Chem. Mater. **2006,** *18,* 198−203

Synthesis and Thermal Stability of Hydroxyapatite−*β*-Tricalcium Phosphate Composites with Cosubstituted Sodium, Magnesium, and Fluorine

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

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

Received August 31, 2005. Revised Manuscript Received November 1, 2005

The preparation of biphasic mixtures (HAP + β-TCP) of controlled ratios with the combined substitution of essential biocompatible trace elements (Na, Mg, and F) was carried out by an aqueous precipitation method. The results showed that incorporated elements have played a significant role in the thermal stability of the apatites up to 1400 °C, and that increased calcium deficiency in the apatites has led to the formation of a higher proportion of β-TCP in the biphasic mixtures. However, minor discrepancies in the structural parameters due to the incorporated trace elements and the matching of phases of the synthesized powders with respect to the stoichiometric HAP were apparent from the present investigation.

1. Introduction

Hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$, HAP) has been regarded as being an important implant material because of its similarities to the inorganic component of vertebrate bone and tooth mineral. Its departure from the chemistry of pure apatites and its similarity to bone lead HAP to be considered an ideal match to living bone.[1,2] The concurrent existence of both HAP and β-tricalcium phosphate [β-TCP, β-$Ca_3(PO_4)_2$] forms biphasic calcium phosphates that combine the excellent bioactivity of HAP with the good resorbability of β-TCP, and thus HAP and β-TCP have been used as materials for bone replacement.[3−5]

The family of apatites, an ionocovalent ($M_{10}(XO_4)_6F_2$) structural model, is ready to accept an array of ionic substituents, both cationic and anionic, which induce modifications in the crystallinity, morphology, lattice parameters, and structural stability without causing significant changes in the structure's hexagonal system.[6] Under this perspective, substitution of trace elements into the apatite structure has been the subject of widespread investigation nowadays because of their impending role in the biological process during implantation studies.[7−13]

To date, a number of studies have been devoted to element substitutions such as F, Mg, and Na on the apatite structure. Each of these mentioned elements plays an essential part in the biological action course: (a) Na is a monovalent ion available in abundance next to calcium and phosphorus, which plays a significant role in bone metabolism and osteoporosis.[14,15] (b) Mg is undoubtedly one of the most important bivalent ions associated with the biological apatite; it has its own significance in the calcification process and on bone fragility, and has indirect influence on mineral metabolism.[16,17] (c) F is well-recognized for its potential behavior relating to the stability of the apatite and for its prevention role in dental caries.[18,19] However, combined substitution of these elements with the simultaneous formation of biphasic mixtures of HAP and β-TCP is a new contribution to improving and refining calcium phosphates in the market. Hence the goal of the present work is an effort toward the synthesis of biphasic mixtures of HAP and β-TCP with combined substitution of Na, Mg, and F through an aqueous precipitation method. Generally, biphasic mixtures are formed by the calcination of calcium-deficient apatites beyond 700 °C, and the proportions of the resulting mixtures

---

* To whom correspondence should be addressed. Tel.: 351-234-370242. Fax: 351-234-425300. E-mail: jmf@cv.ua.pt.

