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

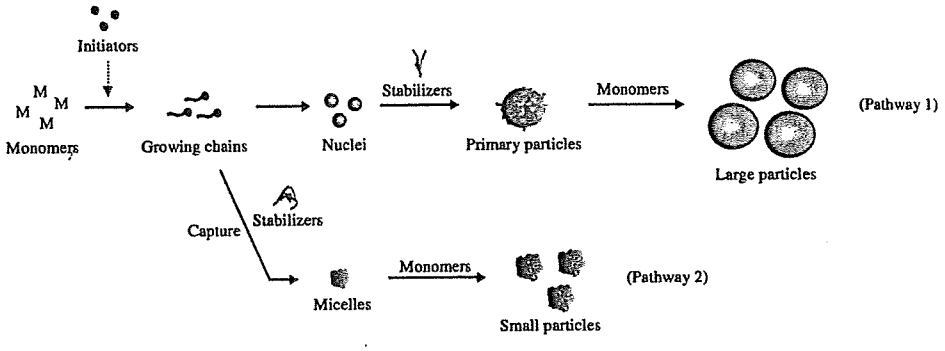

Fig. 10 Schematic representation of particle formation and growth in dispersion polymerization of D,L-lactide with PDMA-*g*-PDLLA

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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Heterogeneous Polymerization with Polyaspartate Macromonomer Having Vinyl Pendant Groups. II. Control of Particle Diameter and Diameter Distribution in Dispersion Copolymerization

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ABSTRACT: To control particle diameter and particle diameter distribution in dispersion copolymerization of styrene and sodium polyaspartate macromonomer containing vinylbenzyl pendant groups, effects of some polymerization parameters, water contents, initiator concentration, styrene monomer concentration, reaction temperature, and type of initiator on the particle diameter and the diameter distribution were investigated. Variation of the water contents from 20 to 80 vol % controls the resultant particle diameter from 0.066 to 0.47 μm. The diameter increased with increasing initiator concentration. This tendency is similar to dispersion polymerization system using a nonpolymerizable stabilizer. Particle diameter distribution broadened with increasing styrene monomer concentration. This trend was attributed to the increase of a period of particle formation. This result indicated that the period of particle formation affected the resultant particle diameter distribution. Particle diameter distribution was successfully improved (CV = 9.1 from 23.6%) by shortening of decomposition time of initiator. © 2009 Wiley Periodicals, Inc. J Polym Sci Part A: Polym Chem 47: 2281–2288, 2009

Keywords: colloids; dispersion polymerization; macromonomers; particle nucleation; particle size distribution

INTRODUCTION

Nano- and microparticles immobilized with polymer chains on the surface have been remarked in recent years. These functional particles have been used for biomedical tools,[1] particulate emulsifier,[2] catalyst,[3–6] and colloidal crystal.[7,8] Functionalization of the polymer chains on the surface can expand the application of these particles.

It is known that heterogeneous polymerization with macromonomer, such as emulsion copolymerization[2,9–13] or dispersion copolymerization,[1,2,13–21] is a one-pot method for preparing particles immobilized with polymer chains on the surface. In this polymerization system, macromonomer plays a role of not only a dispersion stabilizer but a comonomer. Therefore, prepared particles secure high stability and functionality derived from macromonomer chains immobilized onto the surface. Poly (ethylene oxide) (PEO) macromonomer has been used in almost all studies on the heterogeneous polymerization.[11–13,15–21] However, the functionalization of PEO chains is difficult owing to the chemical stability of ethylene oxide units.

We synthesized sodium polyaspartate (PAspNa) macromonomer with vinylbenzyl

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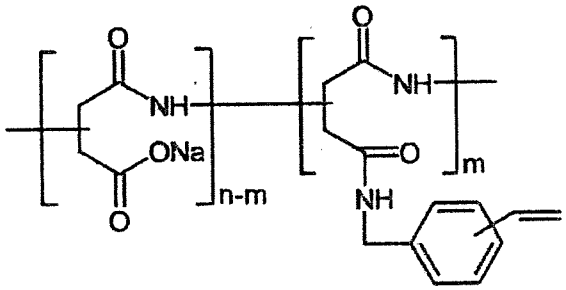

Figure 1. Chemical structure of VBA-PAspNa.

pendant groups (VBA-PAspNa; Fig. 1) as a polymerizable stabilizer in dispersion polymerization.[22] Since poly(succinimide) (PSI), precursor of PAspNa, reacts with various amine compounds without any coupling agent, PAspNa derivatives with various functional pendant groups are easily designed.[23–26] Therefore, dispersion copolymerization with VBA-PAspNa is promising to prepare polymeric particles with polymer chains functionalized as desired on the surface. Submicron sized polymeric particles with broad diameter distribution were obtained by dispersion copolymerization of styrene with VBA-PAspNa in a mixture of ethanol and water.[22]

Adequate ranges of particle diameter in each application fields are different. In addition, monodisperse particles are required for many applications. Therefore, to apply the functional particles produced by dispersion copolymerization with VBA-PAspNa for various application fields, the extension of the control range of particle diameter and improvement of the diameter distribution are important. Many studies about the effects of polymerization parameters on the particle diameter and the distribution in dispersion polymerization have been reported by researchers.[14,15,19–21,27–37] However, there are relatively few studies which discuss the formation mechanism of polydisperse particles in dispersion polymerization in detail. Paine proposed the model of particle formation in dispersion polymerization.[38] In this model, polydisperse diameter distribution results from newborn particle formation and/or coalescence of the particles after stable particle formation. These phenomena result in changes of particle number and diameter distribution of the particles during polymerization. Thus, the investigation of time courses of the particle number and the diameter distribution in dispersion copolymerization is important for elucidation of the formation mechanism of polydisperse particles. In our best knowledge, however, there is no study which discusses about polydispersity of the particle diameter in the term of the time courses of the particle number and the diameter distribution.

In this article, the effects of polymerization parameters such as water contents in media, initiator concentration, styrene monomer concentration, reaction temperature, and type of initiator on the particle diameter and the diameter distribution were examined. Moreover, time courses of the particle number and the diameter distribution during polymerization were investigated with changing the polymerization parameter, which was found to affect the diameter distribution.

EXPERIMENTAL

Material

Styrene, 2,2′-azobisisobutyronitrile (AIBN), 2,2′-azobis(2,4-dimethylvaleronitrile) (ADVN), 4-*t*-butylpyrocatechol and ethanol were obtained from Wako Pure Chemical Industries. Styrene was purified by distillation under reduced pressure. AIBN and ADVN were purified by recrystallization from ethanol. 4-*t*-Butylpyrocatechol was used without purification. Water was purified by a Millipore Milli-Q purification system.

Synthesis of PAspNa Macromonomers

VBA-PAspNa was synthesized by the reaction between PSI and vinylbenzylamine (VBA) and the hydrolysis reaction with sodium hydroxide. The detailed synthesis procedure was described in our previous article.[22] A vinyl group fraction of VBA-PAspNa used in this study was fixed at 10 mol %. Weight-average molecular weight (M_w) and the distribution (M_w/M_n) of the PSI was 29,700 and 2.9, which were measured by gel permeation chromatography (GPC) with polystyrene standard.

Dispersion Copolymerization

Dispersion copolymerization was carried out in a reactor equipped with a reflux condenser and a magnetic stirrer, and which was placed in an oil bath equipped with a temperature control. A typical procedure for dispersion copolymerization of styrene with VBA-PAspNa is presented below: 0.107 g of AIBN and 1.34 g of styrene were dissolved in ethanol 27 mL, and it added into the aqueous solution containing of 0.05 g VBA-

PAspNa 18 mL. The mixture was polymerized in the reactor at 343 K for 6 h under nitrogen atmosphere.

Measurements and Characterization

The diameter and the diameter distribution of particles were measured by scanning electron microscopy (SEM, Hitachi *S*-4700). The number-average particle diameter was obtained by counting 200 particles in SEM photographs. Coefficient of variation (CV) of the particle diameter was calculated from the following equation:

$$CV(\%) = \frac{\text{Standard derivation } (\mu m)}{\text{Number} - \text{average particle diameter } (\mu m)} \times 100 \quad (1)$$

Styrene monomer conversion was calculated from the unreacted styrene monomer concentration measured as follows: Small amount of samples withdrawn at different polymerization intervals was added to methanol with 4-*t*-butylpyrocatechol to terminate polymerization. This solution was centrifuged at 30,000 rpm for 15 min to precipitate and collect polymers, and unreacted styrene concentration in the supernatant was measured by high-performance liquid chromatography (TOSOH SC-8010 system) with a UV–VIS detector (UV-8010, λ = 254 nm) with the mixture of methanol/water = 7/3 (vol/vol) as an eluant. The column was a TSK-Gel ODS-80Ts QA (150 × 4.6 mm, TOSOH). The flow rate and the column temperature were 0.8 mL/min and 313 K, respectively. Particle number was calculated from the particle diameter and the styrene monomer conversion.

