Encapsulation of nanosized magnetic iron oxide by polyacrylamide via inverse miniemulsion polymerization

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Received 8 August 2003; received in revised form 25 September 2003

Abstract

Polyacrylamide particles containing nanosized magnetic iron oxide were prepared via inverse miniemulsion polymerization in this paper. The particle size of magnetic polymeric particles is about 100 nm, and these particles are superparamagnetic. The relative parameters of the miniemulsion polymerization, such as the surfactant content, ultrasonicating time, \( \text{Fe}_3\text{O}_4 \) and \( N, N' \)-methylene bis acrylamide content, were studied in detail. The iron oxide nanoparticles were characterized by X-ray diffraction and transmission electron microscopy (TEM). The final magnetic polymeric particles were characterized by TEM, scanning electron microscopy, dynamic light scattering, magnetization analysis and thermogravimetric analysis.

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PACS: 75.50

Keywords: Nanosized iron oxide particle; Superparamagnetic; Inverse miniemulsion polymerization; Encapsulation; Polyacrylamide magnetic particle

1. Introduction

Due to the widespread applications of magnetic polymeric particles, especially in biological field, such as cell separation [1–5], site-specific drug delivery [6,7], tissue engineering [8] and nucleic acids concentration [9,10], more and more attentions have been paid to preparation of different kinds of magnetic polymeric particles in the past decades, and various strategies have been performed to producing magnetic polymeric particles.

Encapsulation of magnetic particles with preformed natural or synthetic polymers is the simple and classical method to prepare magnetic polymeric particles [11–13], but the particle size and shape prepared by this method are random. In order to control the shape and structure of the magnetic polymeric particles, Ugelstad et al. [14] developed an effective method through direct precipitation of iron salt inside the porous polystyrene particles. The development of emulsion polymerization, such as the conventional emulsion polymerization, soap-free emulsion polymerization, miniemulsion polymerization and microemulsion polymerization, was led to new synthesis methods [15–20]. The typical method based on emulsion polymerization is to suspend magnetic particles in the dispersed phase and then polymerize the monomer in the presence of the magnetic...
particles to form magnetic polymeric particles. Considering the mechanism of different emulsion polymerizations, the miniemulsion polymerization is very suitable for making magnetic polymeric particles. In miniemulsion polymerization, the monomer droplets with magnetic nanoparticles act as “nanoreactors”, the magnetic polymeric particles can be prepared in situ. Recently, Ramirez et al. [20] used a new three-step preparation route including two miniemulsion processes to encapsulate magnetic particles by polystyrene successfully. Wormuth [17] achieved 140–220 nm magnetic polymeric particles using monomers (2-hydroxyethylmethacrylate and methacrylic acid) and a diblock polymer emulsifier (poly(ethylene-co-butylene)-b-poly(ethylene oxide)), via inverse miniemulsion polymerization. In this paper, a one-step inverse miniemulsion polymerization was adopted to synthesize the magnetic polyacrylamide particles using small molecular emulsifier (Span 80), and these magnetic polymeric particles can be attracted easily by magnet.

2. Experimental

2.1. Materials

Acrylamide (Am) (Shanghai LuNiao Co.) was re-crystallized twice from chloroform and then vacuum dried. The cross-linking agent N, N'-methylene bis acrylamide (MBA) (Shanghai Chem Reagent Co.) was re-crystallized from acetone and vacuum dried. FeCl₂·4H₂O and FeCl₃·6H₂O (Merck), polymethacrylic acid (Henkel co.), cyclohexane (Shanghai FeiDa Trade Company), ammonia (Shanghai Chem. Reagent Co.) and Span 80 (Sigma Chemical Co.) were all used as supplied. Hydrophobic initiator 2,2'-azobis (isobutyronitrile) (AIBN) (Aldrich) was recrystallized from ethanol and vacuum dried. In this study, only distilled water was used.

