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Novel Synthesis of Fluorescent Iron-Doped Carbon Nanodots: New Insights on Medical Imaging

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Extended Abstract

Magnetic Resonance Imaging (MRI) is one of the most important non-invasive imaging modalities in clinical diagnostics and research. Nowadays, most of the contrast agents used clinically are Gg-based but, lately, they have been associated with organ damage and accumulation in tissues due to Gd leaking.[1] Although clinically applied contrast agents are considered safe, there is an initial shift to the use of other paramagnetic ions, such as Fe(III). This metal ion is an essential element naturally found in the body and it is expected to show less associated toxicity than Gd(III). Moreover, features such as high magnetic moment and short ion-water distance, make Fe-based contrast agents an emerging alternative to Gd-based ones.[2] Carbon Nanodots (CNDs) are low dimensional particles with quasi-spherical shape mainly made of carbon and abundant functional groups on the surface. These are very appealing materials for biomedical applications, since they show low cytotoxicity, high water solubility, and tuneable fluorescence emission.[3] There are two main approaches to synthesize CNDs: top-down approaches which involve the fragmentation of high-sized carbonaceous materials (i.e., graphene) or bottom-up approaches, occurring by thermal treatment of molecular precursors such as amino acids or sugars. Currently, bottom-up syntheses are very versatile since the careful selection between a large variety of precursors and the possibility to dope with heteroatoms or metal ions *in situ* may tune the physicochemical and magnetic properties of this material to a greater extent.[4] Thus, doping CNDs with Fe(III) allows their use as highly biocompatible T_1 contrast agent for MRI. Accordingly, the project aims to incorporate Fe(III) into the CNDs through a one-pot, microwave-assisted synthesis to fabricate suitable Fe-based nano-contrast agents. This new material is expected to penetrate cells with poor cytotoxicity and possess good biocompatibility *in vivo*. In addition, the dual nature of the nanoparticles enables Fe-doped CNDs (FeCNDs) to act as dual FI/MRI platform and could be superficially decorated with drugs or targeting moieties, enlarging their field of application. FeCNDs were synthetized in a bottom-up approach from β-alanine, a chelating agent and a Fe(III) precursor. The reaction crude was obtained after centrifugation and dialysis. Final FeCNDs were purified from other molecular-like side products through HPLC-SEC. Pure FeCNDs were obtained as negatively charged particles, with spherical-like shape and a size distribution between 1-10 nm, as measured by AFM. The presence of iron in a mixed valence state was confirmed by ICP-MS and XPS measurements. Fluorescence spectroscopy evidenced a strong emission of FeCNDs in the blue region of the spectrum and an excitation wavelength dependent emission, feature commonly attributed to the formation of the carbon nanoparticles. Moreover, FeCNDs exhibit good contrast activity during MRI scanning at 1.5 T, 7 T and 11 T. Dialysis is commonly the last purification step to obtain CNDs. This work highlights the importance of further purification steps to ensure that measured properties arise from CNDs and not from artifacts in the sample. Moreover, purified material shows improved MRI performance as compared to the reaction crude. These results pave the way for the use of FeCNDs as an alternative to Gd-based contrast agents.

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