Amphiphilic graft copolymers: Effect of graft chain length and content on colloid gel

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(Received April 24, 2015, Revised June 8, 2015, Accepted June 9, 2015)

Abstract. A series of amphiphilic graft copolymers were synthesized by varying the number of graft chains and graft chain lengths. The polarity of the hydrophobic graft chain on the copolymers was varied their solution properties. The glass transition temperature of the copolymers was in the low-temperature region, because of the amorphous nature of poly (trimethylene carbonate) (PTMC). The surface morphology of the lyophilized colloid gel had a bundle structure, which was derived from the combination of poly(N-hydroxyethylacrylamide)(poly(HEAA)) and PTMC. The solution properties were evaluated using dynamic light scattering and fluorescence measurements. The particle size of the graft copolymers was about 30-300 nm. The graft copolymers with a higher number of repeating units attributed to the TMC (trimethylene carbonate) component and with a lower macromonomer ratio showed high thermal stability. The critical association concentration was estimated to be between $2.2 \times 10^{-3}$ and $8.9 \times 10^{-2}$ mg/mL, using the pyrene-based fluorescence probe technique. These results showed that the hydrophobic chain of the graft copolymer having a long PTMC segment had a low polarity, dependent on the number of repeating units of TMC and the macromonomer composition ratio. These results demonstrated that a higher number of repeating units of TMC, with a lower macromonomer composition, was preferable for molecular encapsulation.

Keywords: poly(trimethylene carbonate); amphiphilic graft copolymer; colloid gel; critical association concentration; molecular incorporation

1. Introduction

Biomaterials must be versatile, displaying properties such as good biocompatibility, biodegradability, mechanical strength, functionality, specific surface properties, and non-toxicity. A great deal of research is being pursued in order to achieve these properties. Biocompatible polymers such as poly(l-lactic acid) (PLA) and poly(ε-caprolactone) (PCL) have been widely studied for use as biomaterials (Kim et al. 2009, Kim et al. 2006, Amsden et al. 2004) As an aliphatic polycarbonate, poly(trimethylene carbonate) (PTMC) is one of the hydrophobic polymers that have been widely investigated for biomedical applications (Zhang et al. 2006, Andronova...
PTMC has a number of advantageous properties compared with PLA and PCL, including good biocompatibility, excellent biodegradability, and an amorphous structure. In addition, trimethylene carbonate (TMC), the cyclic monomer of PTMC, is widely available as an industrial reagent. TMC is easily polymerized by ring-opening polymerization (ROP) using various catalysts such as organometallic compounds, organic compounds, enzymes, and acids (Watanabe et al. 2008, Cho et al. 2008, Mindemark et al. 2007, Shibasaki et al. 2000, Zheng et al. 2004, Bisht et al. 1998, Hyun et al. 2008). However, recently, concerns have been raised regarding the biosafety of organometallic catalysts. Therefore, we attempted to use 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as a basic organic catalyst because of its reduced cytotoxic potential (Dove 2012).

Amphiphilic polymers with hydrophobic and hydrophilic segments self-assemble to form a hydrophobic domain in aqueous media. Thus, amphiphilic copolymers have enormous potential as drug delivery systems (DDS) to enhance drug-loading efficiency (Siegel and Pitt 1995). DDS vehicles in solution consist of a stable core-shell structure formed by the aggregation of polymer chains. In many studies, biocompatible amphiphilic block copolymers have been designed using poly(ethylene glycol), poly(methacrylic acid), and poly(2-methacryloyloxyethyl phosphorylcholine) as the hydrophilic segment, and PLA, PCL, or PTMC as the hydrophobic segment (Kim et al. 2009, Kim et al. 2006, Nederberg et al. 2007, Nam et al. 2002, Tosaki et al. 2011, Tyson et al. 2009, Ishihara et al. 1999).

