An improved way to prepare superparamagnetic magnetite-silica core-shell nanoparticles for possible biological application

Yongkang Sun, Lei Duan, Zhirui Guo, Yun Duan-Mu, Ming Ma, Lina Xu, Yu Zhang, Ning Gu*

Key Laboratory of Molecular and Biomolecular Electronics, Southeast University, Ministry of Education, Nanjing 210096, PR China

Received 26 April 2004; received in revised form 13 July 2004
Available online 4 August 2004

Abstract

This paper describes an improved approach for the coating of superparamagnetic magnetite nanoparticles with shells of amorphous silica. Magnetite (Fe₃O₄) nanoparticles are prepared by partial reduction coprecipitation method and modified by adding citric acid. The silica coating is conveniently controlled by a dilute silicate solution pretreatment and subsequent Stöber process directly in ethanol. Transmission electron microscopy, photon correlation spectroscopy and zeta-potential analysis results show that the attractions between the superparamagnetic nanoparticles are screened by the silica coating. With enough tetraethylorthosilicate added, the stable core-shell colloid was obtained. Vibrating sample magnetometer characterization shows that the magnetic core-shell structure is superparamagnetic.

© 2004 Published by Elsevier B.V.

PACS: 75.50.M; 75.70.C

Keywords: Magnetite; Nanoparticles; Core-shell; Superparamagnetic

1. Introduction

Magnetic nanoparticles of iron oxide provide attractive possibilities in biomedical applications, such as cell labeling and separation, magnetic resonance imaging (MRI), targeted drug delivery and magnetic ferrofluids hyperthermia (MFH) [1,2]. These applications require magnetic nanoparticles to be well-dispersed in liquid media, chemically stable and uniform in size. Due to the magnetic dipolar attraction, unmodified magnetite nanoparticles incline to aggregate into clusters and inhibit the advantage of the specific properties by...
single-domain. The aggregation associated with magnetite nanoparticles can be avoided by creating an electrostatic double layer [3], using a surfactant steric stabilizer [4], or by shifting the isoelectric point with citric acid and silica coating [5,6]. Usually an inert silica coating on the surface of magnetite nanoparticles prevents their aggregation in liquid and improves the chemical stability. At the same time, the silanol surfaces can be modified with various coupling agents to covalently attach specific bioligands to the surfaces of the magnetic nanoparticles [7,8].

Two different approaches have been used to generate a silica coating on magnetite nanoparticles. The first method is based on microemulsion synthesis, in which micelles or inverse micelles are used as mini-reactor to control the silica coating on the magnetic nanoparticles [9,10]. This method requires tedious steps to separate the magnetic nanoparticles from the surfactants in the microemulsion system. The other method relies on the well-known Stöber process [11], which comprises the hydrolysis and the ploycondensation of tetraethoxysilane under alkaline conditions in ethanol. This method can be directly used to coat SiO2 on clay minerals [12], hematite [13], zirconia and titania [14] due to significant chemical affinity of these materials. Coupling agents (mercaptosilane, or aminosilane) or specific surfactants (PVP) modification turns a broad of nanocrystals from vitrophobic into vitrophilic [15–19]. Water glass also can be used to enhance the silica coating, but it contains multistep processes [20].

In this paper an improved way to coat magnetite nanoparticles with silica will be presented. First, stable ferrofluids were obtained by modifying the magnetite surface with citric acid. Then the ferrofluids were transferred into ethanol. After this, water glass treatment was carried out by directly adding a critical volume of silicate solution into the ethanol. Finally the silica coating was formed by Stöber process.

2. Experimental

All chemicals were of analytical reagents obtained in China and were used freshly opened. Deionized water (18.2 MΩ cm−1, MilliQ) was used in the reactions and double distilled water was used to clean the glassware.

Magnetite nanoparticles were synthesized according to a procedure proposed by Qu et al. [21]. The concentration of Fe3O4 was adjusted to 2 mg ml−1 and the pH was adjusted to 3.0 by HCl (0.1 mol l−1). Citric acid (5% molar ratio of Fe) was added to the suspension under magnetic stirring. After 4 h the solution was washed with water by magnetic decantation 3 times and adjusted to the original volume.

Then 2 ml of the magnetite solution was ultrasonically dispersed in absolute ethanol, and 120 μl sodium-silicate solution (Na2O·SiO2, 0.22 wt% SiO2) was added to the ethanol under vigorous mechanical stirring. After four hours, 4 ml water, 1.4 ml NH3·H2O (27 wt% NH3) and various volume of tetraethylorthosilicate (TEOS) (5, 20, 50, 250 μl, respectively) were consecutively added to the reaction mixture. The hydrolysis of TEOS was carried out under mechanical stirring for 12 h at ambient temperature. The final product was obtained by magnetic separation and washed with water by magnetic decantation 4 times.

