Maghemite Nanoparticles-Templated Assembly of Apoferritin Protein Functionalized with Carbohydrates for Targetting Cells

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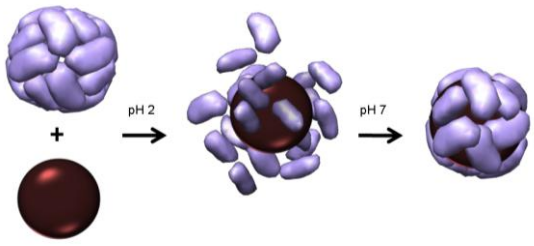
In the last few years there has been an enormous development in the synthesis and functionalization of inorganic nanoparticles for biomedical applications. Of particular interest is the case of magnetic nanoparticles where there is an outbreak of proposed nanostructures for imaging, magnetic hyperthermia or targeted drug delivery.

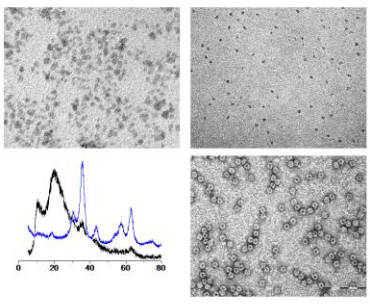
Non-invasive in vivo imaging (MRI, OI, PET CT…) has enormous potential for the early detection and treatment of disease. Imaging techniques using nonspecific-image contrast agents lack of the necessary specificity for obtaining quality imaging, particularly, in the early stages of disease. The identification of specific ligands to target tissues of interest opens the door for development of new probes that can specifically localize and image molecular events in the body in real time.

Magnetite and/or maghemite (Fe_3O_4/γ-Fe_2O_3) nanoparticles have been used extensively as a model magnetic material in the biomedical research field. Considering that the magnetic properties and contrast enhancement capacity of nanoparticles are strongly dependent on various parameters, such as size, shape, surface properties and degree of aggregation, it is important to prepare nanoparticles with high saturation magnetization (Ms) values, while maintaining single domain properties.

Moreover, numerous efforts have been devoted to achieve "active targeting" i. e., ligand-coated nanopartigles bearing an active functionality, such as a targeting molecule for a desired receptor, that enhance selectivity transport based on molecular recognition processes such as antigen-antibody or ligand-receptor interaction.

In this communication we describe a new synthetic method for obtaining carbohydrate-functionalized magnetic nanoparticles. Apoferritin, the cellular iron-storage protein, is a spherical shell composed of 24 polypeptide subunits surrounding a cavity of 8 nm. We used the dissociation at pH 2.0 of the apoferritin into its 24 subunits, followed by its reconstruction at pH 7 to encapsulate maghemite nanoparticles. It is worthy to pointing out that the native mineral formed inside the apoferritin is a ferrihydrite-magnetite core-shell structure of 5 nm of mean size. [1] We have lately shown that apoferritin shell can be successfully functionalized with different dyes or Quantum Dots, as a new type of dual-functional fluorescent-magnetic probes.[2] Herein, we have also succeeded in the functionalization of apoferritin with two types of monosaccharides. The immobilized carbohydrates retained their recognition abilities, as demonstrated by the strong affinity with their corresponding carbohydrate-binding lectins.





References:

[1] N. Gálvez, B. Fernández, P. Sánchez, R. Cuesta, M. Ceolín, M. Clemente-León, S. Trasobares, M. López-Haro, J. J. Calvino, O. Stéphan, J. M. Domínguez-Vera, *J. Am. Chem. Soc*. **2008**, *130*, 8062–8068.

[2] B. Fernández, N. Gálvez, R. Cuesta, A. B. Hungría, J. J. Calvino and José M. Domínguez-Vera. *Adv. Funct. Mater*. **2008**, *18*, 3931-35.