Tunable size Ln:$BaGdF_5$ (Ln= Eu^{3+} and Nd^{3+}) nanoparticles. Luminescence, magnetic properties, and biocompatibility

D. González Mancebo,[1] E. Cantelar[2], F. Cussó,[2] G. Stepien,[3]
J.M. de la Fuente,[4] M. Ocaña[1] and A.I. Becerro[1]

[1]Instituto de Ciencia de Materiales de Sevilla (CSIC-US). c/ Américo Vespucio, 49, 41092 Seville (Spain).
[2]Dpto. Física de Materiales, C-04. Universidad Autónoma de Madrid, 28049 Madrid (Spain).
[3]Instituto de Nanociencia de Aragón, Univ. Zaragoza. c/ Mariano Esquilor s/n. 50018 Zaragoza (Spain)
[4]Instituto de Ciencia de Materiales de Aragón, (CSIC/UniZar), C/ Pedro Cerbuna, 12. 50009 Zaragoza (Spain)

Contact e-mail: anieto@icmse.csic.es

Abstract

Lanthanide-doped rare earth fluoride nanoparticles (NPs) have become a research focus in the last few years in the biomedical field because of their interesting luminescent properties which confer to them important applications as biosensors and optical bioprobes.[1,2] In comparison with oxygen-based systems, fluorides possess very low vibrational energies, which helps to improve their luminescence emission.[3] Among the fluoride systems, the Ln:$BaGdF_5$ compositions (Ln= optically active lanthanide ion) shows, apart from their excellent luminescent properties, interesting added advantages due to the properties of both, Ba^{2+} and Gd^{3+} ions. The former show a large k-edge value as well as high X-ray mass absorption coefficients, which allows Ba-based NPs to be optimal contrast agents for X-ray computed tomography (CT).[4] On the other hand, Gd^{3+} ions show a large magnetic moment and nanoseconds electronic relaxation time, which makes Gd-based NPs very useful contrast agents for magnetic resonance imaging (MRI).[5,6] Most of the synthesis methods reported up to now to obtain $BaGdF_5$ particles led either to uniform >100 nm particles[7,8] or to smaller NPs (12 – 75 nm) with ill-defined morphology or poorly dispersed.[9,10] Only the use of oleic acid as capping agent led to monodispersed $BaGdF_5$ nanospheres (3 to 10 nm).[11] The latter method required, however, the use of very high temperatures (300 ºC) and rendered hydrophobic NPs, which needed then to be acid treated to remove the oleate ligands to obtain hydrophilic NPs suitable for bioapplications.

Herein, we report the synthesis of bifunctional and highly uniform Eu:$BaGdF_5$ and Nd:$BaGdF_5$ NPs using a solvothermal method consisting in the aging at 120 °C of a glycerol solution containing Ln (Gd, Eu and Nd) acetylacetonates (acac) as the Ln source, $Ba(NO_3)_2$ as the Ba source, and the ionic liquid butylmethylimidazolium tetrafluoroborate ([BMIM]BF_4) as the source of fluoride anions. Both the acac and the ionic liquid allowed the controlled release of ions into the solution thus allowing the precipitation of uniform, spherical NPs, without the need of a capping agent. The NP diameter could be tuned from 45 nm to 85 nm, depending on the cations concentration of the starting solution (Fig. 1). The obtained NPs showed a hydrophilic surface due to the absence of surfactants or oleic acid in the reaction medium. The NPs were bifunctional because they showed both optical and magnetic properties. The optical properties were due to the doping ions Eu^{3+} and Nd^{3+} which were selected here for the following reasons: The luminescence of Eu^{3+} is located in the red region of the electromagnetic spectrum, where the auto-fluorescence of tissues is minimal, while Nd^{3+} is excited and emits within the second biological window (1000-1400 nm), in which the radiation is only weakly attenuated by tissues thus improving the sensitivity of the assays. The luminescence decay curves of the nanospheres doped with different amounts of Eu^{3+} and Nd^{3+} were recorded in order to determine the optimum dopant concentration in each case, which resulted to be 5% Eu^{3+} and 0.5% Nd^{3+} (Fig. 2). On the other hand, the presence of the paramagnetic gadolinium ion conferred the NPS with interesting magnetic properties. In this sense, proton relaxation times were measured at 1.5 T in water suspensions of the optimum particles found in the luminescence study. Both NPs types (5%Eu:$BaGdF_5$ and 0.5%Nd:$BaGdF_5$) exhibited r_2/r_1 values lower than 5, which suggest that they could be used as positive contrast agents for MRI. Finally, it was demonstrated that both the 5% Eu^{3+} and 0.5% Nd^{3+}-doped $BaGdF_5$ NPs showed negligible cytotoxicity for VERO cells for concentrations up to 0.25 mg mL^{-1} (Fig. 3).

