Swelling of and Solute Exclusion by Poly(*N*-alkylacrylamide) Gels

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SYNOPSIS

Temperature-sensitive hydrogels of poly(*N*-isopropylacrylamide) poly(*N*,*N*-diethylacrylamide), poly(*N*-*n*-propylacrylamide), copolymer of *N*-isopropylacrylamide and methylacrylamide, and copolymer of *N*,*N*-diethylacrylamide and *N*-*tert*-butylacrylamide were prepared. The swelling characteristics of the gels were studied and gel extraction of macromolecules, based on the solute exclusion by the gel network, were investigated. © 1995 John Wiley & Sons, Inc.

INTRODUCTION

It was discovered recently that the polymer derivatives of acrylamide, when in the form of hydrogel, are temperature-sensitive,[1] i.e., the swelling and deswelling of the gel are a dramatic function of temperature. The gels swell at low temperature and deswell at elevated temperature. Moreover, violent and sometimes discontinuous changes in swelling occur when the gels are near their critical points, which are in analogy to the lower critical solution temperature (LCST)[2,3] of the corresponding polymer solutions.

In this study, gels of homopolymer and copolymer derivatives of acrylamide were prepared. Their swelling characteristics were studied and separation of macromolecules, by taking the advantage of the characteristics of the gels, were investigated.

EXPERIMENTAL

In this research, the monomers of *N*-isopropylacrylamide (NIPA), *N*,*N*-diethylacrylamide (NDEA), *N*-*tert*-butylacrylamide (NTBA), and *N*-*n*-propylacrylamide (NNPA) were synthesized at our laboratory with the procedures similar to those described in Ref. 4. Details of the monomer preparation were published elsewhere.[5] The monomer of methylacrylamide (MAA) of reagent grade was purchased and then purified by recrystallization before use.

The gels were prepared by free-radical solution polymerization. The reaction took place in aqueous solution with *N*,*N*′-methylenebisacrylamide as crosslinking agent, and with ammonium persulfate, sodium metabissulfite, and *N*,*N*,*N*,*N*-teramethyl enthylene diamine as initiators. The crosslinking agent and initiators were used as received.

The composition of gels was described following the method of Hjerten,[6] i.e., the first number after the name of the gel denotes the concentration of overall monomers in weight percentage, and the second number denotes the amount of crosslinking agent expressed as the weight percentage of the total amount of monomers.

The gels to be measured were merged in a water bath, the temperature of which was adjusted by a thermoregulator. When the swelling reached equilibrium, the gel was quickly centrifuged at a proper speed to eliminate the water on the surface of and between the particles. Then the gel was weighed.

The equilibrium swelling of the gels was characterized by swelling degree q or volume fraction v of the polymer network:

$$q = W_s/W_d \tag{1}$$

$$v = 1 + \left(\frac{W_d}{W_s} - 1\right)\frac{\rho_w}{\rho_g} \tag{2}$$

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Journal of Applied Polymer Science, Vol. 56, 285–288 (1995)
 CCC 0021-8995/95/020285-04

