

In Situ Formation and Characterization of Fluorine-Substituted Biphase Calcium Phosphate Ceramics of Varied F-HAP/ β -TCP Ratios

S. Kannan, J. M. Ventura, and J. M. F. Ferreira*

Department of Ceramics and Glass Engineering,
University of Aveiro, CICECO,
3810-193 Aveiro, Portugal

Received February 15, 2005

Revised Manuscript Received April 23, 2005

Calcium phosphate ceramics (CPC) have gained considerable attention in biomedical applications during recent years due to their immense biocompatible features with the living bone. In particular, biphase ceramics phosphate (BCP) [a mixture of hydroxyapatite (HAP) and β -tricalcium phosphate (β -TCP)] belonging to the family of CPC have received more attention from the biomedical arena due to their perfect matches with the human bone.^{1–3} The success of the BCP ceramics in surgical procedures relies on the difference in the degradation properties of HAP (nonresorbable) and β -TCP (resorbable). This variation in their dissolution behavior was found to have a significant impact on the rapid formation of new bone at the implant site when compared to the individual HAP or β -TCP. Very recently, fluorine-substituted hydroxyapatite (F-HAP) was found to be a potential alternative in certain applications of both bone and dental surgical operations due to its presence in trace levels in composition.^{4,5}

Literature reports have revealed enough evidence on the synthesis of F-HAP through varied preparation methods involving sol–gel processing and mechanochemical synthesis and also through wet chemical reactions.^{6–8} Usually, during the preparation of F-HAP, the position of the negatively charged hydroxyl group is replaced by the anionic fluorine. This replacement was found to inhibit the resorption behavior of F-HAP. By this fact, the resorbable behavior of F-HAP can be expressed as β -TCP > HAP > F-HAP. One possible solution is that the poor resorption behavior (low bioactivity) of F-HAP could be rectified by the inclusion of resorbable β -TCP component as a composite. Hence, by this fact F-HAP/ β -TCP ceramics can enhance early stage of bone

ingrowth (favored by β -TCP) and F-HAP can achieve long-term fixation of the implant.

The preparation of F-HAP/ β -TCP composites has been described very rarely in the literature. Recently, the formation of F-HAP/ β -TCP composite was reported by Wong et al.⁹ by the mechanical mixing of individual F-HAP and β -TCP components. However, in situ formation of F-HAP/ β -TCP mixture presents the following advantages: (i) mixing of phases at the crystallite level; (ii) achieving the desired particle size; and (iii) very meagre chance of added impurities into the phases. The present study is an attempt to form F-HAP/ β -TCP mixtures with varied ratios of F-HAP and β -TCP by an in situ method of preparation through wet precipitation. The preparation is carried out by forming powders of calcium-deficient apatites with substituted fluorine and subsequent calcination at higher temperatures to form biphase mixtures. FT-IR and XRD techniques were employed to characterize the powders. Mechanical tests were performed through flexural strength measurements of pellets prepared by uniaxial pressing of the powders. The microstructure of the composites was examined using SEM.

The following details powder preparation. Calcium nitrate tetrahydrate [$\text{Ca}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$], ammonium dihydrogen phosphate [$(\text{NH}_4)_2\text{HPO}_4$], and ammonium fluoride [NH_4F] were used as precursors for the preparation of F-HAP/ β -TCP composite. Calcium-deficient apatites of predetermined Ca/P molar ratios of 1.62 and 1.58, respectively, were formed by adding suitable concentrations of $(\text{NH}_4)_2\text{HPO}_4$ to the solution-containing $\text{Ca}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$ under a constant stirring condition of 1000 rpm. Two different concentrations of NH_4F were added to the solution mixture containing $(\text{NH}_4)_2\text{HPO}_4$ and $\text{Ca}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$ to attain calcium-deficient apatite phases of $\text{Ca}_{10-x}(\text{HPO}_4)_x(\text{PO}_4)_{6-x}(\text{OH})_x(\text{F})_{2-2x}$, where $x = 0.3$ (coded as F-BCP1) and 0.54 (coded as F-BCP2) and $\text{Ca}_{10-x}(\text{HPO}_4)_x(\text{PO}_4)_{6-x}(\text{OH})_x(\text{F})_{1-x}$, where $x = 0.3$ (coded as F-BCP3) and 0.54 (coded as F-BCP4). The pH of the mixed solution was maintained constant at 8–9 by the addition of 8 M ammonium hydroxide (NH_4OH) solution. The precipitated mixture was maintained at a constant stirring rate of 1000 rpm at 60 °C for 2 h. The suspension mixture was then decanted and allowed to settle for 24 h (precipitate maturation). The precipitates were recovered by vacuum filtration and finally dried at 80 °C overnight. The dried cake was crushed to a powder, sieved to <200 μm , and used for characterization studies, as follows.

