Hydrothermal growth of iron oxide NPs with a uniform size distribution for magnetically induced hyperthermia: Structural, colloidal and magnetic properties

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ABSTRACT

Magnetic iron oxide nanoparticles with a narrow size distribution were synthesized by hydrothermally treating suspensions of iron oxide nanoparticles. Ricinoleic-acid-coated magnetic nanoparticles were co-precipitated at room temperature from an aqueous solution of Fe^{2+}/Fe^{3+} cations by the addition of a base. The presence of the ricinoleic acid on the nanoparticles' surfaces strongly suppressed their growth under the hydrothermal conditions. Because of the strong dependency of the rate of particle growth on their size, the size distribution significantly narrowed during the hydrothermal treatment. The size of the nanoparticles was successfully controlled by the temperature of the synthesis and the amount of ricinoleic acid present in the reaction mixture to between 9 and 30 nm. The presence of the ricinoleic acid on nanoparticles' surfaces enabled the preparation of colloidal suspensions in even moderately polar organic liquids. Measurements of the magnetic properties revealed that the nanoparticles smaller than 14 nm exhibited superparamagnetic behavior and nanoparticles larger than 15 nm displayed single-domain ferrimagnetic behavior. The nanoparticles exhibited large values of saturation magnetization of up to 90 emu/g. The strong dependence of the nanoparticles' specific power losses when subjected to an alternating magnetic field on their average size and frequency was demonstrated. The ferrimagnetic nanoparticles showed much higher power losses than the superparamagnetic nanoparticles.

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1. Introduction

Magnetic iron oxide nanoparticles have been intensively studied because of their unique magnetic properties, which are dominated by single-domain ferrimagnetism and superparamagnetism. The transition from the single-domain ferrimagnetic state to superparamagnetic state is observed when the size of the ferrimagnetic material is reduced below a certain critical size [1–3]. A characteristic property of superparamagnetic particles is that they show zero magnetic remanence and coercivity in the absence of an external magnetic field [1,2]. The critical size of the transition depends on the value of the effective magnetic anisotropy constant [1,2]. Depending on the synthesis method used, the critical size for the magnetic iron oxide maghemite is between 14 and 16 nm [4,5]. Such superparamagnetic nanoparticles show a distinct advantage over larger single-domain nanoparticles when colloidal suspensions have to be prepared. Because of the thermally induced randomization of the individual nanoparticles' magnetic moments the net magnetic attraction between the nanoparticles is greatly reduced. Colloidal suspensions of superparamagnetic nanoparticles or magnetic fluids are important in a variety of technological [6]

and biomedical applications [7], such as the contrast agents in MRI [8,9], targeted drug delivery [9] and magnetic hyperthermia [10,11]. Colloidal suspensions of nanoparticles in non-polar or polar organic liquids are also needed in the preparation of different complex materials, such as nanoparticles/polymer nanocomposites [5,12] and composite mulitiferroics [13], to mention just a few.

One of the most promising applications of magnetic nanoparticles in biomedicine is the treatment of cancer by magnetic-mediated hyperthermia—which is already in clinical trials [10,14]. The basis of the treatment is the heating of magnetic nanoparticles that are concentrated in the tumor tissue, induced by an alternating magnetic field. The heat is generated as a consequence of the magnetic losses and two kinds of magnetic nanoparticles can be distinguished: superparamagnetic particles, where the heating effect is related to energy losses during the moment relaxation [15] (Néel), and single-domain (ferri- or ferromagnetic) particles, where the heating is due to hysteresis losses [16–18]. In addition, the rotation of the particles within the carrier liquid (Brownian rotation) can contribute to the total effect [15]. At this point it should be noted that the mentioned separation of the mechanisms responsible for heating is artificial, but the distinction is very persistent in experimental-based articles [17]. The heating ability of magnetic nanoparticles is expressed by the specific loss power (SLP), which is equal to the power losses per material mass. The relaxation time of the Brownian rotation and therefore the heating related to it strongly depends on the hydrodynamic size of the magnetic nanoparticles and the viscosity of the medium [15]. The hydrodynamic size of the nanoparticles when introduced to the human body can change significantly due to the adsorption of proteins and other macromolecules present in body liquids. Furthermore, the application of a magnetic field can induce the formation of agglomerates and chains that have a very different hydrodynamic size in comparison to individual nanoparticles [19,20]. Also, the tissue that is supposed to be heated is more gel-like than liquid-like, meaning that the Brownian rotation of the magnetic nanoparticles when they reach the targeted tumor tissue is at least strongly hindered, if not completely prevented. For this reason it has been suggested that magnetic nanoparticles for magnetic hyperthermia should display a SLP that is independent of such phenomena [17]. In practice this means that measurements of the SLP should be performed on immobilized nanoparticles because the value obtained in such a way is more representative and reflects the nanoparticles' intrinsic properties, which are related to their magnetic properties and not to their hydrodynamic size and the viscosity of the medium.