In our previous study, we proposed and prepared an amphiphilic graft copolymer (Nitta et al. 2012a, b). We evaluated the polarity of the hydrophobic domain formed by poly(N-hydroxyethyl acrylamide) (poly(HEAA)) grafted with PTMC (PHT) in aqueous solution. The driving forces for the self-assembly are hydrogen bonding and hydrophobic interaction, and these properties can be adjusted by changing the composition ratio and the chain length of the macromonomer. Thus, PHT copolymers in aqueous solution could spontaneously form aggregates because of these driving forces (Nitta et al. 2012b).

In this study, we prepared three kinds of amphiphilic graft copolymers. Two of these had similar hydrophobic chain lengths but different monomer composition ratios. The other combination had a similar total chain length, but different lengths of the hydrophobic segments. Thus, the effect of each molecular force such as hydrogen bonding between HEAA units and hydrophobic interaction by PTMC graft chains could be evaluated in terms of polymer colloid formation for molecule encapsulation.

We studied the properties of the PHT copolymers as well as their critical association concentrations (CAC) and partition equilibrium constants ($K_v$). The process of aggregation changes the solution properties, such as surface tension, turbidity, and light scattering intensity. Therefore, determining the values of CAC and $K_v$ is important for DDS, as they help in gauging the drug-loading ability of the aggregates. CACs and $K_v$ of the PHT copolymers were calculated by a fluorescence probe technique using the hydrophobic molecule pyrene, which is commonly employed to evaluate hydrophobic environments in aggregated structures (Shibasaki et al. 2000, Hyun et al. 2008, Kim et al. 2000, Mattanavee et al. 2009). The resulting data regarding the aggregate formation are extremely important for in vivo studies of this DDS vehicle in biomedical applications.

### 2. Experimental methods
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2.1 Materials

In order to synthesize the macromonomer, the conventional ROP was performed. Trimethylene carbonate (TMC) was purchased from Boehringer Ingelheim GmbH (Ingelheim, Germany). HEAA was provided by KOHJIN Co., Ltd., Tokyo, Japan. DBU (Kanto Chemical Co., Ltd., Tokyo, Japan) was used as a basic organocatalyst. The termination reaction of the ROP was performed using benzoic acid (Wako Pure Chemical Industries Co., Ltd., Osaka, Japan). To synthesize amphiphilic graft copolymers with the oligo PTMC segments, radical polymerization was carried out using 2,2′-azobis(isobutyronitrile) (AIBN; Tokyo Chemical Industry Co., Ltd., Tokyo, Japan) as the initiator. All organic solvents were used as received.

2.2 Instruments

Proton nuclear magnetic resonance (1H NMR) measurements were performed using a Unity INOVA AS 500 MHz spectrometer (Varian Technologies Japan Co., Ltd., Tokyo, Japan) and were used to confirm the chemical structures, degree of polymerization (DP), and composition ratios. For the 1H NMR measurements, the macromonomer was dissolved in deuterated chloroform (CDCl3), and the PHT copolymers were dissolved in deuterated dimethyl sulfoxide (DMSO-d6). Chemical shifts were recorded downfield from 0.0 ppm using tetramethylsilane as an internal standard. The average molecular weight and molecular weight distribution of the PHT copolymers were determined using gel permeation chromatography (GPC; Showa Denko Co., Ltd., Tokyo, Japan) and compared with polystyrene standard. All polymer samples were dissolved in N,N-dimethylformamide (DMF) at a concentration of 1 mg/mL in the presence of 10 mmol/L lithium bromide. GPC measurements were performed with a Shodex column (SB-804HQ, Showa Denko Co., Ltd., Tokyo, Japan) with a DMF eluent flow rate at 1.0 mL/min. The morphologies of the lyophilized copolymers were observed using field-emission scanning electron microscopy (FE-SEM; JSM-6340FB, JEOL Co., Ltd., Tokyo, Japan), after sputter-coating with platinum (JFC-1600 AUTO FINE COATER, JEOL Co., Ltd.). The thermal properties of the copolymer were monitored using differential scanning calorimetry (DSC; Thermo Plus DSC8230, Rigaku Co., Ltd., Tokyo, Japan). The polymer aggregate size was determined by dynamic light scattering measurements (DLS; Zetasizer Nano ZS, Malvern Instruments Co., Ltd., Malvern, UK). Fluorescence measurements were performed on a fluorescence spectrophotometer (F-2500, Hitachi Co., Ltd., Tokyo, Japan). Pyrene was used to evaluate the CACs and partition equilibrium constants (Kv).

