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May 2005

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Magnetic studies of iron oxide nanoparticles coated with oleic acid and Pluronic® block copolymer

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(Presented on 9 November 2004; published online 17 May 2005)

We have prepared and studied iron-oxide nanoparticles coated with oleic acid (OA) and Pluronic® polymer. The mean diameter of the iron-oxide nanoparticles was $9.3(\pm)0.8$ nm. Saturation magnetization values measured at 10 K varied from $66.1(\pm 0.7)$ emu/g to $98.7(\pm 0.5)$ emu/g. At 300 K the loops showed negligible coercive field. The peaks in zero-field-cooled susceptibility decreased from 280 to 168 K with increasing OA concentration up to 10.6 wt %, and remained nearly constant for higher concentrations. This suggests that incomplete coverage of the OA allows small, interacting agglomerates to form. © 2005 American Institute of Physics. [DOI: 10.1063/1.1850855]

I. INTRODUCTION

The use of nanoparticles for drug delivery is a topic of vigorous investigation. One approach is to package the drug in a polymer-coated magnetic nanoparticle and use an external magnetic field to target the nanoparticle. The challenges are to develop a biocompatible material that has a long circulation time, can be loaded with the drug, and has a large enough moment for magnetic targeting.

Pluronic® block co-polymers can make phagocyte-resistant nanoparticles with long blood-circulation time.¹ Pluronic® is a water-soluble tri-block copolymer composed of a hydrophobic central segment of poly(propylene oxide) flanked by two hydrophilic segments of poly(ethylene oxide). Pluronic® can be represented as $EO_a-PO_b-EO_a$, where a and b are the number of ethylene oxide and propylene oxide units, respectively.²

Iron oxides are the most-studied materials for magnetic targeting because of their favorable magnetic properties and high biocompatibility. Both are ferrimagnetic with magnetic transitions above 800 K.³ Bulk magnetite and maghemite have the highest saturation magnetizations (M_S) among the iron oxides (92–100 emu/g and 60–80 emu/g, respectively).³

Oleic acid (OA) is used for steric stabilization in nonpolar solutions; however, OA has a low hydrophilic-lipophilic balance (HLB) value of 1, making stabilization in water difficult.⁴ Adding Pluronic® block copolymer, which has a HLB value of 22, as a second layer enhances the dispersion stability.

II. SAMPLE PREPARATION AND MEASUREMENT

Solutions of 0.1 M Fe(III) and 0.1 M Fe(II) in water were mixed with 5 M NH_3 solution and the mixture was stirred for 20 min in a N_2 atmosphere. After stirring, OA was added and the solution was heated to ≈ 353 K for 30 min while stirring. Pluronic® F-127 was added after the solution cooled to room temperature. Iron-oxide nanoparticles were recovered by ultracentrifugation, washed twice with deionized (DI) water and re-dispersed in DI water by sonication. The relative concentrations (in wt %) of iron-oxide, OA and Pluronic® were varied: $0 < \text{Pluronic}^\circ < 60$, $0 < \text{OA} < 21.9$, and $36.5 < \text{iron-oxide} < 100$. Lyophilized powder samples were enclosed in polyethylene bags containing paraffin wax to prevent the particles from rotating in the measuring field.

III. DISCUSSION

Figure 1 shows a typical x-ray diffraction (XRD) powder-diffraction pattern. The similarity of maghemite and magnetite XRD patterns makes it difficult to exclude the formation of maghemite in the samples; however, the value of the saturation magnetization suggests that magnetite comprises a significant fraction of the sample. The iron-oxide nanoparticle diameter for all samples was 9.3 ± 0.8 nm (see inset in Fig. 1) as obtained by an integral breadth analysis of the XRD peaks. This result is in agreement with the mean diameter of 8.9 nm from transmission electron microscopy (TEM). Figure 2 shows a representative TEM micrograph and histogram of the size distribution.