(1) Elliott, J. C. *Structure and Chemistry of the Apatites and Other Calcium Orthophosphates*; Elsevier: Amsterdam, 1994.
(2) Aoki, H. *Science and Medical Applications of Hydroxyapatite*; Japanese Association of Apatite Science: Tokyo, 1991.
(3) Gauthier, O.; Bouler, J. M.; Aguado, E.; LeGeros, R. Z.; Pilet, P.; Daculsi, G. *J. Mater. Sci.: Mater. Med.* **1999**, *10*, 199.
(4) Le Geros, R. Z.; Lin, S.; Rohanizadeh, R.; Mijares, D.; Le Geros, J. P. G. *J. Mater. Sci.: Mater. Med.* **2000**, *14*, 201.
(5) Kannan, S.; Rocha, J. H. G.; Ventura, J. M. G.; Lemos, A. F.; Ferreira, J. M. F. *Scr. Mater.* **2005**, *53*, 1249.
(6) Cazalbou, S.; Combes, C.; Eichert, D.; Rey, C. *J. Mater. Chem.* **2004**, *14*, 2148.
(7) Suchanek, W.; Byrappa, K.; Shuk, P.; Riman, R. E.; Janas, V. F.; TenHuisen, K. S. *Biomaterials* **2004**, *25*, 4647.
(8) Yamasaki, Y.; Yoshida, Y.; Okazaki, M.; Shimazu, A.; Uchida, T.; Kubo, T.; Akagawa, Y.; Hamada, Y.; Takahashi, J.; Matsuura, N. *J. Biomed. Mater. Res.* **2002**, *62*, 99.
(9) Kannan, S.; Ventura, J. M.; Ferreira, J. M. F. *Chem. Mater.* **2005**, *17*, 3065.
(10) Bertoni, E.; Bigi, A.; Cojazzi, G.; Gandolfi, M.; Panzavolta, S.; Roveri, N. *J. Inorg. Biochem.* **1998**, *72*, 29.
(11) Mayer, I.; Schlam, R.; Featherstone, J. D. B. *Inorg. Biochem.* **1997**, *66*, 1.
(12) De Maeyer, E. A. P.; Verbeeck, R. M. H.; Naessens, D. E. *Inorg. Chem.* **1993**, *32*, 5709.
(13) Gibson, I. R.; Bonfield, W. *J. Mater. Sci.: Mater. Med.* **2002**, *13*, 685.
(14) Itoh, R.; Suyama, Y. *Am. J. Clin. Nutr.* **1996**, *63*, 735.
(15) Ginty, F.; Flynm, A.; Cashman, K. D. *Br. J. Nutr.* **1998**, *79*, 343.
(16) Bigi, A.; Foresti, E.; Gregoriani, R.; Ripamonti, A.; Roveri, N.; Shah, J. S. *Calcif. Tissue Int.* **1992**, *50*, 439.
(17) Martini, L. A. *Nutr. Rev.* **1999**, *57*, 227.
(18) Ten Cate, J. M.; Featherstone, J. D. B. *Crit. Rev. Oral Biol. Med.* **1991**, *2*, 283.
(19) Caverzasio, J.; Palmer, G.; Bonjour, J. P. *Bone* **1998**, *22*, 585.

10.1021/cm051966i CCC: $33.50

Table 1. Molar Concentrations of the Precursors Used in the Preparation of Na, Mg, and F Cosubstituted Apatites

sample	molar concentration of the initial precursor salts: Ca	P	Na	Mg	F	Ca:P molar ratio	(Ca+Na+Mg):P molar ratio
HAP	1.0	0.6				1.67	
Nmfap-1	1.0	0.6	0.032	0.02	0.03	1.67	1.75
Nmfap-2	0.948	0.6	0.032	0.02	0.03	1.58	1.67
Nmfap-3	0.924	0.6	0.048	0.028	0.03	1.54	1.67

are dependent on the Ca:P ratios of the precursors.[20,21] This concept was used in the present study for synthesizing biphasic apatites with the combined substitution of Na, Mg, and F in trace levels to mimic both bone and tooth composition. The synthesized powders were characterized using thermal analysis, XRD, elemental analysis, and FT-IR.

2. Materials and Methods

2.1. Powder Preparation. The synthesis was carried out in a fully automated apparatus (capacity = 6 L) with a specific device to control the stirring of suspensions, the addition rate of reactants, and the temperature. Calcium nitrate tetrahydrate ($Ca(NO_3)_2 \cdot 4H_2O$; Vaz Pereira, Portugal), diammonium hydrogen phosphate ($(NH_4)_2HPO_4$; Vaz Pereira, Portugal), sodium nitrate ($NaNO_3$; Vaz Pereira, Portugal), magnesium nitrate hexahydrate ($Mg(NO_3)_2 \cdot 6H_2O$; Merck, Germany), and ammonium fluoride (NH_4F; Riedel-deHaen, Germany) were used as starting chemical precursors, respectively, for calcium (Ca), phosphorus (P), sodium (Na), magnesium (Mg), and fluorine (F). It is important to note that the synthesis was carried out in bulk (every precursor salt was prepared separately in a 1000 mL measuring flask) to ensure the reproducibility of the experimental results. The concentration of each of the trace-element precursors was selected on the basis of its natural abundance in hard tissues (bone and dentine) in such a way that the concentration of Na for all the compositions was kept higher than that of Mg. The fluorine precursor concentration was kept constant for all the compositions.

