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Review

Synthesis of polymer nanoparticles using methylcellulose gel as reactor

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Synthesizing polymer nanoparticles have required large amounts of surfactants, which increase environmental pollution. It is indispensable to develop a synthesis method for polymer nanoparticles that does not require surfactants. In the present study, a methylcellulose (MC) gel was used as a polymerization field to prepare polymer nanoparticles with a particle diameter < 100 nm. MC gel was a biocompatible hydrophilic polymer and low environmental load. This was used as a reactor to carry out the soap-free emulsion polymerization of styrene. The mesh width of the gel decreased with increasing MC concentrations. The three-dimensional network structure of the MC gel prevented the coagulation growth of the particles due to Brownian and thermal motions to decrease the size of the polystyrene particles. Polystyrene particles with the average size of 31 nm were obtained at an MC concentration of 1.0 wt%. In addition, curdlan and melamine foam, which had also three-dimensional network structures, were used as reaction fields of soap-free emulsion polymerization of styrene to make polystyrene particles nanosized.

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Introduction

Polymer nanoparticles have excellent adhesion and permeability and are used as additives for paints and coating agents for paper and leather to improve water resistance and abrasion resistance [1-3]. In recent years, by taking advantage of the diffusion effect of nanoparticles in the body, they have been actively used in the medical field as drug carriers in drug delivery systems and molecular imaging technology [4,5].

Emulsion polymerization is the primary synthesis method for polymer nanoparticles

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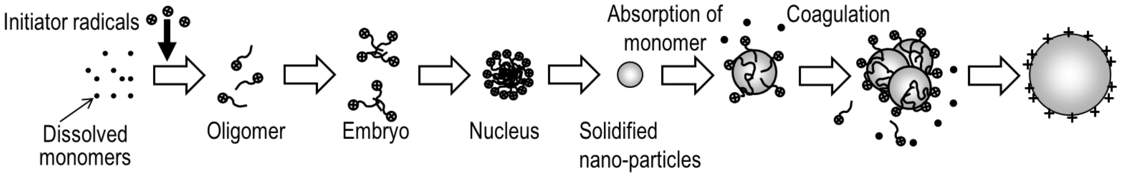

Fig. 1. Particle formation mechanism of soap-free emulsion polymerization of styrene.

[6,7]. However, this method requires the use of large quantities of surfactants. This results in issues such as surfactant contamination of groundwater, adverse impacts on the aquatic ecosystems, and removal costs due to activated carbon and membrane treatment, necessitating a reduction in the usage of surfactants [8].

To address these issues, research has been conducted on polymer particle synthesis methods that reduce surfactant use. For example, emulsion polymerization can occur at surfactant concentrations below the critical micelle concentration. Ishii *et al*. proposed a method for synthesizing nanoparticles by copolymerizing styrene and methyl methacrylate, in which the amount of surfactant added was reduced to approximately 1/10 compared to conventional methods [9].

This study aims to synthesize nanoparticles smaller than 100 nm without using surfactants. The mechanism shown in Figure 1 was proposed for the particle formation of monomers, such as styrene. Nanoparticles are formed during the initial polymerization stage, and the particles aggregate and grow owing to Brownian and thermal motions [10-12]. In this study, we used methylcellulose (MC), which gels when heated, as a reactor and investigated a method for synthesizing polymer nanoparticles of 100 nm or less by suppressing the aggregation growth of particles due to Brownian and thermal motions. We also investigated the effect of the MC concentration on the particle size by changing the mesh width of the gel.

