Preparation and properties of superparamagnetic nanoparticles with narrow size distribution and biocompatible

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Abstract

A chemical co-precipitation method capable of controlling the average size and size distribution of magnetic Fe_3O_4 nano-particles was developed. It was found that the homogeneous variation of the pH value in the solution plays a role in the size distribution of the synthesized Fe_3O_4 particles. In this work, we added urea to the ferrite solution, followed by heating the solution to decompose the urea before titrating a base solution into the ferrite solution. Thus, the variation in pH value in the solution can become uniform, and the uniformity in the particles size can be greatly enhanced. In addition, the average particle size is adjustable via control of the amount of urea decomposing at one time. To be biocompatible, dextran is selected as the surfactant for the Fe_3O_4 particles, because of its non-toxicity and high bio-affinity. The desired bio-probes can be coated on the dextran layer through adequate chemical reactions.
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1. Introduction

Nano-scale materials have brought about many great changes and new research opportunities in physics, chemistry, material science, biology and so on [1,2]. Magnetic nano-particles of single domain are of great interest to researchers because

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of some of their characteristics, such as super-paramagnetism, high field saturation, and extra anisotropy contributions. These characteristics give magnetic nano-particles real and potential applications in biomedicine field. For example, magnetic nano-particles are used as image contrast agents in MRI [3–5], as a magnetic labeling in immunoassay [6–8], for drug delivery [9], or for hyperthermia [10]. For the applications of magnetic nano-particles in biomedicine, the size, size distribution, shape, and surface conditions of the magnetic nano-particles allow the nano-particles to play important roles. Hence, research on the manipulation of the properties of nano-particles is not only important but also represents the most challenges.

At present, many methods have been developed to prepare magnetic Fe_3O_4 nanoparticles such as polyols [11], microemulsions [12], laser pyrolysis [13], sonochemical synthesis [14], and chemical co-precipitation [15–17], etc. Among these reported methods, the chemical co-precipitation may be the most promising one because of its simplicity and productivity. In the chemical co-precipitation procedure, the Fe_3O_4 magnetic nano-particles are formed at a pH of around 10 to 11. But, the pH value of the original ferrite solution containing Fe^{2+} and Fe^{3+} is around 1–2. Thus, base solutions are necessarily added to the ferrite solution. This is usually achieved by pouring or titrating a base solution of KOH, NaOH or NH_4OH into a ferrite solution. In this way, the reaction in the solution is not homogeneous. It is very difficult to control particle size and size distribution. This leads to a fatal disadvantage for further applications in biomedicine.

In this work, we improve the co-precipitation procedure, through which the average size and size distribution of Fe_3O_4 magnetite nano-particles can be easily controllable via the use of NH_4OH as well as urea to manipulate the pH of a ferrite solution homogeneously. In addition, because of its non-toxicity, hydrophilicity and high bio-affinity, dextran was selected as a surfactant on nano-particles here to obtain a water-based magnetic fluid. Many bio-probes can be further coated onto dextran through suitable chemical reactions to make the magnetic nano-particles

bio-compatible. The physical and magnetic properties of dextran-coated magnetic nano-particles are also investigated in this work, and the tunability in the average size of particles through adjustment of the preparation parameters is also discussed.

2. Experimental details

The chemicals of analytical grade and deionized water are used throughout the following preparation procedure. We dissolved a stoichiometric ratio 1:2 ferrous sulfate hepta-hydrate ($FeSO_4 \cdot 7H_2O$) and ferric chloride hexa-hydrate ($FeCl_3 \cdot 6H_2O$) in deionized water under vigorous stirring to prepare total concentration of 0.20-M ferrite solution as an iron source. Concentrated ammonia was then dissolved in an aqueous solution to form 3.5-M ammonium hydroxide (NH_4OH) as a base source. Dextran was dissolved in hot deionized water to form a coating solution.

A 50-ml ferrite solution was mixed with an equal volume of dextran aqueous, then appropriate amount of urea was added into the mixed solution. The mixture was heated gently up to 80–100°C in order to decompose the urea. Thus, the pH can be changed homogeneously all over the mixture. After that, during rigorous stirring, the mixture was titrated to have a pH of around 10–11 by adding drops of 3.5-M ammonium hydroxide at room temperature. It can be observed that the solution became black due to the formation of Fe_3O_4 particles. The black mixture was then heated at 60–70°C in a water bath for 30 min to coat the Fe_3O_4 particles with dextran. Aggregates were then removed by centrifugation in a low-speed centrifuge at 4000 rpm for 5 min. The excess unbound dextran was separated by gel filtration chromatography on Sephacryl-300, using 0.10-M sodium citrate at pH 5.0 as an eluent. The purified water-based magnetic fluid containing dextran-coated Fe_3O_4 nano-particles collected in the void volume had a concentration of about 10 mgFe/ml.

