Growth Condition Dependent Magnetic Properties of CoFe$_2$O$_4$ Nanoparticles and Their Highly T$_2$ Weighted Contrast in MRI

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In this work, we controlled the magnetic properties and water-solubility of CoFe$_2$O$_4$ nanoparticles by adjusting the reaction conditions during the preparation process. The growth condition-dependent crystalline, microstructure and therefore their magnetic properties were investigated in detail. It is found that the crystalline and the size of the nanoparticle become larger with the increasing of both the reaction temperature and reaction time. Consequently, the saturation magnetization (Ms) of our products was highly improved. Specifically, the typical sample prepared at 180 °C for 2 h, which has a higher Ms and good solubility in water was chosen as an alternative agent in magnetic resonance imaging. The results show that it is an effective T$_2$ weighted MRI contrast agent.

Keywords: cobalt ferrite, nanoparticles, solvothermal method, magnetic resonance imaging

1. Introduction

Magnetic nanoparticles (such as Fe$_3$O$_4$, CoFe$_2$O$_4$, NiFe$_2$O$_4$ and γ-Fe$_2$O$_3$) have been investigated widely in recent years owing to their unique properties and a great potential application in magnetic resonance imaging (MRI) [1-4], hyperthermia [5, 6], drug delivery [7, 8], catalyst [9, 10] and Li ion battery [11, 12] etc.. Specially, they were extensively studied as a contrast agent in MRI. For a good contrast agents in MRI, magnetic nanoparticles must show a good chemical, physical and biological stability, moderate saturation magnetization, and high magneto crystalline anisotropy [13-21]. On the basis of this point, CoFe$_2$O$_4$ is an ideal candidate among all of the magnetic nanoparticles and thus attracts a wide research interest. For example, Cai et al. synthesized three-dimensional hierarchical CoFe$_2$O$_4$ porous microspheres through a template-free solvothermal route [22], which was used as a drug delivery carrier. Wang et al. [23] prepared mono-dispersed CoFe$_2$O$_4$ nanoparticles through a sonochemical route. The magnetic properties of CoFe$_2$O$_4$ nanoparticles were also investigated in detail. The in vitro cytotoxicity tests confirmed that the prepared CoFe$_2$O$_4$ nanoparticles had a negligible cytotoxicity and hold potential applications in biomedical fields. A lot of reports have confirmed that all of the size, morphology and magnetic properties of CoFe$_2$O$_4$ nanoparticles are growth condition-dependent [24-26]. Amirabadizadeh et al. reported that CoFe$_2$O$_4$ magnetic nanoparticles were prepared by a co-precipitation method [27]. The reaction time has an influence on their structures, morphologies and magnetic properties. Prabhakaran et al. [28] also demonstrated that the reaction temperature during their co-precipitation process has a great influence on their structures and magnetic behaviors. However, in spite of the significant progress for the magnetic properties of CoFe$_2$O$_4$ nanoparticles have been obtained, many technical restrictions associated with the colloidal stability and magnetic properties for practical applications are still a critical problem that should be overcome.

In this paper, we investigated the relationship between the growth conditions and the magnetic property of CoFe$_2$O$_4$ nanostructures. The growth-condition dependent structure, crystallinity and magnetic properties were studied in detail. It is found that the saturation Ms was changed greatly by varying the growth conditions. Among the products that we prepared under different condition, a sample with a moderate Ms and an excellent water solubility is obtained (prepared condition: keep the temperature at 180 °C for 2 h), which can be employed as a better contrast...
agent in MRI. We believed that the CoFe$_2$O$_4$ nanoparticles we prepared can be explored in the potential application in a more accurate detection and diagnosis.

2. Materials and Methods

2.1. Preparation of CoFe$_2$O$_4$ nanoparticles

All the chemicals used in the experiments were analytical grade without further purification.