Effect of MC concentration on gel network structure and particle size

Styrene (St, Tokyo Chemical Industry Co., Ltd.) was used as a monomer, and 2,2'-azobis[2-(2-imidazolin-2-yl)propane] dihydrochloride (VA-044, Fuji Film Wako Pure Chemical Industries, Ltd.) [13] was used as a polymerization initiator, along with potassium peroxodisulfate (KPS, Fuji Film Wako Pure Chemical Industries, Ltd.). An MC1500 (Shin-Etsu Chemical Co., Ltd.) was used as the MC. Distilled water was prepared using a distilled water manufacturing apparatus (WG250, Yamato Scientific) 15 mL of distilled water was degassed by nitrogen bubbling for 20 min in a 30-mL screw tube. Next, 0.1 g of styrene was added, and ultrasonic waves were applied at 38 kHz for 30 min using an ultrasonic cleaner (US-5KS, SND). After irradiation, a styrene emulsion (with submicron-sized oil droplets) was prepared. After the screw tube was placed in water at 80 °C for 5 min, MC was added and stirred with a shaker for 5 min to disperse the MC. A polymerization initiator was added after allowing it to stand in water at 5 °C and cooling it. The mixture was stirred on a shaker for 5 min to disperse the initiator into the solution. The screw tube was heated at 70 °C for a predetermined time using a temperature controller (RCH-20L, EYELA), and polymerization was

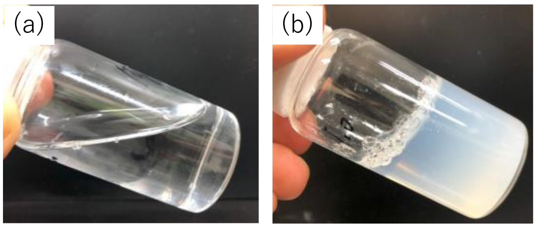

Fig. 2. Photos of the samples at MC concentration of 1.0 wt% and the following temperatures (a) 25 °C and (b) 70 °C.

carried out under stationary conditions without stirring or other mixing operations. This heating caused the MC to gel and become cloudy, as shown in Figure 2. After polymerization, the screw tube was cooled and returned to the sol, the particle dispersion (10 mL) was sampled, and the nanoparticles were recovered using a centrifuge (3700, Kubota) at a rotation speed of 15,000 rpm. The recovered particles were redispersed in 10 mL of distilled water via ultrasonic irradiation for 30 min.

Particle synthesis was considered to have proceeded sufficiently in the gel based on the polymerization ratio. The reaction solution during polymerization was weighed out and placed in a constant temperature bath at 80 °C to remove water and unreacted monomers. The polymer mass was obtained from the weight difference, and the polymerization ratio was calculated from the amount of monomer added. For the sample with added MC, the polymerization ratio was calculated from the polymer mass after subtracting the mass of MC.

The average particle diameter was calculated based on the FE-SEM results. The observation samples were prepared as follows: A small amount of particles redispersed in distilled water was dropped onto the mica piece. After drying, the sample was coated with a thin osmium film via vapor deposition (OPC60A, Filgen). The particle size was calculated by averaging over 200 particle sizes identified from the SEM images using image analysis software, Azo-kun. Zeta potentials of the synthesized particles were measured using Zetasizer (Malvern Panalytical).

To observe the effect of gel mesh width on particle morphology, the gel mesh width was measured with the MC concentrations. Because the MC gel is thermoreversible, it undergoes a sol-gel transition at room temperature and returns to the sol state. The MC was lyophilized (FD-1000, EYELA) in gel form and observed under an electron microscope. Distilled water, which was degassed by bubbling nitrogen for 20 min, was placed in a plastic container. After that, the MC was dissolved by the same method as in the fine particle synthesis described in the previous section and heated at 70 °C for 1 h to form a gel. The gel samples were placed in liquid nitrogen and frozen. The gel was allowed to stand for 24 h in a freeze-dryer to remove the water. The freeze-dried gel was fixed on carbon tape and observed under a scanning electron microscope (FE-SEM, JEOL) [14].

Figure 3 shows SEM images of the MC gels [14]. The mesh grid width of the gel decreased as the MC concentration increased. Because the number of crosslinking points in the gel increases with increasing MC concentration [15], it is thought that an increase in the number of crosslinking points reduces the mesh width.