For the preparation of Na, Mg, and F cosubstituted apatites, $(NH_4)_2HPO_4$ solution was added slowly at a rate of 100 mL/min to the solution mixture containing nitrates of Ca, Mg, and Na, and was stirred at a rate of 1000 rpm. To each of the above solution mixtures was added NH_4F to incorporate fluoride ions (solution concentrations of the precursors are detailed in Table 1). After addition was completed, the measured pH was found to be around 4. The pH of the mixed solution was then increased to 10 by the addition of concentrated ammonium hydroxide (NH_4OH) solution. The reaction mixture was stirred (1000 rpm) continuously for 2 h at a temperature of 90 °C, with maintenance of constant pH in the range of 9.5−10 through the entire stirring time period. A pure stoichiometric HAP without any additives was prepared under the same experimental conditions to compare the results. The precipitated suspension was poured from the reactor, and was allowed to settle for 24 h for the maturation of precipitate. After 24 h, the precipitates were separated through the vacuum filtration technique, and were dried at 80 °C overnight. The dried cakes were ground to fine powders, sieved through a mesh size of 200 μm, and used for characterization studies.

2.2. Characterization Techniques. The dried powders were subjected to thermal analysis with a heating rate of 5 °C/min between 30 and 1000 °C under an air atmosphere (Labsys Setaram TG-DTA/DSC, France) to analyze the thermal behavior during heating. The prepared powders were heat treated at different temperatures ranging from 700 to 1400 °C to study the phase changes. Calcination was carried out in a Thermolab furnace (Pt30%Rh−Pt6%Rh thermocouple) with a heating rate of 5 °C/min to achieve a predetermined temperature range and with a dwelling time of 2 h; the powder samples were again cooled to room temperature at a rate of 5 °C/min. X-ray diffraction studies on the calcined powders were carried out using a high-resolution Rigaku Geigerflex D/Mac C Series diffractometer with Cu Kα radiation ($\lambda = 1.5406$ nm) produced at 30 kV and 25 mA to scan the diffraction angles (2θ) between 20 and 50° with a step size of 0.02° 2θ per second. Lattice constants were determined by least-squares refinements from the well-determined positions of the most intense reflections, which were processed by MDI Jade 6.1 software. For this purpose, the reflection planes (002), (211), (112), (300), (222), and (213) for HAP and the planes (024), (1010), (300), (0210), (220), and (2110) for β-TCP were used for calculations. The volume of the hexagonal unit cell for each HAP formulation and the volume of the rhombohedral unit cell for each β-TCP formulation were calculated from the relationships $V = 2.589a^2c$ and $V = 0.8660a^2c$, respectively.

Quantitative determination of the phase compositions of biphasic mixtures was made using X′Pert HighScore 1.0 *f*, PANalytical BV, using the International Center for Diffraction Data (2004) database. Crystallographic identification of the phases of synthesized apatites was accomplished by comparing the experimental XRD patterns to standards compiled by the International Center for Diffraction Data (ICDD), which were cards 09-0432 for HAP and 09-0169 for β-TCP. Elemental analysis for the presence of all elements except fluorine was made using X-ray fluorescence spectroscopy (Philips PW2400 X-ray fluorescence spectrometer). The vacuum pressure of the chamber was lower then 2 Pa. The error associated with each chemical element could be determined as being ±1 of the last significant digit of the measured values. Fluorine content was measured using the selective ion electrode method. Infrared spectra of the prepared powders and powders calcined at different temperatures were obtained using an infrared Fourier spectrometer (FT-IR, model Mattson Galaxy S-7000, U.S.A.). For this purpose, each powder was mixed with KBr in the proportion of 1:150 (by weight) for 15 min, and was pressed into a pellet using a hand press.

3. Results and Discussion

3.1. Characterization of the Dried Powders. The XRD patterns for the prepared powders are presented in Figure 1. All the powders have indicated the formation of an apatite phase differing only in peak width and absolute intensity of the diffraction patterns. Other powders, except HAP, which can be labeled as nonstoichiometric, are viewed with the broad diffraction peaks indicative of poor crystallinity in comparison with the stoichiometric HAP powder. The

---

(20) LeGeros, R. Z. *Calcium Phosphates in Oral Biology and Medicine*; Monographs in Oral Science; Basel: Karger, 1991.

(21) Ishikawa, K.; Ducheyne, P.; Radin, S. *J. Mater. Sci.: Mater. Med.* **1993**, *4*, 165.

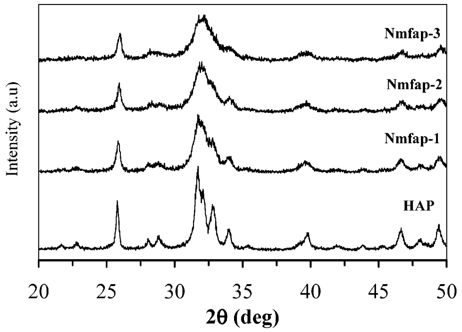

Figure 1. X-ray diffraction patterns for the prepared powders.