In a typical synthesis, 0.6 g of PVP, 1 mmol of Co(NO$_3$)$_2$·6H$_2$O and 2 mmol of Fe(NO$_3$)$_3$·9H$_2$O were dissolved into 25 mL of ethylene glycol at magnetic stirring, followed by the addition of 5 mL of hydrazine hydrate (85 %) into the above orange solution to make a light brown homogeneous slurry. The slurry was transferred into a 50 mL of Teflon autoclave and heated at different reaction conditions. Six samples were prepared, namely CF1 to CF6, and summarized in Table 1. The CoFe$_2$O$_4$ nanoparticles was obtained by magnetic separation and washed several times with DI water and absolute ethanol after the autoclave was cooled down to room temperature. The collected samples were dried at 60 °C for 12 h for further use and characterization. The schematic diagram for solvothermal synthesis of the nanoparticles was illustrated in Figure 1.

2.2. Characterizations

The phase structures of the products were characterized by X-ray powder diffraction spectrometer on an XRD-6000 (Shimadzu Instruments, Japan). The morphology and microstructures of the as-prepared CoFe$_2$O$_4$ nanoparticles were obtained by scanning electron microscope (SEM, S-4800, Hitachi, Japan) with a 5 kV accelerating voltage and transmission electron microscope (TEM, Tecnai G20, FEI, Holland) with a 200 kV accelerating voltage. The X-ray photoelectron spectra (XPS) were collected on an ESCALab MKII X-ray photoelectron spectrometer, using monochromatized Mg Kα X-ray as the excitation source. Infrared spectra (IR) were recorded on NICOLET 5700 infrared spectrophotometer. The magnetic properties of the samples were measured by superconducting quantum interference device magnetometer (MPMS XL-7, Quantum Design, United states of America).

2.3. In vitro MRI experiments

The MRI tests were carried out on a MesoMR21-60H-I MRI scanner system at an ambient temperature. A certain amount of superparamagnetic CoFe$_2$O$_4$ nanoparticles was dispersed in distilled water to make aqueous solution with different concentration ranging from 0.005 to 0.156 mg mL$^{-1}$.

3. Results and Discussion

The phase of the samples were characterized by X-ray diffraction patterns. It is noted that the growth conditions will affect the morphology and thus the magnetic properties of the prepared samples [29-32]. In order to investigate this effect, experiment under different growth conditions were executed. The XRD patterns of the CoFe$_2$O$_4$ samples prepared at different growth conditions was shown in Fig. 2. It can be seen that all the diffraction peaks are well indexed to be the cubic structure of CoFe$_2$O$_4$ (JCPDS No. 22-1086). No any impurity was detected, which demonstrates that the prepared samples are high purity and crystallinity. In addition, the intensity of the diffraction peaks increased with the increasing of the reaction time, which indicates that the crystallinity of the prepared samples is also improved. The reaction temperature is another important factor which affects the structure, morphology and properties of the nanoparticles [28]. The XRD pattern of the samples prepared at different

### Table 1. Experimental conditions of different CoFe$_2$O$_4$ samples.

<table>
<thead>
<tr>
<th>Samples No.</th>
<th>Temperature/°C</th>
<th>Time/h</th>
<th>Morphology</th>
</tr>
</thead>
<tbody>
<tr>
<td>CF1</td>
<td>180</td>
<td>2</td>
<td>Nanoparticles</td>
</tr>
<tr>
<td>CF2</td>
<td>180</td>
<td>6</td>
<td>Nanoparticles</td>
</tr>
<tr>
<td>CF3</td>
<td>180</td>
<td>12</td>
<td>Nanoparticles</td>
</tr>
<tr>
<td>CF4</td>
<td>180</td>
<td>24</td>
<td>Nanoparticles</td>
</tr>
<tr>
<td>CF5</td>
<td>120</td>
<td>2</td>
<td>Nanoparticles</td>
</tr>
<tr>
<td>CF6</td>
<td>150</td>
<td>2</td>
<td>Nanoparticles</td>
</tr>
</tbody>
</table>

Fig. 1. (Color online) Schematic of the solvothermal process that was utilized in the preparation of CoFe$_2$O$_4$ nanoparticles.
temperatures while the reaction time was fixed at 2 h are well assigned to the cubic structure of CoFe$_2$O$_4$ (JCPDS No. 22-1086). The intensity of the diffraction peaks are increasing, while the width of the diffraction peaks is decreasing as the raise of the reaction temperature. These results confirmed that the size was increased and crystallinity was highly improved.

