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Nanocrystalline hydroxyapatite doped with magnesium and zinc: Synthesis and characterization

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Abstract

During recent years, there have been efforts in developing nanocrystalline bioceramics, to enhance their mechanical and biological properties for use in tissue engineering applications. In this research, we made an attempt to synthesize nanocrystalline bioactive hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$, HAp) ceramic powder in the lower-end of nano-range (2–10 nm), using a simple low-temperature sol–gel technique and studied its densification behavior. We further studied the effects of metal ion dopants during synthesis on powder morphology, and the properties of the sintered structures. Calcium nitrate and triethyl phosphite were used as precursors for calcium and phosphorous, respectively, for sol–gel synthesis. Calculated quantities of magnesium oxide and zinc oxide were incorporated as dopants into amorphous dried powder, prior to calcination at 250–550 °C. The synthesized powders were analyzed for their phases using X-ray diffraction technique and characterized for powder morphology and particle size using transmission electron microscopy (TEM). TEM analysis showed that the average particle size of the synthesized powders were in the range of 2–10 nm. The synthesized nano-powders were uniaxially compacted and then sintered at 1250 °C and 1300 °C for 6 h, separately, in air. A maximum average sintered density of 3.29 g/cm^3 was achieved in structures sintered at 1300 °C, developed from nano-powder doped with magnesium. Vickers hardness testing was performed to determine the hardness of the sintered structures. Uniaxial compression tests were performed to evaluate the mechanical properties. Bioactivity and biodegradation behavior of the sintered structures were assessed in simulated body fluid (SBF) and maintained in a dynamic state.

Keywords: Nanostructured bioceramics; Nanocrystalline hydroxyapatite; Nano-powder; Sol–Gel; Calcium phosphate; Biomaterial

1. Introduction

Bioactive and bioresorbable phases of calcium phosphate bioceramics are materials of choice for bone–tissue engineering applications because of their similarity of composition with the mineral phase of the bone, excellent biocompatibility (interaction with the bone tissue to develop a strong bond at the interface), ability to promote cellular functions and expressions, and osteoconductivity (ability to help in the formation of new bone) [1,2]. These bioceramics are primarily used as bone substitutes in both dentistry and medicine. Current dental and medical applications of calcium phosphate ceramics or calcium phosphate-based composites include: repair of bone and periodontal defects, maintenance or augmentation of alveolar ridge, ear and eye implants, spine fusion and adjuvant to uncoated implants. In 1920, Albee reported the first successful medical application of calcium phosphates in humans [3], and in 1975 Nery et al. reported the first dental application of these ceramics in animals [3]. These ceramics are used in medical applications because of the range of properties they offer, from tricalcium phosphates being resorbable to hydroxyapatite being bioactive; they are undeniably the current rage for clinical usage [1,4]. Calcium phosphates exhibit considerably improved biological affinity and activity, compared to other bioceramics. However, unlike alumina and zirconia these ceramics are mechanically weak and exhibit poor crack growth resistance, which limit their uses to non-load bearing applications such as osteoconductive coatings on metallic prosthesis and as powders in spinal fusion.

Among different forms of calcium phosphates, the bioactive hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$) phase has been most extensively researched due to its outstanding biological responses to the physiological environment. However, there is

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a significant difference of properties between natural apatite crystals found in the bone mineral and the conventional synthetic HAp. Bone crystals are formed in a biological environment through the process of biomineralization and are nano-sized. In addition, the bone mineral also contains trace ions like Na^+, $Mg^{2+}$and K^+, which are known to play a role in overall performance [5]. It has been demonstrated that, the resorption of HAp ceramics is quite different from that of bone mineral. Bone mineral crystals are of nano-scale range with large surface areas; therefore, the resorption by osteoclasts is quite homogeneous. Synthetic HAp on the contrary, presents a low surface area and has strong bonding. Resorption takes place in two steps: disintegration of particles and dissolution of the crystals [6]. It has also been shown that the bioactivity of conventional synthetic HAp ceramics is inferior to the bone mineral [5,7,8].

There is a constant need for orthopedic and dental implant formulations that have better osseointegrative properties. One of the approaches to improve overall properties of ceramic biomaterials is by exploring the unique advantages offered by nanotechnology. Nanostructured ceramics can be tailored to obtain desired chemical compositions, surface properties (specifically topography), mechanical properties (ductility) and distribution of grain size similar to those of physiological bone (which contains 70% by weight of hydroxyapatite ceramic with grain sizes less than 100 nm) [9,10].

