Structural insights of mechanically induced aluminum-doped hydroxyapatite nanoparticles by Rietveld refinement

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Abstract

Aluminum doped hydroxyapatite (HA:Al³⁺) nanopowders were successfully prepared via a simple and efficient one-pot mechanochemical route. The effects of dopant loading on phase compositions and structural features were assessed by Rietveld analysis. The XRD-Rietveld refinement revealed the stabilization of HA in hexagonal structure for all the samples. The sharpness and intensity of the apatite-derived XRD peaks decreased as the dopant content increased to 10% due to the increase in lattice imperfections and mechanically induced amorphization. The incorporation of Al³⁺ into the HA lattice decreased the unit cell parameters. From the FTIR measurements, the representing bands of apatite were identified in all cases. The mechanosynthesized nanopowders consisted of nanospheroids with an average size of 44±20 nm and therefore are promising for bone tissue regeneration.

Keywords: Synthesis; Ion exchange; Mechanochemical; Rietveld refinement.

1. Introduction

In recent decades, a great interest in the use of bioceramics to improve the quality of human life has occurred. This is largely due to the inventive use of specially designed bioceramics for the repair and reconstruction of diseased or damaged parts of the human body. These classes of ceramics are potential candidates in the manufacturing of bone-like scaffolds and may also be designed to deliver biologically active substances aimed at repairing, maintaining, restoring or improving the function of organs and tissues in the organism [1–4]. However, insertion of implants to replace the injured parts often gives discomfort to patients, due to the brittleness and insufficient biological properties of the bioceramic implants [5]. Therefore, many attempts have been made to improve the functional specifications of ceramic implants and to regenerate old and deteriorating bones with a biomaterial that can be substituted by a new mature bone without transient loss of a mechanical support [6–9].

Atomic doping or substitution in apatite is a one of the strategy to overcome some intrinsic properties of bioceramic implants or coating [10]. Many recent studies have reported that Ca^{2+} sites in bioceramics can be replaced with various cations such as monovalent (K^+ , Na^+ , Ag^+), divalent (Cd^{2+} , Zn^{2+} , Eu^{2+} , Sr^{2+} , Mg^{2+} , Ga^{2+} etc.), trivalent (Bi^{3+} , La^{3+} , Y^{3+} , Al^{3+} etc.), tetravalent (Zr^{4+}) and pentavalent (Ta^{+5} , V^{+5} , Nb^{+5}), which exactly determine the implant-environment interactions after the implantation [11–15]. Moreover, some studies have focused on the incorporation of monovalent anions (F^- , Cl^- , Br^-) which can replace OH^- ions in the anion channel without charge imbalance and some anionic complexes (CO_3^{2-} , SO_4^{3-} , SiO_4^{3-} , etc.) which can substitute the phosphate groups. These structural modifications can alter the solubility, thermal stability, and mechanical properties as well as the *in-vitro* bioactivity of HA crystals [16–19]. Over the past decades, many different methods have been introduced for the production of various substituted apatites with precise control of the microstructure, particle shape and size [20–24]. Among them, powders synthesized by mechanochemical reactions typically possess a well-defined structure due to the perturbation of surface-bonded species as a result of pressure, which enhances the thermodynamic and kinetic reactions between solids [25–27]. On the other hand, it has been shown that the Rietveld refinement analysis of XRD data allows for quantitative probing of the structural modifications of biomaterials [28,29]. However, to the best of our knowledge, apart from the absence of a comprehensive study on mechanically induced aluminum doping of HA nanoparticles, there are no reports on the effects of the dopant loading on the structural refinement of Al-doped HA by Rietveld analysis.

