New magnetogels based on manganese ferrite nanoparticles and self-assembled peptide hydrogels as drug nanocarriers

Sérgio R. S. Veloso,[a] Ana Rita O. Rodrigues,[a] J. A. Martins,[b] Paula M. T. Ferreira,[b] Elisabete M. S. Castanheira[a]

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

Peptide-based hydrogels are an important class of biomaterials with a wide range of applications, which include among others drug delivery, tissue engineering, *in vivo* imaging and template materials. Particularly, self-assembled biocompatible peptide-based hydrogels have been successfully synthesized and evaluated as nanocarriers for antitumor drugs [1,2].

The incorporation of magnetic nanoparticles in these biocompatible nanosystems, forming nanomagnetogels, will allow their concentration in the therapeutic sites by magnetic forces, allowing the guided transport of anticancer drugs, most of them toxic and with systemic side effects. Therefore, a promising application of these nanomagnetogels in cancer therapy is anticipated, through synergystic magnetically-guided drug delivery and hyperthermia [3,4].

In this work, superparamagnetic manganese ferrite ($MnFe_2O_4$) nanoparticles (Fig. 1), synthesized as previously described [5], were successfully incorporated in self-assembled peptide-derived hydrogels. The new magnetogels were tested as nanocarriers for two fluorescent drugs, curcumin (an anticancer and neuroprotective drug) and a new antitumor thienopyridine derivative [6]. Fluorescence-based techniques (fluorescence emission, FRET and fluorescence anisotropy) were used to assess incorporation of these drugs in the magnetogels and their transport towards models of biological membranes. For that purpose, small unilamelar vesicles (SUVs) of lecithin/cholesterol 7:3 were used as membrane models. Delivery of drugs towards SUVs was monitored through FRET assays from the fluorescent drug (acting as the energy donor) and the dye Nile Red (energy acceptor) included in SUVs (Fig. 2). It can be observed that the drug moves to the model membranes upon interaction of the drug-loaded magnetogels with SUVs. These results are promising for the use of these magnetogels in dual cancer therapy, by combination of chemotherapy and magnetic hyperthermia.

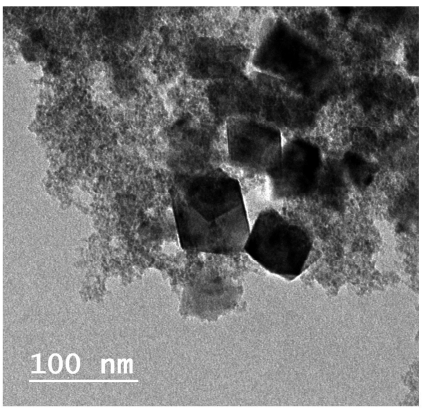

Fig. 1: TEM image of manganese ferrite nanoparticles prepared by coprecipitation method.

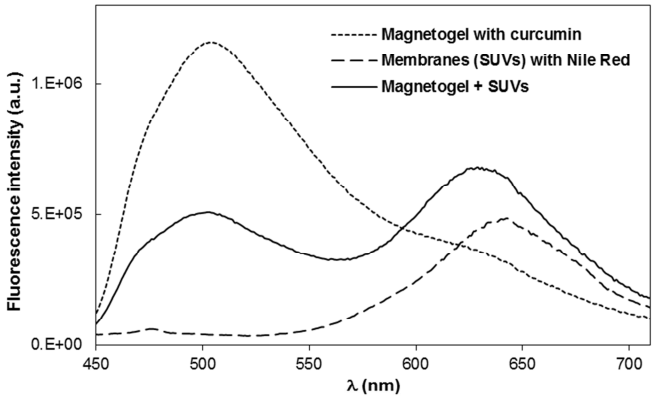

Fig. 2: Fluorescence spectra of curcumin-loaded magnetogel, model membranes (SUVs) with the dye Nile Red, and interaction showing the release of curcumin into SUVs (by FRET, exciting only curcumin).

1) H. Vilaça *et al.*, *J. Mater. Chem. B*, **2015**, *3*, 6355.
2) H. Vilaça *et al.*, *Biomacromolecules*, **2015**, *16*, 3562.
3) A. Akbarzadeh *et al.*, *Nanoscale Res. Lett.,* **2012**, *7*, 144.
4) A. Hervault, N. T. K. Thanh, *Nanoscale*, **2014**, *6*, 11553.
5) A. R. O. Rodrigues *et al.*, *RSC Advances,* **2016**, *6*, 17302.
6) C. N. C. Costa *et al., Photochem. Photobiol. Sci.*, **2014**, *13*, 1730.

Acknowledgements:

This work was supported by the Portuguese Foundation for Science and Technology (FCT) in the framework of the Strategic Funding of CF-UM-UP (UID/FIS/04650/2013) and of CQ-UM (UID/QUI/00686/2013). FCT, POPH-QREN and FSE are acknowledged for the PhD grant of A.R.O. Rodrigues (SFRH/BD/90949/2012) and for financial support to MAP-Fis Joint Doctoral Programme.