Continuous-flow precipitation as a route to prepare highly controlled nanohydroxyapatite

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Hydroxyapatite $Ca_{10}(PO_4)_6(OH)_2$ (HAp) has been widely used for biomedical purposes because of its exceptional biocompatibility, bioactivity and osteoconductivity [1]. As these properties are directly related to HAp particles characteristics (size, morphology and purity), a very good control of the reaction conditions is required to obtain particles with the desired properties. Usually, HAp is synthesized by wet chemical precipitation in stirred tank batch reactors that often lead to inconsistencies in product specifications due to their low mixing efficiency [2].

In this work, a simple apparatus for the preparation of HAp nanoparticles is assessed as an alternative route for commercially solutions presently available in the market. Continuous-flow precipitation of HAp was performed in a scaled-up meso oscillatory flow reactor (OFR) under near-physiological conditions of temperature and pH. Structural (XRD, FTIR), morphological (SEM, size distribution analysis) and biological studies (MTS, DNA and SEM analysis, *in vitro* mineralization in SBF) were carried out. Results obtained showed the synthesis of rod-like HAp nanoparticles with a mean size (d_{50}) of 77 nm and narrow size distribution [3]. Further, *in vitro* biomineralization assays demonstrated the apatite-forming activity of the synthesized HAp nanoparticles and their high surface reactivity. Furthermore, human osteoblastic-like (Saos-2) cells culture evidenced that the synthesized HAp stimulated cell proliferation, especially when applied at low concentrations, although its cellular uptake behavior. Therefore, the prepared HAp shows immense potential for biomedical applications, from bone regeneration to drug and gene delivery vehicle. The results are also very promising regarding further scaling up of the process, as the designed methodology allow for the preparation in a continuous mode of nanosized HAp with controlled physico-chemical properties.

[1] He, Q. J.; Huang, Z. L. Cryst. Res. Technol. (42), 2007, 460—465.
[2] Lawton, S.; Steele, G.; Shering, P.; Zhao, L.; Laird, I.; Ni, X.-W. Org. Process Res. Dev. (13), 2009.
[3] Castro, F.; Ferreira, A.; Rocha, F.; Teixeira, J.A. Ind. Eng. Chem. Res. (52), 2013, 9816—9821.