Development of High Magnetization Fe_3O_4/Polystyrene/Silica Nanospheres via Combined Miniemulsion/Emulsion Polymerization

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Since the pioneering work by Ugelstad on preparation of superparamagnetic polystyrene microspheres using a so-called "activated swelling method" for immunity separation,[1] extensive research has been carried out to develop superparamagnetic organic/inorganic hybrid spheres for biomedical applications.[2,3] These applications include separation and purification of biomolecules, MRI contrast agent, hyperthermia, biosensor, and targeted drug delivery.[4−6] As specifically required for in vitro and in vivo tests,[7] the current research has been focused on synthesizing monodispersed, nanoscale spheres for high sensitivity and efficiency;[8a] achieving high saturation magnetization for fast and sensitive magnetic signal control, manipulation, and detection;[8] and providing hydrophilic surfaces with various functional groups for covalent coupling to antigens, antibodies, enzymes, or DNA/RNA hybridization.[9]

These critical issues have only been partially addressed so far. The major difficulty lies in the interrelated effects in synthesis and assembly. For instance, reducing the particle size to nanometer scale often leads to a wide distribution of particle dimension.[10] Coating the particle surface with a silica layer for hydrophilicity can result in significant reduction in saturation magnetization due to the decrease of the magnetite fraction in each microsphere.[10,11] Recently, a high magnetite fraction was achieved in superparamagnetic nanospheres by a three-step miniemuslion polymerization, but the as-synthesized nanospheres have a nonuniform magnetite fraction in each nanosphere.[8b,12] Therefore, it is of fundamental importance to develop novel methods for the preparation of monosized superparamagnetic spheres that satisfy all major requirements in biomedical applications, in particular, achieving nanospheres with a high volume fraction of magnetite and hydrophilic surfaces.

In this study, we developed a new process to obtain monodispersed, nanoscale, superparamagnetic magnetite/polystyrene (Fe_3O_4/PS) spheres. By uniquely combining modified miniemulsion/emulsion polymerization and the sol−gel technique, not only were the surfaces of monodispersed nanospheres functionalized to be hydrophilic via silica coating, the silica coating also serves as a buffer layer, protecting the magnetite nanoparticles from dissolving in the application environments. The surface silanol groups can easily react with various compounds to form functional groups and reduce nonspecial absorptions[11a] but also exhibit much higher saturation magnetization compared to that in previously reported results.

Figure 1 illustrates the preparation procedure. (1) Magnetite nanoparticles modified by oleic acid with an average particle size ∼10 nm were initially synthesized by a chemical coprecipitation method[13] and dispersed in situ in octane as a ferrofluid. (2) The ferrofluid was added to the aqueous solution with sodium dodecyl sulfate (SDS) as surfactant and treated ultrasonically to obtain miniemulsion A. This miniemulsion was composed of magnetite nanoparticle aggregations of droplets with a typical hydrodynamic size ∼123 nm. (3) Another miniemulsion (B) made of the styrene monomer droplets with uniform hydrodynamic size ∼3.7 μm was prepared by membrane emulsification equipment (SPG). (4) Mini-
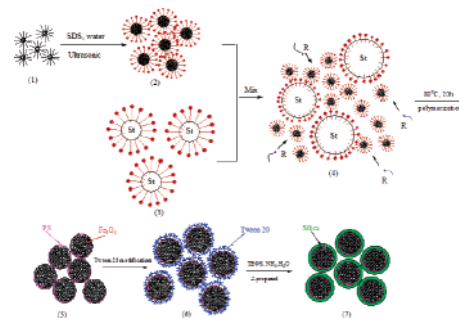

Figure 1. Schematic diagram showing the preparation of hydrophilic magnetic Fe_3O_4/PS nanospheres with high saturation magnetization.

emulsion A was then mixed with miniemulsion B to obtain a double-miniemulsion system, which contained microsized styrene droplets and nanosized magnetite aggregation droplets. (5) The double-miniemulsion system was reacted at 80 °C for 20 h to form Fe_3O_4/PS nanospheres. In this process, potassium peroxodisulfate (KPS) was used as an initiator for the polymerization of styrene. (6) The as-synthesized superparamagnetic Fe_3O_4/PS nanospheres were modified by polyoxyethylene(20) sorbitan monolaurate for dispersing the hydrophobic nanospheres into an aqueous phase. This step ensured that the surfaces of the Fe_3O_4/PS nanospheres came into contact with a rich water layer due to the larger hydrophilic ends of the surfactant. (7) In the final stage, as-synthesized Fe_3O_4/PS nanospheres were coated with a silica layer via a modified Stöber process, during which the hydrolysis, heterogeneous nucleation, and condensation of tetraethylorthosilicate (TEOS) onto the surface of the nanospheres consequently took place. See Supporting Information (SI) for details of preparation conditions.

It was important that the SDS surfactant concentration in processes 2−4 be below the critical micelle concentration (CMC) in order to ensure the absence of micelles. Another key point was that the number of magnetite aggregation droplets in miniemulsion A was much larger than that of St-droplets in miniemulsion B; this ratio was kept at 10^4 in this study.

