Colloid Polym Sci (2009) 287:525–532
DOI 10.1007/s00396-009-1998-z

ORIGINAL CONTRIBUTION

Design of polylactide-grafted copolymeric stabilizer for dispersion polymerization of D,L-lactide

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Received: 27 October 2008 / Revised: 22 December 2008 / Accepted: 28 December 2008 / Published online: 22 January 2009

Abstract Poly(D,L-lactide) (PDLLA) microspheres with narrow diameter distribution were prepared by dispersion polymerization of D,L-lactide in xylene/heptane (1:2, *v*/*v*) using poly(dodecyl methacrylate)-*g*-poly(D,L-lactide) (PDMA-*g*-PDLLA) as a dispersion stabilizer. The particle diameters of PDLLA microspheres were controlled from 200 nm to 5 μm by altering the concentration and the graft chain number of PDMA-*g*-PDLLA. The effect of the copolymer composition on the particle diameter was investigated to clarify an important factor of the copolymer structure for the control of the particle diameter. As a result, it was necessary for anchor block in diblock copolymer as a dispersion stabilizer to have low solubility in the solution rather than the compatibility with particles. Moreover, we confirmed by dynamic light scattering measurement that PDMA-*g*-PDLLA formed micelles in the solution. In conclusion, it was clarified that PDLLA microspheres with a wide range of particle diameter were prepared due to the different kinetic stability of micelles.

Keywords Poly(D, L-lactide) · Microsphere · Dispersion polymerization · Graft copolymeric stabilizer · Copolymeric micelles

Introduction

Heterogeneous polymerization has been of increasing interest for the last three decades, due to the simple preparation of polymeric microspheres with narrow diameter distribution and a wide range of particle diameter [1]. This technique is classified into two methods. The first is emulsion polymerization, which is able to prepare the polymeric microspheres with submicrometer size using reaction medium not dissolving almost monomer. The polymerization takes place in the micelles composed of monomer and emulsifier. The second is dispersion polymerization, which is able to prepare the polymeric microspheres with micrometer size using reaction medium dissolving monomer but not dissolving polymer. The polymerization takes place in reaction medium until the polymer reaches critical molecular weight to precipitate, then the precipitated particles are stabilized by a dispersion stabilizer.

In dispersion polymerization, the dispersion stabilizer which affects the stability of the precipitated particles plays an important role for microsphere preparation. Many workers have prepared monodisperse polymeric microspheres using homopolymeric stabilizers such as poly(vinyl pyrrolidone) and hydroxypropyl cellulose [2–4]. They found that smaller microspheres were obtained at a higher dispersion stabilizer concentration and molecular weight. On the other hand, Dawkins and coworkers have made near-monodisperse polymeric microspheres using diblock copolymeric stabilizer such as poly(styrene-*b*-ethylene-*co*-propylene) and poly(styrene-*b*-dimethylsiloxane) [5–8]. They have investigated the effect of the molecular structure in diblock copolymer such as molecular weight and the alkyl group number of anchoring block on the resultant particle diameter. Winnik et al. confirmed the existence of regular micelles comprising several hundred diblock copolymers and micellar clusters corresponding to the aggregate of tens of micelles in aqueous solution by dynamic light scattering measurement [9–10]. They also

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described that block copolymer with low molecular weight should be used as a stabilizer for dispersion polymerization of styrene in methanol to prepare large and monodisperse microspheres [11].

On the other hand, there have been few papers describing the use of graft copolymer as a stabilizer in dispersion polymerization. Slomkowski et al. reported that Poly(D,L-lactide) (PDLLA) and poly(L,L-lactide) (PLLA) microspheres with narrow diameter distribution were prepared by dispersion polymerization of D,L-lactide and L,L-lactide using poly(dodecyl acrylate)-*g*-poly(ε-caprolactone) as a dispersion stabilizer, respectively [12–13]. They investigated the critical micelle concentration (cmc) of the dispersion stabilizer in 1,4-dioxane/heptane (1:4, *v*/*v*) as a reaction medium. The polymerization occurred at lower concentrations than its cmc, it was found that the particle diameter and the diameter distribution depend on the molecular structures of the dispersion stabilizer [14]. We have also reported that PDLLA microspheres with narrow diameter distribution were prepared by PLLA-grafted copolymer, poly(dodecyl methacrylate)-*g*-poly(L,L-lactide) (PDMA-*g*-PLLA), as a dispersion stabilizer [15]. In this work, we investigated the effect of the molecular structures in PDMA-*g*-PDLLA on the particle diameter of PDLLA microspheres prepared by dispersion polymerization of D,L-lactide in xylene/heptane (1:2, *v*/*v*) to clarify an important factor of molecular structures in the graft copolymeric stabilizer for the control of the particle diameter.