During recent years, attempts have been made in exploring nanotechnology to create nanoscale bioceramics, to improve their properties and to overcome the known limitations. Kong et al. developed zirconia–alumina nano-composite using the Pechini process and had improved the biocompatibility of the composite by addition of hydroxyapatite [11]. Nanostructured materials offer much improved performances than their large-particle-sized counterparts, due to their large surface to volume ratio and unusual chemical/electronic synergistic effects. Nanoscale ceramics can exhibit significant ductility before failure, contributed by the grain-boundary phase. In 1987, Karch et al. reported that, with nanograin size, a brittle ceramic could permit a large plastic strain up to 100% [12]. Nanostructured biomaterials promote osteoblast adhesion and proliferation, osteointegration, and the deposition of calcium containing minerals on the surface of these materials [13]. Also, nanostructured ceramics can be sintered at a lower temperature thereby; problems associated with high temperature sintering processes are eliminated. It is possible to enhance both the mechanical and biological performance of calcium phosphates by controlling the characteristic features of powders such as particle size and shape, their distribution and agglomeration [14]. Nanostructured bioceramics clearly represent a promising class of orthopedic and dental implant formulations with improved biological and biomechanical properties. It is favorable to incorporate trace ions that are naturally present in the bone mineral to improve bioactivity of synthetic HAp [15–17]. It is believed that bone grafts fabricated using these nanocrystalline HAp powder doped with essential trace elements would possess superior mechanical and biological properties, analogous to natural bone.

Though numerous processes have been used to synthesize micron sized HAp ceramic powder, only a few techniques have been developed to synthesize nano-powder. Of these, sol–gel synthesis of HAp nanoceramics has recently attracted much attention [18,19]. The sol–gel method offers a molecular-level mixing of the calcium and phosphorus precursors, which is capable of improving chemical homogeneity of the resulting HAp to a significant extent, in comparison with conventional methods such as solid state reactions [20], polymeric precursor route [21], wet precipitation method [22] and micro emulsion technique [23]. Synthesis of nanoscale HAp powder via other methods has also been attempted [24]. However, in most of these works, a long period of the sol preparation time, 24 h or longer, is commonly reported. In addition, preparation of single-phase HAp powder has been a concern.

In this research, we have developed a simple sol–gel process that could produce HAp nano-powder of size 2–10 nm at a relatively low temperature, with a fairly short synthesis time. Additionally, we have introduced two divalent metal ions, which are known to be present in the bone mineral during synthesis of nano-powder, and analyzed their effects on powder morphology and the properties of nanostructured ceramics developed with this powder. We have also assessed bioactivity and biodegradation behavior of these ceramics using simulated body fluid (SBF), maintained in a dynamic state. This paper presents the synthesis and characterization of pure and doped nanocrystalline HAp ceramic in detail.

2. Experimental procedure

2.1. Materials and method

Pure and doped nanocrystalline HAp powders were synthesized through a water-based sol–gel powder processing method. In this method, 0.025 mol of triethyl phosphite (Fisher Scientific, USA) was first hydrolyzed with a fixed amount of distilled water (the molar ratio of water to phosphite is fixed at 8) in a nalgene bottle under vigorous stirring. A stoichiometric amount of calcium nitrate (Fisher Scientific, USA) dissolved first in 25 ml of distilled water, was added drop wise into the hydrolyzed phosphite sol. The mixed sol solution was then continuously agitated for additional 4 min and kept static (aging) at 50 °C. Measured amount of the mixed sol was sampled, after an aging time of 125 min. This aged sol was then subjected to thermal treatment at 85 °C until a white, dried gel was obtained. The dried gel was ground with a mortar and pestle into fine powder and subjected to different calcination temperatures, *viz.*, 250 °C, 350 °C, 500 °C and 550 °C, at a constant heat rate of 15 °C/min, followed by cooling inside the furnace.

In order to synthesize nanocrystalline HAp powder doped with Magnesium and Zinc, measured quantities of magnesium oxide (MgO, Alfa Aesar, Ward Hill, MA, 96% pure) and zinc oxide (ZnO, Alfa Aesar, Ward Hill, MA, 99% pure) were incorporated into the dried amorphous gel, separately, prior to calcination. The dopants were used in the amount of 1.0, 2.5 and 4.0 wt.% to see their effects on powder morphology and properties of the sintered ceramics. The resultant powders were then