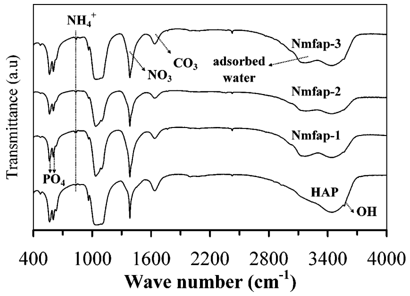

Figure 2. FT-IR spectra for the prepared powders.

substitution of Na, Mg, and F did not appear to affect the diffraction pattern of prepared powders. It should be noted that X-ray diffraction analysis of precipitated apatite powders resulted in diffraction patterns that could resemble HAP even though the Ca:P ratio was greater or less than the stoichiometric molar ratio of 1.67 for HAP.[22,23]

FT-IR spectra displayed in Figure 2 also confirm the formation of an apatite phase for all the powders with the observed fundamental vibrational modes of the PO_4 group at 475, 574, 609, 966, and 1020−1120 cm^{-1}. The bands present at 630 and 3570 cm^{-1} could be attributed to the presence of an OH group of the HAP phase. It is interesting to note from the FT-IR patterns of the cosubstituted powders that the peaks corresponding to OH groups were not as intense as those witnessed in the case of HAP, because the incorporated F would have caused the partial replacement of an OH group. However, it is difficult to explain the role of substituted F as well as that of the cations such as Mg and Na in the prepared powders, because the observed phases exhibit a low crystallinity leading to a lower peak definition in both the XRD patterns and FTIR spectra. Therefore, heat treatments will be required for enhancing crystallinity for a more precise characterization. In fact, the FT-IR patterns also tend to coincide with the results from XRD by the way that the peak resolution of OH and PO_4 bands are viewed with less intensity when compared with those of the stoichiometric HAP. The presence of the adsorbed water could also be detected from FT-IR spectra in the region around 3300−3600 cm^{-1}. Other information from the FT-IR spectra of the powders is the presence of carbonate (CO_3) groups at 1660 cm^{-1}, which might be due to the adsorbed species remaining

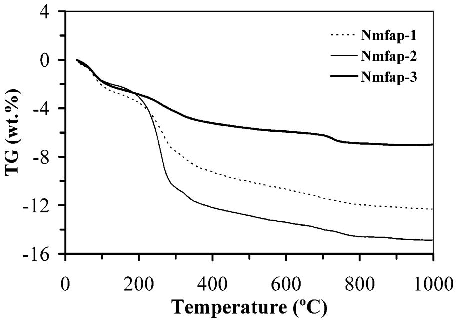

Figure 3. Thermal behavior of the different Na, Mg, and F cosubstituted apatitic powders.

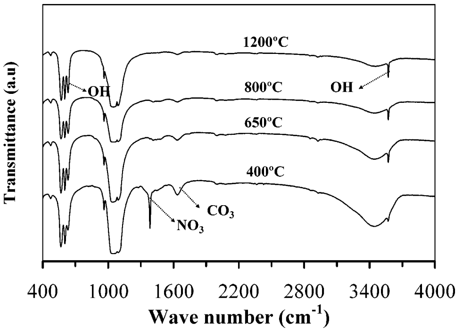

Figure 4. FT-IR spectra for HAP powder heat treated at different temperatures.

from the aqueous precipitation.[24] Because the filtration of the suspension after 24 h of aging was carried out without any washing, the presence of nitrates (NO_3) in the dried powders is obvious, as observed in the FT-IR patterns in the region around 1320−1480 cm^{-1}. The presence of nitrates in the synthesized powders tends to agree with observations made in a previous study.[25]

