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Synthesis and thermally responsive characteristics of dendritic poly(ether-amide) grafting with PNIPAAm and PEG

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Abstract

A series of thermally responsive dendritic core–shell polymers were prepared based upon dendritic poly(ether-amide) (DPEA), modified with carboxyl end-capped linear poly(*N*-isopropylacrylamide) (PNIPAAm-COOH) or both PNIPAAm-COOH and carboxyl end-capped methoxy polyethylene glycol (PEG-COOH) in different ratios via an esterification process to obtain DPEA–PNIPAAm or DPEA–PNIPAAm–PEG. Their molecular structures were verified by gel permeation chromatography, and ^{1}H NMR and FTIR spectroscopy. The temperature-dependent characteristics study has revealed that DPEA–PNIPAAm exhibits a lower critical solution temperature (LCST) of about 34 °C, whereas DPEA–PNIPAAm–PEG polymers with the PNIPAAm/PEG ratio of about 1.0 and 0.4 possess about 36 °C and 39 °C, respectively, compared with 32 °C for homopolymer PNIPAAm. The critical aggregation temperature was investigated using fluorescence excitation spectrum of pyrene as a sequestered guest molecule based upon the sharp increase of the I_{338}/I_{333} value.

Keywords: Poly(*N*-isopropylacrylamide); Temperature-sensitive; Dendritic poly(ether-amide)

1. Introduction

Dendrimers are highly branched monodisperse macromolecules with a large number of ''tunable'' surface groups and an interior [1]. Their globular shape structure and thus unique properties are allowed to be useful in many fields, including drug delivery, catalysis, gene therapy, light-harvesting antennae, chemical sensors, etc. [2–6]. Furthermore, the incorporation of stimuli-sensitive character into dendrimers can significantly expand the scope of these molecules in application [7,8]. The temperature sensitivity is one of the most interesting properties in stimuli-responsive polymers, and has been intensively investigated [9,10]. Temperature-sensitive polymers exhibit a lower critical solution temperature (LCST) in their aqueous solutions, below which the polymers are water soluble, and above which they become water insoluble. These polymers are mostly block copolymers generally composed of temperature-sensitive hydrophilic segments and suitable hydrophobic segments [11]. Up to date, poly(*N*-isopropylacrylamide) (PNIPAAm) and its copolymers have been some of the most extensively studied temperature-sensitive hydrophilic segments, and found several applications, such as separation, controlled release, and enzyme-activity control, etc. [12–14]. However, it has been difficult to graft PNIPAAm chains to the surface of a dendrimer. To obtain a temperature-sensitive dendritic polymer, You and co-workers have reported an approach to graft PNIPAAm chains to the surface of hydroxyl end-capped dendritic polyester by using a reversible addition–fragmentation chain transfer (RAFT) method [10]. A higher generation of dendritic polyester has also been used to graft PNIPAAm chains by the similar method [15]. Nevertheless, this method could not be used to graft both temperature-sensitive PNIPAAm and another hydrophilic chain to a dendrimer surface. It is noteworthy that hydrophilic modification would result in higher LCST of a PNIPAAm copolymer [16,17].

In this study, we synthesized temperature-sensitive dendritic poly(ether-amide)s (DPEAs) grafting both linear PNIPAAm

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and polyethylene glycol (PEG) chains (DPEA–PNIPAAm–PEG), and only PNIPAAm for comparison while the total amounts of grafted chains were kept constant, based upon hydroxyl end-capped DPEA-OH. The temperature-dependent characteristics by LCST and critical aggregation temperatures using fluorescence measurement were investigated.

2. Experimental

2.1. Materials

Dendritic poly(ether-amide) (DPEA-OH) with 12 hydroxyl end-capped groups was synthesized by a three-step procedure with a divergent route starting from pentaerythritol according to the previous work performed in our lab [18]. *N*-Isopropylacrylamide (NIPAAm, Fluka) was recrystallized from a mixture of toluene and *n*-hexane. Methoxy polyethylene glycol (PEG) with a molecular weight of 2000 g/mol (PEG 2000) was purchased from Aldrich, and first purified by precipitation into hexane from tetrahydrofuran (THF), then vacuum-dried to remove hexane. The obtained precipitates were further dried by azeotropic distillation with toluene. Pyrene was obtained from Aldrich and recrystallized from ethanol before use. THF, dimethyl sulfoxide (DMSO), 2-hydroxyethanethiol (HESH), benzoyl peroxide (BPO), and succinic anhydride were purchased from Shanghai First Reagent Co., China, purified before use according to the standard procedures. Diethyl ether, acetone, N, N′-dicyclohexyl carbodiimide (DCC), and 4-dimethylaminopyridine (DMAP) were of analytical grade and purchased from Shanghai First Reagent Co., China, and used as received.

2.2. Synthesis

2.2.1. PNIPAAm-COOH and PEG-COOH

The NIPAAm polymer with a terminal hydroxyl end group (PNIPAAm-OH) was prepared by radical telomerization of NIPAAm monomer using HESH as a chain transfer agent. NIPAAm (15.3 g, 135 mmol), HESH (0.422 g, 5.4 mmol), and BPO (0.055 g, 0.227 mmol) were dissolved in 50 ml of THF, degassed by freeze–thaw cycle and then sealed in vacuum. The polymerization was carried out at 70 °C for 15 h. After removal of a majority of THF by distillation under vacuum, the reactant was precipitated three times in diethyl ether from acetone, and then dried in vacuum. The obtained polymer was named PNIPAAm-OH.

PNIPAAm-OH (5 g, about 2 mmol), succinic anhydride (0.6 g, 6 mmol), and DMAP (0.01 g) were dissolved in 100 ml of CH_2Cl_2. The polymerization was carried out at 25 °C for 48 h. After evaporated a majority of CH_2Cl_2, the reactant was precipitated for three times in diethyl ether from THF, and then dried in vacuum. The obtained polymer was named PNIPAAm-COOH.