Experimental

Materials

D,L-lactide purchased from Purac Biochem BV (Gorinchem, The Netherlands) was purified by the recrystallization from toluene. 2-Hydroxyethyl methacrylate (HEMA) and dodecyl methacrylate (DMA) purchased from Wako Pure Chemical Industries was purified by the distillation under reduced pressure. Toluene, xylene, and heptane (dehydrated-grade) were purchased from Wako Pure Chemical Industries were treated with 4 Å molecular sieves to remove dissolved water. PME-4000, poly(ethylene glycol) macromonomer (MA-PEG), was kindly provided by NOF. FM-0721, polydimethylsiloxane macromonomer (MA-PDMS), was purchased from Chisso were used as received. Other reagents were purchased from Wako Pure Chemical Industries and used as received.

Measurements

Gel permeation chromatography (HLC 8120, Tosoh, GPC) was performed on the basis of the polystyrene standards with tetrahydrofuran as an eluent to determine the number-averaged molecular weight (*Mw*) and the polydispersity index (*Mw*/*Mn*) of synthesized polymer. ^{1}H NMR (AL300 SC-NMR, JEOL) measurement was conducted using $CDCl_3$ as a solvent and tetramethylsilane (TMS) (1%, *v*/*v*) as an internal standard to determine the molecular structure of synthesized polymer. Scanning electron microscopic observation (S-4700, Hitachi, SEM) was performed to determine the particle diameter (*dp*) and the diameter distribution (coefficient of variation, CV) of prepared PDLLA microspheres. Differential scanning calorimetric measurement (SSC5200H, Seiko Instruments, DSC) was conducted to determine the glass transition temperature (T_g) of PDMA-*g*-PDLLA and PDLLA microspheres. The heating rate was kept at 5 K/min, and the atmospheric temperature was scanned from 253 K to 373 K. Dynamic light scattering measurement (FPAR-1000, Otsuka Electronics, DLS) was carried out at 293 K to determine the hydrodynamic diameter (R_h) of micelles that consist of PDMA-*g*-PDLLA in xylene/heptane (1:2, *v*/*v*).

Synthesis

PDMA-g-PDLLA

The preparation of PDMA-*g*-PDLLA serves as a typical example for PDLLA-grafted copolymer. MA-PDLLA was synthesized by ring-opening polymerization of D,L-lactide using HEMA as an initiator in the presence of stannous 2-ethylhexanoate as a catalyst [16]. MA-PDLLA (*Mw*= 3,700, 0.42 mmol), DMA (9.65 mmol), and dehydrated toluene 18 ml as a solvent were placed into a round-bottom reactor. After nitrogen was admitted to remove oxygen, the reactor was immersed in an oil bath at 358 K. Dehydrated toluene dissolving benzoyl peroxide (BPO) (0.63 mmol) was added to initiate the polymerization. The polymerization was conducted for 3 h. After the polymerization, the reaction mixture was poured into excess methanol to remove DMA. The precipitate was recovered and added to 1,4-dioxane/heptane (1:4, *v*/*v*) to remove the remaining MA-PDLLA. After the purification, the polymer was dried under reduced pressure at 313 K.

The number of PDLLA chains in PDMA-*g*-PDLLA, *CN*, was calculated from the ^{1}H NMR spectrum using the integration ratio of DMA and PDLLA unit. It was defined by the following equation:

$$S_{\mathrm{MA-PDLLA}} = \frac{A_{\mathrm{MA-PDLLA}}}{\mathrm{PD}}$$

$$S_{DMA} = \frac{A_{DMA}}{2}$$

where $A_{\mathrm{MA\text{-}PDLLA}}$ and A_{DMA} denote the peak areas of CH for PDLLA unit of MA-PDLLA and $COOCH_2$ for DMA