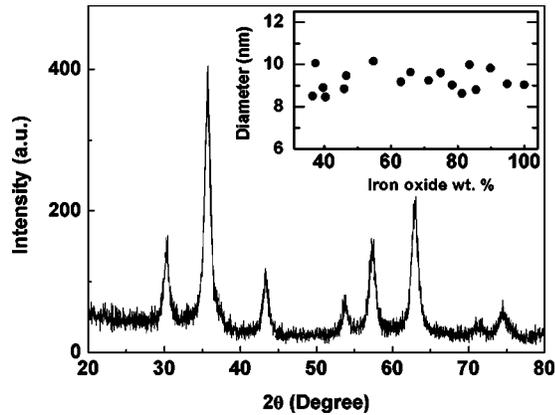


FIG. 1. XRD measurements of OA- and Pluronic®-coated iron-oxide nanoparticle powders. The inset shows the iron-oxide nanoparticle diameters obtained from XRD measurements as a function of iron-oxide concentration.

$M(H)$ loops were normalized to the magnetite mass as determined by atomic absorption spectroscopy (AAS). The saturation magnetization (M_S), remanence ratio ($s = M_r/M_S$), and coercive field (H_c) were determined by fitting the magnetization curve with an analytical model⁵ plus a diamagnetic background contribution.

Figure 3 shows $M(H)$ at 10 and 300 K in a sample with 37.4 wt % of iron-oxide nanoparticles, 40.8 wt % Pluronic®, and 21.8 wt % OA. As a function of OA content, M_S at 10 K increases from 66.1(±0.7) emu/g to 98.7(±0.5) emu/g regardless of the relative concentration of iron oxide and Pluronic®, and s varies from 0.21(±0.01) to 0.31(±0.01). At 300 K the loops show negligible coercive field, and the magnetization at 1.2 T (after the diamagnetic background contribution is removed), ranged from 34.6(±0.8) emu/g to 61.2(±0.8) emu/g. $M(H)$ loops measured at 300 K were fit to a Langevin function weighted by a log-normal distribution of particle sizes, producing a mean particle size comparable to that obtained by XRD and TEM.

The sample without any Pluronic® or OA had a M_S of 66.1(±0.7) emu/g, which is comparable to that reported for 10 nm magnetite nanoparticles.⁶ The M_S values at high OA concentrations are larger than those expected for bulk magnetite. The smaller M_S values relative to bulk magnetite could be due to an increase in the surface anisotropy induced by chemisorption of OA.^{7,8}

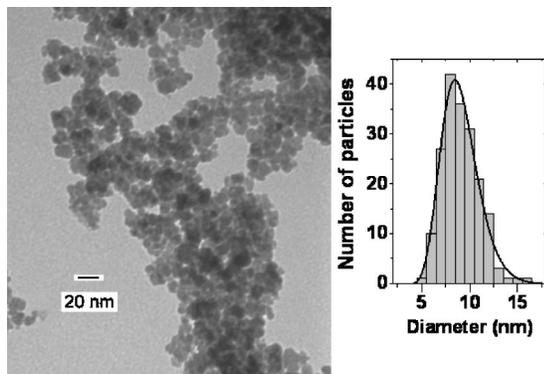


FIG. 2. A representative TEM micrograph and size distribution.

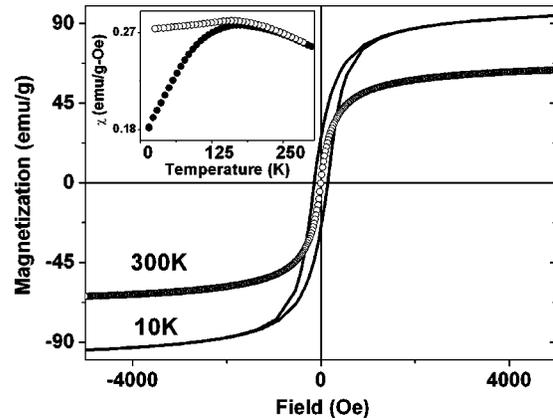


FIG. 3. The magnetization as a function of field for a sample with 37.4 wt % of iron-oxide nanoparticles, 40.8 wt % Pluronic®, and 21.8 wt % OA, measured at 10 K (solid line) and 300 K (circles). The inset shows the FC and ZFC susceptibilities.

The inset of Fig. 3 shows the field-cooled and zero-field-cooled susceptibilities, $\chi_{ZFC}(T)$ and $\chi_{FC}(T)$. The measurement was made at a field of 100 Oe. T_{max} , the position of the peak, was determined from the zero of $d\chi_{ZFC}(T)/dT$. T_{max} vs OA concentration is shown in Fig. 4, where the leftmost two points (at 0 wt % OA) correspond to uncoated and Pluronic®-coated iron-oxide nanoparticles. The particles covered with only Pluronic® have a similar T_{max} as the uncoated particles but a significantly higher M_S of 75.8(±0.5) emu/g. We attribute this to the effect of Pluronic® preventing the nanoparticles from oxidizing and/or agglomerating.