The carboxyl end-capped PEG (PEG-COOH) was prepared by the similar process.

2.2.2. DPEA–PNIPAAm

DPEA–PNIPAAm was prepared via an esterifying process. DPEA-OH (0.1 g, about 1.44 mmol hydroxyl groups) was dissolved in 50 ml of DMSO. Then PNIPAAm-COOH (5.62 g, about 2.16 mmol) and a stoichiometric amount of DMAP and DCC (dissolved in 50 ml of CH_2Cl_2) were added to the above DMSO solution, and stirred for 48 h at 25 °C. After removal of a majority of solvent by distillation under vacuum, the product was dried in vacuum, and further purified to remove the unreacted substance and DCC by ultrafiltration using a filtration membrane with 8000 molecular weight cut-off (Shanghai Sangon Co., China).

2.2.3. DPEA–PNIPAAm–PEGs

DPEA–PNIPAAm–PEG-A with lower PEG substitution degree was prepared by using a similar process with DPEA–PNIPAAm. DPEA-OH (0.1 g, about 1.44 mmol hydroxyl groups) was first dissolved in 50 ml of DMSO. PNIPAAm-COOH (1.88 g, about 0.72 mmol) and a stoichiometric amount of DMAP and DCC (dissolved in 50 ml of CH_2Cl_2) were added to the above DMSO solution, and stirred for 48 h at 25 °C. Then PEG-COOH (1.52 g, 0.72 mmol) and a stoichiometric amount of DMAP and DCC (dissolved in 20 ml of CH_2Cl_2) were added to the above DPEA–PNIPAAm solution and stirred for another 48 h at 25 °C. After removal of a majority of solvent, the product was dried under vacuum, and further purified to remove the unreacted substance and DCC by ultrafiltration using a filtration membrane with 8000 molecular weight cut-off (Shanghai Sangon Co., China).

DPEA–PNIPAAm–PEG-B with higher PEG substitution degree was also prepared by using the same process except that varying the amounts of PNIPAAm-COOH and PEG-COOH. 0.1 g (about 1.44 mmol hydroxyl groups) DPEA-OH reacted with 1.25 g (about 0.48 mmol) PNIPAAm-COOH and 2.02 g (0.96 mmol) PEG-COOH successively.

2.3. Measurements

The ^{1}H NMR spectra were recorded with a Bruker Avance 300 spectrometer (300 MHz) using chloroform-d_1 as a solvent. The chemical shifts were expressed in parts per million using residual protons in the indicated solvent as an internal standard. The IR spectra were recorded on a Fourier transform infrared spectrometer (Perkin–Elmer Spectrum 2000, KBr). The average molecular weight was determined by gel permeation chromatography (GPC, Waters, polystyrene standards) in THF (elution rate: 1 ml/min) at 25 °C.

The optical transmittance spectra of polymer aqueous solutions (1 mg/ml, 0.1 wt%) at various temperatures were measured at 500 nm with a UV–vis spectrometer (Shimadzu UV-240 Apparatus, Shimadzu Co., Japan). The cell-holder temperature was controlled with a thermo-stated circulating bath. The LCSTs of polymer solutions were determined as the temperatures showing the onsets of turbidity.

Fluorescence spectra were recorded on a SPEX Fluorolog 3 spectrometer. The cell-holder temperature was controlled with a thermo-stated circulating bath. Pyrene was used as

a hydrophobic fluorescent probe. For preparing the final concentration of pyrene of 6.0×10^{-7} mol/l, pyrene (1.2×10^{-5} g) in 10 ml of acetone was added to a flask and left to stand at room temperature to allow acetone for evaporation, followed by the addition of 100 ml of the obtained polymer aqueous solution. The emission spectrum was recorded using an excitation wavelength of 335 nm, while the excitation spectrum was recorded using an emission wavelength of 390 nm, with the emission and excitation bandwidths of 5 nm. I_1 and I_3 are the fluorescence intensities of pyrene spectra at 373 and 384 nm, respectively. The ratio of I_1 to I_3 reflects the polarity of microenvironment that pyrene is sensing [19,20].

From the excitation spectrum of pyrene, the intensity (peak height) ratio of I_{338}/I_{333} was analyzed as a function of temperature. The critical aggregation temperature was determined as the temperature showing the onset of an increase in the ratio (I_{338}/I_{333}) [21].