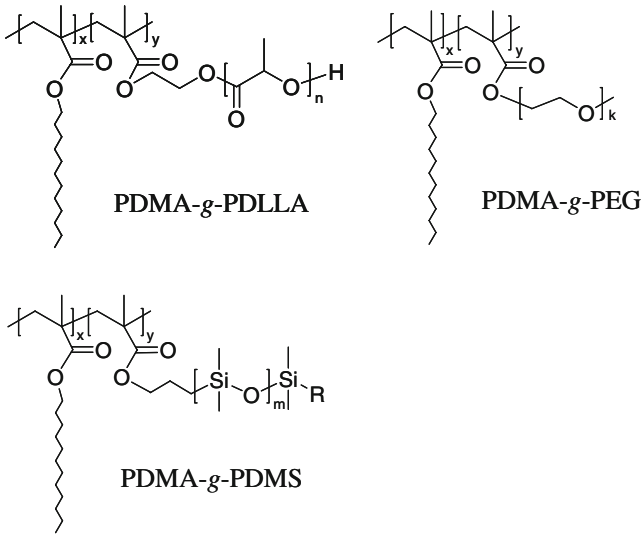


Fig. 1 Chemical structures of the graft copolymeric stabilizers

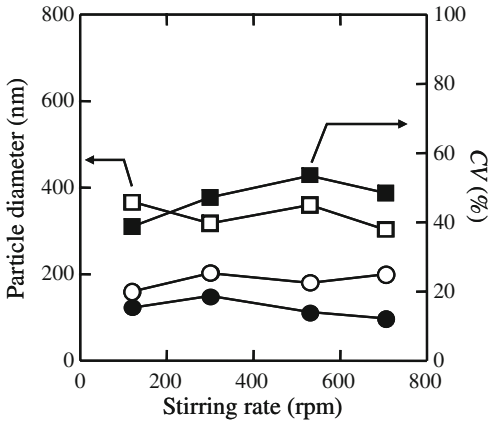


Fig. 2 Effect of stirring rate on the particle diameter and the diameter distribution of PDLLA microspheres prepared using (*open square*, *close square*) G_2 and (*open circle*, *close circle*) G_4 copolymers with different molecular structures; [PDMA-*g*-PDLLA]=10 g/l

unit in ^{1}H NMR spectrum of PDMA-*g*-PDLLA, respectively. And PD denotes the polymerization degree of MA-PDLLA. The number of DMA unit per MA-PDLLA unit, *N*, was defined by

$$N = \frac{S_{\mathrm{DMA}}}{S_{\mathrm{MA-PDLLA}}}$$

$$CN = \frac{Mw_{copolymer}}{(Mw_{DMA} \cdot N + Mw_{MA-PDLLA})}$$

where $Mw_{\mathrm{copolymer}}$, Mw_{DMA}, and $Mw_{\mathrm{MA\text{-}PDLLA}}$ denote the weight-averaged molecular weight of PDMA-*g*-PDLLA, DMA, and MA-PDLLA, respectively.

PDMA-g-PEG

MA-PEG (*Mw*=4,200, 0.55 mmol), DMA (14.49 mmol), and dehydrated toluene 18 ml as a solvent were placed into a round-bottom reactor. After nitrogen was admitted to remove oxygen, the reactor was immersed in an oil bath at 358 K. Dehydrated toluene dissolving BPO (0.47 mmol) was added to initiate the polymerization. The polymerization was conducted for 3 h. After the polymerization, the reaction mixture was poured into excess methanol to remove the remaining MA-PEG and DMA, and then the precipitate was recovered. After the purification, the polymer was dried under reduced pressure at 313 K.

PDMA-g-PDMS

MA-PDMS (*Mw*=8,400, 7.96 mmol), DMA (7.96 mmol), and dehydrated toluene 18 ml as a solvent were placed into a round-bottom reactor. After nitrogen was admitted to remove oxygen, the reactor was immersed in an oil bath at 358 K. Dehydrated toluene dissolving BPO (0.94 mmol) was added to initiate the polymerization. The polymerization was conducted for 3 h. After the polymerization, the reaction mixture was poured into excess methanol. The precipitate was recovered and added to methanol/2-propanol (1:2, *v*/*v*) to remove the remaining MA-PDMS. After the purification, the polymer was dried under reduced pressure at 313 K.

Table 1 Molecular structures of PDMA-*g*-PDLLA

Code	Graft copolymer	Mw^a	Mw/Mn^b	Macromonomer		N^e	CN^f (PDLLA)
				Mw^c	Mw/Mn^d		
G_1	PDMA-*g*-PDLLA	41,300	2.31	3,700	1.30	116	1.3
G_2	PDMA-*g*-PDLLA	34,500	2.23	3,700	1.30	54	2.0
G_3	PDMA-*g*-PDLLA	36,500	2.04	3,700	1.30	27	3.4
G_4	PDMA-*g*-PDLLA	30,700	2.53	6,600	1.40	24	2.4

[a,b,c,d] Determined by GPC
[e] Number of DMA units per MA-PDLLA unit
[f] A grafted PDLLA chain number in a copolymer

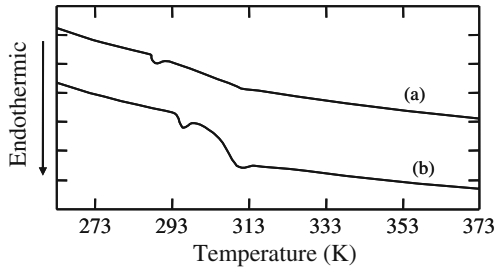


Fig. 3 DSC curves for (*a*) G_4 copolymer and (*b*) PDLLA microspheres prepared with G_4 copolymer; [PDMA-*g*-PDLLA]=10 g/l

