Formation, stabilization & application of polymeric nanoparticles

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SUMMARY: Using microwave irradiation, we were able to prepare a concentrated (up to 40 wt.%) uniform polystyrene nanoparticles (down to ~60 nm) in the presence of 1.82 wt.% of anionic surfactant (sodium dodecylsulfate). Both the nanoparticles and the polystyrene chains inside the nanoparticles were characterized by a combination of static and dynamic laser light scattering (LLS). We also found that various surfactant-free polymeric nanoparticles could be made by microphase inversion; namely, the addition of a polymer solution dropwise into an excess of water or the temperature-induced phase transition. We proposed a stabilization mechanism and experimentally demonstrated that for a given stable dispersion the average surface area (s) occupied per stabilizer is a constant. On the basis of this mechanism, we were able to propose a structural model to control and predict the resultant particle size from the macroscopic monomer/stabilizer weight ratio. We also successfully used the nanoparticles in the studies of enzymatic biodegradation and controllable chemical releasing.

Introduction

Emulsion polymerization is a conventional way to prepare polymeric particles in the size range 10^2 -10^3 nm. Emulsion polymerization has been gradually improved to broaden the size range. The seeded emulsion polymerization was developed to make latexes with a size larger than 10^3 nm[1,2)], while the miniemulsion and microemulsion polymerization were invented for the preparation of smaller particles in the ranges 50-200 nm and 20-50 nm, respectively[3,4)]. It is known that in microemulsion polymerization, a large amount of surfactant/co-surfactant has to be added, which not only limits the dispersion concentration but also is not good for some applications of the nanoparticles. The removal of surfactant from the resultant polymer dispersion without affecting its stability is extremely difficult, if not impossible.

Much effort has been spent on how to increase the solid content and reduce the surfactant. For example, a continuous and slow addition of monomers dropwise into a microemulsion during polymerization and a semicontinuous addition of monomers into a lower solid-content dispersion formed via microemulsion polymerization were developed to make a full use of surfactant to increase the solid content[5,6)]. L. M. Gan *et al.*[7,8)] designed a Winson I-like polymerization system which contains a monomer upper layer saturated with a small amount of water and DTAB and a lower oil-in-water microemulsion layer. The upper layer acted as a monomer reservoir to supply monomers for the microemulsion polymerization in the lower

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layer. In this way, a series of polystyrene latex dispersion in the size range 46-97 nm were prepared with a solid content as high as 15 wt% and a surfactant content as low as 1%.

Up to now, it is still a challenge or a dream to prepare concentrated uniform surfactant-free (or a very small amount of surfactant) polymeric nanoparticles (10-100 nm in size) stable in water. Another standing issue is to quantitatively control and predict the resultant particle size from the initial polymerization composition, i.e., the ratio of monomer to surfactant, or in a more broad sense, the ratio of monomer to stabilizer because polymeric particles can also be stabilized by ionic or hydrophilic groups introduced on the surface and polyelectrolytes or hydrophilic polymer chains grafted or adsorbed on the surface. In this lecture, we will present a novel method of using microwave irradiation to prepare a concentrated (up to 40 wt.%) uniform polystyrene nanoparticles (down to ~60 nm) in the presence of 1.82 wt.% of anionic surfactant (sodium dodecylsulfate) and also surfactant-free polymeric nanoparticles. We will also use the experimental results to show that for a given stable dispersion the average surface area (s) occupied per stabilizer is a constant so that the resultant particle size can be controlled and predicted from the macroscopic monomer/stabilizer weight ratio. In addition, two successful applications of the nanoparticles in the studies of enzymatic biodegradation and controllable chemical releasing will be demonstrated.

Experimental

Materials: Styrene and methyl methylacrylate was purified by a standard procedure. Sodium dodecyl-sulfate (SDS), cetyltrimethylammonium bromide (CTAB), azobis(isobutyronitrile) (AIBN), and potassium persulfate (KPS) were used as received. The PEO macromonomers were specially prepared with either one styrene (St) or methyl methylacrylate (MMA) molecule attached as the end group, i.e., St-PEO and MMA-PEO. In each case, three different molar masses of PEO (M_n = 1000, 2000 and 4000 for MMA-PEO; and M_n = 1000, 2000 and 5000 for St-PEO) were prepared. Deionized water from the Millipore Nanopure water-system with a resistivity of 18 MΩ·cm was used in the experiments.

