Hydroxyapatite (HA) and fluor-hydroxyapatite (FHA) powders were synthesized by a sol–gel method for usage as bone filler and drug carrier. Calcium nitrate and triethyl phosphate were used as precursors under an ethanol–water-based solution. Different amounts of ammonium fluoride (NH₄F) were incorporated for the preparation of FHA powders. With heat treatment above 400°C, a characteristic apatite phase was observed for all the sol–gel powders. However, the crystallization temperature decreased with increasing fluoride addition. The tricalcium phosphate (TCP) phase formed in the heat-treated powders varied corresponding to the fluoride addition, i.e., a gradual decrease in the a-axis, while little change in the c-axis was observed with increasing fluoride addition, indicating a nearly complete substitution of fluoride within the apatite lattice. However, little difference was observed with heat-treatment temperatures (400°C–1000°C). The powders substituted with fluoride exhibited reduced dissolution rates in an in vitro solution as compared with the pure HA powder, suggesting the possibility of tailoring bioactivity with fluoride substitution.

I. Introduction

Hydroxyapatite (HA, Ca₁₀(PO₄)₆(OH)₂) has attracted much interest as an implant material for teeth and bones, due to the similarity of its crystallography and chemical composition to that of human hard tissues. Currently, the HA ceramic is used as a bone filler to heal and regenerate new tissues within the defect sites, in the form of powders, granules, and small porous blocks. In addition, HA finds use as a drug carrier by encapsulating and releasing drugs in a controlled way. In most cases, the solubility of HA is an important factor, since it induces bioactivity, osteoconductivity, and therapeutic effects.

On the other hand, pure fluorapatite (FA, Ca₁₀(PO₄)₆(F)₂) is known to have a much lower solubility than HA, because FA possesses a greater stability than HA, both chemically and structurally. Moreover, the FA forms fluoro-hydroxyapatite (FHA, Ca₁₀(PO₄)₆(OH,F)₂) solid solutions with HA through the replacement of OH⁻ by F⁻. Hence, modulation of the extent of fluoride substitution provides an effective way of controlling the solubility of the apatite. In practice, the fluoride ion itself has been studied widely in dental restoration areas, due to its advantages over other ions in that it prevents the formation of caries in bacteria-existing environments and promotes mineralization and crystallization of calcium phosphates in the formation of bone.

Nevertheless, there have been few reports concerning the fabrication or characterization of the FA or FHA materials. Most studies discussed the possible fabrication of FA powders by precipitation methods or films by thermal spraying techniques. However, the properties and qualities of the powders and films were not so satisfactory due to the formation of byproducts or to other technical problems. On the other hand, the synthesis of HA powder has been performed over the past few years, using different techniques, such as precipitation, hydrothermal, and sol–gel methods. Among these, the sol–gel approach offers many advantages over other techniques due to the chemical homogeneity and finer grain size of the products as well as to the economical and technical viewpoints of the processing. In this study, we have synthesized both the HA and FHA powders by means of the sol–gel method using polymeric precursors and investigated their morphology, phase, and structure changes with thermal treatment. Moreover, their in vitro dissolution rates were observed to examine their bioactivity. Investigation of these powders provides not only important information on the bioengineering field using powders and granules, such as drug delivery systems and bone fillers, but also information on the sol–gel preparation of HA and FHA coatings, which can be used in future studies.

II. Experimental Procedure

(1) Powder Preparation

Triethyl phosphate (TEP, (C₂H₅O)₃P; Aldrich, WI) was hydrolyzed in ethanol with a small amount of distilled water for the preparation of HA (the molar ratio of water to P was kept at 6). Two sets of TEP solutions containing different concentrations of fluorine ion were also prepared, by dissolving ammonium fluoride (NH₄F; Aldrich) in ethanol (the molar ratios of P to F were chosen to be 6 and 3 and designated as FHA1 and FHA2, respectively). The hydrolyzed TEP solutions were added dropwise to the stoichiometric amounts (Ca/P ≈ 1.67) of 2M calcium nitrate [Ca(NO₃)₂·4H₂O] solutions and followed by stirring for 3 h and aging at 40°C for 72 h. After oven drying at 80°C, the powders were heat-treated at 400°C–1000°C for 1 h in air.

