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ORIGINAL CONTRIBUTION

Effects of dispersion stabilizer and reaction solvent on forming monodisperse polystyrene microspheres by dispersion polymerization

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Abstract We used poly(aspartic acid) (PAsp) synthesized by ion exchange with sodium polyaspartate (PAspNa) as a dispersion stabilizer. PAsp improved the dispersion stability and the solubility in the medium for dispersion polymerization. The effects of the stabilizer hydrophobicity on particle formation, conversion, particle diameter, and its distribution of polystyrene microspheres were investigated by using both biodegradable polymers as a dispersion stabilizer. According to these results, we concluded that the polymerization rate of the styrene with PAsp was higher than that of styrene with PAspNa. That is why, smaller and more monodisperse microspheres were prepared with PAsp, compared to those with PAspNa.

Keywords Poly(aspartic acid) · Dispersion polymerization · Monodisperse particle · Biodegradable polymer · Polystyrene

Introduction

Dispersion polymerization is one of the major techniques for the preparation of monodisperse polymer microspheres [1–6]. In dispersion polymerization, monodisperse microspheres are formed in the presence of appropriate polymer dispersion stabilizer such as poly(*N*-vinylpyrrolidone), polyacrylic acid (PAA), and polyethylenimine [7, 8]. However, all commercial dispersion stabilizers used in dispersion polymerization are so far not biodegradable. In general, these water-soluble polymers are difficult to recover from polymer solution. Therefore, these nonbiodegradable dispersion stabilizers cause contamination of polymer microsphere surface and waste-water treatment of polluted water. Furthermore, these are made from fossil fuels. When we thought about sustainable society, cutting our dependence on fossil fuels is essential.

Sodium polyaspartate (PAspNa) synthesized by polycondensation of L-aspartic acid (L-Asp) is one of the typical hydrophilic biodegradable polymers [9, 10]. Since PAspNa is made from plant-derived materials and has biocompatibility, this polymer can be used in medical field, cosmetics, and foods. Thus, we studied dispersion polymerization with PAspNa as a dispersion stabilizer and synthesized monodisperse polystyrene microspheres with PAspNa as a dispersion stabilizer. The particle diameter ranged between 0.25 and 2.3 μm, and the particle size distribution was about 7.7%.

In this work, we synthesized poly(aspartic acid) (PAsp) by ion exchange with PAspNa. Although PAsp is also a typical hydrophilic biodegradable polymer, the solubility in water is lower than PAspNa due to weak-acid polyelectrolyte. We investigated the effect of the stabilizer hydrophobicity on the particle formation, conversion, particle size, and the distribution of polystyrene particles.

Experimental

Materials

All chemicals were purchased from Wako Pure Chemical Industry. Styrene (99%, with 3.0×10^{-3}% 4-tert-butylpyrocatechol stabilizer) was distilled under reduced pressure in a nitrogen atmosphere to remove the inhibitor. 2,2′-Azobis