3.2. Effect of Heat Treatment. The thermograms of the precipitated powders investigated between 30 and 1000 °C are displayed in Figure 3. The weight loss of the powders can be differentiated into three regions. (1) In the 30−200 °C region, all the powders have shown relatively uniform losses of about 2.5%, characteristic of the physisorbed water. (2) In the 200−750 °C region, the differences in weight loss among all the powders are significant, with weight losses of about 9, 12, and 4.5% for the samples Nmfap-1, Nmfap-2, and Nmfap-3, respectively, depending on their stoichiometry and the level of incorporated substituents. The FT-IR patterns for the HAP, Nmfap-1, and Nmfap-3 heat treated at different temperatures are presented in Figures 4−6, respectively. The gradual loss of nitrates and carbonates is evidenced by the decrease in the resolution of corresponding peaks in the region around 1320−1480 and 1660 cm^{-1} that are clearly depicted from the FT-IR spectra obtained at 400 and 650 °C. However, the difference in loss in this temperature range could be solely due to the varied concentrations of the precursors used in the synthesis. In the FT-IR patterns of Nmfap-2 (not presented) and Nmfap-3 (Figure 6) that possess calcium deficiency (Ca:P < 1.67), the presence of hydrogenophosphate ions (HPO_4^{2-}) is apparent at 400 °C, which

---

[22] Kannan, S.; Lemos, I. A. F.; Rocha, J. H. G.; Ferreira, J. M. F. *J. Solid State Chem.* **2005**, *178*, 3190.

[23] Gibson, I. R.; Rehman, I.; Best, S. M.; Bonfield, W. *J. Mater. Sci.: Mater. Med.* **2000**, *12*, 799.

[24] Gibson, I. R.; Best, S. M.; Bonfield, W. *J. Biomed. Mater. Res.* **1999**, *44*, 422.

[25] Raynaud, S.; Champion, E.; Bernache-Assollant, D.; Thomas, P. *Biomaterials* **2002**, *23*, 1065.

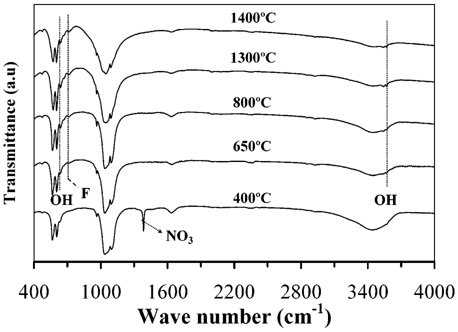

Figure 5. FT-IR spectra for Nmfap-1 heat treated at different temperatures.

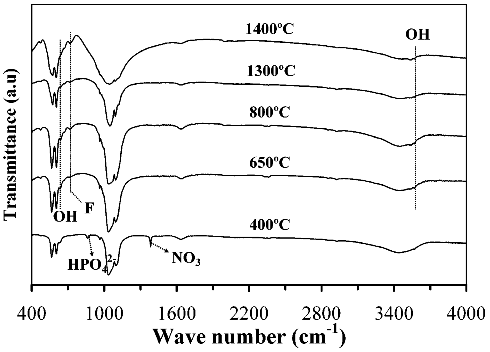

Figure 6. FT-IR spectra for Nmfap-3 heat treated at different temperatures.

was not detected for Nmfap-1 (Figure 5) or for pure HAP (Figure 4) powder. Thus, the similar patterns observed in the FT-IR spectra for both HAP and Nmfap-1 show that the stoichiometric ratio of Ca:P = 1.67 needed to form pure HAP has been retained even in the presence of substituted elements for the powder Nmfap-1. The detected HPO_4^{2-} for Nmfap-2 and Nmfap-3 at 400 °C shows that the pure form of HAP has not been retained for these powders with a ratio of (Ca+Na+Mg):P = 1.67, which behave like calcium-deficient apatites without any substituted elements that have been described elsewhere.[25,26] The FT-IR patterns obtained at 650 °C have indicated the presence of bands corresponding to fluorine at 720 cm^{-1} for both powders Nmfap-1 and Nmfap-3. The presence of OH groups was detected for Nmfap-1 and Nmfap-3 at 645 cm^{-1}, a considerable shift from the normal position at 630 cm^{-1} for HAP, which is due to incorporated fluorine in the apatite lattice. Normally, the condensation of HPO_4^{2-} ions to form pyrophosphates ($P_2O_7^{4-}$) that tends to occur in the temperature range of 200−720 °C for calcium-deficient apatites should be visible at 720 cm^{-1} in the FT-IR spectra. In the present case, the characteristic band identified at 720 cm^{-1} for both Nmfap-1 and Nmfap-3 at 650 °C could be assigned to the incorporated fluorine.[9,27] As a consequence, the characteristic band representative of $P_2O_7^{4-}$ that should appear around 720 cm^{-1} in the FT-IR spectra[22] has been masked by the incorporated fluorine in the apatite lattice.

(3) In the 750−800 °C temperature range, the formation of biphasic mixtures was evident for powders Nmfap-2 and Nmfap-3, and will be detailed in the next section.

