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Synthesis and phase behavior of aqueous poly(*N*-isopropylacrylamide-co-acrylamide), poly(*N*-isopropylacrylamide-co-*N*, *N*-dimethylacrylamide) and poly(*N*-isopropylacrylamide-co-2-hydroxyethyl methacrylate)

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Abstract Poly(*N*-isopropylacrylamide) (PNIPAM) and random copolymers of Poly(*N*-isopropylacrylamide-co-2-hydroxyethyl methacrylate) (PNIPAM-HEMA), poly(*N*-isopropylacrylamide-co-acrylamide) (PNIPAM-AAm), and poly(*N*-isopropylacrylamide-co-*N*, *N*-dimethylacrylamide) (PNIPAM-DMAA) with various volume fractions γ of NIPAM were synthesized by radical polymerization. The phase behavior of the polymers in water was

investigated by means of optical transmittance and dynamic light scattering. With decreasing γ , the cloud point temperature T_{cp} for PNIPAM-HEMA decreased whereas the T_{cp} for both PNIPAM-AAm and PNIPAM-DMAA increased. Increase of hydrodynamic radius around T_{cp} , which resulted from the aggregation of the globules of each polymer, was observed from dynamic light scattering. The relationships between the reciprocal of T_{cp} of the polymer solutions and $1-\gamma$ were linear for the three copolymers in the experimental range of $0.65 < \gamma < 1$. The results are discussed from the aspect of the interaction parameters of copolymer solutions.

Keywords *N*-isopropylacrylamide · Random copolymer · Coil to globule phase transition · Lower critical solution temperature · Hydrodynamic radius

Introduction

Poly(*N*-isopropylacrylamide) (PNIPAM) is a well-known polymer of which the aqueous solution undergoes phase separation on heating beyond 32°C induced by a reversible hydration–dehydration transition [1, 2]. Fujishige et al. [2] reported a change in conformation of individual PNIPAM chains from random coil to compact globule followed by an interchain aggregation due to the phase separation. The phase separation on heating is believed as a phase behavior with the lower critical solution temperature (LCST) [3], which is common to all polymer solutions, although it is still controversial [4]. This phase transition of PNIPAM

was used in attempts to control the enzymatic activity [5–9], affinity precipitation separation [10, 11], and protein recycling systems [12–15]. Another growing area in which this property has been exploited is a targeted delivery of drugs and chemical agents such as anticancer drugs. For the latter purpose, the polymer must be designed to be soluble when injected in vivo but insoluble to accumulate on a locally heated tumor tissue. These specific properties are achieved by using a polymer whose cloud point temperature T_{cp} in water is less than the temperature of a tumor tissue around 42°C under hyperthermia and higher than the physiological body temperature around 37°C [16]. Recently, some groups developed copolymerization of *N*-

isopropylacrylamide (NIPAM) and acrylamide (AAM) [16, 17] or *N,N*-dimethylacrylamide (DMAA) [16, 18–20] and these polymers in water showed higher T_{cp} than that of PNIPAM due to the hydrophilic nature of AAM and DMAA. It was also proved that the rhodamine-poly(*N*-isopropylacrylamide-co-acrylamide) (PNIPAM-AAm) was selectively accumulated in a solid tumor by targeted hyperthermia [17, 20]. Our idea for the drug release using this kind of copolymers is to develop nanospheres containing anticancer drugs with the copolymer chains on the surface. The surface of the nanospheres is hydrophilic at 37°C due to the hydrophilicity of the copolymer; it can recirculate in the blood stream for a long time and will not precipitate on the healthy tissues and cells but will selectively precipitate on the heated cancer tissues and cells because the copolymer becomes hydrophobic at higher temperatures; then the biodegradable nanospheres will gradually degrade and release the drug there to attack the tumor cells. The first step of this project is to find the exact relationship between the volume fraction of kinds of constituent monomers in the copolymer and T_{cp} and to understand the principle of the change of T_{cp} associated by the copolymerization. In this paper, we report the synthesis, characterization, and phase behavior of copolymers in aqueous solution with the incorporation of different comonomers, such as HEMA, AAM, and DMAA to NIPAM with a carboxylic group at the end, which will play the role of a stick on the nanospheres. The experimental results show that the phase separation occurs on raising temperature in response to a small temperature change near the cloud point (or LCST) and the reciprocal of the phase separation temperature is linearly dependent on the volume fraction of NIPAM in the copolymer. This behavior is analyzed by a simple theoretical consideration for designing the most appropriate copolymers for the targeted delivery.

