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Synthesis and swelling behavior of pH- and temperature-sensitive poly[2-(dimethylamino)ethyl methacrylate-*co*-2-acrylamido-2-methylpropane-1-sulfonic acid] hydrogels

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Summary

Poly[2-(dimethylamino)ethyl methacrylate-*co*-2-acrylamido-2-methylpropane-1-sulfonic acid], poly(DMAEMA-*co*-AMPS), hydrogels were prepared by chain polymerization in water at 60 ^{o}C in the presence of tetraethyleneglycol diacrylate (TEGDA) as crosslinking agent. Ammonium persulfate (APS) and *N*,*N*,*N'*,*N'*-tetramethylethylenediamine (TEMED) were used as initiator and accelerator, respectively. Hydrogels with different feed compositions were prepared by keeping the total monomer concentration constant at 1 or 0.5 M. The concentration of TEGDA in the feed was adjusted so that it made for 3 or 2 mol % of the total monomer content while it was 1% for APS. In order to observe the effects of pH and ionic strength of the medium on swelling, the equilibrium swelling behavior of these hydrogels were investigated both in distilled water at various temperatures between 30 and 90 °C and in different buffer solutions with pH of 2.8, 5.3, 7.0, 10.0, and 12.4 at constant ionic strength (I = 0.08 mol/l) at room temperature. The effects of temperature and co-monomer AMPS content on the swelling behavior of poly(DMAEMA-*co*-AMPS) in distilled water were also investigated.

The copolymers with equimolar contents of DMAEMA and AMPS displayed minimum swelling both in distilled water and in buffer solutions due to ionic complex formation. Their swelling values in distilled water between 30 and 90 °C were constant. While equilibrium swelling values of copolymers in buffer solutions with pH between 2.8 and 7 were almost constant, they increased with increasing pH. The increase in the AMPS content and decrease in initial monomer concentration increased the equilibrium swelling values of copolymers.

Introduction

In recent years, the synthesis and characterization of stimulus responsive hydrogels have received increasing importance because of their wide applications such as drug

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delivery and concentration processes [1-4]. These crosslinked polymers can be tailored to a large number of environmental stimuli, e.g. temperature, pH, and ionic strength by modifying their physical/chemical properties. Thermo- and pH-responsive polymers exist in swollen or deswollen (compact) state because of their phase transition behavior below and above the phase transition temperature/pH, respectively [5-9].

Due to extensive work done on *N*-isopropylacrylamide (PNIPAM) homopolymer and copolymers with hydrophobic or hydrophilic comonomers, it is known that the temperature sensitivity is due to the hydrophilicity-hydrophobicity equilibrium of the polymer. In the case of NIPAm copolymer with an ionizable comonomer, the ionization degree of pendant ionic groups on the polymer backbone shows an important effect on the phase transition temperature and induces the copolymer to exhibit pH sensitivity. Linear poly(*N*-isopropylacrylamide), PNIPAM, has been the most frequently studied thermosensitive hydrogel in the last decade. It has a lower critical solution temperature (LCST) in aqueous solutions at ~32 °C [10, 11].

Poly(DMAEMA) is a pH-responsive cationic polyelectrolyte containing tertiary amino groups, showing sensitivity to temperature [12]. Sutani et al. [13] reported the dissociation constant (p*K*a) of DMAEMA as 8.44. The tertiary amine groups on DMAEMA are weakly basic and become charged at low pH, causing the hydrogel to swell. The phase transition pH of DMAEMA homopolymer was found approximately to be 9 by Han et al [7]. However, it decreased upon copolymerization with hydrophobic comonomers such as hydroxypropyl methacrylate (HPMA). The response of DMAEMA-containing hydrogels to temperature has been much less studied than that to pH [3].

In this study, a series of pH- and thermosensitive poly(DMAEMA-*co*-AMPS) hydrogels were synthesized. Due to its pH- and thermosensitive behavior, DMAEMA was used as monomer. In order to investigate the effect of ionic comonomer on swelling, AMPS was incorporated into the polymer structure by copolymerization. The equilibrium swelling values of the hydrogels in distilled water at various temperatures and in buffer solutions with a pH range of 2.8-12.4 at room temperature were determined as a function of monomer compositions of the feed. The effect of crosslinker content was also studied.