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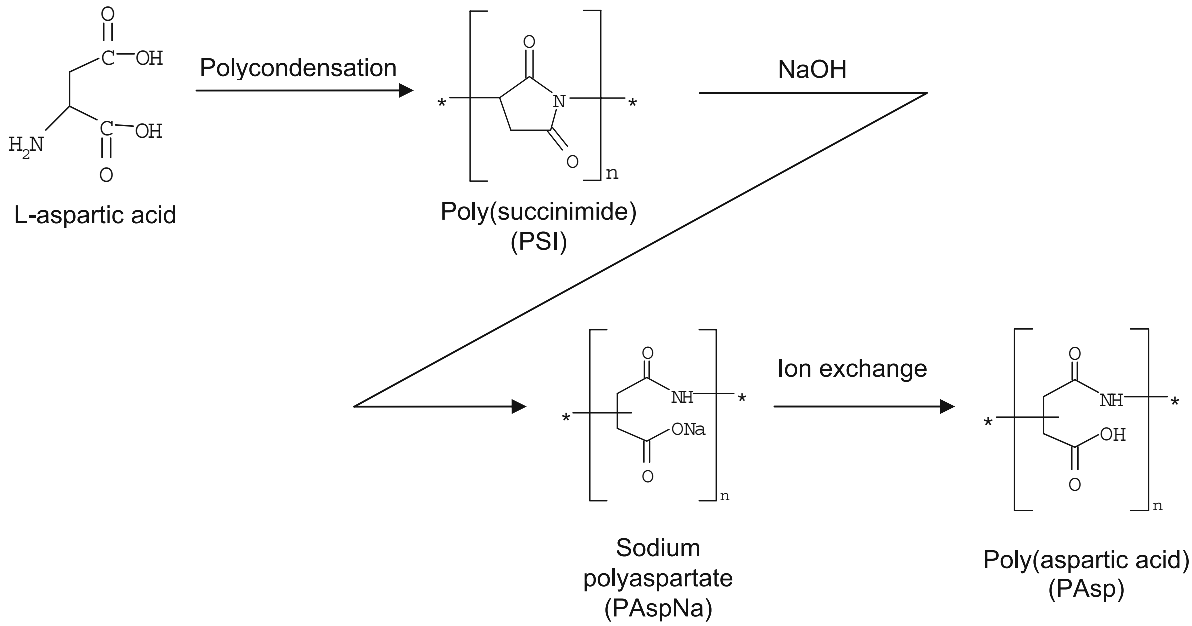

Scheme 1 Synthesis of PSI, PAspNa and PAsp

(isobutyronitrile) (AIBN) was purified by recrystallization from methanol. Water used as a polymerization solvent was purified with a Millipore Milli-Q water purification system.

Synthesis of polysuccinimide

Polysuccinimide (PSI) was synthesized by polycondensation of L-Asp (46.6 g) using phosphoric acid (19.8 g) as a catalyst at 453 K for 8 h. Then, the products were purified, and the weight-average molecular weights were determined by gel permeation chromatography (GPC) as previously reported [11]. The determined molecular weight of PSI was 4.25×10^4. Proton nuclear magnetic resonance (^{1}H NMR) spectra were measured with a JEOL FT NMR System JMN-AL300 (Scheme 1).

Synthesis of PAspNa

PAspNa was prepared by hydrolysis of PSI as already reported [11]. The molecular weight of PAspNa was 6.0×10^4, calculated from the molecular weight of PSI. The chemical structure of PAspNa was confirmed by Fourier transform infrared spectroscopy (FT-IR; KBr method). ^{1}H NMR spectra were measured with a JEOL FT NMR System JMN-AL300.

Synthesis of PAsp

PAspNa was dissolved in purified water, and an ion-exchange resin (Lewatit MonoPlus S100H) was added into the solution. After 24 h, the solution was concentrated under reduced pressure at 313 K [12]. The remaining solution was added into acetone to precipitate PAsp and which was recovered by filtration. The conversion from PAspNa to PAsp was confirmed by FT-IR (KBr method). The ion-exchange efficiency was calculated from natrium ion concentration. The natrium ion concentration was measured with an ion meter (DKK-TOA, IM-55G).

Microsphere preparation

Polystyrene microspheres were prepared by dispersion polymerization under the conditions listed in Table 1. Prepared microspheres were observed with a Hitachi S-3500N scanning electron microscope (SEM), and the average diameter and coefficient of variation (CV) were analyzed from the SEM images by WinRoof (Mitani, Ver.3.53). The average diameter and CV were defined by counting at least 200 individual microspheres from SEM image. The CV was calculated from the average diameter and standard deviation.

