BIOMEDICAL APPLICATIONS OF NANOPOROUS SILICA PARTICLES AND SILICA-BASED COATINGS

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Several attractive features, such as large specific surface areas, narrow pore-size distributions, chemical and mechanical stability, biocompatibility, non-toxicity, and easy surface functionalization of silica-based materials have made them ideal for drug delivery and biosensing applications [1], for transfection [2], as well as for acting as functionalizable coatings on medical devices [3] and on nanoparticles (i.e., contrast agents) [4].

Mesoporous silica shows regular pore openings and can also have different pore arrangements: hexagonal (MCM-41), cubic (MCM-48) and lamellar (MCM-50) with average pore diameters that can be selected between 15 and 100 Å, by adjusting the synthesis conditions and/or by employing surfactants with different chain lengths in their preparation.

For drug-delivery applications a volume-based rather than surface-based approach to drug delivery is also possible. Thus, unlike MCM particles, where the drug is loaded by adsorption on the surface area of the material, with hollow spheres or particles the drug could also be stored in the empty inner volume, thus leading to higher loads per unit mass of drug delivery vector. A variety of preparation methods is now available to produce silica-based hollow spheres, consisting of mesoporous silica and with or without functionalized interiors (e.g., Schult-Eklo et al. [5], Caruso et al. [6], Dong et al. [7], Valtchev and Mintova [8]). These could in principle be used in drug delivery applications given their characteristics of biocompatibility and comparatively high drug loading capability.

For magnetic targeting in drug delivery, a drug or therapeutic radionuclide is bound to a magnetic compound (which can be grafted in a silica based matrix), introduced in the body, and then concentrated in the target area by means of a magnetic field (using an internally implanted permanent magnet or an externally applied field). Depending on the application, the particles then release the drug or give rise to a local effect (irradiation from radioactive microspheres or hyperthermia with magnetic nanoparticles). Drug release can proceed by simple diffusion or take place through mechanisms requiring enzymatic activity or changes in physiological conditions such as pH, osmolality, or temperature; drug release can also be magnetically triggered from the drug-conjugated magnetic nanoparticles.

For diagnosis applications, we have developed different types of silica-coated magnetic nanoparticles as contrast agents for magnetic resonance imaging (MRI). The silica shell provides a hydrophilic surface that helps to retard the process of nanoparticle clearance by the macrophages of the reticuloendothelial system (RES). The silanol groups on the silica coating offer many possibilities for surface functionalization as we mentioned before. The silica shell helps to avoid magnetic and electrostatic agglomeration, since the isoelectrical point of silica is reached at pH 2-3 and therefore silica-coated nanoparticles would display a significant negative surface charge at the pH of the blood.
We have developed silica-coated magnetic nanoparticles functionalized with an antibody as a contrast agent with potential active targeting properties. Superparamagnetism implies that there is not coercivity, and the magnetization is close to zero in the absence of an external

field. To this end, we have: i) synthesized superparamagnetic nanoparticles that can be used as the core of targeted contrast systems; ii) developed a silica shell, on account of the above described advantages of silica, with a size of the core-shell ensemble under 100 nm; iii) attached covalently bio-active entities (an antibody in this case) to the silica coating to develop antibody-conjugated magnetic nanoparticles. The antibody anti-hCG was chosen as a test compound because it is widely studied due to its common use in pregnancy testing kits. Different nanoparticles synthesized are shown below (Figure 1).

