

New biocompatible peptide-based hydrogels as drug nanocarriers

Ana C. L. Hortelão¹, Helena Vilaça², Bruno F. C. Hermenegildo¹, Goreti Pereira², Bing Xu³, Maria-João R. P. Queiroz², José A. Martins², Paula M. T. Ferreira², Elisabete M. S. Castanheira¹

¹Centro de Física, Universidade do Minho, Campus de Gualtar, 4710-057 Braga, Portugal.

²Centro de Química, Universidade do Minho, Campus de Gualtar, 4710-057 Braga, Portugal.

³Department of Chemistry, Brandeis University, Waltham, MA, 02454 USA

*alhortelao@gmail.com

The biocompatibility of peptide-based hydrogels make them ideal for biomedical applications such as drug delivery, biosensing, tissue engineering and wound healing [1,2]. However, the enzymatic hydrolysis of these materials can be regarded as a serious disadvantage. One way to increase the biostability of this type of hydrogels consists in using non-proteinogenic amino acids. In this work, several new hydrogelators were developed, containing a Naproxen or a Naphthalene group, and their critical aggregation concentrations were determined by fluorescence. The influence of pH on the aggregation of these molecules was also investigated. TEM images revealed that these hydrogels contain entangled nanofibers, with width ranging from 9 nm to 18 nm (Figure 1).

The ability of these hydrogels to act as nanocarriers for antitumor drugs was investigated. FRET (Förster Resonance Energy Transfer) assays were performed between the several hydrogels (acting as energy donors) and a new antitumor fluorescent thienopyridine derivative [3] (acting as energy acceptor). Donor-acceptor distances between 2.5 nm and 3.5 nm were determined. The results obtained confirm that the peptide-based hydrogels can be used as drug nanocarriers.

As the antitumor compound tested is especially active against human melanoma cell lines ($GI_{50}=3.5 \mu\text{M}$) [3], these results are promising to the development of hydrogel formulations for topical application.

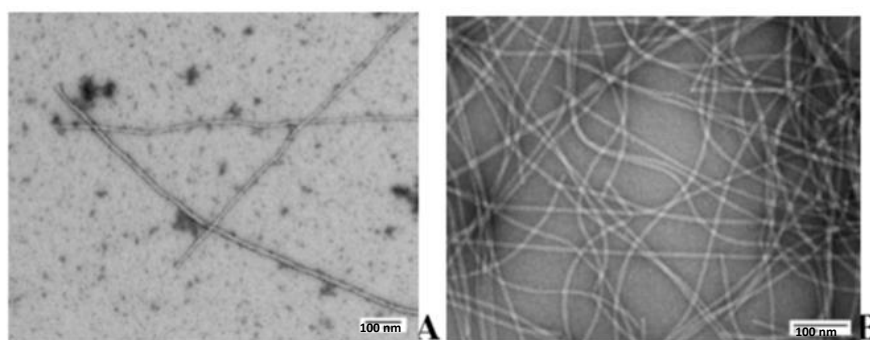


Figure 1. TEM images of two hydrogels: Npx-Phe- Δ Phe-OH (A) and Npx-Phe- Δ Abu-OH (B).

Acknowledgements: Foundation for the Science and Technology (FCT, Portugal), FEDER and QREN for financial support to the Research Centers, CFUM [PEst-C/FIS/UI0607/2013 (FCOMP-01-0124-FEDER-037291)] and CQ/UM [PEst-C/QUI/UI0686/2013 (FCOMP-01-0124-FEDER-037302)]. FCT is also acknowledged for the PhD grant of H. Vilaça (SFRH/BD/7265/2010).

[1] Zhao, F.; Ma, M. L.; Xu, B.; *Chem. Soc. Rev.* **2009**, 38, 883-891.

[2] Zhao, X.; Pan, F.; Xu, H.; Yaseen, M.; Shan, H.; Hauser, C. A. E.; Zhang, S.; Lu, J. R.; *Chem. Soc. Rev.* **2010**, 39, 3840-3898.

[3] Queiroz, M.-J.R.P.; Calhelha, R.C.; Vale-Silva, L.; Pinto, E.; Nascimento, M.S.-J.; *Eur. J. Med. Chem.* **2010**, 45, 5732-5738.