J Nanopart Res (2008) 10:877–880
DOI 10.1007/s11051-007-9311-x

BRIEF COMMUNICATION

Size effects in monodomain magnetite based ferrofluids

I. Nedkov · L. Slavov · T. Merodiiska · P. Lukanov · Ph. Tailhades · M. Gougeon · R. E. Vandenberghe

Received: 13 April 2007 / Accepted: 30 September 2007 / Published online: 2 November 2007

Abstract Ferrofluids based on two types of hybrid particles Fe_3O_4/β-cyclodextrin were prepared: Using monodomain (below 60 nm) magnetite nanoparticles with (A) non-superparamagnetic (non-SPM) behaviour and (B) with superparamagnetic (SPM) behaviour. We found a strong dependence of the hybrid particles' magnetic properties on their size and homogeneity. In both types of ferrofluids we observed hyperthermia upon applying an ac electromagnetic field with frequency 40 kHz and amplitude 30 kA/m. The maximal ΔT upon irradiation with duration of about 12 min for the non-SPM particles was 12 °C, while for the SPM ones it was 3.5 °C.

Keywords Ferrofluids · Magnetite nanoparticles · Hyperthermia · Superparamagnetism · β-Cyclodextrin

I. Nedkov · L. Slavov (✉) · T. Merodiiska · P. Lukanov
Institute of Electronics, Bulgarian Academy of Sciences, 72, Tzarigradsko Chaussee, Sofia 1784, Bulgaria
e-mail: l_slavov@ie.bas.bg

Ph. Tailhades · M. Gougeon
LCMIE - Universite Paul Sabatier, 118 Route de Norbonne, Bat. 2R1, Toulouse 31062, France

R. E. Vandenberghe
Department of Subatomic and Radiation Physics, University of Gent, Gent 9000, Belgium

Introduction

The recent developments in bio-medical applications of the nanotechnologies created opportunities for combating one of the greatest challenges to modern medicine, namely, cancer curing (Bahadur and Giri 2003). The nanosized spherical monodomain magnetite particles are unique in this respect. The critical size for a monodomain particle depends on several factors, including the saturation magnetization and the magneto-crystalline anisotropy of the material. On the other hand, the spherical shape of particles is more suitable for applications in the human body. In the case of magnetite the value for the transition from a polydomain to a monodomain state is around 60 nm (Aharoni and Jakubovocs 1988). Below a certain critical temperature T_κ, these particles retain the properties of the bulk magnetic material. Above it, one observes the phenomenon of "superparamagnetism"(SPM), which is not a paramagnetic behaviour of a single atom, but rather a collective behaviour of antiferromagnetically ordered spin magnetic moments, constrained within the particle's volume. This results in unique magnetic properties of the particle when it interacts with an electromagnetic field. These nanomaterials are considered promising for the development of biocompatible fluids that could deliver drugs in the blood or lymph system to a cancerous tissue. Another application that is now regarded as feasible is the so-called hyperthermia, whereby the ferrofluid already accumulated in the organ to be treated, is heated up by applying an *ac* magnetic field, and so destroying the malignant formation.

We have investigated ferrofluids based on two types of monodomain spherical magnetite nanoparticles. One, with well-expressed SPM properties at room temperature and at the temperature of the human body, and the other with monodomain particles that do not exhibit SPM properties at these temperatures. Data on hyperthermia effect in the ferrofluids is presented. The colloidal stability of the fluids was achieved using tetramethylammonium hydroxide (TMAOH) as a surfactant and β-cyclodextrin (β-CD) as outer shell for the conjugated particles. The formation of inclusion complex between magnetite nanoparticles and the cyclic molecules of β-CD, as reported in (Bocanegra-Diaz et al. 2003), is avoided due to the bigger size (over 4 nm) of the magnetic particles. Thus, cyclodextrin's cavity retains its unique properties and can be used for future biomedical applications.