Experiment

Preparation of samples

NIPAM was purchased from TCI (Tokyo, Japan) and purified by recrystallization from *n*-hexane. AAM was purchased from Sigma (USA). DMAA and 2,2'-azobis(isobutyronitrile) (AIBN) were supplied from TCI. HEMA and 3-mercaptopropionic acid (MPA) were purchased from Wako Pure Chemicals (Tokyo, Japan). NIPAM with or without comonomers (HEMA, AAM, or DMAA) were polymerized by free radical polymerization using AIBN and MPA as an initiator and a chain transfer reagent, respectively, to obtain PNIPAM, poly(*N*-isopropylacrylamide-co-2-hydroxyethyl methacrylate) (PNIPAM-HEMA), PNIPAM-AAm, and poly(*N*-isopropylacrylamide-co-*N,N*-dimethylacrylamide) (PNIPAM-DMAA). Molar fraction of NIPAM in the copolymer x was assumed to be the same as the molar fraction of NIPAM in the monomer mixtures.

x was chosen to be more than 0.85, 0.65, and 0.68 for PNIPAM-AAm, PNIPAM-HEMA, and PNIPAM-DMAA, respectively. Volume fraction γ of NIPAM in each copolymer was estimated from x and the densities of the pair of comonomers. Then 8.4 g of the (mixed) monomer, 0.05 g of AIBN, and 0.01 g of MPA were dissolved separately in 50 cm³ of ethanol (total volume). MPA was used for attaching a carboxylic group at the end of the copolymers. Polymerizations were carried out at 60°C for 16 h under nitrogen atmosphere. The resultant polymers designated as shown in Table 1 were separated and purified by reprecipitation into diethylether and then dried in vacuum. The polymers were dissolved in tetrahydrofuran (THF) for the characterization and in MilliQ water for optical transmittance (OT) and dynamic light scattering measurements.

Viscosimetry and size exclusion chromatography

Viscosity measurements for the copolymers in THF were made at 35°C using an Ubbelohde-type viscometer for samples of PNIPAM, PNIPAM-AAm-4, PNIPAM-AAm-5, and PNIPAM-AAm-6. The Huggins plot and Fuoss–Mead plot were combined to determine $[\eta]$ and the Huggins constant k' . Size exclusion chromatography (SEC) measurements were made on PNIPAM, PNIPAM-AAm-4, PNIPAM-AAm-5, and PNIPAM-AAm-6 in THF at 35°C using a Waters SEC equipment [Waters 515 HPLC Pump, Waters Styragel Columns (HT2 + HT3 + HT4), and Waters 2410 Differential Refractometer]. The flow rate and the

Table 1 Results of polymerization and LCST in water

Sample	x^a	γ^b	Yield (%) ^c	$T_{cp}/^{\circ}\text{C}$
PNIPAM	1.000	1.000	73	32.8
PNIPAM-AAm-1	0.978	0.989	86	34.4
PNIPAM-AAm-2	0.955	0.977	93	36.3
PNIPAM-AAm-3	0.934	0.966	89	38.0
PNIPAM-AAm-4	0.926	0.962	93	38.2
PNIPAM-AAm-5	0.919	0.958	88	39.0
PNIPAM-AAm-6	0.856	0.924	83	43.7
PNIPAM-HEMA-1	0.916	0.920	70	30.3
PNIPAM-HEMA-2	0.830	0.837	64	26.6
PNIPAM-HEMA-3	0.742	0.751	72	21.4
PNIPAM-HEMA-4	0.651	0.662	69	17.0
PNIPAM-DMAA-1	0.893	0.911	83	36.9
PNIPAM-DMAA-2	0.853	0.878	81	38.1
PNIPAM-DMAA-3	0.827	0.855	80	39.8
PNIPAM-DMAA-4	0.788	0.822	84	41.1
PNIPAM-DMAA-5	0.686	0.730	76	46.0

^aMolar fraction of NIPAM

^bVolume fraction of NIPAM

^cDiethylether insoluble fraction

temperature of the column oven were set to be $1 \text{ cm}^3 \text{ min}^{-1}$ and 35°C , respectively. Elution times were converted into molecular weights using a calibration curve constructed with narrow polydispersity polystyrene standards whose molecular weights range from 2,500 to 600,000.

