

## Growth of hydroxyapatite in a biocompatible mesoporous ordered silica

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### Abstract

A novel biomaterial (HA-SBA-15) has been developed based on the growth of calcium phosphate hydroxyapatite (HA) nanoparticles within an organized silica structure (SBA-15). Characterization of the material was carried out using a combination of X-ray diffraction, X-ray fluorescence, transmission electron microscopy, N<sub>2</sub> adsorption–desorption isotherms and nuclear magnetic resonance. Transmission electron microscopy observations and N<sub>2</sub> porosimetry revealed the crystallization of hydroxyapatite nanoparticles inside the mesopore cavities of the silica structure. Specific surface areas of 760 m<sup>2</sup> g<sup>-1</sup> and 260 m<sup>2</sup> g<sup>-1</sup> were measured for the SBA-15 and the HA-SBA-15 material, respectively. The hydroxyl groups present in the silica nanostructure surface have brought about cationic defects in the silicium sites, mainly with those of tetrahedral symmetry, and promoted the formation of siloxanes. <sup>29</sup>Si MAS-NMR analysis shows a significant reduction of the silanol groups concentration with HA growing within the base (SBA-15) material. Studies and brain tissue biocompatibility tests were carried out. Histopathological studies on the SBA-15 implant material showed no changes to the tissue nearby. The results confirmed the synthesis of a silica-based composite containing HA nanoparticles with the potential for biomedical applications.

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### 1. Introduction

Skeletal deficiencies, especially resulting from trauma, tumors or abnormal development, are common, and are usually treated by surgical intervention and grafting to restore mechanical function and reconstruct the operation area. The steadily increasing number of skeletal deficiencies requires bone replacements and effective ways to enhance bone formation [1]. This problem has led scientists to find

a biomaterial with grafting properties which possess biocompatibility, functionality and simplicity and is also economically viable [2,3]. Bone tissue engineering may potentially provide alternative solutions that possess better fixation and mechanical properties than those used currently. Bone tissue engineering is the use of a scaffolding material to either induce formation of bone from the surrounding tissue or to act as a carrier or template for implanted bone cells or other agents. Materials used as bone tissue-engineered scaffolds may be injectable or rigid, the latter requiring an operative implantation procedure [4,5]. Composites obtained by nucleation and growth of inorganic phases inside the pores of bioceramics are a good

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alternative. Hydroxyapatite (HA) can be considered as a leading biomaterial satisfying these conditions. It is the main mineral component of bone and teeth, having the chemical formula of  $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ .

For bone and soft tissues, interfacial bonding with biomaterials occurs because of the biological equivalence of the inorganic portion of the bone and the growing hydroxyl carbonate apatite layer (HCA) on the bioactive implant. This interfacial bonding has been found to be the result of a complex dissolution, polycondensation and readsorption process which involves inorganic and organic ad-species and therefore can be promoted with increasing surface area. Recent molecular biology studies have shown that critical concentrations of soluble Ca and Si ions released from the bioactive materials control the cell cycle of osteoprogenitor cells [6]. The hierarchical organization of bone involves organic and inorganic nanophases. Hartgerink et al. [7] claim that one way to accomplish this hierarchical organization in an artificial system is to prepare an organic nanophase designed to exert control over crystal nucleation and growth of the inorganic component. Bio-inspired morphogenesis of different inorganic phases including phosphate and apatite crystals is currently under intensive research [8–10].

HA has been used as bone graft but it has poor rates of reactivity and integration with existing bone when compared with bioactive glasses and glass–ceramics. The incorporation of Si atoms into HA increases the dissolution processes, enhancing the rate of incorporation of the graft though the precipitation of biological apatite [11].

