Preparation and Morphology Study of Microporous Poly(HEMA–MMA) Particles

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ABSTRACT: Porous poly(2-hydroxyethyl methacrylate-methyl methacrylate) particles crosslinked with ethylene glycol dimethacrylate were synthesized by free-radical suspension copolymerization in an aqueous phase initiated by an oil-soluble initiator, 2,2-azobisisobutyronitrile. 1-octanol was used as a pore forming agent (porogen). The porous structures, the particle morphology, and the swelling capacity of the resultant polymer in water at room temperature were studied at different crosslink densities and under various porogen concentrations. The analysis via Scanning Electronic Microscopy (SEM) indicated that permanent pores remained in the dried polymeric particles prepared in the presence of the porogen at certain crosslink densities. According to the studies via the SEM pictures and the pore size distributions, higher porogen concentration promotes the formation of more pores, and higher crosslink density results in narrower pore size distribution. The swelling capacity of the particles in water at room temperature decreases with an increase in the crosslink density, and the existence of the highly porous structures enhances the swelling capacity of the porous particles of poly(2-hydroxyethyl methacrylate-methyl methacrylate). © 2006 Wiley Periodicals, Inc. J Appl Polym Sci 103: 707–715, 2007

Key words: hydrogels; porous materials; HEMA; MMA; particle; morphology

INTRODUCTION

2-Hydroxyethyl methacrylate (HEMA) hydrogels have been of great interest because of the biocompatibility of their three-dimensional polymeric networks, which can swell in water and retain a significant fraction of water within the structures without dissolving.[1] HEMA hydrogels have been widely used in many areas, especially in biomedical and pharmaceutical areas, such as packing materials in chromatography,[2] sorbents in controlled release or drug delivery,[3] and implanting materials in tissue engineering,[4] etc. In recent decades, how to build uniform porous structures in HEMA hydrogels has received considerable attention since the presence of the porous structures can significantly modify the performance of HEMA hydrogels for more favorable applications.

Basically, porous poly(HEMA) particles can be synthesized by incorporating a multi-vinyl crosslinker, and organic solvents (porogen) by means of free radical suspension polymerization.[5–7] The crosslinker creates the three-dimensional networks, whereas the porogen is a good solvent for monomers but a nonsolvent for poly(HEMA). The porogen is responsible for inducing pores by enhancing phase separation in the polymeric particles. Therefore, the types and the amount of the crosslinker and the porogen used in the reaction systems usually determine the porous structures and the particle morphology, although some other factors, such as reaction temperature and agitation speed, also can affect the formation of pores.

Most of the studies in the area of porous polymer preparation have indicated that the phase separation results in the porous structures in the porous polymers. However, different procedures of the phase separation generate different porous structures and polymer morphology. Okay[8] indicated that expanded or heterogeneous (porous) networks, depending on the suspension polymerization conditions, can be obtained in the polymeric particles as a consequence of the phase separation process. Heterogeneous pores are the permanent pores since they do not collapse easily when removing solvents from the polymers. The porogen separates totally out of the network phase during the reaction.[7] Horak el al.[6] studied the relationship between the phase separation and the porous structures of the poly(HEMA) particles by exploring the porous structures and the particle morphology using SEM. In their studies, the heterogeneous pores resulting from the agglomeration of the separated microgels can be seen. The expanded pores, as also pointed out

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by Gomez et al.,[7] are nonporous networks in a dry state since the networks are collapsed during drying and solvent removal, but they could re-expand to their previous state in a good solvent.

Up until now, most of poly (HEMA) particles were synthesized by introducing a large amount of organic solvents,[5–7] including good solvents and/or nonsolvents, which are not preferred for the applications of these polymers in biomedical areas. On the other hand, if a good solvent, such as cyclohexanol used by Horak et al.,[6] is not used, it will be hard to obtain the spherical poly(HEMA) particles with the proper particle morphology and to control the porous structures because of the hydrophilicity of HEMA.

The crosslinking density of the polymeric networks, the porous structures of the HEMA polymers and swelling capacity of the resultant polymers can be improved by using comonomers. A hydrophobic comonomer with suitable solubility to HEMA will be helpful to produce the spherical particles and decrease the requirement for the amount of the solvents in the reaction.[6]

There is almost no research on the porous structures and the particle morphology for HEMA–MMA system although some copolymers of HEMA with methyl methacrylate (MMA) or some other vinyl monomers have been synthesized,[9–11] and some porous poly (HEMA–MMA) particles have been prepared.[2]

The objectives of the present studies were to synthesize the highly porous HEMA and MMA copolymer particles in the presence of an organic porogen (1-octanol), to characterize the particle morphology using SEM, and to explore the porous structures and their formation mechanisms. The porous characteristics were also described quantitatively in terms of the pore size distribution. The equilibrium weight swelling ratio (q_w) and the equilibrium volume swelling ratio (q_v) in water at room temperature were investigated to characterize the swelling capacity of the porous poly(HEMA–MMA) particles.

EXPERIMENTAL

Materials

Ethylene glycol dimethacrylate (EGDMA, 98%, Aldrich, Ontario, Canada), methyl methacrylate (MMA, 99%, Aldrich), 2-hydroxyethyl methacrylate (HEMA, 97%, Aldrich), and 1-octanol (99%, Sigma) were used without further purification. 2,2-azobisisobutyronitrile (AIBN, Polysciences, Warrington, PA) was used as the initiator. The sodium dodecyl sulfate (SDS, Aldrich) solution of 0.66 wt % was prepared before using. Methanol (Aldrich) was HPLC grade.