Kandori *et al.* [30] examined the effects of modification of HA by trivalent metal ions (Al(III), La(III), and Fe(III)) on protein adsorption behavior using bovine serum albumin (BSA). Their results indicated that both the mean particle length and surface hydrophilicity of Al(III)-, La(III)-, and Fe(III)-substituted HA particles were the determining factors of the adsorption of BSA. Kaygili *et al.* [31] also investigated the HA and HA-based bioceramics with high Al contents by using the sol–gel method. They found that with the increase of Al content, the crystallinity dramatically decreased, and the HA transformed into the new phases, including aluminum calcium

phosphate and/or aluminum phosphate. Here, the possibility of using a one-pot mechanochemical reaction to prepare nanosize Al-doped HA was studied for the first time. The microstructural features and doping mechanism were investigated using microscopic and spectroscopic techniques. Besides, the mechanosynthesized nanopowders were systematically treated by Rietveld refinement to extract the quantitative phase analysis and the structural parameters, to refine the composition of the Al-substituted HA. This unique top-down approach offers a framework for the future design of substituted apatites.

2. Materials and methods

2.1. Chemicals

Calcium hydroxide (Ca(OH)_2 , $\geq 96\%$), phosphorus pentoxide (P_2O_5 , 99%), and aluminum hydroxide (Al(OH)_3) (all from Sigma-Aldrich Co., USA) were used as the precursors without further purification.

2.2. Clarification

With regards to the milling conditions, the mechanochemical reactions can be classified into two main categories: (i) progressive mode where the reaction may expand to a very small volume during each collision and (ii) mechanically induced self-sustaining reactions (MSRs) wherein a self-propagating combustion reaction can initiate and eventually lead to the instantaneous formation of irreversible crystalline phases. It should be mentioned that the second mode could happen if the reaction enthalpy is sufficiently high [14,32]. In this mode, the reaction mechanism can be predicted by calculating the adiabatic temperature or by the parameter $(-\Delta H_{298}/\sum C_p)$. Accordingly, for self-sustaining reaction to take place, it is imperative that these quantities be at least $T_{\text{ad}} > 1800 \text{ K}$ and $-\Delta H_{298}/\sum C_p > 2000 \text{ K}$ [33]. In the present case, due to the lack of high exothermic reactions, it could be considered that the mode of the reaction is gradual, which includes the following steps: (i) the interaction of particles and the reactive absorption of atmospheric carbon dioxide during the early stage of milling, (ii) the mechanically induced reaction between calcium phosphate and the dopant.

Therefore, it is necessary to mention the following assumptions: (i) milling vial is sealed and isolated (ii) all the reactions occur in the standard conditions ($\Delta G = \Delta G^\circ$) (iii) the activity coefficient is equal to 1, and (iv) the reactions occur in the same physical conditions.

2.3. Mechanochemical process

A series of HA:Al³⁺ powders with different doping levels and general formula of Ca_{10-x}Al_x(PO₄)₆(OH)₂ ($0 \leq x \leq 1$) were synthesized by mechanical activation of reagents for 1 h, using a high-energy ball mill (8000M Mixer/Mill) with hardened chromium steel vials (vol.65mL) under air atmosphere without any process control agent (PCA). In all cases, the (Ca + Al) / P ratio was fixed at 1.67, while the Al / (Ca + Al) ratio ranged from 0 to 0.10. The ball-to-powder (BPR) weight ratio, total powder mass and rotational speed were 10:1, 2.2 g, and 1725 rpm (115 V 60 HZ), respectively. The details of the substitution degree are summarized in Table 1.

2.4. Characterization

2.4.1. X-ray powder diffraction (XRD)

X-ray powder diffraction (Bruker D8 Advance ECO (XRD)) using a Cu-K α radiation over a 2θ range from 10° to 70° was employed to determine the phase purity. The "PANalytical X'Pert HighScore" software was used to analyze the XRD profiles, where the patterns were compared to standards compiled by the Joint Committee on Powder Diffraction and Standards (JCPDS), which involved card #24-0033 for HA and #029-0041 for Al(OH)₃. The crystallinity degree was assessed using the well-known equation (Eq. (I)) [34]:

$$X_c \approx 1 - (V_{112/300}/I_{300}) \quad \text{Eq. (I)}$$

2.4.2. Structural refinement

In addition to the above-mentioned approach, *Match!* is an user friendly software was employed for the phase identification process of the powder diffraction data. It compares the diffraction pattern of the sample to a database containing reference patterns to recognize the phases which are present. The additional information about the sample such as phases, elements or density

can also be determined easily. Besides, a quantitative analysis using the Rietveld refinement can be performed as well. The Rietveld refinements can be easily run from *Match!*, and the actual calculations being performed automatically, using the well-known FullProf program [35].