Optical transmittance and dynamic light scattering

OT of aqueous polymer solutions whose polymer concentration c was $5.00 \times 10^{-3} \text{ g cm}^{-3}$ was measured from lower to higher temperatures at 500 nm of wavelength with an optical spectrophotometer (spectrum 721, SP-1105) at the heating rate of 0.1°C/min . A sample cell whose path length is 10 mm was used. The T_{cp} of the polymer solutions were determined as temperatures showing an OT of 50%. Dynamic light-scattering (DLS) measurements were carried out at the scattering angle of 30° for aqueous PNIPAM, PNIPAM-AAm-1, PNIPAM-AAm-2, ..., and PNIPAM-AAm-6 from lower to higher temperatures using a laboratory-made light scattering apparatus [21] with a BI-9000 AT correlator (Brookhaven). Vertically polarized incident light with a wavelength of 532 nm (a diode laser, BWT-50, and B&W) was used. Polymer concentration was set to be $5.00 \times 10^{-3} \text{ g cm}^{-3}$ and the solutions were optically cleaned through a $0.45\text{-}\mu\text{m}$ membrane filter just before measurements. The solutions were equilibrated at given temperatures for 10 min before each measurement and then were heated to the next temperature for the next measurement. A filter lens was added to weaken the incident light when the scattering light became too strong near the cloud point. The DLS measurements were not made in the temperature range where the solutions were turbid because of phase separation. Hydrodynamic radius R_h was estimated from the obtained diffusion coefficient by using the Stokes–Einstein equation.

Results

Polymerization results

Table 1 summarizes the results of the polymerization. The yield determined as diethylether insoluble fraction for each polymer sample was between 64 and 93%. The GPC chart for PNIPAM and three PNIPAM-AAm polymer samples are shown in Fig. 1. A peak for PNIPAM at 20 cm^3 is appreciably larger than those for copolymers. Because small shoulders detected around 27 cm^3 correspond to solvent and/or some impurities with low molecular weight, the peak and distribution from polymer species cannot be obtained exactly as shown in Fig. 1. Therefore, we summarized only the molecular weight M_p corresponding to the peak on each gel permeation chromatography (GPC) chart in Table 2 and did not make the universal calibration using the viscosity data.

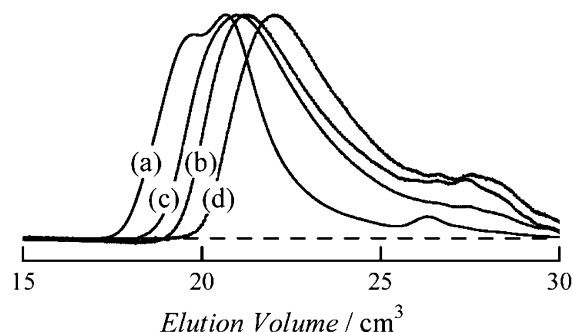


Fig. 1 GPC traces of PNIPAM (a), PNIPAM-AAm-4 (b), PNIPAM-AAm-5 (c), and PNIPAM-AAm-6 (d) in THF at 35°C

Phase behavior

OT determined for PNIPAM-AAm is shown as a function of temperature in Fig. 2a. The OT of aqueous PNIPAM is almost unity at temperatures below 32°C . It decreases rapidly with rising temperature between 32.7 and 33.1°C and vanishes at higher temperatures. For PNIPAM-AAm samples, the transition temperature increases with decreasing γ . Results for PNIPAM-HEMA and PNIPAM-DMAA are illustrated in Fig. 2b,c. The temperature dependence of OT for these three copolymers becomes gentler as γ decreases. The sharpness of the transition was estimated from the temperature distance ΔT between 5% transmittance and 95% transmittance: ΔT was 0.4 K for PNIPAM, 0.6, 0.6, 0.7, 0.9, 1.0, and 1.3 K for PNIPAM-AAm-1 to 6, 1.0, 1.7, 1.0, 2.2, and 3.9 K for PNIPAM-DMAA-1 to 5, and 0.6, 2.4, 2.3, and 3.7 K for PNIPAM-HEMA-1 to 4.