XRD patterns for the calcined powders were recorded using a high-resolution XRD analyzer using monochromatic Cu K α radiation ($\lambda = 1.5405 \text{ \AA}$, XRD, Rigaku Geigerflex D/Mac, C Series, Japan). X-ray patterns were recorded from 20° to 60° 2 θ with a step size of 0.02° 2 θ per second. The lattice parameters were calculated from the XRD patterns as an average of six maximum intensity peaks of the HAP phase (002, 211, 112, 202, 222, and 213 planes) using MDI Jade 6.1 software. Unit cell volumes were determined from

(9) Wong, L. H.; Tio, B.; Miao, X. *Mater. Sci. Eng. C* 2002, 20, 111.

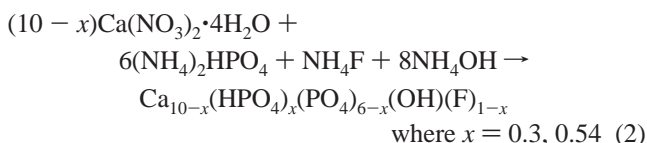
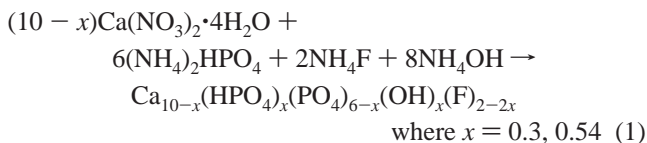
* To whom correspondence should be addressed. E-mail: jmf@cv.ua.pt.

- (1) Han, Y.; Xu, K.; Lu, J.; Wu, Z. *J. Biomed. Mater. Res.* 1999, 45, 198.
- (2) Li, Y.; Klein, C. P. A. T.; Wijn, J. D.; Meer, S. V. D.; de Groot, K. *J. Mater. Sci. Mater. Med.* 1994, 5, 263.
- (3) Hench, L. L.; Wilson, J. *An introduction to bioceramics*; World Scientific: Singapore, 1993.
- (4) Jha, L. J.; Best, S. M.; Knowles, J. C.; Rehman, I.; Santos, J. D.; Bonfield, W. *J. Mater. Sci. Mater. Med.* 1997, 8, 185.
- (5) Kim, H. W.; Noh, Y. J.; Koh, Y. H.; Kim, H. E. *J. Mater. Sci. Mater. Med.* 2003, 14, 899.
- (6) Cheng, K.; Shen, G.; Weng, W.; Han, G.; Ferreira, J. M. F. *Mater. Lett.* 2001, 51, 37.
- (7) Barinov, S. M.; Rustichelli, F.; Orlovskii, V. P.; Lodini, A.; Oscarsson, S.; Firstov, S. A.; Tumanov, S. V.; Millet, P. *J. Mater. Sci. Mater. Med.* 2004, 15, 291.
- (8) Chen, Y.; Miao, X. *Ceram. Int.* 2004, 30, 1961.

the lattice parameters values obtained from XRD patterns. FT-IR spectra for the calcined powders were recorded using the instrument Bruker IFS 55, Specac (Germany). Fluorine analysis was carried out by potentiometry (WTW, pMX 300/pH), using an ionic-selective electrode WTW, F 500, and a reference electrode WTW, R 502, after solubilization by alkaline digestion.

