Novel magnetoliposomes based on shape-anisotropic nanoparticles for combined chemotherapy and magnetic hyperthermia

Beatriz D. Cardoso[a], Ana R. O. Rodrigues[a], Manuel Bañobre-López[b], Bernardo G. Almeida[a], Carlos O. Amorim[c], Vítor S. Amaral[c], Paulo J. G. Coutinho[a], Elisabete M. S. Castanheira[a]

[a] *Centre of Physics (CFUM), University of Minho, Campus de Gualtar, 4710-057 Braga, Portugal*

[b] *Advanced (magnetic) Theranostic Nanostructures Lab, Life Sciences Department, INL – International Iberian Nanotechnology Laboratory, 4715-330 Braga, Portugal*

[c] *Physics Department and CICECO, University of Aveiro, Campus de Santiago, 3810-193 Aveiro, Portugal*

beatrizdiascardoso94@gmail.com

Solid magnetoliposomes (SMLs) are multifunctional lipid nanocarriers urging as a promising therapeutic approach for cancer therapy. These nanocarriers allow the encapsulation of therapeutic drugs, improving their pharmacokinetics and associated pharmacodynamics while enabling their magnetic-controlled release. In this work, a new method for magnetoliposomes synthesis with improved and adequate structural, physicochemical and magnetic properties was developed. Shape-anisotropic cubic calcium-substituted magnesium ferrite nanoparticles ($Ca_{0.25}Mg_{0.75}Fe_2O_4$) were synthesized and characterized, revealing high saturation magnetization (50.07 emu/g at 300 K) and heating abilities. The synthesized nanoparticles were covered with lipid bilayers of different compositions (DPPC, DPPC/Ch and DPPC/DSPE-PEG), originating SMLs with optimal sizes for *in vivo* applications (around or below 150 nm) and low polydispersity index. SMLs revealed high efficiencies of Doxorubicin encapsulation and to reduce its interaction with human serum albumin, highly contributing for a prolonged bioavailability of the drug upon systemic administration.

The overall results confirmed the development of a promising new method for the synthesis of cubic-shaped magnetic ferrite nanoparticles and a novel route for drug-loaded SMLs with improved features. The properties of these multifunctional nanosystems point to their future effective application in cancer therapy.