Preparation of Novel Syndiotactic Poly(vinyl alcohol) Microspheres through the Low-Temperature Suspension Copolymerization of Vinyl Pivalate and Vinyl Acetate and Heterogeneous Saponification

Se Geun Lee,[1] Jae Pil Kim,[1] Won Seok Lyoo,[2] Jin Woo Kwak,[2] Seok Kyun Noh,[3] Chan Sik Park,[4] Jae Hyun Kim[4]

[1]*School of Materials Science and Engineering, Seoul National University 151-742, Korea*
[2]*School of Textiles, Yeungnam University, Kyongsan 712-749, Korea*
[3]*School of Chemical Engineering and Technology, Yeungnam University, Kyongsan 712-749, Korea*
[4]*R&D Center, Dongjin Semichem Company, Gyeonggi-do 445-931, Korea*

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ABSTRACT: Syndiotactic poly(vinyl alcohol) (PVA)/poly(vinyl pivalate/vinyl acetate) [P(VPi/VAc)] microspheres, with a skin–core structure, were prepared through the heterogeneous saponification of copolymers of vinyl pivalate (VPi) and vinyl acetate (VAc). For the preparation of P(VPi/VAc) microspheres with various particle sizes and a uniform particle size distribution (which are promising precursors of syndiotactic PVA embolic materials to be introduced through catheters for the management of gastrointestinal bleeders, arteriovenous malformations, hemangiomas, and traumatic rupture of blood vessels), VPi and VAc were suspension-copolymerized at 30°C with a room-temperature initiator, 2,2′-azobis(2,4-dimethylvaleronitrile). The effects of the polymerization conditions were investigated in terms of the size and size distribution of the suspension particles. P(VPi/VAc) microspheres, with various syndiotactic dyad (s-dyad) contents, were produced through the control of the monomer feed ratio. In addition, monodisperse P(VPi/VAc) particles of various particle diameters were obtained by the separation and sieving of the polymerization product. Monodisperse P(VPi/VAc) microspheres of various particle sizes were partially saponified in the heterogeneous system, and the effects of the particle size and particle size distribution on the saponification rate were investigated in terms of the tacticity and the saponification time and temperature. Novel skin–core PVA/P(VPi/VAc) microspheres of various s-dyad contents and degrees of saponification were successfully produced through the control of the various polymerization and saponification parameters. © 2005 Wiley Periodicals, Inc. J Appl Polym Sci 95: 1539–1548, 2005

Key words: syndiotactic PVA; P(VPi/VAc); microspheres; skin/core; heterogeneous saponification

INTRODUCTION

Poly(vinyl alcohol) (PVA), obtained by the saponification of poly(vinyl ester)s such as poly(vinyl acetate) (PVAc) and poly(vinyl pivalate) (PVPi), is a linear and semicrystalline polymer that has been widely used as fibers for clothing and industrial uses, films, membranes, medicines for drug delivery systems, and cancer-cell-killing embolic materials. PVA fibers and films are potentially high-performance materials because they have high tensile and impact strengths, high tensile moduli, high abrasion resistance, excellent alkali resistance, and oxygen barrier properties that are superior to those of other known polymers.[1–3] To maximize these physical properties, the molecular weight, degree of saponification (DS), and syndiotacticity should be increased.[4–10] In particular, the molecular weight is a fundamental factor affecting the physical properties, and so the improvement of polymerization methods for vinyl acetate (VAc)[11–16] is necessary.

PVA obtained from PVAc, the most common precursor of PVA, is almost atactic, and its syndiotactic dyad (s-dyad) content is about 48–53(%). To enhance the syndiotacticity and molecular weight of PVA, PVPi is selectively used as a precursor of PVA. PVA obtained from PVPi has the highest syndiotacticity of PVAs obtained via radical polymerization, and the s-dyad content of PVA, prepared by the low-temperature polymerization of vinyl pivalate (VPi),[17–26] is greater than 60%. Therefore, we can obtain PVAs with various tacticities through the copolymerization of VAc and VPi, and we can examine the relationship between the physical properties of PVAs and their tacticities.

Correspondence to: W. S. Lyoo (wslyoo@yu.ac.kr).
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Four common polymerization methods for monomeric precursors of PVA are bulk, solution, emulsion, and suspension polymerizations. Suspension polymerization is a powerful process for many reasons, including the ease with which the heat produced by the strongly exothermic reaction can be removed and the possibility of producing polymer particles with diameters of 50–1000 μm, which can be appropriate for many industrial applications.[27,28] As is well known, the molecular weight of a polymer prepared by suspension polymerization is controlled by the type and amount of the initiator and suspending agent, the polymerization temperature, the monomer-to-water ratio, and the agitation speed. The higher the agitation speed is, the higher the molecular weight and conversion are.[29–31] In comparison with the rarity of studies on the suspension polymerization of VPi, there have been many on the suspension polymerization of VAc because it is possible to reach higher conversions with this polymerization method than with other polymerization methods.[32,33]

Embolization is a nonsurgical procedure that occludes an abnormal artery or vein (blood vessel) through the injection of a special embolic material through a catheter. This closes the blood vessel and stops or prevents bleeding. For nearly 30 years, this embotherapy technique has been used as a means of stopping uncontrollable bleeding from the uterus due to cancer, blood vessel malformations, and traumatic rupture of blood vessels. Many different polymeric materials have been used to occlude vessels. Among them, PVA is extensively used for the superselective embolization of vascular lesions because of its good biocompatibility, few foreign-body reactions *in vivo*, high blocking efficiency due to good binding properties, and ease of treatment.[34–36] PVA can be introduced through catheters in the management of gastrointestinal bleeders, arteriovenous malformations, hemangiomas, and traumatic rupture of blood vessels. Because it can be compressed and subsequently reexpands on contact with blood, PVA has been used as an embolic plug to occlude large vessels. Commercial PVA embolic particles, such as Contour and Ivalon, have been obtained through the pulverization of fully saponified PVA sponges.[37–41] The irregularity of the particle size and the shape have caused inflammatory reactions in the walls of embolized vascular tissues and made it difficult to occlude targeted blood vessels selectively.[35,36,40,41] Therefore, the regulation of the particle size homogeneity, spherical morphology, and stability to human blood is required. Until now, there have been few results on the preparation of PVA microspheres with uniform diameters and blood stabilities.