Suspension copolymerization

The dispersed organic phase, which consists of HEMA, MMA, EGDMA, 1-octanol, and AIBN, was charged into SDS solution at room temperature to prepare an emulsion. The emulsion was transferred into a jacketed steel reactor equipped with a powerful 4-pitched blade agitator at room temperature. The reaction was maintained at 70°C for 4 h under an agitation speed of 300 rpm, and then a filtration operation was applied to obtain the polymeric particles. The particles were washed successively using deionized water and methanol, and then were extracted by ether using a Soxhlet extractor for 24 h. Finally, the copolymeric particles were dried in a vacuum chamber at room temperature for 24 h. The copolymerization systems investigated in this study are listed in Table I.

Characterization of the porous particles

LEO 1530 Field-Emission Scanning Electronic Microscope was used to evaluate the particle morphology and the porous structures. The copolymeric particles in a dry state were put on a double-coated electronic tape with a gold coating of 10 nm. SEM photos were taken under different magnification.

Poremaster GT-60, a mercury intrusion porosimetry, was used to investigate the pore size distribution

TABLE I
Copolymerization Systems for Preparing Porous Poly(HEMA–MMA) Particles[a]

Polymer batch	EGDMA content[b] (vol %)	1-octanol content[b] (vol %)	q_w (g/g)	q_v	SEM figure
A	5	50	2.51 ± 0.13	1.95 ± 0.56	1
B	5	100	2.62 ± 0.21	2.46 ± 1.23	2
C	15	50	2.10 ± 0.11	1.96 ± 0.46	3
D	15	100	2.13 ± 0.11	2.26 ± 0.78	4
E	35	50	1.97 ± 0.10	1.45 ± 0.25	5
F	35	100	2.42 ± 0.23	1.98 ± 0.34	6
G	50	50	1.48 ± 0.14	1.47 ± 0.25	7
H	50	100	1.77 ± 0.11	1.44 ± 0.24	8

[a] HEMA–MMA = 2 mL/12 mL; Water = 150 mL; SDS = 1 g; AIBN = 0.1 g; agitation speed = 300 rpm.
[b] The content is with respect to the total volume of HEMA and MMA.

of the polymeric particles. The contact angle between mercury and the polymers was 140°.[2]

The equilibrium concentrations of HEMA, MMA, EGDMA, and porogen in the aqueous phase at room temperature were determined by HPLC (Waters 2690 Separations Module) equipped with a UV detector (996 PDA, wavelength 254.0 nm). The flow phase consists of 60% of methanol and 40% of water.

The equilibrium weight swelling ratio (q_w) was calculated via eq. (1). The dry polymeric particles were weighed (W_{dry}) and put into deionized water at room temperature for 24 h and the swollen particles were filtered and weighed after wiping off surface water using No. 4 filter paper (W_{swell}). Each experiment was repeated three times.

$$q_w = \frac{W_{swell}}{W_{dry}} (g/g) \qquad (1)$$

The equilibrium volume swelling ratio (q_v) was determined by measuring the diameters of the polymeric particles, which were put in a large excess of water for 24 h at room temperature in an equilibrium swelling state (D_{swell}) and in a dry state (D_{dry}), using an optical microscope equipped with a ruler (0.01 mm). q_v was calculated via eq. (2). Each experiment was also repeated three times.

$$q_v = \frac{V_{swell}}{V_{dry}} = \frac{D_{swell}^3}{D_{dry}^3} \qquad (2)$$

where V_{swell} and V_{dry} are the volumes of a single particle in the equilibrium swelling state and in the dry state, respectively.

RESULTS AND DISCUSSION

The dependence of the porous structures and the particle morphology on the porogen concentration and the crosslink density were investigated. Figures 1 through 8 show the porous structures and the particle morphology. These SEM pictures indicate that spherical particles resulted. The equilibrium weight swelling ratio and the equilibrium volume swelling ratio are shown in Table I as well as in Figures 9 and 10.