Figure 4 shows SEM images of the particles synthesized in the MC gel. Particles with a

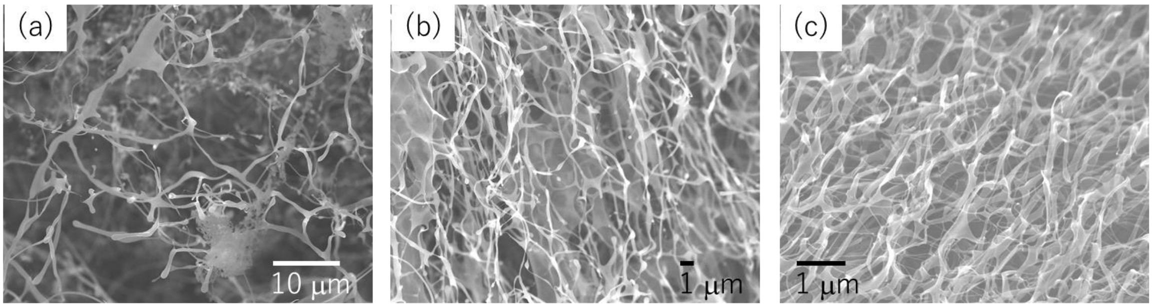

Fig. 3. SEM images of MC gels at the following MC concentrations: a) 0.1 wt%; b) 0.5 wt%; c) 1.0 wt%.

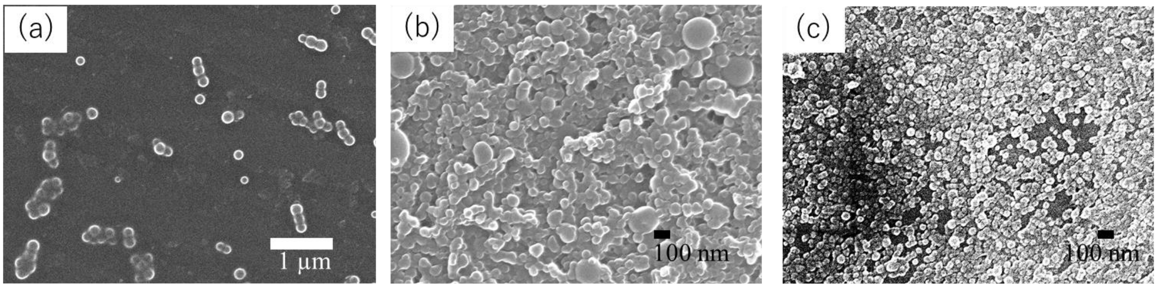

Fig. 4. SEM images of polystyrene nano particles with VA-044 of 2.0 mM at the following MC concentrations: a) 0 wt%; b) 0.1 wt%; c) 0.5 wt%.

diameter of 50 nm or less were observed at an MC concentration of 0.5 wt%. In contrast, when the MC concentration was 0.1 wt%, particles with a diameter of 100 nm or more were synthesized, confirming that the particle diameter was non-uniform.

Based on the above results, we summarized the effect of the MC concentration on the mesh width and particle diameter. The smaller the mesh width of the gel, the smaller the particle size. In particular, we confirmed the synthesis of 31-nm particles at an MC concentration of 1.0 wt%. Presumably, this is because the gel mesh reduces the fluidity of the water in the gel, suppressing the Brownian and thermal motions of the particles and the aggregation growth of the particles.

Particle displacement due to Brownian and thermal motions is affected by the particle diffusion. Water in the gel is in a state of low fluidity, such as hydrated water or intermediate water near the gel mesh [16]. The interface area between the MC gel and water is believed to increase as the MC concentration increases. Consequently, the proportion of hydrated and intermediate water at the interface between the gel network and water increases, and the fluidity of the water in the gel decreases. Therefore, the Brownian and thermal motions were suppressed by lowering the fluidity of water, and the aggregation growth of fine particles was suppressed, resulting in particles of 50 nm or less.

