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Fluoridation of synthetic apatite: Effect on the formation of calcium-deficient hydroxyapatite and the properties of porous scaffold

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Abstract

Fluoridated apatite (FHA) has been considered as a promising bone substitute substance due to its promoting cell proliferation and osteoblastic activity. This paper reports on the synthesis of FHAs via chemical precipitation at room temperature with different KF additions. The prepared samples were characterized using various characterization methods. Both PO_4^{3-} and HPO_4^{2-} ions were found in Fourier transform infrared (FTIR) spectra. X-ray diffraction (XRD) results show that two kinds of $CaHPO_4 \bullet 2H_2O$ (DCPD1, DCPD2) mixed with FHA were present in the final products at the lower content of KF addition. However, the amount of DCPD decreased as the increment of KF added, which hints that fluoridation distinctly accelerates the reaction of transforming DCPD into FHA. Meanwhile, ^{31}P magic angle spinning nuclear magnetic resonance (MAS NMR) spectra indicated that the electron density around P nuclei in FHAs changed with F content. The highly interconnected scaffold with small pores nesting inside large ones had been fabricated by using raw FHA powder and behaved in good bioactivity when examined in simulated body fluid (SBF).

Keywords: D. Apatite; Fluoridation; XRD; NMR

1. Introduction

Calcium phosphate cement (CPC) is widely used for fracture fixation, bone and joint replacement, cosmetic surgery and oral facial bone repair [1] due to its good mechanical strength and bone conduction activity [2]. Calcium-deficient hydroxyapatite (CDHA), with a hexagonal crystal structure, is distinctively similar to human bone among CPCs for its Ca/P molar ratio near to 1.67 [3]. Furthermore, CDHA exhibits excellent biocompatibility of better solubility in body and is conducive to mineral deposition [4]. However, the mechanical properties of CDHA drop rapidly as calcium lost and, similarly to osteoporosis in nature, a progressive metabolic disease presents brittle bones with a concomitant reduce of Ca/P ratio [5]. Therefore, in order to hold or improve the mechanical properties of CDHA, increasing calcium or Ca/P ratio may be an effect method.

Current trends in preparation of CDHA are imperatively coupled with cheap process techniques, and many researchers focus their attentions on the methods of transforming from calcium phosphate salts to CDHA [6–9]. The formation of CDHA are attributed to the low driving force available for the growth in special conditions [8,10–12]. The formation speed of CDHA is affected by several factors. Amorphous α-tricalcium phosphate (α-TCP) [13] and amphiphilic triblock copolymer (pluronic) [8] were observed to accelerate the formation of CDHA. On the

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contrary, alanine-functionalized polyphosphazene nanofibers was found to delay the transformation from precursors to CDHA when adopting $Ca_4(PO_4)_2O$ (TeCP), MCPM and $CaHPO_4$ (DCPA) as starting materials to prepare CDHA [7]. However, the detail mechanisms of the impedance to driving force are still not completely uncovered.

Fluorine exists as a trace element in the mineral phase of bone and teeth. Fluoridate reagent is normally used to improve the stability of HA because of the thermal decomposition and corrosion of HA in the acid environment [14–16]. The enhancement of stability has been confirmed by adding F ion into HA despite of the synthesis methods adopted [14–18]. Fluoridated apatite, as alternative biomedical materials, proves to exhibit a good biocompatibility, thermal stability and corrosion resistance that is benefited for the cell growth in further experiments of cultivating biologic cells [19,20]. Fluoride has also been used to prevent the reduction in bone density associated with osteoporosis [21,22]. Our previous works show that both thermal and chemical stability are improved when FHA synthesized by the sol–gel method [23], and the shape and the distribution of pore in fluoridating-HA scaffolds are also manifestly improved due to the good stability of FHA during the scaffold processing [24]. In the present study, a chemical synthesis method was adopted to prepare FHAs, based on that KF was taken as fluoridating agent, $Ca(CH_3COOH)_2$ and KH_2PO_4 as precursors. It was found that with the addition of F, CDHA preparation exhibited high-hydrolysis effect and promoting driving force. The finding may shed the light on keeping a constant Ca/P ratio in bone and leading to an effective therapeutic treatment for osteoporosis.