RESULTS AND DISCUSSION

Effect of Water Contents in Medium

The polarity of medium significantly affects the diameter of the particles prepared by dispersion polymerization.[27,29–33,37] When oligomers have larger molecular weight than the critical value for precipitation, these are precipitated and coagulated to form particle nuclei. The particle nuclei subsequently coagulate among each other and the number of particle nuclei decreases until enough stabilizers adsorb to stabilize them. Yielding a large number of particle nuclei results in the decrease in the diameter of final particles. The critical value for precipitation strongly depends on the solubility of oligomers in the medium. In addition, since polarity of medium also affects the solubility of dispersion stabilizers, it determines their adsorption behavior and stability. Therefore, the polarity of medium is a principal parameter affecting resultant particle diameter in dispersion polymerization.

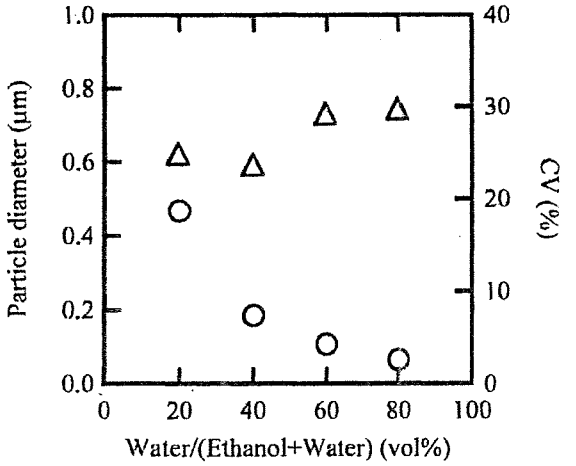

Figure 2. Effect of water contents in the media on particle diameter (○) and CV (△). [Styrene] = 29.8 g/L, [Initiator] = 8 wt %-monomer.

The solvents used in this study were a mixture of ethanol and water because the ratio of the solvent controls the polarity of the medium. Water contents of the standard condition was 40 vol %. Dispersion copolymerization was carried out in the media with different water contents was carried out to examine the effect of the water contents on the particle diameter and CV. Styrene monomer was not completely solved in the media with more than 60 vol % of water, and the polymerization occurred in the heterogeneous system. Effect of the water contents in media on the particle diameter and CV is shown in Figure 2. Particle diameter was significantly decreased with increasing water contents. Variation of the water contents from 20 to 80 vol % facilitates the control of particle diameter from 0.066 to 0.47 μm. The decrease in diameter with increasing water contents is explained as follows: (1) Increasing water contents induces further formation of particle nuclei because the solubility of polystyrene in water is lower than that in ethanol. (2) Since PAspNa is insoluble in ethanol and soluble in water, the solubility of VBA-PAspNa is enhanced with increasing water contents. Thus, the PAspNa chains on the surface of particle nuclei provide

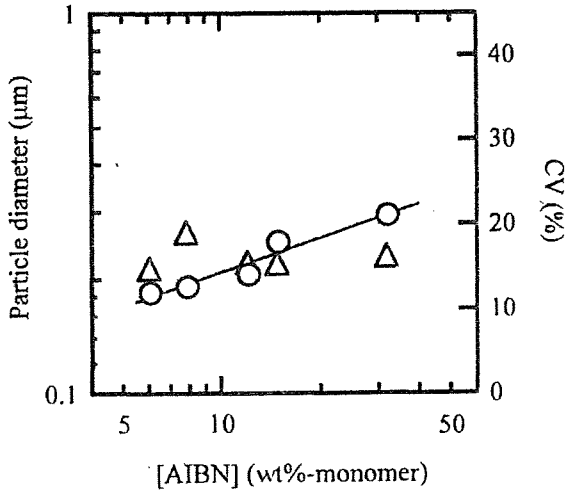

Figure 3. Effect of initiator concentration on particle diameter (○) and CV (△). [Styrene] = 7.5 g/L, ethanol/water = 3/2.

high dispersion stability to the particle nuclei and prevent from coagulating, resulting in the formation of a large number of particle nuclei.

Diameter distribution of the particles prepared in water-rich media was slightly broader than that prepared in ethanol-rich media. When dispersion copolymerization in water-rich solvents is considered, the particle diameter distribution is supposed to be monodisperse because of the high dispersion stability. However, this result indicated opposite tendency to our prediction. Therefore the polymerization was probably occurred in heterogeneous phase.

Effect of Initiator Concentration

Effect of initiator concentration on the diameter and the CV of particles obtained is shown in Figure 3. As seen in this figure, the particle diameter increased with increasing initiator concentration as the follow equation:

$$dp = [\text{Initiator}]^{0.30}$$

Many researchers have reported that a particle diameter increased with increasing initiator concentration in dispersion polymerization with homopolymer as a nonpolymerizable dispersion stabilizer.[28,29,32,36,37] This behavior is explained as follows. The molecular weight of polystyrene formed is decreased by termination reactions with increasing initiator concentration. In dispersion polymerization using homopolymer as a dispersion stabilizer, free radicals generated in the solution abstract the hydrogen atoms from the homopolymer chain during polymerization. Graft polymerization of monomer from these radical sites occurred and led to produce the graft copolymers which adsorb onto the particles. The graft copolymers with shorter polystyrene segment are formed at higher initiator concentration, which make it more soluble in the medium and thus less effective as a stabilizer. This leads to low number of particle nuclei and large particles. Since VBA-PAspNa is a macromonomer containing multiple vinyl groups in the side chains, we can imagine that the stabilization mechanism of VBA-PAspNa is similar to that of homopolymer. Thus, the effect of initiator concentration on the polymerization behavior using VBA-PAspNa was corresponding to that using homopolymer.

Effect of Styrene Monomer Concentration

Effect of styrene monomer concentration on particle diameter and CV is shown in Figure 4. Particle diameter was almost constant regardless of styrene monomer concentration in dispersion copolymerization with VBA-PAspNa. CV of the resultant particles increased with increasing styrene monomer concentration. In the conventional dispersion polymerization of styrene, the particle diameter increases with increasing feed monomer concentration.[28–30] Styrene monomer in a medium acts as a good solvent for the polymer, polystyrene, formed in dispersion polymerization. Thus, at

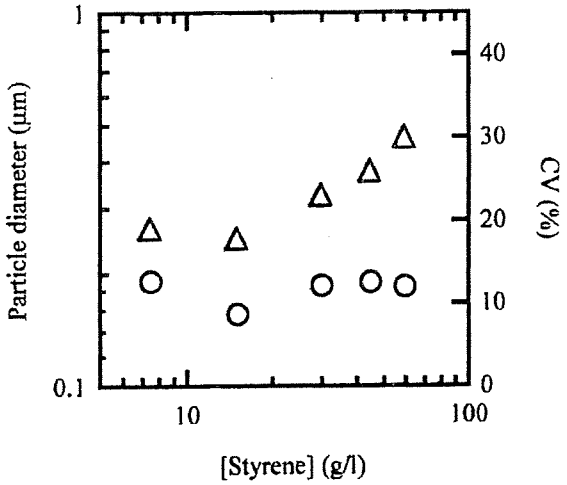

Figure 4. Effect of styrene monomer concentration on particle diameter (○) and CV (△). [Initiator] = 8 wt %-monomer, ethanol/water = 3/2.

high styrene monomer concentration, large particles are produced as described in the above section. However, dispersion copolymerization of styrene with VBA-PAspNa showed a different tendency.

Paine proposed that polydisperse diameter distribution resulted from newborn particle formation and/or coalescence of the particles after initial particle formation. In this model, broadening of the diameter distribution involving increase in the particle number is due to the newborn particle formation, and that involving decrease in the particle number is due to the coalescence of the particles. To clarify the reason why the diameter distribution was broadened with increasing styrene monomer concentration, the time course of particle number and CV in dispersion copolymerization with different monomer concentrations were investigated. The results are shown in Figure 5(a,b). In all of the polymerization conditions, CV increased with polymerization time and then reached on almost constant value. Particle number also increased from the beginning of polymerization and then decreased to a constant value. The period of increase in CV and particle number indicated that particle nucleation continues to occur in this period. Since the newborn particles are smaller than the old particles, the CV was enhanced by the newborn particle formation. Decrease of particle number after the maximum value is probably caused by coagulation of the particles. The particles formed at initial polymerization stage grew to increase the surface area of particles. The increase of surface area advanced the coagulation of particles, and this led to decrease the particle number.