In this study, a room-temperature initiator, 2,2′-azobis(2,4-dimethylvaleronitrile) (ADMVN), was selected for the suspension copolymerization of VPi and Vac to obtain ultrahigh-molecular-weight (UHMW) syndiotactic poly(vinyl pivalate/vinyl acetate) [P(VPi/VAc)] microspheres with higher conversions, various particle sizes, and a uniform size distribution. They are expected to be profitable precursors of UHMW syndiotactic PVA microspheres with high yields. P(VPi/VAc) microspheres, with various s-dyad contents, were produced through the control of the VPi content. Monodisperse P(VPi/VAc) microspheres with various particle sizes and s-dyad contents were then partially saponified in the heterogeneous system. The effects of the particle size and particle size distribution on the saponification rate were considered. The influence of the molecular parameters of the P(VPi/VAc) microspheres and the saponification conditions on the DS of the PVA microspheres was investigated.

EXPERIMENTAL

Materials

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

Suspension copolymerization of VPi and VAc

In a typical reaction, the suspending agent was dissolved in water, under a nitrogen atmosphere and with constant stirring, in a 250-mL reactor fitted with a condenser. After degassing, the VPi and VAc monomers, along with ADMVN, were added all at once at a fixed polymerization temperature. After predetermined times, the reaction mixture was cooled and kept for 1 day to separate and sink spherical P(VPi/VAc) particles. To eliminate residual VPi and VAc and the suspending agent, P(VPi/VAc) was filtered and washed with warm water. The conversion was calculated from the weight of the polymer. The conversion was the average of three determinations. The polymerization conditions are listed in detail in Table I.

Heterogeneous surface saponification of the P(VPi/VAc) microspheres

The following is an example of the heterogeneous saponification of P(VPi/VAc) microspheres. In a flask equipped with a reflux condenser, a thermocouple, a

TABLE I
Suspension-Copolymerization Conditions of VPi and VAc

Type of initiator	ADMVN
Type of suspending agent	PVA
Initiator concentration	0.0001 mol/mol of monomers
Suspending agent concentration	1.5 g/dL of water
VPi/VAc	1/9, 2/8, 3/7, 4/6, and 5/5 mol/mol
Monomers/water	0.50 L/L
rpm	300 and 500
Temperature	30°C

dropping funnel, and a stirring device, an alkali solution (sodium hydroxide/sodium sulfate/methanol or ethanol/water) was made. P(VPi/VAc) microspheres (0.5 g) were slowly added to the flask during stirring. After the reaction, the reaction mixture was poured into cold water and kept for 1 day to separate and sink spherical skin–core PVA/P(VPi/VAc) particles. The solid saponification product was filtered and washed several times with water and was dried *in vacuo* at 40°C for 1 day. PVA/P(VPi/VAc) microspheres, with a skin–core structure, were obtained through the control of the saponification time. Residual ester groups could not be detected in the ^{1}H-NMR spectra of these specimens.

Elimination of the static electricity and sieving of the particles

Polymerized and saponified particles were separated into individual particles with a dispersion agent and an antistatic agent, such as sodium sulfate, potassium sulfate, magnesium sulfate, or sodium chloride, and were sieved with standardized mesh sieves.

Acetylation of PVA[42]

A mixture of 1 g of PVA, 2 mL of pyridine, 20 mL of acetic anhydride, and 20 mL of acetic acid was stirred in a three-necked flask at 100°C for 100 h under an atmosphere of nitrogen. The mixture was poured into cold water to precipitate PVAc. PVAc thus produced was filtered and purified by reprecipitation from methanol and water.

Characterization

The surface morphology of the particles was investigated with a scanning electron microscope (JSM 5800-LV, JEOL, Japan) and an optical microscope.

The particle size and size distribution were measured with a Horiba LA-910 laser scattering particle size distribution analyzer (the range of operational measurements was 20 nm to 1020 μm). The mean diameter, from the data analysis of the Horiba LA-910, was based on the volume-average diameter (D_{vad}). The particle diameters of some samples were also measured directly with scanning electron microscopy (SEM). Before the SEM examination, the samples were dried at room temperature and coated with a thin layer of gold with a JEOL JFC-1100 ion-sputter coating machine. The number-average diameter (D_n) and weight-average diameter (D_w) were calculated with the following equations.[43,44] At least 300 particles [number of added particles (N)] were counted for each calculation:

$$D_n = \sum N_i D_i / \sum N_i \quad (1)$$

$$D_w = \sum N_i D_i^4 / \sum N_i D_i^3 \quad (2)$$

The polydispersity index (PI) of the particle size is expressed as D_w/D_n. With the Horiba LA-910, N_i and D_i correspond to the values of the frequency distribution 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 distributions of particle sizes, and those ranging from 1.1 to 1.2 were regarded as nearly monodisperse distributions. The particle size and size distribution, obtained with the Horiba LA-910, were reproducible and similar to those measured via SEM.

