Multifunctional nanoplatform for in vivo and in vitro biomedical applications

R. Piñol¹, L. Gabilondo¹, J.L. Murillo¹, N.J.O. Silva², R. Bustamante¹, L. Mohamed¹, V. Sorribas³, M. Gutierrez⁴, R. Cornudella⁴, J. A. Moreno⁴, A. Millan¹, F. Palacio¹.

¹ Instituto de Ciencia de Materiales de Aragón. CSIC - Universidad de Zaragoza, and Departamento de Física de la Materia Condensada. Facultad de Ciencias, 50009 Zaragoza, Spain.

² Departamento de Física and CICECO. Universidade de Aveiro, 3810-193 Aveiro. Portugal.

³ Departmento de Toxicologia, Facultad de Veterinaria, Universidad de Zaragoza, 50009 Zaragoza, Spain.

⁴ Departamento de Hematologia, Facultad de Medicina, Universidad de Zaragoza, 50009 Zaragoza. Spain.

pinol@unizar.es

Nanotechnology offers clear advantages with respect to conventional techniques that is resulting in a real breakthrough in biomedical research and health care. One of the best chances along this direction would come from the development of multipurpose nanometric systems incorporating several physical (magnetic, optical) and biological functionalities in a single unit that could perform simultaneously a variety of different operations such as driving, sensing, imaging and therapy. Here, we present a coreshell multifunctional nanoplatform containing magnetic nanoparticles, luminescent centres, anchoring sites for biological active molecules and potentially a molecular thermometer¹. This study involves a variety of research fields and includes researchers from various specialities: chemists, physicists, biology, toxicology and clinical medicine. The magnetic properties of the nanoplatform (magnetic moment, susceptibility, blocking temperature, relaxivity, etc) can be tuned up in the whole superparamagnetic range by changing the size of the magnetic nanoparticles from 2 to 25 nm.² The synthesis is based in a polymeric route, in which polymers play multiple role: a) as templates for the control of inorganic nuclei production; b) as a matrix for the encapsulation of the nuclei; c) as a coating containing hydrophilic residues to achieve stabilitization of the nanoparticles in biological media; and d) for the incorporation of inorganic and organic functionalities. Surface functionalization of the magnetic nanoparticles is achieved by Michael addition chemistry between α,β -unsaturated electrophiles and amine based polymers in aqueous solution at different pH conditions and room temperature to moderated temperatures.³ Michael addition chemistry in water as medium benefits from mild reaction conditions, no by products, high functional tolerance, high conversion and favourable reaction times, non-toxicity and non-hazardous to the environment isolation purification. All the components are biocompatible. The whole particle size, which account for the magnetic nanoparticles and their polymeric multicoating, can be varied from 30 to 150 nm. As it will be shown in this presentation, the nanoplatform is highly stable in biological fluids, shows low toxicity⁴, capability of cell internalization, excellent hematocompatibility, anticoagulation properties, and excellent performance in magnetic resonance imaging⁵ and hyperthermia, substantially better than commercial standards.

This work has been supported by the grants MAT2007-61621 and CONSOLIDER CSD2007-00010 from the Ministry of Education.

References

[1] C. D. S. Brites, P. P. Lima, N. J. O. Silva, A. Millán, V. S. Amaral, F. Palacio, L. D. Carlos, Advanced Materials, **22** (2010) 4499-4504.

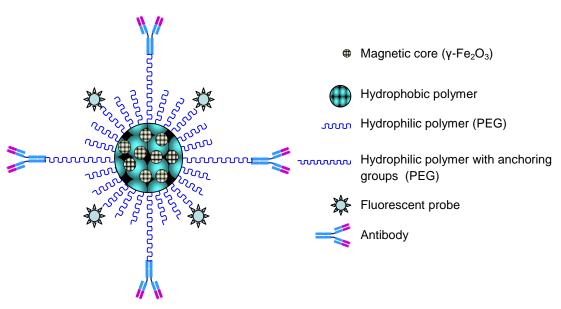
[2] A. Millan, F. Palacio, A. Falqui, E. Snoeck, V. Serin, A. Bhattacharjee, V. Ksenofontov, P. Gütlich and I. Gilbert, Acta Materialia, **55**, (2007), 2201-2209.

[3] R. Piñol, A. Millán, F. Palacio, L. Gabilondo, Spanish Patent no. P201031493 submitted to the Spanish Patent and Trademark Office (07-10-2010).

[4] R.Villa-Bellosta, G. Ibarz, A. Millan, R. Piñol, A. Ferrer-Dufol, F. Palacio, V. Sorribas, Toxicology Letters, **180**, (2008) S221-S221.

[5] H. Amiri, R. Bustamante, A. Millán, N. Silva, R. Pinol, L. Gabilondo, F. Palacio, P. Arosio, M. Corti, A. Lascialfari, "Multifunctional Polymer-based Nanostructured Bio-ferrofluids as MRI Contrast Agents" submitted to Magnetic Resonance in Medicine.

Figures



Scheme of core-shell multifunctional nanoplatform containing magnetic nanoparticles