Monomer partitions between aqueous phase and organic phase

The monomer partitions in the reaction system are important parameters for understanding the polymerization performance of the reaction system. The solubility parameter of each reaction component is shown in Table II, which suggests that the organic phase is a homogeneous mixture because the solubility parameter values do not have much difference from each other. Table III shows the experimental results of the monomer fractions in the aqueous phase. The concentration of 1-octanol in the aqueous phase was too low to be detected; however, it was also found that the monomer contents in the aqueous phase were lower under higher 1-octanol concentration. According to Table III, the fraction of HEMA in the aqueous phase is about 40%, which is very close to the value reported by Horak et al.,[6] even though cyclohexanol, a good solvent for both monomers and poly(HEMA), was not used. According to Horak et al.,[6] cyclohexanol was used to make spherical particles and reduce the solubility of HEMA in the aqueous phase. However, in the present studies, the solubility of HEMA in the aqueous phase was still kept at about 40% with the introduction of MMA instead of cyclohexanol. This implies that the
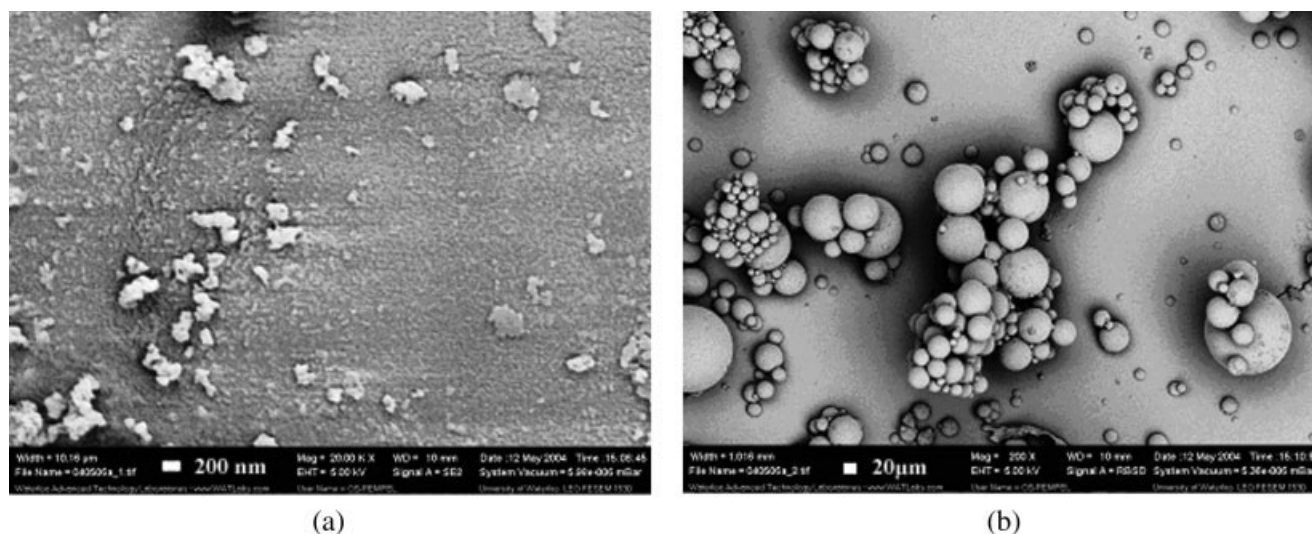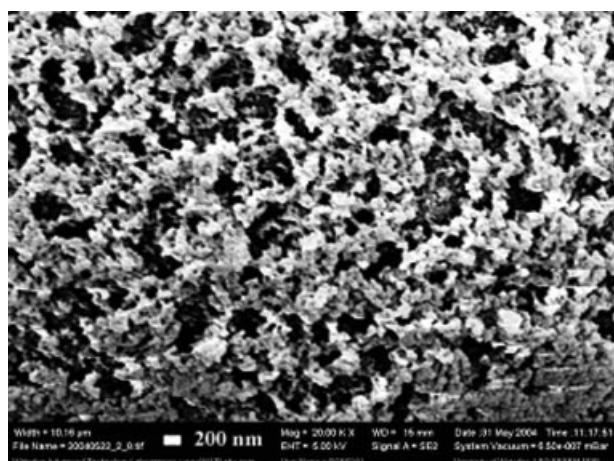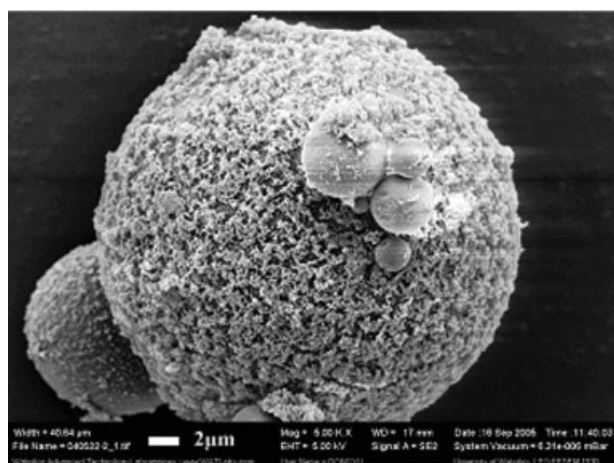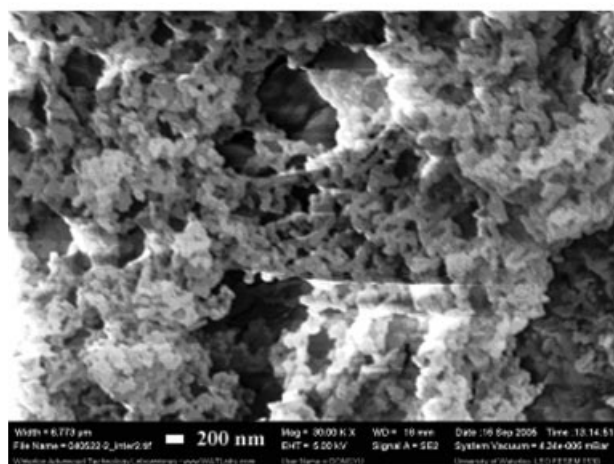

Figure 1 SEM of Sample A in Table I. Particle surface (1a, scale = 200 nm) and particles (1b, scale = 20 μm).

(a)

(b)

(c)

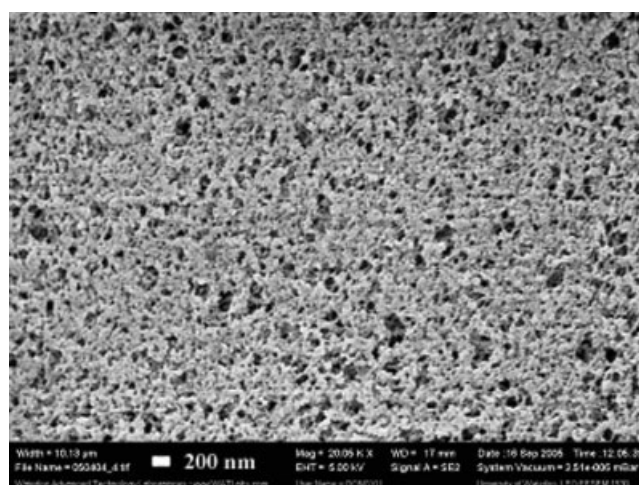**Figure 2** SEM of Sample B in Table I. Particle surface (2a, scale = 200 nm), particles (2b, scale = 2 µm) and interior structures (2c, scale = 200 nm).

introduction of MMA can successfully reduce the solvent required, and produce the spherical particles as well.

