Functionalization-induced improvement in magnetic properties of Fe_3O_4 nanoparticles for biomedical applications

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(Presented 12 November 2008; received 18 September 2008; accepted 2 December 2008; published online 24 March 2009)

Fe_3O_4 were synthesized nanoparticles by thermal decomposition method with oleic acid as the surfactant, and to make them suitable for aqueous environments, dopamine ligand exchange was carried out on the particles. The nanoparticle size and phase was quantified by transmission electron microscopy (TEM) and x-ray diffraction (XRD), respectively. Superconducting quantum interference device magnetometry confirmed superparamagnetic behavior in both nanoparticles. A surprising and significant increase in the remanence M_R, saturation magnetization M_S, and blocking temperature T_B of the particles was found after dopamine functionalization, even though TEM and XRD studies revealed no change in the particles' size and/or structure. The results are consistent with an increase in the magnetic size of the nanoparticle core induced by the dopamine ligand exchange process. These effects are tentatively attributed to surface bonding effects that alter the canted magnetic state of the Fe_3O_4 nanoparticles. © *2009 American Institute of Physics*. [DOI: 10.1063/1.3073654]

I. INTRODUCTION

Magnetic nanoparticles (NPs) in the form of biocompatible iron oxide NPs are key components of next-generation drug delivery systems, magnetic resonance imaging contrast agents, and cell separation systems for disease diagnosis.[1,2] However, most synthesis methods create hydrophobic NPs that must be subjected to ligand exchange procedures to become hydrophilic so as to be soluble in aqueous media and rendered suitable for further conjugation with specific molecules for biomedical applications.[3,4] Optimization of magnetic NPs for these applications requires thorough understanding of the effects of ligand exchange on the magnetic attributes of NPs. To this end, size-controlled Fe_3O_4 NPs were synthesized with oleic acid as the surfactant. The subsequent ligand exchange process was carried out using dopamine. Both oleic acid and dopamine are covalently bound to the surface via a chelating bidentate interaction to the iron species.[5,6] In this paper we report on the magnetic properties of Fe_3O_4 NPs before and after undergoing the dopamine-exchange procedure. It is observed that the dopamine functionalization process produced an unexpected increase in the remanence and saturation magnetization of the NP ensemble, despite the fact that the particles' size and structure remained the same. Other researchers have reported on similar phenomena but to date have not investigated the underlying mechanism of magnetic property alterations.[7–10] The current results are consistent with an increase in the magnetic size of the NP core induced by the dopamine ligand exchange process. This phenomenon is tentatively attributed to surface bonding effects that alter the canted magnetic state of the Fe_3O_4 NPs.

II. EXPERIMENTAL PROCEDURES

High temperature thermal decomposition method was used to synthesize Fe_3O_4 NPs as described by Sun *et al.*[11] The NPs were synthesized by mixing iron (III) acetylacetonate [$Fe(acac)_3$, 2 mmol], 1,2-hexadecanediol (10 mmol), oleic acid (6 mmol), oleylamine (6 mmol), and phenyl ether (20 ml) and magnetically stirred at room temperature under argon. The mixture was first heated to 473 K, maintained at this temperature for 30 min. and then increased to 538 K for an additional 30 min. After cooling to room temperature, the NP were precipitated with ethanol, collected and redispersed in hexane. Larger particles were then grown by mixing the NPs in hexane with the chemical mixture procedure described above. A room-temperature ligand exchange reaction using dopamine was used to convert the NPs from the hydrophobic to the hydrophilic state.[12] Briefly, 10 mg of dopamine was dissolved in dichloromethane; 10 mg of NPs was then added and shaken overnight to facilitate ligand exchange, as shown in Fig. 1. Dichloromethane was evaporated; dopamine-exchanged particles were rinsed with hexane to remove excess surfactant and resuspended in 1X phosphate buffer solution (*p*H 7.4).

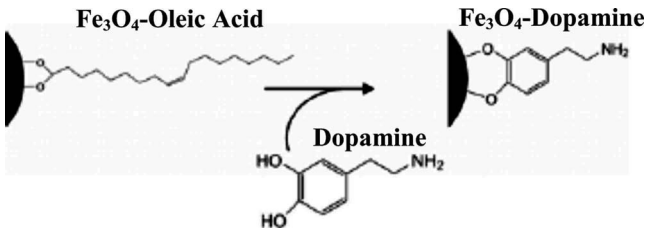

FIG. 1. Schematic illustration of ligand exchange from oleic acid to dopamine surfactant on Fe_3O_4 NPs.

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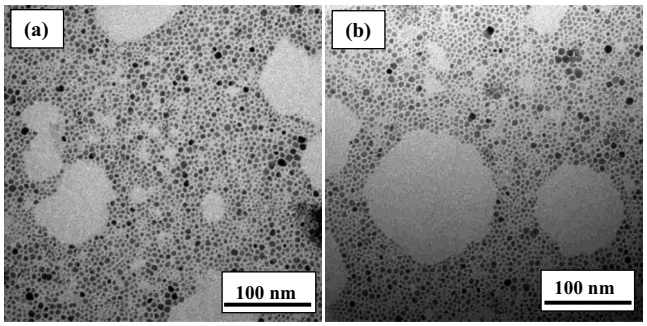

FIG. 2. TEM micrographs of (a) as-synthesized oleic-acid-stabilized NPs and (b) dopamine-stabilized NPs.

