PEGylation of condensed colloidal magnetite nanocrystal clusters for imaging and drug delivery

A. Kolokithas-Ntoukas[1], Y. Sarigiannis[1], A. Bakandritsos[1*], R. Zboril[3], S. Pispas[2], G., Mountrichas[2], Zoppellaro[3], C. Diwoky[4]

[1]University of Patras, Materials Science Dept. [2]Theoretical and Physical Chemistry Institute N.H.R.F., Athens, Greece; [3]RCPTM, Olomouc, Czech Republic; [4]Graz University of Technology, Medical Engineering, Austria

Condensed magnetite colloidal nanocrystal clusters (co-CNCs) have received particular interest due to their application as theranostics. Their development requires solvothermal conditions and/or high temperature.[1] Herein, co-CNCs were synthesized for the first time through one-step soft chemical route in presence of alginate. Co-MNCs, including the present product (MagAlg), display excellent attributes with regard to magnetic manipulation, contrast enhancement in MRI and remotely triggered release.[2] However, they lack colloidal stability upon drug loading and dispersion in blood-isotonic media.

In order to overcome this, installation of a poly(ethylene glycol) (PEG) canopy was pursued through covalent conjugation and, alternatively, through self-assembly with double hydrophilic poly(cationic-b-elthylene glycol) copolymers.

The as-prepared co-MNCs rapidly flocculate at 0.3M NaCl and in presence of doxorubicin. After several trials the appropriate reaction conditions and conjugation reagents were determined, as manifested by the unchanged absorbance in salt-stability assays and light scattering results. In the second PEGylation approach, co-CNCs were incubated with quaternized poly[3,5-bis(dimethylaminomethylene) hydroxystyrene]-b-PEG (QNPHOS-PEG) and poly(L-lysine-b-PEG) (PLL-PEG). After determination of the optimum feeds, PLL-PEG appears to impart excellent entropic stabilization at high alt concentrations. Following the effective PEGylation, doxorubicin loading (10 % wt) was successful without any aggregation (Dh=~100 nm). Drug release was sustained and could be triggered with magnetic hyperthermia.

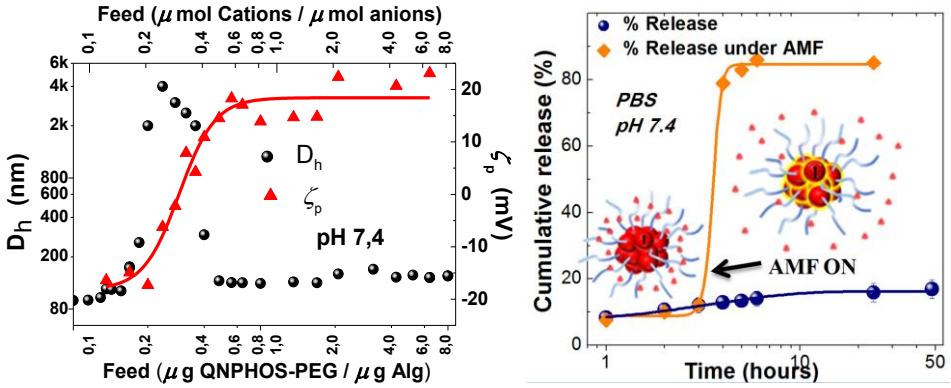

Figure 1. Left: Hydrodynamic diameter and ζ variation at different block-copolymer feeds. Right: Drug release kinetics with and without of magnetic hyperthermia.

References

[1] Z. Lu, Y. Yin, Chem. Soc. Rev., **41**, 687, (2012).

[2] Zoppellaro, G.; Kolokithas-Ntoukas, A.; Polakova, K.; Tucek, J.; Zboril, R.; Loudos, G.; Fragogeorgi, E.; Diwoky, C.; Tomankova, K.; Avgoustakis, C.; Kouzoudis, D.; Bakandritsos, A. Chem. Mater. **26**, 2062, (2014).