

Multifunctional Core-Shell Fe-MgO Nanospheres for biomedicine

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There have been major advances in the availability of magnetic nanoparticles (Nps), both in quality and quantity, which in turn stimulated the worldwide pursuit of NPs for technological applications in fields as diverse as high density memory devices, spintronics or biotechnology. For instance, iron oxide nanoparticles have proven for several decades to be promising for biomedical applications such as tissue engineering, magnetic resonance imaging (MRI), magnetic separation of biological materials, and heating mediators for cancer therapy [R. K. Gilchrist, et al. *Ann. Surg.* 146 (1957) 596]. But in spite of the encouraging progress, expectations have not been fully accomplished: most of the magnetic nanoparticles intended to-date have the disadvantage of either being bio-incompatible or not providing a large enough magnetic stray field for high-resolution detection schemes. The first problem is the poisonous character of pure 3d and 4f ferromagnetic metals and the second one the superparamagnetic fluctuations at the ambient detection temperatures.

One promising solution for overcoming these issues is the development of core-shell structures in which the shell will provide chemical stability and biocompatibility while maintaining the magnetic properties of the core. Here we report on Fe(Co) particles covered by a uniform 3 nm thick MgO epitaxial shell. Among commonly used schemes, we followed simple physics-derived solutions based on gas-aggregation methods that assure industrial scalability and ecology. Nearly spherical crystals with negligible shape anisotropy were obtained [Fig. 1]. MgO forms a continuous and epitaxial shell over the Fe islands, providing exceptional advantages such as environment stability, controlled interparticle interactions, and non-toxic hydroxyl surface groups that would allow for surface attachment of drugs or biomolecules. Hysteresis loops show a much stronger magnetic response (210 emu/g_{Fe}) than any composite material produced up to now involving magnetic nanoparticles encapsulated in inorganic matrices. Worthy, no diminish of the properties was detected over several months' storage under ambience conditions.

To elucidate whether our system is appropriate for *in-vivo* applications, the particles were dispersed in a biological suspension with 7.4 pH. *In-vitro* studies exploring the toxicity of the nanoparticles in 3T3 fibroblast cells and mouse cortical neurons cultures will be presented. Worthy, *in vitro* cultures remained healthy for 72h with solutions above 1 mM total-metal molar concentration. After these encouraging results, the Nps were used in veterinarian trials in mice as MRI contrast agents. In comparison to paramagnetic ion chelates and superparamagnetic iron oxides, our ferromagnetic NPs show higher molar relaxivities and may offer advantages at low concentrations. Thanks to the ferromagnetic character of the NPs, biodistribution could be easily evaluated through magnetic measurements of *ex-vivo* tissue [Fig. 2], from which urinary excretion is considered as possible clearance pathway. Besides, experiments will be presented on the RF-power absorption efficiency so that the performance of the final pharmaceutical product for magnetic cancer hyperthermia treatment can be evaluated.

Figures:

