Preparation of Polymer Microspheres from Solutions

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ABSTRACT: Polymer microspheres are obtained by the dropwise addition of a precipitant, containing a polymeric stabilizer, into a polymer solution, containing a polymeric stabilizer. The polymer and stabilizer concentrations, the stirring speed, and the precipitation temperature determine the size and size uniformity of the microspheres. Seven polymer microspheres of polyimide, poly(ether imide), poly(ether ketone), poly(phenylene oxide), polysulfone, poly(vinylidene fluoride), and cellulose diacetate have been prepared with dimethylacetamide as the solvent, with water as the precipitant, and with poly(vinyl alcohol) as the stabilizer. The size and size uniformity of the obtained microspheres are $d = 2.3\text{--}25.7\ \mu\text{m}$ and $\epsilon = 0.15\text{--}0.50$, respectively ($\epsilon = \sigma/d$, where ϵ is the dispersion coefficient, d is the average diameter, and σ is the standard deviation of the diameter). © 2002 Wiley Periodicals, Inc. *J Polym Sci Part B: Polym Phys* 41: 159–165, 2003

Keywords: microspheres; polymer solution; precipitation; polymeric stabilizer

INTRODUCTION

Polymer microspheres are very useful for making size markers; chromatographic packings; functional coatings; inks and toners; additives for food, medicine, and cosmetics; supports for catalysts; carriers for proteins, enzymes, and cells; reagents for immunological diagnostics; controlled-release or target-specific drugs; and so forth.

The size uniformity of microspheres is characterized by the dispersion coefficient parameter ϵ . ϵ is defined as $\epsilon = \sigma/d$, where d is the average diameter and σ is the standard deviation of the diameter. A small ϵ value means high size uniformity. When ϵ is less than 0.1, the microspheres are monodisperse. In some applications as size markers or chromatographic packings, monodisperse microspheres are necessary or preferred.

The techniques for making microspheres from natural polymers were developed in the 1950s and 1960s.^{1–3} At that time, dextran, agarose, and cellulose microsphere products were commercialized. The preparations can be summarized as follows:

1. Formation of a liquid phase containing the natural polymer.
2. Shaping of the liquid to form spherical droplets.
3. Solidification of the liquid droplets.
4. Final washing.

For the formation of spherical droplets, the liquid is either extruded through suitably sized apertures or dispersed in a medium that does not mix with the liquid phase. The particle size is controlled by the manner in which the fluid passes through the nozzle, by the efficiency of mixing during dispersion, or by the addition of surface-active compounds.

Synthetic polymer microspheres are usually manufactured during polymer synthesis from a

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monomer, for example, in suspension, emulsion, and dispersion polymerizations. Swelling and dispersion polymerization methods have been developed for manufacturing monodisperse microspheres.^{4–6} In the polymer latex industry, artificial latices, which are dispersions of existing solid polymers in an aqueous medium at the nanometer–submicrometer level, are produced by mini-emulsion, solution-precipitation, and phase-inversion techniques, as well as others.^{7,8} There are not many reports on preparing microspheres from existing synthetic polymers. However, in the 1980s and 1990s, techniques for making microspheres from existing crystalline polymers were developed. In 1987, Schaaf et al.⁹ reported that spherical polyethylene globules 1–10 μm in size formed upon the controlled crystallization of semidilute (ca. 1–5%) solutions in poor solvents. The authors concluded that liquid–liquid demixing took place before the crystallization of the polymer. In 1992, Hou and Lloyd¹⁰ reported a fast cooling (1 $^{\circ}\text{C/s}$) method for preparing monodisperse polyamide microspheres ($\epsilon = 0.06$) from dilute solutions in small vials. In 1994, Nicholas and Robertson¹¹ reported the preparation of poly(butylene terephthalate) microspheres through crystallization from a moderately concentrated (5%) solution in a liquid diglycidyl ether of bisphenol A epoxy prepolymer. At the same time, patents for poly(ethylene terephthalate), polyolefin, and nylon microsphere and powder (microsphere aggregate) products were published in Japan.^{12–14} One patent showed that rather homogeneous polypropylene microspheres ($\epsilon = 0.3–0.5$ by our calculation) were obtained at a 5% concentration in diethylethanolamine/xylene (70/30).¹³ The other patent showed that individual nylon microspheres were obtained even at a high concentration of 10% when the polymer crystallized in propylene glycol monomethyl ether/methanol (855/45).¹⁴