It was found that the both periods in which CV and particle number increased were extended and therefore these final values increased with increasing styrene monomer concentration. This means that the particle nucleation period was prolonged with increasing styrene monomer concentration. The time courses of the amount of unreacted styrene and the CV of particle diameter at a different styrene monomer concentration are shown in Figure 5(b,c). From these results, the CV was gradually increased when styrene remained in the system. This indicated that newborn particles were produced as long as styrene monomer was available for polymerization. In general, since particle nuclei after the initial particle nucleation are instantly captured by the growing particles, no formation of newborn particles occurs during polymerization.[27,37] However,

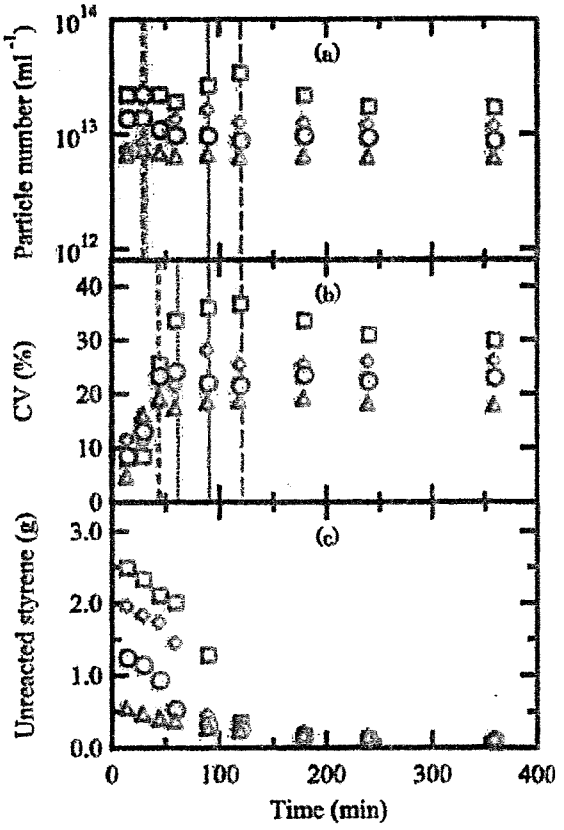

Figure 5. Time courses of (a) particle number, (b) CV, and (c) unreacted styrene amounts in dispersion copolymerization with various concentration of styrene monomer: [Styrene]= 14.9 g/L (△, - - -), 29.8 g/L (○, ·····), 44.7 g/L (◇, —), 59.6 g/L (□, – – –). The lines indicate the times for maximum values of the particle number and CV during polymerization.

Figure 5 implies that capturing particle nuclei by the growing particles is difficult. The surface of particles prepared with VBA-PAspNa would be significantly covered with PAspNa chains at the initial polymerization stage. During dispersion polymerization, styrene oligomers are generated in solution. The oligomers are precipitated and coagulate among each other to form particle nuclei. Graft copolymers are also generated in the solution and adsorb to the particle nuclei to stabilize them. Therefore, stabilizer chain density on the particle surface increases with progress with polymerization.[38] The low solubility of VBA-PAspNa in the ethanol-rich solvent leads to fast adsorption of VBA-PAspNa onto the particle surface. It seems that sufficient surface coverage of PAspNa chains prevents from capturing particle nuclei. The no dependency of styrene

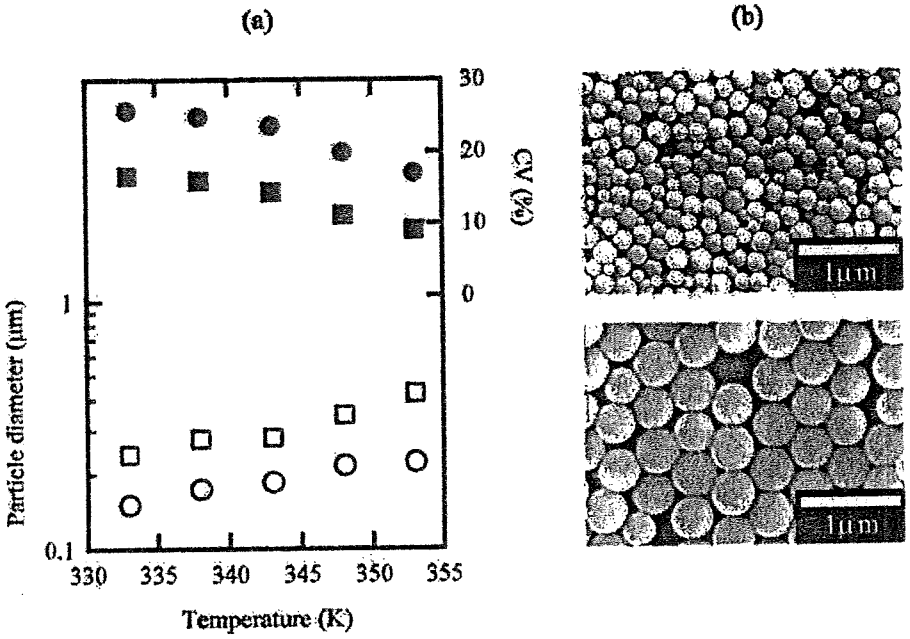

Figure 6. (a) Effects of reaction temperature on particle diameter (open key) and CV (close key) with AIBN (○, ●), ADVN (□, ■) as an initiator. [Styrene] = 29.8 g/L, [Initiator] = 8 wt %-monomer, ethanol/water = 3/2. (b) SEM images of particles prepared with AIBN at 343 K (top) and with ADVN at 353 K (bottom).

concentration on particle diameter is also explained by the decrease in the number-average particle diameter along with the small newborn particle formation.

Effect of Reaction Temperature and Type of Initiator

As mentioned above, the long period of particle nucleation gives rise to broader particle diameter distribution in dispersion copolymerization with VBA-PAspNa. To reduce the CV of the prepared particles, the nucleation time needs to be shortened. Radical generation relates to the particle nucleation. Thus, the period of particle formation expects to decrease by fast decomposition rate of initiator. The decomposition rate of initiator depends on the reaction temperature and the molecular structure. To demonstrate the effect of initiator decomposition rate on the particle diameter distribution, dispersion copolymerization with different reaction temperatures and initiators were carried out. Reaction temperature was varied from 333 K to 353 K. AIBN or ADVN was used as an initiator. The decomposition rate is faster at higher temperature. In addition, the half-life time of ADVN, ~36 min at 343 K, is shorter than that of AIBN, ~340 min at 343 K. The effects of reaction temperature on the particle diameter and the CV of particles with AIBN and ADVN are shown in Figure 6(a). Figure 6(b) shows SEM images of the particles prepared with AIBN at 343 K and with ADVN at 353 K. These results indicated that the elevation of reaction temperature increased the particle diameter and decreased the CV. In addition, large particles with narrow diameter distribution were obtained by using ADVN. The increase of the particle diameter by fast decomposition rate of initiator might be similar to the phenomenon at high initiator concentration.

As expected, dispersion copolymerization with ADVN at high temperature produced particles with low CV. The time courses of particle number and CV of particles prepared by dispersion copolymerization at different reaction temperatures are shown in Figure 7. These results showed that the period of increase in particle number and CV, the period of particle nucleation, was shorter at higher reaction temperature. Likewise, the time courses of particle number and CV of particles prepared by dispersion copolymerization with using AIBN or ADVN are shown in Figure 8. When using AIBN, the CV increased until 60 min. Conversely, when using ADVN, the CV was

almost constant after 45 min, and the particle number was almost constant during polymerization.

From these results, the polymerization using a fast-decomposing initiator at high temperature improves the diameter distribution of the particles obtained owing to the short particle formation period. The optimization of polymerization condition (reaction temperature: 343→353 K, initiator: AIBN→ADVN) successfully reduced the CV of the particles to 9.1 from 23.6% [Fig. 6(b)].

CONCLUSIONS

In dispersion copolymerization of styrene with VBA-PAspNa in a mixture of ethanol and water, polymerization parameters such as water contents in media, initiator concentration, styrene monomer concentration, reaction temperature, and type of initiator affected the particle diameter and the diameter distribution. The particle diameter greatly decreased and CV slightly increased with increasing water contents in the media. Particle diameter increased with increasing initiator concentration. The period of increase of CV and particle number, namely, the period of particle formation increased with increasing styrene monomer concentration. From this result, we found that the particle diameter distribution in the final particles was determined by the nucleation period. Monodispersity of the particles can be improved by shortening of the decomposition time of initiator, which is determined by the reaction temperature and the molecular structure.

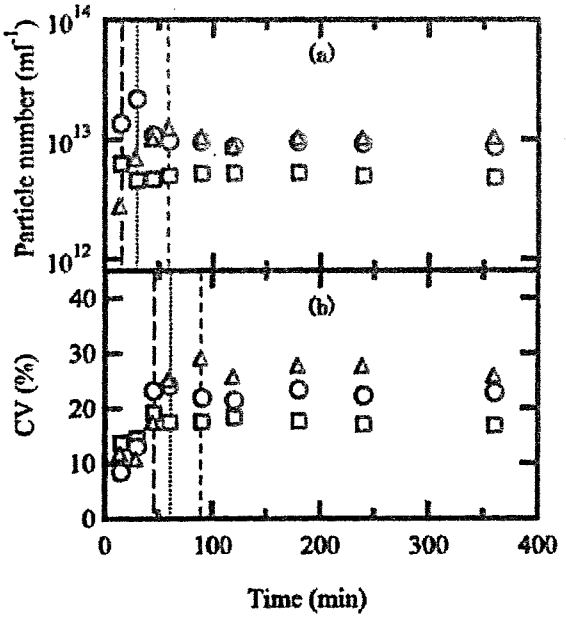

Figure 7. Time courses of (a) particle number and (b) CV in dispersion copolymerization at different reaction temperature: 333 K (△, - - -), 343 K (○, ·····), 353 K (□, – – –). The lines indicate the times for maximum values of the particle number and CV during polymerization.