The crystalline of magnetic particles was analyzed by using powder X-ray diffraction (XRD) of a Siemens D-500 diffractometer using Cu-K$_\alpha$ radiation with a wavelength of 0.15418 nm. The magnetic-particle-size distribution was investigated

with Microtrac Nanotrac 150 based on dynamic laser scattering, in which the particle size was measured by detecting the Brownian motion of the particles through probing the Doppler frequency shift of a scattered light with respect to the incident light. It is noted that the diameter detected via dynamic laser scattering is hydrodynamic diameter. The magnetization properties of the magnetic fluid was examined by a vibration sample magnetometer (VSM) with an EG&G Model 4500.

3. Results and discussion

Fig. 1 shows the XRD pattern of the synthesized Fe_3O_4 particles. It is clear that only the phase of Fe_3O_4 is detectable. There is no other phase such as $Fe(OH)_3$ or Fe_2O_3, which are the usual co-products in a chemical co-precipitation procedure. The results shown in Fig. 1 reveal a high purity for the synthesized Fe_3O_4 magnetic particles. With the XRD pattern, the average core size of the particles can be evaluated from Scherrer equation [18]

$$L = \frac{0.94\lambda}{B(2\theta)\cos\theta},\tag{1}$$

where L is equivalent to the average core diameter of the particles, λ is the wavelength of the incident X-ray, $B(2\theta)$ denotes the full width in radian subtended by the half maximum intensity width of the powder peak, for instance (3 1 1), and θ correspo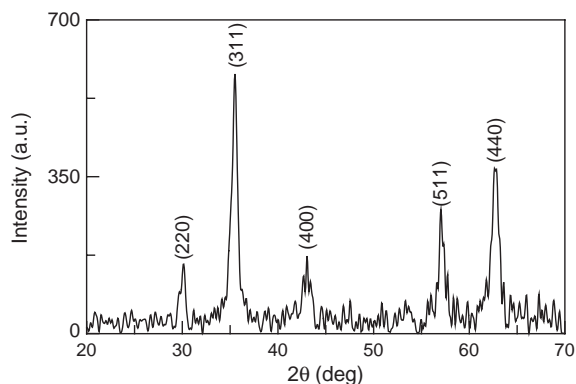nds to the angle of the (3 1 1) peak. For the (3 1 1) peak in the XRD pattern shown in Fig. 1, 2θ is observed as $35.52°$, and $B(2\theta)$ is $0.70°$. With λ being 0.15148 nm, L is obtained as 12.24 nm via Eq. (1). In order to investigate the size distribution of magnetic particles, a dynamic laser scattering (DLS) analysis system is used in this work. It is worth noting that the value for the particle diameter obtained from XRD pattern means the particle core size, where as the size detected using DLS system refers to a hydrodynamic diameter of particles.

According to DLS results, the ratio of the standard deviation to the average value of the diameter distribution of the Fe_3O_4 particles ranges from 0.2 to 0.25. A typical diameter distribution of the Fe_3O_4 particles is shown in Fig. 2. The standard deviation is 5.9 nm and the average is 25.3 nm for this diameter distribution. It is worth noting that the value of 0.2 to 0.25 for the ratio is much lower as compared to published reports through a conventional chemical co-precipitation procedure, in which the ratio is generally higher than 40% [5,17,19,20]. This gives the evidence that the size distribution of particles can be significantly narrowed with the addition of urea into the ferrite solution. The possible mechanism is discussed as follows.
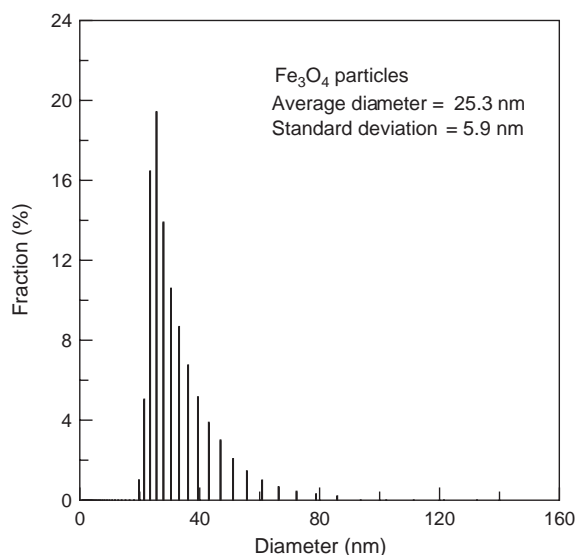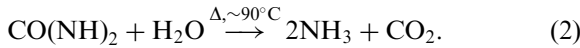
Fig. 1. $\theta{-}2\theta$ X-ray powder diffraction pattern of the synthesized magnetic particles. The indices are for the Fe_3O_4 phase.

Fig. 2. Distribution of the hydrodynamic diameters for the magnetic dextran-coated Fe_3O_4 particles in magnetic fluid.

