Poster

FLUORESCENT AND MAGNETIC NANOPARTICLES FOR BIOLOGICAL IMAGINE

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In this work we describe the preparation of a new type of "two in one" fluorescent-magnetic nanocomposites based on magnetite nanoparticles, a polyhedral octaaminopropylsilsesquioxane ($T_8NH_3^+Cl^-$), and a porphyrin derivative. We also assess their intracellular uptake by bone osteoblast cells and evaluate their potential as MRI contrast agents.

Magnetite nanoparticles were prepared by reacting a mixture of ferrous and ferric chlorides (2:1 molar ratio) and NaCl aqueous solution with ammonia. A suspension of the particles in distilled millipore water was prepared using ultrasound. The suspension was then treated by the octaaminopropylsilsesquioxane hydrochloride $T_8NH_3^+Cl^-$.[1] Finally a solution of 4, 4', 4'', 4'''-(21H, 23H) Porphine-5, 10, 15, 20- tetrayl) tetrakis-(benzoic acid) was added to of the magnetite suspension. Any precipitate was removed by magnetic separation and further aggregates were removed by centrifugation giving a stable suspension of $T_8NH_3^+Cl^-$-porphyrin magnetite nanocomposites in water. These nanocomposites are formed via non-covalent ionic and hydrogen bonding interactions between the magnetic nanoparticle surface, $T_8NH_3^+$ ions and porphyrin molecules which contain terminal carboxylate groups. TEM images of the magnetite-porphyrin nanocomposites have shown the formation of partially aggregated core-shell nanoparticles,. The particle size is found to be 12 ± 2 nm. By analyzing the HRTEM images of a single functionalized magnetite nanoparticle, the lattice spacing between two planes is 4.82 Å, corresponding to the distance of two (111) planes in Fe_3O_4.

The magnetic nature of the nanoparticle composites and their potential MRI contrast efficiency was assessed by nuclear magnetic resonance dispersion (NMRD), where the frequency dependence of the spin-lattice relaxation is measured. The water relaxation rate enhancement due to the superparamagnetic particles is expressed as concentration independent relaxivity, r_1 with units $s^{-1}mM^{-1}$ (of Fe). The relaxivity values obtained for these samples are slightly higher than those for commercial nanoparticulate MRI contrast agents at 20 MHz. TEM demonstrates that the particles are in the superparamagnetic size range, and the observed r_1 maxima clearly indicate that a significant proportion, c. 60 mol%, of the magnetisation is superparamagnetic.[2] However, the high low-field relaxivity shows that the remaining magnetisation is magnetically blocked. This is most likely due to strong anisotropic interparticle interactions in the magnetic nanoclusters, which are more predominant for the $T_8NH_3^+Cl^-$ -magnetite. PCS measurements confirm the presence of clusters in suspension, giving a Z-average cluster size of 82 nm with a PDI of 0.415.

We have investigated the uptake and cellular localisation of porphyrin-$T_8NH_3^+Cl^-$ -magnetite nanocomposites in live THP-1 phagocytic cell line. THP-1 cells were differentiated to macrophages and the nanocomposites were added at a 1 in 100 dilution followed by incubation for the indicated times at 37 ^oC. Vigorous washing with PBS (Phosphate Buffer Saline) followed the incubation period to detach the loosely bound nanoparticles. Confocal imaging found that the porphyrin-$T_8NH_3^+Cl^-$ -magnetite nanocomposites are internalized by the macrophages and sequestered to the cytoplasm within 10 minutes (Fig. 2), significantly increasing the fluorescent signal due to intracellular particle accumulation, compared to the

non-ingested nanocomposites. Thus these fluorescent magnetic nanocomposites are potential organelle specific diagnostic markers which could be detected by MRI or fluorescent confocal imaging. The results of our studies also indicate that these materials could potentially serve as drug delivery systems. We believe that these systems may have important applications in diagnostics and treatment of degenerative and chronic diseases associated with overactive phagocytic responses, such as autoimmune disorders and osteoporosis.

References:

[1] F. J. Feher, K. D. Wyndham, D. Soulivong and F. Nguyen, *J. Chem. Soc., Dalton Trans.,* 1999, **9**, 1491-1497.

[2] S. J. Byrne, S. A. Corr, Y. K. Gun'ko, J. M. Kelly, D. F. Brougham and S. Ghosh, *Chem. Commun.,* 2004, **22**, 2560-2561.

Figures:

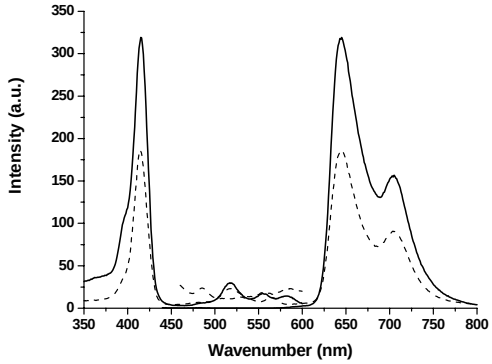

Fig. 1 Emission (right) and excitation (left) spectra of original porphyrin [1.4×10^{-9}M in phosphate buffer] (solid line) and porphyrin -$T_8NH_3^+Cl^-$-magnetite nanocomposites [360 μL of particle suspension, made up to 3mL with phosphate buffer] (dashed line).

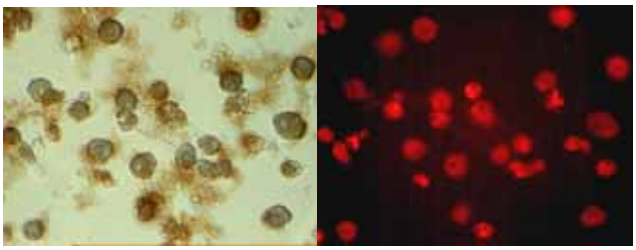

Fig. 2 Porphyrin-$T_8NH_3^+Cl^-$ -magnetite nanocomposites in cultures of macrophages. Left, transmitted light microscopic image of the THP-1 cells interacting with nanocomposite particles. Right, corresponding fluorescent image of the same microscopic field (λ_{ex}= 488 nm, λ_{em}= 650 nm). Remaining non-ingested particles are seen as brown aggregates in transmitted light.