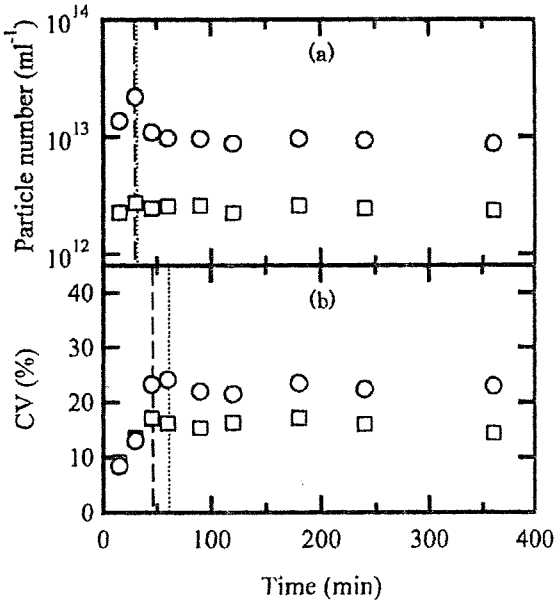

Figure 8. Time courses of (a) particle number and (b) CV in dispersion copolymerization with AIBN (○, ·····), ADVN (□, – – –) as an initiator. The lines indicate the times for maximum values of the particle number and CV during polymerization.

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Role of Dispersion Stabilizer with Hydroxy Groups in Preparation of Monodisperse Polylactide Microspheres

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ABSTRACT: Monodisperse poly(D,L-lactide) (PDLLA) microspheres were prepared by dispersion polymerization of D,L-lactide in xylene/heptane (1/2, *v/v*) with poly[(dodecyl methacrylate)-*co*-(2-hydroxyethyl methacrylate)] (P(DMA-*co*-HEMA)) as a dispersion stabilizer. P(DMA-*co*-HEMA) contains hydroxy groups, which act as an initiation group for pseudoanionic dispersion polymerization. The best coefficient of variation (CV) values concerning particle diameter distribution and the particle diameter of obtained PDLLA microspheres were 3.7% and 5.3 μm, respectively. The particle diameter decreased with increasing concentration of P(DMA-*co*-HEMA) and HEMA maintained low CV (<10%) values. As a result, monodisperse PDLLA microspheres ranging from 1.3 to 5.3 μm were obtained. In addition, it was found that monodisperse PDLLA microspheres were obtained by sufficient capture of growing polymers and monomers in the particle growth stage. Therefore, the HEMA concentration in P(DMA-*co*-HEMA) strongly affecting the capturing capability is the most important factor. © 2009 Wiley Periodicals, Inc. J Polym Sci Part A: Polym Chem 47: 5230–5240, 2009
Keywords: colloids; dispersion polymerization; micelles; monodisperse polylactide microspheres; stabilization

INTRODUCTION

Heterogeneous polymerization for preparing polymeric particles is mainly classified as emulsion,[1] dispersion,[2] and suspension polymerization.[3] Dispersion polymerization, which facilitates the preparation of microparticles with narrow diameter distribution in a single step, has attracted attention for biomedical and chemical applications such as coatings, inks, adhesives, and diagnosis carriers.[4–6] The degree of success in each application depends on the particle diameter and diameter distribution. Therefore, it is important to understand the role of the dispersion stabilizer and how to control the particle diameter and diameter distribution using the dispersion stabilizer.

Dispersion polymerization is carried out in a reaction medium that dissolves monomers, but not polymers. Polymerization continues in the reaction medium until the critical molecular weight of a polymer chain for solubility is reached, and then the precipitated particles are stabilized using the dispersion stabilizer. When using polystyrene-*b*-poly(ethylene glycol), which contains both soluble and insoluble polymer segments in a medium, as a dispersion stabilizer, Winnik and coworkers showed the existence of micelles comprised of several hundred molecules of a diblock copolymer and micellar clusters corresponding to the aggregation of tens of micelles in aqueous solution from dynamic light scattering measurements.[7,8] Moreover, in free radical polymerization,

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as the dissociation of an initiator is relatively slow, the duration of chain initiation is prolonged. Thus, the particle formation period in free radical dispersion polymerization with a diblock copolymeric stabilizer is complex. In contrast, *in-situ* polymerized graft copolymers are used during dispersion polymerization of styrene.[9–11] There are precursor polymers that contain active sites for chain transfer of radicals such as hydroxypropyl cellulose, poly(acrylic acid), and polyvinylpyrrolidone (PVP). As micelle formation of these polymeric stabilizers is negligible at the initial stage of polymerization, it would be promising to prepare monodisperse polystyrene microspheres. In a previous study, El-Aasser and coworkers prepared polystyrene microspheres with narrow diameter distribution by anionic dispersion polymerization using polystyrene-*b*-polybutadiene and *sec*-butyllithium as a dispersion stabilizer and an initiator, respectively.[12] During this anionic dispersion polymerization, all initiator was consumed by 1–2% of monomer.[13] Therefore, it is a favorable condition for understanding the role of the dispersion stabilizer.

Biodegradable polymeric microspheres have been recently developed for chemical materials such as coatings, inks, adhesives, and controlled drug delivery systems.[14–17] A typical biodegradable polymer, polylactide (PLA), exhibits good mechanical properties, biodegradability, and biocompatibility for use in those areas.[18–20] Slomkowski and coworkers reported that PLA microspheres with narrow diameter distribution, and a coefficient of variation (CV) of 12%, were prepared by dispersion polymerization of lactide in 1,4-dioxane/heptane (1:4, *v/v*) using poly(dodecyl acrylate)-*g*-poly(ε-caprolactone) as a dispersion stabilizer.[21–23] We also reported that poly(D,L-lactide) (PDLLA) microspheres with narrow diameter distribution and a CV of 12.5%, were prepared by dispersion polymerization of D,L-lactide in xylene/heptane (1:2, *v/v*) using copolymer grafting PLLA, poly(dodecyl methacrylate)-*g*-polylactide, as a dispersion stabilizer.[24,25] However, monodisperse PDLLA microspheres with a CV < 10%, have not been obtained.

We have synthesized poly[(dodecyl methacrylate)-*co*-(2-hydroxyethyl methacrylate)] (P(DMA-*co*-HEMA)) containing hydroxy groups, which act as an initiation group for pseudoanionic dispersion polymerization, leading to the formation of the PDLLA-grafted copolymer, P(DMA-*co*-HEMA)-*g*-PDLLA. Consequently, P(DMA-*co*-HEMA) brought about monodisperse PDLLA microspheres by pseudoanionic dispersion polymerization of D,L-lactide.[26] The advantage of P(DMA-*co*-HEMA) was the formation of a graft copolymer *in situ*. Omi et al. reported that the addition of a small amount of L-ascorbic acid (AA) provided monodisperse polystyrene microspheres during dispersion polymerization with PVP as a dispersion stabilizer.[27] AA acted as an antioxidant, and the oxidized form of AA takes part in the abstraction of a hydrogen atoms from PVP. As a result, monodisperse polystryrene microspheres were prepared by promoting the grafting of PVP. Therefore, the grafting of a dispersion stabilizer produced *in situ* is the most important factor in preparing monodisperse polymeric microspheres by dispersion polymerization. P(DMA-*co*-HEMA) contains initiation points of polymerization, and the number of points are controllable. Therefore, we expect there exists an optimal graft chain number in a grafted copolymeric stabilizer for preparing monodisperse PDLLA microspheres. We investigated the role of P(DMA-*co*-HEMA) in the control of particle diameter and diameter distribution during dispersion polymerization and suggested a solution for preparing monodisperse PDLLA microspheres.

EXPERIMENTAL

Materials

D,L-Lactide (Purac) was purified by recrystallization from toluene. 2-Hydroxyethyl methacrylate (HEMA), dodecyl methacrylate (DMA) (Wako Pure Chemical Industries, Ltd.), and tin(II) 2-ethylhexanoate (Aldrich) were purified by distillation under reduced pressure.[28,29] Xylene and heptane (dehydrated-grade) (Wako Pure Chemical Industries, Ltd.) were stored in a glove box filled with argon gas. Other reagents (Wako Pure Chemical Industries, Ltd.) were used as received.

P(DMA-*co*-HEMA) Synthesis

The synthesis of P(DMA-*co*-HEMA), C_2 in Table 1, is described as a typical example of synthesis. DMA (7.9 g, 31.18 mmol), HEMA (81 mg, 0.62 mmol), and dehydrated toluene (24 mL) were placed into a round-bottom reactor. After nitrogen was added to remove oxygen, the reactor was immersed in an oil bath at 358 K. Dehydrated toluene dissolved in benzoyl peroxide (BPO) (304 mg, 1.25 mmol) was added to initiate polymerization. Polymerization was conducted for 3 h.