Table 1 Recipe for the preparation of monodisperse polystyrene microspheres

Ingredients	Units	Values
Styrene	g	1.35
AIBN	g	0.107
Dispersion stabilizer	g	0.15
Aqueous ethanol solution	Ml	45

343 K; 6 h; N_2; in flask with stirring rate, 360 rpm
AIBN 2,2′-Azobisisobutyronitrile

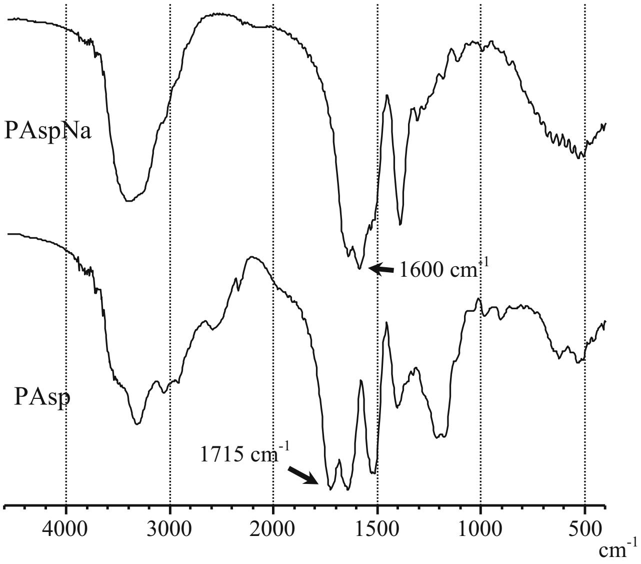

Fig. 1 FT-IR spectra of PAspNa and PAsp

Measurements of time course of conversion, particle diameter and its distribution, and particle numbers

A small amount of polymerization solvent with PAspNa or PAsp was withdrawn at different polymerization intervals. The samples were dissolved in methanol with a small amount of 4-tert-butylcatechol to terminate the polymerization. The concentrations of residual styrene monomer dissolved in methanol solution were determined by HPLC to estimate the conversion. The samples were also measured with the SEM to determine the particle diameters of the prepared microspheres at different polymerization intervals. Particle numbers were calculated from the conversion and particle diameters.

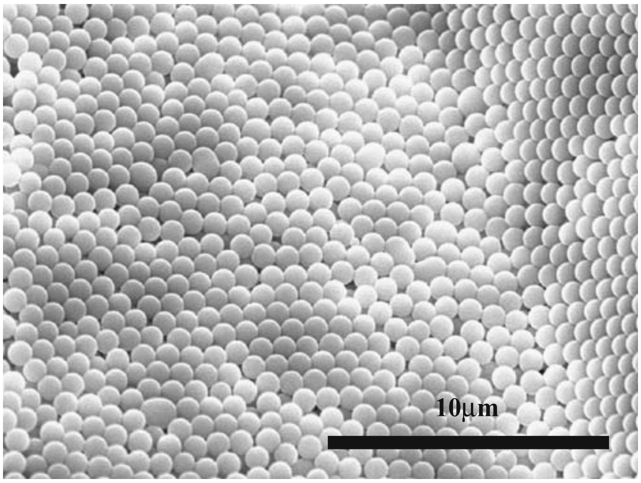

Fig. 2 SEM image of polymeric microspheres synthesized with PAsp. Volume fraction of EtOH=60 vol.%

Results and discussion

Characterization of synthesized PSI, PAspNa, and PAsp

The chemical structures of synthesized PSI and PAspNa were characterized by ^{1}H NMR as previously reported [11, 13].

The residues of synthesized PAspNa and PAsp were determined by FT-IR [12, 14, 15]. Figure 1 shows FT-IR spectra of PAspNa and PAsp. Attention was directed to the frequency of the carboxylate group band in order to investigate the preparing of the PAsp. The spectrum of PAspNa shows a large absorbance at 1,610 cm^{-1} assigned to the carboxylate anion (–COO$^-$). Meanwhile, the carboxylate anion band disappeared in the spectrum of PAsp. At