No report has previously been published on preparing microspheres from amorphous polymers, although many high-performance polymers and specialty polymers are amorphous. It will be of great significance if these microspheres are prepared. In this article, we introduce a method for preparing microspheres from existing amorphous polymers. Instead of the solution being cooled, as is done for crystalline polymers, the addition of a precipitant is adopted for creating the liquid–liquid phase separation. A polymeric stabilizer is added to the solution. Seven polymers have been chosen for experiments, which cover

wide categories. The controlling factors for the sizes and size distributions of the microspheres have been studied.

EXPERIMENTAL

Materials

Polyimide [PI; weight-average molecular weight (M_w) = 25,000] was a product of the Shanghai Institute of Synthetic Resins (China). Poly(ether imide) [PEI; M_w = 30,000, number-average molecular weight (M_n) = 12,000] was a product of General Electric (United States) with the trade name Ultem 1000. Phenolphthalein poly(aryl ether ketone) (PEK-C; M_n = 12,000) was a product of Xuzhou Chemical Factory (China). Poly(2,6-dimethyl-1,4-phenylene oxide) (PPO; M_w = 35,000), bisphenol A polysulfone (PSF; M_w = 59,000), poly(vinylidene fluoride) (PVDF; M_w = 200,000), cellulose diacetate (CA; M_w = 34,000, combined acetic acid = 54.5–56.0%), and poly(vinyl alcohol) (PVA; M_w = 77,000, degree of hydrolysis = 88%) were all produced in China. Scheme 1 shows the structures of some of the polymers. Dimethylacetamide (DMAc) was analytically pure.

Preparation of the Microspheres

In a 5000-mL, three-necked bottle was placed 1000 mL of PI (0.02 g/mL) and PVA (0.02 g/mL) in a DMAc solution. PVA (0.02 g/mL) in a water solution was added dropwise (drop size = 0.05 mL) into the bottle under stirring at 250 rpm at 70 $^{\circ}\text{C}$. The second drop was added only when the precipitate caused by the first drop almost disappeared in the solution. After 100 mL of the precipitant was dropped, the precipitate no longer disappeared. The addition of the precipitant continued until 2000 mL was added. The suspension was stirred overnight. On the 2nd day, the microspheres were collected by filtration and washed with water until DMAc and PVA were completely removed. After weighing, the dry product recovery was obtained.

In addition to PI, microspheres of PEI, PEK-C, PPO, PSF, PVDF, and CA were also prepared. The preparation was studied at different polymer and PVA concentrations, stirring speeds, and temperatures.

Scheme 1. Structures of PI, PEI, and PEK-C.

Determination of the Sizes and Size Distributions of the Microspheres

The values of d and ϵ were obtained from the statistics of over 200 microspheres in the SEM micrographs.

RESULTS AND DISCUSSION

The reason that microspheres of crystalline polymers are first prepared and even commercialized is related to the phase behavior of these polymers in solution. A crystalline polymer solution has a liquid-liquid phase separation followed by crystallization of the polymer.^{9,11} During cooling, the dilute solution first undergoes a liquid-liquid demixing by which the polymer concentrated-phase droplets form. Having a crystallization temperature higher than the solution temperature, the concentrated phase crystallizes. Because the solvent is completely excluded from the crystallizing polymer in the droplets, the liquid droplets shrink substantially and solidify quickly. Individual microspheres are easily obtained.