Microwave irradiation: A domestic microwave oven (Whirlpool-VIP20) with a double emission system, operating at 2450 MHz with a maximum output power of 900 W was used. The oven was slightly modified so that a flask equipped with a glass stirrer, a reflux condenser, a thermometer, and a feeding head could be assembled inside it (Figure 1). It should be noted that a brass tube was connected to the open hole on the top to prevent the leakage of microwave. Another modification was the addition of an electric On-and-OFF controller (the box on the top) so that the output microwave power could be better regulated.

Typically, under the irradiation, the reaction temperature of ~70 °C could be reached within 1-2 minutes and the monomers were polymerized at ~70 °C under N_2 with a reduced microwave irradiation of only 80 W. In this way, more than 98% of styrene monomer were polymerized within ~40 minutes.

Laser light scattering. A modified commercial LLS spectrometer (ALV/SP-125) equipped with a multi-τ digital time correlator (ALV-5000) and a solid-state laser (ADLAS DPY 425II, output power ≅ 400 mW at λ_o = 532 nm) was used. The principle of LLS can be found elsewhere.[9,10] In static LLS, the measurements of the angular dependence of the scattered light intensity from a set of dilute dispersions or solutions can lead to the weight average molar mass (M_w), the average radius of gyration $<R_g>$ and the second virial coefficient (A_2). In dynamic LLS, the hydrodynamic radius distribution ($f(R_h)$) can be determined from the measured time correlation function. A combination of static and dynamic LLS can also lead to other parameters, such as the average number of the PS chains inside each particle and the particle density. In this study, all the LLS measurements were conducted at 25.0 ± 0.1 °C and the specific refractive index increment (dn/dC) of the PS latices in water and the PS chains in toluene are 0.256 and 0.110 mL/g, respectively.

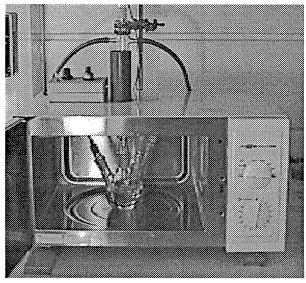

Figure 1. Modified microwave oven for emulsion and microemulsion polymerization of polymeric nanoparticles.

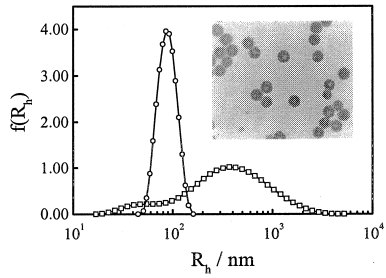

Figure 2. Comparison of the hydrodynamic radius distribution $f(R_h)$ of PS nanoparticles prepared with (the sharp peak, while the insert is a TEM photo) and without microwave irradiation.

Results and discussion

Preparation of polymeric nanoparticles by microwave irradiation[11,12]

A mixture of proper amounts of freshly distilled styrene or methyl methylacrylate monomers and water with and without surfactant was added into the flask and stirred for 10 minutes at a speed of 3×10^2 rpm under N_2 before a given amount of initiator, potassium persulfate (KPS),

was added to start the polymerization. The total volume of the reaction mixture is 250 mL. Typically, under the microwave irradiation, the reaction temperature of ~70 °C was reached within only 1-2 minutes and maintained by adjusting the microwave power. The reaction was carried out at ~70 °C under N_2 for 1 hour with a reduced microwave irradiation of only 80 W. In this way, more than 98% of styrene monomer were polymerized within ~40 minutes. It should be stated that even without the addition of surfactant the resultant nanoparticles were narrowly distributed and stable over months.

Both the polystyrene nanoparticles in water and individual polystyrene chains in toluene were characterized by using a combination of static and dynamic LLS. Figure 2 shows a typical hydrodynamic radius distribution $f(R_h)$ of the nanoparticles. In comparison, if using a water-bath to heat the same reaction mixture under an identical condition, the polymerization not only took a much longer time to reach the same extent of conversion, but also resulted in a more broader size distribution. Using microwave irradiation, we also prepared narrowly distributed stable surfactant-free poly(methyl methylacrylate) nanoparticles.