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Table 1. Molecular Structure of P(DMA-*co*-HEMA)

Code	M_n	M_w/M_n	F_{HEMA} (mol %)	N_{HEMA} (units)
H_1	8,200	2.16	0.0	0.0
C_1	16,900	2.42	0.9	0.6
C_2	16,300	2.48	1.3	0.8
C_3	18,200	2.44	2.3	1.7
C_4	17,000	2.24	4.1	2.9

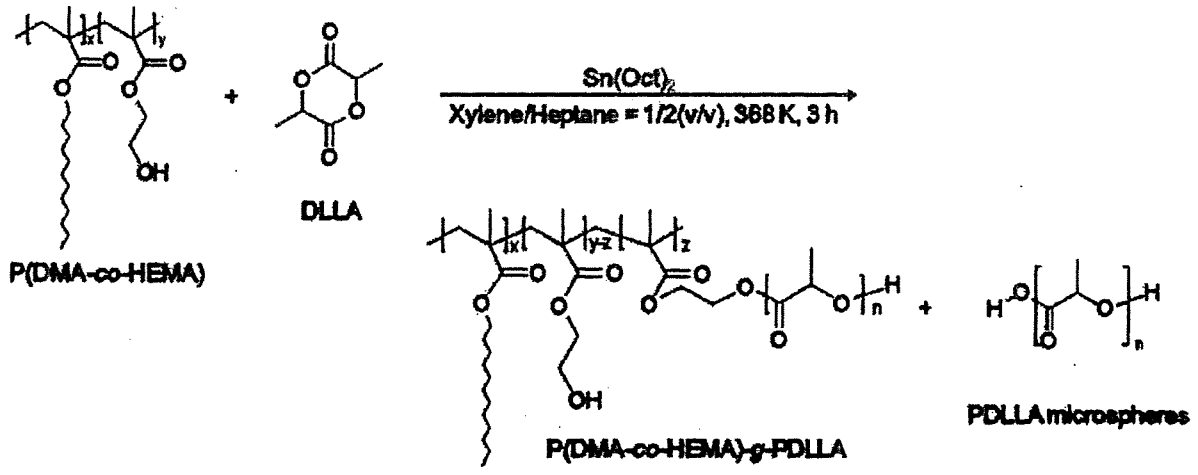
Afterward, the reaction mixture was poured into excess methanol to remove the remaining DMA and HEMA. After purification, the obtained polymer was dried under reduced pressure at 313 K.

PDLLA Microspheres Preparation

PDLLA microspheres were prepared according to a typical preparation procedure of PDLLA microspheres shown in Scheme 1. D,L-lactide (500 mg, 3.47 mmol) was added into dehydrated xylene/heptane (1:2, *v/v*) (17 mL) dissolved in P(DMA-*co*-HEMA). The solution was stirred at 120 rpm with a magnetic stirrer. Dehydrated xylene/heptane (1:2, *v/v*) (3 mL) dissolved in stannous 2-ethylhexanoate (475 mg, 0.12 mmol) as a catalyst was prepared. This was added into the solution using a syringe, and polymerization was conducted at 368 K for 3 h. After polymerization, the reaction solution was poured into excess cold heptane. The solution was centrifuged for 3 min at 6000 rpm, and the collected microspheres were redispersed into heptane. This solution was filtered to collect the prepared microspheres. During polymerization, aliquots of the sample were periodically withdrawn through a syringe for intermittent characterization of the polymerization progress.

Characterization

The chemical structures of the synthesized polymers were confirmed with ^1H NMR (AL300 SC-NMR, JEOL) using $CDCl_3$ as a solvent. The weight-averaged molecular weight (M_w) and the polydispersity index (M_w/M_n) of the synthesized polymers were measured using gel permeation chromatography (HLC 8120, Tosoh, GPC) equipped with a refractive index detector based on polystyrene standards with tetrahydrofuran as an eluent. A scanning electron microscope (S-4700, Hitachi, SEM) was used to study the morphology of PDLLA microsphers, particle diameter, and diameter distribution. Dynamic light scattering measurement (FPAR-1000, Otsuka Electronics Co., DLS) was carried out at 293 K using a He-Ne laser with a wavelength of 633 nm to determine the hydrodynamic diameter (R_h) of the micelles of P(DMA-*co*-HEMA) and P(DMA-*co*-HEMA)-*g*-PDLLA in xylene/heptane (1:2, *v/v*). The mean hydrodynamic diameter was evaluated using the cumulant method. The conversion of D,L-lactide was measured using high-performance liquid chromatography (LC-6A, Shimazu, HPLC) with methanol/water (1:49, *v/v*) as an eluent and a UV-detector at 216 nm.



Scheme 1. Preparation of PDLLA microspheres.

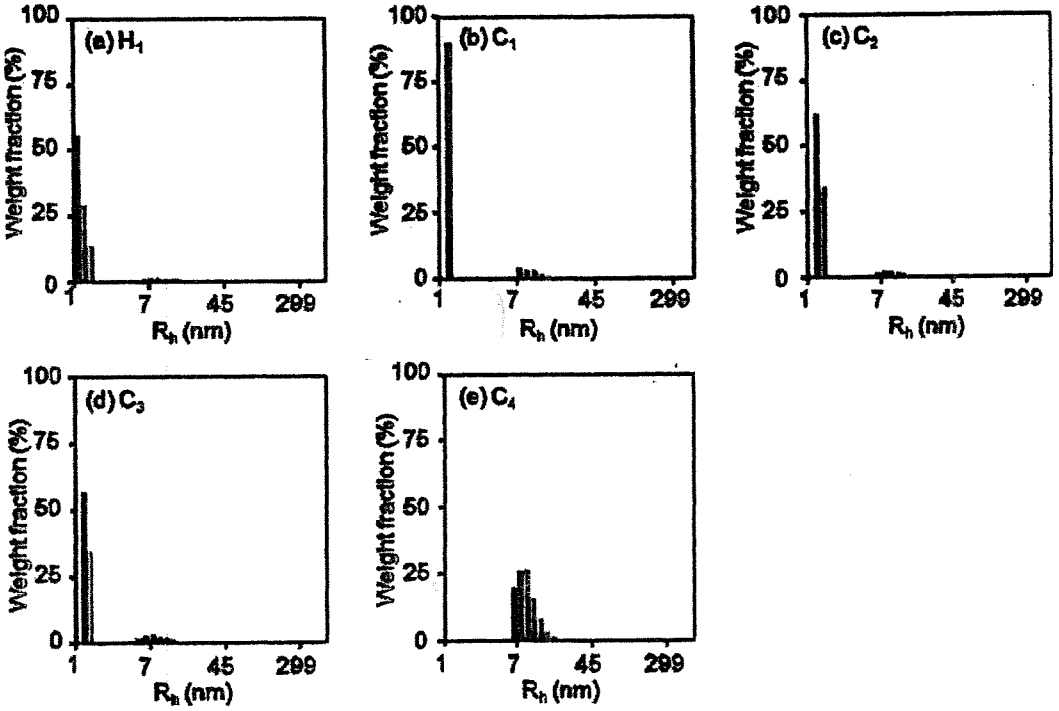


Figure 1. Size distributions of P(DMA-*co*-HEMA) in xylene/heptane (1:2, *v/v*); (a) H_1 (R_h = 1.1 and 8.6 nm), (b) C_1 (R_h = 1.2 and 8.6 nm), (c) C_2 (R_h = 1.3 and 8.8 nm), (d) C_3 (R_h = 1.3 and 7.4 nm), and (e) C_4 (R_h = 7.9 nm), [P(DMA-*co*-HEMA)] = 10 g/L.

RESULTS AND DISCUSSION

P(DMA-*co*-HEMA) Synthesis

P(DMA-*co*-HEMA) was successfully obtained by free radical copolymerization of DMA and HEMA using BPO as an initiator. The analytical results of synthesized copolymers are summarized in Table 1. To investigate the effect of the molecular structure of P(DMA-*co*-HEMA) on the particle diameter and diameter distribution of PDLLA microspheres, five kinds of P(DMA-*co*-HEMA) with different HEMA concentrations were synthesized. The ^{1}H NMR spectrum of P(DMA-*co*-HEMA) showed peaks at 3.9 ppm ($COOCH_2$ for DMA unit) and at 4.1 ppm ($COOCH_2$ for HEMA unit). Furthermore, there were no peaks detected around 5.6 and 6.1 ppm (double bond for DMA and HEMA) in the spectrum. Therefore, P(DMA-*co*-HEMA) was finally identified. The fraction of HEMA units in P(DMA-*co*-HEMA), F_{HEMA}, was calculated by the integration ratios corresponding to 3.9 ppm ($COOCH_2$ for DMA unit) and 4.1 ppm ($COOCH_2$ for HEMA unit) in the ^{1}H NMR spectrum.

This was defined by the following equation:

$$F_{HEMA} = \frac{A_{HEMA}}{(A_{DMA} + A_{HEMA})}$$

where A_{HEMA} and A_{DMA} denote the peak areas of $COOCH_2$ for HEMA and DMA units in the ^{1}H NMR spectrum of P(DMA-*co*-HEMA), respectively. The number of HEMA units in P(DMA-*co*-HEMA), N_{HEMA}, is defined as follows:

$$N_{HEMA} = \frac{M_{n\,copolymer}}{(M_{n\,DMA}\frac{A_{DMA}}{A_{HEMA}} + M_{n\,HEMA})}$$

where $M_{n\,copolymer}$, $M_{n\,DMA}$, and $M_{n\,HEMA}$ denote the number-averaged molecular weight of P(DMA-*co*-HEMA), DMA, and HEMA, respectively.