2.3 Preparation of amphiphilic graft copolymers using macromonomer method

The graft copolymers in this study were synthesized using a macromonomer method. Conventional ROP of TMC from HEAA was first performed to obtain HEAA–PTMC macromonomer according to a previously reported procedure (Nitta et al. 2012a). The DP of PTMC in the macromonomer was calculated from the 1H NMR spectrum. The synthesized HEAA–PTMC macromonomers contained 10 or 50 TMC units. 1H NMR (500 MHz, CDCl3) δ: 2.1 (m, 2H, –CH2–CH2–CH2–), 3.6 (q, 2H, –CH2–CH2–O–), 3.7 (t, 2H, –NH–CH2–CH2–), 4.2 (t, 4H, –CH2–CH2–CH2–), 5.6 (d, 1H, H–CH=CH–), 6.1 (q, 1H, CH2=CH–CO–), 6.2 (br, 1H, –CO–NH–CH2–), 6.3 (d, 1H, H–CH=CH–).

Next, the graft copolymer was synthesized according to our previously reported method (Nitta
et al. 2012b). The composition ratio of HEAA to HEAA–PTMC macromonomer in the graft copolymer was calculated from the \(^1\)H NMR measurement. The number of graft chains in the copolymer was found to be approximately 1 to 10 mol%. \(^1\)H NMR (500 MHz, DMSO-\(d_6\)) \(\delta:\)

1.1–1.6 (br, 3H, –CH\(_2\)–CH–CO–), 1.9 (m, 2H, –CH\(_2\)–CH\(_2\)–CH\(_2\)–), 3.4–3.5 (br, 4H, –NH–CH\(_2\)–CH\(_2\)–), 4.1 (t, 4H, –O–CH\(_2\)–CH\(_2\)–O–), 7.2–7.9 (br, 1H, –CO–NH–CH\(_2\)–).

2.4 Observation of lyophilized colloid gel morphology

The resulting graft copolymer was dissolved in DMF and dialyzed in deionized water for 48 h (molecular weight cut-off was 3.5 kDa). The water was replaced every 2 h for the first 6 h and then at longer intervals. The final aqueous solution of the polymer was then lyophilized using liquid nitrogen. For the SEM observation, the lyophilized PHT copolymer was fixed by carbon tape to a sample stage, and then electro-conductive paste (DOTITE; Fujikura Kasei Co., Ltd., Tochigi, Japan) was spotted onto the corner of the sample. All samples were sputter-coated with platinum prior to observation.

2.5 Thermal analysis

The thermal properties of the graft copolymer were investigated using DSC. The glass transition temperature \((T_g)\) of the lyophilized graft copolymer was recorded from −50 to 150 °C using liquid nitrogen at a scanning rate of 10°C/min.

2.6 Particle size and their thermal stability

The synthesized graft copolymers spontaneously formed aggregates in aqueous media. In order to measure the size of these aggregates, the lyophilized graft copolymer was dissolved in water, with ultrasonic agitation, for a short time, and then filtered (pore size 0.8 \(\mu\)m). The copolymer solution was adjusted to a concentration at 1 mg/mL and DLS measurements were performed at temperature ranging from 20 to 70°C.