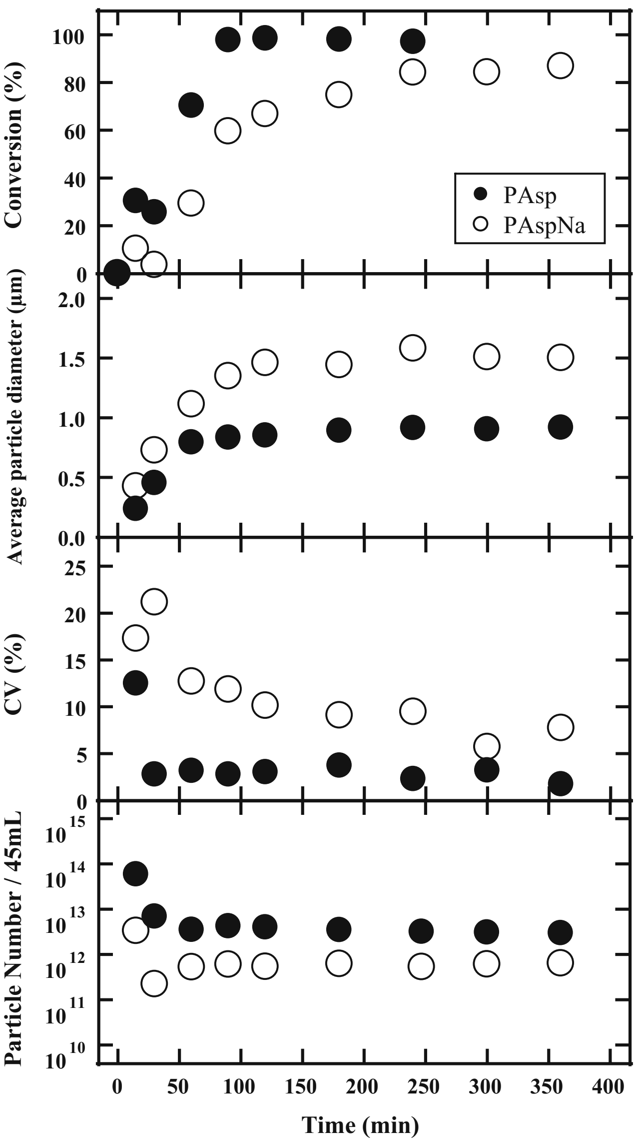

Fig. 3 Time course of conversion, particle diameter, CV, and particle number. Concentration of dispersion stabilizer = 3.33 mg/mL. Volume fraction of EtOH=60 vol%

the same time, a new band appeared at 1,720 cm^{-1}. This was assigned to the carboxylate group (–COOH).

In addition, the ion-exchange efficiency was calculated from the natrium ion concentration. It was measured before and after ion exchange of PAspNa solution. As a result, the natrium ion concentration after an ion-exchange process was very low. It was considered that almost all natrium ions of PAspNa were exchanged into hydrogen ions.

Thus, it was concluded that PAsp was successfully prepared from PAspNa by ion-exchange resin.

Kinetics of dispersion polymerization of styrene with PAspNa or PAsp

Figure 2 shows the SEM image of the polystyrene microspheres prepared with PAsp in an EtOH/water mixture with 60 vol.% EtOH. The particle diameter was approximately 0.91 μm. The CV was approximately 3.1%. The monodisperse polystyrene microspheres were clearly observed. This result indicates that PAsp acts as a dispersion stabilizer.

Figure 3 shows the time courses of styrene conversion, particle diameter, CV, and particle numbers of polystyrene microsphere in the dispersion polymerization using PAspNa or PAsp. The concentration of dispersion stabilizer was 3.4 mg/ml.

The final conversion with PAspNa is 87%. Meanwhile, the final conversion with PAsp came up to about 100%. Furthermore, the polymerization rate of styrene with PAsp was higher than that with PAspNa. The polymerization mechanism observed is similar to that in our previous studies concerning dispersion polymerization [16, 17].