Experimental

Materials

DMAEMA and AMPS were purchased from Merck-Schuchardt (Hohenbrunn, Germany). The initiator ammonium peroxodisulfate (APS) and the accelerator *N*,*N*,*N'*,*N'*-tetramethylethylenediamine (TEMED) were provided by Riedel de Haen (Seelze, Germany) and Serva Electrophoresis GmbH (Heidelberg, Germany). The crosslinker tetraethyleneglycol diacrylate (TEGDA) was from Aldrich. All the reagents were used as received. Buffer solutions were prepared using potassium diphosphate, potassium hydrogen phthalate, potassium hydrogenphosphate, sodium hydrogencarbonate, sodium chloride, potassium hydroxide, and hydrochloric acid. All buffer reagents were from Merck (Germany).

Preparation of poly(DMAEMA-co-AMPS) hydrogels

A series of hydrogels from 2-(dimethylamino)ethyl methacrylate and 2-acrylamido-2-methylpropane -1-sulfonic acid were prepared by free radical copolymerization in water at 60 °C for 24 h in the presence of tetraethyleneglycol diacrylate (TEGDA) as crosslinking agent. The polymerizations were performed in glass tubes with an inner diameter of 1.3 cm and a length of 15 cm. Instead of the well-known crosslinker N,N′-methylenebisacrylamide (NMBA), TEGDA was used as crosslinking agent since it imparts flexibility to the polymer chain. Aqueous ammonium persulfate (APS) solution (4.25 g APS/100 mL) and *N*,*N*,*N′*,*N′*-tetramethylethylenediamine (TEMED) were used as initiator and accelerator, respectively. Hydrogels with different feed compositions were prepared by keeping the total initial monomer concentration constant at 1 and 0.5 M. While the APS content in the feed was 1.0 mol % of total monomer content, that of TEMED was equal to the weight amount of APS. The amount of the crosslinking agent, TEGDA, was adjusted to 3.0 and 2.0 mol % of the two monomers. Before the polymerization, the monomer solution containing crosslinker was bubbled with nitrogen for 20 min, which was followed by the addition of APS and TEMED. After completion of the reaction at 60 °C in 24 h, the glass tubes were broken without destroying the cylindrical hydrogels. Afterwards, these hydrogels were sliced into small cylinders and then immersed in distilled water for 2 days changing the water every 12 h in order to remove the residual unreacted monomers and linear polymers. The resulting swollen hydrogels were dried in a vacuum oven at 40 °C until no change in weight was observed. Thus, dry gels were obtained. Feed compositions of hydrogels are given in Table 1.

Table 1. Feed composition[a].

Hydrogel code[b]	DMAEMA (mol %)	AMPS (mol %)	TEGDA (mol %)	APS (mol %)	Total monomer concentration in feed (mol/L)
D60A40(I)	60	40	3	1	1
D50A50(I)	50	50			
D40A60(I)	40	60			
D30A70(I)	30	70			
D60A40(II)	60	40	2	1	1
D50A50(II)	50	50			
D40A60(II)	40	60			
D30A70(II)	30	70			
D20A80(II)	20	80			
D50A50(III)	50	50	3	1	0.5
D40A60(III)	40	60			
D30A70(III)	30	70			
D20A80(III)	20	80			

a: The TEMED content was equal to the weight amount of APS

b: The numbers I,II, and III in hydrogel codes denote experimental series

Swelling measurements

Effect of temperature on the equilibrium swelling values of poly(DMAEMA-co-AMPS) gels

The equilibrium swelling (ES) values of DMAEMA-AMPS copolymers in distilled water were determined at 30, 40, 50, 60, 70, 80, and 90 °C by gravimetric method. A given amount of dry gel was placed in distilled water and kept at the desired temperature for 24 h in order to attain the swelling equilibrium. At the end of the swelling time, the swollen gels were taken out of distilled water, blotted with a piece of filter paper to remove excess water, and weighed. Then, these swollen gels were dried in air for 2 days followed by drying in vacuum at 40 °C until constant weight was reached. ES values of hydrogels were determined by the following equation:

$$\mathrm{ES}\ (\mathrm{gH_2O/g_{copolymer}}) = (W_s - W_d)/W_d$$

where W_s and W_d are the weights of swollen and dry gels, respectively.

The effect of pH of buffer solution on the equilibrium swelling values of poly(DMAEMA-co-AMPS) gels

Dry gels were placed in different buffer solutions with constant ionic strength (I = 0.08 mol/l) at room temperature for 24 h for the investigation of the effect of pH of the medium on the equilibrium swelling values. The ionic strength of each buffer solution was kept constant at 0.08 mol/l using NaCl when necessary. Different formulations of buffer solutions in a wide range of pH were prepared [14], e.g. potassium hydrogen phthalate - HCl at pH 2.8, potassium hydrogen phthalate - NaOH at pH 5.3, potassium diphosphate - NaOH at pH 7, sodium hydrogencarbonate - NaOH at pH 10.0, KCl - NaOH at pH 12.4. After swelling, the samples were taken out of the buffer solutions, and their ES values were determined by the procedure and using the equation above.