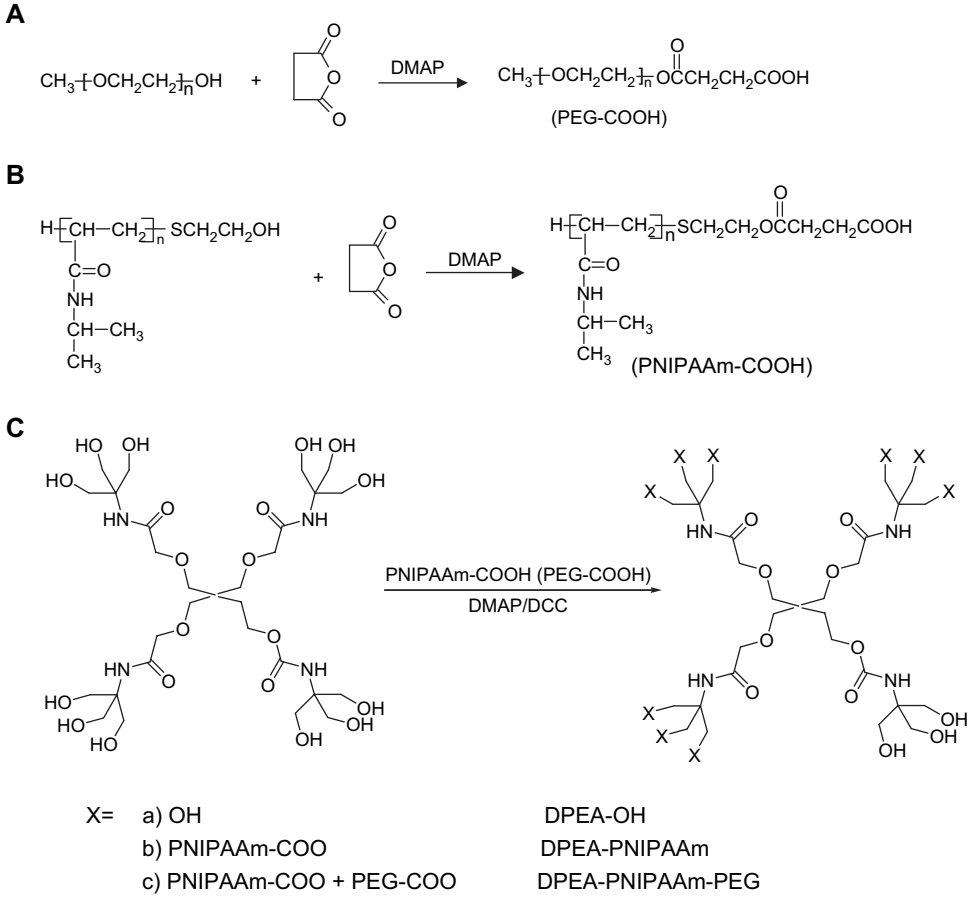
3. Results and discussion

3.1. Characterization

Thiol compounds are well known to participate actively in the telomerization of vinyl monomers [22]. NIPAAm is considered to be easily telomerized with thiol compounds [23,24]. Therefore, hydroxyl end group was thereby introduced to one terminal end of the formed PNIPAAm during telomerization with hydroxyethanethiol as a chain transfer agent. By adjusting the amount of hydroxyethanethiol, PNIPAAm-OH was obtained with a number average molecular weight of about 2500 g/mol.

PNIPAAm-COOH and PEG-COOH were then prepared by the reactions of PNIPAAm-OH and PEG-OH with succinic anhydride, as shown in Scheme 1, respectively. Their molecular structures were confirmed by the ^{1}H NMR spectra, as shown in Fig. 1.

DPEA–PNIPAAm was prepared by an esterification process of DPEA-OH with PNIPAAm-COOH. An excess amount of PNIPAAm-COOH was used for increasing the esterification degree. The unreacted reactants were removed by ultrafiltration using a filtration membrane. From the ^{1}H NMR spectrum of obtained DPEA–PNIPAAm, as shown in Fig. 2, the signals attributed to PNIPAAm moiety at the shell (l for $CH_2CHCONHCH\mathit{Me}_2$, j for $CH_2C\mathit{H}CONHCHMe_2$, i for $C\mathit{H}_2CHCONHCHMe_2$, k for $CH_2CHCONHC\mathit{H}Me_2$) and the signals attributed to DPEA-OH moiety as a core (a for $CC\mathit{H}_2OCH_2CH_2CONHC(CH_2O-)_3$, b for $CCH_2OC\mathit{H}_2CH_2$-$CONHC(CH_2O-)_3$, d for $CCH_2OCH_2CH_2CONHC(C\mathit{H}_2O-)_3$, respectively) are observed. The signal c for $CCH_2OCH_2C\mathit{H}_2$-$CONHC(CH_2O-)_3$ was covered with PNIPAAm moiety. The signal d′ is attributed to unreacted $CCH_2OCH_2CH_2CONHC$-$(C\mathit{H}_2O-)_3$. From the integration ratio of signal l to signal



Scheme 1. Synthesis schemes for PEG-COOH (A), PNIPAAm-COOH (B), and DPEA–PNIPAAm and DPEA–PNIPAAm–PEGs (C).

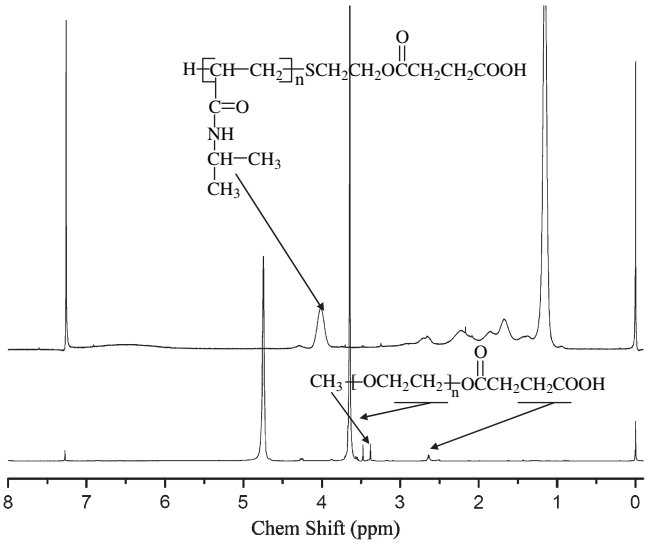


Fig. 1. ^{1}H NMR spectra of (a) PNIPAAm-COOH and (b) PEG-COOH.