Preparation of PLA microspheres

The preparation of PDLLA microspheres is shown as a typical example. D,L-lactide (0.5 g, 3.47 mmol) was added into 17 ml of dehydrated xylene/heptane (1:2, *v*/*v*) dissolved PDMA-*g*-PDLLA. In this study, the concentration of dispersion stabilizer ranged from 0.01 to 0.2 g. The solution was stirred at 120 rpm with a magnetic stirrer. Three milliliters of dehydrated xylene/heptane (1:2, *v*/*v*) dissolving stannous 2-ethylhexanoate (0.0475 g, 0.12 mmol) as a catalyst and lauryl alcohol (0.011 g, 0.06 mmol) as an initiator was prepared. The solution was added with a syringe and the polymerization was conducted at 368 K for 9 h. After the polymerization, the reaction solution was poured into excess cold heptane. The solution was centrifuged for 5 min at 9,000 rpm and the microspheres were redispersed into excess heptane. The solution was filtered to obtain the prepared microspheres.

Results and discussion

Synthesis of PDMA-*g*-PDLLA

Figure 1 shows the chemical structures of synthesized graft copolymers with different grafted polymer chains. MA-PDLLA was synthesized by ring-opening polymerization of D,L-lactide using HEMA as an initiator. Subsequently, MA-PDLLA was copolymerized with DMA by free radical polymerization using BPO as an initiator to obtain PDMA-*g*-PDLLA. The ^{1}H NMR spectrum of PDMA-*g*-PDLLA had peaks in the range of 1.5–1.7 ppm (CH_3 for PDLLA unit), 5.1–5.3 ppm (CH for PDLLA unit) and around 3.9 ppm ($COOCH_2$ for DMA unit). Furthermore, peaks at 5.6 and 6.2 ppm (CH_2=CH for MA-PDLLA) were not detected in the spectrum. Therefore, PDMA-*g*-PDLLA was finally identified. The molecular structures of synthesized PDMA-*g*-PDLLA were summarized in Table 1.

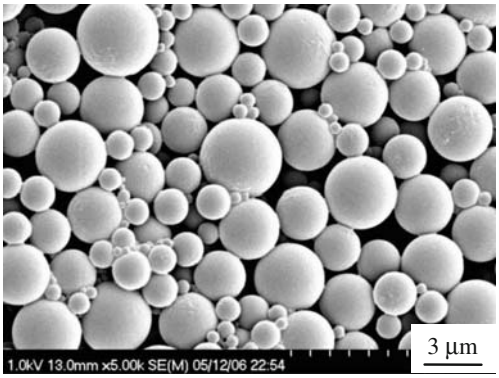


Fig. 4 SEM image of PDLLA microspheres prepared with PDMA-*g*-PEG as a dispersion stabilizer; (*dp*=1,420 nm, CV=48.2%), [PDMA-*g*-PEG]=10 g/l

Synthesis of PDMA-*g*-PEG

PDMA-*g*-PEG was synthesized by free radical polymerization of DMA and MA-PEG as a macromonomer using BPO as an initiator. The ^{1}H NMR spectrum of PDMA-*g*-PEG had peaks in the range of 3.6 ppm ($COOCH_2CH_2$ for PEG unit) and around 3.9 ppm ($COOCH_2$ for DMA unit). Furthermore, peaks at 5.5 and 6.1 ppm (CH_2=CH for MA-PEG) were not detected in the spectrum. Therefore, PDMA-*g*-PEG was finally identified. The MA-PEG number in PDMA-*g*-PEG, *CN*, was calculated by the similar method to PDMA-*g*-PDLLA.

Synthesis of PDMA-*g*-PDMS

PDMA-*g*-PDMS was synthesized likewise using MA-PDMS. The ^{1}H NMR spectrum of PDMA-*g*-PDMS had

Table 2 Molecular structures of graft copolymeric stabilizers

Graft copolymer	*Mw*[a]	*Mw*/*Mn*[b]	Macromonomer		*N*[e]	*CN*[f] (Macromonomer)
			Mw[c]	*Mw*/*Mn*[d]		
PDMA-*g*-PEG	27,500	2.38	4,200	1.09	22	2.8
PDMA-*g*-PDMS	39,000	2.05	8,400	1.11	23	2.8

PEG poly(ethylene glycol), *PDMS* poly(dimethyl siloxane)
[a,b,c,d] Determined by GPC
[e] Number of DMA units per macromonomer unit
[f] A grafted macromonomer chain number in a copolymer