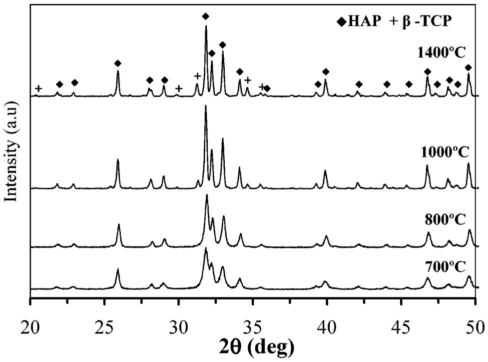

Figure 7. XRD patterns for powder Nmfap-1 heat treated at different temperatures.

3.3. Evolution of Phases. The X-ray diffraction patterns for the cosubstituted powders Nmfap-1, Nmfap-2, and Nmfap-3 over a wide calcination temperature range (700−1400 °C) are illustrated in Figures 7−9, respectively. The diffraction patterns obtained at 700 °C confirm the presence of a poorly crystalline HAP phase with no other extra peaks detected from the XRD spectra. However, calcination at 800 °C has affected the formation of the β-TCP phase for powders Nmfap-2 and Nmfap-3, which could be attributed to the transformation of deficient apatite to biphasic mixtures, as evident from Figures 8 and 9.

As explained in the previous section, the behavior of Nmfap-2 and Nmfap-3 was similar to that of the calcium-deficient apatite without any substituted elements, and hence, it follows the condensation mechanism proposed by Mortier et al.,[26] which can be expressed in the form of the equations given below.

$$Ca_{10-z}(HPO_4)_{2z}(PO_4)_{6-2z}(OH)_2 \rightarrow Ca_{10-z}(P_2O_7)_{z-s}(PO_4)_{6-2z+2s}(OH)_{2(1-s)} + (z + s)H_2O \quad (1)$$

$$Ca_{10-z}(P_2O_7)_{z-s}(PO_4)_{6-2z+2s}(OH)_{2(1-s)} + (z + s)H_2O \rightarrow (1 - z)Ca_{10}(PO_4)_6(OH)_2 + Ca_3(PO_4)_2 + (z - s)H_2O \quad (2)$$

The calculated β-TCP content for powder Nmfap-3, which possesses a higher degree of calcium deficiency, was 32%, compared to only 19% β-TCP detected for powder Nmfap-2. However, the powder Nmfap-1 has shown a pure HAP phase at 800 °C that possesses a Ca:P molar ratio of 1.67, which clearly indicates that HAP derived from this composition retains its stoichiometry at this temperature despite the presence of added Na, Mg, and F. However, calcination at 1000 °C (Figure 7) led to the formation of a small amount (8%) of β-TCP phase, and thus we anticipate some extent of lattice distortion caused by the substituted ions.

3.4. Thermal Stability of the HAP and β-TCP Composites. One of the essential criteria in the apatite-based materials for medical applications is their aptitude for maintaining thermal stability. Some of their critical applications as (i) porous or granulated materials useful in bone surgery, (ii) additives to organic polymers that improve their biofunctionality, and (iii) coatings, plasma sprayed or prepared by laser ablation, necessarily need treatments of the materials at elevated temperatures. The pure HAP has not shown thermal stability above 1200 °C (Figure 10) by the present method of synthesis, whereas the biphasic

---

(26) Mortier, A.; Lemaitre, J.; Roushet, P. G. *Thermochim. Acta* **1989**, *143*, 265.
(27) Rodriguez-Lorenzo, L. M.; Hart, J. N.; Gross, K. A. *Biomaterials* **2003**, *24*, 3777.

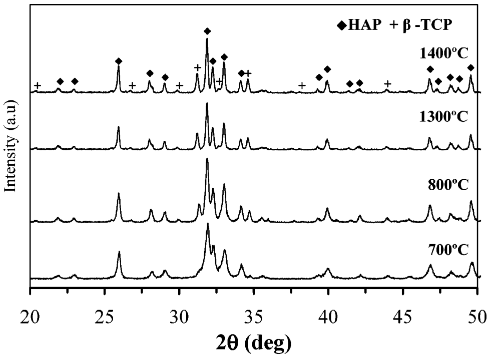

Figure 8. XRD patterns for powder Nmfap-2 heat treated at different temperatures.