XRD was used to confirm the structure and phase purity, and inductively coupled plasma-optical emission spectroscopy (ICP-OES) was employed to determine the iron content of the particles before and after dopamine exchange. In addition, Fourier transform-infrared (FT-IR) spectroscopy was utilized to confirm ligand exchange. The size and morphology of the NPs were characterized using TEM 75 kV. Magnetic studies were carried out using a superconducting quantum interference device magnetometer. Field-cooled and zero-field-cooled (FC/ZFC) curves were collected from 2 to 300 K at the applied field $H_{\text{appl}}=100$ Oe and hysteresis curves were measured at temperatures of 6, 10, 50, 150, 200, 250, and 300 K in the field range $-5\ \text{kOe} \leq H_{\text{appl}} \leq 5\ \text{kOe}$. The saturation magnetization M_S was estimated from the measured hysteresis loops using the $1/H$ law approach[13] while the particle diameter was determined by applying the Langevin function to the data; the Langevin function was modified to include a paramagnetic contribution present in the hysteresis measurements:[14]

$$M(H) = M_S\left[\coth\left(\frac{\mu_p H}{k_B T}\right) - \frac{k_B T}{\mu_p H}\right] + \chi_a H, \tag{1}$$

where μ_p is the magnetic moment per particle provided as $\mu_p = M_s \pi D^3/6$ emu with D equal to the particle diameter in centimeters, k_B is the Boltzmann constant, and χ_a is the high field susceptibility attributed to the organic stabilizer and hypothesized paramagnetic surface contributions in the iron oxide NPs. All data have been normalized to the mass of iron present in each sample, determined from elemental analysis.

III. RESULTS AND DISCUSSION

TEM micrographs of both the as-synthesized and dopamine-exchanged particles are shown in Fig. 2. Uniform spherical NPs are seen with no clustering. Particle size distribution yielded an average particle diameter of 10 nm for both oleic-acid- and dopamine-stabilized NPs. XRD (results not shown) confirmed attainment of cubic spinel-type Fe_3O_4 with a particle size of approximately 9.3 nm derived from Scherrer broadening analysis of the (311) Bragg peak;[15] the calculated lattice parameter of $a=8.416\pm0.026$ Å agrees well with literature values.[16] The iron content was determined by ICP-OES analysis to be $54.1\pm0.8\%$ and $54.7\pm0.1\%$ by mass for the as-synthesized and the dopamine-stabilized NPs, respectively, confirming no loss of iron upon ligand exchange. FT-IR spectra (results not shown) of oleic acid and oleic-acid-stabilized NPs showed the characteristic CH_2 asymmetric (2922 cm^{-1}) and symmetric (2852 cm^{-1}) stretches. Also in the case of NPs C=O stretch at ~1710 cm^{-1} significantly decreased indicating the binding of oleic acid through these carboxyl group on the NP surface. Upon ligand exchange with dopamine, all the characteristic peaks of oleic acid have completely disappeared, indicating successful and complete exchange of oleic acid with dopamine.

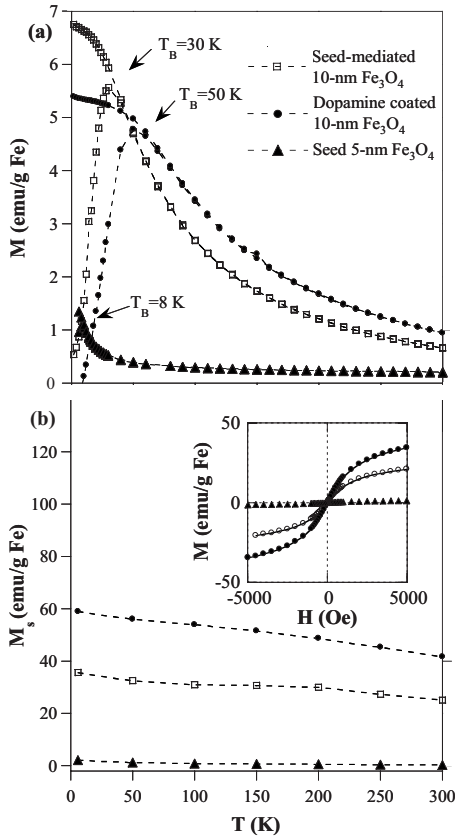

FIG. 3. Magnetic characterization of iron oxide NPs as function of temperature. (a) FC/ZFC curves of as-synthesized 5 nm seed (-▲-), 10 nm seed mediated (-□-), and 10 nm dopamine-coated (-●-) Fe_3O_4 particles and (b) saturation magnetization using $1/H$ law approach at six different temperatures and inset shows hysteresis curves at 300 K for the three particle samples. Langevin function represented by curve fit of seed-mediated and dopamine hysteresis data.

