

## Synthesis of Amphiphilic Superparamagnetic Ferrite/Block Copolymer Hollow Submicrospheres

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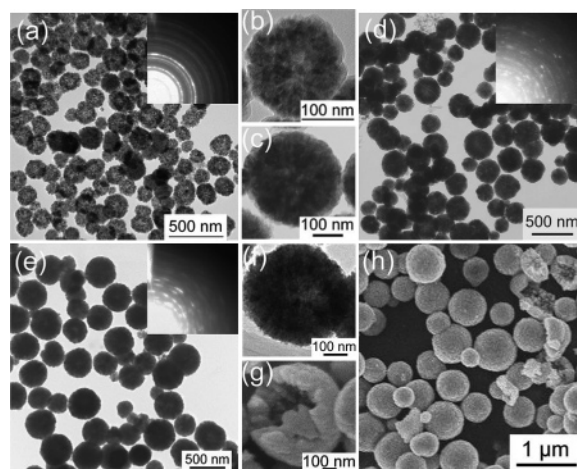
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Hollow spheres with nanometer-to-micrometer dimensions, tailored structures, and optical, magnetic, and surface properties are widely applicable in areas,<sup>1–16</sup> such as catalysis and biotechnology. Conventional methods for preparation of hollow spheres usually require sacrificial templates, including hard ones, such as polystyrene and silica spheres,<sup>3–6</sup> and soft ones, such as liquid drops,<sup>7</sup> microemulsion droplets,<sup>8</sup> polymer micelles, or vesicles.<sup>9</sup> These template-based approaches involve a multistep process in which preparation of a template, coating of the template with a shell, and removal of the template to create the hollow center are successively conducted. Recently, self-assembly strategies for hollow sphere preparation, which are more straightforward, have also been reported.<sup>10–15</sup>

For practical applications, especially in biomedicine, the hollow spheres need to be nontoxic, biocompatible, dispersible in various solvents, and superparamagnetic for drug delivery and separation of biochemical products and cells.<sup>1,7</sup> Most importantly, it is necessary to find an economical and efficient process for large-scale synthesis of hollow spheres with the tailored properties, whereas the hollow sphere preparation techniques reported so far cannot meet all the requirements. Herein, we describe a facile route for preparation of submicrometer ferrite hollow spheres which are amphiphilic and superparamagnetic and may find wide applications in biomedicine and biotechnology. This unique approach involves the formation of ferrite nanoparticles and the simultaneous self-assembly of nanoparticles and block copolymer poly(ethylene oxide)-*block*-poly(propylene oxide)-*block*-poly(ethylene oxide) (PEO-*PPO*-PEO), a widely used biocompatible polymer,<sup>17</sup> into hollow spheres. Furthermore, this approach is general for the preparation of a series of  $M_{1-x}Fe_{2+x}O_4$  ( $M = Fe, Co, Mn, 0 \leq x \leq 1$ ) ferrite hollow spheres. Unlike conventional hollow spheres, which are either hydrophobic<sup>18</sup> or hydrophilic,<sup>16</sup> the products we obtained exhibit excellent dispersibility in both polar and nonpolar solvents, widening their use to a considerable extent.

In a typical synthesis of 300 nm  $Fe_3O_4$ /PEO-*PPO*-PEO hybrid hollow spheres, 0.811 g (3.0 mmol) of  $FeCl_3 \cdot 6H_2O$ , 3.6 g (43.9 mmol) of  $CH_3COONa$ , and 0.998 g (0.525 mmol) of PEO-*PPO*-PEO block copolymer (Aldrich,  $M_n = 1900$ ) were dissolved in 35 mL of ethylene glycol and stirred vigorously until homogeneous. The mixture was sealed in a 50 mL PTFE-lined stainless steel autoclave and heated at 200 °C for 4 h followed by slow cooling to room temperature. The resulting product was thoroughly washed with absolute ethanol to remove all residual reagents and separated by centrifugation. During the reaction,  $Fe^{2+}$  species formed via reduction of a fraction of  $Fe^{3+}$  ions by solvent.<sup>19</sup> For  $M_{1-x}Fe_{2+x}O_4$  ( $M = Co, Mn$ ), the procedure was the same as described above except that  $FeCl_3 \cdot 6H_2O$  was replaced by the mixture of  $MCl_2$  ( $M = Co, Mn$ ) and  $FeCl_3 \cdot 6H_2O$  ( $Fe^{3+}/M^{2+} = 2$ ).

