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ORIGINAL CONTRIBUTION

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Synthesis of monodisperse, magnetic latex particles with polystyrene core

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Abstract. A novel method for producing monodisperse, submicron-sized magnetic latex particles is described. The method provides coating of polymer particles with surface-modified magnetic particles during soap-free polymerization. Experiments were performed with styrene monomer, potassium persulfate initiator, Fe_3O_4 magnetic particles, and silane-coupling reagents of methacryloxypropyltrimethoxysilane (MPTMS) and methacryloxypropyldimethoxysilane (MPDMS). The morphology of the magnetic particles depended on the silane-coupling reagents. Use of the tri-functional coupling reagent MPTMS produced particles having a disk-like or concave-like shape, whereas use of the di-functional coupling reagent MPDMS produced spherical particles that had a coefficient of variation of 4.4%, which was much smaller than the standard criteria of monodispersity, 10%.

Keywords Soap-free polymerization · Magnetic latex particle · Silane-coupling reagent · Heterogeneous coagulation · Particle shape

Introduction

Development in magnetic labeling techniques for polymer microspheres has expanded into high gradient magnetic separations in biotechnology [1, 2, 3, 4, 5, 6, 7, 8, 9, 10]. An old and simple method for preparing magnetic microspheres is coating or encapsulation of magnetic particles with preformed polymers [11, 12, 13]. This method produces various types of magnetic particles employing natural, synthetic, and composite polymers. Another method is vinyl polymerization, initiated chemically [14] or by γ-ray irradiation [15] in the presence of magnetic particles. However, the magnetic particles produced by these methods or their combinations are not ideally suitable for immunological and medical purposes because of their inhomogeneity in particle size.

More suitable methods have been developed with emulsion polymerization in the presence of freshly prepared Fe_3O_4 ferrofluid or commercial ferrofluids [16, 17]. Ugelstad developed a novel method based on a two-step swelling technique and succeeded in the preparation of monodisperse magnetic particles [18, 19, 20, 21], which are now commercially available.

The present work proposes an alternative method for producing monodisperse magnetic particles. Figure 1 presents a conceptual scheme of the method in which coating of polymer particles with surface-modified magnetic particles occurs during soap-free emulsion polymerization. The magnetic particles are nanometer-sized Fe_3O_4 and their surface can be modified with silane-coupling reagent possessing vinyl groups. After the appearance of negatively charged polymer particles during soap-free emulsion polymerization in the presence of the same coupling reagent, a suspension of the magnetic particles is continuously added to the reaction system in which the polymerization still proceeds. In acidic conditions, the magnetic particles have positive charges on their surface because of the isoelectric point of Fe_3O_4. Under these conditions, the magnetic particles can be expected to cause heterogeneous coagulation with