Experimental

The ferrofluids examined are based on hybrids between TMAOH/β-CD coating and magnetite monodomain particles (with 30 nm and 5 nm average particle size (patent BG, 2003)). The wet precipitate (with 100 mg magnetite fraction per 1 g wet precipitate) was mixed with 1 ml of surfactant—tetramethylammonium hydroxide—$N(CH_3)_4OH$- and then homogenised by intensive stirring. A subsequent dilution was performed, using 10^{-2}M water solution of β-cyclodextrin. The ferrofluids thus obtained were heated and stirred for 20 min. The experiment was conducted at atmospheric pressure and room temperature.

The XRD data exhibited consistently a single-phase spinel structure for the samples examined. The Scherrer formula applied to the $< 311 >$ line was used to calculate the average particle size (Nedkov et al., 2006). Previously conducted Mössbauer investigations confirmed magnetite's magnetic properties (Vandenberghe et al. 2005). Heating experiments were performed in a simple arrangement using a coil of three windings. The *ac* field was generated by means of a homemade generator with a power of 10 kW (40 kHz). The temperature was measured by Cu-Constantan thermocouples placed at different distances from the heating source.

Results and discussions

The process of "hyperthermia" is observed in highly viscous media containing nanosized magnetic particles, the so-called ferrofluids. Figure 1 illustrates the hyperthermia effect in the two types of ferrofluids studied. It is obvious that the magnetite's magnetic properties are the reason for the different processes of energy dissipation in the two types of ferrofluids. The hyperthermia effect is considerably better expressed (ΔT) in monodomain particles that have no superparamagnetic properties at the respective temperatures. In both types of ferrofluids we observed hyperthermia upon applying an *ac* magnetic field with frequency 40 kHz and amplitude 30 kA/m at room temperature. In the case of a fluid containing non-superparamagnetic particles, the temperature difference, ΔT, due to the application of an external electromagnetic field was larger. The maximal ΔT upon irradiation with duration of about 12 min for the non-superparamagnetic particles was 12 °C, while for the superparamagnetic ones it was 3.5 °C.

Using Magnetic Force Microscopy (MFM) we studied the homogeneity and the particles size distribution in the fluid with non-superparamagnetic behavior. In contrast with the behavior of the superparamagnetic one, this ferrofluid preserves its magnetic characteristics at room temperature, even in the absence of external magnetic field. That can lead to a number of side effects like agglomeration of the particles. Simple calculations, using MFM statistics

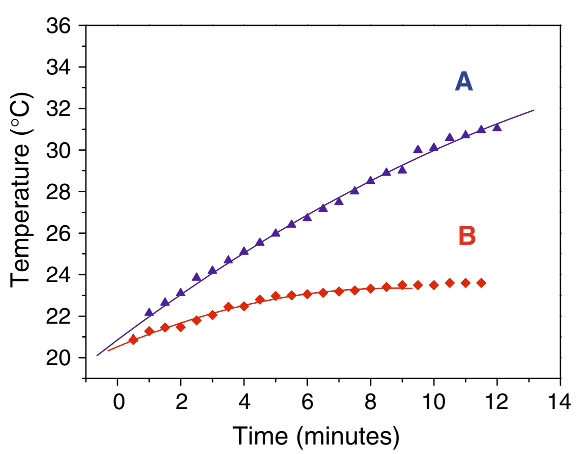

Fig. 1 Effect of hyperthermia in ferrofluids based on A non-SPM monodomain hybrid particles Fe_3O_4/β-CD and B, on SPM particles