Fourier transform infrared spectra were recorded in KBr with a Jasco FT/IR-430 spectrometer, and a 100% KBr disk was used as a control.

RESULTS AND DISCUSSION

Suspension copolymerization of VPi and VAc

P(VPi/VAc) can be obtained with the following copolymerization methods: bulk, solution, emulsion, and suspension copolymerizations. However, it is impossible to produce spherical particles by bulk and solution polymerizations, and it is difficult to obtain particles over approximately 100 μm in diameter that are appropriate for embotherapy by emulsion polymerization. In suspension polymerization, the particle size and its distribution can be controlled by various polymerization conditions, including the stabilizing agent and its concentration, the monomer/water ratio, the stirring method and rate, and the polymerization temperature. Until now, the suspension copolymerizations of VPi and VAc were carried at polymerization temperatures greater than 50°C, and so it was impossible to obtain spherical P(VPi/VAc) particles with a uniform diameter because of the fast polymerization rate. The effects of the polymerization conditions were examined to determine the optimum conditions for the production of P(VPi/VAc) particles. The micro-

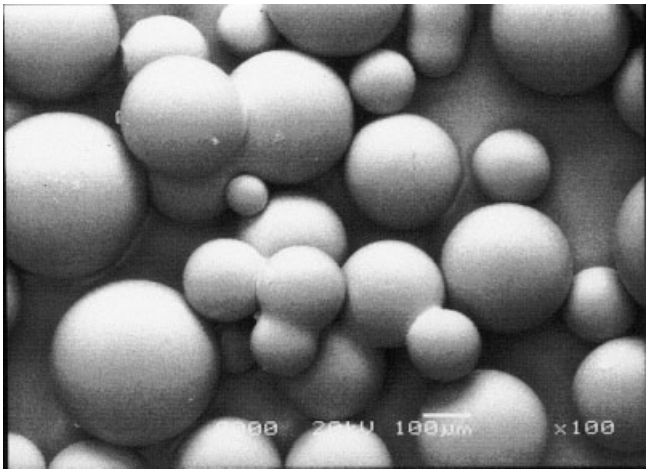


Figure 1 SEM micrograph of nonsieved P(VPi/VAc) microspheres prepared by the suspension copolymerization of VPi and VAc at 30°C with a suspending agent concentration of 1.5 g/dL of water, a monomer/water concentration of 0.5 L/L, a VPi/VAc feed molar ratio of 4/6, and an agitation speed of 300 rpm with an ADMVN concentration of 0.0001 mol/mol of monomers.

spheres of P(VPi/VAc), with diameters ranging from 75 to 600 μm, and higher conversions were obtained at a polymerization temperature of 30°C through control over the stirring rate and with other factors fixed (Fig. 1). Microspheres of P(VPi/VAc), with various s-dyad contents of 56.2–58.5%, were obtained through variations in the VAc/VPi feed ratio (Fig. 2).

Elimination of the static electricity and the sieving of particles

The size and size distribution of particles are the most important parameters of embolic materials. Because vessels occluded by embolic materials differ according to diseases (e.g., arteriovenous malformations, uterine fibroids, and malignant tumors),[38,39,40] it is necessary to produce embolic particles of various sizes for successive occlusions of the vessels.

The homogeneity of the particle size can be evaluated by PI of the particle diameter:

