Preparation of Poly(vinyl acetate) Microspheres with Narrow Particle Size Distributions by Low Temperature Suspension Polymerization of Vinyl Acetate

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ABSTRACT: To estimate influences of suspension polymerization conditions including conversion, polymerization temperature, stirring rate, initiator concentration, monomer concentration, and suspending agent concentration on the volume average diameter (D_{avg}) and particle size distribution (PSD) of poly(vinyl acetate) (PVAc) microspheres, vinyl acetate (VAc) was suspension-polymerized at low temperature using 2,2′-azobis(2,4-dimethylvaleronitrile) as an initiator. The effects of each condition, on D_{avg} of PVAc microspheres, were expressed as follows, D_{avg} = [conversion]^a[temperature]^b[rpm]^c[ADMVN]^d[VAc]^f [suspending agent]^g. Logarithms of D_{avg} were linearly proportional to those of polymerization conditions, and their exponents, a, b, c, d, f, and g were calculated as 0.27, −13.7, −1.37, −0.21, 0.58, and 0.29, respectively. Variations of PSDs, according to polymerization conditions, were examined by considering polymerization rate, droplet or suspension viscosity, and droplet break-up/coagulation equilibrium. From these results, PVAc microspheres with various sizes and narrow PSDs were obtained effectively under carefully controlled polymerization conditions, which can be used as promising precursors of novel PVA microspheres through heterogeneous surface saponification. © 2006 Wiley Periodicals, Inc. J Appl Polym Sci 101: 4064–4070, 2006

Key words: suspension polymerization; PVAc; microspheres; narrow PSD

INTRODUCTION

Suspension polymerization is a common industrial process for many reasons, including the ease with which the heat produced by the strongly exothermic reaction and the large increase in the viscosity of the reaction media over the course of polymerization can be removed and the possibility of producing polymer particles with diameters in the range 50–1000 μm, which can be appropriate for different applications. Polymer particles, produced by suspension polymerization, have been used in chromatographic separations, ion-exchange chromatography, and biomedical applications such as enzyme immobilization, drug delivery, cell culturing, embolization, and immunochemistry.[1–13]

Among various properties, particle size distribution (PSD) plays an important role in many applications. For example, polymer particles with narrow PSD make it possible to occlude target blood vessel selectively in embolization. And, if the polymer is used as bone cement, the PSD strongly affects the thermal effect during implantation and the mechanical and ageing behavior of the final product. While the theoretical and experimental methodologies available for the estimation and measurement of the molecular weight distribution (MSD) are well developed, the same cannot be stated with regard to the PSD.[14]

PSD is a complex function of drop break up and coalescence rates during the polymerization. Those are affected by several parameters such as the densities and viscosities of each phase, interfacial tension, type and concentration of suspending agent, dispersed-phase hold up, type of impeller, and stirring speed.[15–17] In suspension polymerization, especially for the case of batch process, the evolution of drop size is more complex because drop viscosity increases continuously as polymerization proceeds, and the particles obtained have a broad PSD due to the different mechanisms for particle formation coexisting in suspension polymerization.[18]

There have been many studies relating to the influences of the conformation of the PSD in suspension polymerization. A theoretical model of suspension polymerization using a particle population balance was

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proposed,[19] and influences of polymerization conditions, such as conversion, temperature, stirring speed, suspending agent concentration, monomer concentration, and initiator concentration on PSD, were examined.[14,19–21]

In general, suspension polymerization, using benzoyl peroxide or 2,2′-azobis isobutyronitrile as initiator, is conducted at a polymerization temperature of over 50°C and the resulting polymer beads have a wide PSD. We thought that, to obtain polymer beads with a narrow PSD, a stable steady state of monomer droplets is necessary, and excessive coalescence should be excluded at the growth stage, which may be realized by lowering the polymerization temperature. Furthermore, at higher polymerization temperature, it is more difficult to control the polymerization system closely due to increased polymerization rate and the resulting viscosity increase in droplets.