2.7 Determination of CAC and partition equilibrium constant \((K_v)\)

In order to dissolve the hydrophobic pyrene probe in an aqueous solution, it was first dissolved in THF at 1.2×10\(^{-3}\) mol/L (Cho et al. 2008, Hyun et al. 2008). This solution was then added dropwise to water (6.0×10\(^{-7}\) mol/L) and vigorously stirred. THF was removed by rotary evaporation at 40°C for 2 h. A solution of the graft copolymer containing pyrene was then prepared. The final concentration of pyrene was 6.0×10\(^{-7}\) mol/L. Several graft copolymer solutions were prepared, with concentrations varying in the range of 10\(^{-5}\) to 1 mg/mL. The excitation spectrum of pyrene was measured using a fluorescence spectrophotometer at room temperature. The emission was measured at 373.0 nm with a slit-width of 5.0 nm and a scan speed of 300 nm/min.

3. Results and discussion

3.1 Preparation of macromonomer and amphiphilic graft copolymer
The polymerization of TMC was initiated from the hydroxyl end-group of HEAA, and then the synthesized HEAA–PTMC macromonomer was used in a typical radical polymerization. The chemical structure of the graft copolymer is shown in Scheme 1. Table 1 shows the results of the polymer synthesis. The sample code of PH$_{99}$T$_{11}$ refers to the compound with an HEAA monomer composition ratio of 99 mol% with 11 repeating units of TMC in the macromonomer; the same system of nomenclature was applied to PH$_{92}$T$_{9}$ and PH$_{99}$T$_{52}$. Both the number of repeating units of TMC in the macromonomer and the composition ratio of the graft copolymer were calculated from the $^1$H NMR spectra. PH$_{99}$T$_{11}$ and PH$_{92}$T$_{9}$ were similar in terms of the number of repeating units of TMC, whereas PH$_{99}$T$_{11}$ and PH$_{99}$T$_{52}$ were similar in macromonomer composition. PH$_{92}$T$_{9}$ had a higher molecular weight and a larger $M_w/M_n$ than the others. The GPC result showed the effect of the interaction between the graft copolymers, because of the Tyndall phenomenon was observed on PH$_{92}$T$_{9}$ solution in DMF. Particularly, the interaction of PH$_{92}$T$_{9}$ was much enhanced.

Scheme 1 Chemical structure of amphiphilic graft copolymer (PHT)

3.2 Characterization of graft copolymer

In Fig. 1, SEM images show the surface morphology of each copolymer. In the case of poly(HEAA), the punched-sheet morphology was observed. The diameter of the observed fibrils was approximately 2 μm. The pore size was roughly 2-5 μm, and the pores were spread over the entire area. In contrast, the surface morphology of the graft copolymer hydrogel appeared as a fibrous entangled structure of aggregates derived from PTMC.

On the other hand, PH$_{92}$T$_{9}$ showed bundles of random entanglements. The surface morphologies are formed from the aggregate due to its modification by a stronger interaction among the PTMC segments (Mattanavee et al. 2009, Chandler-Temple et al. 2010). Because the hydrophobic PTMC prevented the invasion of water molecules, there is no pore on the surface.

As an amorphous polymer, PTMC has a low $T_g$, below 0°C (Kim et al. 2006, Amsden et al. 2004, Terao et al. 2012, Tyson et al. 2009). For the graft copolymers, the values of $T_g$ were higher (Fig. 2), with poly(HEAA), PH$_{99}$T$_{11}$, PH$_{92}$T$_{9}$, and PH$_{99}$T$_{52}$ demonstrating endothermic transitions at 61.3, 52.3, 36.6, and 36.3°C, respectively. The flexible PTMC segment showed to be in micro-
Brownian motion, so that $\text{PH}_{99}T_{11}$, $\text{PH}_{92}T_{9}$, and $\text{PH}_{99}T_{52}$ displayed lower $T_g$ values than did poly(HEAA). The $T_g$ was influenced by the DP of PTMC, rather than the composition ratio of the macromonomer, in the copolymers with a similar number of TMC units. $\text{PH}_{92}T_{9}$ and $\text{PH}_{99}T_{52}$ showed approximately equal values of $T_g$. We concluded that this is because the strength of the interaction in both polymer segments was similar. Additionally, the $T_g$ data indicated good compatibility between the poly(HEAA) and PTMC segments.