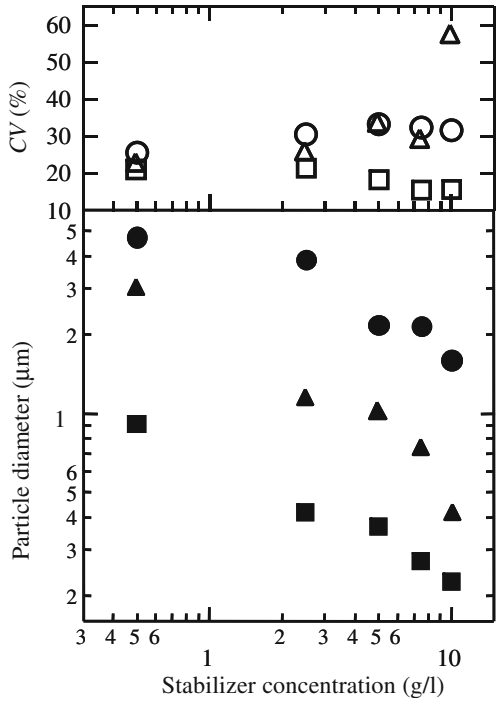


Fig. 5 Effect of concentration of (*open circle*, *close circle*) G_1, (*open triangle*, *close triangle*) G_2, and (*open square*, *close square*) G_3 copolymers with different number of graft chains on the particle diameter and the diameter distribution of PDLLA microspheres

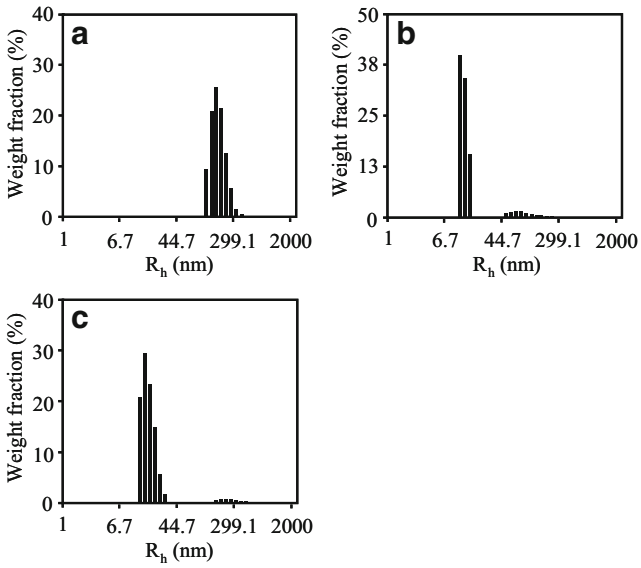
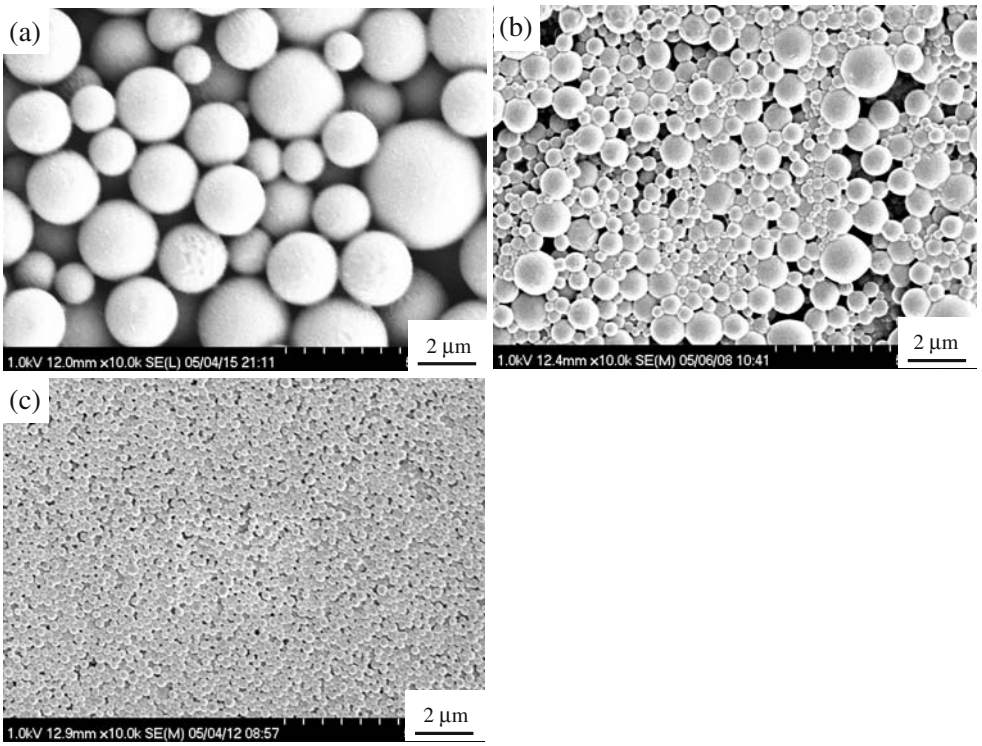