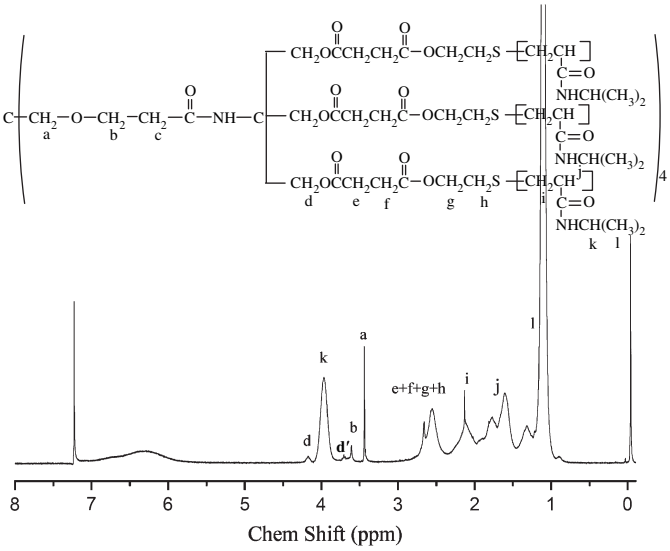


Fig. 2. ^{1}H NMR spectrum of DPEA–PNIPAAm.

b in Fig. 2, an average of eight PNIPAAm arms are conjugated to each dendrimer molecule. This implies that approximately 67% terminals were covered by PNIPAAm arms. Consequently, the number average molecular weight of DPEA–PNIPAAm was estimated to be about 21, 500 g/mol from the ^{1}H NMR spectrum.

PNIPAAm is a well-known thermo-sensitive polymer showing the reversible hydration–dehydration change in response to a small temperature change. The LCST of an amphiphilic polymer resulting from hydrophilic PNIPAAm and its copolymer depends on both the copolymer's composition and its molecular weight. Due to a given molecular weight of the polymer desired for the purpose of controlled release, the LCST of an amphiphilic polymer is usually adjusted by the composition of hydrophilic segment [11]. In the present study, PEG was employed as a hydrophilic segment to adjust the LCST of the polymer. It is noteworthy that PEG chain had a LCST (>70 °C) much higher than the transition temperature (32–40 °C), and thus is insensitive to changes in temperature. Therefore, PEG chain did not contribute to the enhanced hydrophobicity of the copolymer to an appreciable extent in the range of temperature investigated [16].

Grafting both PNIPAAm and PEG at higher PEG substitution degree to the surface of DPEA is shown in Scheme 1. The ^{1}H NMR spectrum for DPEA–PNIPAAm–PEG-B, as shown in Fig. 3, is similar to that for DPEA–PNIPAAm, except for the signals at 3.64 ppm ($-CH_2CH_2O-$) and 3.38 ppm (CH_3O-) for PEG moiety. As the signals attributed to DPEA-OH moiety were covered with the signals of ($-CH_2CH_2O-$) for PEG moiety, the ^{1}H NMR spectrum of intermediate semi-DPEA–PNIPAAm was used to calculate the average of PNIPAAm arms conjugated to each dendrimer molecule. For DPEA–PNIPAAm–PEG-B, the intermediate semi-DPEA–PNIPAAm was conjugated with the average of 2.3 PNIPAAm arms. Then, from the integration ratio of the signals for PNIPAAm moiety to the signals for PEG moiety, the PNIPAAm/PEG chain ratio was calculated to be 0.4, and thus the number average molecular weight of DPEA–PNIPAAm–PEG-B was estimated to be 18,867 g/mol. For DPEA–PNIPAAm–PEG-A, the PNIPAAm/PEG chain ratio and the number average molecular weight were calculated with the same method as for DPEA–PNIPAAm–PEG-B to be 1.0 and 19,612 g/mol, respectively. The FTIR spectra of three polymers show the similar absorption (Fig. 4). The peaks at 3305–3437 cm^{-1} (N–H, O–H), 1628–1650 cm^{-1} (C=O), 1540–1545 cm^{-1} (C–N) are observed distinctly.

The GPC spectra for DPEA–PNIPAAm and DPEA–PNIPAAm–PEGs are shown in Fig. 5 with acceptable polydispersities. The data are given in Table 1.

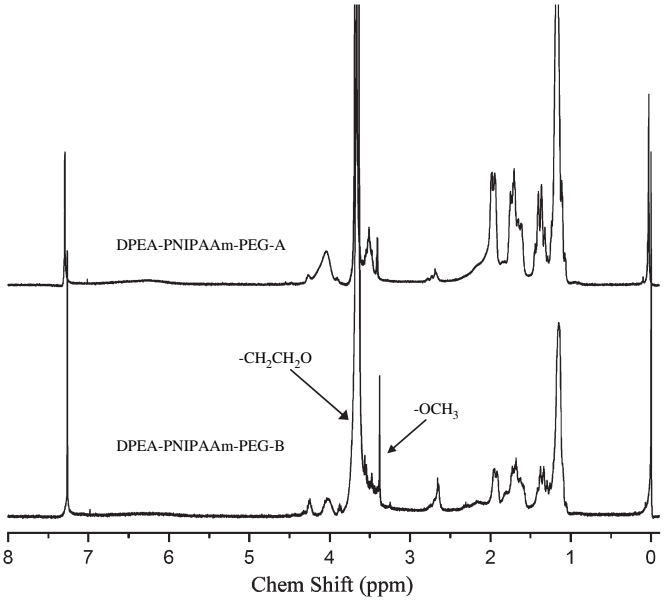


Fig. 3. ^{1}H NMR spectra of DPEA–PNIPAAm–PEGs.

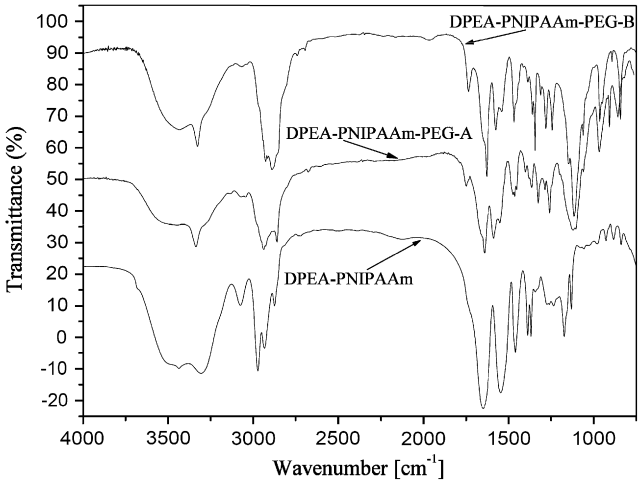


Fig. 4. FTIR spectra of DPEA–PNIPAAm and DPEA–PNIPAAm–PEGs.