2.2. Synthesis of hydrophilic magnetic nanoparticles

The hydrophilic magnetic nanoparticles were prepared according to the procedure as reported by Shen et al. [19]. In addition to Shen et al. recipe, a dispersant agent of polymethacrylic acid was adopted to stabilize the ion oxide nanoparticles during the coprecipitation of FeCl₂ and FeCl₃ by ammonia under N₂ atmosphere at 60°C. The dispersion was then heated to 90°C and held for 0.5h. The dispersion was then cooled to room temperature and the pH was adjusted to 4 with 3 M HCl. The magnetic nanoparticles were collected with the help of magnet and washed five times with distilled water to remove Cl⁻. Finally, the magnetic nanoparticles were redispersed in dilute ammonia for further use (solid content is about 20 wt%).

2.3. Synthesis of magnetic polymeric particles

A suitable amount of Am, MBA and magnetic fluid were mixed homogenously at first, and then was added to a Span 80 cyclohexane solution under stirring. After 1 h of stirring, the miniemulsion was prepared by ultrasonically in a Cole-Parner sonifier CP600. Before polymerization, the miniemulsion was purged with N₂ for 30 min. Then the reaction system was heated to 65°C and the initiator (AIBN) was added. This reaction is very quick and finishes in several minutes. To ensure full conversion of the monomer, the reaction mixture was stirred at 65°C for 2 h. After the polymerization, the magnetic polymeric particles were washed by cyclohexane under the help of magnet for three times.

2.4. Measurements

2.4.1. X-ray diffraction analysis

A crystallographic study of the iron oxide powder was performed on a rotating anode X-ray diffractometer (Rigaku, Japan) using Cu Kα radiation. The X-ray diffraction (XRD) graphics were compared to the ASTM XRD graphics in order to deduce the crystal structure of the product.

2.4.2. Vibrating-sample magnetometer analysis

A vibrating-sample magnetometer (VSM, EG&G Princeton Applied Research Vibrating Sample Magnetometer, Model 155) was used to study the magnetic properties of hydrophilic
magnetic nanoparticles and magnetic polymeric particles at room temperature.

2.4.3. Transmission electron microscopy analysis
Transmission electron microscopy (TEM) images were obtained using a Hitachi HU-11B TEM operating at 250 kV. The sample was prepared as follows: A drop of very dilute magnetic dispersion was mounted on carbon-coated copper grid and dried at room temperature.

2.4.4. Scanning electron microscopy analysis
Scanning electron microscopy (SEM) was performed using a Philips XL30 SEM at an accelerating voltage of 27 kV. Samples were mounted on a small piece of glass substrate and sputter-coated with gold to minimize charging.

2.4.5. Thermogravimetric analysis
The content of Fe$_3$O$_4$ in hydrophilic magnetic nanoparticles or magnetic polymeric particles was measured by thermogravimetric analysis (TGA). About 5 mg sample was placed into platinum crucible with increasing temperature (10°C/min) in a controlled, flowing air atmosphere, and heated from 25°C to 600°C. In air, Fe$_3$O$_4$ was converted to Fe$_2$O$_3$ at about 200–300°C. The content of Fe$_3$O$_4$ was achieved relative to the content of Fe$_2$O$_3$ in sample.

2.4.6. Dynamic light scattering analysis
The size and size distribution of magnetic polymeric particles dispersed in cyclohexane were measured by dynamic light scattering analysis (DLS, Malvern 4700). Before measurement, the prepared magnetic polymeric latexes were highly diluted and filtered through a 0.45 μm filter to remove impurities, then the sample was charged into a thermostated scattering cell at 25°C.