Fig. 7 Size distributions for micellar aggregates of **a** G_1 (R_h=194 nm), **b** G_2 (R_h=13 nm, 93 nm) and **c** G_3 (R_h=18 nm, 276 nm) copolymers in xylene/heptane (1:2, *v*/*v*) at 293 K; [PDMA-*g*-PDLLA]=10 g/l

peaks in the range of 0.0 ppm ($Si(CH_3)_2$ for PDMS unit) and around 3.9 ppm (OCH_2 for DMA unit). Furthermore, peaks at 5.4 and 6.0 ppm (CH_2=CH for MA-PDMS) were not detected in the spectrum. Therefore, PDMA-*g*-PDMS was also finally identified. The MA-PDMS number in PDMA-*g*-PDMS, *CN*, was calculated likewise.

Fig. 6 SEM images of PDLLA microspheres using **a** G_1 (*dp*= 1,600 nm, CV=31.6%), **b** G_2 (*dp*=414 nm, CV=57.2%), and **c** G_3 (*dp*=225 nm, CV=15.8%) copolymers. They have different number of graft chains; [PDMA-*g*-PDLLA]=10 g/l



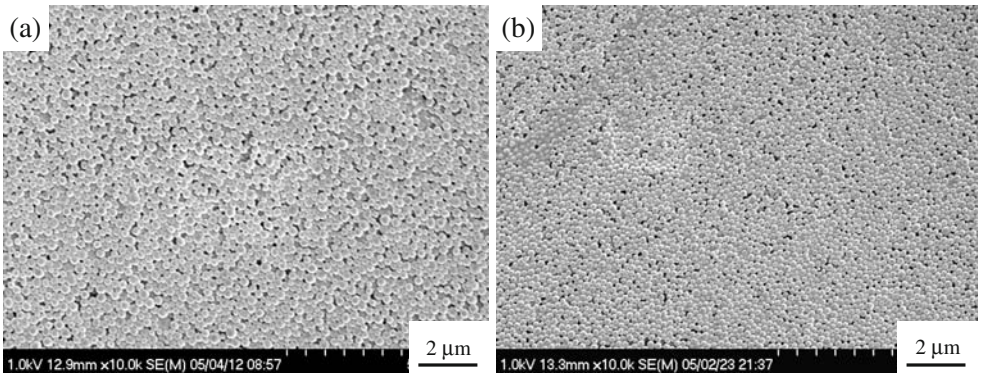


Fig. 8 SEM images of PDLLA microspheres using **a** G_3 (dp=225 nm, CV=15.8%) and **b** G_4 (dp=160 nm, CV=15.4%) copolymers. They have different graft chain length; [PDMA-*g*-PDLLA]=10 g/l

Effect of stirring rate

Figure 2 shows the effect of the stirring rate in the solution on the particle diameter of PDLLA microspheres prepared using G_2 and G_4 copolymers with different molecular structures. As shown in this figure, the stirring rate did not affect the particle diameter.

In addition, in the case with G_2 copolymer, the particle diameter exhibited larger than that in the case with G_4 copolymer. This result implied that the adsorption rate of G_4 copolymer was larger than that of G_2 copolymer because G_4 copolymer shows lower solubility in the solution than G_2 copolymer. As a result, G_4 copolymer prevented primary particles from further aggregation, leading to the formation of small particles with narrow diameter distribution. Thus, it was suggested that the particle diameter depended on the adsorption rate of PDMA-*g*-PDLLA on the surface of primary particles. Namely, it was expected that the particle diameter of PDLLA microspheres was controlled by the molecular structures in PDMA-*g*-PDLLA.

The surface characterization of polymeric microspheres prepared by dispersion polymerization using a dispersion stabilizer with nitrogen element has been performed with X-ray photoelectron spectroscopy (XPS) and Fourier transform infrared spectroscopy (FT-IR) [17–18]. They exhibited the existence of diblock copolymeric stabilizer immobilized on the surface of the polymeric microspheres. For PDMA-*g*-PDLLA, however, XPS and FT-IR are not available. Therefore, we confirmed the existence of PDMA-*g*-PDLLA with ^{1}H NMR. Moreover, we also confirmed the T_g based on PDMA-*g*-PDLLA with DSC. Figure 3 shows the DSC curves of G_4 copolymer and PDLLA microspheres prepared by dispersion polymerization with G_4 copolymer. From this figure, T_g based on PDMA in G_4 copolymer was 287 K. In addition, T_g of G_4 copolymer was confirmed from the DSC curve of the resultant PDLLA microspheres and the T_g shifted higher to 294 K. Therefore, it was suggested that PDLLA anchor blocks in G_4 copolymer were strongly adsorbed on surface of the primary particles.