The calcined powders were uniaxially pressed using a steel die at 125 MPa to form rectangular bars of size $4 \times 5 \times 50$ mm and the pressed bodies were sintered at 1200 °C to analyze the mechanical strength. Flexural strength measurements were made using a mechanical testing machine AG-1S, Shimadzu (Japan). At least 10 specimens have been tested for each single-point measurement. The densities of the sintered bodies were measured by Archimedes method by immersion in mercury. The morphology of fracture surfaces of the different samples was observed by a scanning electron microscope (SEM) (4100-1, Hitachi, Japan), coupled with energy dispersive spectroscopy (EDS) analysis.

During the course of wet chemical precipitation reaction, generally Ca/P molar ratios of the precursors less than 1.67 form calcium-deficient apatites as represented by the formula $\text{Ca}_{10-x}(\text{HPO}_4)_x(\text{PO}_4)_{6-x}(\text{OH})_{2-2x}$, hypothesized by Winand.¹⁰ Usually, these deficient apatites are not stable beyond particular temperature ranges and tend to transform into a biphasic mixture comprising HAP and β -TCP ceramics, as described elsewhere.^{11,12} In the apatite structures, it is true that the positions occupied by the hydroxyl group could be replaced by similar ions of the same charge. It is not surprising the fact that fluorine ion (F^-), which possesses charge identical to that of hydroxyl ion (OH^-), could replace OH^- partially or completely without significant distortion of hexagonal apatite structure, except for some changes in the positions occupied by the replaced groups. In the present study, two different concentrations of fluorine were attempted to replace the hydroxyl groups irrespective of the Ca/P ratio of precursors added. Hence the substituted fluorine in the nonstoichiometric apatites ($\text{Ca/P} < 1.67$) form fluorine-substituted calcium-deficient apatites, which are deduced in the form of equations given below:



As discussed above that deficient apatites are not stable, hence the formed nonstoichiometric apatites decompose to mixtures of fluorine-substituted hydroxyapatite and β -whitlockite (β -TCP) ceramics with calcination at higher temper-

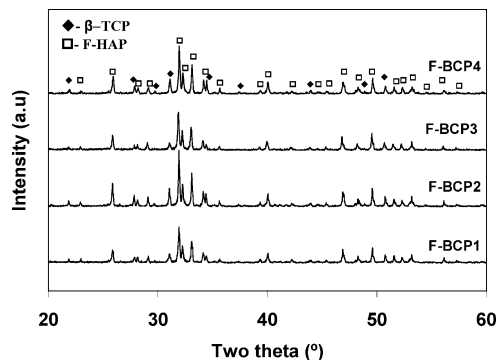
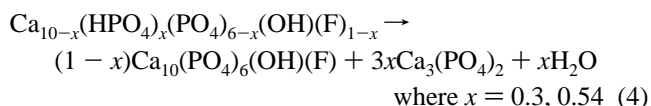
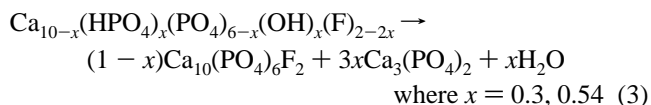


Figure 1. XRD patterns for the different fluorine-substituted apatitic powders calcined at 1200 °C.