Our results showed that the average hydrodynamic volume of the nanoparticles is a linear function of the initial monomer concentration if the initiator concentration was kept as a constant, indicating that on average each nanosphere contained a constant number of individual polystyrene chains. Our results showed that the average number of the polymer chains inside each nanosphere is independent of the monomer concentration, but increases with the initiator concentration; and the average length of the polystyrene chains formed inside the nanoparticles is independent of the initiator concentration, but increases with monomer concentration.

Moreover, we found very recently that the microwave irradiation could be used to prepare a very concentrated (up to 40 wt.%) uniform polystyrene nanoparticles (down to ~60 nm) in the presence of only 1.82 wt.% of anionic surfactant (sodium dodecylsulfate). The results showed that the monomer conversion reached ~90% within 20 minutes, after which there was no change in the size and molar mass of the nanoparticles as well as in the average length and number of the polystyrene chains inside the nanoparticle.

It should be stated that using microwave irradiation to initiate a reaction is not new in chemistry, but it has several distinct advantages in the preparation of polymeric nanoparticles. For example, it can quickly and uniformly heat the entire reaction mixture to a desired temperature so that a simultaneous initiation is expected, which is reflected in the narrow distribution of the resultant polymer chains. Also, the fast variation of electric and magnetic

field during microwave irradiation can introduce a micro-stirring of water molecules. The method presented here can be used to prepare other types of colloid particles.

Formation of surfactant-free polymeric nanoparticles by microphase inversion[13-15)]

Using controllable microphase inversion, we have successfully prepared a range of novel surfactant-free polymer nanoparticles. For example, it is known that randomly carboxylated polystyrene ionomers are insoluble in water. However, we recently found that adding their tetrahydrofuran (THF) solution of such ionomers into an excess of water or vice versa, the ionomer chains can undergo a microphase inversion to form surfactant-free colloidal nanoparticles (~5-50 nm) stable in water. A combination of static and dynamic LLS results showed that 1) a lower initial ionomer concentration and a higher ionic content could lead to smaller nanoparticles; and 2) using Na^+ instead of Mn^+ as a counterion could result in smaller particles (Figure 3). We also found that the order of mixing the ionomer THF solution with water could influence the size distribution of the resultant nanoparticles.

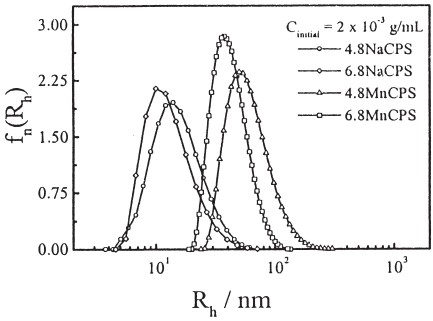

Figure 3. Surfactant-free nanoparticles made of randomly carboxylated polystyrene ionomers (four different weight ratios of NaCPS to PS) dispersed in water by means of microphase inversion.

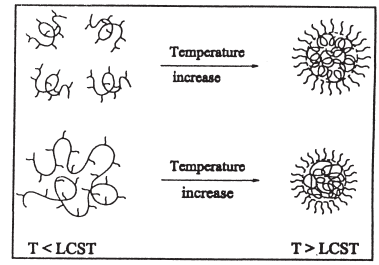

Figure 4. Schematic representation of the self-assembly of PNIPAM-PEO copolymer chains (or chain) in water to form core-shell structure with PNIPAN as the core and PEO as the shell.

Another successful example is that the copolymer chains, poly(*N*-isopropylacrylamide) (PNIPAM) grafted with poly(ethylene oxide) (PEO), could form the polymeric nanoparticles with a core-shell structure if the temperature increased from 25 °C to ~32 °C or higher. This is because at room temperature, both PNIPAM and PEO are water-soluble, while at temperatures higher than ~32 °C, PNIPAM becomes hydrophobic and undergoes an intrachain "coil-to-globule" transition and an interchain aggregation to form nanoparticles. Our results showed that the particle size decreased as the number of the PEO chains grafted on the PNIPAM chain backbone increased; and a lower copolymer concentration and a fast heating rate could also lead to smaller nanoparticles. With a proper control of the formation conditions, we were able, for the first time, to suppress the interchain aggregation to prepare and study a single chain core-shell nanostructure (Figure 4).