Vinyl acetate (VAc) and vinyl pivalate, which are precursors of poly(vinyl alcohol) (PVA), could be polymerized at room temperature using the low-temperature initiator, 2,2′-azobis(2,4-dimethylvaleronitrile) (ADMVN).[22–27] Especially, when VAc and VPi was suspension-polymerized at low temperature, the resulting PVAc and PVPi had ultrahigh molecular weight and was obtained at high yield, over 90%.[28,29]

In this study, VAc was suspension-polymerized at low temperature, using ADMVN, to obtain PVAc microspheres with a narrow PSD, which is expected to be a profitable precursor of PVA microspheres applicable to embolization. The effect of suspension polymerization conditions including conversion, temperature, stirring speed, suspending agent concentration, monomer concentration, and initiator concentration on the volume average diameter (D_{avg}) and PSD was investigated.

EXPERIMENTAL

Materials

VAc, purchased from Shin-Etsu, was washed with an aqueous solution of $NaHSO_3$ and water and dried over anhydrous $CaCl_2$, followed by distillation under reduced pressure of nitrogen. The initiator ADMVN (Wako, 99%) was recrystallized twice from absolute methanol before use. PVA, with number-average molecular weight of 127,000 and degree of saponification of 88% (Aldrich), was used as a suspending agent. Other extra-pure grade reagents were used without further purification. Water used for all the procedures was deionized.

Suspension polymerization of VAc

In a typical reaction, suspension agent was dissolved in water under a nitrogen atmosphere and constant stirring in a 250-mL reactor fitted with a condenser. After degassing, VAc along with the ADMVN was added all at once at a fixed polymerization temperature. After predetermined times, the reaction mixture was cooled and kept for 1 day to effectively separate and to sink spherical PVAc particles. To eliminate residual VAc and suspension agent, the PVAc polymerized was filtered and washed with warm water. The washed PVAc microspheres were dried in a vacuum oven at 40°C for 48 h before weighing. The conversion was determined by the following expression

$$\text{Conversion} = (W_p/W_m) \times 100 \quad (1)$$

where W_P and W_m are the weight of dry microspheres and the total weight of the monomers initially charged in the reactor, respectively. The detailed polymerization conditions are listed in Table I.

TABLE I
Standard Suspension Polymerization Conditions

Initiator concentration	0.001 mol/mol of VAc
Suspending agent concentration	1.5 g/dL
Rpm	300
Temperature	30°C
Conversion	40%
VAc/water	0.5 L/L

Characterization

The surface morphology of the PVAc specimens was investigated using a scanning electron microscope (SEM, JSM 5800-LV, JEOL, Japan).

The particle size and size distribution were measured with a Horiba LA-910 laser scattering particle size distribution analyzer (the range of operational measurements is from 20 nm to 1020 μm.). The mean diameter obtained from this data analysis was the volume-average diameter (D_{vad}). The particle diameters of some samples were also measured directly from SEM. Prior to SEM examination, the samples were dried at room temperature and coated with a thin layer of gold, using a JEOL ion-sputter JFC-1100 coating machine. The number-average diameter (D_n) and weight-average diameter (D_w) were calculated from the following equation.[30,31] At least 300 particles (N) were counted for each calculation.

$$D_n = \sum N_i D_i / \sum N_i \quad (2)$$

$$D_w = \sum N_i D_i^4 / \sum N_i D_i^3 \quad (3)$$

The polydispersity index (PI) of the particle size is expressed as D_w/D_n. When using the Horiba LA-910, N_i and D_i correspond to the values of frequency dis-

tribution and mean diameter, respectively, for the calculation of D_w/D_n. The D_w/D_n values ranging from 1.0 to 1.1 were regarded as monodisperse particle size distributions and those ranging from 1.1 to 1.2 as near-monodisperse size distributions. The particle size and size distribution obtained from Horiba LA-910 were reproducible and were similar to those measured by the SEM.

RESULTS AND DISCUSSION

In embolization, there has been a need for various PVA particles with narrow PSD to occlude, selectively, blood vessels of which diameters are diversified with diseases, including tumor, arteriovenous malformation, and uterine fibroid. Furthermore, PSD is the more significant property, because PVA particles with larger or smaller diameter than the target vessel's may block others, causing harmful side effects.

