Aqueous synthesis and transmission electron microscopy observation of seed-grown spherical ferrite nanoparticles

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Abstract. Uniform-sized spherical iron ferrite nanoparticles grew on seed crystals in an aqueous solution containing sucrose. Using the seed crystals which were highly dispersed in acidic or alkaline seed-crystal suspension without relation to pH of the suspension, we widely controlled the particle diameter in the range 20–200 nm by changing the additive amount of the seed crystals. By transmission electron microscopy observation and X-ray diffraction analysis, it indicated that the particles were highly crystalline but not amorphous. Selected area diffraction patterns of the particles by using transmission electron microscope revealed that the particles were composed of one to several crystals. Thus we provided the evidence that the particles grew on clusters composed of one to several seed crystals to which those of several dozen seed crystals were disintegrated.

1. Introduction

Functional magnetic nanoparticles have been developed for biomedical applications such as bio-separation, drug delivery systems, magnetic resonance imaging and hyperthermia therapy [1,2]. Especially, iron ferrite (intermediate between Fe₃O₄ and γ-Fe₂O₃) nanoparticles have high potential for the biomedical applications due to high biocompatibility and corrosion resistance. To enhance the quantifiablility and reproducibility of the biomedical applications, magnetic nanoparticles should have spherical shape and uniform size, which endow the nanoparticles with high dispersibility and uniform surface-immobilization, magnetic and hydrodynamic properties. Moreover, the particle size should be optimally controlled between several dozen and several hundreds nanometers in accordance with each biomedical application to obtain high throughput and high sensitivity. In previous studies, uniform-sized spherical iron ferrite particles were synthesized by various chemical syntheses, which were however limited to ≤ 30 nm or ≥ 200 nm in diameter [3–9].
We have already developed a synthesis method of uniform-sized spherical iron ferrite nanoparticles in an aqueous solution containing a disaccharide and ferrite seed crystals [10]. We found that disaccharides enable spherical growth of the ferrite nanoparticles and seed growth makes the particle size distribution narrow. We have also widely controlled the particle diameter in the range 20–200 nm by changing the amount of ferrite seed crystals highly dispersed in a HNO$_3$ solution [11]. By the relation between the adding seed crystal amounts and the resultant spherical particle diameters, we theoretically considered that clusters composed of the several dozen seed crystals were disintegrated into smaller clusters of a few seed crystals and then the spherical ferrite nanoparticles grew on the smaller clusters.

In this paper, we report the effect of seed-crystal suspensions on seed growth of uniform-sized spherical iron ferrite nanoparticles. We also show crystal morphology of the spherical ferrite nanoparticles by transmission electron microscopy (TEM) observation and present an evidence to support that the spherical ferrite nanoparticles grew on the disintegrated seed-crystal clusters.

2. Experimental
Iron ferrite seed crystals were prepared by a coprecipitation method. A NaOH solution is added to an aqueous solution of FeCl$_2$+2FeCl$_3$. The prepared ferrite seed crystals were separated from the reaction solution by a magnet and then washed in distilled water several times. They were dispersed into a HNO$_3$ solution and a tetramethylammonium hydroxide (N(CH$_3$)$_4$OH) solution based on Massart’s method [12]. Thus we obtained acidic and alkaline suspensions of the seed crystals. The concentration of the seed crystals in the suspensions was measured as Fe concentration by spectrophotometric method using 2,2'-bipyridyl [13].

Uniform-sized spherical iron ferrite nanoparticles were synthesized by the seed-growth method from an aqueous solution containing sucrose [11]. An aqueous solution containing NaOH (10 mmol), NaNO$_3$ (20 mmol), and sucrose (50 mmol) was heated to 70 °C, to which the acidic or the alkaline seed-crystal suspension (about 1–1000 µmol Fe) and a FeCl$_2$ solution (7.5 mmol) were sequentially added. The mixed reaction solution was adjusted to 100 mL. The mixed solution was kept at 70 °C for 3 h under stirring and N$_2$ gas bubbling. The grown ferrite nanoparticles were separated from the solution by a magnet and then washed in distilled water.

The hydrodynamic diameter and zeta potential were measured by a dynamic light scattering method. The crystal structure and morphology were assessed by TEM operating at 200 kV and X-ray diffraction (XRD) using a Cu-Kα radiation source. For TEM observation of crystal structure, we prepared observation samples by slicing the spherical ferrite nanoparticles, about 150 nm in size, embedded in resin.