The citric acid modified magnetic nanoparticles and silica-coated nanoparticles were characterized by transmission electronic microscopy (TEM, JEOL, JEM-2000EX, 120 kV). Powder X-ray diffraction (XRD, Rigaku, D/Max-RA, Cu Kα) and electronic diffraction (ED) were used to determine the crystal structure of the pristine magnetic nanoparticles. A Beckman-Coulter Delsa 440SX apparatus was used for the zeta potential analyses of particles at pH 7.0. Temperature was fixed at 25°C and the applied electric field was 20 V cm−1. The hydrodynamic mean diameter measurements of the magnetic particles were carried out using Beckman-Coulter N4-plus Submicron Particle Size Analyzer. The scattered light was measured at 90° from the incident beam and temperature was fixed at 20°C and pH of the solution was tuned to 7.0. The hysteresis loops of bare magnetite nanoparticles and those coated with silica (50 μl TEOS) were measured by a vibration sample magnetometer (VSM, Lakeshore, Model 7300).
3. Results and discussion

X-ray diffraction (XRD) and electron diffraction (ED) were used to determine the crystal structure of the magnetic nanoparticles obtained by reduction coprecipitation method, which are shown in Figs. 1 and 2(A). There are many different possible iron oxide structures such as magnetite (Fe$_3$O$_4$), hematite (α-Fe$_2$O$_3$), maghemite (γ-Fe$_2$O$_3$), or ferric hydroxide (β-FeOOH) [22]. The d spacings calculated from the patterns are close to those of magnetite and maghemite (Table 1), both of which are inverse spinel structures. Thus the magnetic nanoparticles are close to magnetite. The magnetite particles are approximately spherical and the mean size was about 7.6 nm according to the TEM image. This agrees well with the mean diameter (7.1 nm) calculated from the XRD pattern using Scherrer formula, which is usually smaller than that of the TEM.

Usually, stable ionic ferrofluids can be obtained by surface modification with citric acid [23], and the mechanism is well illustrated [24]. Based on the stable ferrofluids, magnetite-silica core-shell structures may be developed by TEOS hydrolysis on magnetite nanoparticles. Although a first sodium silicate solution treatment in water can enhance the silica coating in ethanol, dialysis will be carried out to remove the surplus silicate [4]. In this experiment, we directly pretreated the magnetite nanoparticles with thin sodium silicate solution in ethanol instead of water. Due to the low solubility in ethanol (5 x 10$^{-4}$ wt% SiO$_2$) [25], the silicate solution tended to precipitate and a sudden turbidity appeared when adding excess sodium silicate. TEOS precursor condensed on the small nuclei and the silica coating on magnetite nanoparticles was inhibited. However with less or without sodium silicate, irregular clusters of magnetite nanoparticles were coated with silica. Hence, the appropriate amount of sodium silicate solution added in the ethanol was a prerequisite. In this experiment, 120 μl dilute silicate solution (10 times of the solubility in ethanol) was added into the ethanol to enhance the vitrophilicity of magnetite nanoparticles modified with citric acid.

Due to the magnetic dipole attractions, magnetite nanoparticles tend to aggregate, as is shown in Fig. 2(A). Silica coating stabilizes the magnetite nanoparticles in two different ways. One is by sheltering the magnetic dipole interaction through

![Fig. 1. XRD patterns of the magnetite nanoparticles prepared by reduction coprecipitation.](image)

![Fig. 2. (A) TEM and ED photography of the magnetite nanoparticles prepared by reduction coprecipitation method and modified by citric acid, (B, C, D, E) TEM images of the magnetite nanoparticles coated with silica by 5, 20, 50, 250 μl TEOS precursor respectively, and (F) the low magnification view of E. Scale bar: 10 nm for A–E; 500 nm for F.](image)
the silica shell. The magnetic dipole attraction in a simplified head to tail configuration is proportional to the \(1/r^3\) (\(r\) the center distance of two dipoles)\[4\]. The attraction decreases quickly with the increase of thickness of silica shell. And the other is by bringing charges to the magnetic particles. The point of zero charge (PZC) of silica and magnetite are about 2.0 and 7.3 in water, respectively. In neutral biological media, the pristine magnetite nanoparticles are nearly free of charges. On the other hand, the silica nanoparticles are negatively charged. In Fig. 3, the \(\zeta\)-potential of magnetite nanoparticles changed from nearly zero (10 mV) to negative (−42.2 mV) through silica modification. And \(\zeta\)-potential of final core-shell with 250 \(\mu\)l TEOS precursor agrees well with that of pure silica (−40.5 mV). So the silica coating enhanced the coulomb repulsion of the magnetic nanoparticles. Thus the magnetic dipole interactions between the magnetic nanoparticles were greatly screened.