(2) Characterization

The powder morphologies were analyzed with transmission electron microscopy (TEM; Philips, CM20, Holland). Each powder heat-treated was ultrasonically dispersed in an acetone solution for 1 min. The powder emulsion was picked up with a carbon-coated copper mesh using a filter paper. The thermal property of

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the powders was investigated using differential thermal analysis (DTA) from room temperature to 900°C under air flow conditions at a ramping rate of 5°C/min. The phase of each powder was investigated using X-ray diffraction (XRD; M18XHF-SRA, Mac Co., Japan) at a scanning speed of 0.2°C/min with CuKα radiation (wavelength = 1.54056 Å). The structural change of the powder was observed with Fourier transform infrared (FT-IR; BoMems DA8, Canada) analysis using KBr as a standard. The crystallinity of the powder was estimated from the XRD data using the following Eq. (1):20

\[ X_c = 1 - \left( \frac{V_{123000}}{I_{300}} \right) \]  

(1)

where \( X_c \) is the degree of crystallinity, \( V_{123000} \) is the intensity of the shoulder between (112) and (300) diffraction peaks, and \( I_{300} \) is the intensity of the (300) peak. The crystallite size of the powder was evaluated from the peak broadening of XRD patterns based on Scherrer’s formula as follows:21

\[ X_s = 0.9\lambda / (\text{FWHM} \times \cos \theta) \]  

(2)

where \( X_s \) is the crystallite size (nm), \( \lambda \) is the wavelength of the monochromatic X-ray beam (\( \lambda = 0.154056 \) nm for CuKα radiation), FWHM is the full width at half-maximum for the diffraction peak under consideration (rad), and \( \theta \) is the diffraction angle (deg).

(3) In Vitro Dissolution Test

After heat treatment at 500°C, 1 g of powder was placed in 100 mL of phosphate buffered saline solution (PBS, \times 10 concentrated, Sigma-Aldrich, U.K.), which was stirred and maintained at 37°C in a water bath, for periods up to 7 days. At predetermined periods of time, the powders were filtered using a filter unit Millex-GP 0.22 μm (Millipore, MA). The filtered solution was analyzed to detect Ca²⁺ and F⁻ ions using inductively coupled plasma-atomic emission spectrometer (ICP-AES, Shimadzu, Japan) and ion analyzer (microprocessor ion analyzer 901, Orion Research, U.K.), respectively.

III. Results and Discussion

(1) Morphology

Figures 1(A)–(C) show the TEM analyses of the HA and FHA powders after heat treatment at 500°C. All the powders consisted of nanosized (30–50-nm) particles. The particle size of FHA appeared to be slightly larger than that of HA. From the selected area electron diffraction pattern, all the powders were observed to have apatite structures with diffraction spots on the weak ring pattern (manifest in (002) and weak in (112) directions), confirming the evolution of polycrystalline apatite powders. The diffraction spots appeared to be clearer with increasing fluoride, suggesting the enhanced crystallinity and increased crystallite size.13,22

(2) Thermal Properties

Figure 2 shows the DTA curves of each dried powder during heating up to 900°C in air. Regardless of the powders, the curves behaved in a similar manner. Strong peaks at 280° (endothermic) and 550°C (exothermic) corresponded to the decomposition of...
nitrate from the Ca precursor and the liberation of carbonate groups, respectively (which is evidenced in the FT-IR data shown below). The carbonate groups were believed to be incorporated into the apatite lattice during the preparation of sols. Notably, the weak exothermic peak observed at ~400°C in all cases was due to the formation of the crystalline apatite (which is illustrated in the XRD data shown below). On closer examination, the crystallization temperature was observed to be slightly lower with F substitutions; FHA2 (398°C) < FHA1 (405°C) < HA (411°C).

