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A COMPARATIVE STUDY ON HYDROXYAPATITE PRECIPITATION IN A STIRRED TANK AND IN AN OSCILLATORY FLOW MESO-REACTOR

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ABSTRACT

Hydroxyapatite (HAp) $Ca_{10}(PO_4)_6(OH)_2$ has been extensively used in bone replacement applications due to its biocompatibility, bioactivity and osteoconductivity (Kumta *et al*. 2005). In this context, it is desirable that HAp particles meet specific requirements such as high specific surface area, narrow size distribution and high purity, in order to optimize bone-related cells growth around them (Gómez-Morales *et al* 2001; Wang *et al*. 2006).

HAp is usually prepared by precipitation from solution (Kuznetsov *et al.* 2007), where HAp particles with different morphology, size and purity can be obtained depending on the experimental conditions like stirring speed, reactants addition rate, calcium/phosphate (Ca/P) molar ratio, reaction temperature and pH (Wang *et al*. 1998; Kumta *et al*. 2005; Han *et al*. 2007; Mobasherpour 2007). Moreover, as regards the use of HAp for biomedical purposes, there is a concern in preparing HAp particles under conditions that are more conductive to the survival of cells. The synthesis conditions have to follow specific criteria about pH, temperature, composition of raw materials, as well as purity of the final product (Kumta *et al*. 2005). But difficulties have been encountered in synthesizing HAp at physiological pH and temperature (Elliot 1994; Koutsopoulos 2002).

Commonly, precipitation of HAp is carried out in stirred tank. In this kind of system, inhomogeneous distribution of the mixing power and energy within the process volume leads to a heterogeneous distribution of supersaturation in the medium, affecting thus crystal size distribution and chemical purity of the particles precipitated. The problem becomes magnified as the scale of operation increases and can be particularly pronounced in fast precipitation systems (Jones *et al*. 2005). This calls for the development of a system that provides an efficient and intense mixing. In that way, the oscillatory flow reactor (OFR) appears as a good candidate to promote ideal conditions for the controllability of HAp particles properties. It has proved to result into significant enhancement in processes such as mass transfer (Ni *et al.* 1995a; Ni *et al*. 1995c), particle mixing and separation (Mackley *et al*. 1993), and crystallization. A novel meso-OFR has been developed at CEB, University of Minho. The reactor provides very controllable hydrodynamic conditions just by regulating the frequency and amplitude of the oscillations (Reis *et al*. 2004; Reis *et al*. 2005). Further, it can be easily scaled up to the industrial level (Lopes *et al*. 2011).

In the present work, HAp synthesis was carried out in batch, in a 1 L stirred tank and in the meso-OFR developed at CEB, with a volume of about 4.5 mL. Precipitation started by the quick addition of an orthophosphoric acid aqueous solution to a saturated calcium hydroxide aqueous solution. The experiments were performed under the same conditions of temperature (T=37 ºC), initial Ca/P molar ratio and power density (31.5 W/m^3). The constant power density applied to both reactors was used as the reference criteria. The effectiveness of both mixing methods for a given power input was studied in terms of reaction time and characteristics of precipitated particles. Reaction time was assessed by pH measurements, considering that most of the reaction is complete when pH stabilizes. For the experiments done in the stirred tank, pH was measured through a pH electrode. For the meso-OFR experiments, a methodology was developed to obtain the pH profile during the precipitation of HAp. A pH indicator, bromothymol blue, was added to each reagent and through an optical fibre the absorbance of the

reaction medium was measured. As to the characterization of the precipitated particles, X-ray diffraction, Fourier transform infrared spectroscopy (FTIR) and scanning electron microscopy (SEM) techniques were used.

Particles precipitated in the stirred tank were proved to be HAp. They come in the form of aggregates in the order of hundreds of µm. From FTIR results, formation of HAp was also verified in the meso-OFR. Besides, it has been proved that it is possible to determine pH during the HAp precipitation in the meso-OFR, by monitoring the changes in absorbance in the reaction medium. However, pH values obtained were slightly different from one experiment to another. This can be justified by the presence of the HAp particles that scatter and absorb light, changing thus the spectrum of the light field.
The experimental set-up of the meso-OFR has to be improved. Some problems were found in the injection system. A manual injection system was used, leading to problems of reproducibility between experiments. Therefore, an automatic injection system has to be implemented, being syringe pump a good alternative. Finally, a dead volume was observed in the reagents' injection point. This may be due to the design of the reactor and to the fact that the reagents are injected one at a time and not simultaneously. This dead volume could not be eliminated, however it was attenuated by optimizing the relation frequency/amplitude.

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