Development of nickel-based magnetoliposomes

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

In this work, magnetic nanoparticles of nickel core with silica shell were prepared by soft chemical methods, using tetraethyl orthosilicate (TEOS) and different surfactants as templating media. Magnetic nickel ferrite nanoparticles were also prepared by coprecipitation method.

These 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-C_6-HPC (NBD acting as donor) included in the second lipid layer and rhodamine DHPE (acceptor) in the first lipid layer. A FRET efficiency of 31% was obtained from which an average donor-acceptor distance of 7.6 nm was estimated. This distance is comparable to the typical thickness of lipid bilayer.

The systems were characterized by Dynamic Light Scattering (DLS) and SEM. SEM images of the dry magnetoliposomes (Figure 1) show that they are approximately uniform in size (diameter between 58 nm and 76 nm). The magnetic properties of the nickel nanoparticles were also evaluated by SQUID, showing a typical ferromagnetic behavior with a coercive field of 80 Oe (Figure 2), which is lower than the coercive fields obtained for Ni nanoparticles prepared by similar methods [3].

The non-specific interaction between the prepared magnetoliposomes and models of biological membranes was investigated. Giant Unilamellar Vesicles (GUVs) were used as membrane models. Membrane fusion between the aqueous magnetoliposomes and the GUVs was confirmed by FRET between the labeled lipid NBD-C_6-HPC (donor) and the hydrophobic dye Nile Red (acceptor). When both donor and acceptor are incorporated in the same vesicle, efficient energy transfer is observed. Upon fusion of the aqueous magnetoliposomes with GUVs, the membrane size increases, rising the donor-acceptor average distance, with a consequent decrease in energy transfer efficiency from the NBD moieties to Nile Red (Figure 3) [4].

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Figures

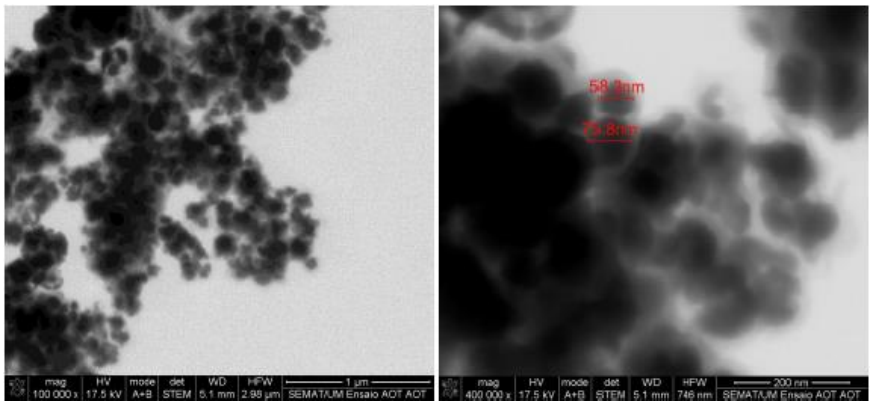

Figure 1. SEM images of dry magnetoliposomes of nickel nanoparticles covered by the double chain surfactant AOT (sodium bis(2-ethylhexyl) sulfosuccinate).

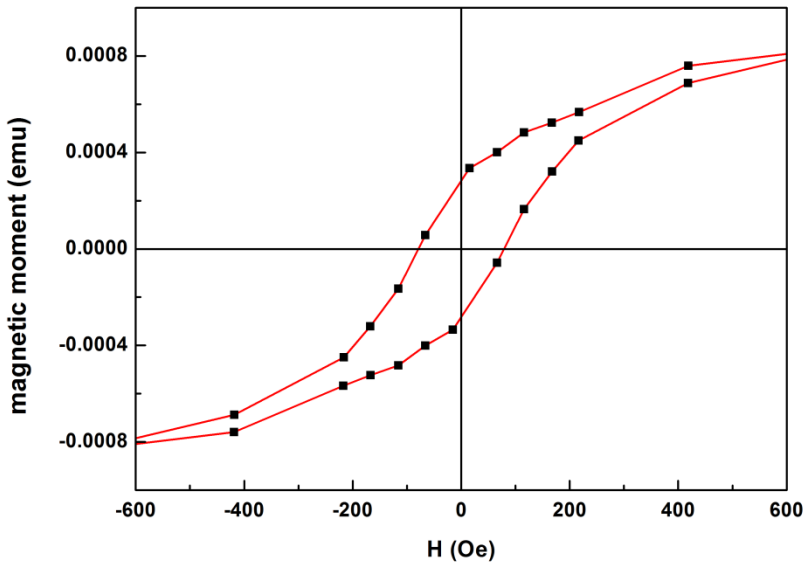

Figure 2. Hysteresis loop of Ni nanoparticles at room temperature obtained by SQUID.

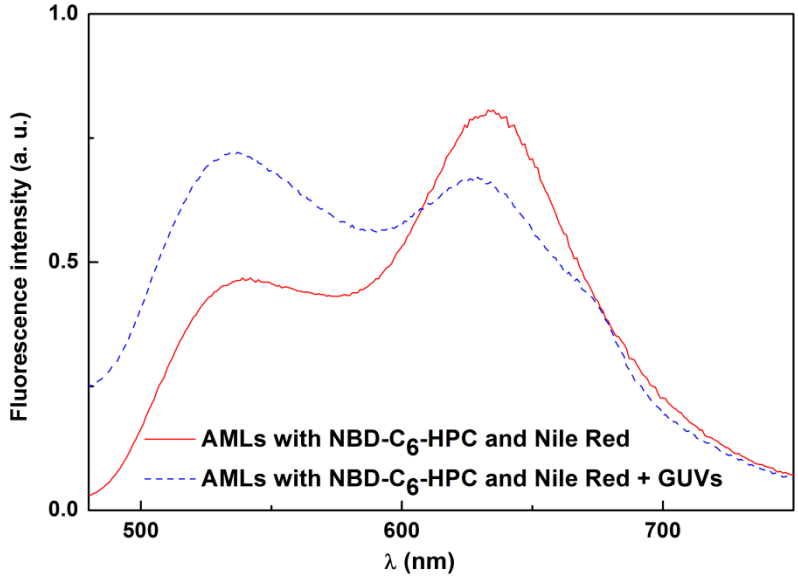

Figure 3. Fluorescence spectra (λ_{exc}=400 nm) of AMLs of egg-phosphatidylcholine with Ni/silica core/shell nanoparticles with Nile Red (2×10^{-6} M) and NBD-C_6-HPC (10^{-6} M); and with GUVs.