3. Results and discussion

3.1. Magnetic particles modified with hydrophilic polymer
Magnetic nanoparticles, which have a large ratio of surface to volume, tend to agglomerate in order to reduce their surface energy. Therefore, one of the main problems in producing stable magnetic fluid is to prevent the agglomeration during the synthesis and coating process. The double surfactant layers were usually used for stabilization of magnetic particles [21]. The first layer surfactant attached to magnetic particles by hydrophilic group and the second layer helped to disperse in aqueous carrier liquid by its hydrophilic group. A basic weakness in this design is its dependence on van der Waals forces between the two layers, and the secondary layer is very easy to be removed by polar organic solvents such as acetone. In this work, we improved the stability of magnetic fluid by replacing the double surfactants with polymethylacrylic acid. The modified magnetic iron oxide nanoparticles could be redispersed into dilute ammonia easily and it was very stable under magnetic fluid. As there are several different structures of ironoxide, such as magnetite (Fe$_3$O$_4$), hematite (α-Fe$_2$O$_3$) and maghemite (γ-Fe$_2$O$_3$), etc. [22], excess ammonia was added to an aqueous mixture of ferric and ferrous salts and the precipitation temperature was kept at 90°C to ensure the synthesis of Fe$_3$O$_4$.

3.1.1. XRD analysis
In order to obtain the structure information of the product, the crystallographic structure of magnetic particles was analyzed by X-ray powder diffraction (XRD) (Fig. 1). The XRD graphics of the magnetic particles is similar to the ASTM XRD graphics of Fe$_3$O$_4$. The detail information was listed in Table 1. XRD results show that the iron oxide particles are composed of magnetite (Fe$_3$O$_4$). In our synthetic process, the precipitation temperature of 90°C and the excess amount of ammonia, ensure the formation of Fe$_3$O$_4$ over Fe$_2$O$_3$ [23,24].

3.1.2. TEM analysis
The sizes and size distributions of the magnetic particles were characterized by TEM. Fig. 2 shows that the Fe$_3$O$_4$ particles are somewhat irregularly shaped from oval to sphere. The particle size was determined to be around 10 nm, which is a common value for monodomains of
superparamagnetic iron oxide nanoparticles as reported by Shinkai et al. [25].

3.1. Magnetic properties

The magnetic particles were analyzed by VSM. Fig. 3 shows a typical magnetization variation ($M$) versus the applied magnetic field ($H$). The saturation magnetization of the synthetic magnetic particles was found to be equal to 61 emu/g at 300 K. Since only 90 wt% $\text{Fe}_3\text{O}_4$ in the hydrophilic particles as determined by TGA, the saturation magnetization of the pure magnetic particles is 68 emu/g, similar to the results reported in literature [18,26]. In addition, the magnetization decreases from the plateau value and reaches zero (i.e. no remanence effect) when the magnetic field intensity decreases. The behavior shows that the iron oxide particles correspond to a single crystal domain exhibiting only on orientation of the magnetic moment and magnetite in structure.

3.2. Encapsulation of nanosized magnetic iron oxide

3.2.1. Particle size and size distribution of magnetic polymeric particles

A series of magnetic polymeric particles were prepared by miniemulsion polymerization. The results were listed in Table 2. On increasing the

<table>
<thead>
<tr>
<th>2θ (exp.)</th>
<th>$d$ (exp.)</th>
<th>$d$ (Fe$_3$O$_4$)</th>
</tr>
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<tr>
<td>18.320</td>
<td>4.839</td>
<td>4.852</td>
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<td>30.260</td>
<td>2.951</td>
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<td>2.094</td>
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<td>62.760</td>
<td>1.479</td>
<td>1.484</td>
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</table>

Table 1: Summary data of experimental $d$ (Å) spacings from X-ray patterns ($d$ (exp.)) and from ASTM data cards for iron oxide ($d$ (Fe$_3$O$_4$)).

Fig. 1. XRD spectrum of the synthesized magnetite.

Fig. 2. TEM image of magnetic iron oxide nanoparticles.

