MASTER project 31.10.2017

Project : Laboratory internship

Main Laboratory ICCF – SIGMA Clermont (Clermont-Ferrand, France)

Collaboration : SAINBIOSE- MSE (Saint-Etienne, France)

Overview

Calcium phosphates (CaPs) are mineral constituents of hard tissue (69 wt% of bone). They are composed of ions found in physiological environment (Ca^{2+}, P^{5+}, Na^{+}, Mg^{2+}, CO_3^{2-}, F^{-}, Cu^{2+}, etc). Their great biocompatibility as well as resemblance in composition with inorganic phase of bone allows them to be implanted inside the human body. They are commonly applied in medicine, particularly in dentistry and orthopedics, as bone substitutes and grafts. Hydroxyapatite, with chemical formula $Ca_{10}(PO_4)_6(OH)_2$ (HA), is the most important calcium phosphate in the field of bone substitutes. It is due to its bioactivity and biocompatibility with the human bone, and its osteoconductive capacity. However, HA shows limited ability to stimulate the development of new bone tissue (bone apposition), has a very low rate of biodegradation (slow osseointegration) and as such can elicit inflammatory response and be the subject of bacterial infection. A potential method of improving the bioactivity of HA and bringing it new functionalities is to dope HA with biologically active ions, such as Sr^{2+}, Zn^{2+}, Cu^{2+}…. Besides its antimicrobial activity, copper is an essential trace element, necessary for mammalian life and it plays a role in the cross-linking of collagen and elastin of bone [1-3]. Cu^{2+} ions have been reported to enhance angiogenesis potential, osteostimulation and antibacterial properties [4-6], to stimulate the proliferation of endothelial cells [7], to promote wound healing in rats [8,9], and to enhance cell activity and proliferation of osteoblastic cells [10]. Recent study on copper containing glass-ceramic has shown the interesting potential of Cu^{2+} doping for bioactivity and biocompatibility, with the necessity to control the CuO content, i.e. to manage the Cu^{2+} release, in order to tune cells activity and viability [11]. Recent work performed in our laboratory has put forward a non-conventional incorporation mechanism of copper ions in the HA phase while demonstrating non-cytotoxicity and antibacterial potential [12].

Study goal and tasks of the project

This scientific study aims to develop a new bioceramic material for bone substitute and/or coating on metallic prostheses that would combine the bioactivity of HA with antimicrobial and pro-angiogenic properties.

In this scientific framework, the proposed internship will be dedicated to the manufacturing of copper-doped hydroxyapatites (**CuHA)** bioceramics for biological evaluations. The production of a ceramic consists of three main successive steps: (i) **powder synthesis**, (ii) **shaping**, and (iii) **sintering**. The sintering consists in a high-temperature thermal treatment which leads to the final ceramic part by elimination of pores contained in the shaped body.

The first part of this project will be focused on the synthesis of CuHA with different copper content. CuHA will be prepared by a conventional aqueous precipitation method using salts of copper, calcium and phosphorus. These powders will be analyzed by means of several physico-chemical techniques, such as powder X-Ray Diffraction, vibrational spectroscopy (FTIR and Raman) and chemical analysis (XRF and MP-AES), in order to determine their phase and chemical composition. In the second step, we will study (i) the thermal stability of the CuHA powders, by means of thermal analyses (e.g, TGA-DT, infrared spectrometry, X-Ray Diffraction), and (ii) the influence of the powder characteristics (e.g., specific surface area, particle size distribution) on the ceramic sintering. Once the powder features optimized, pellets will be produced by a uniaxial pressing at 40 MPa of powder in a 12.6 mm diameter stainless steel die, followed by a cold isostatic pressing under 3000 MPa. Finally, these pellets will be sintered then mirror polished up to 1 µm with diamond paste. Biological evaluation will be performed at ICCF under the supervision of Pr S. Descamps and Ms A. Jacob in the framework of her PhD work (2017-2020, ICCF).

This work is a collaborative project between the team Materials For Health at ICCF, SIGMA Clermont (Clermont-Ferrand, France) and the Center for Health Engineering (CIS), Mines de Saint-Etienne (Saint-Etienne, France). The student will be mainly based at CIS in Saint Etienne but will also spend some time at ICCF in Clermont-Ferrand.

Profile

A Master student with formation in the field of materials, ceramics, and/or biomaterials is expected. The student will have to conduct all tasks from chemical synthesis of CuHA materials up to the shaping of the materials. The student must show good skill for collaborative work and will have to move between the two laboratories (1 h distance) even if mainly localized at Mines Saint-Etienne. The student may have to present his work in national conferences during the internship period. Classical gratification will be proposed for this 6-months master level internship. The project should be continued through a PhD thesis.

Contacts

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