3 Structure Change

Structural changes of the HA and FHA powders during heat treatment were analyzed with FT-IR, as shown in Fig. 3. In the HA powder as-dried, strong N–O bands (~1100 and 1400 cm⁻¹) were observed due to the presence of the organic precursor, and the broad H–P–O band (~1150 cm⁻¹) indicated that the P-precursor remained in the form of HPO₄ rather than the PO₄ apatite group. However, after heat treatment at 400°C, P–O bands (~500–600 and ~900–1000 cm⁻¹), characterizing the typical apatite structure, were observed, and the H–P–O band disappeared. Moreover, the O–H stretching mode was observed at 640 cm⁻¹, confirming the formation of characteristic apatite structure, containing an hydroxyl group. However, a strong N–O band at 1400 cm⁻¹ was still observed. The P–O band became sharp and strong at 500°C, indicating an improvement in the atomic arrangement of the apatite structure. After heat treatment at 800°C, the O–H band (HA) was slightly attenuated and the P–O bands were broadened. This fact suggested the formation of TCP, which was consistent with the XRD data. The band structures of the FHA1 powders exhibited a trend similar to those of the HA powders. However, the intensities of the P–O bands were slightly higher at all temperatures and the broadening of the P–O bands at 800°C was attenuated when compared with the HA powder. The O–H band (640 cm⁻¹) of the FHA1 was slightly lower than that of the HA powder, suggesting the partial substitution of F⁻ for OH⁻. Unlike the HA and FHA1, the FHA2 powders showed no O–H stretching band (640 cm⁻¹) between 400° and 800°C, suggesting the liberation of the O–H bond, presumably due to the nearly complete replacement of OH⁻ by F⁻. Moreover, the P–O bands were still sharp and strong even after the heat treatment at 800°C, confirming the high stability of the apatite structure in the FHA2 powders. Notably, the C–O bands (~870 and 1460 cm⁻¹) observed in the powders as-dried and heat-treated at low temperatures (400° and 500°C), were stronger in the order HA > FHA1 > FHA2, confirming that the HA powder contained carbonate groups within the apatite structure to a higher degree. The incorporation of the carbonate group is closely related with the nonstoichiometry of an apatite.

4 Phase Change

The phase changes of the HA and FHA powders were analyzed by XRD, as shown in Fig. 4, following heat treatment at various temperatures. The as-dried HA powder displayed poorly crystalized apatitic structure peaks at 2θ ~ 32°. After heating at 400°C, the apatite peaks at 2θ ~ 32° increased and the other apatite peaks started to appear, confirming the onset of the crystallization of an apatite at ~400°C, which was in good agreement with the DTA analysis. However, there was a strong overlap between the peaks at 2θ ~ 32°, confirming the low degree of crystallinity of the apatite. After heat treatment at 500°C, the apatite peaks became sharper and more manifest, along with the peak separation at 2θ ~ 32° becoming more apparent. With further increase in temperature up to 800°C, the trends were more pronounced. Such a fact suggests the improved crystallinity of the apatite. Notably, additional TCP peaks appeared at 600°C, and the amount became pronounced at 800°C. Compared with the HA, similar trends were
observed in the FHA1 with respect to the heat-treatment tempera-
ture. However, for all the heat-treatment temperatures, the peak
intensities of the FHA1 were much higher than those of the HA. In
the FHA1, the TCP peaks were also observed at 800°C; however
the amount was lower as compared with the HA. The apatite peaks
became sharper and narrower in FHA2. Moreover, the TCP peaks
were not observed in this powder for all heat-treatment tempera-
tures. There have been several reports on the formation of TCP
above 700°C–800°C in the preparation of HA powders.17–19 In
these reports, the formation of TCP was attributed to the decom-
position of a nonstoichiometric HA, which contained \( \text{CO}_3^{2-} / \text{HPO}_4^{2-} \)
groups in a \( \text{PO}_4 \) site or vacancies in a Ca site, at elevated
temperatures.18,19 The attenuation of TCP in the FHA powder
showed that the substitution of fluoride made the apatite structure
more stable and stoichiometric.