The morphologies of the CoFe$_2$O$_4$ nanoparticles prepared at different growth conditions were obtained using TEM imaging technique (Fig. 3). It can be seen that the samples show a sphere shape with an average diameter of about 20 nm. From Fig. 3, it can be seen that the size of the samples increased slightly with increasing of the reaction temperature and reaction time. The nanoparticles tend to aggregate due to their ultrasmall sizes and the interaction

![Fig. 2.](Image) (Color online) XRD patterns of the samples growth under different conditions.

![Fig. 3.](Image) TEM images of CoFe$_2$O$_4$ samples: (a): CF5, (b): CF6, (c): CF1, (d): CF2, (e): CF3, (f): CF4 (The insert in (c) are the HRTEM image of a single nanoparticle and the corresponding SAED).

![Fig. 4.](Image) (a) XPS spectrums of CF1 sample, (b, c) high resolution XPS spectrum of Co2p and Fe2p and (d) FT-IR spectra of CF1 and pure PVP.
of magnetic force between different nanoparticles. In Fig. 3(c), the pattern inserted shows the HRTEM image of the CF1 sample, the crystal lattice was seen clearly, which confirmed that the samples have a good crystallinity. The lattice spacing was measured to be 0.30 nm, which corresponds to the value of (220) crystalline plane of CoFe$_2$O$_4$. Additionally, the SAED pattern demonstrates that the prepared CoFe$_2$O$_4$ nanoparticles were polycrystalline of cubic spinel crystal structure (the inserted in Fig. 3(c)). There were six diffraction rings from the center, which corresponding to (220), (311), (222), (400), (422), (511), (440) and (533) lattice planes of crystalline CoFe$_2$O$_4$, respectively.

The elemental composition and status of the CoFe$_2$O$_4$ nanoparticles were characterized by XPS, as shown in Fig. 4. The general profile of the CoFe$_2$O$_4$ nanoparticles indicate that the product are mainly composed of Co, Fe, O and C. The high resolution XPS spectra of Co and Fe were shown in Fig. 4(b)-(c). In the Co2p spectrum, there are four peaks centered at 780.1, 786.2, 795.7 and 802.5 eV, which could be assigned to Co2p3/2 and Co2p1/2, respectively (Fig. 4(b)) [22, 23, 33]. The spectrum of Fe2p was exhibited in Fig. 4(c). There are two main peaks located at 710.4 and 724.0 eV, which could be indexed to Fe2p3/2 and Fe2p1/2, respectively. The results confirmed that the as-prepared sample was Fe$_2$O$_3$, which are consistent with the previous study that conducted by XRD characterization.

The bonding status of PVP on the surface of the prepared CoFe$_2$O$_4$ nanoparticles was checked using a wave-length-dependent transmittance spectrum obtained by Fourier transformed infrared spectrum. There are five absorption bands for the pure PVP spectrum centered at around 3480, 2956, 1670, 1425 and 1281 cm$^{-1}$, which correspond to OH stretching, CH$_2$ asymmetric stretching, C=O symmetric stretching, CH$_3$ scissoring, C-N symmetric stretching, respectively (Fig. 4(d)) [34]. Two characteristic peaks centered at about 3480 cm$^{-1}$ and 1670 cm$^{-1}$ respectively slightly shift to lower frequency in the spectra of PVP coated CoFe$_2$O$_4$ nanoparticles, because of the interaction between PVP and CoFe$_2$O$_4$ nanoparticles [23]. The sharp peak centered at 587 cm$^{-1}$ was assigned to Fe-O in the CoFe$_2$O$_4$ nanoparticles [35, 36]. The peak centered at 587 cm$^{-1}$ was absent in pure PVP spectrum. The results reveal that the PVP polymer was coated on the surface of CoFe$_2$O$_4$ nanoparticles.

