

Ultra-high transversal relaxivity and hyperthermia-induced drug delivery in superparamagnetic solid lipid nanoparticles

Carolina L. Moura^{1,2}, Juan Gallo², Nágila M. P. S. Ricardo¹ and Manuel Bañobre-López²

¹Department of Organic and Inorganic Chemistry, Federal University of Ceará, CX 12200 Fortaleza, Brazil.

²Advanced (magnetic) theranostic nanostructures Group, International Iberian Nanotechnology Laboratory, INL, Braga, Portugal.

manuel.banobre@inl.int

Abstract

Magnetic hybrid self-assemblies have been found to open new perspectives for biomedical and environmental applications [1]. In particular, solid lipid nanoparticles (SLNs) have received great interest as suitable bioactive encapsulating agents and carriers due to their biocompatibility, low toxicity and ability to influence the bioactive delivery profile [2,3]. Recently, hybrid organic-inorganic solid lipid nanocomposites have been explored as a synergistic approach that combines the modified bioactive release induced by the lipidic encapsulation and the intrinsic physico-chemical properties from the inorganic counterpart [4]. In this context, magnetic solid lipid nanocomposites (MSLNs) dual loaded with a bioactive compound and superparamagnetic iron oxide nanoparticles (SPIONs) were obtained showing good multifunctional performance as improved T₂-contrast agents and heat generating sources in magnetic resonance imaging (MRI) and magnetic hyperthermia (MH), respectively.

A method based on oil-in-water emulsions was employed to prepare SLNs from carnauba wax containing different concentration of ~10 nm superparamagnetic oleic acid coated magnetite (Fe₃O₄@OA) nanoparticles. Successful incorporation of the magnetic nanoparticles was confirmed by transmission electron microscopy (TEM), and the results showed that they accumulate preferentially inside the organic lipidic core. Dynamic light scattering (DLS) and ζ-potential measurements showed a relatively narrow size distribution of spherical-shaped magnetic nanocomposites with an average particle size of ~180 nm and a surface charge around -60 mV. In terms of magnetic characterization, hysteresis loops showed MSLNs to behave as superparamagnetic particles. Interestingly, MSLNs showed an anomalous ultra-high transversal relaxivity (r₂) with values higher than 900 mM(Fe)⁻¹s⁻¹, what clearly translated into dark contrast effects when sample phantoms were imaged at 3 T. On the other hand, an anticancer drug was encapsulated and its delivery profile assessed without and with the application of an oscillating magnetic field (MH). MH resulted to be efficient to externally induce a drug release increase. *In vitro* results will be also shown and discussed.

References

- [1] C. Sanson, O. Diou, J. Thévenot, E. Ibarboure, A. Soum, A. Brûlet, S. Miraux, E. Thiaudière, S. Tan, A. Brisson, V. Dupuis, O. Sandre and S. Lecommandoux. *ACS Nano*, **5** (2011), 1122.
- [2] W. Mehnert and K. Mader., *Adv. Drug Delivery Rev.* **47** (2001), 165.
- [3] E. Andreozzi, P. Wang, A. Valenzuela, C. Tu, F. Gorin, M. Dhenain and A. Louie, *Bioconjugate Chem.*, **24** (2013), 1455.
- [4] K. Oumzil, M. A. Ramin, C. Lorenzato, A. Hemadou, J. Laroche, M. J. Jacobin-Valat, S. Mornet, C.-E. Roy, T. Kauss, K. Gaudin, G. Clofent-Sanchez and P. Barthelemy, *Bioconjugate Chem.*, **27** (2016), 569.

Acknowledgment: Edital CAPES/INL.

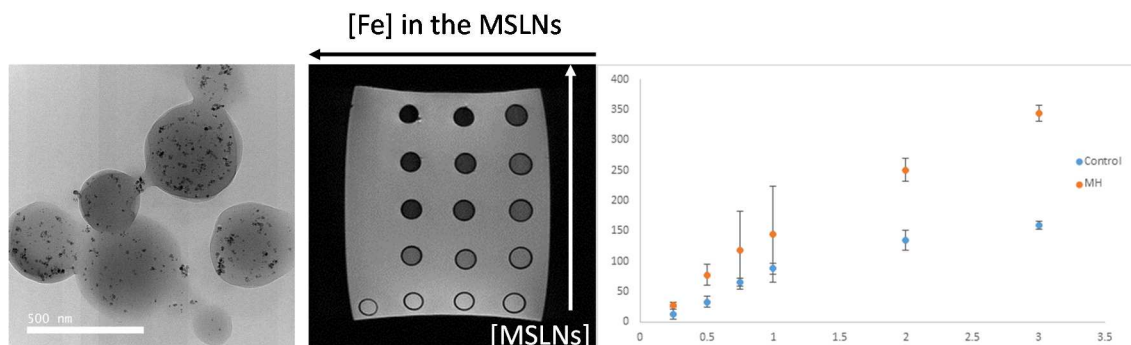


Figure 1: (left) TEM image of MSLNs; (middle) T₂-weighted MRI image of MSLNs; (right) Drug delivery profiles without and with applying MH.