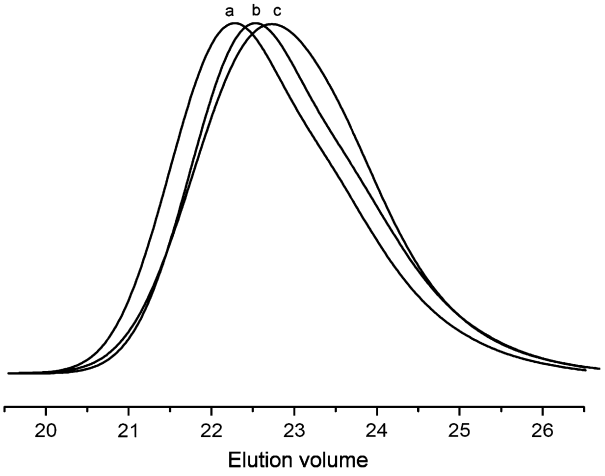


Fig. 5. GPC charts of (a) DPEA–PNIPAAm, (b) DPEA–PNIPAAm–PEG-A and (c) DPEA–PNIPAAm–PEG-B.

Table 1
GPC results of DPEA–PNIPAAm and DPEA–PNIPAAm–PEGs

Polymer	M_n[a]	M_w[b]	M_w/M_n[c]
DPEA–PNIPAAm	23,051	33,592	1.46
DPEA–PNIPAAm–PEG-A	21,225	29,078	1.37
DPEA–PNIPAAm–PEG-B	18,867	24,452	1.31

[a] Number-averaged molecular weight.
[b] Weight-averaged molecular weight.
[c] Polydispersity.

3.2. Effect of PEG on LCST

To construct covalently fixed stable amphiphilic core–shell nanoparticles, cross-linked block copolymer consisting of hydrophilic chains as a shell and hydrophobic chains as a core was usually used [25,26]. Star-shaped block copolymer can also form stable core–shell nanoparticles [27,28]. The synthesized DPEA–PNIPAAm contains PNIPAAm chains as its hydrophilic shell and dendritic poly(ether-amide) as its hydrophobic core, and thus possesses temperature-sensitive character. Fig. 6 shows the LCST curves of DPEA–PNIPAAm and

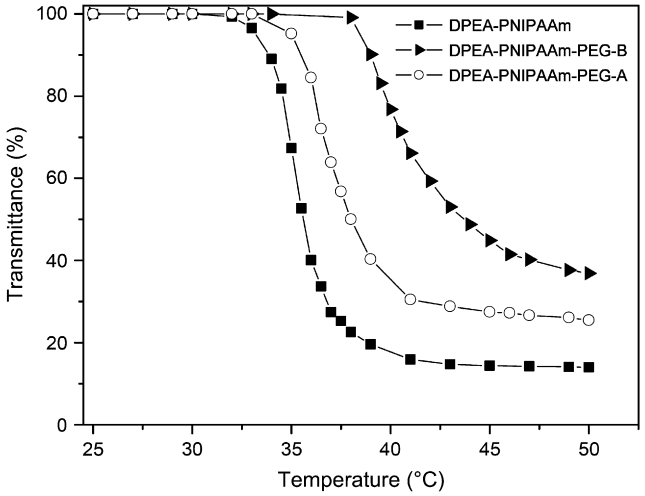


Fig. 6. Transmittance changes of aqueous solutions of DPEA–PNIPAAm and DPEA–PNIPAAm–PEGs as a function of temperature.

DPEA–PNIPAAm–PEGs. The LCST of DPEA–PNIPAAm is estimated to be 34 °C, which is higher than that of traditional linear PNIPAAm or its copolymers (32 °C). This is suggested to be due to the dendritic core, which having a few –CONH– groups possessing hydrophilic property [29], and also perhaps a few unreacted hydroxyl end groups of dendritic poly(ether-amide) [23]. Consequently, the LCST of DPEA–PNIPAAm–PEG-A was estimated to be 36 °C, even higher than that of DPEA–PNIPAAm. For DPEA–PNIPAAm–PEG-B, as PEG content increased, a higher LCST of 39 °C was obtained.

As well known, the conformation and solubility of PNIPAAm chain in water can be changed with temperature. Fig. 7 shows the schematic diagram of proposed mechanism for forming a dendritic core–shell nanostructure with a temperature-sensitive and water-soluble shell. PNIPAAm chains collapse at the temperature higher than the LCST, 34 °C for DPEA–PNIPAAm. This can be interpreted that, at the temperatures below the LCST, the strong hydrogen bonding between the hydrophilic groups –CONH– groups of PNIPAAm chains and water exceeds the hydrophobic interaction between hydrophobic side groups ($-CH(CH_3)_2$) and water, resulting in good solubility of the polymer in water [10,29]. As the temperatures increase, the hydrogen bonding weakens, while the hydrophobic interaction increases. At the temperature above the LCST, the interaction between hydrophobic groups becomes dominant, leading to the PNIPAAm chains collapse [29,30]. However, for DPEA–PNIPAAm–PEG-A, due to the incorporation of hydrophilic PEG chains, the polymer solution remains transparent until the temperature reaches to 36 °C. In the range of 34–36 °C, the hydrophilic PEG chains compensate the compacting behavior of PNIPAAm chains. At the temperature above 36 °C, DPEA–PNIPAAm–PEG-A becomes water insoluble. For DPEA–PNIPAAm–PEG-B, due to the incorporation of more hydrophilic PEG chains, in the higher temperature range of 36–39 °C, PEG chains still compensate the compacting behavior of PNIPAAm chains. At the temperature above 39 °C, DPEA–PNIPAAm-PEG-B also becomes water insoluble.