Table 1. Calculated Lattice Parameter Values of Fluorine-Substituted Apatitic Samples Heat-Treated at 1200 °C

samples	lattice parameters a and c and unit cell volumes (V)		
	a	c	V
pure HAP (JCPDS No-9-0432)	9.418	6.884	1586.3
pure FHAP (JCPDS No-71-0880)	9.363	6.878	1561.1
pure β -TCP (JCPDS No-09-0169)	10.429	37.38	3960.8
F-BCP1	9.3652	6.8843	1568.6
F-BCP2	9.3670	6.8851	1569.4
F-BCP3	9.3788	6.8692	1569.7
F-BCP4	9.3810	6.8642	1569.3

atures. Accordingly, the transformation reactions can be represented by the following equations:



XRD patterns for the different powders calcined at 1200 °C are presented in Figure 1. This temperature was selected because the phase mixtures showed to be thermally stable up to this temperature, while calcination at 1300 °C led to the formation of α -TCP. The X-ray patterns reveal the presence of a biphasic mixture of phases comprising F-HAP and β -TCP and no other extra phases were detected from the patterns. The powders F-BCP1, F-BCP2, F-BCP3, and F-BCP4 yielded F-HAP/ β -TCP ratios of approximately 80/20, 70/30, 80/20, and 70/30, respectively. It can be noticed from the X-ray patterns that formation of phase mixtures were dependent on the calcium deficiency ($\text{Ca/P} < 1.67$) in the samples rather than the added fluorine. This can also be interpreted by the way the observed shift in the 2θ values of the 211 plane of the F-HAP phase showing exact matches with that of fluorapatite phase of JCPDS PDF# 71-0880. Lattice parameters (a and c) and unit cell volumes for the calcined powders at 1200 °C are presented in Table 1. The unit cell volumes have indicated the shrinkage in volume and the lattice parameter a has shown significant contraction with respect to pure HAP (JCPDS PDF# 09-432). Small irregular changes have been observed in the c axis values with respect to pure HAP. Similar findings have been reported in previous work on fluorine-substituted hydroxy-

(10) Winand, L. *Ann. Chim. Ser.* **1961**, *136*, 941.

(11) Reynaud, S.; Champion, E.; Bernache-Assolant, D.; Thomas, P. *Biomaterials* **2002**, *23*, 1065.

(12) Lazic, S.; Zec, S.; Milijevic, N.; Milonjic, S. *Thermochim. Acta* **2001**, *374*, 13.

Table 2. Calculated Mechanical Test Values of Fluorine-Substituted Apatitic Samples Heat-Treated at 1200 °C

samples	density ^a (g/cm ³)	flexural strength (MPa)	fluorine content (wt %)
F-BCP1	3.096 ± 0.005	42.2 ± 6.3	0.52 ± 0.02
F-BCP2	3.084 ± 0.005	39.1 ± 7.9	0.88 ± 0.02
F-BCP3	3.072 ± 0.005	33.1 ± 8.2	0.49 ± 0.02
F-BCP4	3.006 ± 0.005	29.2 ± 14.5	0.51 ± 0.02

^a For comparison purposes, the theoretical density values for pure HAP, pure FHAP, and pure β -TCP are 3.160, 3.170, and 3.070 g/cm³, respectively.

apatites.¹³ This may be due to the nonstoichiometry of the precursors Ca/P ratio adapted during the present system.

Usually the apatite structure can be viewed by the unconnected PO₄³⁻ tetrahedra oriented toward Ca²⁺ ions along the *a* axis and the electronegative elements X⁻ (OH⁻ or F⁻ or Cl⁻) are placed perpendicular to the Ca²⁺ ions along the *c* axis.¹⁴ It has been proposed that X⁻ ions can be easily exchanged by other ions at higher temperatures without any crystal distortion.¹⁵ Although the electronegative group OH⁻ and F⁻ ions have the same charge, their size difference (OH⁻ = 1.68 Å and F⁻ = 1.32 Å) causes the lattice strain and hence the contraction of *a* axis occurs as observed in the present case, either by the partial or complete replacement of the OH⁻ group by F⁻ ions. This is in accordance with the previous results which have indicated similar *a* axis contraction due to F⁻ ions substitution in HAP.¹⁶ Also, it could be revealed from the present results that the higher replacement level of OH⁻ group by F⁻ ions has caused a more significant contraction in the *a* axis parameter for the powders F-BCP1 and F-BCP2 when compared to the lower replacement level, which have indicated comparably low *a* axis contraction for the samples F-BCP3 and F-BCP4. Table 2 reports the calculated density, the measured flexural strength values, and the fluorine contents of the samples. It can be seen that the final fluorine content of the samples after calcination at 1200 °C is almost independent of the added amounts (3.78 wt % for samples F-BCP1 and F-BCP2 and 1.89 wt % for samples F-BCP3 and F-BCP4). These results show that there is a significant loss of fluorine upon calcinations. Moreover, lower levels of fluorine addition can be used since the final concentration is still about 20–25 times higher than that in the human bone.³