![Fig. 1 SEM images of the freeze-dried polymers (Scale bar, 10 μm): (a) Poly(HEAA), (b) $\text{PH}_{99}T_{11}$, (c) $\text{PH}_{92}T_{9}$, (d) $\text{PH}_{99}T_{52}$](Fig1)

![Fig. 2 DSC thermograms of lyophilized poly(HEAA) and PHT copolymers](Fig2)
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3.3 Thermal stability of graft copolymer aggregates in aqueous media

The amphiphilic PHT graft copolymers spontaneously formed aggregates in aqueous media, driven by the hydrophobic interactions among the PTMC segments and the hydrogen bonding derived from HEAA. These aggregates consisted of a shell, covered with hydrophilic poly(HEAA) segments, and a core of PTMC domains. The particle size of the PHT copolymers at a concentration of 1 mg/mL in aqueous media was analyzed by DLS measurements. The particle sizes of PH$_{99}$T$_{11}$, PH$_{92}$T$_{9}$, and PH$_{99}$T$_{52}$ were approximately 30, 75, and 250 nm at 25°C, respectively. For each PHT copolymer, the total amount of PTMC segments was different. For PH$_{99}$T$_{11}$ and PH$_{92}$T$_{9}$, the HEAA–PTMC macromonomer contents were significantly different, although the DP of the PTMC segment was almost the same. Therefore, these two copolymers should have different hydrophobic properties. By comparison with PH$_{99}$T$_{11}$, the PH$_{99}$T$_{52}$ copolymer had a PTMC segment whose DP was five times higher, although the macromonomer content was quite similar. This result indicated that the larger particle size was observed as a result of the higher hydrophobicity caused by the PTMC environment.

In addition, the small shoulder of the particle size distribution indicated that the unimer was formed due to the intramolecular aggregation of PHT. The thermal stability of the particle as a function of temperature was measured using DLS (Fig. 3). The concentration of the polymer solution was 1 mg/mL and the temperature range was from 20 to 70°C. Both PH$_{92}$T$_{9}$ and PH$_{99}$T$_{52}$ remained highly stable and unchanging, but the particle size of poly(HEAA) and PH$_{99}$T$_{11}$ increased in the interval from 60 to 70°C. By heating, it showed an unstable aggregate structure due to a dissociation of hydrogen bonding formed by amide and hydroxyl groups on the HEAA unit at higher temperatures. Therefore, in this temperature range, the particle size of poly(HEAA) was about 80 nm. On the other hand, the particle size of PH$_{99}$T$_{11}$ changed from about 115 to 140 nm.
nm in the process of forming the aggregate from the hydrophobic interaction of PTMC and its association through hydrogen bonding. This behavior indicated that graft copolymers as colloid gels were in a swelled state. Additionally, the particle size reversibly increased and decreased due to change in temperature. We considered that the physical cross-linking such as hydrogen bonding and hydrophobic interaction was dominant for the colloid gel association and disassociation.

### 3.4 Evaluation of graft copolymer aggregate by fluorescence measurements

The CAC and $K_v$ values of the PHT copolymers were determined in aqueous media at different concentrations using fluorescence measurements, with pyrene as a hydrophobic fluorescent probe. The fluorescence spectrum of pyrene in solution is known to shift depending on the polarity of the surrounding environment (Kim et al. 2000, Wilhelm et al. 1991). Fig. 4 shows that by increasing the polymer concentration in aqueous media, the maximum value in the excitation spectra ($\lambda_{ex}$) of pyrene shifts from 333.5 to 336 nm, where it was considered that pyrene was incorporated into the hydrophobic PTMC domain. This shift in the excitation spectra was observed for all of the graft copolymers. The total intensities of the spectra varied depending on both the copolymer concentration and the total amount of hydrophobic PTMC segments.