Particle morphology

Particle morphology has a great impact on the end-use properties of porous polymers. For many applications, separated spherical particles with minimized agglomerated particles of irregular shapes are preferred. In this study, some agglomerated particles of irregular shapes were observed when the porogen concentration and the crosslink density were relatively high, such as Samples E and H shown in Figures 5 and 8. Among the investigated reaction systems shown in Table I, the amounts of HEMA and MMA used in the reactions are identical. Thus, a higher crosslink density and/or porogen concentration implies higher viscosity in the reaction system. For a given reaction system, as the copolymerization proceeds, the viscosity of each droplet increases. The collisions between these droplets will make it difficult to set these droplets apart if the viscosity of each droplet
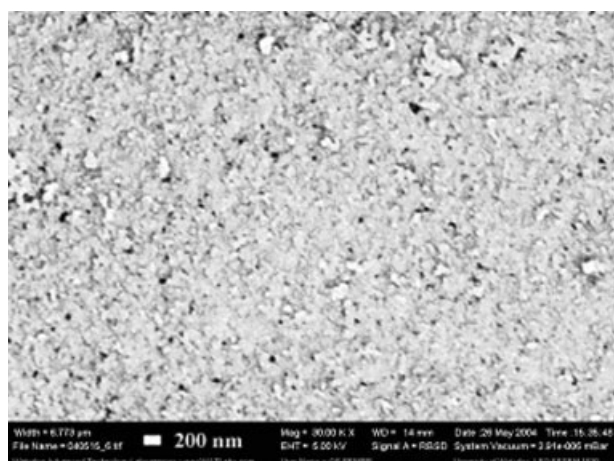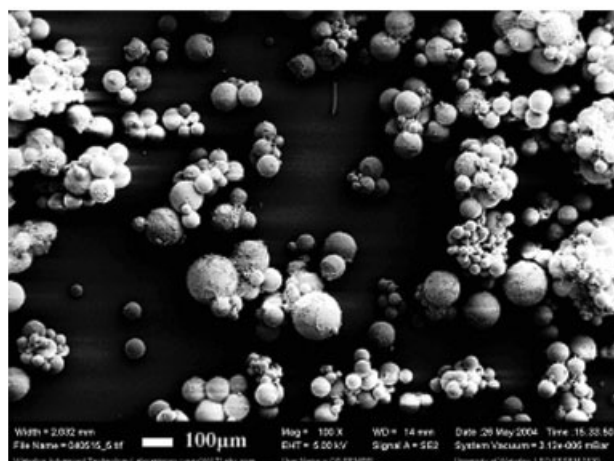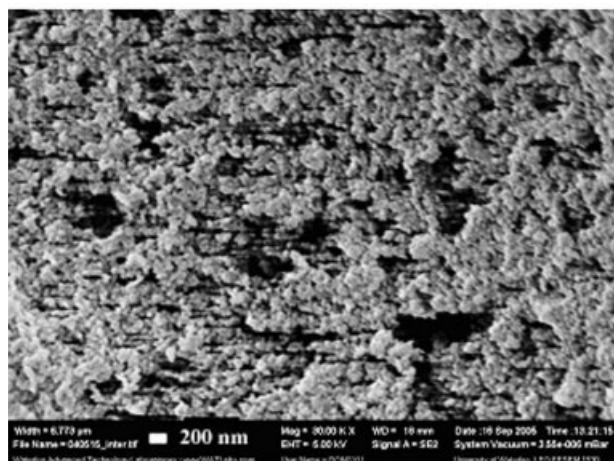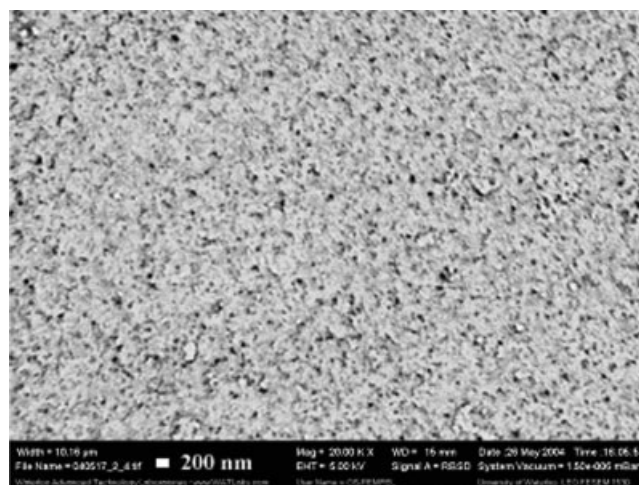

(a)
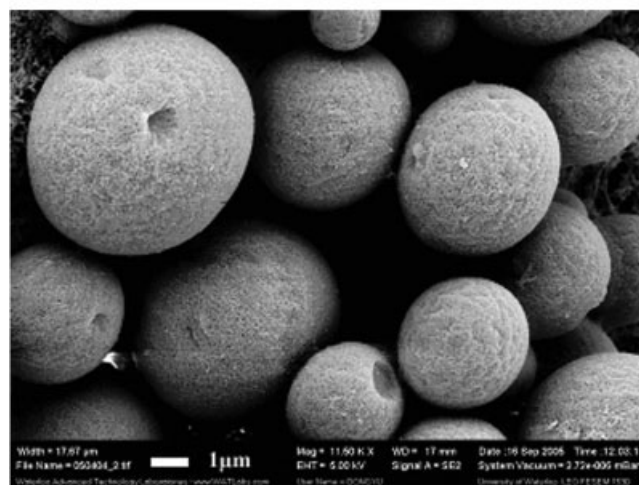
(b)

