyethyl methacrylate + methacrylic acid) as a function of the molar ratio of the monomeric units and as a function of the water content. The results of these measurements are reported elsewhere (2).

The freezing and melting of water in p-hydroxyethyl methacrylate (p-HEMA) gels have been studied. Preliminary results have already been published (3). After having compared a cooling and a heating process, it appeared, that there is a large hysteresis between the heat effects involved. During the cooling process a slow exothermal process apparently takes place. From the melting peak of water the melting enthalpy of the water in p-HEMA has been calculated, which is about 200 J/g. This value is much lower than that of pure water (320 J/g). The large discrepancy between these two values can have two causes:

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a. The enthalpy of melting of water in the hydrogel is different from that of pure water due to polymer-water interactions;
b. A part of the water does not freeze. In literature this part of the water has been referred to as "non-freezing" or "bound" water.

In order to determine to what extent the large discrepancy is caused by enthalpic water-hydrogel interactions we have measured these interactions with an isoperibol calorimeter.

EXPERIMENTAL

Purification

Before polymerization the monomers have been purified as follows: Hydrochinon, which serves as an inhibitor, has been removed from the monomers by elution over an Amberlite A26 column. Traces of Methacrylic Acid (MAA) are removed, if necessary, by elution with a basic Al_2O_3 column.
p-HEMA: The polymers have been synthesized by using $(NH_4)_2S_2O_8$ as initiator. Traces of ethylene glycol dimethacrylate (EDMA) in HEMA serve as a cross-linker. The cross-linker content is 0.03 % w/w.
p-(HEMA + MAA): A molar ratio of 1:3 has been chosen. As initiator AIBN (azo isobutyronitril) has been used. As cross-linker EDMA has been added to the monomeric solution (0.5 % w/w).

Measurements

After washing the hydrogels to remove the remaining traces of monomers, the hydrogels have been dried at a temperature of 110 °C under vacuum. Then the hydrogels were swollen in aceton, grained and again dried. In order to obtain a series of polymers with increasing water content, the polymers were brought into contact with the equilibrium vapour phases of different salt solutions. After two months a variation less than 1 % in water content was observed during 1 week. The heat effect of immersing these conditioned hydrogels into a large amount of water (1 g gel/360 ml water) was measured with an isoperibol calorimeter. The measurements were carried out in duplo. A short description of the apparatus is given below. A detailed description is given elsewhere (4).

Calorimeter

The calorimeter vessel has a content of 180 ml and is made of gold-plated copper. The calorimeter is placed in a stainless-steel enveloppe which is evacuated and placed in a thermostat. The change in temperature in the calorimeter vessel is measured by a Wheatstone bridge. The output of the bridge is measured with a D.V.M. (Keithley). A signal of 1μV corresponds to a change in temperature of $1.72\ 10^{-5}$ K. The standard deviation during stabilization ranges from 0.2 to 0.4 μV over a period of 1000 seconds. In the measuring range the bridge is almost linear, the deviation being less than 1 percent. A correction for this deviation has been applied. The measuring curves were corrected for the heat-exchange between the calorimeter and the bath. The performance of the calorimeter was checked by measuring the heat of solution of KCl. For seven measurements a standard deviation of 0.03

Table 1

Water content and measured heat effects (ΔH) of immersion in water, both given per gram dry polymer.

p-(HEMA+MAA)		p-HEMA	
Water content (g)	Heat effect (J)	Water content (g)	Heat effect(J)
0	-82.6 ± 0.5	0	-26.7 ± 0.1
0.03	-65.6 ± 0.7	0.01	-23.9 ± 0.4
0.09	-44.6 ± 0.5	0.04	-15.5 ± 0.5
0.13	-34.1 ± 0.2	0.07	-10.5 ± 1.0
0.19	-15.9 ± 0.2	0.13	- 2.4 ± 1.0
0.37	- 0.4 ± 0.1	0.32	- 0.2 ± 0.2

percent was found. The larger deviations in these measurements is due to the long reaction time of the hydrogel and water. For p-(HEMA + MAA) samples (dry) it took about 2 hours before the reaction was completed. In the case of p-HEMA the small particles (roughly cubes of about 0.5 mm sides) immediately clotted together as soon as they were immersed in water. This inhibited further contact with water and increased the reaction time to 3 to 4 hours.