An amorphous polymer solution has a phase behavior similar to that of a crystalline polymer (Fig. 1). Instead of crystallization, liquid-liquid phase separation is followed by vitrification of the concentrated phase. When the temperature is lower than the glass-transition temperature, the concentrated-phase droplets vitrify. Because the solvent is not excluded from the droplets during vitrification, the droplets solidify slowly. In this case, aggregates of the microspheres form easily. This is why amorphous polymer microspheres are difficult to prepare from their solutions. In 1988, Hikmet et al.¹⁵ reported the phase transformation and morphology of an atactic polystyrene/cyclohexanol system. They showed that three morphological structures were obtained from the system (Fig. 1): (1) a dispersed polymer-rich glassy phase in a solvated matrix at low concentrations, (2) a dispersed solvated phase in a glassy matrix at high concentrations, and (3) bicontinuous interpenetrating networks at intermediate concentrations. However, they did not obtain individual microspheres and only observed 1–2- μm beads collapsed in the structure.

Figure 1. Phase diagram of an amorphous polymer solution. A dispersed polymer-rich glassy phase (black points) in a solvent matrix at low concentrations, a dispersed solvated phase (white points) in a glassy matrix at high concentrations, and bicontinuous interpenetrating networks at intermediate concentrations are obtained during phase separation at low temperatures.

To solve the aggregation problem, two measures are taken in our preparation. First, the addition of a precipitant is adopted for creating the liquid–liquid demixing. The precipitant addi-

tion continues after the phase separation begins for completing the precipitation (conservation). Because of the large quantity of the precipitant, the droplets are isolated, and the solvent in the droplets are removed. For the crystalline polymer microspheres to be made from their solutions, further cooling is adopted for completing the phase separation. The droplet concentration remains unchanged in the system. Second, a polymeric stabilizer (PVA) is added in solution. PVA is a good stabilizer for suspension polymerization in water. With the protection of PVA, the collision and aggregation of the droplets are greatly suppressed.

Sizes and Size Distributions of the Microspheres

Controlling the size and size uniformity is important in the preparation of polymer microspheres. In our preparation, the particle size increases in two ways: the coagulation of the droplets or the absorption of the polymer in solution into the droplets. The size distribution broadens in several ways: the coagulation or breakup of the droplets, the formation of the secondary droplets, or the nonequal absorption of the polymer into the droplets. Coagulation should be suppressed because it reduces size uniformity. In Table 1 are listed the experimental conditions and results. Figure 2 provides a representative example of the prepared PI microspheres. The size and size uniformity are dependent on the polymer and stabilizer concentrations, stirring speed, and precipitation temperature.

Table 1. Preparation of the Polymer Microspheres

Polymer	Polymer Concentration (g/mL)	PVA Concentration (g/mL)	Stirring Speed (rpm)	T (°C)	d (μm)	ε	Recovery (%)
PI1	0.02	0.02	250	70	8.3	0.28	52
PI2	0.005	0.02	250	70	6.9	0.50	41
PI3	0.02	0.04	250	30	4.9	0.20	52
PI4	0.05	0.02	250	70	25.7	0.34	58
PI5	0.02	0.06	250	70	8.9	0.16	62
PI6	0.02	0.04	250	70	9.5	0.15	67
PI7	0.02	0.04	1100	70	4.9	0.16	57
PEI	0.04	0.02	250	90	8.1	0.20	40
PEK	0.01	0.02	250	80	5.7	0.27	47
PPO	0.01	0.02	250	80	2.3	0.14	—
PSF	0.02	0.02	250	30	19.8	0.26	91
PVDF	0.04	0.02	250	95	3.0	0.23	82
CA	0.02	0.04	250	40	8.7	0.25	53

Figure 2. SEM micrograph of PI6 microspheres.

Polymer Concentration

With increasing polymer concentration, the size of microspheres increases, but ϵ decreases. The data (PI2, PI1, and PI4 in Table 1) show that the size increases from 6.9–8.3 to 25.7 μm , whereas ϵ decreases from 0.50 to 0.28–0.34, when the polymer concentration increases from 0.005 to 0.05 g/mL. This indicates that a high concentration increases the ratio of the polymer concentration to the primary droplet number in solution. Both a larger particle size and a narrower size distribution result because every droplet absorbs more polymer equally from the solution during precipitation.