$$\mathrm{PI} = D_w/D_n \tag{3}$$

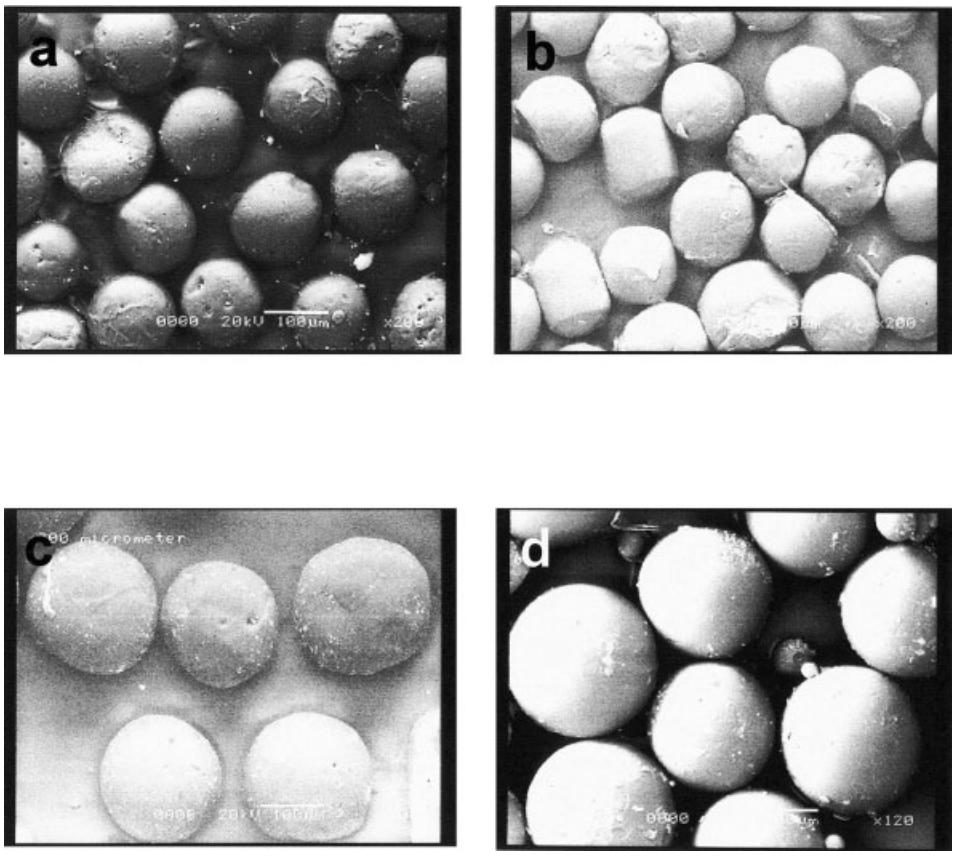


Figure 2 SEM micrographs of sieved monodisperse P(VPi/VAc) microspheres prepared by the suspension copolymerization of VPi and VAc at 30°C with a suspending agent concentration of 1.5 g/dL of water, a monomer/water concentration of 0.5 L/L, and an agitation speed of 300 rpm with an ADMVN concentration of 0.0001 mol/mol of monomers and various VPi/VAc feed molar ratios. The molar ratios, D_{vad} values, and PI values were (a) 2/8, 107 μm, and 1.01, (b) 3/7, 154 μm, and 1.04, (c) 4/6, 208 μm, and 1.07, and (d) 5/5, 352 μm, and 1.14, respectively.

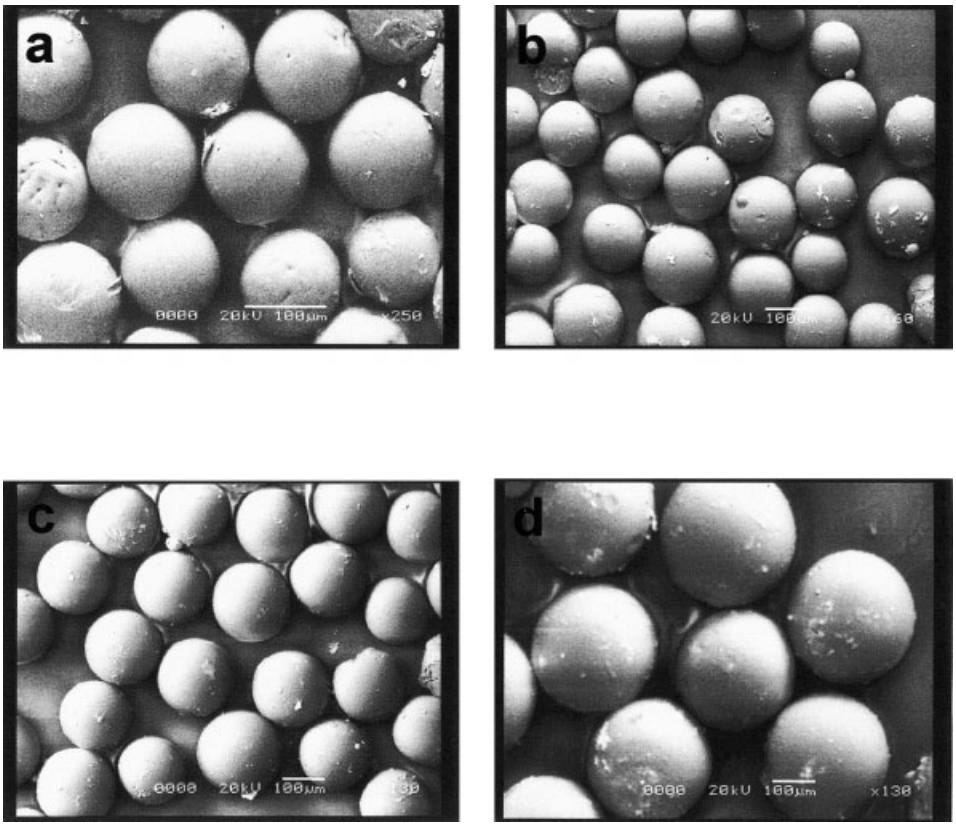


Figure 3 SEM micrographs of sieved monodisperse P(VPi/VAc) microspheres with various particle sizes prepared by the suspension copolymerization of monomers with a 4/6 VPi/VAc molar ratio. The D_{vad} and PI values were (a) 105 μm and 1.01, (b) 131 μm and 1.05, (c) 183 μm and 1.08, and (d) 256 μm and 1.11, respectively.

A particle PI value of 1.0–1.1 is considered monodisperse and is necessary for the superselective occlusion of the targeted vessel. Thus, in this study, for obtaining monodisperse P(VPi/VAc) particles, 1 g of P(VPi/VAc) particles was placed in a cup with 0.5 g of sodium sulfate, potassium sulfate, magnesium sulfate, and sodium chloride individually and was suitably ground. The ground particles were sieved with standardized mesh sieves. After the sieving, statically or adhesively aggregated P(VPi/VAc) microspheres were completely separated into individual particles with D_{vad} values of 90 $\pm$ 15, 125 $\pm$ 20, 180 $\pm$ 20, 250 $\pm$ 25, 300 $\pm$ 50, 400 $\pm$ 50, and 600 $\pm$ 50 μm (Fig. 3).

Relationship between the DS and the particle size

The heterogeneous surface saponification of insoluble P(VPi/VAc) particles in water is limited to the surface of the particles because the reaction progresses in a suspended phase in the alkali solution. Therefore, if we make the size of the particles uniform and the mass the same, the velocity of the saponification reaction is proportional to the surface area of the particle; as a result, under the same reaction conditions, DS would have a different value depending on the diameter of the particle. Therefore, we consider the relationship between the size of the particles and the DS to control the appropriate DS.