Figure 3 SEM of Sample C in Table I. Particle surface (3a, scale = 200 nm) and particles (3b, scale = 1 µm).
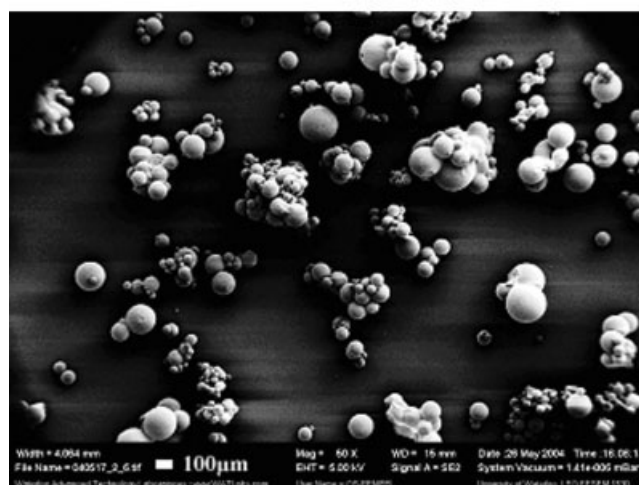
phase could transfer radicals from the organic phase to the aqueous phase during the reaction, and these radicals can react with other pendant vinyl groups on the surface of the droplets to result in the aggregates. To obtain better particle morphology, the introduction of other effective stabilizers would be helpful.

Porous structures

If the polymeric networks absorb most of the solvents up to the gel point during the reaction, the porous structures can then be induced by removing the solvent from the polymer. However, collapse of the pores can happen during the course of the porogen removal. At a certain low crosslink density, these pores can completely disappear to form nonporous particles in the dry state. However, the porous structures can be restored or partly restored when these particles are put in suitable solvents.[7] Since these pores can be
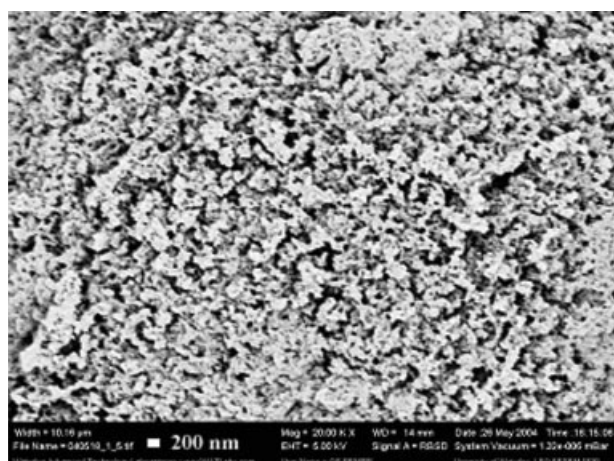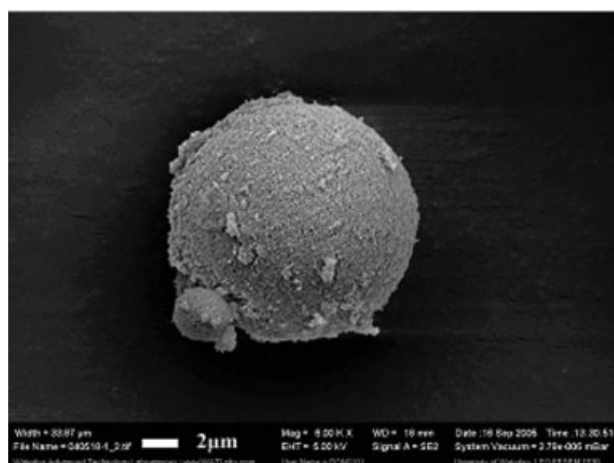
Figure 4 SEM of Sample D in Table I. Particle surface (4a, scale = 200 nm), particles (4b, scale = 100 μm), and interior structures (4c, scale = 200 nm).

Figure 5 SEM of Sample E in Table I. Particle surface (5a, scale = 200 nm) and particles (5b, scale = 100 μm).

is high enough and the protection of the droplets is not effective. In addition, the data shown in Table III implies that the monomers dissolved in the aqueous

(a)

(b)

(c)

Figure 6 SEM of Sample F in Table I. Particle surface (6a, scale = 200 nm), particles (6b, scale = 2 μm), and interior structures (6c, 200 nm).

generated in the swelling process, this type of pores was called ''swelling pores'' in the present study. Although it has a similar meaning as that of the

''expanded pores,''[7] it was used here to emphasize the fact that these pores could be generated during the swelling process. At a low crosslink density (e.g., 5 v/v% EGDMA) and under relatively low porogen concentration (e.g., 50 v/v%), the particles with fewer permanent pores were observed as shown in Figure 1. However, these particles have relatively high values of q_w and q_v as can be seen in Table I. This implies that the polymeric networks are greatly swollen, trying to restore to their original state at the end of the reaction. Therefore, this proves that the swelling pores that collapsed during drying are regenerated in the swelling process so that the water regain can be enhanced.