As we know, urea is decomposed at around 80–90°C.

$$CO(NH)_2 + H_2O \xrightarrow{\Delta, \sim 90°C} 2NH_3 + CO_2. \quad (2)$$

In water, the NH_3 can generate hydroxyl OH^- to raise the pH value of the solution for particles formation.

$$NH_3 \cdot H_2O \rightarrow NH_4^+ + OH^-. \quad (3)$$
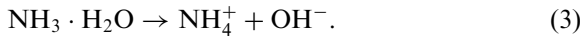
In case, urea was distributed homogeneously in the solution. OH^- was generated all over the solution when heated up to 80–90°C. This led to a uniform increase in the pH value of the solution, and a homogeneous environment was achieved for the formation of Fe_3O_4 particles as a concentrated NH_4OH solution was titrated. Therefore, a more uniform distribution was the result for the Fe_3O_4 particles size.

In addition to the reduction in the size distribution, we were able to control the decomposition of urea to obtain various average sizes of Fe_3O_4 particles. Fig. 3 plots the size distribution of Fe_3O_4 particles, where in the synthesis process more amount of urea is decomposed with respect to that of Fig. 2 via lasting the duration at 80–90°C. It was
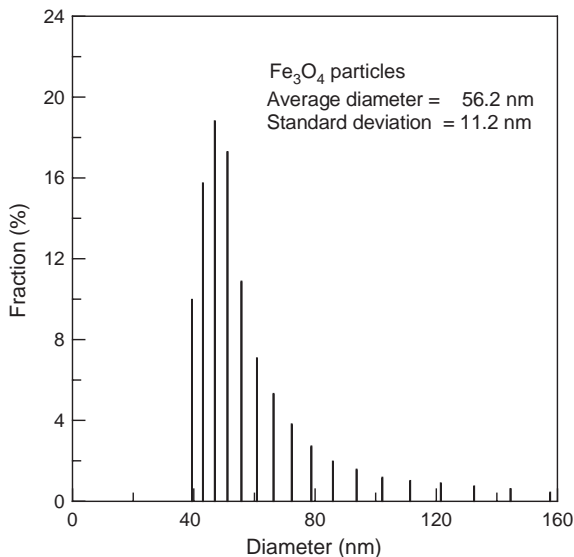

Fig. 3. Hydrodynamic diameter distribution of magnetic dextran-coated Fe_3O_4 particles in magnetic fluid. Here, more amount of urea is decomposed with respect to that of Fig. 2 via lasting the duration at 80–90 °C.
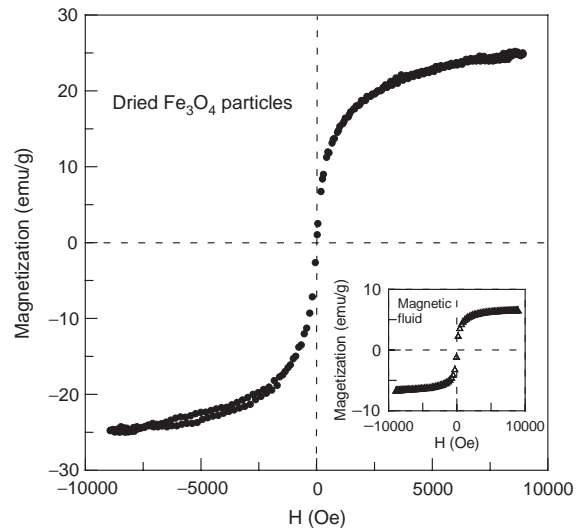

Fig. 4. Magnetization loop of the dextran-coated dried Fe_3O_4 particles. The inset shows a magnetization loop of magnetic fluid containing the Fe_3O_4 particles.

found that a larger average diameter ($= 52.6\,nm$) results. The corresponding standard deviation of the distribution in Fig. 3 is 11.2 nm. Thus, the ratio of the standard deviation to average diameter of particles is 0.22. Through the preparation procedure developed in this work, the average diameter of the synthesized Fe_3O_4 particles can be adjusted from 8 to 50 nm, depending on the decomposition of urea in the ferrite solution.

Fig. 4 gives the magnetization loop of dextran-coated Fe_3O_4 dried particles at room temperature. The magnetic hysteretic curve exhibits super-paramagnetic behavior. The super-paramagnetism was also observed for the magnetic fluids when we dispersed the dextran-coated Fe_3O_4 particles into water, as shown in the inset of Fig. 4. In our experience, the dextran-coated can be reliably dispersed in water without self-agglomeration.

4. Conclusion

We developed a chemical co-precipitation procedure to synthesize magnetic Fe_3O_4 nano-particles of high quality. We found that with the addition of urea into a ferrite solution, the

variation in pH is homogeneous all over the solution. Thus, the size distribution of magnetic Fe_3O_4 nano-particles can be significantly narrowed down. In addition, by controlling the decomposing amount of urea via adjustment of the decomposing duration, the average hydrodynamic diameters of magnetic Fe_3O_4 particles can be manipulated. In this work, the average hydrodynamic diameter of Fe_3O_4 particles is tunable from 8 to 50 nm.

Acknowledgements

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