Results and discussion

Swollen poly(DMAEMA-*co*-AMPS) hydrogels prepared in this work were completely transparent at all feed compositions. After the preparation, hydrogel diameters were the same as inner diameters of the glass tube except those of the copolymers of anionic (AMPS) and cationic (DMAEMA) monomers used at equimolar amounts in the feed. In the latter case, the hydrogel diameter was apparently smaller than that of the glass tube and the hydrogel was not as elastic as those at other feed compositions, but it preserved its shape during slicing.

The influences of crosslinking agent and DMAEMA contents on the equilibrium swelling values of poly(DMAEMA-co-AMPS) hydrogels

ES values of dry poly(DMAEMA-*co*-AMPS) gel samples in distilled water at room temperature were presented in Figure 1. As seen in Figure 1, the ES values of

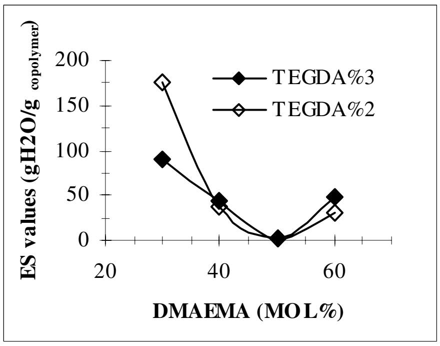


Figure 1. The variation of ES values of dry DMAEMA-AMPS(I) (TEGDA 3 %) and DMAEMA-AMPS (II) (TEGDA 2 %) gels in distilled water at room temperature as a function of the DMAEMA content in the feed depending on the crosslinker content.

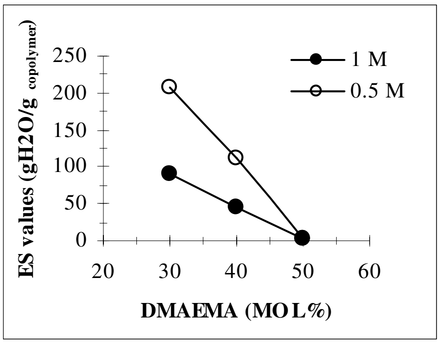


Figure 2. The variation of ES values of dry DMAEMA-AMPS(I) (1 M) and (III) (0.5 M) gels as a function of DMAEMA content depending on initial monomer concentration in the feed, in distilled water at room temperature.

copolymers decrease with the increasing DMAEMA content up to 50 % and then increase with further increase in DMAEMA content. The increase in the TEGDA content from 2 to 3 % for D30A70 gels led to a decrease in ES values of polymer as expected, but for the copolymers prepared at the other feed compositions, it has practically no influence on their swelling values. The minimum ES values observed for the copolymer containing DMAEMA and AMPS in equimolar amounts can be envisaged for an ionic complex between the anionic and cationic units of the copolymer, and the least contribution to swelling due to lowest ionic repulsion. These results are well in agreement with the findings of Sutani et al [13].

The influence of initial monomer concentration in the feed on the ES values of DMAEMA-AMPS copolymers was also studied. Figure 2 shows the change in ES values of DMAEMA-AMPS(I) and (III) gels as a function of initial monomer concentration in the feed where TEGDA was kept constant at 3 %. At both monomer concentrations, 0.5 and 1 M, ES values decreased linearly with the increase in the DMAEMA content. The ES values of DMAEMA-AMPS copolymers prepared at the lower monomer concentration (0.5 M) are higher than those prepared at higher monomer concentration except that for the polymer (D50A50) with equimolar anionic and cationic monomer contents. In that case, the ES values of the copolymer D50A50 for both initial monomer concentrations are the same due to the formation of ionic complex.

The influence of pH on the equilibrium swelling values of poly(DMAEMA-co-AMPS) hydrogels

The ES values of dry poly(DMAEMA-*co*-AMPS) hydrogels in different buffer solutions with pH of 2.8, 5.3, 7.0, 10.0, and 12.4 at constant ionic strength (I = 0.08 mol/l) at room temperature are demonstrated in Figure 3. The pH responsiveness studies of poly(DMAEMA-*co*-AMPS) hydrogels showed that D50A50(I-III) copolymers have the lowest ES values in comparison with the hydrogels prepared at other feed compositions as seen in Figures 3-5, due to ionic complex formation. As can be seen from the figures, the ES values of poly(DMAEMA-*co*-AMPS) gels depended strongly on pH. Thus, the ES values are low and almost constant at pH between 2.8 and 7 and increase with increasing pH from 7 to 12.40. Although the hydrogels were prepared at various feed compositions of DMAEMA and AMPS, in addition to different initial total monomer and crosslinker concentrations, they showed a similar swelling behavior.

