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Polymer 42 (2001) 1863–1867

polymer

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Volume phase transitions of poly(acryloyl-L-proline methyl ester) gels in response to water–alcohol composition

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Received 19 January 2000; received in revised form 17 April 2000; accepted 31 May 2000

Abstract

The volume phase transitions of poly(acryloyl-L-proline methyl ester (A-ProOMe)) gels in mixtures of water and various alcohols (methyl, ethyl, propyl, and *t*-buthyl alcohols) were investigated. The poly(A-ProOMe) gels showed two swelling phases (first swell, 0–10 vol%; second swell, 50–80 vol%) and two shrinking phases (first shrink, 10–50 vol%; second shrink, 80–100 vol%) in the presence of each aqueous alcohol under alcohol concentrations ranging from 0 to 100 vol%. The swelling profiles at second swell and second shrink varied in terms of the solvent alcohols; this difference was quantitatively elucidated by taking into account the hydrophobicity of the solvents using dynamic hydration numbers as a parameter of the alcohol's hydrophobicity. The gels showed a shrinking phase in the region of high alcohol concentration (second shrink), which had not been observed in other hydrogels such as NIPAAm. Infrared spectra of the poly(A-ProOMe) revealed that the hydrogen bonding of the amide moiety of poly(A-ProOMe) plays a key role in the gel's sensitivity to the solvent composition, resulting in the sudden shrinking. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: Volume phase transition; Poly(acryloyl-L-proline methyl ester) gel; Solvent composition

1. Introduction

The volume phase transition of a thermo-responsive gel plays an important role in applications such as drug delivery systems, selective membranes, and biosensors [1–4]. Poly(*N*-isopropylacrylamide (NIPAAm)) gels have been widely investigated in light of their thermo-responsiveness and characteristic reversible phase transition between swollen and shrunken states in water at transition temperatures between 31 and 35°C [5–7]. This transition temperature range is near the lower critical solution temperature (LCST) of the corresponding linear polymers with these LCST behaviors resulting from the polymer chain's sudden change from hydration to dehydration. Therefore, the volume phase transition of the gel is considered to be the consequence of a balance between hydrophilic and hydrophobic moieties on gel networks. It has also been reported that poly(NIPAAm) gels exhibit a volume phase transition in response to solvent composition in mixtures of water and organic solvents [8–10].

We have focused on the volume phase transition behavior of the self-bridged gels that contain amino acid residues on the side chain. These self-bridged gels are prepared by radiation-induced polymerization without any crosslinkers, initiators, or accelerators [11,12]. This allows us to control physical properties such as the density of cross-linking and the porosity of the gels in the absence of chemical impurities. Amino acid residues in self-bridged gels are expected to manifest a biocompatibility in vivo for biological and medical applications. Recently, we have found that the self-bridged gel of acryloyl-L-proline methyl ester (A-ProOMe) exhibits a volume phase transition at around 14°C, which is a lower temperature than that of poly(NIPAAm) gel [13,14]. Since the lower transition temperature of poly(A-ProOMe) gel indicates its higher hydrophobic interaction in comparison with that of poly(NIPAAm) gel, we assumed that poly(A-ProOMe) gel could recognize slight differences in the hydrophobicity of solvents. We report herein the volume phase transition behavior of poly(A-ProOMe) gel in response to the solvent composition. The volume phase transition behavior was elucidated by the effect of the alkyl moieties of alcohol molecules. Moreover, the hydrogen bonding of amide and ester moiety