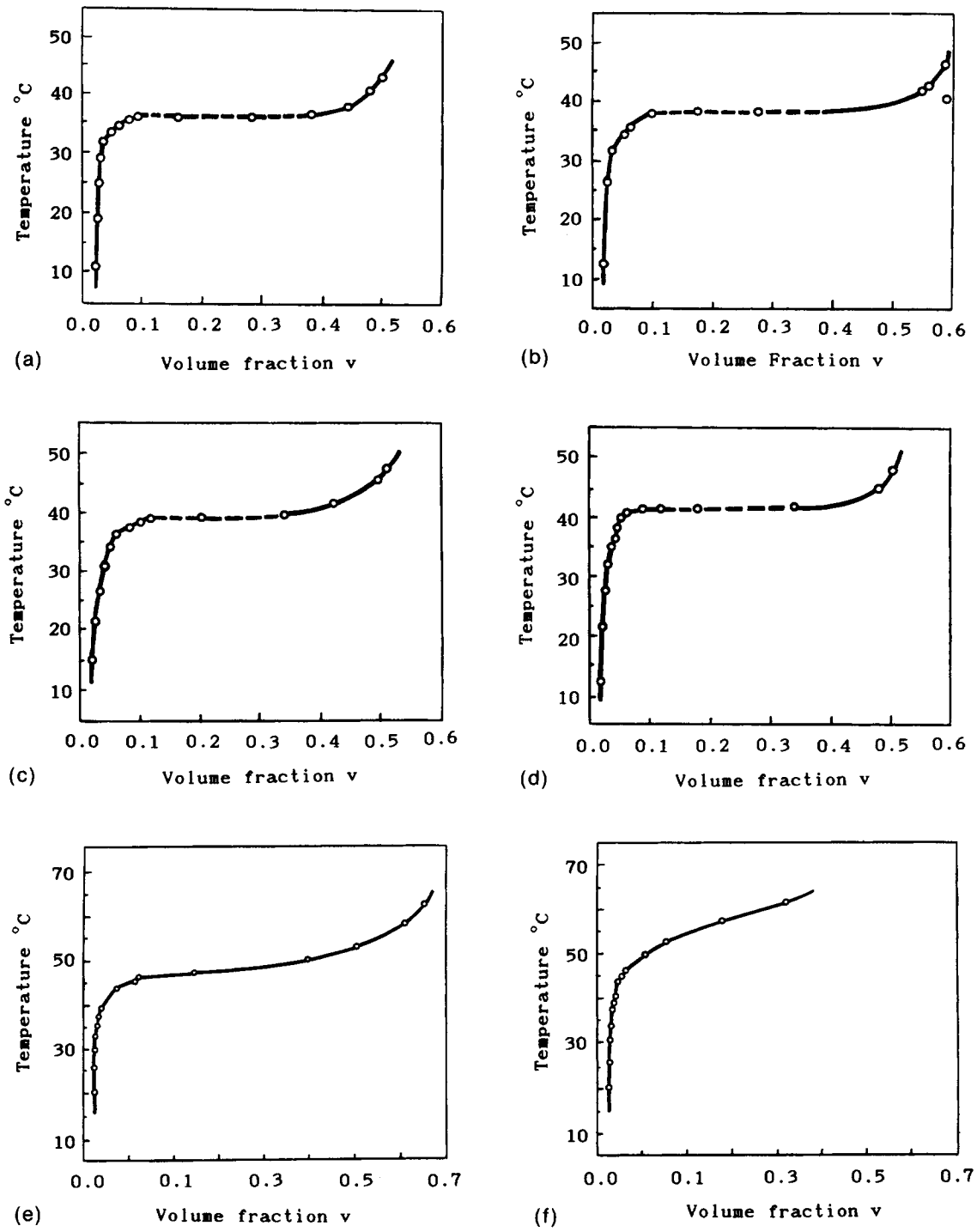

Figure 1 Equilibrium swelling of NIPA gels and NIPA + MAA gels: (a) NIPA 8 × 1, (b) NIPA 10 × 1, (c) NIPA 12 × 1, (d) NIPA 8 × 2, (e) NIPA/MAA (8/10) × 2, (f) NIPA/MAA (8/20) × 2.

where W_d, W_s are weights of dry and swollen gel, respectively, ρ_w and ρ_s denote, respectively, the density of water and swollen gel. When the swelling degree is large, which is usually the case in this research, ρ_s approximates ρ_w, and therefore the volume fraction v can be roughly taken as:

$$v = W_d/W_s \quad (3)$$

and thus

$$q = 1/v \quad (4)$$

RESULTS AND DISCUSSION

The swelling of gels of polymer NIPA and copolymer of NIPA and MAA are shown in Figure 1. It can be observed that the critical temperatures of the NIPA gels are about 37°C. With the increase of overall monomer concentration, the critical temperature slightly increases, while the volume fraction difference at swollen and collapsed state becomes smaller upon the same change. These phenomena can be attributed to the increase of crosslinking density, the enhancement of the interactions between the polymer chains, and the loss of elasticity of the network. With the increase of the overall monomer concentration in the per-gel solution, there would be an increase of the probability of entanglements, which function as crosslinker to resist the gel from further swelling. It can also be noticed that the monomer composition of a gel has a considerable effect on its critical temperature [Fig. 1(e) and (f)]. With higher concentration of more hydrophilic MAA in the gel, higher temperature is needed to cause the gel to collapse. The change of overall monomer concentration and monomer composition provides us with a way of adjustment to meet specific requirement in application.

The swelling behavior of NDEA gels change regularly with the crosslinking concentration, under the condition that the overall monomer concentrations

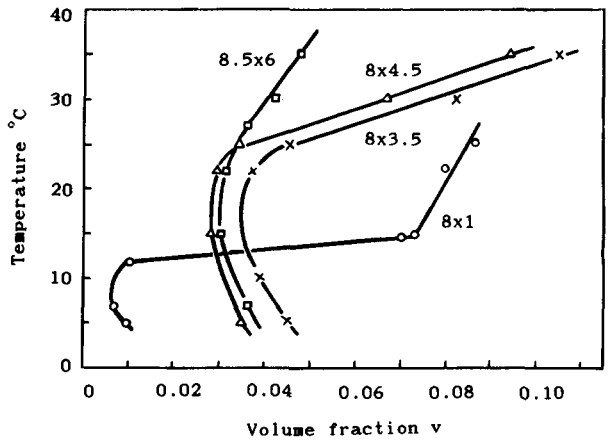

Figure 2 Equilibrium swelling of NDEA gels of varying crosslinking concentration.