Table 2 shows that the samples F-BCP1 and F-BCP2 had shown comparably higher density values when compared to the samples F-BCP3 and F-BCP4. However, the samples with higher proportions of β -TCP due to increased nonstoichiometry have caused low-density values. These trends are according to the theoretical density values for pure phases (HAP, FHAP, and β -TCP) given at the bottom of Table 2 for comparison purposes. The transformation of HAP into β -TCP involves a volumetric expansion and the generation of mechanical stresses within the samples. This explains why the samples richer in β -TCP present lower values of flexural

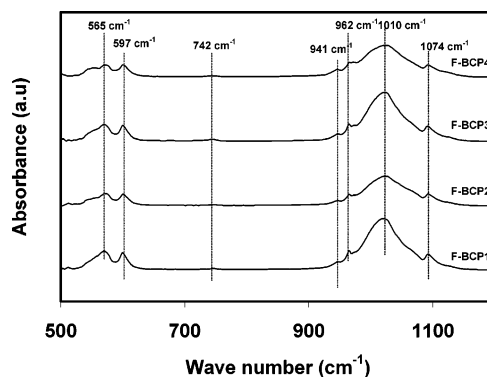


Figure 2. FT-IR spectra for the different fluorine-substituted apatitic powders calcined at 1200 °C.

strength (Table 2). Although the evolution of flexural strength is also consistent with the decreasing trend observed in the density of the samples, this can hardly be attributed to the small apparent differences in porosity.

FT-IR patterns for the different powders calcined at 1200 °C are displayed in Figure 2. The presence of PO₄ groups of apatite phase is evident from the bands observed at regions 1010 and 1074 cm⁻¹ (ν_3), 565 and 597 cm⁻¹ (ν_4), and 962 cm⁻¹ (ν_1). The evidence for the presence of β -TCP in the phase mixture is indicated by the vibrational frequencies observed at 941 cm⁻¹ for all the samples. Close examination of this particular peak revealed that peak resolution increases with increasing the content of the β -TCP. The most interesting feature of the FT-IR spectra was the band observed at 742 cm⁻¹ due to the presence of fluorine in all the samples. However, the characteristic band for the partial presence of OH groups in the powders F-BCP3 and F-BCP4 were not observed in the FT-IR patterns. This is due to the coupling effect caused by the fluorine to mask the characteristic band of hydroxyl group to form F--OH as explained by Rodriguez et al.¹³

SEM images for the fractured surfaces of the sintered bodies at 1200 °C of different samples are presented in Figure 3. The pictures reveal the uniform distribution of phase mixtures throughout the surface. The differences in the content of β -TCP in the biphasic mixtures are evident from the images of which higher content of β -TCP in the samples (F-BCP2 and F-BCP4) are viewed with comparably large grain size in comparison with the lower contents of β -TCP samples (F-BCP1 and F-BCP3) showing tiny pores (F-BCP1) and a high relative densification level (F-BCP3). Whenever required, tailored porous structures might be produced,¹⁷ which will contribute to a rapid resorption when biphasic mixtures with considerable amounts of β -TCP are implanted, causing remodeling around the implant site.