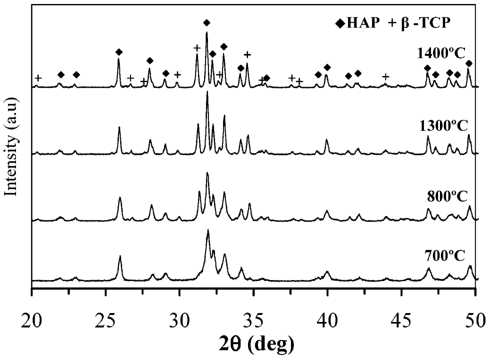

Figure 9. XRD patterns for powder Nmfap-3 heat treated at different temperatures.

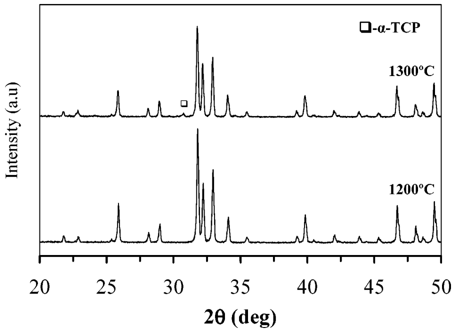

Figure 10. XRD patterns for stoichiometric HAP powder heat treated at 1200 and 1300 °C (unmarked peaks refer to HAP).

Table 2. Elemental Analysis of the Synthesized Apatites[a]

sample	Ca	P	Na	Mg	F
	concentration of element (wt %)				
HAP	39.89	18.51	∼0.02	∼0.01	
Nmfap-1	39.64	18.67	0.502	0.412	0.099
Nmfap-2	38.11	18.81	0.516	0.422	0.087
Nmfap-3	37.27	19.12	0.723	0.617	0.089
bone[b]	24.5	11.5	0.7	0.55	0.02
enamel[b]	36.0	17.7	0.5	0.44	0.01

[a] For HAP, elemental analysis was done at 1200 °C. For powders Nmfap-1, Nmfap-2, and Nmfap-3, analysis was done at 1400 °C. [b] See ref 30.

mixtures with substituted elements have indicated thermal stability to 1400 °C (Figures 7−9) without decomposition to undesirable phases such as α-TCP. It is a well-established fact that pure β-TCP undergoes allotropic transformation to α-TCP beyond 1120 °C,[28,29] and therefore, the high thermal stability of phase mixtures obtained from the present method of synthesis confirms the positive influence of additives. The FT-IR spectra recorded at 1400 °C have shown the presence of a HAP phase. Bands representative of PO_4 tetrahedra are visible at 485 (O−P−O bending υ_2), 576 (O−P−O antisymmetric bending υ_4), 605 (O−P−O bending υ_4), 980 (P−O stretching υ_1), and 1095 cm^{-1} (P−O stretching υ_3). The presence of incorporated F was also apparent in the FT-IR spectrum as a band detected around 720 cm^{-1} even at 1400 °C. The bands corresponding to OH groups (630 and 3570 cm^{-1}) are not clearly visible in the FT-IR spectra of Nmfap-1 and Nmfap-3, as in case of pure HAP, which is due to the incorporated F replacing the OH group in the apatite lattice. However, their presence can be ascertained by the low resolution of the bands observed at 645 and 3570 cm^{-1}.

The elemental analysis for the calcined powders presented in Table 2 confirms the incorporation of Na, Mg, and F in the structure. The measured values also had a good correlation with the initial concentrations of the precursors used. It can be seen from the Table 2 that elements incorporated at a trace level closely match the composition of natural bone and tooth enamel as proposed by Le Geros et al.[30] It is true that natural bone and tooth enamel do not possess similar composition, which may vary depending upon species, age, dietary factors, and pathologies.[31,32] Hence, from the available results, it can be inferred that attainment of the necessary concentrations of elements in the apatite structure can be achieved from the present method of synthesis by adjusting the initial concentration of the precursors.

3.5. Influence of Additives. In the case of synthetic HAP with substituted elements, the existing scientific reports have documented the behavior of single-element substitution in the apatite lattice well. It is reasonable to state that although the apatite structure accommodates the incorporation of foreign ions in its lattice, their inclusion can induce subtle changes in the resulting crystallographic parameters of the apatite phase depending upon its concentration, the nature of the additives, and, most critically, its size. Regarding Na (0.97 Å), its incorporation is facilitated depending on the nature of precursors.[33,34] With certain additives, it has been proved that Na incorporation is favored by the formation of pure HAP, whereas in certain cases trace levels of β-TCP and calcium oxide (CaO) have been detected in the resulting powder after heat treatment.[34] In the case of Mg, its stabilization role in the β-TCP phase upon heat treatment above 800 °C has been well-recognized. There are reports on its significant influence on the lattice constant values due to a size mismatch with Ca (Ca = 0.99 Å, Mg = 0.66 Å). In the case of anionic F (1.36 Å), the prevailing reports strongly suggest it is substituting for OH (1.68 Å) groups