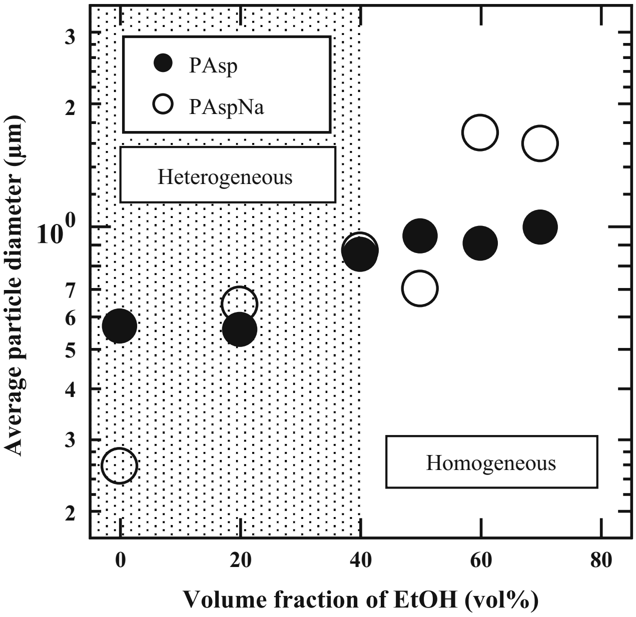

Fig. 4 Effect of EtOH volume fraction on particle diameter. Concentration of dispersion stabilizer = 3.33 mg/mL

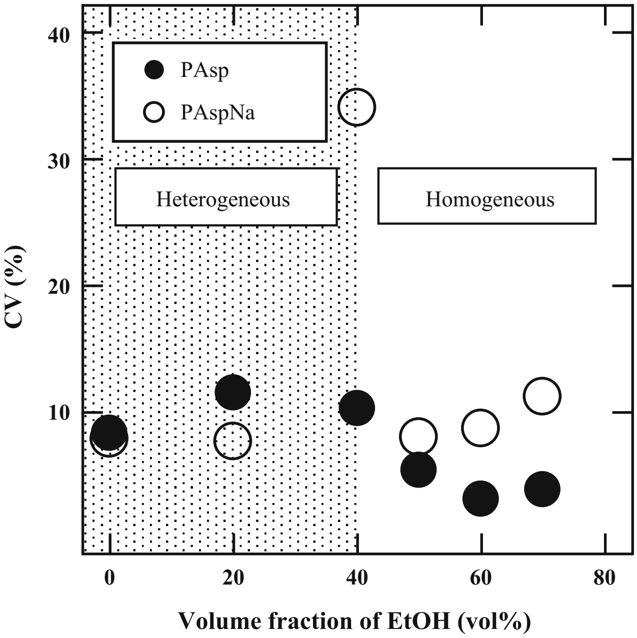

Fig. 5 Effect of EtOH volume fraction on CV. Concentration of dispersion stabilizer = 3.33 mg/mL

The diameter of particle prepared with PAsp was smaller than that prepared with PAspNa. In addition, the growth rate of microspheres with PAsp was faster than that with PAspNa.

The CVs obtained with PAsp and PAspNa decreased with time, and the CV obtained with PAsp was smaller than that with PAspNa.

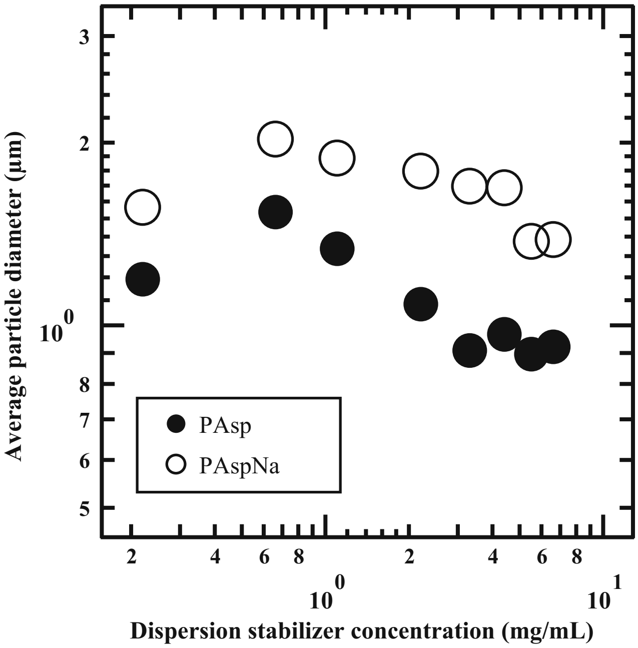

Fig. 6 Effect of dispersion stabilizer concentration on particle diameter. Volume fraction of EtOH = 60 vol%