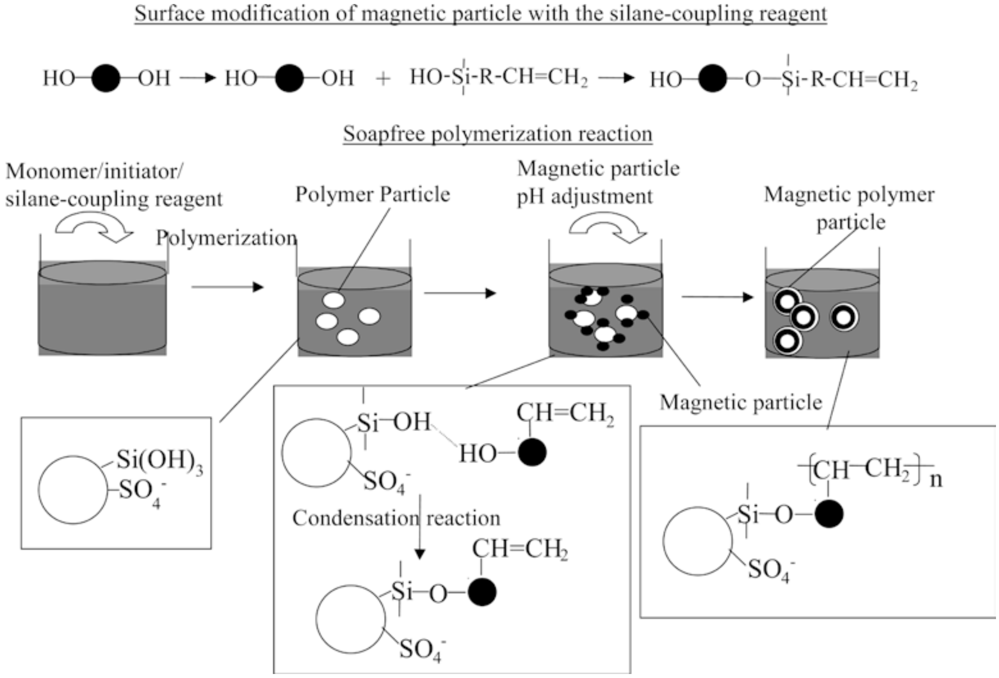

Fig. 1 Conceptual scheme of magnetic polymer particle synthesis

the polymer particles, accompanied by polymerization of the vinyl groups and condensation of the SiOH groups on the magnetic and polymer particles. To examine this possibility, the present work carried out coating experiments employing styrene monomer and potassium persulfate initiator in the presence of the coupling reagent of methacryloxypropyltrimethoxysilane (MPTMS) or methacryloxypropydimethoxysilane (MPDMS) under various reaction conditions.

Experimental

Materials

Styrene (99%, Wako Pure Chemical Industries, Osaka, Japan) was distilled under reduced pressure with a nitrogen atmosphere. Potassium persulfate (KPS) (98%, Nacalai Tesque Chemicals., Kyoto, Japan) was used without further purification. NH_3 (25%), acetic acid (99.7%), sodium hydroxide (99.7%), iron (III) chloride, and tetramethylammonium hydroxide (TMA, 15%) were obtained from Wako (Osaka, Japan) and used as received. Iron (II) chloride (Superpurification Science Laboratory, Saitama, Japan) was used as received. MPTMS (95%) and MPDMS (95%) were obtained from Shinetsu Chemicals (Tokyo, Japan) and used without further purification. Water was deionized and distilled to have an electric resistance higher than 18 MΩ cm.

Preparation of the magnetic particles

Fe_3O_4 particles were prepared according to the coprecipitative reaction method of Massart [22]. Aqueous solution of 5 cm^3 that contained HCl and $FeCl_2$ at an equal concentration of 2 $kmol/m^3$ was mixed with 20 cm^3 of $FeCl_3$ aqueous solution at 1 $kmol/m^3$. Then, this mixed solution was dissolved into 250 cm^3 of NH_3 aqueous solution at 0.7 $kmol/m^3$, and stirred for 1 h to cause complete reaction for the formation of Fe_3O_4 particles. The particles were sedimented with a magnet placed under the vessel of the solution, and supernatant liquid was removed. Residual solution of the particles was mixed with 30 cm^3 aqueous solution containing dispersion stabilizer TMA at 1 $kmol/m^3$, and then diluted with the deionized water to a total volume of 250 cm^3.

The suspension of Fe_3O_4 particles was transferred to a flask, to which MPTMS or MPDMS was added under stirring to initiate the surface modification of the Fe_3O_4 particles. The suspension stood for more than 0.5 h under stirring. All the reactions in the preparation of the suspension were carried out at ambient temperatures.

Synthesis of magnetic latex particles

Magnetic latex particles were synthesized in a batch reactor (7.5 cm i.d. and 15 cm height) equipped with a 6-bladed 45°pitch paddle with an impeller diameter of 6 cm. The impeller was located one-third of liquid height from the bottom. Styrene and buffer solution were charged into the reactor and then deoxygenated by bubbling with nitrogen for 0.5 h under stirring. After heating the reactant mixture up to 70 °C, the bubbling was stopped and the initiator solution was added to the reaction mixture to initiate polymerization. After a given reaction time, the suspension of the magnetic particles was continuously supplied to the reaction system by a micro-feed pump (Sinko MRP-IX) at a fixed speed. All coating experiments were carried out at a stirring speed of 350 rpm. The pH of the system was measured with a potentiometer (Horiba D-24SE).

Characterization

The Fe_3O_4 particles prepared with the coprecipitative reaction method were observed with a scanning electron microscope (SEM) (Zeiss, LEO 912 OMEGA) operated at 3.2 kW and 80 mA. An X-ray diffractometry (XRD) (Rigaku Denki, RU-200) was used to measure crystalline structures of the Fe_3O_4 particles.

