Superparamagnetic core-shell nanoparticles: synthesis, characterization and application in targeted drug delivery

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Abstract

In recent years, since research into the targeting and delivery of therapeutics is right at the forefront of nanomedicine, scientists have developed different kinds of drug delivery systems. In this field, the design of chemical and physical stimuli-responsive gated mesoporous materials have recently demonstrated to be an excellent approach for the development of smart nanodevices. In fact, the unique characteristics of functionalized mesoporous silica supports such as high homogeneous porosity, inertness, robustness, thermal stability, the presence of tunable pore sizes, homogeneous pore distribution and high loading capacity, makes these scaffoldings ideal for hosting functional guest molecules. Additionally, the possibility of incorporating in the external surface functional groups able to open or close at will or including capping molecules, provides advanced control release applications. One of the most captivating features of such systems is the possibility to prepare "zero release" devices that deliver entrapped guests exclusively upon the application of an external stimulus [1,2]. Among different physical triggers, such as light and temperature, the use of magnetic fields is captivating [3,4].

This work reports the on-command cargo controlled delivery using an alternating magnetic field (AMF) from magnetic silica mesoporous supports capped with a lipid bilayer [5]. Silica mesoporous nanoparticles containing superparamagnetic iron oxide nanocrystals (solid S1) were synthesized and loaded with the dye methylene blue [6]. Further, the pores were capped with a lipid bilayer of 1,2-dioleoyl-sn-glycero-3-phosphocholine (solid S2). The synthesis procedure is summarized in Figure 1.

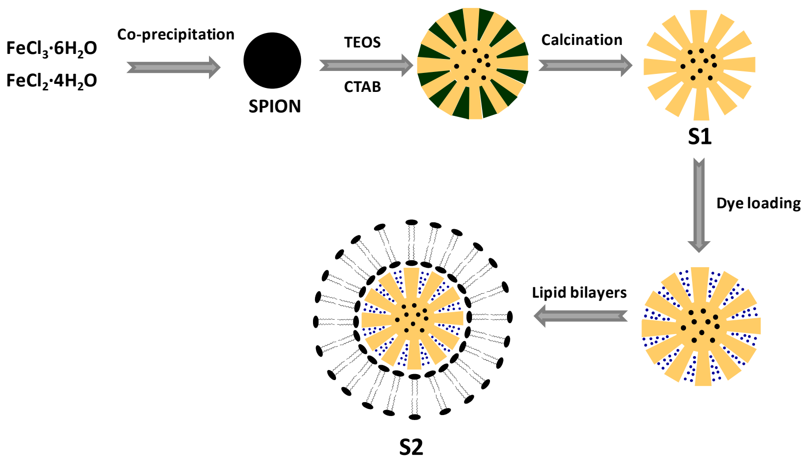

Figure 1. Synthesis of superparamagnetic core-shell nanoparticles.

Delivery of the dye from S2 in the presence of an isolated AMF (50 Hz and 1570 G) was studied in a phosphate-buffered saline medium (PBS; pH 7.4) at 20 ºC and compared with the release behavior in absence of the magnetic field (see Figure 2).

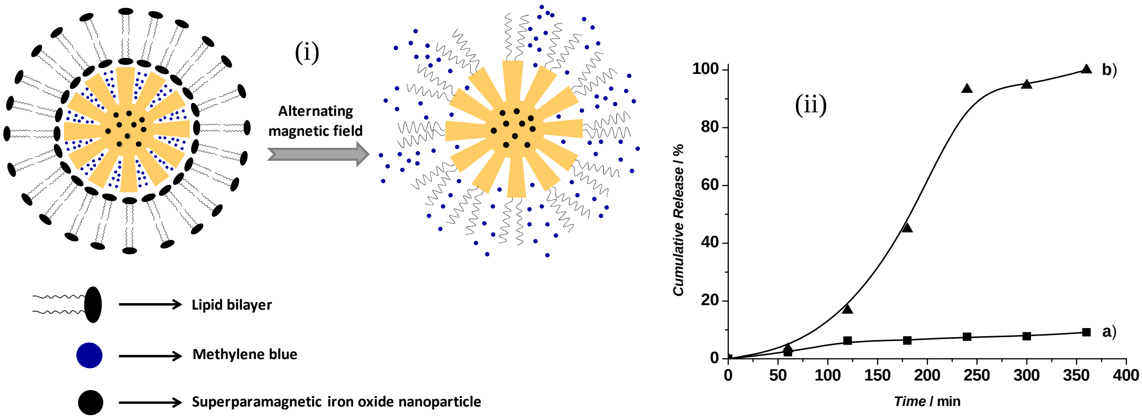

Figure 2. i) Solid S2 expected performance; ii) Cumulative release profile of methylene blue from solid S2 a) without AMF and b) in the presence of an AMF.

Whereas solid S2 displayed no release of the cargo, the application of an AMF induced the delivery of more than 90% of the maximum deliverable methylene blue dye during the first four hours. Delivery mechanism occurs most likely due to changes in the permeability of the lipid bilayer (and eventually its total or partial rupture) promoted by the vibration of the nanoparticles in the presence of an AMF.

The easy preparation of the nanomaterial, the robustness and high loading capacity of the cargo reservoir, the wide range of possibilities as well as the biocompatibility of lipid bilayers, combined with the remote release activation using a friendly simple alternating magnetic field make these new hybrid nanomaterials attractive systems for the future design of on command delivery nanodevices in a wide range of applications.

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References

[1] Aznar, E.; Martínez-Máñez, R.; Sancenón, F. Expert Opin. Drug Deliv.**6** (2009) 643-655.
[2] Cotí, K.; Belowich, M. E.; Liong, M.; Ambrogio, M.W.; Lau, Y.A.; Khatib, H.A.; Zink, J.I.; Khashab, N.M.; Stoddart, J.F. Nanoscale, **1** (2009) 16-39.
[3] Ruiz-Hernández, E.; Baeza, A.; Vallet-Regí, M. ACSNano, **5** (2011) 1259-1266.
[4] Bringas, E.; Köysüren, O.; Quach, D.V.; Mahmoudi, M.; Aznar, E.; Roehling, J.D.; Marcos, M.D.; Martínez-Máñez, R.; Stroeve, P. submitted, Angew. Chemie Int. Ed. (December 2011).
[5] Zhang, L.; Longo, M.L.; Stroeve, P. Langmuir, **16** (2000) 5093-5099.
[6] Bruce, I.J.; Taylor, J.; Todd, M.; Davies M.J.; Borioni, E.; Sangregorio, C.; Sen, T. J. Magnet. Magnet. Mater. **284** (2010) 145-160.