DLS Measurement of P(DMA-*co*-HEMA)

DLS measurements clarified the presence of P(DMA-*co*-HEMA) micelles, as shown in Figure 1. P(DMA-*co*-HEMA) exhibited a bimodal size distribution based on unimers and polymeric micelles

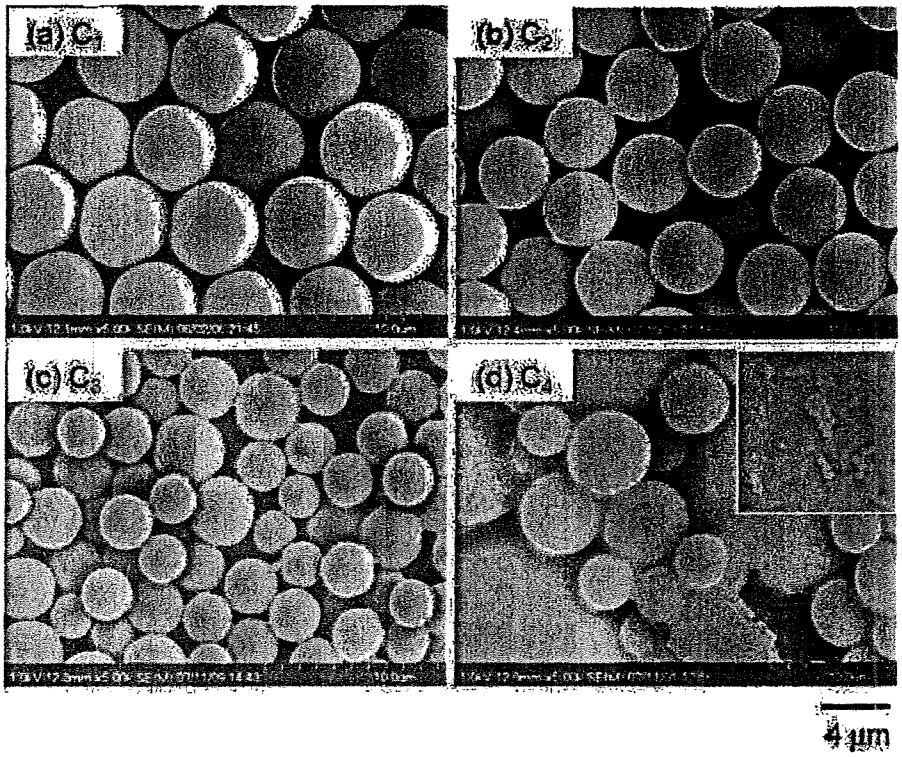


Figure 2. SEM images of PDLLA microspheres prepared by dispersion polymerization using P(DMA-*co*-HEMA) with different HEMA concentrations; (a) C_1 (dp = 5.3 μm, CV = 3.7%), (b) C_2 (dp = 4.5 μm, CV = 4.9%), (c) C_3 (dp = 3.2 μm, CV = 13%), and (d) C_4 (polydispersity), [P(DMA-*co*-HEMA)] = 1.0 g/L.

in xylene/heptane (1:2, *v/v*) when using H_1, C_1, C_2, and C_3 (refer Table 1). The mean hydrodynamic diameter (R_h) of unimers and polymeric micelles were about 1.3 and 8.0 nm, respectively. In addition, most of the P(DMA-*co*-HEMA) were in a unimer state in the solution. In contrast, when using C_4, P(DMA-*co*-HEMA) exhibited a single size distribution based on the polymeric micelles in the solution. This result indicated that the formation of polymeric micelles was induced by the existence of hydroxy groups in P(DMA-*co*-HEMA), which showed a low affinity to the medium. Winnik and coworkers reported that the large molecular weight block copolymers showed the presence of micellar aggregates in methanol, which might induce the polydispersity of the particles during dispersion polymerization.[8] Therefore, it was assumed that the HEMA concentration in P(DMA-*co*-HEMA) affecting micelle formation should be a contributing factor to prepare monodisperse PDLLA microspheres during dispersion polymerization of D,L-lactide.

Effect of HEMA Concentration on Particle Size Distribution

Figure 2 shows SEM images of PDLLA microspheres prepared by dispersion polymerization using P(DMA-*co*-HEMA) with different HEMA concentrations. As shown in Figure 2, monodisperse PDLLA microspheres were obtained using only C_1 and C_2. The best value of CV and the particle diameter of PDLLA microspheres were 3.7% and 5.3 μm, respectively [Fig. 2(a)]. In contrast, PDLLA microspheres were not obtained during dispersion polymerization using H_1, which had no HEMA unit. These results suggested that the preparation of spherical PDLLA microspheres require a dispersion stabilizer containing PDLLA segments to interact with the precipitated particles. The PDLLA segment in a dispersion stabilizer physically adsorbs on the surface of the precipitated particles, and the PDMA segment creates high solubility in the medium. In addition, the CV increased with increasing HEMA concentrations in P(DMA-*co*-HEMA), and polydisperse

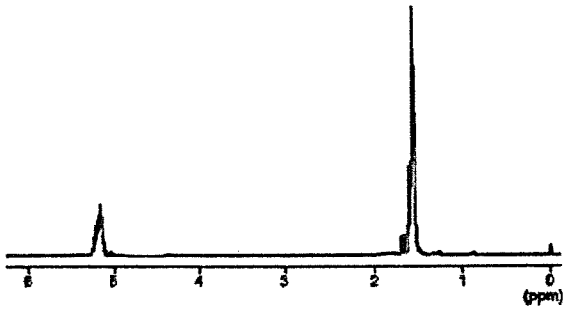


Figure 3. ^{1}H NMR spectrum of PDLLA microspheres prepared by dispersion polymerization using P(DMA-*co*-HEMA) (C_2).

PDLLA microspheres were prepared during dispersion polymerization using C_3 and C_4 [Fig. 2(c,d)]. In particular, many nanoparticles of P(DMA-*co*-HEMA)-*g*-PDLLA were obtained when using C_4 because most monomers were consumed by the hydroxy groups in P(DMA-*co*-HEMA) during polymerization. Therefore, we concluded that there is an optimal HEMA concentration for preparing monodisperse PDLLA microspheres.

Characterization of PDLLA Microspheres

Figure 3 shows the ^{1}H NMR spectrum of PDLLA microspheres prepared by dispersion polymerization using C_2 as a dispersion stabilizer. The spectrum showed peaks at 1.7 and 5.2 ppm (CH_3 and CH for PLA), but no peaks of P(DMA-*co*-HEMA)-*g*-PDLLA were detected. During dispersion polymerization of styrene or methyl methacrylate using a conventional stabilizer, PVP and the existence of a graft copolymer on the surface of particles were confirmed using FTIR and X-ray photoelectron spectroscopy.[30,31] This suggests that the adsorption of P(DMA-*co*-HEMA)-*g*-PDLLA on the particle surface was weak. In addition, no peak at 4.1 ppm ($COOCH_2$ for HEMA unit) was detected in the ^{1}H NMR spectrum of P(DMA-*co*-HEMA)-*g*-PDLLA. Therefore, all hydroxy groups in P(DMA-*co*-HEMA)reacted, and PDMA-*g*-PDLLA was produced *in situ*. The number-averaged molecular weight of the graft chain was approx. 14,000. Furthermore, Figure 4 shows the size distribution of PDMA-*g*-PDLLA in the supernatant of the medium after dispersion polymerization. The resultant graft copolymer, PDMA-*g*-PDLLA, exhibited a single size distribution based on the polymeric micelles through self-aggregation. Consequently, it was confirmed that

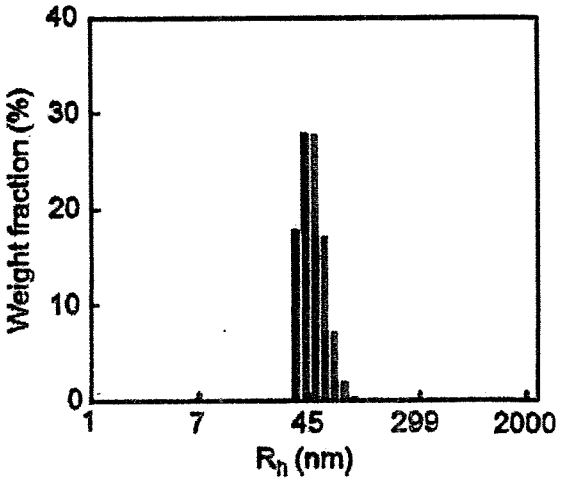


Figure 4. Size distribution of P(DMA-*co*-HEMA)-*g*-PDLLA in supernatant of medium after dispersion polymerization; [P(DMA-*co*-HEMA) (C_2)] = 1.0 g/L.

hydroxy groups in P(DMA-*co*-HEMA) played a key role as an initiation group during polymerization of D,L-lactide.