During the polymerization for the preparation of the magnetic latex particles, small amounts of reaction mixture were withdrawn from the reactor. Hydroquinone was added to the mixture to terminate the polymerization. Then, the mixture was dried with lyophilization equipment (Tokyo Rika, FD-5 N) and analyzed with thermal gravimetric (TG) analysis, from which content of Fe_3O_4 in the magnetic latex particles was determined. Monomer-to-polymer conversion of styrene was calculated by subtracting the weights of Fe_3O_4, hydroquinone, initiator, and silane-coupling reagent from the weight of the dried mixture.

Particle size distributions of the magnetic latex particles were determined with transmission electron microscopy (TEM) (Zeiss, LEO 1420). More than 200 particle diameters were measured for each distribution and used to calculate the volume-averaged diameter, d_v, and coefficient of variation, C_v, defined as follows:

$$d_V = \left(\sum n_i d_i^3 / \sum n_i\right)^{1/3} \tag{1}$$

$$C_V = \frac{\left(\sum \left(d_i - \left(\sum n_i d_i / \sum n_i\right)\right)^2 / \sum n_i\right)^{1/2}}{\left(\sum n_i d_i / \sum n_i\right)} \times 100 \tag{2}$$

where n_i is the number of particles with diameter d_i.

Results and discussion

Synthesized Fe_3O_4 particles

Figure 2 shows the TEM photograph of the Fe_3O_4 particles. Most of the particles had sizes from 10 nm to 20 nm, and the average size of the particles was 14.6 nm with a C_v value of 12.8%. XRD measurements confirmed that the particles had the crystalline structure of Fe_3O_4. These particles were surface-modified and used for the coating experiments.

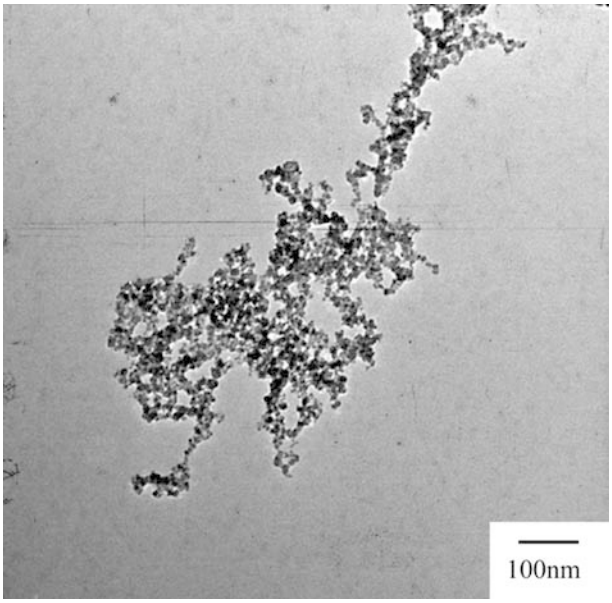

Fig. 2 TEM photograph of Fe_3O_4 magnetic particles

Magnetic latex particles synthesized with coupling reagent of MPTMS

Figure 3 shows photographs of the particles observed during a coating experiment at a styrene concentration of 0.61 $kmol/m^3$ H_2O, a KPS concentration of 8 mol/m^3 H_2O, and a MPTMS concentration of 13 mol/m^3 H_2O, at pH 4.4. In this experiment, the suspension that contained the magnetic particles at 2.1 wt% was continuously supplied to the reaction system for 4 h at a volumetric rate of 15 cm^3/h after a reaction time of 0.5 h. It can be seen from Fig. 3a that, at the reaction time when the supply of magnetic particles started, polymer particles were already generated in the reaction system. The particles grew in size and had the regular shape seen in Fig. 3b. The shape, however, was not spherical but concave around the center, and resembled blood cells in appearance. The particles grew further and retained their shape (Fig. 3c). After completion of the reaction, free magnetic particles were not observed in the reaction system. The content of Fe_3O_4 in the magnetic latex particles determined with the TG analysis was 6.1 wt%, which was consistent with the calculated amount (6.8 wt%) of magnetic particles added.