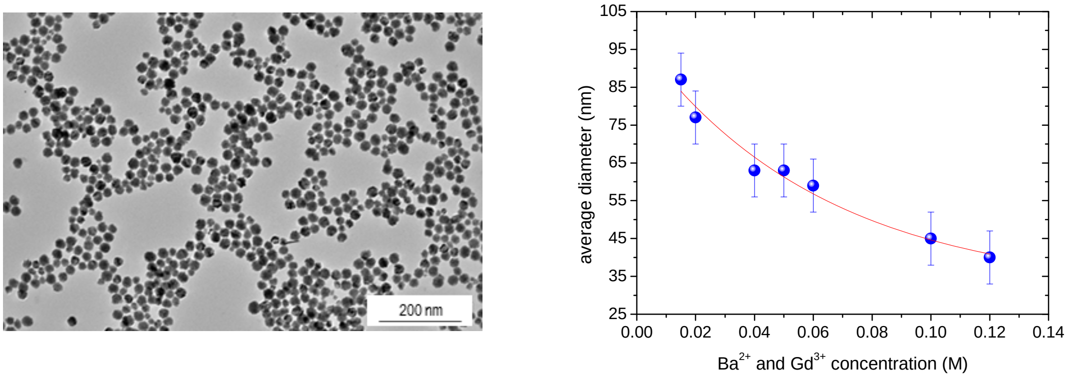

Figure 1: <u>Left</u>*:* TEM micrograph showing uniform spherical (~45 nm diameter) NPs. *<u>Right:</u>* Exponential decay of the average diameter of the particles with increasing Gd^{3+} and Ba^{2+} concentrations.

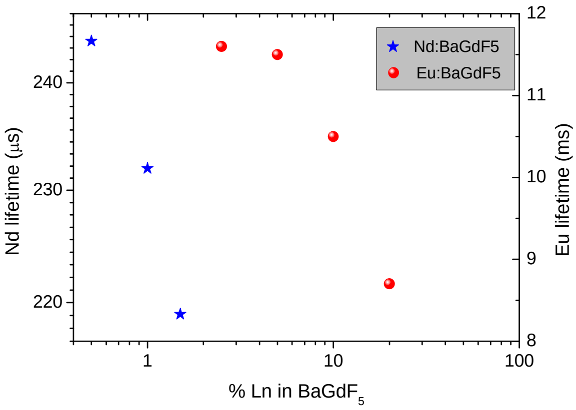

Figure 2: Evolution of the average lifetimes, recorded at the dominant emission of Nd^{3+} and Eu^{3+}, with the ion contents.

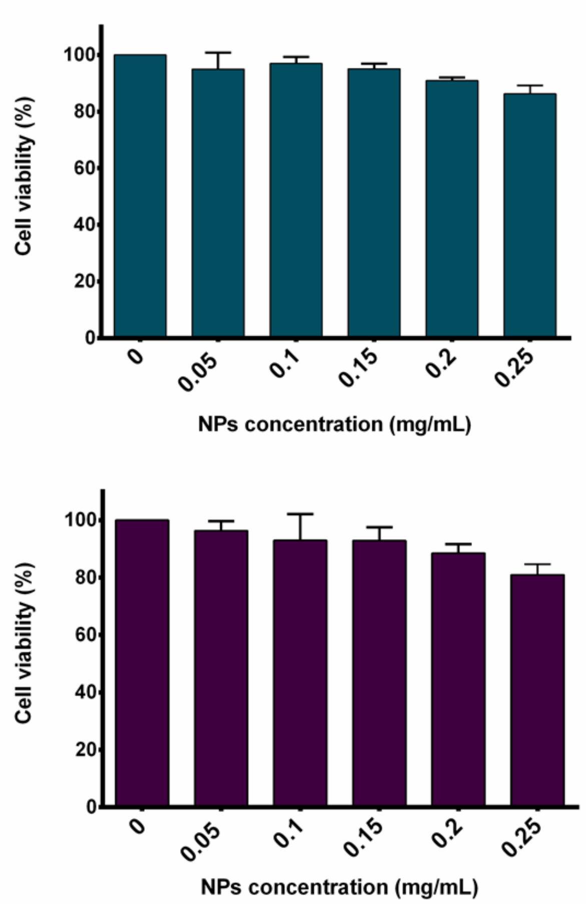

Figure 3: Cytotoxicity profiles of 5% Eu^{3+} and 0.5%Nd^{3+}-doped $BaGdF_5$ NPs (top and bottom, respectively) with Vero cells, determined by MTT assay. Percentage of viability of cells was expressed relative to control cells (n = 5). Results are represented as mean ± standard deviations.

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