Fig. 3. Magnetization vs. applied magnetic field for iron oxide nanoparticles modified with PMAA at 300 K.
amount of Span 80 from 0.25 to 0.75 g as shown in Table 2, the particle size of the magnetic microspheres decreased from 109 to 81 nm. At the same time, we also noticed the residue in the system decreased sharply with the increase of emulsifier, similar to that reported by Landfester et al. [27]. This observation indicates that the amount of Span 80 in this polymerization system has significant effect on the particle size and formation of stable latex. In Table 2, stable miniemulsion can be achieved with 0.75 g of Span 80.

When the sonifier is used to form the miniemulsion, the ultrasound waves can break up the monomer droplets. The drop size decreases with ultrasonicating time which means the particles of latex will follow this trend. On increasing in the ultrasonicating time from 4 to 16 min, the particle size of the magnetic polymer microspheres decrease from 136 nm (ML4) to 67 nm (ML7).

Table 2 also shows the effect of the ferrofluid content on the particle diameter. An increase in the ferrofluid content in the polymerization system reduced the particle size of the magnetic polymer microspheres, which means the amount of Fe₃O₄ has also a great influence on the particle size. This is because during the fusion/fission process in ultrasonication, the droplets favored to fission than fusion with the increase of the amount of Fe₃O₄.

To study the effect of the MBA concentration on the final particle size of the composite miniemulsion, different MBA amounts were used in the recipe. DLS analysis in Table 2 showed that the particle size of magnetic polymeric latex (ML6, ML11, ML12 and ML13) fluctuated around 80 nm, this means that the amount of MBA in this polymerization system did not have much effect on the particle size.

Fig. 4a shows a typical size distribution profile of sample ML11. The $z$-average particle size of the polymeric magnetic particles was 81 nm. DLS studies showed that the microspheres obtained had values ranging from 40 to 170 nm. Phase inversion method was applied to change sample ML11 from W/O latex to O/W dispersion. Fig. 4b shows particle size distribution profile in aqueous solution. The $z$-average particle (200 nm) is much larger than that before phase inversion, because the particles in aqueous phase had been swollen.

### Table 2

The influence of varying synthesis parameters on the particle size of magnetic polymeric latex

<table>
<thead>
<tr>
<th>Code</th>
<th>Span 80 (g)</th>
<th>Ultrasonicating time (min)</th>
<th>Fe₃O₄ dispersion (g)</th>
<th>Am (g)</th>
<th>MBA (g)</th>
<th>$D_{h}^{b}$ (nm)</th>
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<tbody>
<tr>
<td>ML1</td>
<td>0.250</td>
<td>10</td>
<td>1.40</td>
<td>2.25</td>
<td>0</td>
<td>109</td>
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<tr>
<td>ML2</td>
<td>0.500</td>
<td>10</td>
<td>1.40</td>
<td>2.25</td>
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<tr>
<td>ML3</td>
<td>0.750</td>
<td>10</td>
<td>1.40</td>
<td>2.25</td>
<td>0</td>
<td>81</td>
</tr>
<tr>
<td>ML4</td>
<td>0.750</td>
<td>4</td>
<td>1.40</td>
<td>2.25</td>
<td>0</td>
<td>136</td>
</tr>
<tr>
<td>ML5</td>
<td>0.750</td>
<td>8</td>
<td>1.40</td>
<td>2.25</td>
<td>0</td>
<td>104</td>
</tr>
<tr>
<td>ML6</td>
<td>0.750</td>
<td>10</td>
<td>1.40</td>
<td>2.25</td>
<td>0</td>
<td>84</td>
</tr>
<tr>
<td>ML7</td>
<td>0.750</td>
<td>16</td>
<td>1.40</td>
<td>2.25</td>
<td>0</td>
<td>67</td>
</tr>
<tr>
<td>ML8</td>
<td>0.750</td>
<td>10</td>
<td>0.250</td>
<td>2.25</td>
<td>0</td>
<td>160</td>
</tr>
<tr>
<td>ML9</td>
<td>0.750</td>
<td>10</td>
<td>0.950</td>
<td>2.25</td>
<td>0</td>
<td>116</td>
</tr>
<tr>
<td>ML10</td>
<td>0.750</td>
<td>10</td>
<td>1.85</td>
<td>2.25</td>
<td>0</td>
<td>67</td>
</tr>
<tr>
<td>ML11</td>
<td>0.750</td>
<td>10</td>
<td>1.40</td>
<td>2.14</td>
<td>0.11</td>
<td>81</td>
</tr>
<tr>
<td>ML12</td>
<td>0.750</td>
<td>10</td>
<td>1.40</td>
<td>2.04</td>
<td>0.21</td>
<td>82</td>
</tr>
<tr>
<td>ML13</td>
<td>0.750</td>
<td>10</td>
<td>1.40</td>
<td>1.95</td>
<td>0.30</td>
<td>81</td>
</tr>
</tbody>
</table>