Figure 2a,b shows the transmission electron microscopy (TEM) images of as-synthesized Fe_3O_4/PS nanospheres. As can be seen in Figure 2a, the size of the monodispersed spheres is 105 nm and the nanospheres all assume well proportioned spherical geometry, arranged in an orderly hexagon pattern in a single layer on the sample substrate. Figure 2b is the TEM image of as-synthesized Fe_3O_4/PS nanospheres at a higher magnification. Within each sphere, nanosized Fe_3O_4 crystals on the order of 10 nm are randomly embedded in the polymer matrix. Figure 2c,d shows the TEM images of the nanospheres after the silica coating. As can be seen, the outer silica-coating layer is quite uniform with a thickness of 20 nm (Figure 2c) and 5 nm (Figure 2d). From the TEM images, the core−shell structure and sphere size uniformity can be clearly seen. For comparison, laser size analyzing equipment was used to further determine the particle size (see SI). The experimental results
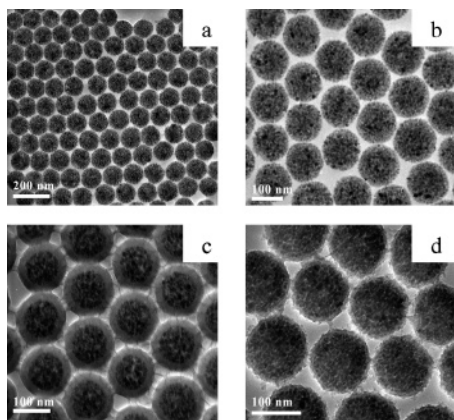
Figure 2. (a,b) TEM images of as-synthesized magnetic Fe_3O_4/PS nanospheres and (c,d) silica-coated magnetic Fe_3O_4/PS nanospheres.
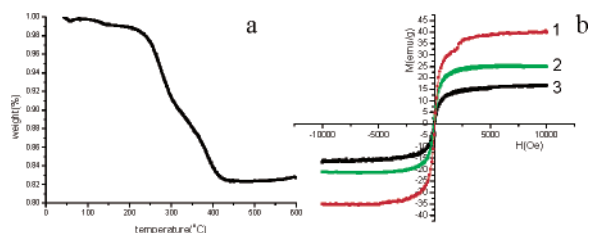
Figure 3. (a) TGA results of as-synthesized Fe_3O_4/PS nanospheres. (b) Magnetization curves at 300 K of as-synthesized magnetic Fe_3O_4/PS nanospheres with (1) 2, (2) 10, and (3) 30 nm silica coating.

on as-synthesized nanospheres indicate that the hydrodynamic size of the magnetic polymer nanospheres is 133 nm, whereas the polydispersity index is 0.060, consistent with the monodispersed core of Fe_3O_4/PS nanospheres shown in Figure 2a. The preparation method used in this study can avoid the irregular morphology of the Fe_3O_4/PS core, ensuring even growth of the silica layer.

Figure 3a shows the TGA results of the as-synthesized Fe_3O_4/PS nanospheres. The weight loss of 20% at 400 °C is the typical burn out temperature of polystyrene. This result implies at least 80 wt % of magnetite in the Fe_3O_4/PS nanospheres, much higher than reported previously.[8,12] Figure 3b shows the room-temperature magnetization curves of as-synthesized silica magnetic nanospheres with silica thicknesses of 2, 10, and 30 nm, respectively, adjusted by the content of TEOS. The same Fe_3O_4/PS nanosphere cores were used in the silica-coating experiments. As shown in this figure, the saturation magnetization value of silica magnetic nanospheres is 40 emu/g at 300 K (2-nm shell thickness) and decreases with increasing the shell thickness due to the decrease of the magnetite fraction in each microsphere. The zero coercivity and the reversible hysteresis behavior indicate the superparamagnetic nature of the nanospheres. The volume fraction of magnetite can be further increased by reducing the thickness of silica coating.

In this novel approach, since large numbers of nanosized magnetite aggregation droplets are mixed with a few microsized styrene droplets, the magnetite aggregation droplets become the major nucleation sites initiated by KPS, while styrene monomer droplets act as monomer reservoirs similar to traditional emulsion polymerization.[14] As a result of SDS concentration lower than that of CMC, there are no free or monomer-swollen micelles in the reaction system. In this situation, nucleation is entirely suppressed in free or monomer-swollen micelles, allowing the magnetite aggregation droplets to be the only nucleation sites. The excellent dispersion of magnetite in octane results in a high volume fraction of magnetite and nanoscale Fe_4O_3/PS spheres.

In surface functionalization for hydrophilicity, the as-synthesized Fe_3O_4/PS nanospheres are not ideal for silica coating. Their surfaces are therefore modified by a coating of polyoxyethylene(20) sorbitan monolaurate. The surfactant hydrophobic chains are inserted into the exterior polystyrene chains of Fe_3O_4/PS nanospheres. The hydrophilic chains made of three soft polyoxyethylene(n) chains ($n = 20$) would extend in water, as a result of special hydrophilicity.[15] A great number of water molecules are locked in the hydrophilic polyoxyethylene chains to form a rich water region on the surface of Fe_3O_4/PS nanospheres. This in turn enhances hydrolysis and condensation of TEOS onto the surface of nanospheres.

In conclusion, we have developed a new process combining double-miniemulsion/emulsion polymerization with sol−gel technology to synthesize monodispersed hydrophilic magnetic nanospheres that exhibit a much higher saturation magnetization due to a large fraction of magnetite compared to others reported in the current literature. The nanospheres are also surface modified by a thin layer of silica with a controlled thickness. The nanospheres are shown to be superparamagnetic, which allows them to serve as ideal candidates for biomedical applications such as nucleic acid extraction, cancer diagnosis and treatment, biosensors, and drug delivery.

Supporting Information Available: Experimental preparations for **1** and supporting characterization for **2**−**5**. This material is available free of charge via the Internet at http://pubs.acs.org.

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