In general, PVAc, as the precursor of PVA, is obtained by bulk, solution, emulsion, or suspension polymerization of VAc. It is impossible to obtain spherical PVAc particles through bulk or solution polymerization. In the case of emulsion polymerization, the particle size is too small to be used for embolic material of which diameter is over 50 μm at least. Particle size and PSD of suspension-polymerized particle are affected by the type and amount of initiators and suspending agents, monomer ratio to water, stirring method and speed, and polymerization temperature. For example, the higher the stirring speed, the higher the conversion of monomer, and molecular weight of polymer becomes higher and narrower the PSD.[32,33]

As most suspension polymerizations of VAc have been carried out at polymerization temperatures over 50°C, it was very difficult to obtain PVAc particles with adequate size and narrow size distribution available to embolization due to increased polymerization rate. In this study, ADMVN was used as an initiator to obtain PVAc microspheres with a narrow PSD by lowering polymerization temperature. Effects of polymerization conditions, including conversion, polymerization temperature, stirring speed, initiator concentration, monomer concentration, suspending agent concentration, D_{avg} and PSD, were examined by verifying one of the polymerization conditions with others fixed, as shown in Table I.

The effects of each condition on D_n of PVAc microsphere were expressed as exponents (eq 4), by which it was estimated how the conditions affect.

$$D_{avg} = [\text{conversion}]^a[\text{temperature}]^b[\text{rpm}]^c[\text{ADMVN}]^d [\text{VAc}]^f[\text{suspending agent}]^g \quad (4)$$

The logarithm of D_{avg} and PI of PVAc microspheres versus the logarithm of conversion are shown in Figure 1. Log[D_{avg}] linearly increased with log[conversion], and exponent a was calculated at 0.27. At the early stage of the polymerization, average size and PI of the particles obtained are similar to that of monomer drops, where the rate of drop break-up is higher than that of drop coalescence, resulting in small D_{avg} and narrow PI. As the drop viscosity increased owing to polymerization, drops could not be easily broken up, but they could still undergo coalescence. As a result, D_{avg} increased and PI broadened. It is interesting to see that PI showed a steep rise over the conversion of 50%, and resulting degree of homogeneity of PVAc microspheres was very low. This is attributed to the newly formed particles resulting from polymerization of small drops, whereas the existing large particles were stopped in their growth because there was no coalescence owing to their solid-like property and, therefore, little consumption of monomers owing to frequent chain transfer reactions between polymers which were the results of the gel effect.[21,28,29]

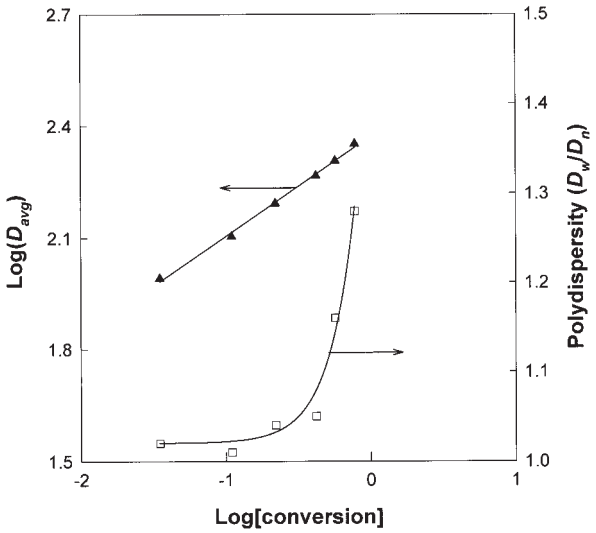

Figure 1 Effect of fractional conversion of VAc into PVAc on the D_{avg} and PI of PVAc particles obtained by the suspension polymerization using ADMVN concentration of 0.001 mol/mol of VAc, suspending agent concentration of 1.5 g/dL, VAc/water of 0.5 L/L, and agitation speed of 300 rpm at 30°C.