(Table 1) show that some 96% of the particles in the fluid are with sizes below 30 nm, thus confirming good homogeneity of the material. The rest 4% of the particles are in a cluster form, reaching sizes up to 67 nm, due to agglomeration. The presence of such aggregates gives us reason to believe that applying such fluids in vivo for accumulation in tumor cells will be hindered by the clusters' large size, in spite of the stronger dissipative processes and, respectively, the larger ΔT. Nevertheless, the persentige observed of larger particles (4%) in the fluid is much smaller than we anticipated. We presume that the bigger the particles, the bigger the probability for them to loose their colloidal stability and to precipitate. That is precisely what was observed: Figs. 2 and 3 presents respectively MFM and TEM images of large clusters with sizes around 0.4 µm. found in precipitate, sedimented from the fluid in the first 48 h. Such formations were not observed for the SPM particles. We link the behavior of the non-SPM particles with their better expressed dipol interactions, which in cases of local piling of particles leeds to the formation of clusters.

The heating of magnetic nanoparticles is due to the movement of the magnetic moment away from the crystal axis called the Néel mode ($\tau_N = \tau o \ exp \ KV/kBT$) and to the oscillation of the whole nanoparticle, called the Brownian mode ($\tau_B = 4\pi\eta r2/kBT$). It is a strong function of the size of the nanoparticles (Rosensweig 1982). These two relaxation effects cause a mechanical motion and friction with the media so that heat is released. When an *ac* electromagnetic field is applied to the system (medium/discretely dispersed particles), the particle rotate so as the total magnetic moment is oriented along the easy magnetization axis and begins a motion of precession along the magneto-crystalline anisotropy, with a certain time of relaxation (Néel's relaxation). When the observation time of the electromagnetic measurements is

Table 1 MFM statistical data (from A)

	Mean	Minimum	Maximum	Sigma
Height (nm)	2.016	1.070	7.446	0.958
Area (nm^2)	452.95	15.259	3524.8	674.39
Diameter (nm)	20.174	4.408	66.992	13.028
Length (nm)	25.660	5.524	82.124	15.652
Width (nm)	15.832	5.524	63.355	10.807

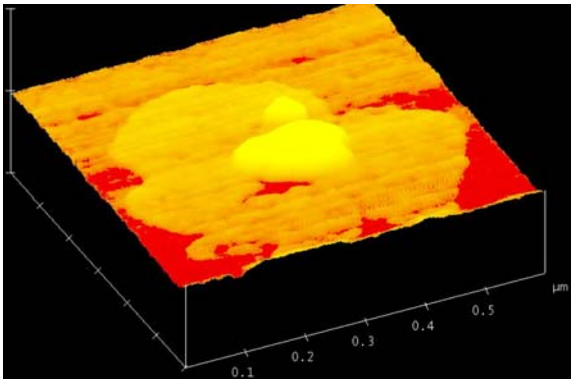

Fig. 2 MFM of agglomerate containing monodomain non-SPM magnetite (from A)

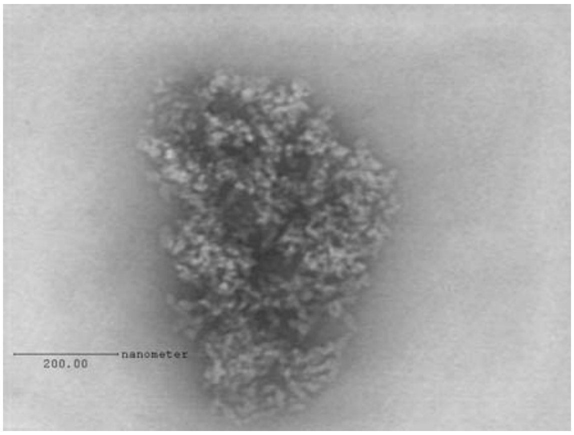

Fig. 3 HRTEM of agglomerate containing monodomain non-SPM magnetite (from A)

comparable to the resonance frequency of the magnetic particles in the fluid, f_r, then the M relaxes during the measurement and the phenomenon known as "magnetic viscosity" appears. The magnetization as a function of time after an *ac* field is applied is as follow (Dormann et al. 1997):