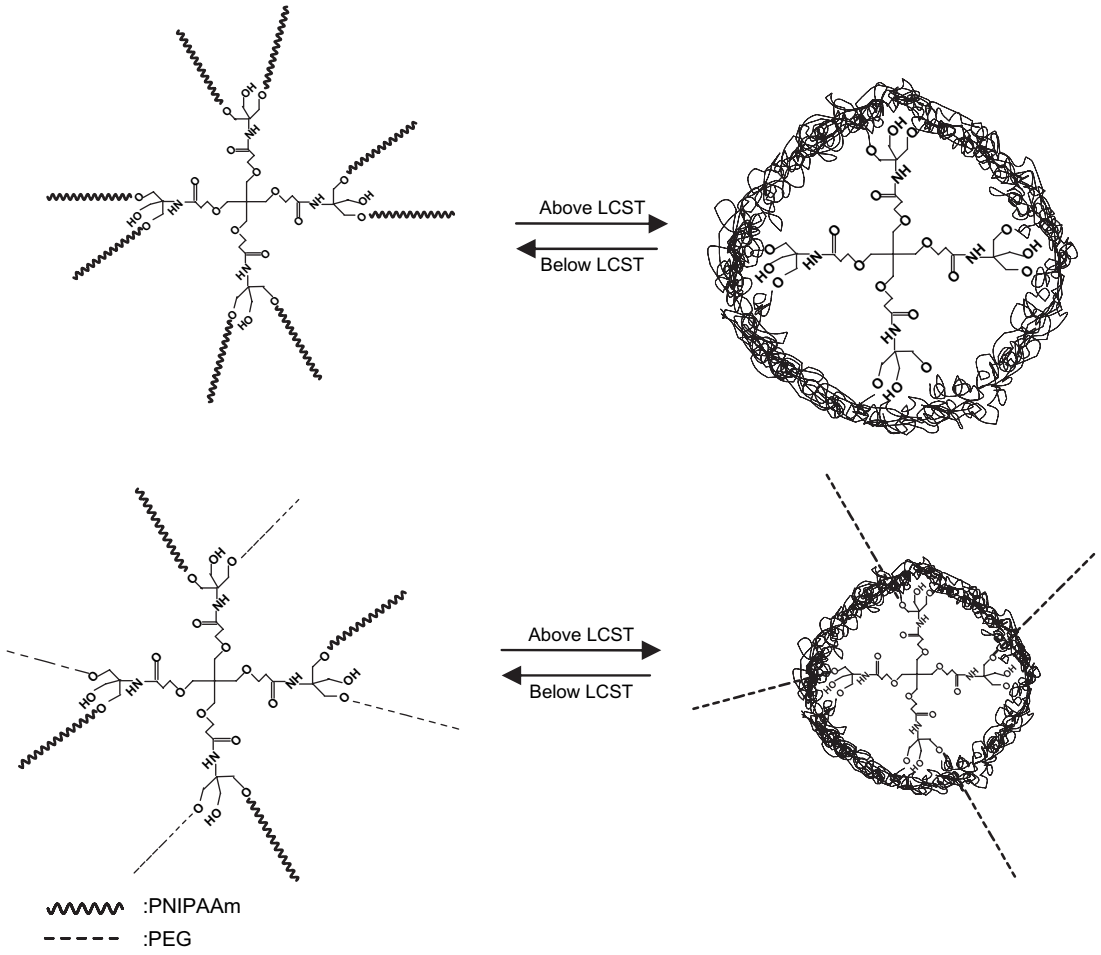


Fig. 7. Schematic diagrams of forming dendritic nanostructures with the temperature-sensitive and water-soluble shell.

3.3. Effect of PEG on the critical aggregation temperature

Fluorescence spectroscopy is a well-established method for detecting micelle formation using pyrene as a molecular probe whose emission and excitation spectra are sensitive to the surrounding environment [20]. It has been reported that two features of the absorption and emission spectrum can be changed when micellization occurs. Firstly, a change in the vibrational fine structure takes place, as the transfer of pyrene from a polar to a nonpolar environment suppresses the allowance of the symmetry forbidden (0, 0) band, which can be described in terms of the ratio I_1/I_3, where I_1 and I_3 are the intensities of the first band (373 nm) and third band (384 nm) in the emission spectrum, respectively. Secondly, the excitation spectrum of pyrene exhibits a red shift when the environment is changed [19].

Figs. 8 and 9 show the emission and excitation spectra of pyrene in the aqueous solutions of DPEA–PNIPAAm and DPEA–PNIPAAm–PEG-B at different temperatures, respectively. For DPEA–PNIPAAm aqueous solutions with a concentration of 1 mg/ml, the intensity ratio of the first to third vibrational band, I_1/I_3 decreases from 1.37 at 25 °C to 1.16 at 38 °C. For DPEA–PNIPAAm–PEG-B aqueous solutions with a concentration of 1 mg/ml, the same phenomenon occurs, where I_1/I_3 decreases from 1.43 at 25 °C to 1.16 at 45 °C. For DPEA–PNIPAAm–PEG-B aqueous solutions with the same concentration, I_1/I_3 also decreases from 1.40 at 25 °C to 1.16 at 39 °C. This indicates that as the temperature reaches a given range, the polarity of pyrene environment would be changed from a polar to a nonpolar.