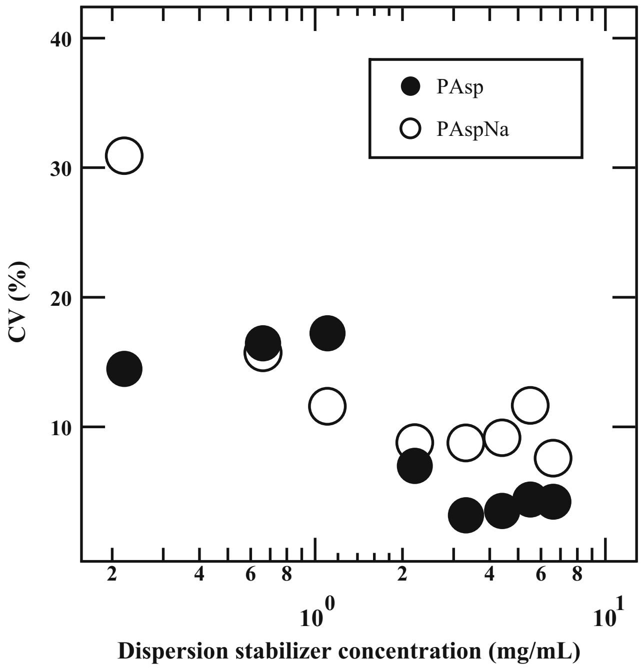

Fig. 7 Effect of dispersion stabilizer concentration on CV. Volume fraction of EtOH = 60 vol%

Both of the particle numbers decreased with time until the particle diameter became constant.

These results show that the number of particles synthesized with PAsp was higher than that synthesized with PAspNa. This is because the increase of hydrophobicity of dispersion stabilizer provided more loci for polymerization in the reaction solution. Since PAsp was more hydrophobic than PAspNa, the affinity of PAsp to EtOH was higher than that to PAspNa. These results also lead to the fact that higher polymerization rate used PAsp as a dispersion stabilizer.

Effect of EtOH volume fraction on average diameter and CV

Figure 4 shows the effect of the EtOH volume fraction in a polymerization medium on the average diameter when using PAspNa or PAsp. The EtOH volume fraction was between 0 and 70 vol.% with 3.4 mg/ml PAspNa or PAsp. The feed styrene monomer was completely dissolved in the EtOH/water solvent in which the EtOH content was above 40 vol.%, and the solution was homogeneous before polymerization.

The particle diameter obtained with PAspNa or PAsp increased with increasing EtOH volume fraction. There are two reasons for this result. One is that the amount of dissolved styrene was increased during EtOH volume fraction between 0 and 40 vol.%. Another reason is the critical chain length of styrene in precipitation increased with increasing EtOH volume fraction. The increasing critical chain length of styrene caused the reduction of the number of particle nuclei.

However, at higher EtOH volume fraction, microspheres synthesized with PAsp were smaller than those with PAspNa. This result concerned with the length of polymer chains in the reaction solvent. The solubility of PAsp into water was decreased as compared with that of PAspNa. In fact, however, PAsp dissolved in reaction solvent well. At the same time, PAsp had an affinity to organic solvents such as methanol and EtOH. Therefore, it was thought that PAsp solvated under condition of more spread own polymer chain at higher EtOH volume fraction. Thus, PAsp preserved the dispersion stability at higher EtOH volume fraction.

Figure 5 shows the effect of EtOH volume fraction in a polymerization medium on CV with PAspNa or PAsp. Polystyrene microspheres up to CV 10% were synthesized with PAspNa or PAsp under most conditions. At above 40 vol.% of EtOH volume fraction, the CV of prepared microspheres with PAsp was lower than those with PAsp. For the reason given above, PAsp preserved the higher dispersion stability under EtOH-rich conditions. Furthermore, the higher CV with PAspNa at 40 vol.% of EtOH was avoided using PAsp. Bimodal distribution of the particle diameter was observed when we prepared microspheres with PAsp at EtOH volume fraction of 40 vol%. We are not sure yet of the reason for the mechanism of the formation.