The T_{cp} is the temperature at which the solution becomes turbid due to the formation of polymer-rich emulsion droplets [22]. T_{cp} of PNIPAM aqueous solution is roughly independent of molecular weight and concentration of PNIPAM [2]. Therefore, it is plausible to assume that T_{cp} is independent of the molecular weight in the range that the value of γ of the copolymers is sufficiently small. In this paper, T_{cp} was determined when the OT of the solutions crosses 50% as the temperature increases. The observed T_{cp} are summarized at the fifth column of Table 1 and Fig. 3. The T_{cp} of PNIPAM was 32.8°C , which was slightly higher than the reported value of 32°C [2]. This is considered to result from hydration contributions from polar terminal

Table 2 Results from GPC and viscosimetry in THF at 35°C

Sample	$M_p/10^4$	$[\eta]/\text{cm}^3 \text{ g}^{-1}$	k'
PNIPAM	1.97	15.6	0.54
PNIPAM-AAm-4	1.56	12.4	0.76
PNIPAM-AAm-5	1.69	12.6	0.80
PNIPAM-AAm-6	0.97	9.5	1.40

M_p is determined by GPC with conventional calibration while $[\eta]$ is determined by Ubbelohde viscometer

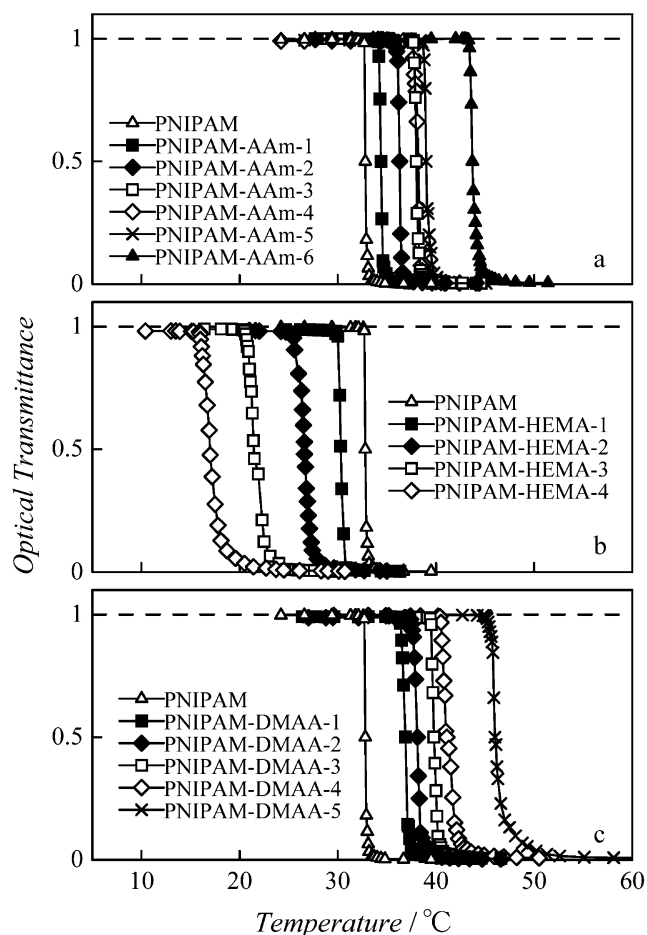


Fig. 2 Temperature dependence of OT of indicated copolymers in water ($c=5.00 \times 10^{-3} \text{ g cm}^{-3}$) for PNIPAM-AAm (a), PNIPAM-HEMA (b), and PNIPAM-DMAA (c)

carboxyl groups in the polymer. The temperature dependence of the hydrodynamic radius R_h of PNIPAM-AAm is shown in Fig. 4 where the dashed lines indicate the T_{cp} given in Table 1. At lower temperatures, R_h is almost

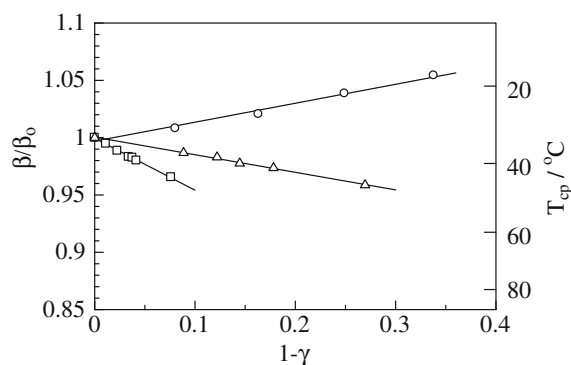


Fig. 3 T_{cp} and the reduced one β/β_0 as a function of $1-\gamma$ of PNIPAM for PNIPAM-AAm (squares), PNIPAM-HEMA (circles), and PNIPAM-DMAA (triangles) in water

