Highly monodisperse spindle-like calcium hydroxyapatite and fluoroapatite nanoparticles for biomedical applications

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Abstract

Calcium phosphate nanostructures are attracting great interest in nanomedicine in both colloidal state, due to their applications in transfection, gene silencing, drug delivery and imaging techniques [1], and bulk systems (i.e. bioactive coatings, cements, and nanocrystalline bulk synthetic ceramics for bone tissue engineering) [2-3]. This is explained for its high biocompatibility and good biodegradability. In fact, calcium phosphate is the inorganic mineral of human bone and teeth [4]. In general terms, most of these applications require uniform nanoparticles or nanostructures with controlled size, shape, composition, surface chemistry, and other physicochemical properties [5]. A high colloidal stability is also required in case of the dispersed systems. This is normally achieved after an appropriate functionalization process, which also provides anchors for adding functional ligands such as antibodies, peptides, proteins, and some anticancer drugs [6].

We report the synthesis of highly monodisperse calcium hydroxyapatite and calcium fluoroapatite nanoparticles functionalised with poly(acrylic acid) (PAA) which exhibit a new spindle-like morphology. The nanoparticles are synthesised through a one-pot microwave-assisted hydrothermal method from aqueous basic solutions containing calcium nitrate, sodium phosphate monobasic, and PAA, as well as sodium fluoride in the case of the fluoroapatite particles. The size of the nanospindles is 142 (26) × 28 (4) nm for calcium hydroxyapatite (Figure 1A) and 160 (14) × 40 (5) nm for calcium fluoroapatite. Both apatite-based nanoparticles show negligible toxicity for Vero cells (Figure 1B) and a very high (up to at least one week) colloidal stability in 2-(N-morpholino)ethanesulfonic acid (MES) 50 mM at pH 6.5 (Figure 2A), which is a commonly used buffer for physiological pH. As a result of their formation mechanism, which consists of an aggregation process of smaller subunits, the nanoparticles show high specific surface area (85 $m^2 g^{-1}$). This makes them suitable for targeted drug delivery systems.

In addition, the particles can be made luminescent by doping with Eu^{3+} (Figure 2B) so that they can be used as biolabels. It is also shown that the luminescence is more efficient for the fluoroapatite particles than for the hydroxyapatite, which is attributed to the presence of OH^- quenchers in the latter. All these features make both kinds of apatite-based nanoparticles promising tools for biomedical applications.

References

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Figures

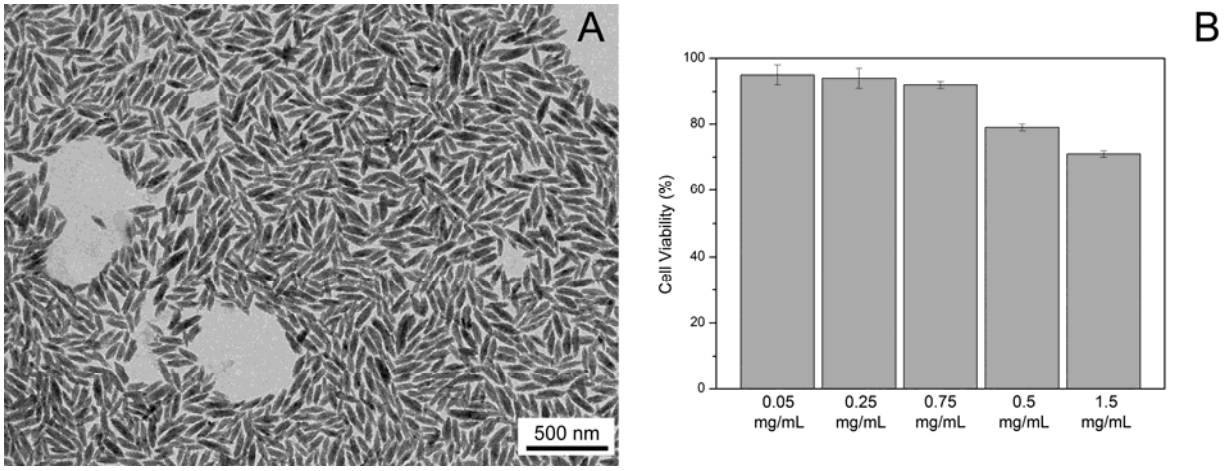

Figure 1A: TEM micrograph of highly monodisperse calcium hydroxyapatite nanospindles functionalised with PAA. **Figure 1B:** Viability assays performed with Vero cell line for PAA-functionalised calcium hydroxyapatite nanospindles at different nanoparticle concentrations.

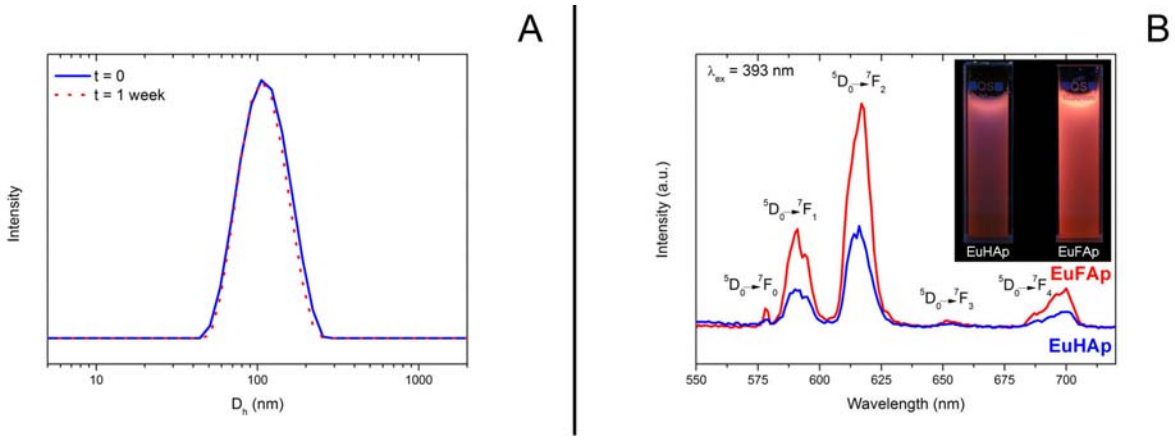

Figure 2A: Size distributions determined by DLS for PAA-functionalised calcium hydroxyapatite suspensions in MES 50 mM at pH 6.5 after different aging times. **Figure 2B:** Emission spectra (λex= 393 nm) of aqueous suspension of PAA-functionalised Eu-doped hydroxyapatite (EuHAp, blue line) and fluoroapatite (EuFAp, red line) nanospindles. The inset shows the red luminescence of suspensions of both europium-doped nanophosphors when irradiated with UV light.

More details can be found in Alberto Escudero et al., Langmuir, **29** (2013) 1985−1994. http://pubs.acs.org/doi/abs/10.1021/la304534f