Zhai et al. [15] determined the isoelectric point (IEP) for the copolymers of DMAEMA and acrylic acid (AAc) as a function of feed composition, which was found to decrease

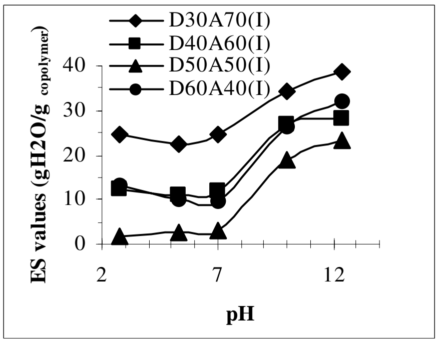
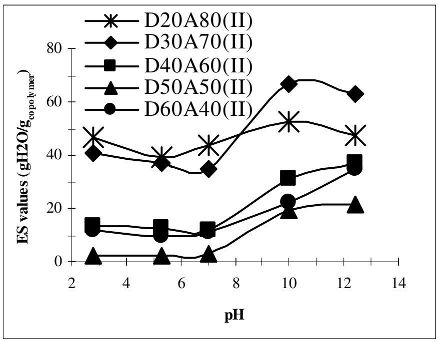


Figure 3. Variation of ES values of poly(DMAEMA-*co*-AMPS)(I) hydrogels as a function of pH at room temperature.

with decreasing DMAEMA content in the feed. They observed that IEP had a value of pH between 7.2 and 8.0 for the copolymers with 50-70 mol % DMAEMA and 4.0 for the copolymer containing 40 % DMAEMA. At the IEP, the hydrogels had the lowest ES values. In the case of our hydrogels, although there is not an apparent isoelectric point like in DMAEMA-AAc copolymers [15], it can be concluded that the transition of hydrogels from the swollen to a more swollen state occurs at pH ca 7. It is known that the DMAEMA and AMPS homopolymers are weakly basic and strongly acidic, respectively. The former homopolymer exists in the swollen state at acid pH's, and the latter swells in alkaline solutions. The reason for exhibiting higher ES values of DMAEMA-AMPS copolymers at pH values higher than 7 may be the dominant effect of strongly acidic SO_3H groups in AMPS on swelling in comparison with weakly basic tertiary amine groups in DMAEMA. Formation of ionic complex between pendant groups of DMAEMA and AMPS may occur at the other feed compositions in addition to the equimolar comonomer composition. In that case, at pH values lower than 7, the free SO_3H groups remaining after formation of a ionic complex of positively charged DMAEMA groups of and SO_3H groups of AMPS exist in protonated form. These protonated SO_3H groups ionize and this ionization increases the ES values of copolymers at higher pH as seen in Figures 3-5.

Although the crosslinker content did not seem to have an apparent influence on the swelling of DMAEMA-AMPS copolymers in distilled water (Fig. 1), its decrease from 3 to 2 % led to an increase in ES values of the copolymers in buffer solutions as



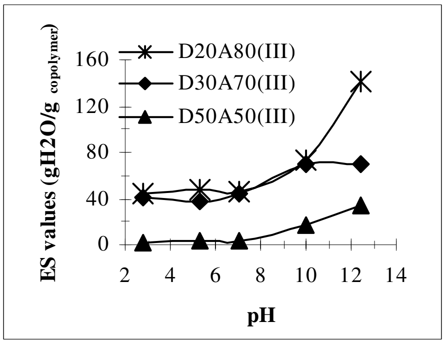


Figure 4. Variation of ES values of poly(DMAEMA-*co*-AMPS)(II) hydrogels as function of pH at room temperature.

Figure 5. Variation of ES values of poly(DMAEMA-*co*-AMPS)(III) hydrogels as function of pH at room temperature.

seen in Figures 3 and 4. The decrease in initial monomer concentration from 1 to 0.5 M at the same crosslinker content (3 % TEGDA) increased the ES values of copolymers in buffer solutions at room temperature as seen in Figures 3 and 5, respectively. The incorporation of high amounts of AMPS into the polymer structure resulted in AMPS-rich DMAEMA-AMPS copolymers exhibiting an anionic polymer behavior during swelling in buffer solutions of various pH.