3. Results and discussion
The diameter of the synthesized iron ferrite seed crystals had geometric average $d_i = 8.8$ nm and geometric standard deviation $\sigma_i = 1.37$ as measured from TEM images. Table 1 shows properties of the acidic and the alkaline suspensions of the seed crystals. The seed crystals were highly dispersed as small clusters with approximate 20 nm in hydrodynamic diameter in both suspensions. They had high positive and negative surface charges in the acidic and the alkaline suspension, respectively. These are because pHs of the suspensions are far from the Fe$_3$O$_4$ isoelectric point of 6.5–6.8 and NO$_3^-$ and N(CH$_3$)$_4^+$ are low polarizing ions [12].

Table 1. Properties of the acidic and the alkaline suspensions of ferrite seed crystals.

| Solution     | pH  | Hydrodynamic diameter (nm) (average ± S.D.) | Zeta potential (mV) |
|--------------|-----|--------------------------------------------|---------------------|
| HNO$_3$      | 1.7 | 22.8 ± 5.4                                 | 42                  |
| N(CH$_3$)$_4$OH | 12.8 | 23.0 ± 5.6                                | −43                 |
We have already reported the result of seed-grown spherical iron ferrite nanoparticles synthesized by using the acidic seed-crystal suspension [11]. As the additive concentration of the seed crystals in the reaction solution \(m_s\) decreased from 11,500 to 11.5 µmol Fe/L, the geometric average diameter of the synthesized nanoparticles \(d\) increased from 19 to 209 nm and geometric standard deviation of the diameter \(\sigma\) narrowed from 1.38 to 1.11 (figure 1(a)–(c) and 2). Here \(m_s\) was calculated from the seed-crystal concentration in the suspensions, the additive volume of the seed-crystal suspension to the reaction solution and total volume of the reaction solution. The size distribution became narrowed by a large amount of the seed crystals, because it suppresses secondary nucleation. The relationship between \(d\) and \(m_s\) follows

\[
d = \left( n^{1/3} d_s m_s^{1/3} \right) m_s^{-1/3}
\]

where \(m\) is Fe concentration supplied from green rust, intermediate product, for the ferrite growth in the reaction solution [14], \(d_s\) average diameter of the seed crystals and \(n\) average number of the seed crystals composing clusters on which the ferrite growth occurs. The \(d\) vs. \(m_s\) curve obtained for \(d_s = 8.8\) nm and \(m = 50\) mmol Fe/L was best fitted by equation (1) with a nominal value of \(n = 3.4\) (figure 2). The value was considerably smaller than \(n = 17\) which was calculated from the relation \(n = (d_s'/d_s)^3\) where \(d_s' = 22.8\) nm is the hydrodynamic diameter of the seed crystal clusters measured in the acidic suspension before the ferrite growth experiments (Table 1). This suggested that the original clusters composed of several dozen seed crystals in the suspension were disintegrated to those of a few seed crystals during the ferrite growth in the reaction solution.

Figure 1(d)–(f) and table 2 show spherical iron ferrite nanoparticles grown on seed crystals by adding the alkaline (N(CH\(_3\))\(_4\)OH) seed-crystal suspension. The particle diameter \(d\) also widely controlled from 212 to 22 nm as \(m_s\) increased from 11.3 to 11,300 µmol Fe/L (figure 2). The standard deviation \(\sigma\) also decreased from 1.30 to 1.15 as \(d\) increased from 22 to 116 nm. However, the largest nanoparticles \((d = 212\) nm) were accompanied by fine particles (figure 1(d)) similarly to those synthesized by using the acidic suspension (figure 1(a)). This is because that secondary nucleation could not be suppressed enough by the smallest amount of the seed crystals. The relationship between \(d\) and \(m_s\) was also fitted by equation (1) and \(n\) was nominally estimated to 4.6 seed crystals (figure 2). The value was also smaller than \(n = 18\) calculated from the hydrodynamic diameter \(d_s' = 23.0\) nm in the alkaline suspension. The clusters composed of seed crystals in the alkaline suspension were also inferred to be resolved to those of a few seed crystals during the ferrite growth. On the other hand, we have shown that particle diameter could not be controlled by using the large amount of seed crystals aggregated in alkaline NH\(_3\) solution [11]. Thus, regardless of whether pH of the seed-crystal suspension is acidic or alkaline, size of the spherical nanoparticles is widely controlled by using the seed crystals highly dispersed in the suspensions.
Figure 1. TEM images of spherical ferrite nanoparticles grown on seed crystals. Seed crystals were dispersed in HNO$_3$ solution ((a) 11.5, (b) 115 and (c) 1150 µmol Fe/L) and in N(CH$_3$)$_4$OH solution ((d) 11.3, (e) 113 and (f) 1130 µmol Fe/L).
Figure 2. Relationship between diameter of seed-grown spherical ferrite nanoparticles $d$ and additive concentration of seed crystals in reaction solution $m_s$. Curves are calculated from equation (1) with nominal average number of seed crystals $n$ which compose clusters on which seed growth occurs. Chain line shows estimated curve of each nanoparticle grown on one seed crystal ($n = 1$).