Structural models for the stabilization of polymeric nanoparticles[16-19)]

The aggregation of polymeric particles could be prevented by various kinds of "stabilizers", such as ionic or non-ionic surfactant; ionic groups introduced by initiation, copolymerization or surface modification; and water-soluble polymer or polyelectrolytes chains grafted or adsorbed on the particle surface (Figure 5). It has been speculated that for a given stable dispersion, the average surface area (s) occupied by each stabilizer should be a constant.

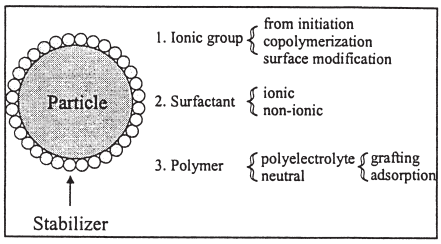

Figure 5. Schematic representation of stabilization of polymeric nanoparticles where the surface area per stabilizer is a constant for a given dispersion.

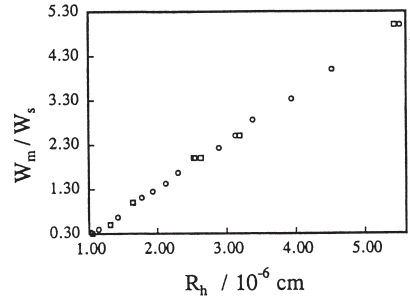

Figure 6. A typical plot of W_m/W_s versus R for the emulsion polymerization of styrene in the presence of CTAB as a stabilizer and AIBN as an initiator.

We have studied a range of dispersions, such as systems obtained by microemulsion polymerization of styrene, ionic group stabilized surfactant-free polystyrene nanoparticles, and the PEO grafted polystyrene latexes. Our LLS results confirmed our speculation and led to the following scaling between the macroscopic monomer/stabilizer weight ratio (W_m/W_s) and the radius (R) of the particle,

$$\frac{W_m}{W_s} \approx \gamma s \frac{N_A \rho}{3M_s} R + \gamma(s \frac{N_A \rho}{3M_s} b - 1) \qquad (1)$$

where ρ, M_s, b, and γ are the particle density, the molar mass of stabilizer, the thickness of the stabilizer shell, and the percentage of stabilizers adsorbed on the particle surface, respectively. Figure 6 shows a typical plot of W_m/W_s versus R for the systems obtained by microemulsion polymerization of styrene in the presence of surfactant, cetyltrimethylammonium bromide (CTAB), and a lypophilic initiator, azobis(isobutyronitrile) (AIBN). On the basis of eq 1, Figure 6 leads to s ~ 0.2 nm^2 and b ~ 1 nm.

Another example is the surfactant-free latex particles stabilized with the short PEO chains grafted on the particle surface. We found that for both the polystyrene (PS) and poly(methyl methylacrylate) (PMMA) latexes, W_m/W_s is a linear function of R even for PEO chains with different lengths (Figure 7). It is interesting to notice that for the PMMA microspheres (the

filled symbols) the slope is much larger, indicating that each PEO macromonomer can stabilize a larger surface area when the core is made of PMMA. This is understandable because the acrylate group on MMA is relatively more hydrophilic than the benzene ring on styrene, so that it requires less PEO macromonomer to stabilize the same surface area or each PEO macromonomer can stabilize more surface. Knowing γ, we can find **s**. On the other hand, Knowing **s**, we can estimate γ, i.e., the amount of the stabilizers on the surface. In addition, our results showed that s/M_s is nearly a constant for different PEO chains, indicating that the PEO chains were in the Flory Θ-state.

We also studied the adsorption of linear poly(*N*-isopropylacrylamide) (PNIPAM) chains on surfactant-free polystyrene nanoparticles and found that the average hydrodynamic volume of the chain adsorbed on the surface can be scaled by the number of the chains adsorbed on each particle (Figure 8), which leads to the following important conclusion. Considering that on a unit area (the x-y plane), the density profile ($\rho(z)$) of the adsorbed chains is a function of the distance (z) away from the surface, we have $\int_o^\infty \rho(z)\, d(z) = W_{polymer} \propto n_{chain}$. Assuming that $\rho(z)$ can be scaled by a characteristic length (ξ), we have $\xi \int_o^\infty \rho(z/\xi)\, d(z/\xi)$. The observed scaling, $v_{chain} \propto n_{chain}$, suggests that $\xi \propto n_{chain}$ and $\rho(z/\xi)$ is an invariant.