The values of d_v and C_v of the particle diameters and the monomer-to-polymer conversion of styrene are presented in Figs. 4 and 5. The final d_v was 550 nm, and the C_v value was about 5% through the reaction after 0.5 h. The polymerization almost finished at 7 h, which gave about 100% in product yield.

Besides the experiment of Fig. 3 at pH 4.4, other experiments were also conducted at pH 9.5, 5.4, and 3.8. TEM photographs of final particles are shown in Fig. 6. At pH 9.5, most magnetic particles were not contained in the polymer particles but remained free in the system. At pH 5.4 (close to the isoelectric point 6.5 of Fe_3O_4) some of the magnetic particles were contained in the polymer particles and free magnetic particles were also observed. At pH 3.8 (lower than the isoelectric point) most magnetic particles were contained in polymer particles which, however, aggregated, probably in the late stage of the reaction. Among the pH conditions examined, the most favorable result was obtained at pH 4.4, as shown in Fig. 3.

At pH values much higher than the isoelectric point, the magnetic particles are expected to have a large electric potential of the same sign as the polymer particles, which might prevent the magnetic particles from incorporation into the polymer particles, as observed at pH 9.5. On the other hand, at pH values much lower than the isoelectric point, the magnetic particles and the polymer particles have opposite and strong electric surface potential, which could be the reason for the aggregation at pH 3.8.

To study the effect of MPTMS, we conducted reactions under the same conditions as in Fig. 3 except for

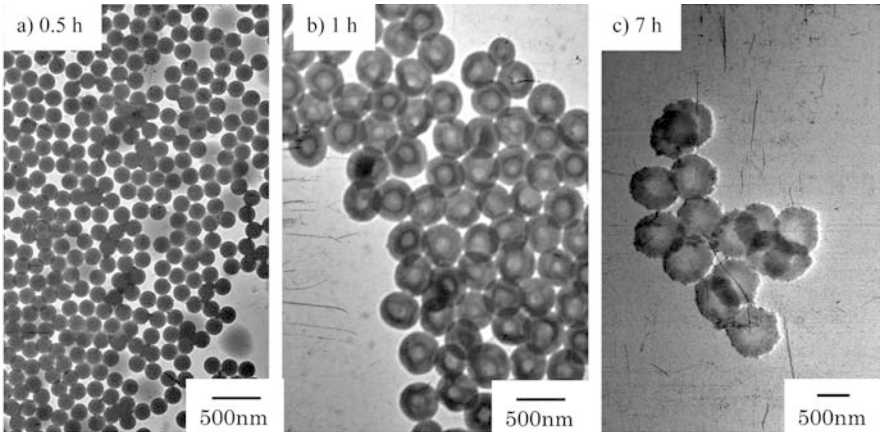

Fig. 3a–c TEM photographs of the particles at reaction times of **a** 0.5 h, **b** 1 h, and **c** 7 h at initial concentrations of [St] = 0.61 kmol/m^3 H_2O, [KPS] = 8 mol/m^3 H_2O, and [MPTMS] = 13 mol/m^3 H_2O for pH 4.4 ([CH_3COOH] = 20 mol/m^3 H_2O, [CH_3COONa] = 10 mol/m^3 H_2O). A 2.1 wt% Fe_3O_4 suspension of a volume 60 cm^3 was continuously supplied after 0.5 h in reaction at a supply rate of 15 cm^3/h

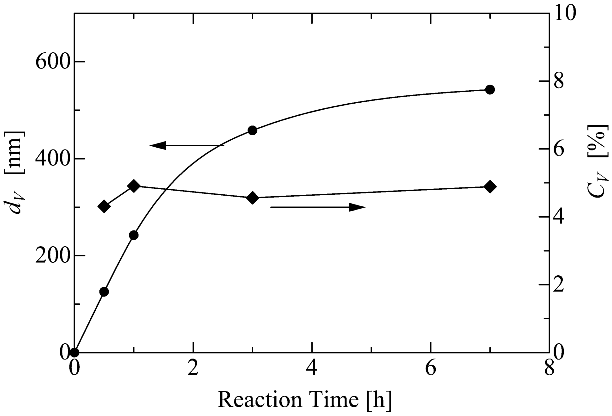

Fig. 4 Volume-averaged diameter d_V and coefficient of variation of particle sizes C_V versus reaction time (see Fig. 3 for conditions)