On the other hand, Figures 3a shows that the gel mesh is non-uniform at an MC concentration of 0.1 wt%, and some parts are sparse in the mesh. At an MC concentration of 0.1 wt%, the particle size increased, and particles with a particle size of 100 nm or more were observed shown in Figure 4b. One reason for this is that the fluidity of water is relatively high in the sparsely meshed part, and it is difficult to suppress the aggregation growth of

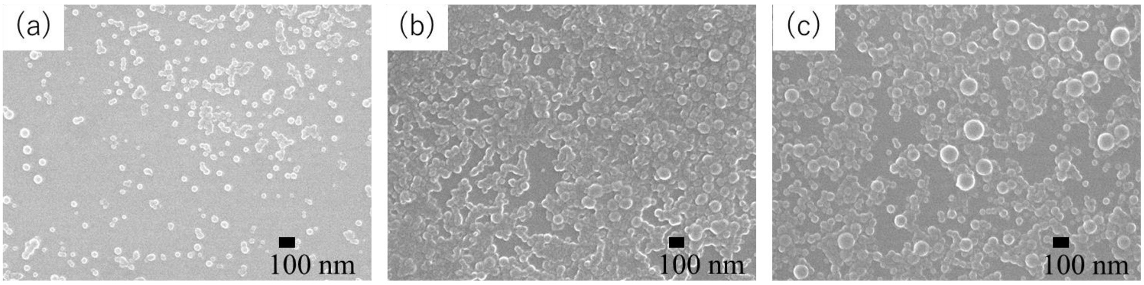

Fig. 5. SEM images of polystyrene nano particles with MC concentration of 0.5 wt% at the following VA-044 concentrations: a) 1.0 mM; b) 5.0 mM; c) 10 mM.

particles.

As shown in Figure 5, when the initiator concentration increased, the average particle size increased, making it possible to control the size of the nanoparticles. This is probably because an increase in the initiator concentration can generate the secondary particles which make contributions to particle growth through the coagulations [17].

As shown in Figures 3a and 4b, the particle size distribution of the polymerized particles in the gel was wide, and the coefficient value, which was defined as the standard deviation divided by average size, exceeded 20%. In general, soap-free emulsion polymerization produces particles with high particle size uniformity because of particle aggregation was occurred during the particle growth. On the other hand, the particles polymerized in the gel suppressed the aggregation of the particles; therefore, it can be assumed that the uniformity of particle coagulation did not progress, and the particle size distribution widened.

From the above observations, the particle generation mechanism in the MC gel was as followed. Styrene monomers dissolved in water from styrene oil droplets react with a water-soluble initiator. As the polymerization progresses, the polymer aggregates and precipitates to form particle nuclei. Subsequently, the particle nuclei agglomerate in water to form nanoparticles. Because the fluidity of water in the gel is low, the aggregation between nanoparticles is suppressed.

Effect of enzymatic degradation reaction of MC on dispersion stability of microparticles

When the MC gel was used as reactor, the synthesized particles were covered with MC. Therefore, their dispersion stabilities were unstable. Using enzymatic degradation reaction, we attempted to improve the dispersion stability of the nanoparticles synthesized in the MC gels.

The dispersion stability of the nanoparticles synthesized in MC gel is an important. Because nanoparticles have large surface energies and are unstable, adhesion and agglomeration of particles are likely to occur. Therefore, in this study, MC was enzymatically degraded to improve the dispersibility of the nanoparticles in water. Cellulase (sucrase ™ C, Mitsubishi Chemical Co.) was used to degrade the MC. Enzymatic degradation is a reaction that hydrolyzes the β1-4 bond of cellulose and can decompose water-soluble cellobiose [18].

Enzymatic decomposition experiments were performed in two ways. These included enzymatic decomposition experiments of MC alone and an enzymatic decomposition experiment of the

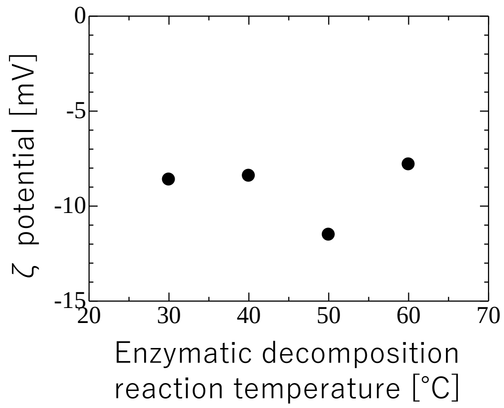

Fig. 6. Effect of enzymatic decomposition reaction temperature on zeta potential of particle synthesized by KPS with a concentration of 2.0 mM.