Polymerization temperature has a significant effect on the control of particle size and PSD. As polymerization temperature increases, polymerization rate of VAc increases severely and rheological properties change. As polymerization temperature increased, the polymerization rate of VAc increased rapidly and rheological properties changed significantly. Thus, polymerization temperature might be the major factor influencing particle size and PSD of PVAc. Polydispersity indices of polymerized particles had higher values than 1.1 at temperatures over 40°C. The log D_{avg} was linearly proportional to that of temperature and D_{avg} decreased with temperature (Fig. 2).

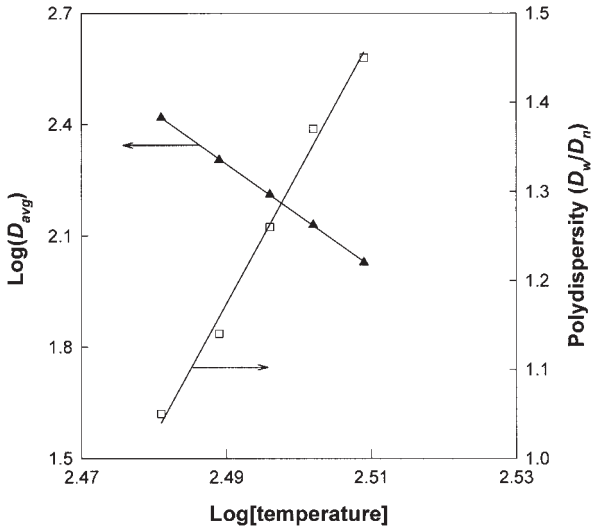

Figure 2 Effect of polymerization temperature on the D_{avg} and PI of PVAc particles obtained by the suspension polymerization using ADMVN concentration of 0.001 mol/mol of VAc, suspending agent concentration of 1.5 g/dL, VAc/water of 0.5 L/L, and agitation speed of 300 rpm (PVAc was sampled at similar conversion of ~40%.).

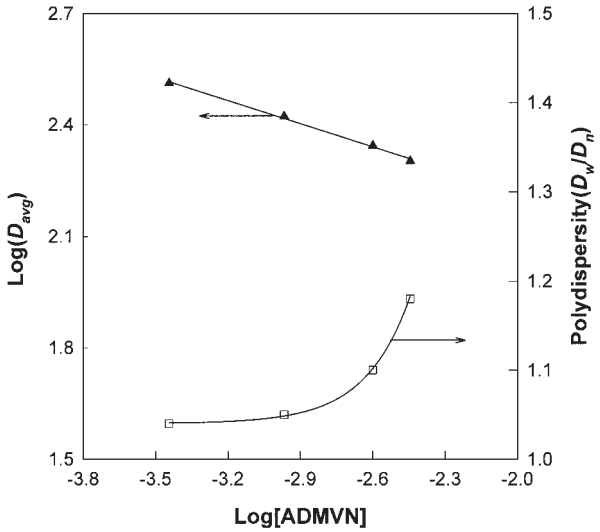

Figure 4 Effect of initiation concentration ([ADMVN]) on the D_{avg} and PI of PVAc particles obtained by the suspension polymerization using suspending agent concentration of 1.5 g/dL, VAc/water of 0.5 L/L and agitation speed of 300 rpm at 30°C (PVAc was sampled at similar conversion of ~40%.).

Figure 3 shows that D_{avg} was decreased with increasing stirring rate due to dominant break-up of monomer droplets at high stirring rates and the value of exponent c was −1.3. The magnitude of exponent c was smaller than that of temperature. Thus, stirring rate might have less of an influence on D_{avg} and PI than polymerization temperature; however, D_{avg} and PSD could be controlled more effectively because they were not as sensitive to change as varying stirring rate. As stirring rate increased, monomer droplet break-up and aggregation were equilibrated rapidly and suspensions became stable, so PSD became narrow.