To further investigated the applications of our finding in MRI imaging, we first studied the magnetic properties of the samples that were prepared at different growth conditions (Fig. 5). The hysteresis loops of the prepared samples were all typical “S” shape, which implies that they all have superparamagnetic properties. The saturation Ms, remnant magnetization (Mr) and coercivity (Hc) were summarized in Table 2. We can observe that the Ms, Mr and Hc of the samples increased with increasing solvothermal treatment duration. When the reaction time increased to 24 h, the saturation magnetization increased to 83.0 emu/g, which is nearly close to the value of pure bulk CoFe$_2$O$_4$ (94 emu/g) [18]. The decrease of Ms value may be caused by the existence of PVP, the small size of nanoparticles and the surface defect of nanoparticles [37]. When the reaction temperature evaluated from 120 to 180 °C, the Ms of the samples gradually increased from 43.6 to 58.5 emu/g, while the coercivity of the samples prepared at different temperature showed nearly zero Oe, respectively (Table 2). From the photo inserted in Figure 5, it is clearly to be seen that the obtained CoFe$_2$O$_4$ nanoparticles are absorbed to the wall when a magnet are put besides the wall of the vial. The suspension change into a nearly transparent solution, because of the interaction between PVP and CoFe$_2$O$_4$ nanoparticles [23]. The sharp peak centered at 587 cm$^{-1}$ was absent in pure PVP spectrum. The results reveal that the PVP polymer was coated on the surface of CoFe$_2$O$_4$ nanoparticles.

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<table>
<thead>
<tr>
<th>Sample No.</th>
<th>Ms (emu/g)</th>
<th>Mr (emu/g)</th>
<th>Hc (Oe)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CF1</td>
<td>58.5</td>
<td>3.9</td>
<td>45.5</td>
</tr>
<tr>
<td>CF2</td>
<td>66.0</td>
<td>12.4</td>
<td>359.6</td>
</tr>
<tr>
<td>CF3</td>
<td>72.3</td>
<td>11.2</td>
<td>350.1</td>
</tr>
<tr>
<td>CF4</td>
<td>83.0</td>
<td>13.7</td>
<td>365.8</td>
</tr>
<tr>
<td>CF5</td>
<td>43.6</td>
<td>2.2</td>
<td>39.2</td>
</tr>
<tr>
<td>CF6</td>
<td>50.1</td>
<td>3.1</td>
<td>42.6</td>
</tr>
</tbody>
</table>

Fig. 5. (Color online) M-H hysteresis loops of different samples (the insert illustrates the digital photo of the CoFe$_2$O$_4$ nanoparticles with and without an external magnetic field).
relatively low remnant magnetization, the samples may be stable when the external magnetic field was removed. These properties are necessary for a MRI contrast agent.

The stability of the colloid is important for a MRI contrast agent [38]. We therefore investigated the stability of different samples, as shown in Fig. 6. The samples were dispersed into DI water, and put in air for one month. It can be seen that the CF1 has the best stability (Fig. 6c).

Based on the above results, we chosen the CF1 samples.
to explore the MRI contrast effect in MesoMR21-60H-I scanner system at an ambient temperature. The relaxivity value of $r_1$ and $r_2$ was calculated to be 1.8462 and 90.047 mg mL$^{-1}$ s$^{-1}$ from the linearly plots in Fig. 7(a) and (b) respectively. The ratio of $r_2/r_1$ was 48.77, revealed that the as-prepared PVP coated CoFe$_2$O$_4$ nanoparticles may be a potential $T_2$-weighted contrast agent. From the color maps in Fig. 7(c), it is observed that the color of the maps changed from red to deep blue with the increase of the agent concentration. The results were in consistent with the observation of the grey maps as shown in Fig. 7(c). With increasing agent concentration, the color of grey maps changed from slight white to deep dark. It was confirmed that the PVP coated CoFe$_2$O$_4$ nanoparticles is a high $T_2$-weighted MRI agent.

4. Conclusions

In summary, CoFe$_2$O$_4$ magnetic nanoparticles coated with PVP were synthesized by a solvothermal route. A series of controlled experiments were carried out to investigate the influence of reaction time and temperature on the structure, morphology and magnetic properties of CoFe$_2$O$_4$ nanoparticles. The results demonstrated that the growth conditions had vital influences on their crystallinity and magnetic properties. The MRI experiments confirmed that the synthesized CoFe$_2$O$_4$ magnetic nanoparticles coated with PVP can enhance the MRI contrast effect and used as high efficient $T_2$ weighted contrast agent. This method can be used to synthesize other ferrites such as MnFe$_2$O$_4$, Fe$_3$O$_4$, NiFe$_2$O$_4$, and ZnFe$_2$O$_4$ etc.

Acknowledgements

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References

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