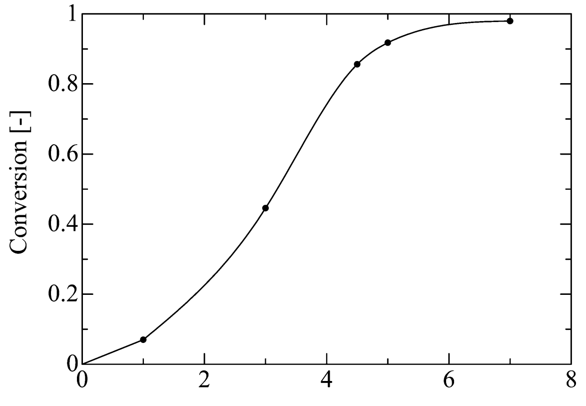

Fig. 5 Monomer-to-polymer conversion versus reaction time (see Fig. 3 for conditions)

the MPTMS concentration. In reaction in the absence of MPTMS, free magnetic particles were observed together with polymer particles that had polydisperse sizes of super micrometers. The polydispersity and the large sizes suggest that coagulation of the polymer particles occurred for long period in the reaction. On the other hand, at a MPTMS concentration of 3 mol/m^3 H_2O, free magnetic particles were not observed and the composite particles prepared had irregular shapes. At a MPTMS concentration of 6.5 mol/m^3 H_2O, polymer particles contained most magnetic particles and had a more irregular shape than those at 13 mol/m^3 H_2O, as shown in Fig. 3.

In our experiments, we also changed initiator concentration, reaction temperature, supply rate of the magnetic particle suspension, and starting time of the supply. The magnetic latex particles obtained in these experiments were not spherical. Very thin, disk-shaped particles were obtained in an experiment where MPTMS was added at a reaction time of 1 h accompanied with continuous supply of the magnetic particle suspension started at 1.5 h. TEM photographs of the particles taken in this experiment are shown in Fig. 7. The spherical shape of polymer particles that appeared at 1 h changed to a disk-like shape at 3 h. The magnetic particles were contained in the polymer particles, possibly in the portion of the particle periphery that looked dark. The image of overlapping of the particles in Fig. 7b indicates very thin particles.

Figure 8 shows the TEM photograph of polymer particles formed in an experiment performed without the supply of magnetic particles. The shape of the particles was concave around their centers and similar to that in Fig. 3. Since the shape of polymer particles in soap-free polymerization without the addition of MPTMS is spherical [23], it can be thought that the appearance of the concave shape arose from the addition of MPTMS.

Magnetic latex particles synthesized with coupling reagent of MPDMS

Using a di-functional coupling reagent MPDMS instead of the tri-functional reagent MPTMS, we carried out coating experiments at KPS concentrations of 8 and

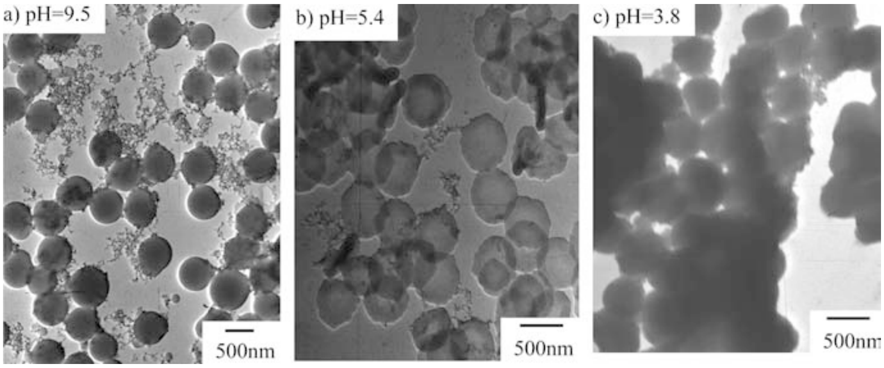

Fig. 6a–c TEM photographs of final particles at **a** pH 9.5 ($[NH_3] = 10\ mol/m^3\ H_2O$, $[NH_4Cl] = 10\ mol/m^3\ H_2O$), **b** pH 5.4 ($[CH_3COOH] = 10\ mol/m^3\ H_2O$, $[CH_3COONa] = 40\ mol/m^3\ H_2O$), and **c** pH 3.8 ($[CH_3COOH] = 80\ mol/m^3\ H_2O$, $[CH_3COONa] = 10\ mol/m^3\ H_2O$) (Reaction conditions are given in Fig. 3)