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PII: S0032-3861(00)00416-X

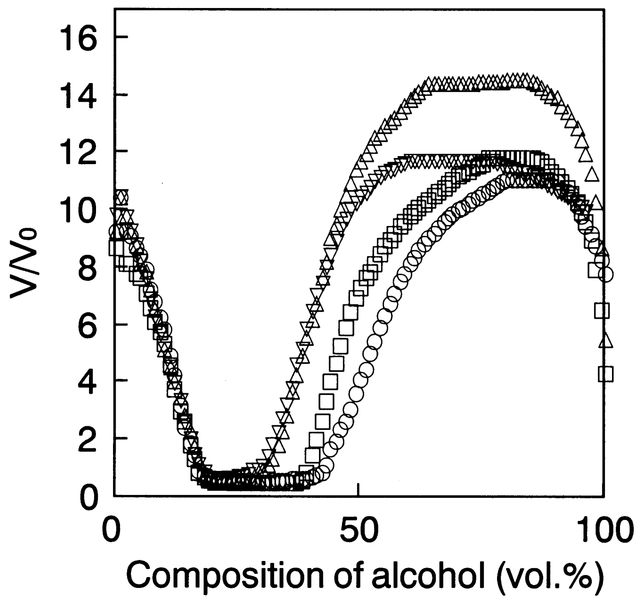

Fig. 1. Swelling ratio (V/V_0) of poly(A-ProOMe) gel in water–alcohol mixed solvents as a function of alcohol concentration at 5°C, (○) methanol; (□) ethanol; (△) 1-propanol; and (▼) 2-methyl-2-propanol.

of poly(A-ProOMe) was analyzed using the infrared absorption spectra to gain insight into the behavior of the poly(A-ProOMe) gel in a mixture of water and alcohol.

2. Experimental

2.1. Materials

Acryloyl-L-proline methyl ester (A-ProOMe) was synthesized as described in previous papers [15,16]. Methanol, ethanol, 1-propanol, 2-methyl-2-propanol, and acetone of special grade were obtained from Wako Pure Chemical Industries, Ltd. (Osaka, Japan) and used without any purification. Deuterium oxide was purchased from Merck (Darmstadt, Germany).

2.2. Preparation of poly(A-ProOMe) gels and the corresponding polymer

Poly(A-ProOMe) gels were obtained without any crosslinkers by the following procedure. A-ProOMe (0.6 ml) was dissolved in a mixed solvent (1.4 ml) of acetone/water (40/60 v/v%). After bubbling a dry nitrogen, this solution was transferred into a 0.8 mm diameter cylindrical ampoule. The cylindrical ampoules were degassed and sealed off in vacuo. The ampoules were irradiated with 30 kGy at 25°C using γ-rays from a ^{60}Co source (10 kGy/h). The obtained gels were taken out of the ampoules and immersed into a large amount of acetone to wash out unreacted monomers and sol fractions. The cylindrical gels were cut into pieces of about 20 mm in length and immersed into distilled deionized water kept at 0°C in a vial.

The corresponding A-ProOMe polymer was prepared without crosslinker by radiation-induced polymerization of A-ProOMe with 10 kGy at 25°C. The irradiated sample was dissolved in acetone, followed by precipitation into water at 80°C. The obtained polymer was lyophilized in vacuo.

2.3. Swelling ratio

The gel was attached to a sample holder, which was designed according to literatures [17,18], in a glass cell. A gel diameter (d) was measured by a calibrated microscope after the gels reached to its equilibrium at each composition of the mixed solvents. A swelling ratio (V/V_0) of the gels was calculated according to the following equation:

$$V/V_0 = (d/d_0)^3$$

where d_0 is the diameter of the gel at preparation of the gel, i.e. $d_0 = 0.8$ mm.

2.4. FT-IR measurement in deuterium oxide–alcohol

Poly(A-ProOMe) (10 mg/ml) was dissolved in a mixture of deuterium oxide and alcohols. It is necessary to use deuterium oxide for the IR measurements instead of water because the latter has strong absorption in the IR region. The infrared absorption spectra were measured with Jasco FT-IR/5300 spectrophotometer, employing a pair of solution cells of 0.1 mm path length with calcium fluoride windows. Peak separation of each spectrum was performed by a least-squares curve-fitting methods using Jasco spectrum-manager on a personal computer (Hitachi FLORA).