In conclusion, the present study is achieved with the in situ preparation of a biphasic mixture of phases comprising F-HAP and β -TCP with two different ratios. The observed experimental results have conveyed that formation of phase mixture is dependent on the calcium deficiency of the precursors. Fluorine is incorporated into the apatite matrix by the marginal shift observed in the XRD patterns of apatite

(13) Rodriguez-Lorenzo, L. M.; Hart, J. N.; Gross, K. A. *Biomaterials* **2003**, *24*, 3777.

(14) Calderin, L.; Stott, M. J. *Phys. Rev.* **2003**, *B67*, 134106.

(15) Cazalbou, S.; Combes, C.; Eichert, D.; Rey, C. *J. Mater. Chem.* **2004**, *14*, 2148.

(16) Narasaraaju, T. S. B.; Phebe, D. E. *J. Mater. Sci.* **1996**, *31*, 1.

(17) Lemos, A. F.; Ferreira, J. M. F. *Key Eng. Mater.* **2004**, *254–256*, 1037.

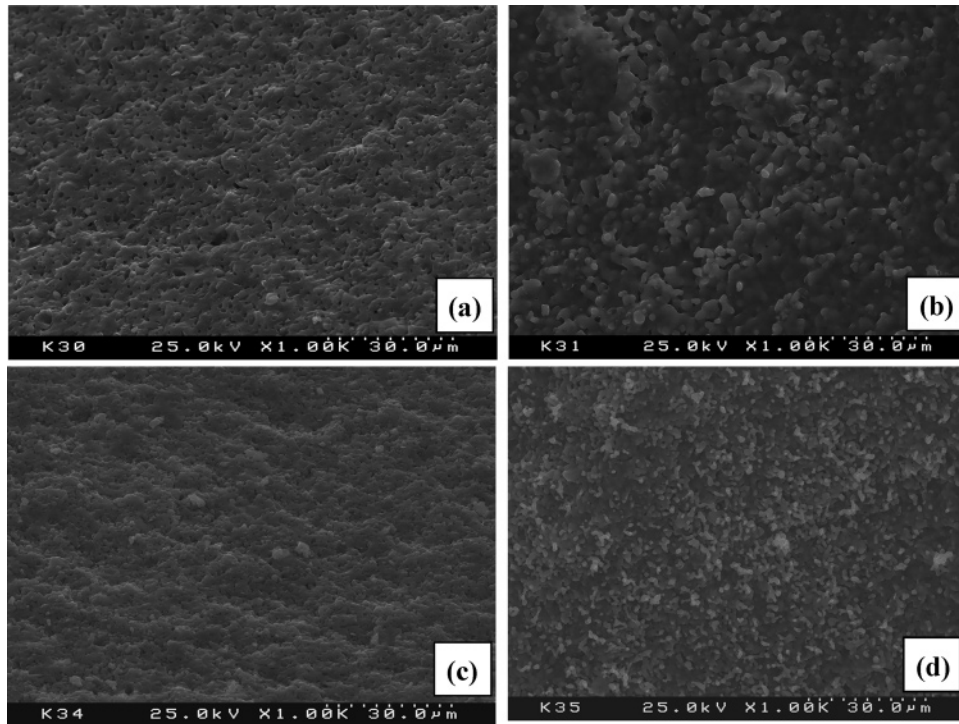


Figure 3. SEM pictures for the different fluorine-substituted apatitic samples sintered at 1200 °C. (a) F-BCP1, (b) F-BCP2, (c) F-BCP3, and (d) F-BCP4.

phase showing close proximity with the fluorapatite (JCPDS PDF # 71-0880). The partial replacement of hydroxyl group by fluorine has been indicated in the FT-IR patterns, which has shown no characteristic peak for an hydroxyl band. Higher density and improved flexural strength for higher fluorine content confirms the stable nature of F-HAP in the biphasic mixture. Finally, SEM images are viewed with the

uniform distribution of phase mixtures throughout the surface.

Acknowledgment. Thanks are due to the Portuguese Foundation for Science and Technology for financial support, project POCTI/CTM/60207/2004 and SFRH/BPD/18737/2004 grant. CM050342+