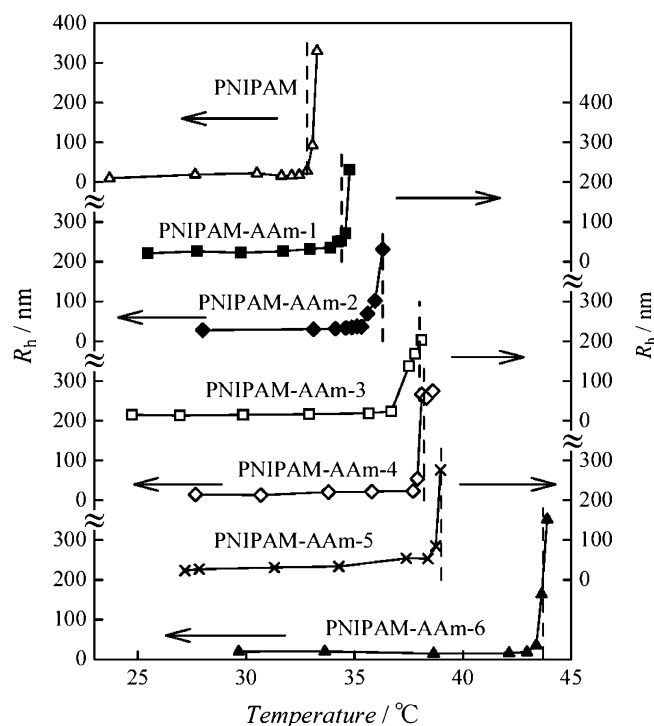


Fig. 4 Temperature dependence of R_h of indicated copolymers in water ($c=5.00 \times 10^{-3} \text{ g cm}^{-3}$). Dashed lines indicate T_{cp} for each sample

independent of temperature. It increases rapidly near the T_{cp} with increasing temperature due to the aggregation of the polymers in the solutions. The behavior of the sharpness of the transition observed in R_h for different γ is similar to that observed in OT as shown in Figs. 2 and 4. The coil-globule transition of polymer chains was not observed in Fig. 4 because the decrease in R_h due to the conformation change is much smaller than the increase in R_h due to the chain aggregation.

Discussion

Condition for preparing copolymers

The copolymers coherent to the current strategy need to change from hydrophilic type to hydrophobic type around 40°C and the change must be very sensitive to temperature change. Because the transition temperature would coincide with the T_{cp} , these conditions can be satisfied for both PNIPAM-AAm and PNIPAM-DMAA as shown in Figs. 2, 3 and 4. From the experimental results for the copolymers of PNIPAM-AAm, T_{cp} determined by the OT is almost the same as the temperature where the aggregation of the copolymers occurs probably due to the conformational change from coil state to globule state. This is the same behavior as that observed for the PNIPAM homopolymer [2]. Here we emphasize that the aggregation happens just

when the temperature reaches the hydrophilic-hydrophobic transition temperature, which is one of the most important factors for the current drug delivery scheme. The optimum γ for this scheme can be obtained from Fig. 3.

Theoretical consideration of composition dependence of interaction parameter of random copolymer

It is desired to develop a methodology to find appropriate pairs of comonomers. Because the coil-globule transition

and chain aggregation are caused by the interaction between segments, we start from the interaction parameter χ of a solution composed of a solvent and a two-species copolymer. The species 1 segment of the copolymer corresponds to NIPAM and the species 2 segment corresponds to AAm, HEMA, or DMAA. We introduce volume fractions of species 2 in total copolymer $\tilde{\gamma}$ ($= 1 - \gamma$). The coordination number of the lattice model used here is taken to be z . By following the conventional method, we express

$$\chi = \frac{1}{2}\beta \left[\varepsilon_{00} - 2\varepsilon_{10}(1 - \tilde{\gamma}) - 2\varepsilon_{20}\tilde{\gamma} + \varepsilon_{11}(1 - \tilde{\gamma})^2 + 2\varepsilon_{12}\tilde{\gamma}(1 - \tilde{\gamma}) + \varepsilon_{22}\tilde{\gamma}^2 \right] \quad (1)$$

where $-\varepsilon_{00}/z$, $-\varepsilon_{10}/z$, $-\varepsilon_{20}/z$, $-\varepsilon_{11}/z$, $-\varepsilon_{12}/z$, and $-\varepsilon_{22}/z$ are the interaction energies of the nearest neighboring pairs of solvent-solvent, solvent-species 1 segment of the copolymer, solvent-species 2, species 1-species 1, species 1-species 2, and species 2-species 2, respectively, and β is the “inverse temperature” given by $\beta=1/(k_B T)$.