Table 2. Relationship between additive concentration of seed crystals in reaction solution and diameter of spherical ferrite nanoparticles grown on the seed crystals measured from TEM images. The seed crystals were dispersed in alkaline suspension before particle synthesis.

| Seed crystals concentration $m_s$ (µmol Fe/L) | Spherical ferrite nanoparticles |
|---------------------------------------------|----------------------------------|
|                                             | Geometric average diameter $d$ (nm) | Geometric standard deviation $\sigma$ |
| 11.3                                        | 212$^a$                          | 1.29$^a$                          |
| 113                                         | 116                              | 1.15                              |
| 1130                                        | 58                               | 1.25                              |
| 11300                                       | 22                               | 1.30                              |

$^a$ Smaller particles in figure 1(d) were neglected.
Figure 3 show XRD profiles of seed-grown spherical ferrite nanoparticles whose diameter was controlled. All the nanoparticles had a single phase with a spinel structure and the diffraction spectrum became sharp as the particle diameter increased. As shown in figure 4, the uniform lattice fringe was observed at part of a seed-grown spherical ferrite nanoparticle although the nanoparticle had the concavo-convex surface. They clearly indicate that the spherical nanoparticles are highly crystalline but neither amorphous nor aggregate of smaller particles. The concavo-convex surface of the nanoparticles might be formed by growth suppression with weak adsorption of sucrose on the surfaces.

**Figure 3.** Powder XRD profiles of seed-grown uniform-sized spherical ferrite nanoparticles controlled their diameters by changing the additive concentration of seed crystals.

**Figure 4.** A high-resolution TEM image of part of a seed-grown spherical ferrite nanoparticle at an ultrahigh magnification.
Figure 5(a) and (b) shows dark- and bright-field TEM images of a seed-grown spherical ferrite nanoparticle. The dark-field image consists of several domains. The selected area diffraction (SAD) patterns of the particle at areas A–D, shown in figure 5(c)–(f), had clear diffraction spots and were different from one another. Their superposition gives a pattern similar to that taken on the whole area of the crystal (figure 5(g)). All spots are assigned as diffractions from crystal planes of spinel structure of ferrite (figure 5(h)). Thus it indicates that the nanoparticle is composed of several single crystals.

Figure 5. TEM images and electron diffraction patterns of a spherical ferrite nanoparticle composed of several crystals. (a), (b) Dark-field and bright-field TEM images. (c)–(f) SAD patterns obtained at areas A–D. (g) Diffraction pattern of the whole particle. (h) Crystal planes responsible for the diffraction spots in figure (g).
As shown in figure 6(a), another spherical ferrite nanoparticle gave a dark-field TEM image with smooth brightness gradation over the whole range, which suggests that the particle is essentially single crystalline. This was confirmed because each of the SAD patterns taken at areas A–C in figure 6(b) was composed mainly of (002) diffraction spots arrayed on a line (figure 6(c)–(e) and (g)). Also each SAD pattern was similar to that taken on the whole area of the crystal (figure 6(f)). Therefore TEM observation revealed that seed-grown spherical ferrite nanoparticles are composed of one to several single crystals. Since the seed crystals were single crystalline, ferrite growth occurred on clusters composed of one to several seed crystals as we expected. Thus we successfully proved that the clusters each composed of several dozen seed crystals were disintegrated to those composed of a few seed crystals during the ferrite growth.

Figure 6. TEM images and electron diffraction patterns of a spherical ferrite nanoparticle which is single crystal. (a), (b) Dark-field and bright-field TEM images. (c)–(e) SED patterns obtained at areas A–C. (f) Diffraction pattern of the whole particle. (g) Crystal planes responsible for the diffraction spots in figure (e).
4. Conclusions
Using seed crystals highly dispersed in their acidic or alkaline suspension independently of the suspension pH, uniform-sized spherical ferrite nanoparticles grew on seed crystals and the particle diameter were controlled in the range 20–200 nm by changing the additive concentration of the seed crystals. TEM observation revealed that seed-grown spherical ferrite nanoparticles were highly crystalline and composed of one to several single crystals. Therefore we provided that the spherical ferrite nanoparticles grew on clusters composed of one to several seed crystals to which those of several dozen seed crystals resolved during the particle growth.

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