The heterogeneous pores are the permanent porous structures when the polymeric particles are in the dry state. According to Dusek,[12] the heterogeneous pores may appear as a result of the interaction of the polymer and the solvent when a poor solvent (χ-induced syneresis) is used, or by increasing the crosslink
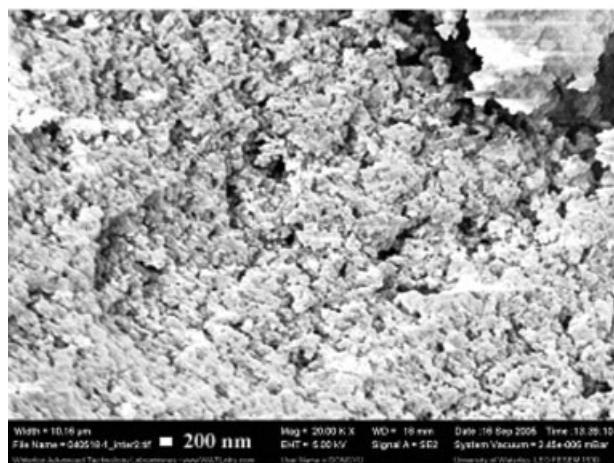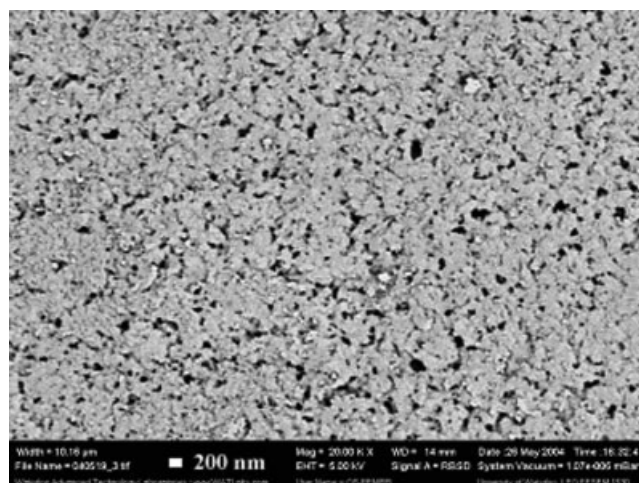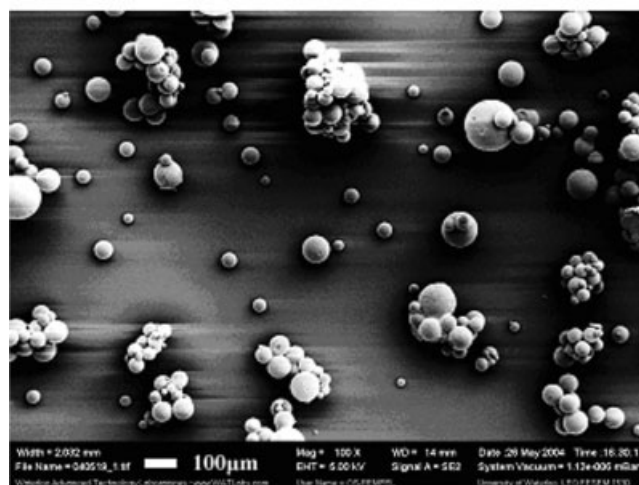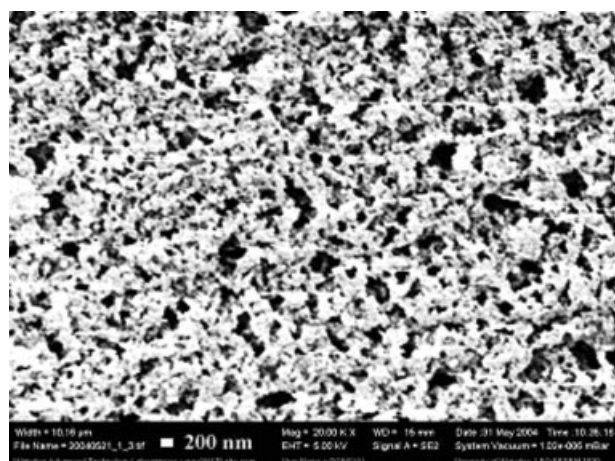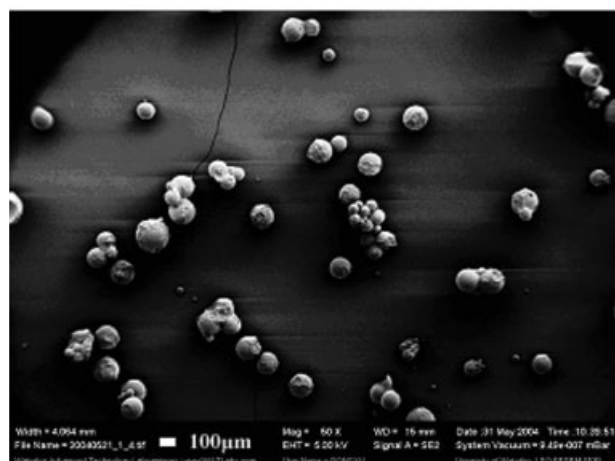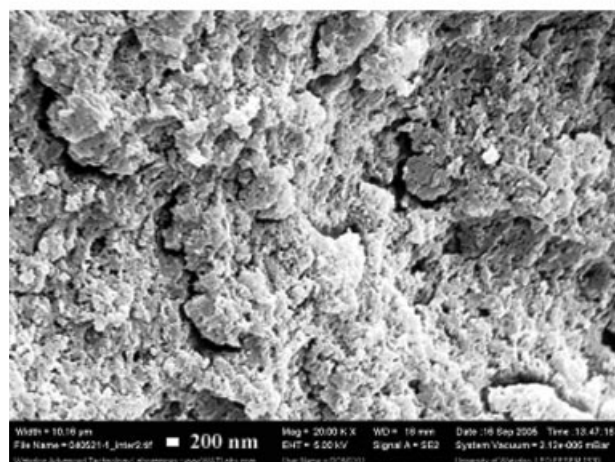

(a)

(b)

Figure 7 SEM of Sample G in Table I. Particle surface (7a, scale = 200 nm) and particles (7b, scale = 100 μm).