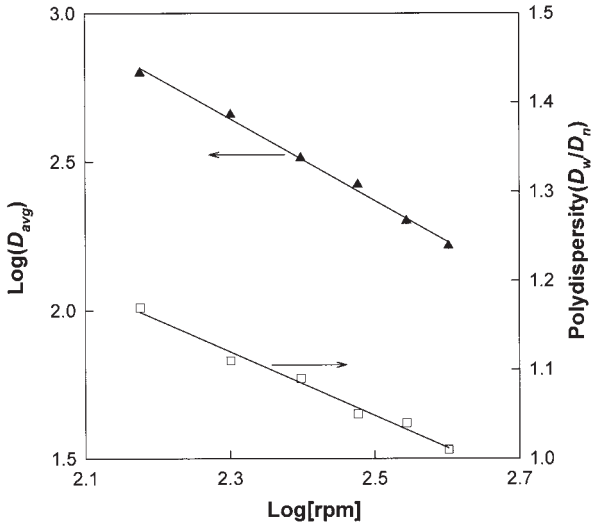

Figure 3 Effect of agitation speed (rpm) on the D_{avg} and PI of PVAc particles obtained by the suspension polymerization using ADMVN concentration of 0.001 mol/mol of VAc, suspending agent concentration of 1.5 g/dL, VAc/water of 0.5 L/L at 30°C (PVAc was sampled at similar conversion of ~40%.).

In radical polymerization, as initiator concentration increased, polymerization rate increased and molecular weight of obtained polymer decreased. In this study, to obtain PVAc particles with narrow PSD, suspension polymerizations were carried out fixed at 30°C, which is relatively low compared to others, using the low-temperature initiator, ADMVN. With increasing ADMVN concentration, D_{avg} decreased and PSD became narrow due to rapid polymerization rate (Fig. 4). Consequently, PVAc particles with low PI and high molecular weight were obtained, which were promising precursors to PVA microsphere when monodisperse particles were prepared through heterogeneous surface saponification.[34]

For VAc concentration, frequent collisions between monomer droplets took place at higher concentration. D_{avg} became larger and it was difficult to equilibrate droplet break-up and coagulation resulting in broad PSD (Fig. 5). The significant increase of polydispersity at higher VAc concentration was affected by two factors at least, as follows

1. Monomer droplet coagulation is proportional to the square of [VAc], but break-up to [VAc].
2. Suspension was unstable at high [VAc], because suspending agent concentration was fixed at 1.5 g/dL_{water}.

In general, partially saponified PVA is one of the most useful suspending agents and widely used in suspen-

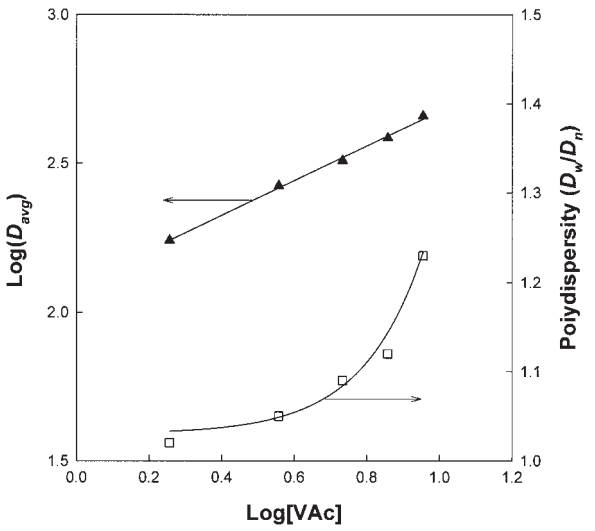

Figure 5 Effect of monomer concentration ([VAc]) on the D_{avg} and PI of PVAc particles obtained by the suspension polymerization using ADMVN concentration of 0.001 mol/mol of VAc, suspending agent concentration of 1.5 g/dL, and agitation speed of 300 rpm at 30°C (PVAc was sampled at similar conversion of ~40%.).