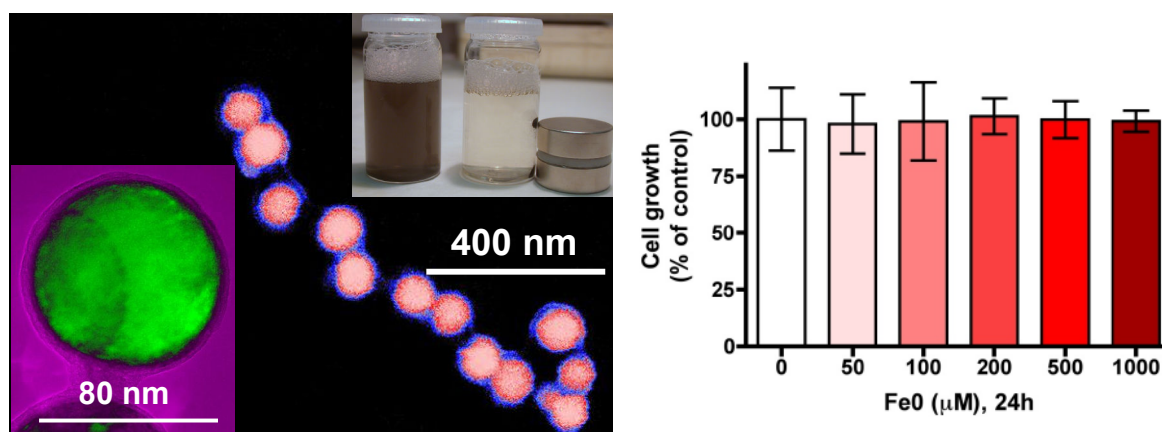


Fig. 1. On the left, electron micrograph of a chain of magnesia-coated Fe with average diameter close to 75 nm. Before these NPs can act as contrast agents, they must be stabilized in water at physiological pH. Inset shows the feasibility of magnetic separation in suspensions. On the right, fibroblast cell cultures demonstrate no toxic response.

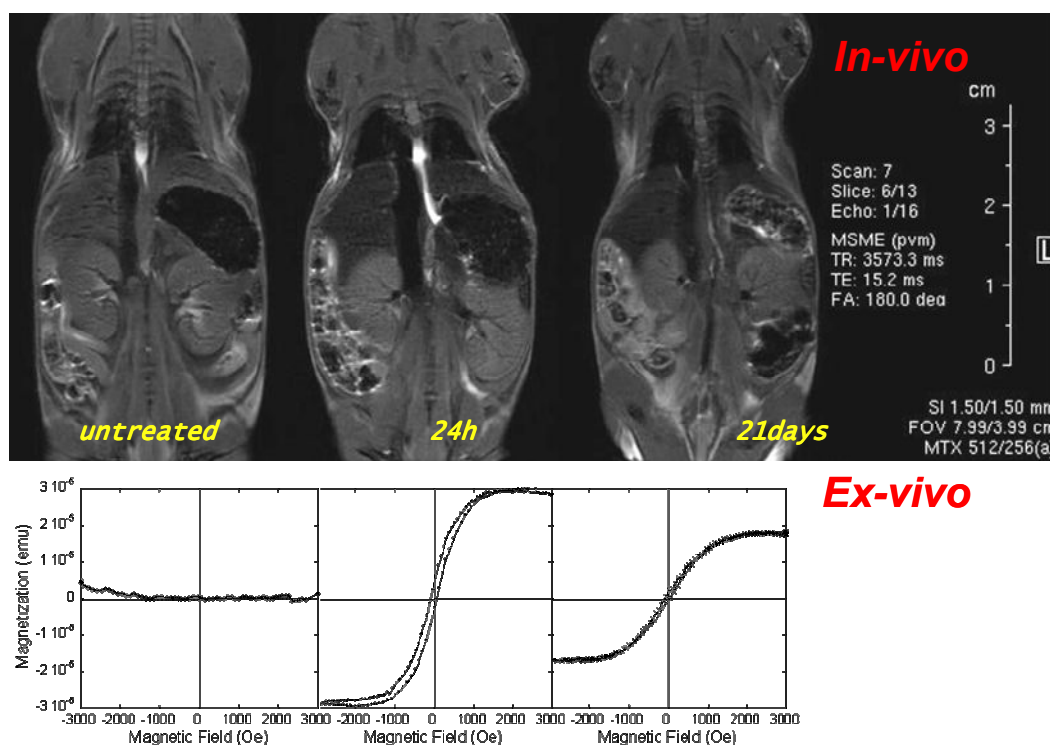


Fig. 2. In vivo 7 Tesla Bruker MRI T2-weighted images of mice injected with NPs (upper) and magnetic estimation of hepatic iron concentration measured from postmortem liver tissue (300K). Authors acknowledge the Servei de Resonancia Magnètica Experimental from IDIBAPS (Barcelona) for MRI measurements.