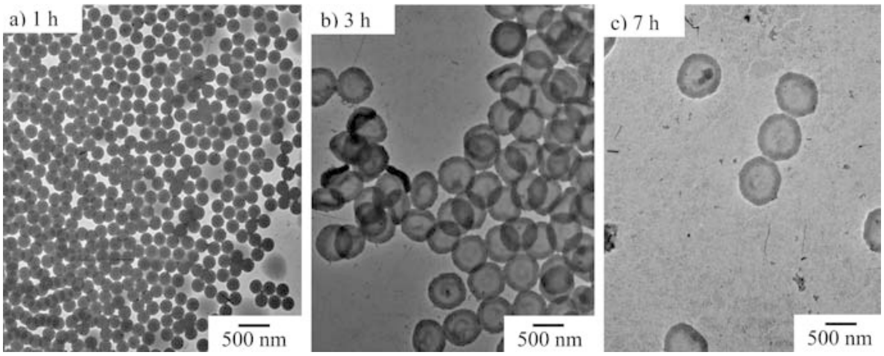

Fig. 7a–c TEM photographs of particles at reaction times of **a** 0.5 h, **b** 3 h, and **c** 7 h with the addition of MPTMS at 1 h. [MPTMS] was $13\ mol/m^3\ H_2O$ and Fe_3O_4 suspension was continuously supplied after 1.5 h (Reaction conditions are given in Fig. 3)

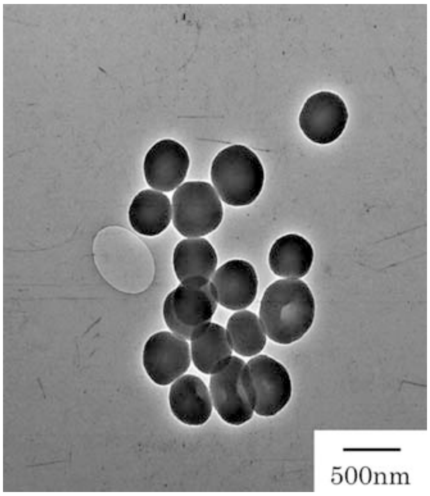

Fig. 8 TEM photograph of final particles without the supply of magnetic particle at $[St] = 0.61\ kmol/m^3\ H_2O$, $[KPS] = 8\ mol/m^3\ H_2O$ and $[MPTMS] = 13\ mol/m^3\ H_2O$ for pH 4.4 ($[CH_3COOH] = 20\ mol/m^3\ H_2O$, $[CH_3COONa] = 10\ mol/m^3\ H_2O$)

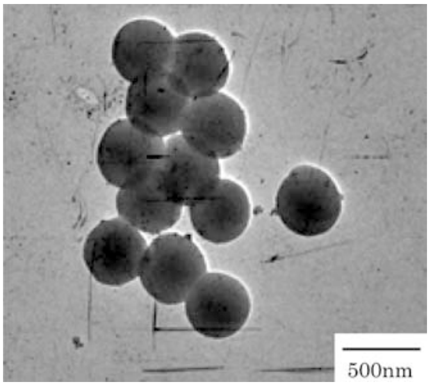

Fig. 9 TEM photograph of final particles at $[MPDMS] = 13\ mol/m^3\ H_2O$ and $[KPS] = 16\ mol/m^3\ H_2O$. Other reaction conditions are the same as in Fig. 3

$16\ mol/m^3\ H_2O$. The other reaction conditions were the same as in Fig. 3. In the experiment at $8\ mol/m^3$, spherical magnetic latex particles appeared during the reaction and agglomeration composed of several particles was observed in the final stage of the reaction. The increase in the initiator concentration to $16\ mol/m^3$ raised the stability of the magnetic latex particles and the agglomeration was not observed. TEM image of the magnetic latex particles is presented in Fig. 9. Free magnetic particles were not observed in the reaction system. The content of Fe_3O_4 in the magnetic latex particles determined with the TG analysis was 6.1 wt%, which was consistent with the calculated amount (6.8 wt%) of magnetic particles added. The shape of the particles was spherical. The size distribution of the particles is shown in Fig. 10. The average diameter d_v was 321 nm, and the C_v value of the particles was 4.4%,