sion polymerization up to the present. In this study, PVA, with degree of saponification 88% and molecular weight 127,000, was used as suspending agent. Especially, little effort was needed to separate suspending agent from PVAc particles, as, after suspension polymerization of the VAc, most PVAc particles were used as the precursor of PVA, and PVAc particles and partially saponified PVA as suspending agent were converted to the same PVA by heterogeneous surface saponification.[34] By increasing the concentration of the suspending agent, D_{avg} became decreased owing to lowered surface free energy and increased suspension viscosity causing frequent monomer droplet break-up. Polydispersity indices were lower than 1.1, around the suspending agent concentration [PVA] of 1.5 g/dL. At low [PVA], suspending agent did not work effectively at the interface of monomer droplet and water, and suspension was unstable, so it was difficult to attain to equilibrium state of monomer droplet size. Although increasing the concentration of suspending agent leads to higher stability of droplets, globules of the molecules of suspending agent appear in the water phase. Polymer particles made by such globules were very small and, therefore, PSD becomes extremely wide (Fig. 6).[19]

Exponents of polymerization conditions, including conversion, temperature, stirring rate, initiator concentration, VAc concentration, and suspending agent concentration, are expressed in eq. (5). As mentioned earlier, they may be changed with polymerization systems; however, it can be estimated which condition has a major effect on D_{avg} and, furthermore, what we can do to control precisely particle size and particle size distribution.

$$D_{avg} = [\text{conversion}]^{0.27}[\text{temperature}]^{-13.7}[\text{rpm}]^{-1.37}[\text{ADMVN}]^{-0.21}[\text{VAc}]^{0.58}[\text{suspending agent}]^{0.29} \quad (5)$$

Figure 7 shows scanning electron micrographs images of PVAc particles obtained at various stirring rates and calibrated by excluding PVAc particles with extremely large or small diameters using standard sieves, which process is necessary especially when they are used as a precursor of new embolic PVA microspheres. D_{avg} of PVAc particles, having narrow PSD, could be successfully diversified by careful control of polymerization conditions.

CONCLUSIONS

Polymerization conditions, including conversion, temperature, stirring rate, initiator concentration, VAc concentration, and suspending agent concentration, influenced D_{avg} and PSD of suspension-polymerized PVAc particles and their influences over D_{avg} were expressed as exponents, 0.27, −13.7, −1.37, −0.21, 0.58, and 0.29, respectively. D_{avg} was significantly affected by polymerization temperature and could be controlled effectively by verifying stirring rate. PSD became narrow at low conversion, low temperature, high stirring rate, low ADMVN concentration, low VAc concentration or adequate suspending agent concentration. Influences of such polymerization conditions on PI were examined by considering polymer-

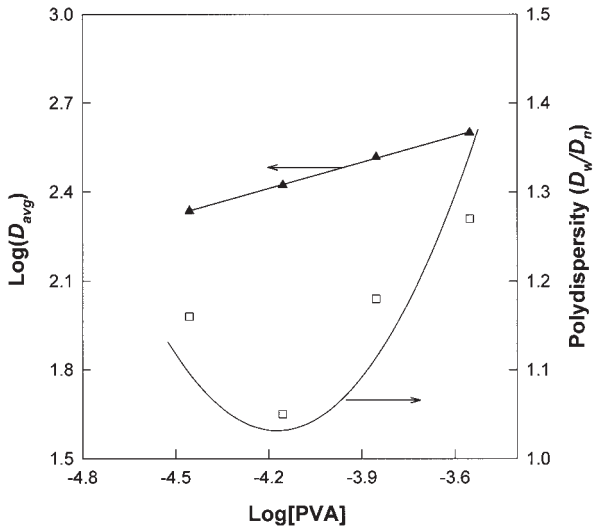

Figure 6 Effect of suspending agent concentration ([PVA]) on the D_{avg} and PI of PVAc particles obtained by the suspension polymerization using ADMVN concentration of 0.001 mol/mol of VAc, VAc/water of 0.5 L/L, and agitation speed of 300 rpm at 30°C (PVAc was sampled at similar conversion of ~40%.).