When the concentration of the added saponification reaction catalyst is constant, the velocity of the heterogeneous surface saponification reaction is proportional to the total surface area of the added particle (S_A):

$$d\mathrm{DS}/dt \propto kS_A \tag{4}$$

If we consider that the size distribution of the added particles is monodisperse

$$S_A = 4\pi N/(d/2)^2 \tag{5}$$

where d is the diameter of the added particle.

We can derive the relationship between S_A and d by making the mass of the added particles (M) the same during the reaction:

$$M = 4/3\pi N\rho_c(d/2)^3 \tag{6}$$

$$S_A = 4\pi N(d/2)^2 = 3M/\rho(d/2)^{-1} \tag{7}$$

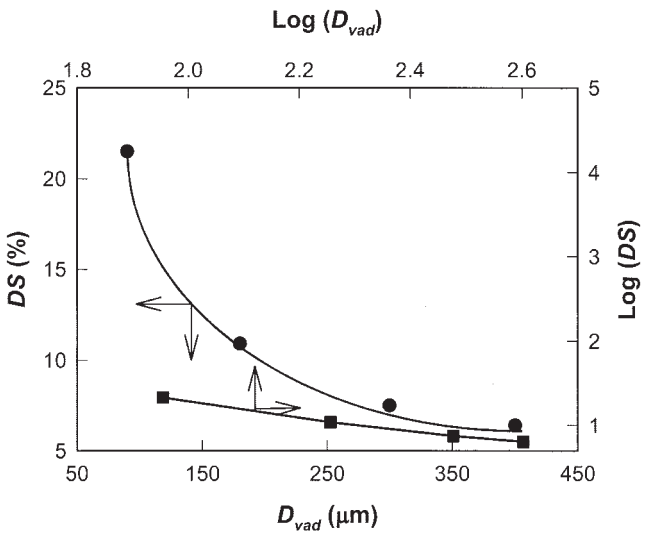


Figure 4 Effect of the initial diameter of the P(VPi/VAc) microspheres on DS of PVA obtained by heterogeneous surface saponification during a constant time.

where ρ_c is the density of the P(VPi/VAc) particle. As eq. (7) shows, the velocity of the initial heterogeneous surface saponification is inversely proportional to the diameter of the particle. In other words, the smaller the particle is, the faster the velocity is of the saponification reaction.

Figure 4 shows the DS of the PVA/P(VPi/VAc) microspheres evaluated through the changes in the diameter of the monodisperse P(VPi/VAc) particles. DS decreases with increasing particle diameter. For the common logs of individual values, the value of the slope is −0.97. This result corresponds to the theoretical equation with the aforementioned assumption.

Because PVA prepared by the saponification of P(VPi/VAc) particles is a crystalline polymer, unlike

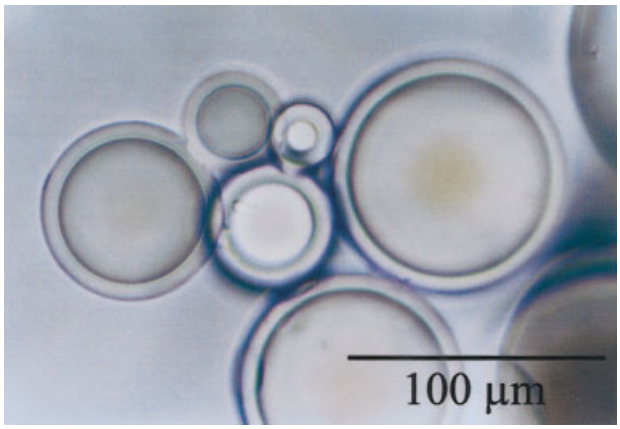


Figure 5 Optical micrograph of nonsieved PVA/P(VPi/VAc) microspheres with a skin–core structure produced by heterogeneous saponification in an alkali/ethanol/water solution.

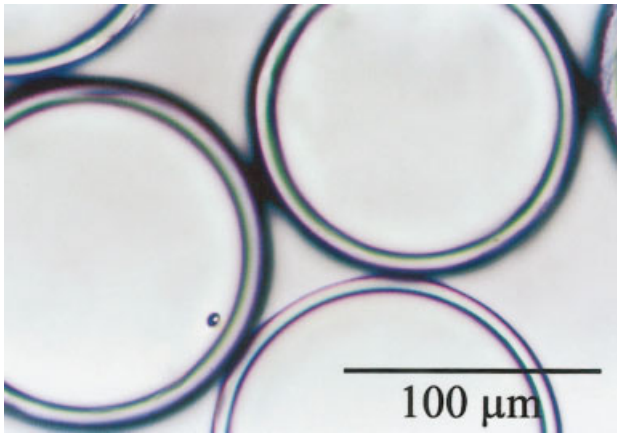


Figure 6 Optical micrograph of sieved monodisperse PVA/P(VPi/VAc) microspheres with a skin–core structure produced by heterogeneous saponification in an alkali/ethanol/water solution.

P(VPi/VAc), which is amorphous, particles produced by heterogeneous surface saponification shows differences in the size of the P(VPi/VAc) particles added initially; this arises from some shape contraction by density fluctuation. The size and size distribution of particles for embolic materials are important factors in making the selected vessels able to be occluded; therefore, we tried to change the particle size, which depended on the DS, according to heterogeneous surface saponification.

The weight of the remaining P(VPi/VAc), which is not saponified, is

$$M_c = M_0(1 - \mathrm{DS}) \tag{8}$$

where M_0 is the mass of the P(VPi/VAc) particle added initially and M_c is the mass of the remaining P(VPi/VAc) that is not saponified.