Table I Swelling Characteristics of Copolymer (NDEA + NTBA) Gels and Homopolymer NNPA Gel

Gel $C_T \times C_B$	Critical Temperature, °C	Swelling Degree (at 20°C)
(NDEA + NTBA) (5 + 5) × 4	17	23
(NDEA + NTBA) (7.5 ± 2.5) × 4	23	23
(NDEA + NTBA) (8.8 ± 1.2) × 4	24	23
NNPA 8 × 4	25	25

are almost the same, as shown in Figure 2. The swelling of NDEA8X1 gel is a very sharp function of temperature at about 12–15°C, and the maximal degree of swelling approaches 170. The other NDEA gels are less sensitive to temperature, owing to the several times higher concentration of the crosslinking agent. For all the NDEA gels observed, the degree of swelling increases as the temperature decreases, which has been explained by a "hydrogen-bonding" mechanism.[7] The formation and orientation of hydrogen bonds at low temperature decrease the entropy of the gel–solvent system, so that further mixing of gel and solvent, i.e., swelling of gel, should happen to keep the entropy change positive. At lower temperature, however, the gels deswell because of the decrease of internal energy and elasticity of the gel network.

The swelling characteristics of copolymer (NDEA + NTBA) gels and homopolymer NNPA gel are shown in Table I. The concentration of crosslinking of all gels are the same (C_B = 4), and the degree of swelling ranges from 23 to 25 at 20°C. The overall monomer concentration of the copolymer gels are kept unchanged, whereas the NDEA portion varies from 5 to 8.8. It can be seen that the critical temperature increases with the increase of NDEA portion in the copolymer gel. NDEA comonomer is more

Table II Separation Efficiency of BSA by Gel Extraction with NIPA Gels

Gel	NIPA 10 × 1	NIPA 10 × 2	NIPA 10 × 3	NIPA 10 × 5
η% (BSA 0.1%)[a]	86.4	92.2	88.6	87.5
η% (BSA 0.03%)[a]	85.0	92.9	95.9	69.5

[a] Feed concentration.

Table III Separation Efficiency of BD by Gel Extraction with NIPA Gels

Gel	NIPA 8 × 1	NIPA 8 × 2	NIPA 8 × 4	NIPA 8 × 6	NIPA 10 × 1	NIPA 10 × 3
$\eta\%$[a]	98.4	99.7	98.7	98.0	98.0	98.0

[a] Feed concentration 0.028%.

hydrophilic than NTBA, because the volume of the hydrophobic tertbutyl group is larger than that of the diethyl group. Therefore, for a gel with more NDEA composition, higher temperature is needed to deswell it. Thus the gel has higher swelling–collapsing transition temperature.

Temperature-sensitive gels have a great variety of potential applications, among which gel extraction was particularly interested in this research. In a gel extraction process, feed solution is mixed with gel particles, which swell by absorbing solvent and small solutes. Large solutes are excluded by gel networks and thus concentrated at the solution phase. Then the gel particles are separated from the concentrated solution by filtration or centrifugation. Finally, the gel was warmed above its critical temperature so that most of the absorbed solvent and solutes can be released.

The efficiency η of a gel extraction process can be expressed as

$$\eta = \frac{C_R - C_F}{C_{\max} - C_F} \tag{5}$$

where C_F is the concentration of target solute in feed solution, and C_R, $C_{\max}$ denote, respectively, the practical and maximal concentration of target solute after separation. Generally, C_R is smaller than $C_{\max}$, the latter can only be achieved in the case of complete exclusion.

The concentration of bovine serum albumin (BSA) (MW 69,000) and blue dextran (BD) (MW 2 × 10^6) from water by gel extraction with NIPA gel was examined. Assay was performed with a model 53W UV-VIS spectrophotometer. The separation results in the cases of different gels and different concentrations of feed solution are summarized in Tables II and III. Depending on the size of the solute molecules, the separation efficiency in concentrating BD is rather close to 100%, whereas the efficiency is appreciably lower for separation of smaller BSA molecules. The lower efficiency may also attributed to the surface adsorption of BSA to the gel.

Generally, with the increase of monomer concentration or crosslinking concentration of the gel, its pore size should become smaller and thus separation efficiency should increase, as reflected by some of the data in Tables II and III. However, inhomogeneity of the gel may develop with the increase of crosslinking concentration or even with aging, adsorption of solute may occur at the gel surface and the presence of solute may cause the gel to deswell. These effects may become so serious under certain conditions that the influence of gel density on the separation efficiency is totally screened.

Gel extraction process may have advantages in separating bioactive macromolecules while keeping the activity from losing considerably, for very mild and gentle separation condition can be arranged.

To fit conditions required in various applications, one can change the swelling degree, pore size, and swelling–collapsing transition temperature of the gel to a certain extent by varying the monomer concentration, crosslinker concentration, and the monomer composition.

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Received April 12, 1994
Accepted November 2, 1994