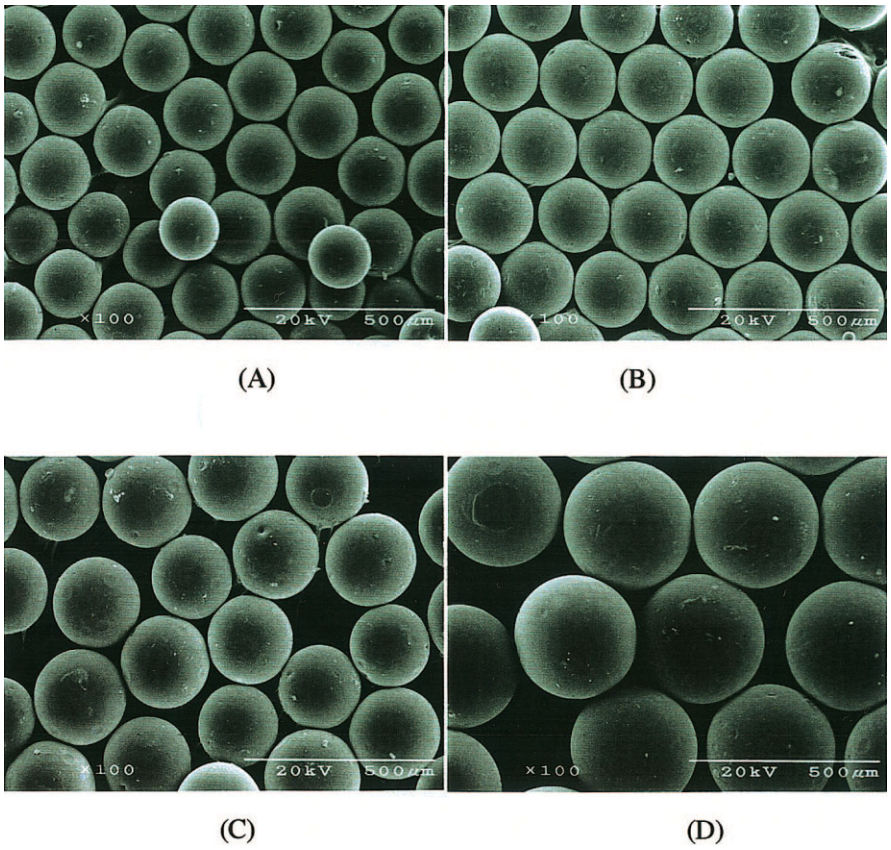

Figure 7 Scanning electron micrographs of PVAc microspheres obtained by the suspension polymerization using ADMVN concentration of 0.001 mol/mol of VAc, suspending agent concentration of 1.5 g/dL, and VAc/water of 0.5 L/L at 30°C: (A) 163 μm at 400 rpm; (B) 223 μm at 350 rpm; (C) 281 μm at 300 rpm; and (D) 340 μm at 250 rpm (PVAc was sampled at similar conversion of about 40%.). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

ization rate, droplet or suspension viscosity, and droplet break-up/coagulation equilibrium. In the near future, we will report on the monodisperse PVA microspheres prepared by the heterogeneous saponification of PVAc polymerized in this study.