Effect of graft chain structure

We investigated the effect of the molecular structures in PDMA-*g*-PDLLA on the particle diameter to clarify an important factor of the molecular structure for the adsorption on the surface of primary particles. As the first point, Ober et al. reported that the anchor block in copolymeric stabilizer should be compatible with the particles [19]. In contrast, Baines et al. suggested that the compatibility was not an essential requirement [20]. We synthesized copolymers with different grafted polymer chains to experimentally prove the point mentioned above. PDLLA and PDMS bring hydrophobicity to the copolymer but PEG brings hydrophilicity. In addition, PDLLA and PEG show low solubility in xylene/heptane (1:2, *v*/*v*) during dispersion polymerization. In contrast, PDMS shows high solubility in the solution. The characteristics of the synthesized graft copolymers were summarized in Table 2. Figure 4 shows the SEM image of PDLLA microspheres prepared by dispersion polymerization with PDMA-*g*-PEG as a stabilizer. As a result, in cases with PDMA-*g*-PDLLA and PDMA-*g*-PEG, PDLLA microspheres were prepared. Thus, PDMA-*g*-PEG played a role of a dispersion stabilizer even PEG chain brought no good compatibility with PDLLA particles. In contrast, PDMA-*g*-PDMS gave rise to an undefined-shaped product in the solution even PDMS chain had better compatibility with PDLLA particles than PEG chain. In conclusion, it is necessary for an anchor block in diblock copolymer as a dispersion stabilizer to have low solubility in the solution rather than the compatibility with particles.

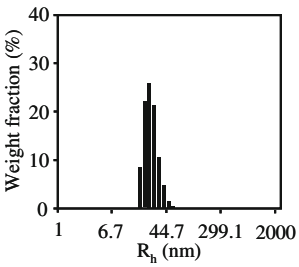


Fig. 9 Size distribution for micellar aggregates of G_4 copolymer in xylene/heptane (1:2, *v*/*v*) at 293 K; R_h=24 nm, [PDMA-*g*-PDLLA]=10 g/l

Effect of graft chain number

Figure 5 shows the effect of the graft chain number and the concentration of PDMA-*g*-PDLLA on the particle diameter and the diameter distribution of PDLLA microspheres. As shown this figure, the particle diameter decreased with increasing the graft chain number and the concentration of G_1, G_2, and G_3 copolymers. Moreover, it was able to control the particle diameter from 200 nm to 5 μm by altering the graft chain number and the concentration of PDMA-*g*-PDLLA. However, as regarding the particle diameter distribution, they were not correlated. Figure 6 shows the SEM images of PDLLA microspheres using G_1, G_2, and G_3 copolymers. In the case with G_1 copolymer, large PDLLA microspheres were prepared. In contrast, in the case with G_3 copolymer, small PDLLA microspheres with narrow diameter distribution were prepared. In addition, in the case with G_2 copolymer, PDLLA particle with a bimodal size distribution were prepared. From these results, it was suggested that the adsorption rate of PDMA-*g*-PDLLA on the surface of primary particles was determined by the kinetic stability of PDMA-*g*-PDLLA micelles in the reaction medium. Winnik et al. and Stejskal et al. reported similar opinions in dispersion polymerization of styrene and methyl methacrylate using poly(ethylene oxide-*b*-styrene) and poly(styrene-*b*-ethylene-*co*-propylene) as a dispersion stabilizer, respectively [11, 21]. The copolymers with low molecular weight in the micelles can undergo relatively rapid exchange with unimers because the copolymer acts as a steric stabilizer. In contrast, high molecular weight copolymers slowly exchange with unimers, causing the polymerization to take place within the micelles. We measured the hydrodynamic diameter (R_h) of PDMA-*g*-PDLLA micelles in xylene/heptane (1:2, *v*/*v*) by DLS measurement. Figure 7 shows the size distributions for the micelles of G_1, G_2, and G_3 copolymers in xylene/heptane (1:2, *v*/*v*) at 293 K. It was confirmed that the G_1 copolymer exhibited a single size distribution and formed larger micelles than that of G_2 and G_3 copolymers because the longer PDMA segment shows higher solubility in the solution. In contrast, G_2 and G_3 copolymers exhibited a bimodal size distribution. It was suggested that both peaks corresponded to the micelles with different R_h because the graft copolymer with various graft chain number exists in the synthesis by free radical polymerization. The micelles of G_3 copolymer are thermodynamically less stable than that of G_1 and G_2 copolymers because G_3 copolymer shows the lowest solubility in the solution. Therefore, the adsorption capability of PDMA-*g*-PDLLA on the surface of primary particles was increased with increasing the graft chain number.