Among the different magnetic materials, the magnetic iron oxides magnetite (Fe_3O_4) and maghemite (γ-Fe_2O_3) are by far the most studied, mainly because they are considered to be non-toxic. The superparamagnetic iron oxide nanoparticles (also known as SPIONs) were also approved by the US Food and Drug Administration (FDA) for specific in-vivo applications [21]. Current state-of-the-art magnetic nanoparticles exhibit large SLP values when their size is in the range between 15 nm and 20 nm [22–25]. Despite their outstanding SLP values the synthesis methods used to obtain such particles have severe drawbacks. The methods are complex, multi-stage and the synthesis is conducted in expensive, toxic, organic reagents, at elevated temperatures of up to 300 °C in an inert atmosphere. Magnetic iron oxide nanoparticles can be synthesized by other methods as well. By far the most common method used to synthesize magnetic nanoparticles is the co-precipitation of Fe^{3+} and Fe^{2+} from aqueous solutions by the addition of a base [26]. The method has clear advantages, such as the use of cheap and green reagents, the reproducibility of the particles' properties and it can be easily scalable to produce large quantities of magnetic nanoparticles. Nevertheless, it suffers from

some drawbacks, such as poor control of the magnetic nanoparticles' size and size distribution. In addition, it is not possible to synthesize particles larger than 12 nm. Using hydrothermal growth, especially when performed in the presence of surfactants that adsorb onto the magnetic nanoparticles' surfaces, such limitations can be overcome [27]. Because the synthesis is conducted at elevated temperatures, the growth of the magnetic nanoparticles is promoted, but not exaggerated due to the presence of a surfactant that inhibits the secondary re-crystallization. Relatively good control over the size of the magnetic iron oxide particles was achieved by applying the hydrothermal method, but in most cases the nanoparticle surfaces were not coated and therefore the preparation of colloidal suspensions is difficult because of their tendency to agglomerate [28–32]. Taniguchi et al. synthesized oleic-acid-coated nanoparticles, which can only be dispersed in non-polar organic liquids [31]. Thomas et al. synthesized LDOPA-coated nanoparticles in a continuous hydrothermal apparatus and demonstrated colloidal stability in aqueous media of biological relevance [30]. Ricinoleic acid, which is structurally similar to oleic acid, the only difference being the presence of an −OH group in the tail, enables the preparation of colloidal suspensions of magnetic nanoparticles in non-polar and moderately polar organic liquids [33]. Dispersability in a relatively broad range of organic liquids and the −OH group in the tail enable the covalent bonding of a wide range of hydrophilic molecules or polymers to the particles' surface, which leads to colloidal stability in aqueous media.

In this work we present a systematic study of the influence of the temperature and the concentration of ricinoleic acid on the size and magnetic properties of iron oxide nanoparticles. The goal was to develop a method that provides control over the nanoparticles' size in the region where superparamagnetism dominates to the region where ferrimagnetism dominates the magnetic properties and the effect of the magnetic properties and the size on the heating in AC fields. Moreover, the influence of ricinoleic acid on the dispersibility in moderately polar organic solvents was also studied.

2. Materials and methods

2.1. Materials

Iron (III) sulfate hydrate ($Fe_2(SO_4)_3 \cdot xH_2O$, reagent grade), iron (II) sulfate ($FeSO_4 \cdot H_2O$, 99+%), were purchased from Alfa Aeasar. Ammonia solution (NH_4OH, 25% for analysis), 1,2-dichlorobenzene (DCB) ($C_6H_4Cl_2$, for synthesis), nitric acid (HNO_3, 65%, for analysis) were purchased from Merck. Ricinoleic acid (RA) ($C_{18}H_{34}O_3$, technical grade ~80%) was purchased from Aldrich. Methanol (CH_4O, reagent grade) and acetone (C_3H_6O, reagent grade) were purchased from Sigma-Aldrich. Fe_2O_3 (99.999%) was purchased from Ventron. $FeTiO_3$ (99.9%) was purchased from Alfa Aesar.

2.2. Synthesis

Iron oxide nanoparticles were synthesized by the aqueous co-precipitation of Fe^{2+} and Fe^{3+} cations with ammonia at room temperature. In brief, to the 80 mL of cations solution (0.113 mol/L Fe^{3+} and 0.135 mol/L Fe^{2+}) 64 mL of ammonia solution was added in a single rapid pour (within 1 s) during vigorous stirring in a Teflon vessel. For the configuration (dimension of Teflon vessel, diameter of stirrer and dynamic viscosity of water at 25 °C) used for the synthesis the estimated Reynolds number was Re~20 000. Since Re > 10,000, fully turbulent flow can be assumed (sample NPRT). Over the 30-min time interval the specified amount of RA was added drop-wise (Table 1). The amount of the added ricinoleic acid is reported as the ratio between the mass of the added ricinoleic