particle dispersion after particle synthesis. First, for the enzymatic degradation experiment of MC alone, a 0.5 wt% MC sol was prepared, and cellulase was added. Enzyme decomposition was performed by heating at 30 – 60 °C for 24 h. After completion of the decomposition reaction, the enzymatic reaction was stopped by cooling at 5 °C. After that, it was heated to 70 °C, and gelation was confirmed visually. For enzymatic decomposition of the particle dispersion, 0.02 g of cellulase was added to the particle dispersion prepared using KPS. After heating for 24 h at 30 – 60 °C for enzymatic decomposition, 10 mL of the particle dispersion was sampled and centrifuged to collect the fine particles. The recovered particles were redispersed in 10 mL of distilled water using ultrasonic waves, and the dispersion stability of the particles in water was evaluated using dynamic light scattering (DLS, Malvern Panalytical) and Zetasizer.

Figure 6 shows the relationship between the enzymatic decomposition reaction temperature and the zeta potential of the polystyrene particles synthesized by KPS. The zeta potential of the synthesized particles showed -0.2 mV before the enzymatic degradation reaction, which was not originated from KPS-derived sulfate ions (SO4$^-$). However, their dispersion stabilities were improved after the degradation reaction, as shown in Figure 6. In addition, because the zeta potential after the enzymatic decomposition reaction was negative, the SO4$^-$ covered with MC were exposed on the surface because of the decomposition of MC. As the enzymatic decomposition reaction temperature increased, the enzymatic decomposition activity increased; however, the dispersion stability of the particles did not improve. This was probably because the methoxy group of MC was thermally aggregated, the enzyme could not be efficiently adsorbed onto the particle surface, and part of the enzyme was heat-inactivated [19]. The optimized reaction temperature was found to be 50 °C. The SEM images of the particles at each degradation reaction temperature were shown in Figure 7. MC, which covered with particles, were degraded to keep some distances between the

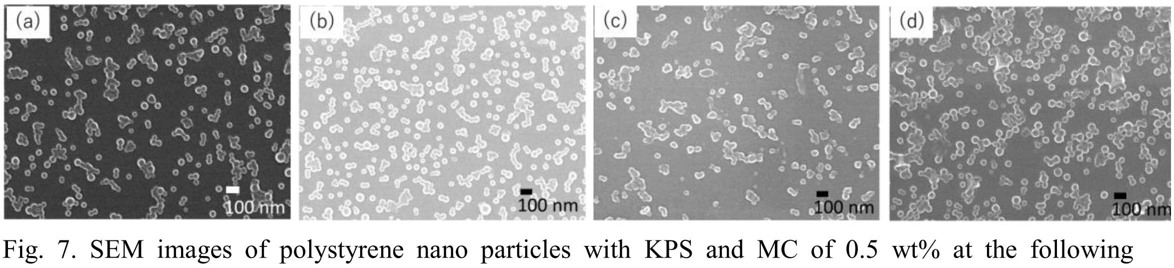

Fig. 7. SEM images of polystyrene nano particles with KPS and MC of 0.5 wt% at the following degradation reaction temperatures: a) 30 °C; b) 40 °C; c) 50 °C; d) 60 °C.

particles, which showed enhancement of their dispersion stabilities.

The average size of particles not subjected to enzymatic degradation measured by DLS ranged between 700 ~ 800 nm, which is larger than the average particle size obtained by SEM. In addition, the zeta potential of the particles was almost zero, suggesting that the MC molecules adhered to the particle surface and the particles formed aggregates. The average particle size measured by DLS after enzymatic degradation, 100 ~ 200 nm was smaller than that of the particles not subjected to enzymatic degradation. This is thought to be because of the decrease in the amount of MC adhering to the particle surface and the redispersion of the particles due to the decomposition of MC.