RESULTS

The results of the measurements are given in Table 1. The heat effect is exothermal and rather large. An increase in initial water content leads to a smaller negative heat effect, as is expected. In figure 1 the heat effect is plotted against the initial water content per gram dry polymer. From this figure it is observed, that the measured heat effect decreases linearly with increasing initial water content and therefore a straight line can be drawn through the experimental points with exception of the samples with the highest water contents. The data of these samples are not shown in figure 1. Probably the very small but significant heat effect of these samples is caused by wetting the polymer; wetting of the polymeric chains at the surface leads to a reorientation of the chains at the surface. The measurements show, that part of the water has strong enthalpic interactions with the polymer. The heat effect per gram water, determined from the slope of the curves in Fig. 1, being -180 J/g and -360 J/g for p-HEMA and p-(HEMA+MAA) respectively. The latter value is even larger than the enthalpy of crystallization of water. Extrapolation of the straight line to zero heat effect corresponds to a water content of 0.14 g/g dry polymer for p-HEMA and 0.23 g/g dry polymer for p-(HEMA+MAA).

In the case of p-HEMA this value corresponds with 1 molecule of water per monomeric unit. In the case of p(HEMA+MAA) the amount of water per monomeric unit at zero heat effect is somewhat higher, namely 1.2 molecules per monomeric unit.

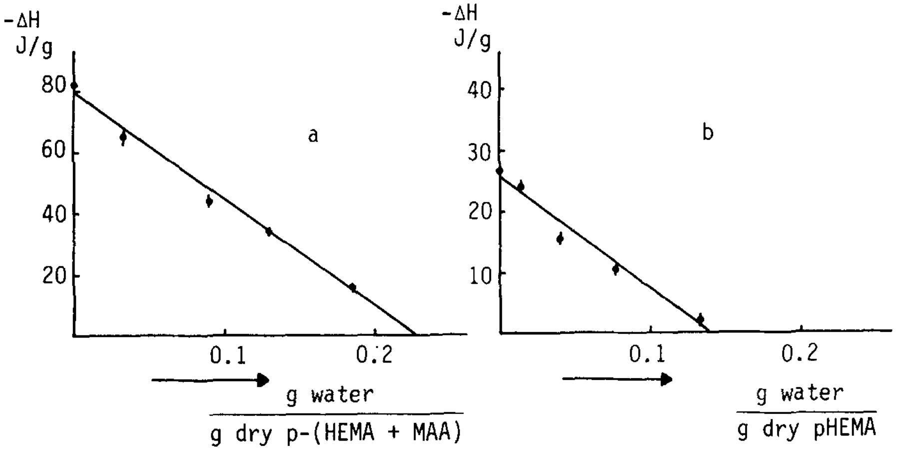

Figure 1. The enthalpy change has been plotted against the water content (g) per gram dry polymer.
a) p-(HEMA + MAA)
b) p-HEMA

DISCUSSION

Pouchly and Biros et al. (5, 6) measured the excess heat capacity of hydrogels above as well as below 0 °C. They concluded, that the excess heat capacity (Cp^E) of these kind of systems is very small. Therefore, the heat effect measured at room temperature can be extrapolated to the melting temperature of ice, without introducing large errors. Moreover, they stated from their measurements ($Cp^E = 0$), that no strong interactions occur between water and polymer. In our opinion, not the interaction but the dependence of the interaction on the temperature is small; our measurements show, that a strong enthalpic interaction occurs between a part of the water and the polymer. Warren and Prins (7) indirectly calculated the heat of dilution for p-HEMA gels from elasticity measurements. They found a small exothermal effect, which is strongly temperature dependent. These measurements are not in agreement with ours and those of Pouchly. Finally, it is clear, that the smaller melting enthalpy of water in the polymer is at least partly due to a large exothermal enthalpy of binding. We are planning additional measurements using copolymers with varying concentration of the monomeric units HEMA and MAA. In the case of p-HEMA the cross-linker content will be varied. Together with these additional measurements a more detailed discussion will be given, combining the enthalpy of mixing and the enthalpy of fusion of ice in hydrogels.

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