2. Materials and methods

2.1. Material synthesis

For the preparation of FHAs, $Ca(CH_3COOH)_2 \cdot H_2O$, KH_2PO_4 and $KF \cdot 2H_2O$ (component concentrations listed in Table 1) were adopted as reactants to synthesize samples at room temperature. No carbonated hydroxyapatites, a kind of product of HA reacting with CO_2 in the air, as well as other impurities were found in the final products. The prepared samples were named as Sample 00–10F based on the amount of KF added. 0.04 mol Ca $(CH_3COOH)_2 \bullet H_2O$ was dissolved with 200 ml ultra-pure water, and 0.024 mol KH_2PO_4 with different additions of $KF \cdot 2H_2O$ were dissolved with 120 ml ultra-pure water. The pH value of each solution was adjusted to 7 by KOH. Then the two solutions were dropwise mixed at the rate of 2–3 drops per second, with cling film wrapping around the reaction vessel to avoid CO_2 in the air involving in the reaction. The solution has been electromagnetically stirred for 4 h and the pH value was adjusted per hour to keep it at 7. Precipitates were aged for 24 h, then washed and dried.

Table 1
The preparing recipe of FHAs

Apatite type (F)	Reactant compositions (mol)		
	$Ca(CH_3COOH)_2 \cdot H_2O$	KH_2PO_4	$KF \cdot 2H_2O$
00	0.04	0.024	0
02	0.04	0.024	0.0016
04	0.04	0.024	0.0032
06	0.04	0.024	0.0048
08	0.04	0.024	0.0064
10	0.04	0.024	0.008

2.2. Instrumental characterization

Ca, P and K concentrations were determined using ICP (Thermo, iCAP 6300). A 0.05 g quantity of specimen was dissolved with a solution composed of HCl, HNO_3 and HF, then dried out. After that, it was dissolved with another 500 ml solution including HCl and HNO_3 in a volumetric flask with ultra-pure water. The later solutions were used for ICP measurements. C concentration of specimen was determined using High Frequency Infrared Ray Carbon Sulfur Analyzer (CSI) (Shanghai Bao Ying Optoelectronics, CS-206). Finally, F and O concentrations were determined using Sequential X-ray Fluorescence Spectrometer (XRF) (SHIMADZU, XRF-1800), operating at 40 kV and 95 mA. The F and O concentrations were measured by a FP method referring to the concentrations of Ca, P, K and C gained from ICP and CSI. The measurements of F concentration were precisely averaged for 4 times.

XRD patterns were collected using a diffractometer (type D8 Advance, Bruker, Germany) with Cu Kα radiation, operating at 40 kV and 40 mA, scanning within a 2θ range 10–80°,at a scanning speed of 4°/min. The compositions of Sample 00F and Sample 02F as-synthesized were determined with a multiphase Rietveld refinement on the X-ray diffraction patterns. Crystal size was determined by using the Scherrer equation. The morphologies of sample particles were observed by using a TEM (H8000, Hitachi Co., Japan) under a high voltage of 200 kV. FTIR spectra were used to study the molecular structure of samples. 1 mg of dried sample was mixed with KBr in a ratio of 1:300 and pressed using a tableting machine. With an FTIR spectrometer (Thermo Fisher, Nicolet 6700), a scanning within the range from 400 to 4000 cm^{-1} were performed. The morphologies of scaffold were observed by using SEM (Carl Zeiss Ultra 55).

^{31}P MAS NMR spectra were obtained using a Bruker Avance III (9.4T) spectrometer at the phosphorus resonance frequency of 161.976 MHz, equipped with a wide broad band CP/MAS probe. For ^{31}P MAS experiment, the ^{31}P 90° pulse length was 1.30 μs. A tppm15 sequence was used for proton decoupling with a pulse length of 100.00 μs. The sample cells were 4 mm cylindrical zirconia rotors. The samples were spun at the spinning speed 9 kHz. The acquisition time was 0.00633 s with a spectral width of 81,521.74 Hz and the pulse repetition time was 4 s. Numbers of scan of samples 00F, 04F, 10F were 300, 300, 1024, respectively. Chemical shifts were ascertained relative to KH_2PO_4 (0 ppm).