If we suppose that x is the radius of P(VPi/VAc) in the PVA/P(VPi/VAc) particle with a skin–core structure

$$4/3 \times \pi x^3 N \rho_c = M_0(1 - \mathrm{DS}) \tag{9}$$

As shown in eq. (10), we obtain the result by dividing the total mass by the mass of one particle because N does not change during the reaction:

$$N = M_0/[4/3 \times \pi(d/2)^3 \rho_c] \tag{10}$$

Therefore, we could get x from eqs. (9) and (10):

$$x = d/2[(1 - \mathrm{DS})]^{1/2} \tag{11}$$

After the heterogeneous surface saponification reaction stops, the skin of the resulting particle is PVA,

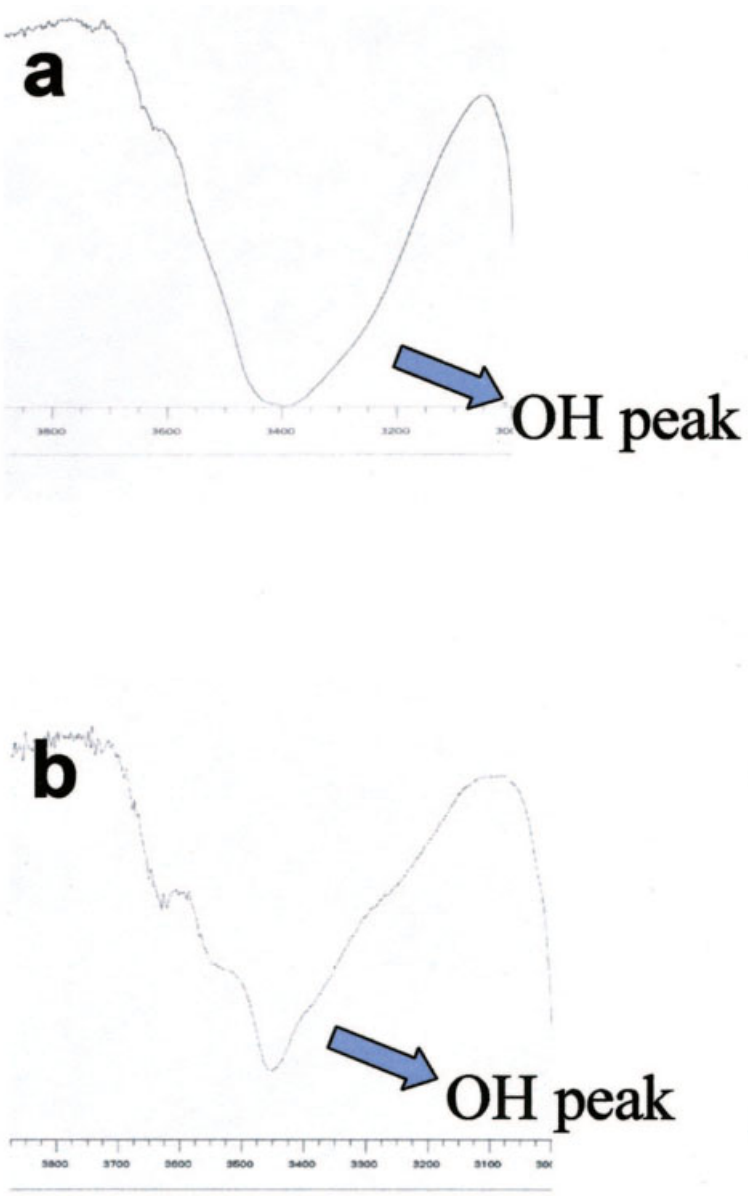


Figure 7 IR spectra of sieved PVA/P(VPi/VAc) microspheres with a skin–core structure produced by heterogeneous saponification in (a) alkali/ethanol/water and (b) alkali/methanol/water solutions.

and we derive the following equation to get r, the thickness of the skin part.

If we call M_a the mass of produced PVA

$$M_a = m_a/m_a \times M_0\mathrm{DS} \quad (12)$$

where m_a is the molecular weight of PVA and m_c is the molecular weight of P(VPi/VAc)

Supposing that ρ_a is the density of PVA, we find that the mass of PVA and M_a converted by x and r are the same:

$$4/3 \times \pi[(r + x)^3 - x^3]\rho_a N = m_a/m_c \times M_0\mathrm{DS} \quad (13)$$

Thus, we could derive r from eqs. (12) and (13):

$$r = [x^3 + \rho_c m_a/\rho_a m_c \times \mathrm{DS}(d/2)^3]^{1/3} - x \quad (14)$$

Heterogeneous surface saponification of the P(VPi/VAc) microspheres

The general method for preparing PVA is the saponification reaction of P(VPi/VAc) in a solution state; a concentrated aqueous solution of sodium hydroxide is dropped into a completely dissolved P(VPi/VAc)/methanol solution. Some problems arise in its application to the embolization because of its irregular surface and broad particle size distribution. To preserve the spherical shapes of P(VPi/VAc) particles with a uniform size distribution, we restricted saponification to the surface of the particles by suspending P(VPi/

VAc) particles in an aqueous alkali solution, and skin–core particles were obtained.

To prepare alkali solutions in a flask, we stirred 20 g of sodium hydroxide, 20 g of sodium sulfate, and 20 g of methanol (ethanol) with a magnetic stirrer with 200 g of purified water. Separated P(VPi/VAc) particles (0.5 g) were added to the flask and slowly stirred under various saponification conditions. After the saponification of P(VPi/VAc) particles, the solid saponification product was filtered and washed several times with water and dried *in vacuo* at 40°C for 1 day.