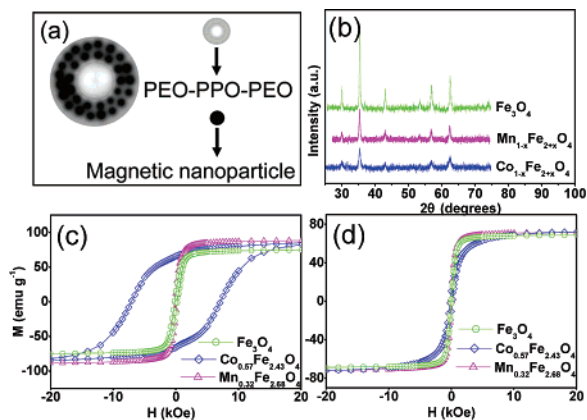
The average diameter of the spheres can be tuned from 170 to 610 nm (Figure S2) by varying the reaction time and reactant



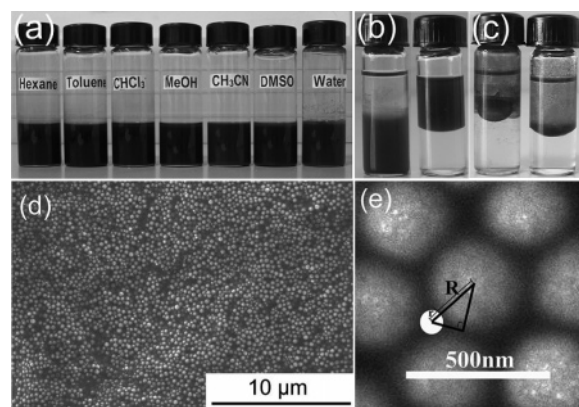
**Figure 1.** TEM images of (a and b) 170 nm  $Co_{0.57}Fe_{2.43}O_4$ , (c and d) 280 nm  $Fe_3O_4$ , and (e and f) 400 nm  $Mn_{0.32}Fe_{2.68}O_4$ , and FESEM images of (g and h) 610 nm  $Fe_3O_4$  hollow hybrid spheres. The insets are the SAED patterns.

concentration. Taking  $Fe_3O_4$  for example, 610 nm hollow spheres were obtained by increasing the concentrations of the reactants to 0.42 M ( $FeCl_3$ ), 1.29 M ( $CH_3COONa$ ), and 0.045 M (PEO-*PPO*-PEO), and the reaction time to 48 h. Nevertheless, there was no obvious linear correlation between sphere size and reaction time or concentration of reactants, as also observed for the preparation of other nano- and microparticles.<sup>19</sup> Figure 1a–f shows the transmission electron microscope (TEM) images of  $Co_{0.57}Fe_{2.43}O_4$ ,  $Fe_3O_4$ , and  $Mn_{0.32}Fe_{2.68}O_4$  hybrid hollow submicrospheres. The remarkable feature of the spheres is the obvious contrast between the dark edge and the pale center, as reported for other hollow particles with a central cavity. From the high-resolution transmission electron microscope (HRTEM) images (Figure S3) and the selected-area electron diffraction (SAED) patterns (insets in Figure 1a,d,e), it is seen that small nanocrystals are assembled together in the shell of the hollow spheres. Infrared spectroscopy (FTIR) and thermogravimetric and differential thermal analysis (TG-DTA) (Figures S4 and S5) reveal the presence of PEO-*PPO*-PEO copolymer, which plays a role in the assembly of the inorganic nanocrystals (Figure 2a) in the hollow spheres. In addition, the field-emission scanning electron microscope (FESEM) images of several broken  $M_{1-x}Fe_{2+x}O_4$ /PEO-*PPO*-PEO hybrid spheres also reveal the hollow feature of the spheres, as shown in Figure 1g,h and Figure S1e–h.