(a)

(b)

(c)

Figure 8 SEM of Sample H in Table I. Particle surface (8a, scale = 200 nm), particles (8b, scale = 100 μm) and interior structures (8c, 200 nm).

density (ν-induced syneresis). As show in Figure 2 (Sample B), according to the surface pores and the interior structures, although the crosslink density was
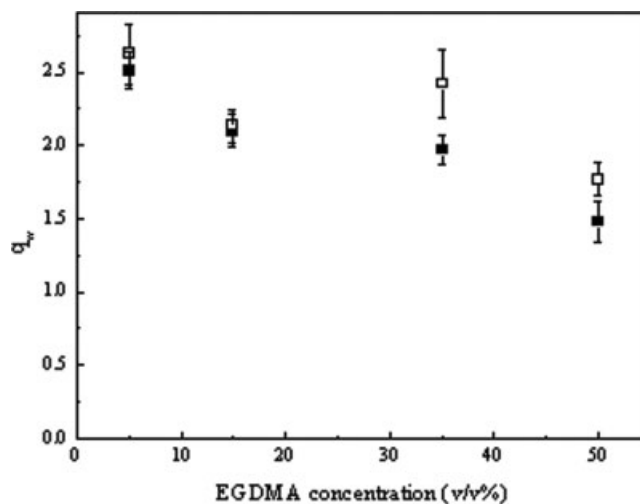

Figure 9 The values of q_w under different EGDMA concentration and porogen concentration. ■: 1-octanol = 50 v/v%, Samples A, C, E, and G; □: 1-octanol = 100 v/v%, Samples B, D, F, and H.

still 5 v/v%, which is the same as that of Sample A, the permanent pores were generated because the porogen concentration was too high to be completely absorbed by the polymeric networks, which resulted in the dispersion of the free porogen (separated phase, χ-induced syneresis) in the polymer. As the reaction proceeds, the spaces, occupied by the free porogen, can be fixed by the crosslinking to form voids (pores). In this case, the porogen lies in these voids (pores) and the permanent pores are generated, whereas the rest of the porogen is present in the polymeric networks to form swelling pores and these swelling pores would collapse or shrink during drying operations but they can be recovered during swelling. Sam-
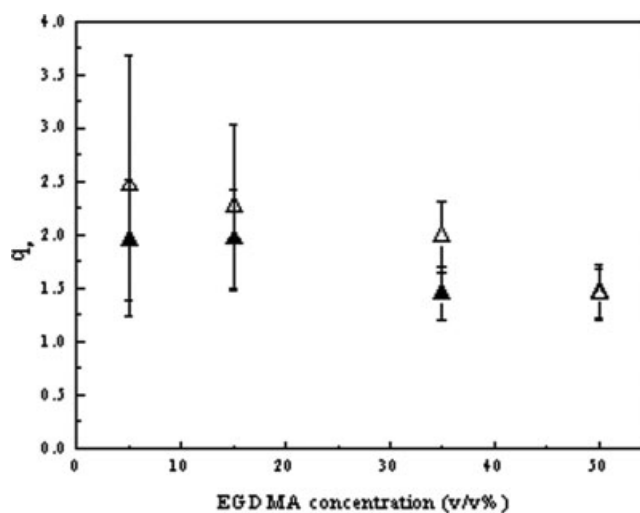

Figure 10 The values of q_v under different EGDMA concentration and porogen concentration. ▲: 1-octanol = 50 v/v%, Samples A, C, E, and G; Δ: 1-octanol = 100 v/v%, Samples B, D, F, and H.

TABLE II
Solubility Parameter Values of Monomers and Porogen[1,13]

Chemicals	Solubility parameter $(Mpa)^{1/2}$
HEMA	23
EGDMA	18.2
MMA	18
1-Octanol	~ 21

ple B has relatively higher q_w and q_v values showing good water regain and swelling capacity, which implies the existence of both permanent pores and swelling pores. So the swelling porosity of the heterogeneous porous particles is thus accompanied by the permanent porosity under a certain crosslink density and porogen concentration, which is consistent with other researchers' observations.[6,7]

The mechanism of the phase separation will be the ν-induced syneresis if the crosslink density keeps increasing.[8] The permanent pores formed by the agglomeration of many microgels can be observed in Figures 3 through 8. The porous morphology shown in Figures 5 through 8 illustrates the heterogeneity as a result of the agglomeration of a large amount of separated microgels. Figures 7 and 8 also show the interior structures of the particles, illustrating the identical structures inside and outside the particles. According to Okay,[8] a higher crosslink density (e.g., 35 v/v% and 50 v/v% in Samples E through H) results in the microgels that are separated earlier than the original gel point without being greatly swollen by the solvents or the reaction mixture. Under this situation, the organic phase becomes a continuous phase, which is full of the separated microgels. These microgels agglomerate to form the porous aggregates. The voids between these agglomerated gels are occupied by the porogen to form the permanent pores after the porogen is removed from the polymeric particles.

Swelling performance

The swelling capacity of poly(HEMA–MMA) particles was characterized by the equilibrium swelling ratios,

q_w and q_v. The q_w and q_v values are listed in Table I. Figures 9 and 10 show the dependence of the q_w and q_v values on reaction conditions. They indicate that the particles synthesized under higher porogen concentrations have higher q_w and q_v values. However, under the same porogen concentration, the q_w and q_v values decrease with an increase in the crosslink density. The equilibrium volume swelling ratio, q_v, shown in Table I, illustrates that the polymeric networks are easier to be swollen at lower crosslink density (higher q_v values).

According to the discussion on the porous structures, the swelling capacity is higher at a lower crosslink density and higher porogen contents since more swelling pores can be produced. Therefore, the decrease of q_v values implies the absence of the swelling pores although the permanent porous structures are shown. The swelling of the polymeric network becomes more difficult at the higher crosslink density since the relaxation time for the polymeric networks becomes longer. But the q_w values are still considerable. This thus implies that water fills in the pores even without greatly swelling the networks.