Figure 5 shows polydisperse PVA/P(VPi/VAc) microspheres with a skin–core structure after saponification. This saponification method produces spherical and uniform-surface particles. Saponified particles were separated into individual particles with a dispersion agent and an antistatic agent (sodium sulfate) and were sieved with standardized mesh sieves (Fig. 6). Figure 7 shows IR spectra of PVA/P(VPi/VAc) microspheres produced by heterogeneous saponification in alkali/water/methanol or ethanol solutions. With these results, we confirmed the —OH peak as evidence of saponification.

Finally, four things are worth noting about the preparation of monodisperse PVA/P(VPi/VAc) microspheres through the control of various heterogeneous saponification conditions. First, the saponification of monodisperse P(VPi/VAc) particles, with different s-dyad contents, was conducted under the same conditions. This showed that the DS changed with the s-dyad content of the precursor (Fig. 8); that is, the DS of the particles decreased with an increase in the s-dyad content. In other words, saponification was more difficult with higher syndiotacticity microspheres. Second, the effect of the saponification temperature on the DS was investigated. Figure 9 shows monodisperse PVA/P(VPi/VAc) microspheres with 3/7 (mol/mol) VPi/VAc produced by heterogeneous surface saponification for 4 h at 40 or 50°C and sieved. There was little difference in the DS values despite saponification temperature differences of 10°C. Third, the effect of the saponification time on the DS was investigated. Figure 10 presents monodisperse PVA/P(VPi/VAc) microspheres with 4/6 VPi/VAc produced by saponification at 40°C for 72 and 126 h and sieved. There was a big difference with the two saponification times. The second and third results showed that the saponification time had a large affect on the DS, in comparison with the saponification temperature. Lastly, syndiotactic PVA/P(VPi/VAc) microspheres from 4/6(VPi/VAc) and atactic PVA/PVAc microspheres from VAc were boiled to test the possibility of their use as embolic materials with good durability. After the boiling, the skin part of the PVA/PVAc microspheres was destroyed with PVA/P(VPi/VAc) microspheres, whereas syndiotactic PVA was unchanged. Therefore, PVA/P(VPi/VAc) microspheres are expected to exhibit high stability and durability in blood at 37°C when they are used as embolic materials *in vivo*.

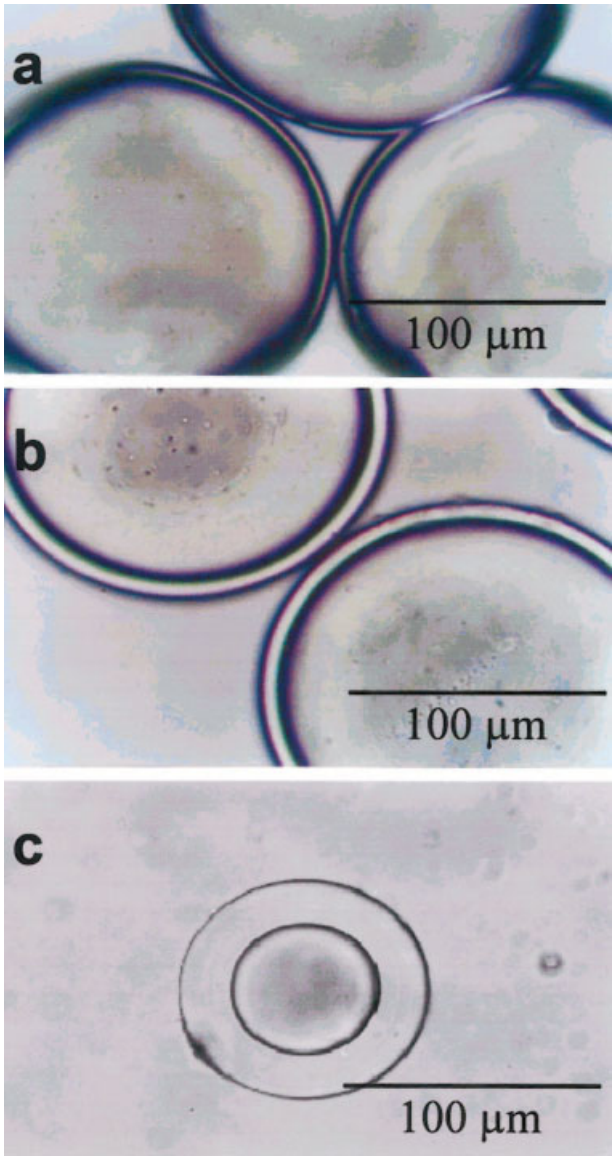
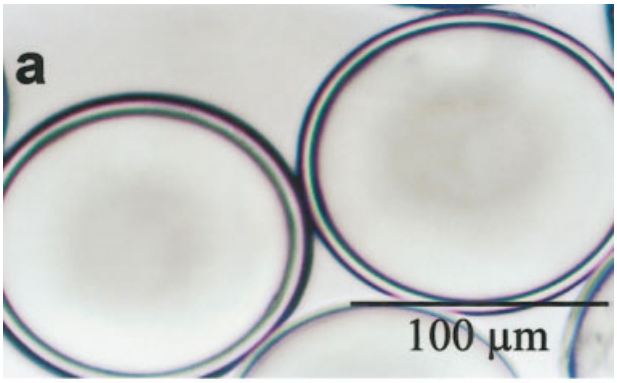


Figure 8 Optical micrographs of sieved monodisperse PVA/P(VPi/VAc) microspheres with skin–core structures and various DS values prepared by heterogeneous saponification in alkali/ethanol/water solutions at 40°C for 4 h according to the different s-dyad contents. The s-dyad contents and DS values were (a) 58.5 and 8.4%, (b) 57.6 and 13.2%, and (c) 56.7 and 38%, respectively.