*a* Cyclohexane: 24.0 g, (Fe₃O₄ dispersion (20 wt%)+H₂O): 3.0 g, AIBN: 75 mg.

*b* The $z$-average particle size of magnetic polymeric latex without further treatment.

3.2.2. Morphology of magnetic polymeric particles

As described in the Section 2, the PMAA coated magnetic iron oxide nanoparticles dispersed in monomers were dispersed into cyclohexane and polymerized. In our study, the latex particles that do not contain magnetic iron oxide nanoparticles are formed simultaneously, but they can be easily separated from the magnetic polymeric particles.
by magnetic field. A representative transmission electron image of the magnetic polymeric particles obtained from ML9 (Table 2) is shown in Fig. 5. In Fig. 5, a large number of nanosized iron oxide can be observed in one magnetic polymeric particle, and the iron oxide particles mainly located inside of the polymer particles. In order to further confirm the iron oxide location, SEM image was obtained of ML9 (Fig. 6), we can clearly see that the surface of the magnetic polymeric particles is very smooth and this hints that the iron oxide nanoparticles were mainly located inside of the polymeric particles instead of on the surface of the particles. The size of these magnetic polymeric particles was about 50–200 nm which was similar to the result (116 nm) of DLS in Table 2.
3.2.3. Magnetic properties of magnetic polymeric particles

The magnetic properties of magnetic polymeric particles were studied using a vibrating sample magnetometer. Fig. 7 shows the magnetization curve of the sample ML9. Obvious superparamagnetic properties can be observed for the magnetic polymeric particles, no remanence was observed when the magnetic field is removed. The saturation magnetizations obtained for ML9 is 8.2 emu/g. Consequently, the magnetite concentration in polymer particles is 13% (wt/wt), which is in agreement with the magnetite concentration of TGA result (Fig. 8). In initial recipes the magnetite concentration is only 7.8 wt%, which is less than above results. This means that some blank microspheres formed in the polymerization and had been removed by purification.

4. Conclusion

Hydrophilic magnetic nanoparticles with excellent stability were achieved by adding poly(methacrylic acid) during the preparation of magnetic iron oxide. Such particles dispersed readily in dilute ammonia and formed a stable magnetic fluid. In an inverse system, hydrophilic monomer was dissolved in above magnetic fluid and the inverse miniemulsion polymerization was conducted successfully. The experimental results demonstrate that the inverse miniemulsion polymerization is an effective way to synthesize magnetic polymeric particles. The magnetic polymeric particles are spherical and their size range from 60 to 160 nm depending on the reaction parameters. The nanosized iron oxide particles can be well encapsulated in polyacrylamide particles and the magnetic polymeric particles are superparamagnetic. These crosslinked magnetic polyacrylamide particles can be dispersed in water easily and can be recommended as a candidate for the biological application.

Acknowledgements

This work was supported by the National Science Foundation of China (Grant No. 50173005).

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