Fig. 5 shows the fluorescence intensity ratio ($I_{336}/I_{333.5}$) in the pyrene excitation spectra at 373 nm versus the logarithm of the PHT concentration. Above the CAC, the fluorescence intensity increased exponentially, as the number of molecules of pyrene increased. On the other hand, below the CAC, absorption only occurred near the surface of the aggregates where the pyrene molecules cohered. The fluorescence intensity increased when the pyrene was solubilized in the hydrophobic domain. The fluorescence intensity also increased with increasing PHT copolymer concentration. The increase in the intensity ratio indicated the onset of aggregate formation. From the result of Fig. 3, the particle size of PH$_{99}$T$_{11}$ increased over 55°C due to the dissociation of hydrogen bonding on the HEAA units. Aggregation of the polymer would be enhanced. The CAC of PH$_{99}$T$_{11}$ was quite high, so hydrophobic interaction was not so strong. Therefore, the CAC can be defined as the intersection of two straight lines in the low concentration range. The CAC values of PH$_{99}$T$_{11}$, PH$_{92}$T$_{9}$, and PH$_{95}$T$_{52}$ were estimated to be approximately 8.9×10$^{-2}$, 3.2×10$^{-3}$, and 2.2×10$^{-3}$ mg/mL, respectively (Table 2). The CAC of the graft copolymer decreased with not only the chain length of PTMC, but also with the macromonomer composition ratio. In the case of PH$_{99}$T$_{11}$, the

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**Fig. 4** Excitation spectra of pyrene (6.0×10$^{-7}$ mol/L) as a function of polymer concentration (10$^{-5}$–1 mg/mL) in aqueous solution at 25°C. (a) PH$_{99}$T$_{11}$, (b) PH$_{92}$T$_{9}$, (c) PH$_{95}$T$_{52}$
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Fig. 5 Plot of $I_{336}/I_{333.5}$ (from the pyrene excitation spectra) versus log $C$, where $C$ is the concentration of the graft copolymers. PH$_{99}$T$_{11}$: ●, PH$_{92}$T$_{9}$: ●, PH$_{99}$T$_{52}$: ●

CAC had the lowest value among the copolymers, showing lower association forces. The repeating unit of TMC and the macromonomer composition both influenced the formation polymer colloids. In this case, the higher number of repeating units of TMC appears to be dominant; otherwise, a higher macromonomer composition would be necessary. The slope reached a plateau above 1.2 of $I_{336}/I_{333.5}$ for PH$_{92}$T$_{9}$ and PH$_{99}$T$_{52}$ samples, indicating that the hydrophobic domain was saturated with incorporated pyrene.

To quantify the separation of pyrene into the hydrophobic domain during aggregation, Wilhelm et al. (1991) devised an equation to calculate the $K_v$ value of the hydrophobic domain in graft copolymer aggregates (Wilhelm et al. 1991). The concentration of pyrene in the hydrophobic domain of the PHT copolymer was calculated using Eqs. (1)-(4), where $[Py]_A$ and $[Py]_w$ represent the concentrations of pyrene in the aggregated and aqueous phase, respectively. The $K_v$ value for pyrene was calculated from the ratio of the pyrene concentrations ($[Py]_A/[Py]_w$). In this approach, $[Py]_A/[Py]_w$ can be corrected to the volume ratio of each phase: which can be rewritten as

$$[Py]_A/[Py]_w=K_vV_A/V_w$$

Moreover, $[Py]_A/[Py]_w$ can be written as

$$[Py]_A/[Py]_w=K_vx(c-CAC)/1000\rho$$

where $x$ is the weight fraction of the PTMC segment, $c$ is the concentration of the graft copolymer, and $\rho$ is the density of the PTMC aggregation domain, which is assumed to be the value of bulk PTMC (1.0 g/cm$^3$ ≅ g/mL).

$$[Py]_A/[Py]_w=(F-F_{min})(F_{max}-F)$$

which can be rewritten as

$$K_v=\text{slope} \times 1000\rho/x$$
Fig. 6 Plots of \((F-F_{\text{min}})/(F_{\text{max}}-F)\) versus concentration of graft copolymers. PH$_{99}$T$_{11}$: •, PH$_{92}$T$_{9}$: ●, PH$_{99}$T$_{52}$: ○.