3. Results and discussion

In Fig. 1, the swelling ratios of poly(A-ProOMe) gels at 5°C are plotted as a function of the alcohol concentration (vol%) in the mixture of water and alcohol. We can clearly distinguish among four different phases: first swell (0–10 vol%), first shrink (10–50 vol%), second swell (50–80 vol%), and second shrink (80–100 vol%) in all the aqueous alcohols as the alcohol concentration in solvent increased from 0 to 100 vol%. In the case of methanol, the swelling ratio of the poly(A-ProOMe) gel gradually decreased with increase in the alcohol fraction from 0 to 20 vol%, corresponding to the transition from first swell to first shrink. From 20 to 43 vol%, the gel was completely collapsed with swelling ratio of less than 0.5 (first shrink). As the methanol concentration in the solvent increased, the collapsed gel reswelled and reached a maximum swelling ratio ($V/V_0 = 11$) in the second swell. Furthermore, with an increase in the methanol concentration from 80 to 100 vol%, the swelling ratio of the gel gradually decreased again from 11 to 8 (second shrink). This second shrink has not been observed in the other hydrogels such as NIPAAm in mixtures of water and alcohol. Even in other alcohols

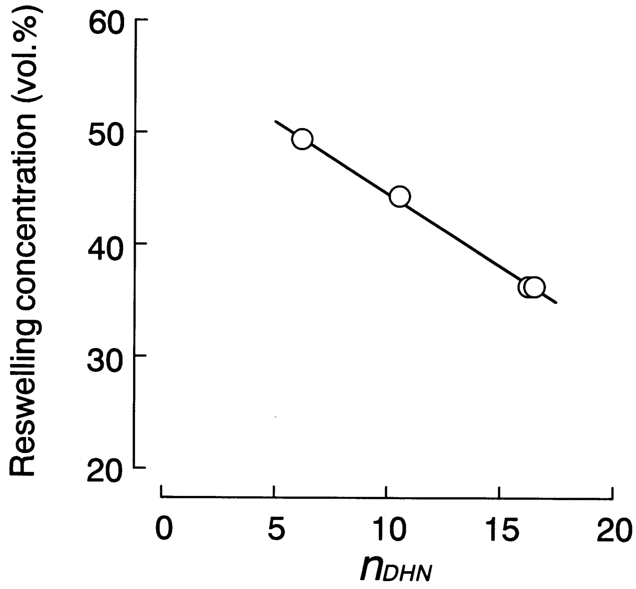

Fig. 2. Relationship between the alcohol concentrations, at which second swell commences and the n_{DHN} of the corresponding alcohols.

containing larger alkyl groups (Et, Pr, and *t*-Bu), the behavior of the volume phase transitions can be divided into four phases.

In the presence of any alcohol the swelling ratio of the gels gradually decreased with increase in alcohol concentration from 0 to 20 vol%; then, the shrunken gels reswelled in different alcohol concentrations ranging from 30 to 43 vol%, depending on the alcohols. The similar swelling profile from the first swell to second swell has also been observed in poly(NIPAAm) gel in binary mixture [10,18]. The change of swelling ratio corresponding to water–alcohol composition may be explained by the entropy of mixing and the alcohol partial molar volume in water–alcohol mixtures. The alcohol concentrations at which the gel shrinkage reaches to minima in first shrink nearly agree with those of the entropy of mixing and the alcohol partial molar volume of water–alcohol mixtures [19–21]. The decrease in entropy of mixing is ascribed to the increase of interaction between water and alcohol molecules, which results in the cluster formation of alcohol and water. Therefore, the similar profiles of the swelling ratio of the gels to those of the entropy of mixing and the alcohol partial molar volume indicates that water should prefer cluster formation with alcohols to hydrophobic hydration around the polymer, as resulting in the shrinking of the gels.

