Magnetogels based on iron oxide nanoparticles and peptide hydrogels containing Naproxen and/or RGD

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Peptide-based hydrogels constitute 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, naproxen-containing peptide-derived hydrogels have been successfully synthesized and evaluated as drug nanocarriers [1,2].

The incorporation of magnetic nanoparticles in these biocompatible nanosystems, forming nanomagnetogels, will allow their concentration in the desired area of the patient's organs by magnetic forces, allowing the guided transport of biologically active substances, most of them toxic and with systemic side effects. A promising application of these nanomagnetogels in cancer therapy is anticipated, through magnetically-guided drug delivery and hyperthermia [3]. Moreover, targeted therapy is also being addressed through hydrogels with the RGD sequence (arginine-glycine-aspartic acid; Arg-Gly-Asp), recognized by integrins, these receptors being involved in the regulation of cellular proliferation and apoptosis. The integrin $\alpha_v\beta_3$ is overexpressed in some tumor cells and has been implicated in the growth of solid tumours and in the development of metastases.

In this work, iron oxide nanoparticles, with diameters around 12 nm (Fig. 1), were synthesized by coprecipitation method in aqueous solution. These nanoparticles exhibit a superparamagnetic behavior, with a coercive field of 9.7 Oe and a blocking temperature of 118 K [4].

The nanoparticles were successfully incorporated in peptide-based hydrogels containing naproxen (Npx) and/or RGD (Fig. 2). The ability of these magnetogels to act as drug nanocarriers is being investigated, aiming at developing multifunctional therapeutic nanosystems.

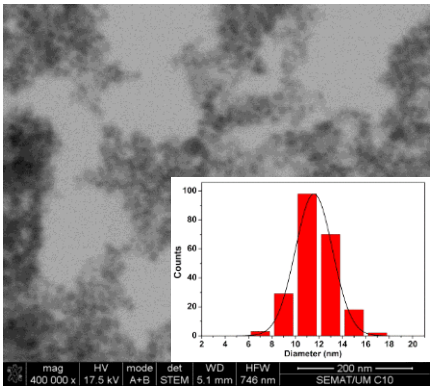

Fig. 1: SEM image of iron oxide nanoparticles. Inset: Particles size histogram and fitting to a Gaussian distribution.

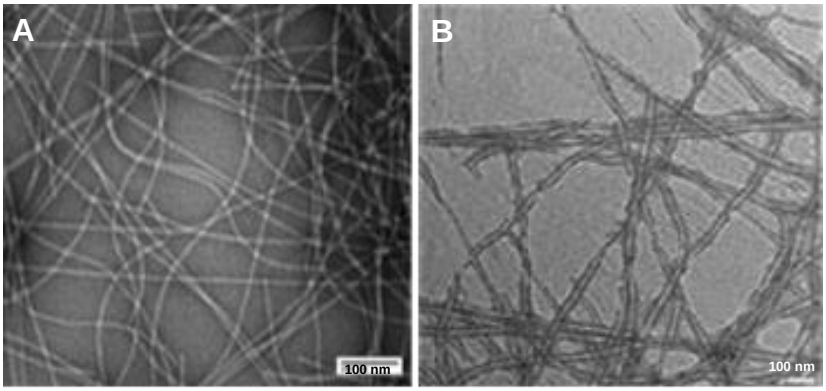

Fig. 2: TEM images of hydrogels. **A**: Npx-Phe-ΔAbu-OH. **B**: Npx-Ala-ΔPhe-Gly-Arg-Gly-Asp-Gly-OH. (Npx: Naproxen; Phe: Phenylalanine; Abu: Aminobutyric acid; Ala: Alanine; Gly: Glycine; Arg: Arginine; Asp: Aspartic acid).

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. R. O. Rodrigues *et al.*, *Coll. Surf. B,* **2017**, *in press.*

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