Magnetic liposomes based on nickel ferrite and manganese ferrite nanoparticles for biomedical applications

Ana Rita O. Rodrigues^{1*}, José M. F. Ramos¹, B. G. Almeida¹, I. T. Gomes^{1,2}, J. P. Araújo², E. M. S. Castanheira¹, P. J. G. Coutinho¹

¹CFUM - Centro de Física, Univ. do Minho, Campus de Gualtar, 4710-057 Braga, Portugal ²IFIMUP/IN - Instituto de Nanociência e Nanotecnologia, R. Campo Alegre, 4169-007 Porto, Portugal *ritarodrigues@fisica.uminho.pt

Magnetoliposomes (liposomes entrapping magnetic nanoparticles) are of large importance in drug delivery, as they can be guided and localized into the therapeutic site of interest by external magnetic field gradients and used in cancer treatment by hyperthermia [1,2].

In this work, nickel ferrite and manganese ferrite nanoparticles were synthesized by coprecipitation method. The systems were characterized by SEM, AFM, DLS, XRD and EDX. The magnetic properties were measured by SQUID. Both types of nanoparticles exhibit superparamagnetic behavior at room temperature (with coercive fields of 12 Oe for nickel ferrites and 6 Oe for manganese ferrites), being suitable for biomedical applications.

The resulting magnetic nanoparticles were either covered with a lipid bilayer, forming dry magnetoliposomes (DMLs), or entrapped in liposomes, originating aqueous magnetoliposomes (AMLs). Dry magnetoliposomes synthesis, based on a new promising route, results in two lipid layers surrounding one or more nanoparticles. This structure was confirmed by FRET (Förster Resonance Energy Transfer) measurements between the fluorescent-labeled lipids NBD-C₁₂-HPC (NBD acting as donor) included in the second lipid layer and rhodamine B DOPE (acceptor) in the first lipid layer. An average donor-acceptor distance of 3.1 nm was estimated.

Preliminary assays of the non-specific interactions of magnetoliposomes with biological membranes (modeled using giant unilamellar vesicles, GUVs) were performed. Membrane fusion between the magnetoliposomes and GUVs was confirmed by FRET between the labeled lipid NBD-C₁₂-HPC (donor) and the hydrophobic dye Nile Red (acceptor) (Figure 1).

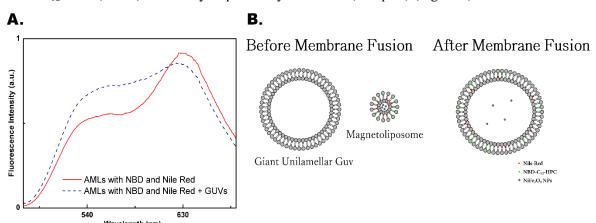


Figure 1. A: Fluorescence spectra of AMLs (containing nickel ferrite NPs) labeled with Nile Red and NBD- C_{12} -HPC, before (—) and after (– –) interaction with GUVs. B: Schematic representation.

Acknowledgements: FEDER through the COMPETE Program and FCT in the framework of CFUM Strategic Project [PEst-C/FIS/UI0607/2011 (F-COMP-01-0124-FEDER-022711)]; MAP-Fis PhD Programme for support; FCT and POPH/QREN for A.R.O. Rodrigues PhD grant (SFRH/BD/90949/2012).

- [1] Lubbe, A. S.; Bergemann, C.; et al., D. G.; J. Magn. Magn. Mat. 1999, 194, 149-155.
- [2] Dandamudi, S.; Campbell, R. B.; *Biomaterials* **2007**, 28, 4673-4683.