The blocking temperature T_B is defined as $T_B = KV/25k$, where V is the volume of the nanoparticles, K is the magnetic anisotropy constant (which ranges from 1.4×10^4 to 5×10^4 J/m³ for magnetite^{3,9}), and k is the Boltzmann constant. T_{max} will be equal to T_B only in systems with negligible inter-particle magnetic interaction. XRD and TEM measurements show that the iron-oxide size is roughly constant for all samples. If the particles were noninteracting and superparamagnetic, T_{max} should be similarly constant; however, T_{max} varies from a maximum value of 280(±5) K to 168(±5) K as the OA concentration increases. The T_{max} observed at low OA concentration could be due to incom-

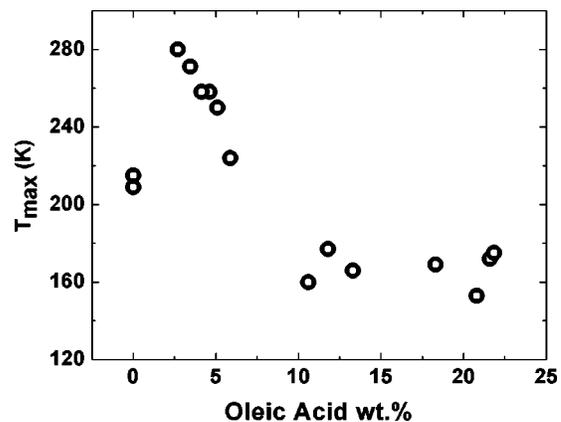


FIG. 4. T_{max} vs OA concentration in wt %.

plete coverage of the iron-oxide nanoparticles by the surfactant, allowing some nanoparticles to aggregate.

Using $K=1.4 \times 10^4 \text{ J/m}^3$ (for magnetite) yields a blocking temperature of 168 K, which would require a mean nanoparticle diameter of about 20 nm. This is twice the size obtained from XRD, TEM, and magnetization measurements. Furthermore, the ratio M_r/M_s is smaller than the value of 0.5 expected for noninteracting, randomly oriented single-domain particles.¹⁰

The most likely explanation of the observed phenomena is that one or more layers of Pluronic® surround a small group of OA-coated iron-oxide nanoparticles. Inside the aggregate, the nanoparticles are separated by the OA layers, and this distance decreases interactions and determines the value of T_{max} . The higher value of T_{max} could be due to dipolar magnetic interactions among the iron-oxide nanoparticles. These interactions slow the magnetic relaxation and increase T_{max} , as has been observed experimentally,^{9,11} and theoretically.¹² T_{max} increases at low OA concentrations, indicating that the iron-oxide nanoparticles are closer to each other, which is consistent with incomplete covering by the OA.

The process of magnetically targeted drug delivery involves binding a drug to biocompatible magnetic nanoparticles. Paclitaxel is a potent anti-neoplastic drug, but its high hydrophobicity makes it difficult to develop into an effective drug delivery system.¹³ Drug-loaded nanoparticles with OA and Pluronic® F-127 showed good dispersibility in aqueous media. A 5.4 wt % of paclitaxel could be incorporated into the nanoparticles, which allowed sustained release over ten days under *in vitro* conditions.

IV. CONCLUSIONS

We have synthesized iron-oxide nanoparticles coated with oleic acid and Pluronic® tri-block polymer. Magnetic measurements suggest that OA-coated iron-oxide nanoparticles tend to aggregate. Pluronic® decreases aggregation, improves the stability of the suspension in water and increases blood circulation time. The combination of magnetic properties, the ability to incorporate acceptable amounts of drug into the particles, and the stability of the particles in aqueous suspension suggest that these materials are ideal candidates for magnetically targeted drug delivery.

ACKNOWLEDGMENTS

This work was supported by the Nebraska Research Initiative and the MRSEC Program of the NSF. The authors thank F. Erwin Harvey and Kelli Warren for assistance in making AAS measurements.

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