References

1. Kahovec, J.; Jelinkova, M.; Coupek, J. Polym Bull 1987, 18, 495.
2. Kahovec, J.; Coupek, J. React Polym 1988, 8, 105.
3. Chang, M.; Colvin, M.; Rembaum, A. J Polym Sci Polym Lett Ed 1986, 24, 603.
4. Kamei, S.; Okubo, M.; Matsumoto, T. J Appl Polym Sci 1987, 34, 1439.
5. Robert, C. C. R.; Buri, P. A.; Peppas, N. A. J Controlled Rel 1987, 5, 151.
6. Scranton, A. B.; Bowman, C. N.; Klier, J.; Peppas, N. A. Polymer 1992, 33, 1683.
7. Dawson, R. M.; Broughtn, R. L.; Stevenson, W. T. K.; Sefton, O. Biomaterials 1987, 8, 360.
8. Stevenson, W. T. K.; Sefton, O. Biomaterials 1987, 8, 449.
9. Horak, D.; Svec, F.; Adamyan, A.; Titoca, M.; Voronkova, O.; Kokov, L.; Gumargalieva, K. Biomaterials 1986, 7, 467.
10. Horak, D.; Svec, F.; Kalal, J.; Adamyan, A.; Titova, M.; Voronkova, O.; Trostenyuk, N.; Vishnevski, V.; Gusienov, E.; Gumergalieva, K. Clin Mater 1990, 6, 287.
11. Horak, D.; Svec, F.; Isakov, Y.; Polyaeva, Y.; Adamyan, A.; Konstantinov, K.; Shafranov, V.; Voronkova, O.; Nikanorov, A.; Trostenyuk, N. Clin Mater 1992, 9, 43.
12. Rembaum, A.; Yen, S. P. S.; Sheng, E.; Wallave, S.; Molday, R. S.; Gordon, J. L.; Dreyer, W. J. Macromolecules 1976, 9, 328.
13. Rembaum, A.; Yen, S. P. S.; Molday, R. S. J Macromol Sci A 1979, 12, 603.
14. Polacco, G.; Palla, M. and D. Semino Polym Int 1999, 48, 392.
15. Brooks, B. W. Makromol Chem Macromol Symp 1990, 35/36, 121.
16. Yuan, H. G.; Kalfas, G.; Ray, W. H. J Macromol Sci Rev Macromol Chem Phys 1991, C31, 215
17. Vivaldo-Lima, E.; Wood, P. E.; Hamielec, A. E.; Penlidis, A. Ind Eng Chem Res 1997, 36, 939.
18. Cunningham, M. F. Poly React Eng 1999, 7, 231.
19. Gritzkova, I. A.; Adebayo, G. G.; Krasheninnikova, I. G.; Kaminsky, V. A. Colloid Polym Sci 1998, 276, 1068.
20. Tuncel, A. Colloid Polym Sci 2000, 278, 1126.
21. Jahanzad, F.; Sajjadi, S.; Brooks, B. W. Macromol Symp 2004, 206, 255.
22. Lyoo, W. S.; Han, S. S.; Choi, J. H.; Ghim, H. D.; Yoo, S. W.; Lee, J.; Hong, S. I.; Ha, W. S. J Appl Polym Sci 2001, 80, 1003.
23. Lyoo, W. S.; Kim, B. C.; Lee, C. J.; Ha, W. S. Eur Polym Mater 1997, 33, 785.
24. Lyoo, W. S.; Yeum, J. H.; Ghim, H. D.; Ji, B. C.; Yoon, W. S.; Kim, J. P. J Korean Fiber Soc 2000, 37, 487.
25. Lyoo, W. S.; Blackwell, J.; Ghim, H. D. Macromolecules 1998, 31, 4253.

26. Lyoo, W. S.; Kim, B. J.; Ha, W. S. J Korean Fiber Soc 1996, 33, 231.
27. Lyoo, W. S.; Kim, J. H.; Ghim, H. D. Polymer 2001, 42, 6317.
28. Lyoo, W. S.; Lee, S. G.; Kim, J. P.; Han, S. S.; Lee, C. J. Colloid Polym Sci 1998, 276, 951.
29. Lyoo, W. S.; Park, C. S.; Yeum, J. H.; Ji, B. C.; Lee, C. J.; Lee, S. S.; Lee, J. Y. Colloid Polym Sci 2002, 280, 1075.
30. Capek, I.; Riza, M.; Akashi, M. Makromol Chem 1992, 193, 2843.
31. Saenz, J. M.; Asua, J. M. J Polym Sci Part A: Polym Chem 1995, 33, 1511.
32. Bamford, C. H.; Jenkins, A. D.; Johnston, R. J Polym Sci 1958, 29, 355.
33. Sorenson, W. R.; Campbell, T. W. In Preparative Methods of Polymer Chemistry, 2nd ed.; Wiley Interscience: New York, 1968; p 238.
34. Lee, C. J.; Lyoo, W. S.; Kwon, I. C.; Lee, S. G.; Kim, J. P.; Han, M. H. US Pat. 6,191,193 (2000).