Materials in the ternary system  $\text{SiO}_2\text{--CaO--P}_2\text{O}_5$  obtained by a sol–gel process have demonstrated excellent bioactivity. From the early stages of biomaterials research it was clear that a high surface area of the bioactive material plays a substantial role in increasing bioactivity [12,13]. Both a negative surface charge and a porous substrate have been reported to be required for HCA formation [14,15]. An HCA layer can be formed on a porous pure silica gel in a solution containing  $\text{Ca}^{2+}$  and  $\text{HPO}_4^{2-}$  ions. The layer formation is enhanced by the presence of pores of between 2 and 50 nm diameter in sol–gel derived glasses, which increased the surface area/volume ratio compared to that of melt derived glasses [15].

An alternative to the use of organic templates for the hierarchical control of crystal growth could be the use of mesoporous ordered inorganic materials. Mesoporous SBA-15 type silica's have surface areas in the range of  $600\text{--}1000\text{ m}^2\text{ g}^{-1}$  and may accomplish the hierarchical requirements for growing apatite crystals resulting in a high surface area organized  $\text{SiO}_2\text{--CaO--P}_2\text{O}_5$  system.

This paper reports the synthesis and the physicochemical characterization of a HA–silica composite biomaterial which has the potential to be used in the development of bone-fixation devices and could also be considered as a porous matrix for performing in situ controlled delivery of chemotherapy drugs.

## 2. Materials and methods

### 2.1. Synthesis

The synthesis of the material has been carried out using a two-step procedure which is detailed in the following two sections:

#### 2.1.1. Preparation of the Ca-doped silica matrix

The first step (low pH step) consisted of the preparation of a calcium doped silica matrix which was obtained by means of a variation of the methodology described in Ref. [16]. Pluronic<sup>®</sup> 123 block copolymer ( $\text{EO}_{20}\text{PO}_{70}\text{EO}_{20}$ ; molecular weight 5750 g/mol) donated from the BASF Corporation was used as a template. The block copolymer was dissolved in an aqueous solution containing HCl (Pan-reac, PA-ACS-ISO 37%) and  $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$  (Alfa-Aesar 99%) at a pH of  $\approx 1$  and 313 K. Tetraethyl orthosilicate (TEOS) (Alfa-Aesar 99%) was used as the silica source. The mixture was stirred for 24 h and subjected to a hydrothermal treatment at 353 K for 24 h. The product was dried in an oven at 353 K.

Using similar synthesis conditions a base mesoporous silica (SBA-15), without  $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$  addition, and heat-treated in air at 773 K, was also synthesized as reference material.

#### 2.1.2. HA crystallization inside of the Ca-doped matrix

In the second step (high pH step) the Ca-doped silica was dropped into a  $(\text{NH}_4)_2\text{HPO}_4$  (Merck  $\geq 99\%$ ) solution and was submitted to a second hydrothermal treatment at 353 K for 24 h. The powder was then washed and heat-treated in air at 773 K to obtain the final (HA-SBA-15) material.

### 2.2. Materials characterization

#### 2.2.1. Transmission electron microscopy

Micrographs were recorded using a Philips CM200 transmission electron microscope (TEM) with a  $\text{LaB}_6$  filament as the electron source, operated at 200 kV. Material samples were mounted on a microgrid carbon polymer, supported on a copper grid, by placing a few droplets of a suspension of the sample in water followed by drying at ambient conditions.

#### 2.2.2. X-ray diffraction analysis

X-ray diffraction (XRD) powder analysis was performed with a Philips X'Pert diffractometer using  $\text{Cu-K}_\alpha$  radiation ( $\lambda = 0.15418\text{ nm}$ ). The diffractometer was operated at 40 kV and 40 mA. Small-angle X-ray diffraction (SAXRD) measurements were carried out using a step size of  $0.002^\circ$ , a 20 s exposure time and a position sensitive detector (PSD) length of 0.5170 ( $2\theta$ ). Wide-angle X-ray diffraction (WAXRD) patterns were recorded using a step size of  $0.05^\circ$ , a 100 s exposure time and a PSD length of 2.1180 ( $2\theta$ ).

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