$$M(\tau) = M_0\left(1 - \int_0^E e^{f^\tau} n(E)dE\right) \quad (1)$$

where *n(E)dE* is the fraction of particles having an energy between *E* and *E-dE*. The existence of so-called "boundary effect" (Dormann et al. 1997) in the magnetic nanoparticles leads to a decrease in the particles' magnetization in comparison with that of bulk magnetite. Our previous investigation (Nedkov et al. 2006) shows that to a depth of about 3 nm the nanoparticles have a quasi-maghemite structure. The magnetic characterisation of the particles in the fluids show that as the particles size diminishes, the effective surface augments its share and exerts increasing influence on the nanoparticles magnetic properties. This has a strong impact on the hyperthermia effect of the ferrofluids. It is obvious that the magnetite's magnetic properties are the reason for the different processes of energy dissipation in the two types of ferrofluids. The hyperthermia effect is considerably better expressed $\Delta(T)$ in monodomain particles that have no superparamagnetic properties at the respective temperatures. In contrast with the SPM particle, however, the non-SPM one preserves its magnetic behaviour at room temperature in the absence of an external electromagnetic field. This can lead to a number of side effects, such as aggregation (Figs. 2 and 3), dipole interactions, etc., which can hamper the possible bio-applications of such particles. This is an issue that still remains in the domain of theoretical disputes between scientists active in the field of magnetism of the nanosized state, as clear quantitative experimental data are lacking on the respective contributions of the monodomain SPM and non-SPM particles to the hyperthermia effect.

Conclusions

Ferrofluids based on two types of hybrid particles Fe_3O_4/β-CD, with monodomain non-superparamagnetic and with superparamagnetic magnetite are investigated. Strong dependence of the hybrid particles' magnetic properties on their size and homogeneity was found. In both types of ferrofluids we observed hyperthermia upon applying an *ac* electromagnetic field with frequency 40 kHz and amplitude 30 kA/m. In the case of a fluid containing non-superparamagnetic particles, the temperature difference, ΔT, due to the application of an external electromagnetic field was larger for the same τ. The maximal ΔT upon irradiation with duration of about 12 min for the non-superparamagnetic particles was 12 °C, while for the superparamagnetic ones it was 3.5 °C. In the fluid conteining non-SPM particles cluster formation was observed with sizes of up to 67 nm, which tend to grow with time, as seen in the precipitate examined. The presence of such aggregates gives us reason to believe that applying such fluids in vivo for accumulation in tumor cells can in spite of the stronger dissipative processes be hindered by the large size of the clusters, and the larger ΔT respectively.

Acknowledgements This work was supported by Bulgarian National Science Fund under TH-1/01 in co-operation with CNRS, France and FWO—Flanders, Belgium.

References

Aharoni A, Jakubovocs JP (1988) Cylindrical domains in small ferromagnetic spheres with cubic anisotropy. IEEE Trans Magn 24:1892

Bahadur D, Giri Jyotsnendu (2003) Biomaterials and magnetism. Biomater magn 28:639

Bocanegra-Diaz A, Mohallem NDS, Sinisterra RD (2003) Preparation of a ferrofluid using cyclodextrin and magnetite. J Braz Chem Soc 14(6):936–941

Dormann JL, Fiorani D, Tronc E (1997) Magnetic relaxation in fine-particle systems. Adv Chem Phys 98:283

Nedkov I, Merodiiska T, Slavov L, Vandenberghe RE, Kusano Y, Takada J (2006) Surface oxidation, size and shape of nano-sized magnetite obtained by co-precipitation. J Magn Magn Mater 300:358–367

Patent (2003) BG No 107837/22.05.2003

Rosensweig RE (1982) Magnetic fluids. Sci Am 247:136

Vandenberghe RE, Merodiiska T, Nedkov I, Slavov L (2005) Surface oxidation control of nano-sized magnetite and Mössbauer measurements. Hyperfine Interact 165:267–271