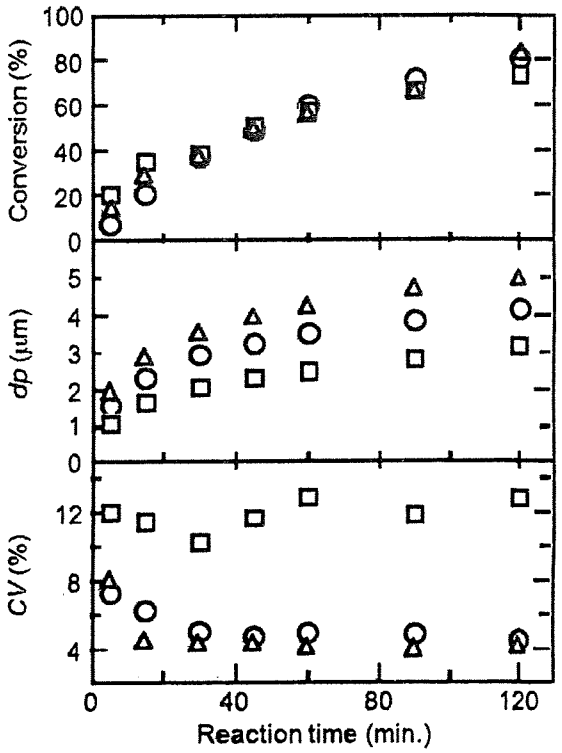


Figure 5. Dependence of monomer conversion, particle diameter, and diameter distribution of PDLLA microspheres on polymerization times, P(DMA-*co*-HEMA); C_1 (△), C_2 (○), C_3 (□), [P(DMA-*co*-HEMA)] = 1.0 g/L.

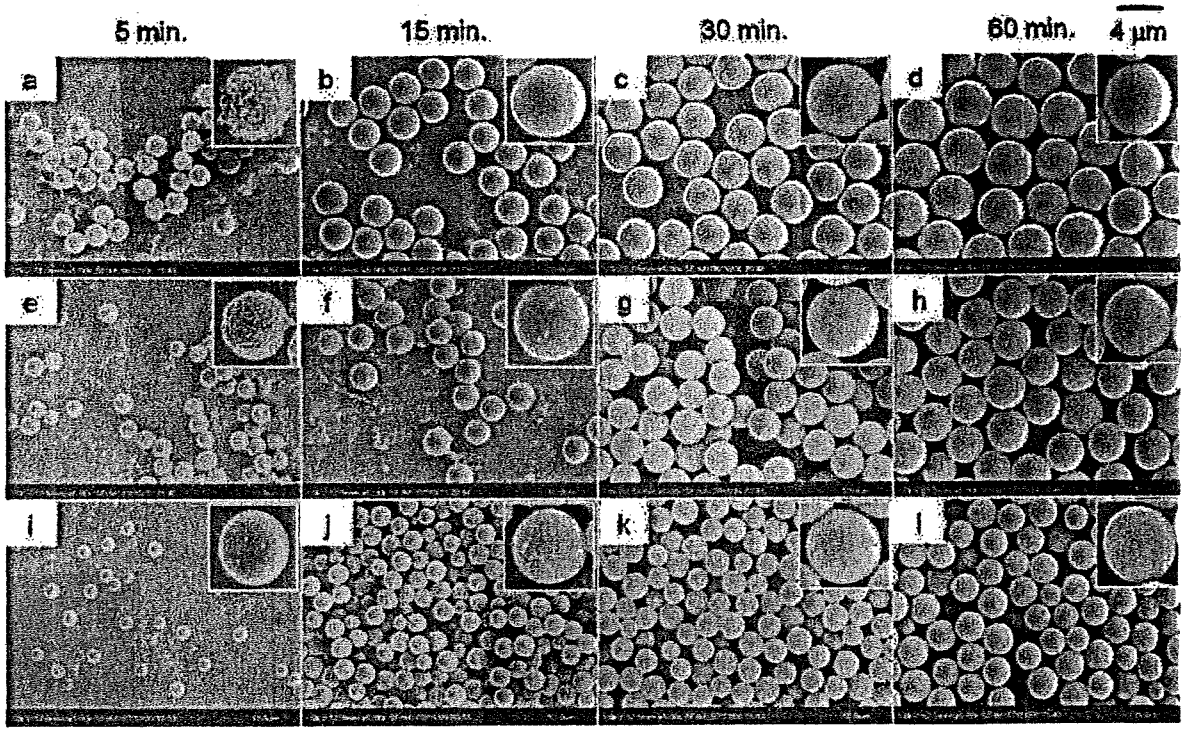


Figure 6. SEM images of PDLLA microspheres at 5, 15, 30, and 60 min of dispersion polymerization using P(DMA-*co*-HEMA) with different HEMA concentrations; (a–d) C_1, (e–h) C_2, (i–l) C_3, [P(DMA-*co*-HEMA)] = 1.0 g/L.

Time Courses of Particle Growth

The effects of polymerization time on monomer conversion, the particle diameter and particle diameter distribution on HEMA concentration in P(DMA-*co*-HEMA) were investigated for preparing monodisperse PDLLA microspheres. The results are shown in Figure 5. From Figure 5, the CV decreased with increasing polymerization time when using C_1 and C_2. The decrease in CV was induced by the capture of growing polymers and monomers into the particles from a continuous phase in the particle growth stage.[32,33] In contrast, CV did not decrease with increasing polymerization time when using C_3. In soap-free polymerization, Yamamoto et al. reported that the rough surface of polystyrene latex particles became smooth by the addition of styrene monomers in the particle growth stage.[34,35] We observed the surface morphology of the particles, which changed with increasing polymerization time, using SEM as well as these reports. Figure 6 shows SEM images of PDLLA microspheres at 5, 15, 30, and 60 min of dispersion polymerization using P(DMA-*co*-HEMA) with different HEMA concentrations. C_1 exhibited the roughest particle surface at 5 min, becoming smooth at 15 min. In contrast, the surface became smooth at 60 min with C_3. These results suggest that the growing polymers and monomers were not sufficiently captured into the particles in the particle growth stage because many monomers were consumed by the hydroxy groups in P(DMA-*co*-HEMA) during polymerization. Therefore, with C_3, the CV did not decrease due to insufficient capture of growing polymers and monomers. With C_1 and C_2, monodisperse PDLLA microspheres were obtained by sufficient capture of growing polymers and monomers. In conclusion, the HEMA concentrations in P(DMA-*co*-HEMA) strongly affected the capability of capturing monomers and growing polymers, and P(DMA-*co*-HEMA) with 0.9 mol % of HEMA was the optimal molecular structure.

Effect of P(DMA-*co*-HEMA) Concentration

P(DMA-*co*-HEMA), a dispersion stabilizer, plays an important role in preparing monodisperse PDLLA microspheres during dispersion polymer-

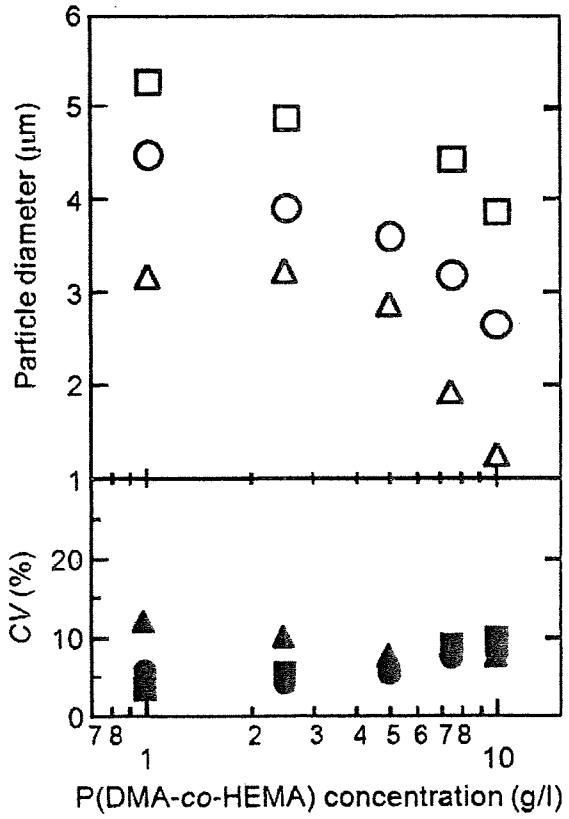


Figure 7. Effect of P(DMA-*co*-HEMA) concentration on particle diameter and diameter distribution of PDLLA microspheres; C_1 (□, ■), C_2 (○, ●), C_3 (△, ▲).

ization. P(DMA-*co*-HEMA) and P(DMA-*co*-HEMA)-*g*-PDLLA adsorb onto the surface of particles through physical interaction. In fact, *in-situ* produced P(DMA-*co*-HEMA)-*g*-PDLLA acts as a true dispersion stabilizer to form spherical stable particles and inhibits particle coagulation. Figure 7 shows the effect of P(DMA-*co*-HEMA) concentration on the particle diameter and diameter distribution of PDLLA microspheres prepared using P(DMA-*co*-HEMA) with different HEMA concentrations. From Figure 7, the particle diameter decreased with increasing P(DMA-*co*-HEMA) concentration because a large number of P(DMA-*co*-HEMA) molecules adsorbed onto the large surface area of particles to reduce the surface energy. In addition, the particle diameter decreased with increasing HEMA concentration in P(DMA-*co*-HEMA) because the adsorption rate to the surface of particles was larger when using P(DMA-*co*-HEMA) with a number of PDLLA chains, which showed a high affinity to the particles. In conclusion, the particle diameters of monodisperse PDLLA microspheres were controlled from 1.3 to 5.3 μm by the P(DMA-*co*-HEMA) and HEMA concentrations. Figure 8 shows the largest and smallest monodisperse PDLLA microspheres obtained in this study.