---

(28) Bigi, A.; Foresti, E.; Gandolfi, M.; Gazzano, M.; Roveri, N. *J. Inorg. Biochem.* **1997**, *66*, 259.
(29) Kwon, S.; Jun, Y.; Hong, S. H.; Kim, H. *J. Eur. Ceram. Soc.* **2003**, *23*, 1039.
(30) Le Geros, R. Z.; Le Geros, J. P. *An Introduction to Bioceramics*; World Scientific: Singapore, 1993.
(31) Le Geros, R. Z.; Balmain, N.; Bonel, G. *Calcif. Tissue Res.* **1987**, *41*, 137.
(32) Handschin, R. G.; Stern, W. B. *Clin. Rheumatol.* **1994**, *13*, 75.
(33) Lin, F. H.; Liao, C. J.; Chen, K. S.; Sun, J. S. *Biomaterials* **1998**, *18*, 1101.
(34) Suchanek, W.; Yashima, M.; Kakihana, M.; Yoshimura, M. *Biomaterials* **1998**, *18*, 923.

Table 3. Calculated Lattice Parameters[a]

	cell parameters for HAP phase			cell parameters for β-TCP phase		
sample	*a*-axis (Å)	*c*-axis (Å)	*V* (Å^3)	*a*-axis (Å)	*c*-axis (Å)	*V* (Å^3)
HAP	9.4087	6.8489	1571.35			
Nmfap-1	9.4069	6.8695	1573.80	10.4476	37.1587	3512.46
Nmfap-2	9.4094	6.8645	1573.49	10.4063	37.1905	3487.72
Nmfap-3	9.4016	6.8687	1571.84	10.4210	37.1952	3498.03

[a] Calculation was done at 1200 °C for HAP and at 1400 °C for powders Nmfap-1, Nmfap-2, and Nmfap-3. HAP (JCPDS PDF 09-0432): $a = 9.418$ Å, $c = 6.884$ Å, $V = 1580.84$ Å^3. β-TCP (JCPDS PDF 09-0169): $a = 10.429$ Å, $c = 37.38$ Å, $V = 3520.91$ Å^3.

while being incorporated into the apatite structure, causing a contraction of the *a*-axis without causing significant changes in the *c*-axis parameter.[35] Some studies have indicated that partial substitution of F for the OH group can cause the formation of trace levels of the β-TCP phase upon heat treatment.[27,36] Thus the effect of single-element substitutions on the apatite structure can be understood from the existing reports. The calculated lattice parameters (Table 3) for both the HAP and β-TCP phases of the biphasic mixtures obtained from the synthesized powders in the present study have confirmed the presence of hexagonal HAP and rhombohedral β-TCP phases. Minor irregular changes in the values of cell parameters are apparent from the present results. However, the reason for these minor discrepancies is difficult to explain, as the combined incorporation of Na, Mg, and F is more complex and needs extensive structural investigation.

4. Conclusions

The trace elements (Na, Mg, and F) have been successfully incorporated into the biphasic mixtures of apatites by the aqueous precipitation method by adjusting the initial molar ratios of the precursors. The phase stability and the concentrations of the incorporated elements have been verified by X-ray diffraction and elemental analysis. FT-IR spectra also confirm the presence of apatites at 1400 °C. However, minor variations in both the matching of phases and the lattice parameters (*a*, *c*, and *V*) have been observed because the incorporated elements play a crucial role. The exact structure and occupancy factors for the incorporated ions in the apatite lattice cannot be determined from the present results. Finally, it can be concluded that because the natural bone or tooth mineral is not perfectly stoichiometric, the apatites synthesized by the present method with substituted elements will certainly be a better material when compared to the pure HAP or biphasic mixtures without any substituted trace elements.

Acknowledgment. We thank the Portuguese Foundation for Science and Technology for financial support, Project POCTI/CTM/60207/2004 and Grant SFRH/BPD/18737/2004.

CM051966I

---

(35) Chen, Y.; Miao, X. *Ceram. Int.* **2004**, *30*, 1961.
(36) Chen, Y.; Miao, X. *Biomaterials* **1998**, *26*, 1205.