Approximating $\varepsilon_{11} \cong \varepsilon_{12} \cong \varepsilon_{22} \cong \varepsilon_{pp}$, Eq. 1 is reduced as

$$\begin{aligned} \chi &\cong \frac{1}{2}\beta [\varepsilon_{00} + \varepsilon_{pp} - 2\varepsilon_{10}(1 - \tilde{\gamma}) - 2\varepsilon_{20}\tilde{\gamma}] \\ &= \beta \left[\frac{\varepsilon_{00} + \varepsilon_{pp}}{2} - \varepsilon_{10}(1 - \tilde{\gamma}) - \varepsilon_{20}\tilde{\gamma} \right] \end{aligned} \quad (2)$$

The weak interactions derived from such hydrophobic bondings contribute to the energy ε_{i0} ($i=1,2$) which depends on temperature strongly. Near the room temperature such interaction energies decrease with increasing temperature [23]. The expansion of ε_{i0} as a function of β around $\beta=\beta_*=1/(k_B T_*)$ where T_* is the room temperature results in

$$\varepsilon_{i0} = \varepsilon_{i0}(\beta) \cong \varepsilon_{i0}(\beta_*) + \varepsilon'_{i0}(\beta_*)(\beta - \beta_*) \equiv u_i + k_i\beta \quad (3)$$

where

$$k_i \equiv \varepsilon'_{i0}(\beta_*) > 0 \quad (4)$$

and

$$u_i \equiv \varepsilon_{i0}(\beta_*) - \varepsilon'_{i0}(\beta_*)\beta_* \quad (5)$$

Then Eq. 2 is reduced as

$$\begin{aligned} \chi &= \beta \left[\frac{\varepsilon_{00} + \varepsilon_{pp}}{2} - (u_1 + k_1\beta)(1 - \tilde{\gamma}) - (u_2 + k_2\beta)\tilde{\gamma} \right] \\ &\equiv \beta B_0(\tilde{\gamma}) - \beta^2 B_1(\tilde{\gamma}) \end{aligned} \quad (6)$$

where

$$B_0(\tilde{\gamma}) = \frac{\varepsilon_{00} + \varepsilon_{pp}}{2} - u_1(1 - \tilde{\gamma}) - u_2\tilde{\gamma} \quad (7)$$

and

$$B_1(\tilde{\gamma}) = k_1(1 - \tilde{\gamma}) + k_2\tilde{\gamma} \quad (8)$$

The T_{cp} could be located just above the coil-globule transition point because the chain aggregation is followed by the collapse of individual polymer chains [2]. The coil to globule transition occurs as temperature passes through the theta temperature where $1-2\chi=0$ [24]. Actually the coil-globule transition becomes broader as the degree of polymerization decreases [25]; however, the theta-temperature could be some measure of the transition point even though the molecular weight is rather small as in the present case. From the relation $1-2\chi=0$, we have

$$1 - 2\beta B_0 + 2\beta^2 B_1 = 0 \quad (9)$$

The solution of the above equation with respect to β is obtained as

$$\beta = \frac{B_0 \pm \sqrt{B_0^2 - 2B_1}}{2B_1} \quad (10)$$

For the coil to globule transition, we have the transition inverse temperature:

$$\beta_c = \frac{B_0 + \sqrt{B_0^2 - 2B_1}}{2B_1} \quad (11)$$

Equations 7 and 8 are rewritten as

$$B_0(\tilde{\gamma}) = B_0(0) + (u_1 - u_2)\tilde{\gamma} \quad (12)$$

and

$$B_1(\tilde{\gamma}) = k_1 + (k_2 - k_1)\tilde{\gamma} \quad (13)$$

The composition dependencies ($\tilde{\gamma}$ dependencies) of $B_0(\tilde{\gamma})$ and $B_1(\tilde{\gamma})$ lead to those of the transition inverse temperature β_c . When the differences of thermodynamic properties between species 1 and 2 are small, the differences $u_1 - u_2$ and $k_1 - k_2$ are also small. Then, the zeroth and the first order terms in the power expansion of β_c with respect to $\tilde{\gamma}$ are dominant; we have a linear composition dependence of