(5) Crystallinity and Crystallite Size

Of special note in the XRD data were the variation in intensity
and width of the apatite peaks among the different powders, and
this variation was closely related to the crystallinity and crystallite
size. Figure 5 shows the crystallinity and crystallite size of the
heat-treated apatite powders. For all the HA and FHA powders,
the crystallinity increased with heat-treatment temperature. Notably,
the fluoride substitution improved the crystallinity for all the
heat-treatment temperatures, with crystallinity being on the order
FHA2 > FHA1 > HA. The crystallite size was calculated from
Scherrer’s formula. The (002) peak was chosen since the peak was
developed well and separate from others; also the apatite crystal is
known to grow along the \( c \)-axis direction preferentially.14,20,21 A
similar trend was observed in the crystallite size as was in the
crystallinity, that is, an increase in the crystallite size with
increasing heat-treatment temperature and fluoride addition. Prac-
tically, it is known that the existence of fluorine within the apatite
structure promotes the crystallization of the apatite structure,
especially along the \( c \)-axis direction.13,14

On the basis of above results regarding the phase and structure
changes during thermal treatment, it was deduced that the incor-
poration of fluoride enables the powder to be matured to a higher
degree and to retain higher thermal stability. These properties,
the crystallization and thermal stability, are closely interrelated,
in that the enhanced apatite crystallization induced by the
incorporation of fluoride adds to the stability of the apatite
structure, thereby preventing its decomposition at elevated
temperatures.

(6) Lattice Parameters

The changes in lattice constants, which occurred due to the
replacement of \( \text{OH}^- \) by \( \text{F}^- \), were calculated for all heat-treatment
temperatures, as represented in Fig. 6. When there was no fluoride
incorporation, both values, \( \approx 9.41–9.42 \text{ Å} \) for the \( a \)-axis and
\( \approx 6.87–6.88 \text{ Å} \) for the \( c \)-axis, showed no significant changes with
temperature, and these were very close to the reported values for
pure HA (\( a = 9.4218 \text{ Å} \) and \( c = 6.8814 \text{ Å} \)).23 However, in the case
of the FHA powders there were manifest decreases in the \( a \)-axis,
though little changes were observed in the \( c \)-axis, which was
well-reported in the fluoride-substituted apatites.8,11,24 When the
molar ratio of P to F was set at 3 (FHA2), which was intended to

Fig. 4. XRD patterns of the HA and FHA powders before and after heat
treatment at various temperatures: TCP (●) and HA/FHA (others).

Fig. 5. Crystallinity and crystallite size of the powders after heat-treating
at various temperatures. Data obtained from XRD results. The (002)
diffraction peak was chosen for crystallite size calculation.
Fluoride-substituted hydroxyapatite powders (FHA) were successfully fabricated via a sol–gel technique with the incorporation of different levels of fluoride ions. Nearly complete substitution of the OH\(^{-}\) by F\(^{-}\) occurred with heat treatment, which was confirmed by lattice parameter calculation. All the powders started to crystallize to an apatite structure at about 400°C, and the structure was highly matured above 500°C. However, the phase stability and crystallinity were different depending on the level of fluoride substitution. In pure HA, a large amount of HA decomposed to β-TCP with heat treatment above 800°C, but this was suppressed with the fluoride substitution. Moreover, the crystallinity and crystallite size of the powders increased with fluoride substitution. These improvements in the crystallization and phase stability of the apatite structure, resulting from the fluoride substitution via the sol–gel process, suggest enhanced performance of the FHA powders from the standpoint of purity and the thermal stability of the product. The prepared powders showed a controlled release rate in vitro, that is, retarded ion dissolution in the powder containing the higher fluoride substitution.

**IV. Summary and Conclusions**

Fluoride-substituted hydroxyapatite powders (FHA) were successfully fabricated via a sol–gel technique with the incorporation of different levels of fluoride ions. Nearly complete substitution of the OH\(^{-}\) by F\(^{-}\) occurred with heat treatment, which was confirmed by lattice parameter calculation. All the powders started to crystallize to an apatite structure at about 400°C, and the structure was highly matured above 500°C. However, the phase stability and crystallinity were different depending on the level of fluoride substitution. In pure HA, a large amount of HA decomposed to β-TCP with heat treatment above 800°C, but this was suppressed with the fluoride substitution. Moreover, the crystallinity and crystallite size of the powders increased with fluoride substitution. These improvements in the crystallization and phase stability of the apatite structure, resulting from the fluoride substitution via the sol–gel process, suggest enhanced performance of the FHA powders from the standpoint of purity and the thermal stability of the product. The prepared powders showed a controlled release rate in vitro, that is, retarded ion dissolution in the powder containing the higher fluoride substitution.

**References**