CONCLUSIONS

Generally, it is known that both commercial atactic PVA embolic materials with irregular shapes (Contour) and spherical particle-type embolic materials of atactic PVA, which is made via the suspension polymerization of VAc, have deficiencies[40,41] because the effects of occlusions of the vessels decrease after treat-

ment, with respect to the treatment time. We obtained PVPi particles, prepared by the room-temperature suspension polymerization of VPi in high yields, to prepare syndiotactic PVA particles with a skin–core structure. After heterogeneous surface saponification of the PVPi particles, PVA/PVPi particles with skin–core structures were prepared. However, the particles had irregular surfaces, and saponification was very difficult. Therefore, to reduce the very high stereoregularity to some extent, we suspension-copolymerized VPi and VAc with VPi/VAc molar ratios of 1/9 to 6/4. The surfaces of the PVA/P(VPi/VAc) particles, via the heterogeneous surface saponification of the P(VPi/VAc) particles, were very uniform. The durability of the syndiotactic PVA/P(VPi/VAc) particles was superior to that of atactic PVA/PVAc particles. Whether we used nontoxic ethanol or toxic methanol, there was no difference in the formation of PVA skin on the P(VPi/VAc) core. Various PVA particles with high syndiotacticity and skin–core structures were successfully produced through changes in the concentrations of alkali and alcohol and the saponification time and temperature. Consequently, novel syndiotactic PVA particles of various sizes, uniform size distributions, and high stability in blood were obtained and are expected to be useful as drug carriers for controlled-release applications. In the near future, we will report that PVA forms a blue complex with iodine immersed in an aqueous solution of iodine and potassium iodide and that P(VPi/VAc) forms a red complex instead of being radiopaque.



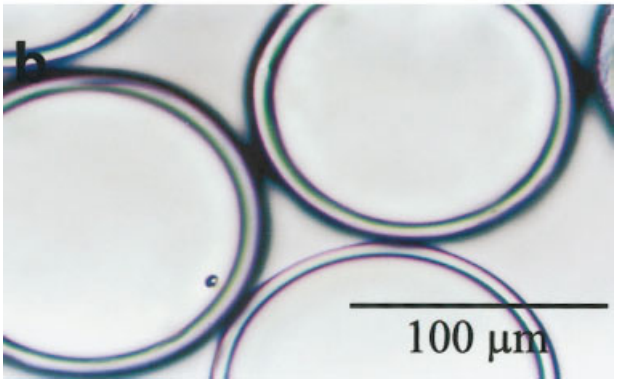
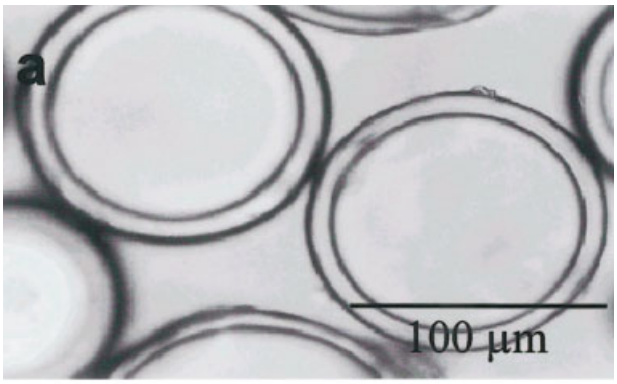


Figure 9 Optical micrographs of sieved monodisperse PVA/P(VPi/VAc) microspheres with skin–core structures and different DS values prepared by heterogeneous saponification in alkali/ethanol/water solutions for 8 h according to different saponification temperatures. The saponification temperatures and DS values were (a) 40°C and 13.7% and (b) 50°C and 14.6%, respectively. The microspheres were prepared from P(VPi/VAc) with D_{vad} values of 90–106 μm and a monomer feed ratio of 3/7 (mol/mol) VPi/VAc.



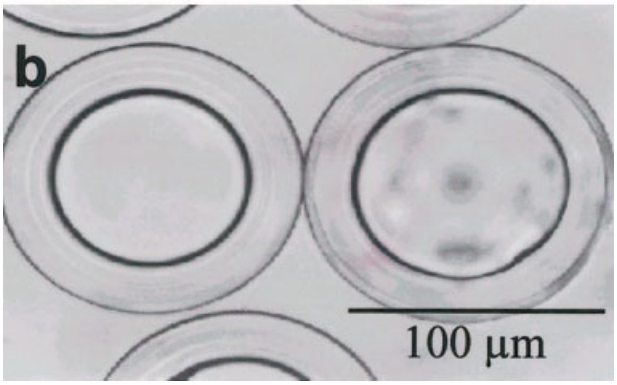


Figure 10 Optical micrographs of sieved monodisperse PVA/P(VPi/VAc) microspheres with skin–core structures and different DS values prepared by heterogeneous saponification in alkali/ethanol/water solutions at 40°C according to different saponification times. The saponification times and DS values were (a) 72 h and 16.6% and (b) 126 h and 36.4%, respectively. The microspheres were prepared from P(VPi/VAc) with D_{vad} values of 106–125 μm and with a monomer feed ratio of 4/6 (mol/mol) VPi/VAc.

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