Effect of MC gel on polymerization ratio

The polymerization ratios at reaction times of 6 and 24 h were 32%, and 41%, respectively [20]. In a previous study, the polymerization ratio in the soap-free emulsion polymerization of styrene was approximately 30% for the same reaction time, 6 h, and it was assumed that a sufficient amount of nanoparticles could be synthesized in 6 h using this method. As styrene forms a submicron-sized emulsion, the interfacial area between water and styrene increases, promoting monomer diffusion, and the polymerization ratio becomes comparable to that of conventional soap-free emulsion polymerization.

In addition, the polymerization ratio of soap-free emulsion polymerization, in which styrene was emulsified and synthesized in water without agitation, was 11.5% during the same period, and the polymerization ratio of soap-free emulsion polymerization in the MC gel was much higher. This is attributed to the low fluidity of water in the MC gel, which prevents the styrene monomer droplets from coalescing owing to Ostwald ripening and phase separation in the upper part of the reactor, allowing the monomers to be efficiently used for polymerization.

Three-dimensional network reactor

Using curdlan to make the three-dimensional network reactor, polystyrene nano particles were obtained by soap-free emulsion polymerization of styrene, as shown in Figure 8.

Applying the present method to melamine foam (Figure 9c) as reactor enabled us to synthesize polystyrene nano particles [21, 22] shown in Figure 9, because the fluidity of the solvent was decreased due to the hydrogen bonds between water molecules and triazine rings of the melamine resin [23].

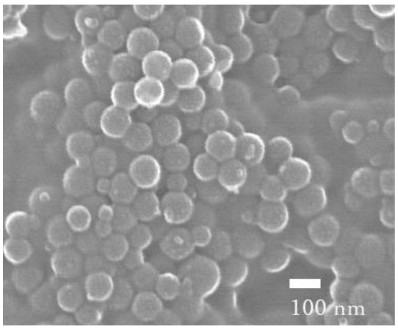

Fig. 8. SEM image of polystyrene nano particles synthesized by reactor using curdlan to carry out soap-free emulsion polymerization of styrene.

Conclusions

Polystyrene nanoparticles were synthesized using an MC gel as the polymerization field and investigated in terms of particle size and degree of polymerization. The MC gel was enzymatically decomposed to improve the dispersion stability of the particles. The following conclusions were drawn:

(1) The particle size decreased as the mesh width of the MC gel decreased. We succeeded in synthesizing 31-nm nanoparticles at an MC concentration of 1.0 wt%. This is probably because the smaller the mesh width, the lower the fluidity of the water in the gel and the suppression of aggregation growth due to the Brownian and thermal motions of the particles.

(2) The dispersion stabilities of the nanoparticles were poor because MC was attached to the surfaces of the nanoparticles, however, they were improved by the enzymatic degradation reaction for MC.

(3) A sufficient amount of polymer nanoparticles was synthesized after 6 h of polymerization using the MC gel as reactor for soap-free emulsion polymerization of styrene.

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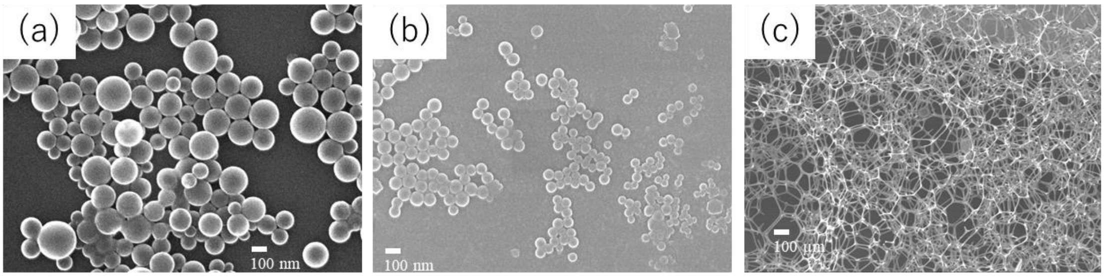

Fig. 9. SEM images of polystyrene particles with KPS using the following reactors: a) conventional reactor; b) melamine foam reactor shown in (c).

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