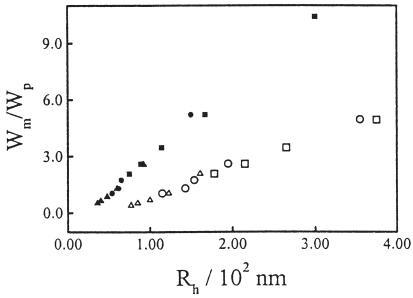

Figure 7. Typical plot of W_m/W_s versus R for dispersions obtained by emulsion polymerization of styrene in the presence of the short PEO chain as a stabilizer.

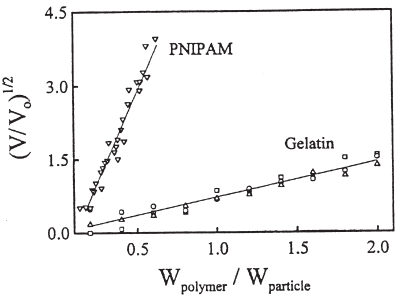

Figure 8. Adsorption dependence of the average hydrodynamic volume of the adsorbed polymer layer on the particle.

Application of polymeric nanoparticles[20,21)]

Polymeric latex particles have been widely used in various aspects. Here, we only use several of our own experimental results to illustrate their novel applications. For example, studying the degradation of polymeric nanoparticles provided us not only an accurate, reliable and microscopic method, but also a novel and fast way to evaluate the biodegradability of a given polymer. Using poly(ε-caprolactone) (PCL) as a typical example, we have shown that its biodegradation time can be shortened by a factor of more than ~10^3 times in comparison with

the time required to biodegrade a thin film (10 x 10 x 0.1 mm^3). Moreover, the biodegradation kinetics can be monitored *in-situ* in terms of the decrease of the time-averaged scattering intensity and the number of the nanoparticles. A comparison of static and dynamic LLS results revealed that the enzyme, Lipase Pseudomonas, "eats" the nanoparticles in an one-by-one manner and the biodegradation of PCL follows a zero-order kinetics (Figure 7). On the basis of our results, we proposed an enzymatic biodegradation mechanism in which an additional equilibrium between the inactive and active enzyme/polymer complexes was introduced besides the equilibrium between the inactive complex and polymer.

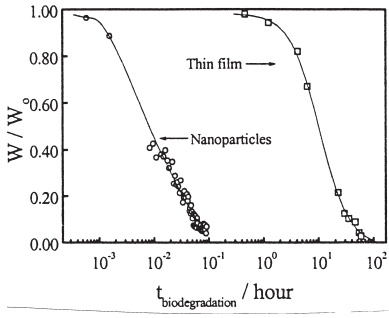

Figure 9. Comparison of biodegradation of a PCL thin film and nanoparticles under the same enzyme concentration.

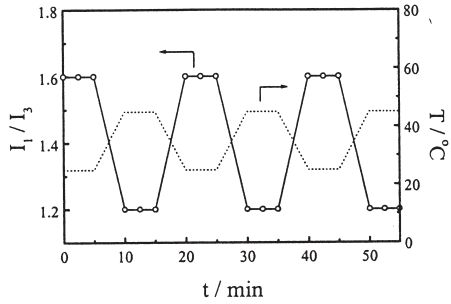

Figure 10. Temperature dependence of the fluorescence intensity ratio of pyrene in the presence of the core -shell PNIPAM-g-PEO nanoparticles.

Another example is that using the core-shell PNIPAM-PEO nanoparticles, we could load and release hydrophobic chemicals by a simple temperature variation. Figure 8 shows an imitation in terms of the temperature dependent fluorescence intensity ratio (I_1/I_3) of pyrene in the presence of PNIPAM-PEO, where the pyrene concentration is ~2 x 10^{-7} M. It is known that the intensity ratio I_1/I_3 is very sensitive to microenvironmental polarity; namely, in pure water, I_1/I_3 ~1.8, while in a hydrophobic domain, I_1/I_3 could be as low as 1.2. The change of I_1/I_3 between ~1.6 and ~1.2 clearly shows that PNIPAM-PEO can release and encapsulate pyrene when temperature changes between 25 to 45 °C. It should be noted that the change of I_1/I_3 would be a step function if the temperature jump is fast.

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