The powder X-ray diffraction (XRD) patterns for  $M_{1-x}Fe_{2+x}O_4$  ( $M = Fe, Co, Mn$ ) hollow spheres indicate that the inorganic components are pure-phase ferrites with a cubic structure (Figure 2b), but nonstoichiometry has been found for the Co- and Mn-containing compounds (Table S1). The magnetic properties of the products were investigated using a superconducting quantum



**Figure 2.** (a) Schematic representation for the structure of a hollow sphere. (b) XRD patterns of 400 nm  $M_{1-x}Fe_{2+x}O_4$  ( $M = Fe, Co, Mn$ ) hollow spheres. (c) Magnetization curves of 400 nm  $M_{1-x}Fe_{2+x}O_4$  ( $M = Fe, Co, Mn$ ) hollow spheres measured at 4 K and (d) at 300 K.



**Figure 3.** (a) Suspensions of the 300 nm  $Fe_3O_4$  spheres in (from left to right) hexane, toluene, chloroform, methanol, acetonitrile, dimethyl sulfoxide, and water. (b) Hollow spheres originally dispersed in water (left) or hexane (right) to which hexane or water was added. (c) Thin film formed at water/hexane interface. (d) SEM image of the thin film formed by 300 nm hollow spheres. (e) Amplified SEM image and the relationship of the pore diameter  $r$  with the sphere diameter  $R$  calculated as  $r \approx 0.155R$ .

interference device (SQUID) magnetometer. Typical hysteresis loops have been observed for 400 nm  $M_{1-x}Fe_{2+x}O_4$  hybrid hollow spheres at 4 and 300 K (Figure 2c,d, respectively). It is seen that the spheres are ferromagnetic at 4 K but nearly superparamagnetic at 300 K, which is consistent with the small size of the primary ferrite nanoparticles composing the hollow spheres.

The products show excellent dispersibility and re-dispersibility in most of the common solvents. For instance, the as-synthesized powder of the 300 nm hollow spheres can be well dispersed in polar and nonpolar solvents (Figure 3a) and form stable colloids in ethanol, acetonitrile, dimethyl sulfoxide, and water. Under optimal conditions, the colloidal solution of 300 nm hollow spheres in ethanol remains stable for several weeks. Without shaking or sonication, the hollow spheres prefer to stay in the polar solvent (represented by water as shown in Figure 3b, left) or in the nonpolar solvent (represented by hexane as shown in Figure 3b, right), in which they are originally dispersed. This phenomenon demonstrates the amphiphilic nature of the magnetic spheres, and it is believed that the amphiphilic behavior of the spheres originates from the PEO-PPO-PEO block copolymer. Gentle shaking or sonication easily move the amphiphilic spheres to the water/hexane interface (Figure 3c), and a black thin film forms at the interface and expands

upward along the wall of the glass bottle. The thin film is formed by close-packed spheres as shown in Figure 3d. Because of the spherical shape of the spheres, the interstices between the spheres turn into an array of pores. Therefore, the magnetic hollow spheres can be excellent building blocks for selectively permeable capsules.<sup>20</sup> As the pore diameter can be tuned by varying the sphere diameter (Figure 3e), the permeability of the capsules may be adjusted conveniently.

These hollow amphiphilic magnetic spheres are proved to be of great potential use for controlled manipulation of liquid droplets of water in organic phase or droplets of oil in water phase.<sup>21</sup> With the help of the amphiphilic magnetic spheres, we can cut a droplet into smaller ones, combine two droplets together to form a large one, and deliver the droplets to certain targets under ambient magnetic field, as shown in the Supporting Information (Movies S1 and S2 and Figure S7).

In summary, we have successfully prepared hollow amphiphilic superparamagnetic ferrite submicrospheres via a facile one-step solvothermal route. This synthetic approach, using nontoxic and inexpensive reactants with the reaction yields higher than 90%, is easy to scale up for industrial need. It is promising that these biocompatible, amphiphilic, and superparamagnetic hollow spheres can be readily used in various realms of biomedicine and biotechnology.

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**Supporting Information Available:** Further SEM, TEM, and HRTEM images, particle size distribution histograms, FTIR, TG-DTA, ICP, magnetization data, experimental process in detail, and movies and images for manipulating droplets. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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