Fig. 7 Schematic illustration of aggregation and pyrene-loading-related CAC and $K_v$ for the graft copolymers.

Table 2 CAC and $K_v$ of PHT copolymers (25°C)

<table>
<thead>
<tr>
<th>Sample</th>
<th>CAC (mg/mL)</th>
<th>$K_v/10^4$</th>
</tr>
</thead>
<tbody>
<tr>
<td>PH$<em>{99}$T$</em>{11}$</td>
<td>8.9×10$^{-3}$</td>
<td>2.0</td>
</tr>
<tr>
<td>PH$<em>{92}$T$</em>{9}$</td>
<td>3.2×10$^{-3}$</td>
<td>8.0</td>
</tr>
<tr>
<td>PH$<em>{99}$T$</em>{52}$</td>
<td>2.2×10$^{-3}$</td>
<td>9.8</td>
</tr>
</tbody>
</table>

where $F_{\text{min}}$ and $F_{\text{max}}$ correspond to the average magnitudes of the peak ratio in the region of high and low concentration ranges shown in Fig. 5, respectively, and $F$ is the fluorescence intensity ratio \((I_{336}/I_{333.5})\) in the intermediate concentration range of the conjugates [Eqs. (2)-(3)]. The slope
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was determined by a linear approximation and the $K_v$ values were calculated using Eq. (4).

The fluorescence study using pyrene also reflected the polymer structure, including the grafting degree and PTMC chain length. PH$_{92}$T$_9$ and PH$_{99}$T$_{52}$ had higher slope, as calculated by Eq. (3), by changing each polymer concentration. The $K_v$ values of PH$_{99}$T$_{11}$, PH$_{92}$T$_9$, and PH$_{99}$T$_{52}$ were estimated to be approximately 2.0×10$^{-4}$, 8.0×10$^{-4}$, and 9.8×10$^{-4}$, respectively (Fig. 6).

The $K_v$ of PH$_{92}$T$_9$ was four times as large as that of PH$_{99}$T$_{11}$. We concluded from these results that PTMC segments played a role in both molecular incorporation and cross-linking. Therefore, the $K_v$ of PH$_{92}$T$_9$ was not in agreement with the theoretical value. Table 2 and Fig. 7 summarize these results. The chain length of PTMC rather than the macromonomer composition ratio decreased the $K_v$ values of graft copolymers. Therefore, the hydrophobic domain in PH$_{99}$T$_{52}$ proved to have a more significant influence than in PH$_{92}$T$_9$.

4. Conclusions

Amphiphilic graft copolymers with homogeneous graft chain lengths of PTMC segments were prepared using a macromonomer method. The $T_g$ values of the graft copolymers were measured to be from 35 to 60°C, and the PTMC fraction showed a flexible nature at temperatures close to body temperature. These copolymer associations formed core-shell structures in an aqueous solution. The particle size of the PHT aggregates in aqueous solution was about 30-300 nm and was comparatively stable relative to changes in temperature. In particular, PH$_{99}$T$_{11}$ and PH$_{92}$T$_9$ have suitable particle sizes for common DDS. The CAC of the PHT copolymers were in the range of 2.2×10$^{-3}$ to 8.9×10$^{-2}$ mg/mL. The $K_v$ values were dependent to the increase in TMC units. We deduced that the particle size, CAC, and $K_v$ values for the copolymers depended mostly on the chain length of the hydrophobic PTMC. The graft copolymer with a longer PTMC chain length underwent strong hydrophobic interactions, leading to an increase in the particle size, $T_g$, and $K_v$. From these results, the function of the hydrophobic PTMC domains seemed to be slightly different according to the number of TMC repeating units. We confirmed that the aggregates formed from the graft copolymers with PTMC domains might be used as potential drug delivery vehicles for loading hydrophobic molecules.

Acknowledgments

Part of this study was financially supported by a Grant-in-Aid from the Hirao Taro Foundation of the Konan University Association for Academic Research.

References


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