These two kinds of actions have been reflected by the morphology and the mean hydrodynamic diameter of the different magnetic nanoparticles. The typical magnetic core-shell structures prepared by this method with different volume of TEOS precursor are shown in Fig. 2(B–F), in which the sizes were 10.5, 30.2, 44.9 and 135 nm, respectively. The unmodified and those modified with little TEOS precursor (Fig. 2(A, B)) existed in general aggregation. When the thickness of the silica shell increased, the magnetic nanoparticles changed from aggregates to discrete ones (Fig. 2(D, E)). The intermediate form can be seen in Fig. 2(C). In discrepancy with the results by the TEM, the hydrodynamic diameter of the core-shell structures did not increase steadily with the amount of TEOS precursor. When the TEOS volume was up to 20 \(\mu\)l, the mean hydrodynamic diameters (pH = 7) and the polydispersity by photon correlation spectroscopy (PCS) decreased compared with those of bare magnetite nanoparticles, the modified with citric acid or with 5 \(\mu\)l TEOS (Fig. 4). The larger hydrodynamic diameters are due to the particle aggregations caused by the incompletely screened magnetic dipole interactions without or with less TEOS precursor. In contrary, those of relative smaller hydrodynamic sizes are the results of improved sheltering of magnetic interactions by silica coating.

The hysteresis loops of magnetite nanoparticles and magnetite-silica core-shell structures with 50 \(\mu\)l TEOS precursor are shown in Fig. 5. Both magnetic particles showed superparamagnetic character. The saturation magnetization of magnetite nanoparticles by reduction coprecipitation method was 46.3 emu/g, which agreed well with the reported value [26]. For the core-shell structure,

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>(R) (cm)</td>
<td>0.71</td>
<td>1.15</td>
<td>1.35</td>
<td>1.63</td>
<td>1.98</td>
<td>2.11</td>
<td>2.30</td>
</tr>
<tr>
<td>ED results-(d) (Å)</td>
<td>4.84</td>
<td>3.00</td>
<td>2.55</td>
<td>2.12</td>
<td>1.74</td>
<td>1.63</td>
<td>1.49</td>
</tr>
<tr>
<td>XRD results-(d) (Å)</td>
<td>4.78</td>
<td>2.95</td>
<td>2.53</td>
<td>2.09</td>
<td>1.71</td>
<td>1.61</td>
<td>1.48</td>
</tr>
<tr>
<td>Theory values-(d) (\text{Fe}_3\text{O}_4) (Å)</td>
<td>4.85</td>
<td>2.97</td>
<td>2.53</td>
<td>2.10</td>
<td>1.71</td>
<td>1.62</td>
<td>1.48</td>
</tr>
<tr>
<td>Theory values-(d) (\gamma)-(\text{Fe}_2\text{O}_3) (Å)</td>
<td>4.82</td>
<td>2.95</td>
<td>2.51</td>
<td>2.09</td>
<td>1.70</td>
<td>1.61</td>
<td>1.47</td>
</tr>
<tr>
<td>Crystalline plane (hkl)</td>
<td>(1 1 1)</td>
<td>(2 2 0)</td>
<td>(3 1 1)</td>
<td>(4 0 0)</td>
<td>(4 2 2)</td>
<td>(5 1 1)</td>
<td>(4 4 0)</td>
</tr>
</tbody>
</table>
it was 13.9 emu/g due to the mass proportion of the magnetite nanoparticles.

In conclusion, the magnetite nanoparticles modified with citric acid can be coated with silica by the so-called one step way through a direct sodium silicate pretreatment in ethanol. Thickness of the shell can be easily tuned by different volume of TEOS precursor, the same with the magnetic attraction. Thus the stable superparamagnetic core-shell structures in neutral condition may find application in biological use. And this method needs to be improved to get the strict tunable core-shell structure with a single magnetite nanoparticle core.

**Acknowledgement**

This work was supported by the High Technology Research Project of Jiangsu Province in China (BG2001006) and the National Natural Science Foundation of China (No. 60171005, 60121101, 60371037). We thank Mr Aiquan Xu of Southeast University for TEM characterization and Ms Wenqing Zhou of Nanjing University for VSM measurements.

**References**