The characteristic feature of excitation spectrum, that is, band (0, 0) shift from 333 to 338 nm upon pyrene partition into the micellar hydrophobic core, was also utilized to determine the critical aggregation behavior of the conjugates in water [31]. The critical aggregation temperature curves of polymers determined from the intensity ratios (I_{338}/I_{333}) of excitation spectra of pyrene in aqueous polymer solutions are shown in Fig. 10. For both DPEA–PNIPAAm and DPEA–PNIPAAm–PEGs, at lower temperature ranges, the negligible changes of intensity ratios (I_{338}/I_{333}) are observed. However, at given temperatures the intensity ratios exhibit substantial increases, suggesting that pyrene molecules are incorporated into the hydrophobic core region upon micellar aggregation. Therefore, the critical aggregation temperatures for three samples are determined from the crossover points at the low temperature ranges. The critical aggregation temperatures of DPEA–PNIPAAm and DPEA–PNIPAAm–PEG-A are about

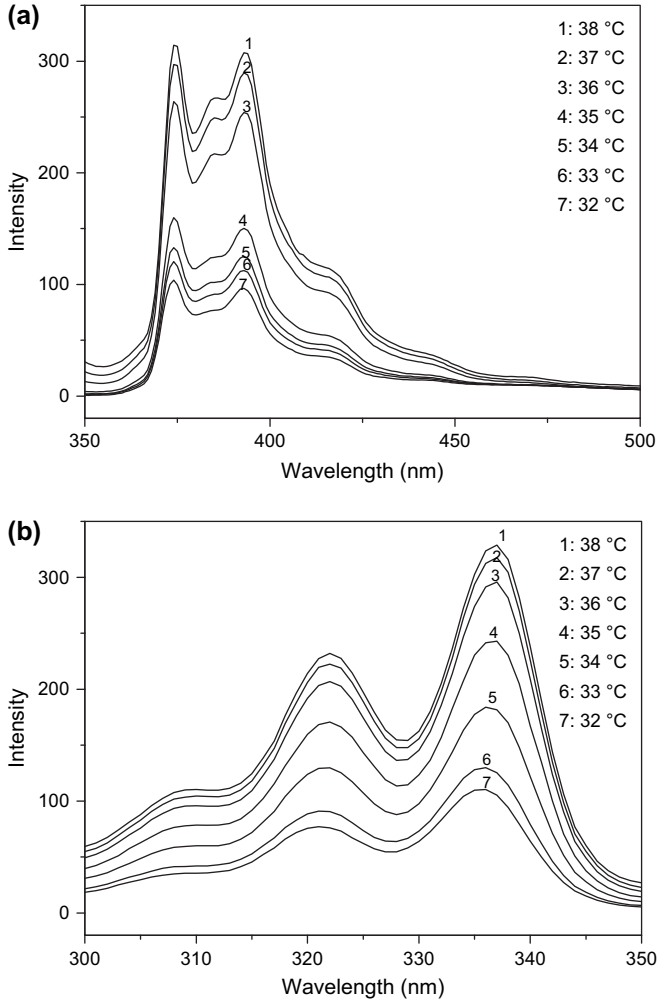


Fig. 8. Emission (a) and excitation (b) spectra of pyrene as a function of temperature in DPEA–PNIPAAm solution.

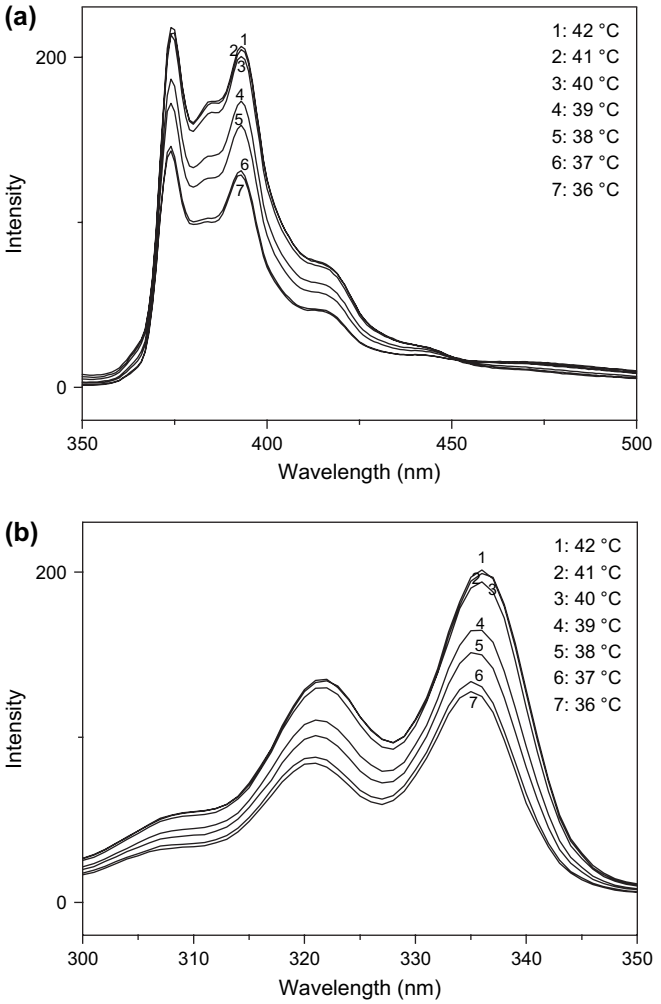


Fig. 9. Emission (a) and excitation (b) spectra of pyrene as a function of temperature in DPEA–PNIPAAm–PEG-B solution.

34 °C and 36 °C, respectively. For DPEA–PNIPAAm–PEG-B, as PEG content increased, the critical aggregation temperature also increases to 39 °C. The critical aggregation temperatures of aqueous DPEA–PNIPAAm–PEG solutions are higher than that of aqueous DPEA–PNIPAAm solution apparently due to the incorporation of hydrophilic PEG chains in the polymer structure. Especially, the critical aggregation temperature of polymer solution may be adjusted by varying PEG content. This result is also consistent with the LCST determination.