Figure 3(a) displays the FC/ZFC magnetization trends with temperature obtained from both the as-synthesized (seed and seed-mediated growth) and dopamine-stabilized NPs. All samples exhibited superparamagnetic behavior with zero remanence and zero coercivity for $T > T_B$ and significant remanence and coercivity (~200 Oe) at $T < T_B$, where the blocking temperature T_B marks the delineation between the coercive and the superparamagnetic states. It is noted that T_B increases with increasing particle size from 8 K (5 nm seed) to 30 K (10 nm particle). Unexpectedly, a consistent increase in T_B, up to $T_B=50$ K, was obtained upon functionalization of the NPs with dopamine, despite the fact that the physical particle size did not change. This phenomenon also manifests in magnetization measurements [Fig. 3(b)] that indicate that the temperature-dependent saturation magnetiza-

tion $M_S(T)$ attains a much higher value for the dopamine-exchanged NPs as compared to the as-synthesized oleic-acid-stabilized particles. The net $M_S(T)$ value increases from 38 emu/g Fe for 10 nm oleic-acid-stabilized NPs to 60 emu/g Fe for dopamine-exchanged 10 nm iron oxide NPs. Application of the Langevin function to the 300 K $M(H)$ data [Fig. 3(b), inset] yields room-temperature M_S values of $3.81\mu_B$/Fe (as-synthesized particles) and $3.87\mu_B$/Fe atoms (dopamine-functionalized particles), close to the bulk value of $4\mu_B$/Fe atom in Fe_3O_4.[17] The Langevin fit yielded a calculated magnetic particle diameter $D\sim 7$ nm for both the seed-mediated and the dopamine-coated NPs that are smaller than the physical diameter of 10 nm. This result of comparable magnetic diameters was not expected, but it should be noted that the paramagnetic contribution χ_a determined from the Langevin fit provided a paramagnetic contribution from the seed-mediated sample (1.94×10^{-7} emu/Oe) that was over 50% larger than that obtained from the dopamine-coated sample (1.25×10^{-7} emu/Oe). Thus the resulting 7 nm diameter can be attributed to the fit and the paramagnetic contributions from the stabilizing surfactant.

The magnetic data on the as-made and dopamine-exchanged NPs attest to an improvement in the magnetization and an increase in the blocking temperature of the iron oxide NPs upon functionalization to become hydrophilic. The ligand exchange process produces no observed change in the physical size or structure of the NPs, as confirmed by TEM, XRD, and elemental analysis. It is thus hypothesized that the dopamine functionalization process alters the surface magnetic state of the particles such that the reported magnetic "dead" layer[18,19] with a canted zero-moment surface structure is restored, to some degree, to a collinear ferromagnetic structure[20,21] of nonzero moment. A similar phenomenon has been reported by Crespo *et al.*[22] for Au NPs, where thiol-derivatized Au NPs were shown to exhibit ferromagnetic magnetization versus alkyl ammonium protected gold particles which showed a diamagnetic behavior. Recently, Daou *et al.*[23] reported a similar increase in M_s induced by changes to dead magnetic layer upon varying the functional groups that are bound to NP surfaces. These conclusions are supported by the results obtained from the Langevin fitting to the magnetic data that indicate that the paramagnetic contribution of the particles, hypothesized to originate from the oxide surface layer as well as from the surfactants, decreases upon NP functionalization with dopamine. The magnetic dead layer is thus hypothesized to be "rejuvenated" by dopamine functionalization, resulting in a higher magnetization and an assumed larger magnetic diameter.

The origin of the improvement in the magnetic properties of the Fe_3O_4 NPs upon functionalization is hypothesized to lie in the steric interaction between the surfactant molecules (oleic acid and dopamine), arising from their strongly covalent interaction with the Fe atoms on the oxide NP surface to form a chelating bidentate bond. It has been reported that removal of a ligand bound to surface Fe atoms, as during the exchange process, can also remove the bound Fe atom.[9] It is expected that this process would lead to complete rearrangement of the NPs' surfaces and result in a significant decrease in particle size. As this effect was not observed in the current study, the phenomena reported in this paper are attributed to collinear realignment of canted-surface spins.

The current results are of significance because biomedical devices employing magnetic NPs,[24] especially those that target field-driven cell separation systems, are more sensitive and more efficient with higher magnetization values. The results presented here provide a means to understand and ultimately tailor the surface of magnetic oxide NPs toward optimal states for biomedical usage.

ACKNOWLEDGMENTS

This work was supported by the IGERT Nanomedicine and Science Program (NSF Contract No. DGE-0504331), the Vietnamese Education Foundation, and Northeastern University. The authors would like to thank Dr. C. N. Chinnasamy for assistance with XRD analysis and Professor Daniel Burkey for access to the FT-IR.

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