On the other hand, higher MMA contents are expected to reduce the q_w and q_v values since MMA is a hydrophobic comonomer. According to Brazel et al.,[9] the poly(HEMA–MMA) polymer containing 75 mol % of MMA was synthesized without using any porogen, and the q_w values of the polymer were up to 1.3 at 25°C. Whereas the poly(HEMA) particles synthesized using porogen, but without using the comonomer MMA, as reported by Horak et al.,[6] showed a q_w value up to 2.6 at 25°C. However, in the present study, the MMA content was about 80 mol %, and q_w values up to 2.6 were obtained, close to the values of the poly(HEMA) particles reported by Horak et al.[6] This once again implies that the presence of both the permanent pores and the swelling pores enhances the swelling capacity.

Generally speaking, the more swelling pores the particles have, the higher the q_w and q_v values. The swelling capacity was greatly enhanced because of the presence of highly porous structures, even if a hydrophobic comonomer was used. Therefore, the porous

TABLE III
Monomers and Porogen Concentration in the Aqueous Phase

Polymer batch	HEMA/MMA/EGDMA/1-octanol	Fraction (%) in aqueous phase[a]			
		HEMA	MMA	EGDMA	1-octanol
C	2 mL/12 mL/2.1 mL/7 mL	49.8	8.2	0.59	–
D	2 mL/12 mL/2.1 mL/14 mL	38.2	6.2	–	–
E	2 mL/12 mL/4.9 mL/7 mL	41.7	6.7	0.36	–
F	2 mL/12 mL/4.9 mL/14 mL	41.4	6.1	0.36	–
G	2 mL/12 mL/7 mL/7 mL	50.5	8.3	0.45	–
H	2 mL/12 mL/7 mL/14 mL	43.1	5.9	0.37	–

[a] Related to the total content of particular compounds in the polymerization mixture.

particles synthesized under high porogen concentration and at low crosslink density will have higher overall q_w and q_v values.

Pore size distribution

The porous structures were also studied quantitatively in terms of the pore size distribution as shown in Figures 11 and 12. These figures indicate that most of the pores are below 100 nm. The peaks shown in Figure 12 are much higher than those in Figure 11, demonstrating that more pores are produced under the higher porogen concentration.

On the other hand, each distribution profile has several peaks showing various pore sizes. Since the polymeric networks are swollen by the porogen during synthesis, the collapse and the shrinking of the pores can result in the various pore sizes during the porogen removal.

It was also found that the pore size distribution profiles have fewer peaks at higher crosslink density, which means that the pore size distribution induced by ν-syneresis is more uniform than those induced by χ-syneresis because of less pore collapse.

CONCLUSIONS

The highly porous spherical poly(HEMA–MMA) particles were synthesized by free radical suspension copolymerization. Nano-pores were produced in the particles. The crosslink density and the porogen concentration have a great effect on the porous structures, the particle morphology, and the swelling capacity.
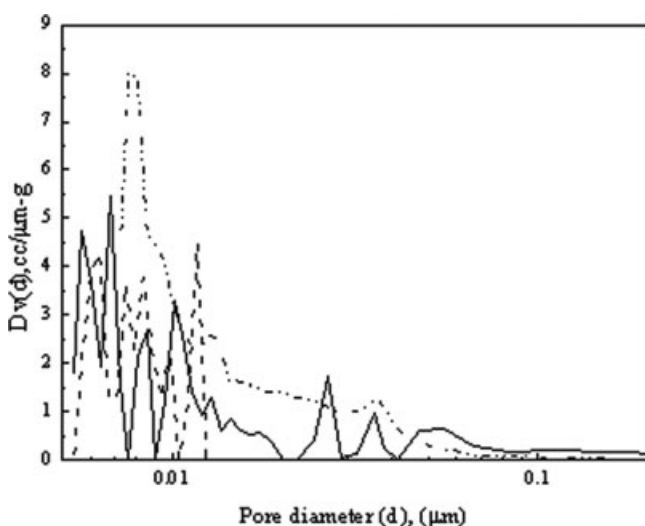
Figure 11 Pore size distributions of Sample C, Sample E, and Sample G. - - -: Sample C; —: Sample E; –●●–: Sample G.
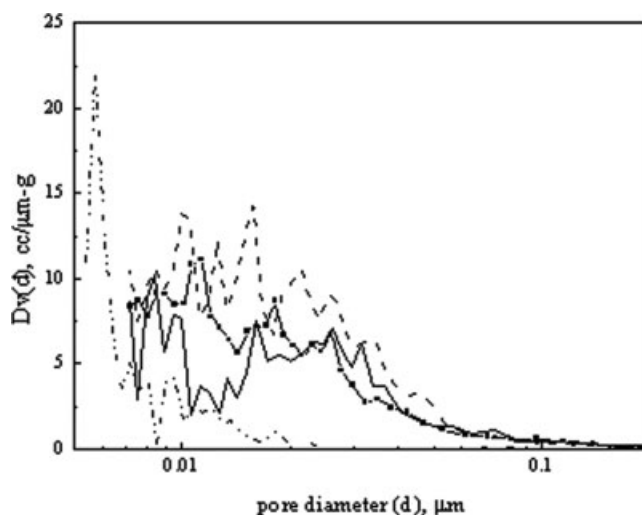
Figure 12 Pore size distributions of Sample B, Sample D, Sample F, and Sample H. –●●–: Sample B; - - -: Sample D; —: Sample F; –■–: Sample H.

More pores were produced under higher porogen concentration, and the pore size distribution is narrower for the particles prepared at higher degrees of crosslink density. The swelling capacity of these particles in water at room temperature was reduced with an increase in the crosslink density. Although the swelling pores determine the water regain of the particles, the presence of the permanent pores enhances the water regain because water can fill in the porous structures resulting in the high q_w values.

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