$$\beta_c \cong \beta_0 + \beta_1 \tilde{\gamma} = \beta_0 + \beta_1(1 - \gamma) \quad (14)$$

with

$$\beta_0 = \frac{B_0(0) + \sqrt{B_0^2(0) - 2k_1}}{2k_1} \quad (15)$$

and

$$\begin{aligned} \beta_1 &= \frac{\beta_0(u_1 - u_2) - \beta_0^2(k_2 - k_1)}{2\beta_0 k_1 - B_0(0)} \\ &= \beta_0 \frac{(u_1 - u_2) - \beta_0(k_2 - k_1)}{\left|k_1\beta_0 - \frac{1}{2\beta_0}\right|} \\ &\cong \beta_0 \frac{\varepsilon_{10}(\beta_0) - \varepsilon_{20}(\beta_0)}{\left|k_1\beta_0 - \frac{1}{2\beta_0}\right|} \end{aligned} \quad (16)$$

Note that β_0 is the transition inverse temperature for the polymer composed of only the species 1 segments.

Equation 16 indicates that the coefficient β_1/β_0 (or T_0/T_1) is proportional to the interaction energy difference between the solvent-species 1 and the solvent-species 2. Figure 3 illustrates linear dependences of β_1/β_0 (or T_0/T_1) against $\tilde{\gamma}(=1 - \gamma)$ with the slope being -0.4525 , 0.1654 , and -0.1534 for PNIPAM-AAm, PNIPAM-HEMA, and

PNIPAM-DMAA, respectively. Eq. 16 is rewritten by using interaction parameters χ_1 and χ_2 defined as

$$\begin{aligned} \chi_1(\beta) &= \beta \left(\frac{\varepsilon_{00} + \varepsilon_{11}}{2} - \varepsilon_{10}(\beta) \right) \\ \chi_2(\beta) &= \beta \left(\frac{\varepsilon_{00} + \varepsilon_{22}}{2} - \varepsilon_{20}(\beta) \right), \end{aligned}$$

which are those of homopolymers of the species 1 segments and species 2 segments, respectively. Using the approximation $\varepsilon_{11} \cong \varepsilon_{22} \cong \varepsilon_{pp}$ and the relation $\chi_1(\beta_0) = 1/2$, we obtain

$$\begin{aligned} \varepsilon_{10}(\beta_0) - \varepsilon_{20}(\beta_0) &= -\frac{\chi_1(\beta_0) - \chi_2(\beta_0)}{\beta_0} \\ &= \frac{1}{\beta_0} \left(\frac{1}{2} - \chi_2(\beta_0) \right). \end{aligned}$$

Substituting this relation into Eq. 16, the expression for β_1 is obtained as

$$\beta_1 = -\frac{\beta_0}{|1 - 2k_1\beta_0^2|} (1 - 2\chi_2(\beta_0)). \quad (17)$$

Equation 17 shows that the coefficient β_1/β_0 is proportional to $1 - 2\chi_2$, which is a parameter proportional to the second virial coefficient for a solution of the homopolymer of the species 2 segments. By choosing comonomers with appropriate value of $\chi_2(\beta_0)$, we can obtain desired copolymers for our purpose. Because the prefactor $-\beta_0/|1 - 2k_1\beta_0^2|$ is always negative, the sign of the coefficient β_1/β_0 is opposite to that of $1 - 2\chi_2$. Hence, to raise (or to lower) the theta or transition temperature, we choose the comonomer whose polymeric chain in water is in the random coil state (or in the globule state).

Conclusion

In this paper, we studied the thermosensitive behavior of copolymers with the incorporation of different comonomers HEMA, AAm, and DMAA to NIPAM with various volume fraction γ of NIPAM in the copolymers prepared by radical polymerization. The reciprocals of the T_{cp} of the aqueous solution of PNIPAM-HEMA decreased and those of PNIPAM-AAm and PNIPAM-DMAA increased linearly against $1 - \gamma$ where the slope was related to the interaction energy difference between the solvent-species 1 and the solvent-species 2. The temperature sensitivity of the conformation change at the transition temperature was

fairly well for the latter two kinds of copolymers. From these results, it is expected that PNIPAM-AAm and PNIPAM-DMAA can be used for anticancer drug carriers to target the cancer cells.

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