References:

[1] I. I. Slowing, B.G. Trewyn, S. Giri, V.S.Y. Lin, Advanced Functional Materials, (Early view, 2007).
[2] C. Kneuer, M. Sameti, U. Bakowsky, T. Schiestel, H. Schirra, H. Schmidt, C.M. Lehr, Bioconjugate Chemistry, 11 (2000) 926.
[3] L.M. Pérez, M. Arruebo, S. Irusta, L. Gracia-Villa, J Santamaría, J.A. Puértolas, Microporous and Mesoporous Materials, 98 (2007) 292.
[4] M. Arruebo, R. Fernández-Pacheco, B. Velasco, C. Marquina, J. Arbiol, S. Irusta, M. Ricardo Ibarra, J. Santamaría, Advanced Functional Materials, (Early View 2007).
[5] G. Schult-Eklo, J. Rathousk, A. Zukal, International Journal of Inorganic Materials, 1 (1999) 97.
[6] F. Caruso, H. Möhwald, Science, 282 (1998) 1111.
[7] A. Dong, Y. Wang, D. Wang, W. Yang, Y. Zhang, N. Ren, Z. Gao, Y. Tang, Y, Microporous and Mesoporous Materials, 64(2003) 69.
[8] V. Valtchev, S. Mintova, Microporous and Mesoporous Materials 43 (2000) 41.

Figures:

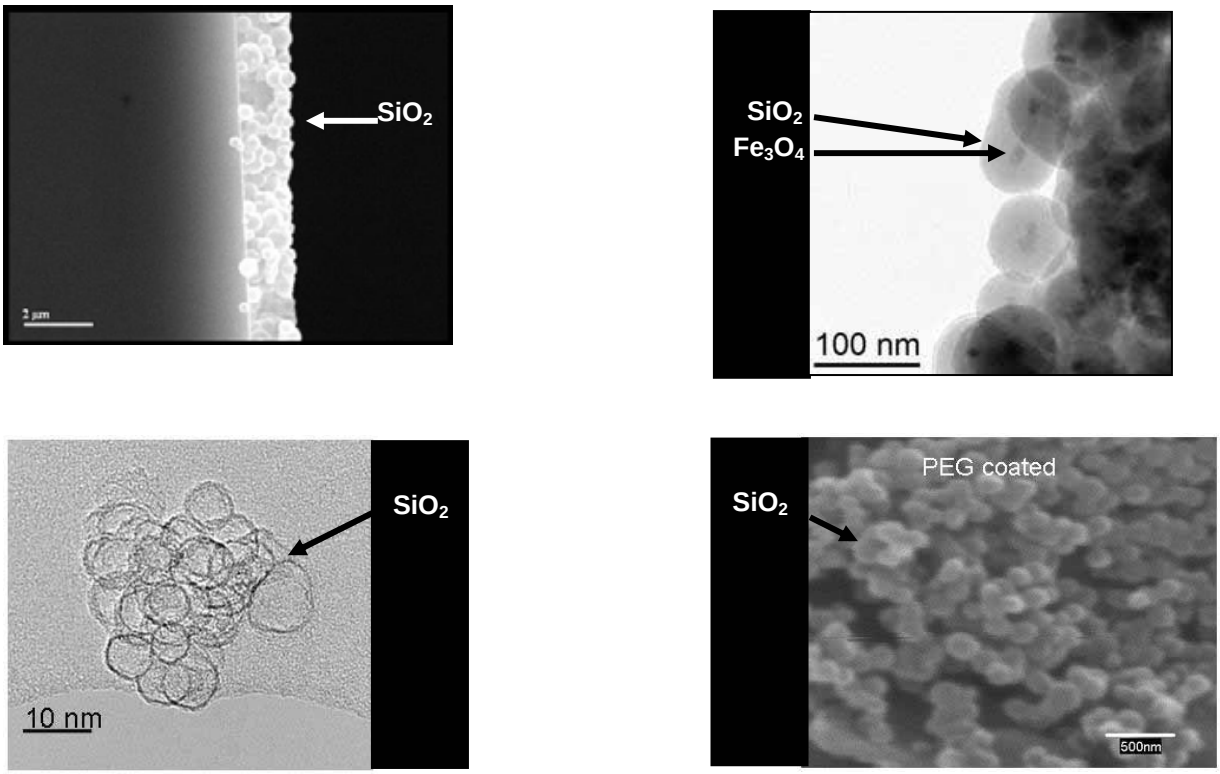

Figure 1. Silica-based nanoparticles synthesized by the Aragon Nanoscience Institute.