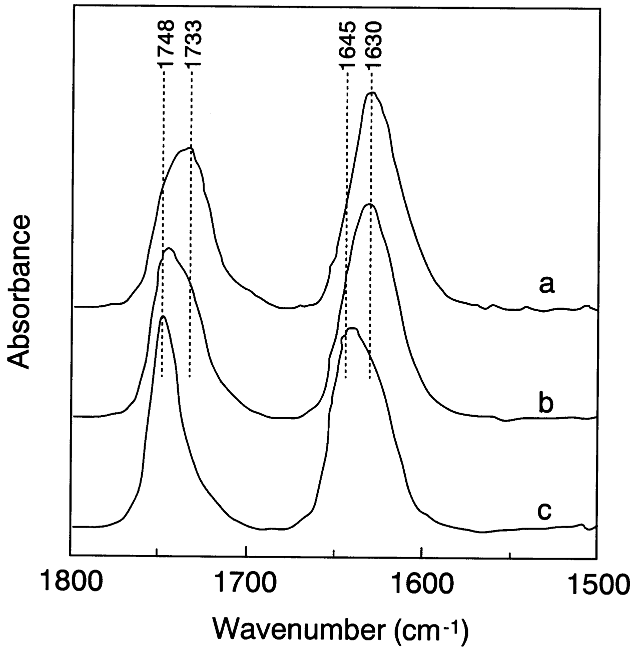

Fig. 3. FT-IR spectra of ester and amide I band of poly(A-ProOMe) in binary mixed solvents. The alcohol concentrations in mixed solvents were (a) 50; (b) 90; and (c) 100 vol%.

In alcohol concentration above 20 vol%, the entropy of mixing and alcohol partial molar volume in water–alcohol mixtures increases with increasing its concentration [19–21]. These increases may result from the decrease of the interaction between water and alcohols, suggesting that the hydrophobic interaction between the polymer and alkyl moieties of alcohols overcomes the interaction between gel networks at alcohol concentrations above 20%. This reversal of interaction results in the second swell, which commences at alcohol concentration in the range of 30–43 vol%.

Since there have been no quantitative elucidation of the hydrophobic recognition of poly(NIPAAm) gels, we introduce dynamic hydration numbers (DHNs) as a parameter of the hydrophobicity of alcohols. The DHN has been used to express the hydrophobicity of proteins by taking into account the static and dynamic hydration of water molecules around the target proteins [22,23] and is applicable to the evaluation of the hydrophobicity of organic molecules. The relationship between the alcohol concentrations at which the second swell commence, and the DHNs of the corresponding alcohols are shown in Fig. 2, where the DHNs of methanol, ethanol, 1-propanol, and 2-methyl-2-propanol are 6, 10.4, 16, and 16.3, respectively [24–26]. The second swell commenced at alcohol concentrations, which are proportional to their corresponding DHNs. This linear correlation indicates that the second swell of poly(A-ProOMe) gel depends quantitatively on the hydrophobicity of the mixed solvents.

The poly(A-ProOMe) gel in the mixed solvents containing all the alcohols shrank in the region of alcohol concentration above 80 vol% (second shrink), which has not been observed in the other gels such as NIPAAm. Furthermore, as the alcohol concentration increased from 80 to 100 vol%, the swelling ratio of the gel decreased by 70, 40, and 38% in methanol, ethanol, and propanol, respectively. In other words, the gel shrank to a greater extent in ethanol and propanol, which are relatively more hydrophobic, than methanol.

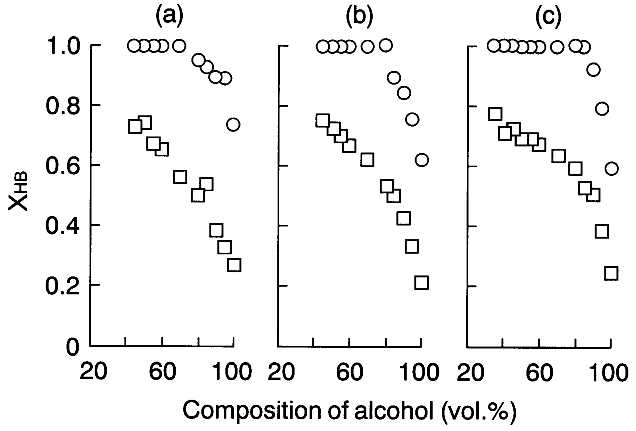

Fig. 4. The hydrogen bonding degrees of C=O stretching (X_{HB}) of (□) ester and (○) amide I bands as a function of alcohol concentration. (a) Methanol; (b) ethanol; and (c) 1-propanol.

