New dextrin nanomagnetogels: production, characterization and *in vivo* performance as dual modality imaging bioprobe

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Abstract

Dual modality contrast agents, such as radiolabelled magnetic nanoparticles, are promising candidates for a number of diagnostic applications, since they combine two complementing imaging modalities, namely photon emission computed tomography (SPECT) and magnetic resonance imaging (MRI). The benefit of such combination lies on the ability to interpret more accurately abnormalities *in vivo*, by integrating the high sensitivity of SPECT with the superb spatial resolution and anatomical information provided by MRI [1]. Superparamagnetic iron oxide nanoparticles (SPION) have been extensively studied as MRI contrast agents [2]. SPIONs need to be coated in order to allow formulation in aqueous solutions and to increase *in vivo* stability [3].

Dextrin nanomagnetogels consists on superparamagnetic iron oxide nanoparticles (γ-Fe_2O_3) stabilized within hydrophobized-dextrin nanogel (scheme 1). The nanomagnetogel formulation, with about 4 mM of iron and a diameter of 100 nm, presents relevant features such as superparamagnetic behaviour, high stability, narrow size distribution and potential for magnetic guidance to target areas by means of an external magnetic field [4]. The functionalization of the dextrin nanomagnetogel with a DOTA-monoamide ω-thiol metal chelator and radiolabelling with ^{111}In were used to ascertain its *in vivo* stability and behavior (blood clearance rate and organ distribution) after intravenous administration in mice model. The surface modification of the nanomagnetogel with PEG 5,000 was accomplished in an attempt to escape the phagocytic system. The unloaded radiolabeled dextrin nanogel (around 30 nm) showed lower uptake in the liver, spleen and kidneys than the nanomagnetogel loaded with SPIONs (around 110 nm). This difference in biodistribution profile can be ascribed to the differences in the particle size.

Nanomagnetogel pegylation resulted in lower liver and spleen accumulation. The blood half-life obtained was approximately 4 hours for all formulations. A good correlation between the amount of polymer (quantified through radioactivity) and the amount of iron (ICP measurement) in the spleen was observed, indicating that leakage of iron from the nanomagnetogels after intravenous administration was negligible. The pilot imaging study demonstrated good performance of dextrin nanomagnetogels as dual modality imaging (MRI and SPECT) bioprobes as expected by the high transverse relaxivity (215-248 $mM^{-1}s^{-1}$) obtained *in vitro*, higher than those of commercial available formulations (160-177 $mM^{-1}s^{-1}$). The production of the nanomagnetogel is simple and easy to scale up, thus offering great technological potential.

References

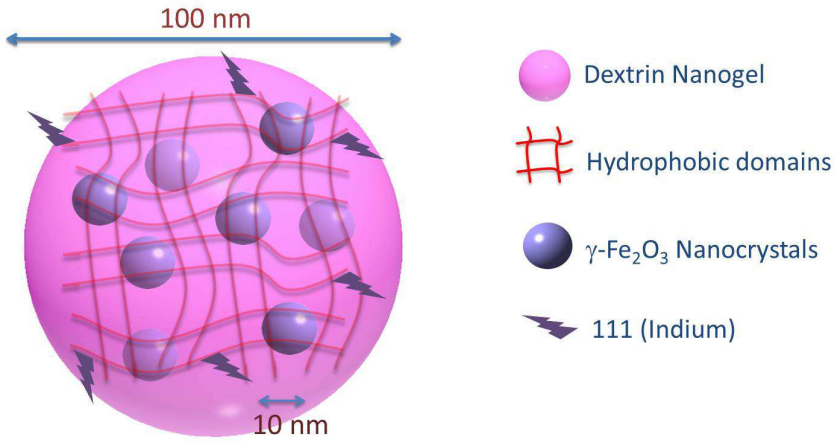
[1] R. Misri, D. Meier, A. C. Yung, P. Kozlowski, U. O. Hafeli, Nanomedicine, **8** (2012) 1007.

[2] X. H. Peng, X. M. Qian, H. Mao, A. Y. Wang, Z. Chen, S. M. Nie, D. M. Shin, International Journal of Nanomedicine, **3** (2008) 311.

[3] W. Yu, E. Chang, C. M. Sayes, R. Drezek, Colvin V.L., Nanotechnology, **17** (2006) 4483.

[4] C. Gonçalves, Y. Lalatonne, L. Melro, G. Badino, M. F. M. Ferreira, L. David, C. F. G. C. Geraldes, L. Motte, J. A. Martins, F. M. Gama, J. Mater. Chem. B, **DOI:10.1039/C3TB21063D** (2013).

Figures



Scheme 1. Schematic dextrin nanomagnetogel as dual modality imaging bioprobe (MRI and SPECT).