Table 2 The conditions for preparing monodisperse microspheres in EtOH/water-mixed solution with PAA, PAspNa, or PAsp as a dispersion stabilizer

Ingredients	PAA (M_w, 2.0×10^5) (non-biodegradable)	PAspNa (M_w, 6.0×10^4) (biodegradable)	PAsp (M_w, 4.25×10^4) (biodegradable)
Ethanol volume fraction in polymerization solvent (vol.%)	70	60	60
Concentration of dispersion stabilizer (mg/ml)	10.0	3.33	3.33
Concentration of monomer (mmol/ml)	1.93	2.89×10^{-1}	2.89×10^{-1}
Average diameter (μm)	1.80	1.69	0.91
CV (%)	5.8	7.7	1.7

Effect of dispersion stabilizer concentration on average diameter and CV

Figure 6 shows the effect of dispersion stabilizer concentration on particle diameter. In this study, the volume fraction of EtOH was fixed at 60 vol.%. The dispersion stabilizer concentration was varied from 2.2×10^{-1} to 6.7 mg/ml. This figure shows that the particle diameter decreased from approximately 2.0 to 1.4 μm by increasing the concentration of PAspNa. On the other hand, by changing the concentration of PAsp, the particle diameter decreased from approximately 1.5 to 0.9 μm. This is because the high initial stabilizer concentration causes the increasing amounts of stabilizer related to form particle nuclei in the initial stage of polymerization. Another reason is the enhancement of stabilizer absorbed on the nuclei and protected against aggregation processes in polymerization. In addition, smaller microspheres were prepared with PAsp as compared with PAspNa. This result indicated the PAsp worked as a dispersion stabilizer more effectively than PAspNa at 60 vol.% of EtOH.

Figure 7 shows the effect of dispersion stabilizer concentration on CV. The volume fraction of EtOH was 60 vol.%. The CV decreased with increasing dispersion stabilizer concentration. The monodisperse microspheres were prepared at the concentration more than 2.2 mg/ml. Thus, Figs. 6 and 7 indicate that we can control the particle diameter of monodisperse microspheres in the case of applying appropriate dispersion stabilizer to a reaction solution.

The effect of the relation between dispersion stabilizer and reaction solvent on forming monodisperse microspheres

Table 2 shows the conditions for preparing monodisperse microspheres in EtOH/water-mixed solution with several dispersion stabilizers [1]. The monodisperse microspheres with similar size were prepared using PAA or PAspNa as previously reported. PAspNa is biodegradable, and the concentration for preparing monodisperse microspheres is about one third of that of PAA.

In this study, we applied PAsp as a dispersion stabilizer to dispersion polymerization. Monodisperse microspheres were prepared at higher EtOH volume fraction, and the CV obtained was lower than that with PAspNa. Furthermore, smaller microspheres than that with PAspNa were prepared at higher EtOH volume fraction. However, at less than 40 vol.% of EtOH volume fraction, it was difficult to prepare monodisperse microspheres with PAsp. This suggested that, monodisperse microspheres were obtained when using the dispersion stabilizer having an affinity to a reaction solvent.

Conclusion

We synthesized PAsp by ion exchange of PAspNa. We applied PAsp as a dispersion stabilizer to dispersion polymerization. The monodisperse microspheres were obtained with PAsp as a dispersion stabilizer. It suggested that PAsp acts as a dispersion stabilizer for styrene polymerization. In addition, the polymerization rate of styrene with PAsp was higher than that with PAspNa. The particle diameter with PAsp increased as the EtOH volume fraction increased. At high EtOH volume fraction, microspheres prepared with PAsp were smaller than those with PAspNa. Consequently, we obtained monodisperse microspheres by using PAsp at higher EtOH volume fraction.

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