Effect of graft chain length

Figure 8 shows the SEM images of PDLLA microspheres prepared using PDMA-*g*-PDLLA with different graft chain length. From this figure, the particle diameter was decreased with increasing the graft chain length in PDMA-*g*-PDLLA. Figure 9 shows the size distribution of G_4 copolymeric micelles in xylene/heptane (1:2, *v*/*v*) at 293 K. It was confirmed that the micelles of G_4 copolymer showed a similar size to those of G_2 and G_3 copolymers. This result indicated similar tendency to the effect of the graft chain number. Thus, it was concluded that the particle diameter strongly depended on the kinetic stability of copolymeric micelles in the solution.

Particle formation mechanism

Based on the results in above sections and the proposed mechanism of anionic dispersion polymerization of styrene [22, 23], a particle formation mechanism in the dispersion polymerization of D,L-lactide in xylene/heptane (1:2, *v*/*v*) is proposed as shown in Fig. 10. The graft copolymeric stabilizer, PDMA-*g*-PDLLA, forms micelles in the solution. D,L-lactide does not swell the micelles and D,L-lactide is completely soluble in the solution. Therefore, the polymerization of D,L-lactide takes place in the homogeneous medium until the polymer chains achieve a critical chain length to precipitate from the medium. After particle nuclei are formed by the aggregation of precipitated polymer chains, the graft copolymeric stabilizer adsorbs on the

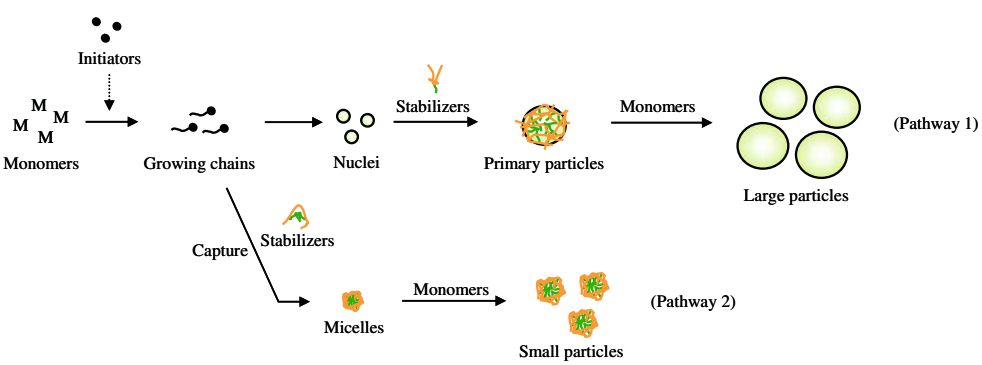


Fig. 10 Schematic representation of particle formation and growth in dispersion polymerization of D,L-lactide with PDMA-*g*-PDLLA

surface of aggregates of particle nuclei to prevent further aggregation. The process of stabilizer adsorption continues until all the surface is occupied, and which forms primary particles. Then the polymerization in the particle goes on through the monomer diffusion from the medium to the particle inside (pathway 1). Moreover, we suggested that the graft copolymeric stabilizer with low solubility in the medium such as G_3 copolymer rapidly exchanged to unimer state and it captured the precipitated polymer chains in the micelles before aggregation. Subsequently, further polymerization of D,L-lactide takes place within the micelles, leading to the formation of small particles with narrow size distribution (pathway 2).

Conclusions

We investigated the effect of molecular structures in the graft copolymer, PDMA-*g*-PDLLA, on the particle diameter of PDLLA microspheres prepared by dispersion polymerization of D,L-lactide in xylene/heptane (1:2, *v*/*v*). The particle diameters of prepared PDLLA microspheres were controlled from 200 nm to 5 μm by altering the concentration and the graft chain number of PDMA-*g*-PDLLA. The anchor block having low solubility in the solution was important for the graft copolymer as a stabilizer. Such copolymers readily formed micelles in the solution. Thus, PDLLA microspheres with a wide range of particle diameter were prepared due to the different kinetic stability of micelles. In addition, the graft chain number and length of PDMA-*g*-PDLLA affect the kinetic stability of micelles. In conclusion, the particle diameter of PDLLA microspheres in dispersion polymerization is controllable by the molecular design of graft copolymeric stabilizer.

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