The swelling behavior from first swell to second swell is interpreted by taking account of the entropy of mixing in the mixed solvent, whereas the second shrink cannot be elucidated in the change of the entropy of mixing. This is because the entropy of mixing simply increases with increase of alcohol concentration up to 100%. However, the reshrinking of the gels, which varied in terms of alcohol molecules, could be understood by taking into account the hydrogen bonding of ester and amide C=O in the mixed solvents. Fig. 3 shows the infrared spectra of the ester and amide I region of poly(A-ProOMe) in deuterium oxide–alcohol mixed solvents. The maximum peaks of the ester and amide I region shift to a higher frequency by 15 cm^{-1}, i.e. from 1748 to 1733 cm^{-1} in ester and from 1645 to 1630 cm^{-1} in amide, as the alcohol concentration increased. These frequency shifts of ester and amide C=O were in good agreement with the difference between the absorption of free and hydrogen bonded C=O [27]. The absorption bands in the C=O region were divided into two absorption peaks, assigned to ester and amide I, by a least-squares fitting method. The hydrogen bonding degrees of ester and amide C=O defined as X_{HB} (X_{HB} = absorption intensity of hydrogen bonded C=O/the sum of absorption intensity of free and hydrogen bonded C=O).

In Fig. 4, the hydrogen bonding degrees of ester and amide C=O (X_{HB}) plotted as the function of alcohol concentration. The X_{HB} of ester and amide C=O in both ethanol and propanol drastically decrease in alcohol concentrations above 80 vol%, in which the second shrink of the gels started. On the other hand, the X_{HB} of ester and amide C=O gradually decrease with increases of methanol concentration up to 100 vol%. From these results, it is obvious that the second shrink of the gel is directly related to the decreasing of hydrogen bonds of ester and amide C=O by the solvent molecules. Furthermore, the X_{HB} of amide C=O in ethanol and propanol decreased suddenly just when the alcohol concentration reached 85 vol%, whereas the X_{HB} of ester C=O decreased gradually even from a 40 vol% alcohol concentration. This sharp decrease of the X_{HB} of amide C=O strongly indicates that the gel's amide group very sensitively recognizes the hydrophobicity of the mixed solvents.

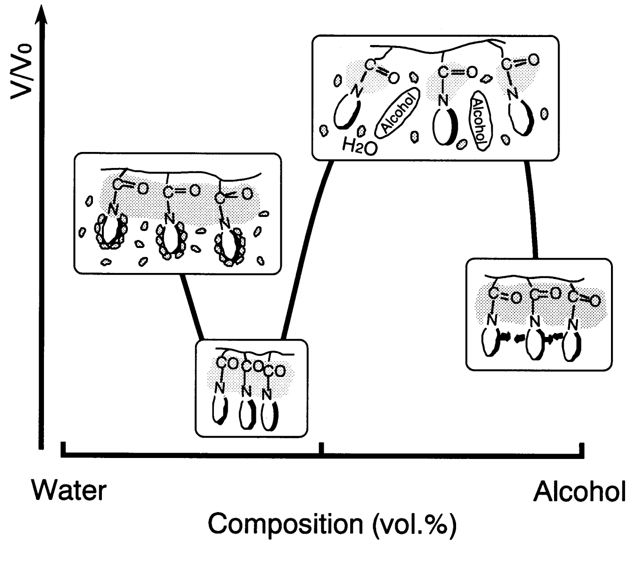

Fig. 5. Schematic illustration of swelling–shrinking behavior of poly(A-ProOMe) gel in water–alcohol mixed solvents.

4. Conclusions

Poly(A-ProOMe) gel showed two swelling phases (first swell: 0–10 vol%, second swell: 50–80 vol%) and two shrinking phases (first shrink: 10–50 vol%, and second shrink: 80–100 vol%) in all the aqueous alcohol solutions when the alcohol concentration was increased from 0 to 100 vol% (Fig. 5). The swelling profiles at second swell and second shrink varied in terms of the solvent alcohols. The different profiles at second swell were quantitatively elucidated by taking into account the solvent's hydrophobicity using DHNs as a parameter of the hydrophobicity of alcohols. The gels showed a shrinking phase in the region of high alcohol concentration (second shrink), which has not been observed in other hydrogels such as NIPAAm. Infrared spectra of the poly(A-ProOMe) revealed that the hydrogen bonding of amide C=O was sufficiently sensitive to solvent hydrophobicity and played a key role in the gel's sudden shrinking at high alcohol concentrations.

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