The CV increased with increasing P(DMA-*co*-HEMA) concentration when using C_1 and C_2. The decrease in CV was induced by the capture of growing chains and monomers into the particles

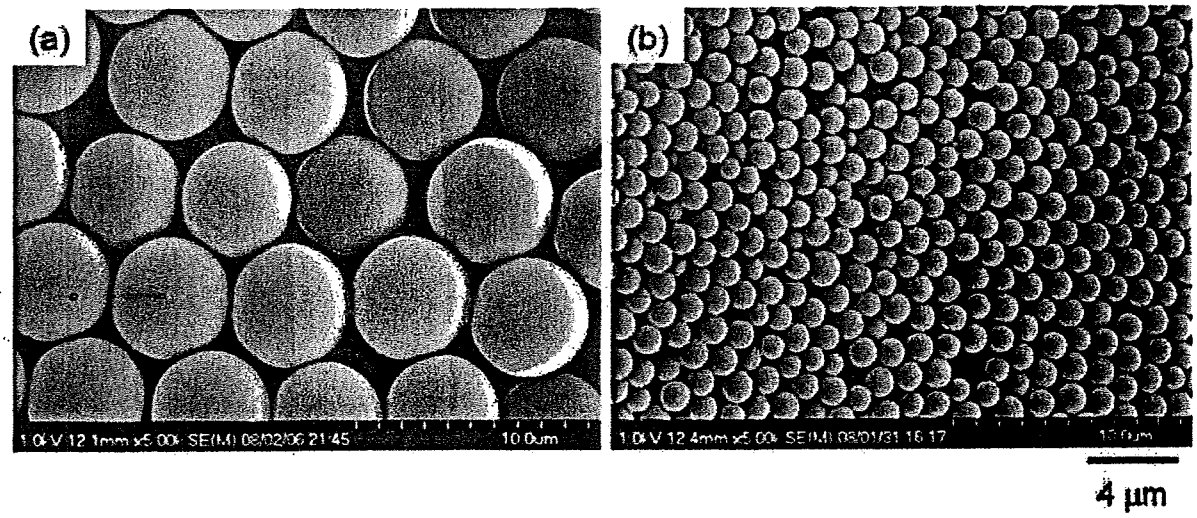


Figure 8. SEM images of PDLLA microspheres prepared with different concentrations of P(DMA-*co*-HEMA); (a) [C_1] = 1.0 g/L (dp = 5.3 μm, CV = 3.7%), (b) [C_3] = 10 g/L (dp = 1.3 μm, CV = 7.7%).

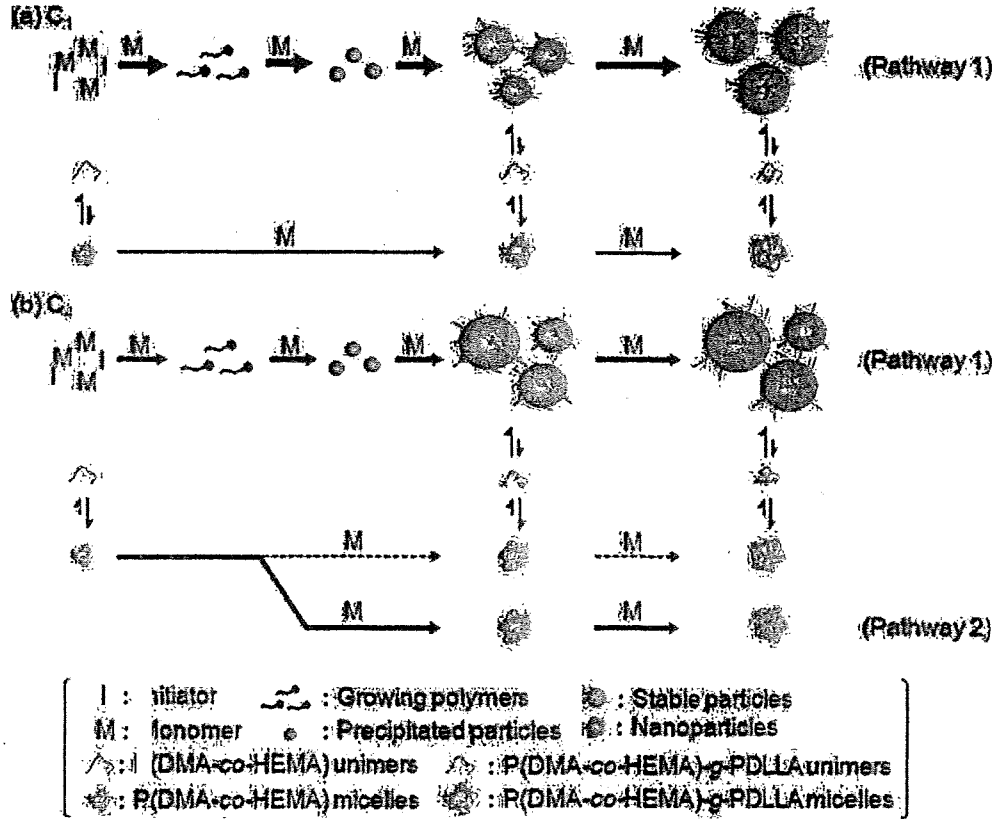


Figure 9. Schematic representation of particle formation and growth during dispersion polymerization of D,L-lactide with P(DMA-*co*-HEMA), (a) C_1, (b) C_4, [P(DMA-*co*-HEMA)] = 1.0 g/L.

from a continuous phase in the particle growth stage. Therefore, with increasing P(DMA-*co*-HEMA) concentration, captured monomers in the particles decreased due to the fact that many monomers were consumed by polymerization from the hydroxy groups in P(DMA-*co*-HEMA). On the other hand, with C_3, the CV decreased with increasing P(DMA-*co*-HEMA) concentration. This result indicated that more monomers were consumed by the hydroxy groups in P(DMA-*co*-HEMA) during polymerization because C_3 had more hydroxy groups, and hence P(DMA-*co*-HEMA)-*g*-PDLLA quickly formed at the initial stage. As a result, the anchoring of P(DMA-*co*-HEMA)-*g*-PDLLA onto the precipitated particles inhibited coagulation of precipitated particles at the stable particle formation stage.

Formation Mechanism of Particles

In general, regardless of the molecular structures of the dispersion stabilizer, the formation mechanism of particles for dispersion polymerization is basically the same as the one we proposed.[36,37] Based on the results in the above sections and the proposed mechanism earlier in the literature for dispersion polymerization of lactide, the formation mechanism of particles during dispersion polymerization of D,L-lactide in xylene/heptane (1:2, *v/v*) using P(DMA-*co*-HEMA) with different HEMA concentrations is illustrated in Figure 9. C_1, C_2, and C_3 with <2.30 mol % of HEMA exhibited a unimer state in the medium. Therefore, polymerization occurs in a homogeneous medium, and then the generated polymer chains grow until reaching the critical chain length where they precipitate to form particles. These precipitated particles are unstable and easily aggregate with each other. Simultaneously, the graft copolymeric stabilizer produced *in situ*, P(DMA-*co*-HEMA)-*g*-PDLLA, adsorbs on the aggregates of the precipitated particles, forming stable particles. The stable particles grow by capturing monomers and growing polymers into the particles from a

continuous phase, which results in PDLLA microspheres (Pathway 1). In particular, monodisperse PDLLA microspheres are obtained by the sufficient capture of growing polymers and monomers into the particles from a continuous phase in the particle growth stage when using C_1 with the lowest HEMA concentration [Fig. 9(a)]. Moreover, nanoparticles of P(DMA-*co*-HEMA)-*g*-PDLLA are formed when using C_4 with the highest HEMA concentration because most monomers are consumed by the hydroxy groups in P(DMA-*co*-HEMA) during polymerization (Pathway 2). As a result, the number of P(DMA-*co*-HEMA)-*g*-PDLLA, which stabilizes PDLLA microspheres in pathway 1, decreases, and polydisperse and larger PDLLA microspheres are obtained [Fig. 9(b)].

CONCLUSIONS

We developed monodisperse PDLLA microspheres by dispersion polymerization in xylene/heptane (1/2, *v/v*) using P(DMA-*co*-HEMA) as a dispersion stabilizer containing hydroxy groups. When using P(DMA-*co*-HEMA) with 0.9 mol % of HEMA, the best result in the CV of PDLLA microspheres obtained in this study was 3.7%, and the particle diameter was 5.3 μm. In addition, by keeping CV low (<10%), the particle diameter was controllable from 1.3 to 5.3 μm by altering the concentrations of P(DMA-*co*-HEMA) and HEMA, which affect the adsorption of *in-situ* polymerized P(DMA-*co*-HEMA)-*g*-PDLLA onto the precipitated particles until stable particles are formed. When monodisperse PDLLA microspheres were obtained, the CV decreased with increasing polymerization time by the sufficient capturing of growing polymers and monomers into the particles from a continuous phase in the particle growth stage. The capturing depended on the consumption of monomer by polymerization from hydroxy groups in P(DMA-*co*-HEMA). Therefore, the HEMA concentration in P(DMA-*co*-HEMA) strongly affected the capturing capability, which was the most important factor. Consequently, preparation of modisperse PDLLA microspheres and the particle diameter control were attained using a new molecular design of a dispersion stabilizer.

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