4. Conclusions

The molecular structures of dendritic core–shell polymers based upon dendritic poly(ether-amide) were confirmed through FTIR, ^{1}H NMR and GPC. These polymers are supposed to have temperature-sensitive characteristics, and the LCST of 34 °C, 36 °C, 39 °C for DPEA–PNIPAAm, DPEA–PNIPAAm–PEG-A, and DPEA–PNIPAAm–PEG-B aqueous solution, respectively. All LCSTs are higher than that of traditional linear PNIPAAm or its copolymers. This

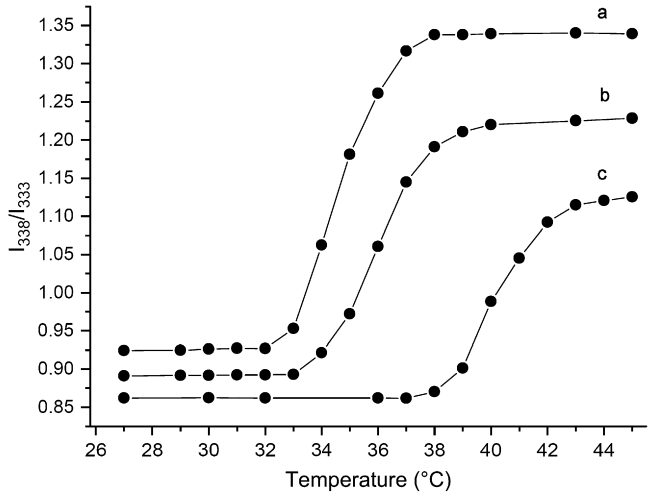


Fig. 10. Intensity ratio (I_{338}/I_{333}) of pyrene from the excitation spectra as a function of temperature in (a) DPEA–PNIPAAm, (b) DPEA–PNIPAAm–PEG-A and (c) DPEA–PNIPAAm–PEG-B solutions.

behavior is attributed to the combination of dendritic poly(ether-amide) (which –CONH– groups possess hydrophilic property) as a core, and water-soluble PEG chains as the shell.

Especially, as the content of grafted PEG increased, the LCST of polymer solution also increased. Their critical aggregation temperatures were investigated using the fluorescence excitation spectrum of pyrene as a sequestered guest molecule in the solution. The sharp increase in the value of I_{338}/I_{333} implies the occurrence of aggregation.

Acknowledgment

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References

[1] Fréchet JMJ, Tomalia DA. Dendrimers and other dendritic polymers. Chichester, UK: John Wiley and Sons Ltd; 2001.
[2] Zou JH, Shi WF, Wang J, Bo J. Macromol Biosci 2005;5:662.
[3] Knapen JWJ, van der Made AW, de Wilde JC, van Leeuwen PWNM, Wijkens P, Grove DM, et al. Nature (London) 1997;372:659.
[4] Bielinska A, Kukowska-Latallo JF, Johnson J, Tomalia DA, Bake Jr JR. Nucleic Acids Res 1996;24:2176.
[5] Bar-Haim A, Klafter J, Kopelman R. J Am Chem Soc 1997;119:6197.
[6] Zhao M, Crooks RM. Angew Chem Int Ed 1999;38:364.
[7] Gillies ER, Jonsson TB, Fréchet JMJ. J Am Chem Soc 2004;126:11936.
[8] Kojima C, Haba Y, Fukui T, Kono K, Takagishi T. Macromolecules 2003; 36:2183.
[9] Aathimanikandan SV, Savariar EN, Thayumanavan S. J Am Chem Soc 2005;127:14922.
[10] You YZ, Hong CY, Pan CY, Wang PH. Adv Mater 2004;16:1953.
[11] Liu XM, Wang LS. Biomaterials 2004;25:1929.
[12] Maeda T, Kanda T, Yonekura Y, Yamamoto K, Aoyagi T. Biomacromolecules 2006;7:545.
[13] Ramanan RMK, Chellamuthu P, Tang L, Nguyen KT. Biotechnol Prog 2006;22:118.
[14] Lee H, Park TG. Biotechnol Prog 1998;14(3):508.
[15] (a) Xu J, Luo SZ, Shi WF, Liu SY. Langmuir 2006;22:989;
(b) Luo SZ, Xu J, Zhu ZY, Wu C, Liu SY. J Phys Chem B 2006;110: 9132.
[16] Hsu YH, Chiang WH, Chen CH, Chern CS, Chiu HC. Macromolecules 2005;38:9757.
[17] Motokawa R, Morishita K, Koizumi S, Nakahira T, Annaka M. Macromolecules 2005;38:5748.
[18] Wei HY, Shi WF, Nie KM, Zhang YC. Chem J Chin Univ 2001;22: 1605.
[19] Kalyanasundaram K, Thomas JK. J Am Chem Soc 1977;99:2039.
[20] Wilhelm M, Zhao CL, Wang Y, Xu R, Winnik MA, Mura JL, et al. Macromolecules 1991;24:1033.
[21] Chung JE, Yokoyama M, Okano T. J Controlled Release 2000;65:93.
[22] Okano T, Katayama M, Shinohara I. J Appl Polymer Sci 1978;22:369.
[23] Fukashi K, Kiyotaka S, Aoyagi T, Yokoyama M, Sakurai Y, Okano T. J Controlled Release 1998;55:87.
[24] Choi CY, Chae SY, Nah JW. Polymer 2006;47:4571.
[25] de la Fuente JL, Wilhelm M, Spiess HW, Madruga EL, Fernández-Garcia M, Cerrada ML. Polymer 2005;46:4544.
[26] Groß M, Maskos M. Polymer 2005;46:3329.
[27] Strandman S, Hietala S, Aseyev V, Koli B, Butcher SJ, Tenhu H. Polymer 2006;47:6524.
[28] An SG, Li GH, Cho CG. Polymer 2006;47:4154.
[29] Feil H, Bae YH, Feijen J, Kim SW. Macromolecules 1993;26:2496.
[30] Kubota K, Fujishige S, Ando I. J Phys Chem 1990;94:5154.
[31] Chang YK, Park CY, Kim KT, Kim CH. Langmuir 2005;21:4334.