Stabilizer Concentration

In this study, a polymeric stabilizer has been used that functions as a surfactant surrounding the droplets and as a thickener increasing the viscosity of the solution. Therefore, the polymeric stabilizer effectively prevents the collision and coagulation of the droplets. This favors the size uniformity of the obtained microspheres. From the data of PI1, PI6, and PI5, we can see this trend. When the PVA concentration increases from 0.02 to 0.06 g/mL, ϵ decreases from 0.28 to 0.15–0.16. However, the microsphere size remains almost constant. This indicates that the stabilizer concentration does not influence the number of the primary droplets.

Stirring Speed

When the stirring speed increases from 250 to 1100 rpm, the particle size decreases from 9.5 to

4.9 μm , but ϵ remains constant (PI6 and PI7 in Table 1). The reason for the particle size decreasing at a high stirring speed is quite similar to that for suspension polymerization: high-speed stirring breaks the liquid droplets. The constancy of the size distribution is a result of the compensation of two opposite processes. High-speed stirring brings homogeneity to the system, greatly suppressing the formation of the secondary droplets and providing equal absorption of the polymer into the droplets. It also breaks the droplets.

Precipitation Temperature

When the precipitation temperature increases from 30 to 70 $^{\circ}\text{C}$, the microsphere size increases from 4.9 to 9.5 μm , whereas ϵ slightly decreases from 0.20 to 0.15 (PI3 and PI6 in Table 1). At a high temperature, the number of the primary droplets forming at the beginning of liquid–liquid demixing is small, and this makes the ratio of the polymer concentration to the primary droplet number large. At a high temperature, the viscosity of the solution decreases, and this partly compensates the improvement in the size uniformity.

Recovery

Recovery is not high in our preparation. This term is determined by the thermodynamics of liquid–liquid phase separation and is calculated as follows (Fig. 1):

$$\text{Recovery} = \phi' C_p' / (\phi' C_p' + \phi'' C_p'') \\ = (C_p - C_p'') C_p' / [(C_p - C_p'') C_p' + (C_p' - C_p) C_p'']$$

where ϕ' and ϕ'' are the phase volumes of the concentrated and dilute phases, respectively. C_p , C_p' , and C_p'' are the concentrations of the polymer in the solution, concentrated phase, and dilute phase, respectively. The binodal curve of the polymer solution is extremely unsymmetrical, and as the concentration of the concentrated phase is not high, the difference between the polymer and dilute-phase concentrations is small; therefore, the recovery is low. The dilute phase exists as fine particles ($<1 \mu\text{m}$) and is washed out afterward.

Polymers

In this work, seven polymers have been chosen for making microspheres, among which PI, PEI, and PEK-C are high-performance condensation poly-

Figure 3. SEM micrographs of polymer microspheres.

mers, PPO and PSF are engineering condensation polymers, PVDF is a fluorine-containing addition polymer, and CA is a derivative of a natural polymer. The preparation conditions and results are also listed in Table 1. The images in Figure 3 are of PEI, PEK-C, PPO, PSF, PVDF, and CA microspheres.

Because of the differences in the thermodynamics of the phase separation and efficiency of the stabilizer in the systems, it is not surprising to see that the particle sizes obtained range from 2.3 to 19.8 μm . Very high recoveries are obtained for PSF and PVDF, and so it is possible that these solutions have broad binodal curves. Like PI, PEI, PEK-C, and PSF particles have smooth surfaces, whereas PPO and PVDF have rough surfaces, and CA even has holes on the surface. This indicates that the efficiency of water is different in precipitating the polymer solutions.

The preparations give us the confidence to prepare more polymer microspheres, but only if the proper solvent, precipitant, and polymeric stabilizer are found.

CONCLUSIONS

Precipitating a polymer solution slowly in the presence of a polymeric stabilizer produces polymer microspheres. A high polymer concentration, a low stirring speed, and a high precipitation temperature are favorable for obtaining large polymer microspheres. Increasing the polymer

and stabilizer concentrations improves the uniformity of the microspheres.

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