Influence of temperature on the equilibrium swelling values of poly(DMAEMA-co-AMPS) hydrogels

The influence of temperature on the equilibrium swelling values is illustrated in Figures 6-8. It can be deduced from the ES values of copolymers prepared at the same monomer concentration of 1 M at various crosslinker contents, 3 and 2 %, as given in Figures 6 and 7, that ES values increase with AMPS content. They also slightly increase with temperature between 50 and 90 °C for D40A60–D60A40 copolymers with 3 and 2 % TEGDA contents. The ES values of D30A70(I) and D20A80(II) copolymers are apparently higher than those of copolymers prepared at the rest of feed compositions and drastic increases in ES values of former gels at 80 and 90°C were observed in comparison to those of rest of the gels. The decrease in initial monomer concentration in the feed from 1 to 0.5 M increased the ES of D40A60(III) (Figure 8) in distilled water by a factor of 2 in

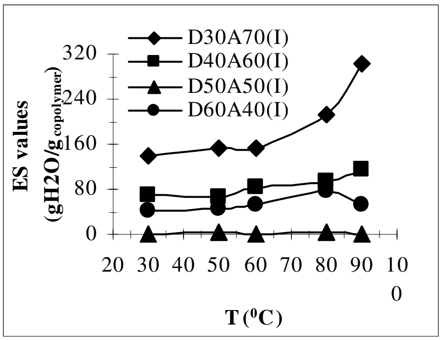


Figure 6. Variation of ES values of poly(DMAEMA-*co*-AMPS)(I) hydrogels as a function of temperature in distilled water.

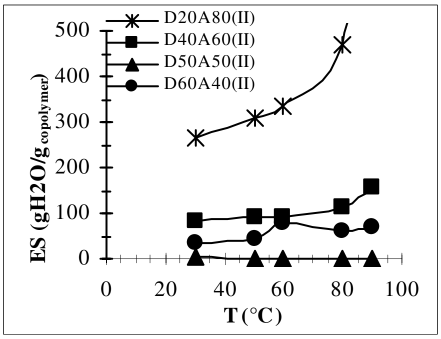


Figure 7. Variation of ES values of poly(DMAEMA-co-AMPS)(II) hydrogels as a function of temperature in distilled water (ES of D20A80(II) at 90 °C is 1143 g H2O/g copolymer).

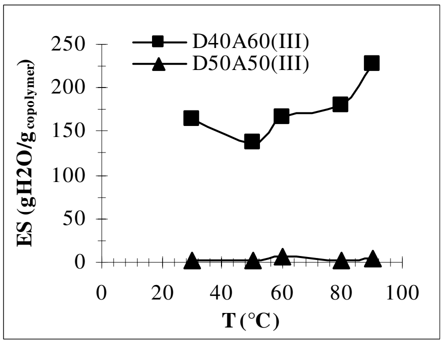


Figure 8. Variation of ES values of poly(DMAEMA-co-AMPS)(III) hydrogels as a function of temperature in distilled water.

comparison with that of D40A60(I) (Figure 6). D50A50 copolymer has the lowest ES values in distilled water (Figure 6-8) similar to those in buffer solutions with various pH.

Conclusion

In this study, DMAEMA-AMPS copolymers were synthesized by chain polymerization in water at 60 °C using APS/TEMED and TEGDA as initiator system and crosslinker, respectively. Swelling behavior of hydrogels in distilled water was investigated as a function of the DMAEMA content, initial monomer concentration, and temperature. It was observed that equilibrium swelling values decreased with increasing DMAEMA content in the feed up to 50 % and then increased with further increase. The minimum ES values in case of hydrogels with equimolar comonomer composition showed the ionic complex of the anionic and cationic units of the polymer. This ionic complex is stable in distilled water between 30 and 90 °C since the ES values of copolymers in distilled water are constant in this temperature range. This applies also to buffer solutions with pH lower than 7, but not for higher pH since the ES values of copolymers with equimolar contents of DMAEMA and AMPS increase with increasing pH starting from 7.

Lower ES values in distilled water at room temperature were observed in hydrogels prepared at higher initial monomer concentration in comparison with those at lower monomer concentrations.

The copolymers, in particular the AMPS-rich ones, displayed an increasing swelling in distilled water with increasing temperature starting from 50 °C.

pH vs. swelling of DMAEMA-AMPS copolymers was also investigated. At low pH values, the copolymers demonstrated low ES values and a steady increase in ES values of the hydrogels of all compositions was observed with increasing pH from 7.0 to 12.4. It was observed that DMAEMA-AMPS copolymers prepared in this work exhibited swelling behavior typical of anionic polymers in swelling in buffer solutions of various pH. It was concluded that this behavior resulted from the ionization of SO_3H groups at higher pH, remaining after complex formation from pendant groups of DMAEMA and AMPS.

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