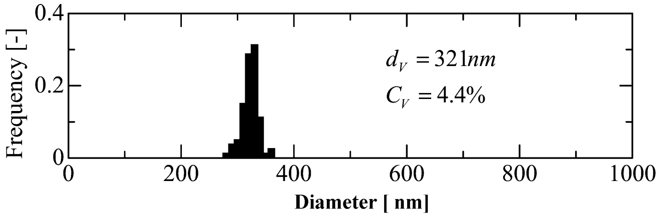

Fig. 10 Size distribution of final particles in the experiment of Fig. 9

which is much smaller than the standard criteria for monodispersity, 10%.

Conclusion

In the coating experiments with styrene, Fe_3O_4 particles and silane-coupling reagents of MPTMS and MPDMS, we were able to produce monodisperse, magnetic latex particles. At a pH of 4.4, most Fe_3O_4 particles were contained in the polymer particles, no aggregation of polymer particles occurred, and almost 100% in product yield was obtained.

The morphology of the magnetic particles depended on the silane-coupling reagents. Use of the tri-functional coupling reagent MPTMS produced non-spherical particles and the shape of particles changed with the addition time of the coupling reagent. Concave-shaped particles like blood cells were obtained when MPTMS was added before the initiation of the reaction. On the other hand, disk-shaped particles were obtained when MPTMS was added after the initiation of the reaction. Use of the di-functional coupling reagent MPDMS instead of MPTMS produced spherical particles that had a coefficient of variation of 4.4%, which is much smaller than the standard criteria for monodispersity, 10%.

References

1. Setchell CH (1984) J Colloid Interface Sci 97:465
2. Shinkai M, Honda H, Kobayashi T (1991) Biocatalysis 5:64
3. Lea T et al. (1988) J Mol Recog 1:1
4. Uheln M (1989) Nature 340:733
5. Kondo A, Kamura H, Higashitani K (1994) Appl Microbiol 41:99
6. Papisov M (1995) Advanced Drug Delivery Reviews 16:127
7. Bach-Gansmo T (1993) Acta Radiologica Suppl 34:2
8. Molday R, Mackenzie D (1982) J Immunol Methods 52:353
9. Carlsen J, Moller M, Lund J (1980) J Nucl Med 21:126
10. Gref R, Minamitake Y, Pracchia M, Trubetskoy V, Torchilin V, Langer R (1994) Science 263:1600
11. Sugibayashi K, Okumura M, Morimoto Y (1982) Biomaterials 3:181
12. Povey AC, Brouet I, Nixon JR, O'Neill IK (1987) J Pharm Sci 76:201
13. Kharkevich DA, Alyautdin R , Filippov VI (1989) J Pharm Sci,41:286
14. Kronick PL, Campbell GL, Joseph K (1978) Science 200:1074
15. Molday RS, Yen SPS, Rembaum A (1977) Nature 268:437
16. Yanase N, Noguchi H, Asakura H, Suzuta T (1993) J Appl Polym Sci 50:765
17. Noguchi H, Yanase N, Uchida Y, Suzuta T (1993) J Appl Polym Sci 48:1359
18. Ugelstad J, Kaggeurd KH, Hansen FK, Berg A (1979) Makromol Chem 180:737
19. Ugelstad J, Kaggeurd KH, Hansen FK, Berg A (1979) Makromol Chem 180:737
20. Ugelstad J, Mork PC, Kaggerud KH, Ellingsen T, Berg A (1980) Adv Colloid Interface Sci 13:1201
21. Ugelstad J, Mork PC, Nordhuus I, Mfutakamba H, Soleimany E, Berg A, Ellingsen T, Khan AA (1985) Makromol Chem, Suppl 10:215
22. Massart (1981) IEE Trans Magn MAG-17:1247
23. Gu S, Konno M (1997) J Chem Eng Japan 30:742