2.4.3. Fourier transformed infrared spectroscopy (FTIR)

Fourier transformed infrared spectroscopy (FTIR, Bruker Tensor 27, USA) was employed to assess the functional groups and structural changes during the mechanical activation in a frequency range of 4000–400 cm⁻¹.

2.4.4. Electron microscopy

Specimens were prepared by ultrasonically dispersing the mechanosynthesized powders in ethanol and then depositing them onto carbon coated copper grids. Scanning electron microscopy (FEI Helios Nanolab 400 SEM) was applied to observe the size and morphology of the samples. Energy dispersive X-ray spectroscopy (EDS) and elemental mapping analysis coupled to SEM were also employed to identify the elemental compositions and the spatial distributions of elements. Transmission electron microscopy (JEOL JEM 1200 EXII) and high-resolution transmission electron microscopy (HT-7700, Hitachi, Japan) were performed to investigate the morphological features and lattice fringes of the nanoparticles, respectively. A full particle size distribution can be obtained based on a count of many particles using automated counting techniques. These experimental data are typically represented as a number average [14]:

$$\bar{d}_n = \sum_i n_i d_i / \sum_i n_i \quad \text{Eq. (II)}$$

where n_i represents the number of particles with a diameter, d_i , which in practice is typically a mean value within a specified size. However, of greater use is the surface-weighted average diameter:

$$\bar{d}_s = \sum_i n_i d_i^3 / \sum_i n_i d_i^2 \quad \text{Eq. (III)}$$

which allows the comparison of crystallite sizes determined by chemisorption methods, and the volume-weighted average diameter:

$$\bar{d}_v = \frac{\sum_i n_i d_i^4}{\sum_i n_i d_i^3} \quad \text{Eq. (IV)}$$

which allows the comparison of crystallite sizes obtained from the XRD analysis or magnetic measurements. Generally, a narrow crystallite size distribution will lead to similar values for equations (III) and (IV), and these are frequently in good agreement with the XRD measurements. Additionally, the broader distribution brings about a greater disparity among the different $\bar{d}$ values. A bimodal crystallite size distribution can also cause large discrepancies among these differently weighted $\bar{d}$ values, regardless of the method used during the characterization. The standard deviation from the average particle size was calculated, using Eq. (V):

$$\sigma = \sqrt{\frac{1}{N} \sum_{i=1}^N (d_i - d_s)^2} \quad \text{Eq. (V)}$$

where N is the total number of particles and σ is the standard deviation from the average particle size.

3. Results and discussion

3.1. Effects of the dopant loading

Figure 1 shows the XRD profile of the dopant agent. As can be seen, the dopant precursor is highly pure gibbsite, $\text{Al}(\text{OH})_3$, which exhibits a monoclinic structure (space group $P1\ 21/n1$) with lattice parameters: a , b , and c of 8.6635, 5.0675, and 9.7138 Å, respectively. The XRD patterns of the 1 h milled specimens in the absence (S1) and presence of different amounts of dopant (S2–S6) are shown in Fig. 2. In the absence of dopant, due to the fast completion of the mechanochemical reaction, a crystalline form of HA was produced after only 1 h of milling. Similar patterns were perceived in the presence of different values of dopant and therefore the XRD profiles showed a major Al-doped HA ($\text{Ca}_{10-x}\text{Al}_x(\text{PO}_4)_6(\text{OH})_2$; where $0 \leq x \leq 0.8$) phase. The main peaks attributed to $\text{HA}:\text{Al}^{3+}$ are as follows: (0 0 2) plane at $2\theta = 25.82^\circ$, (1 0 2) plane at $2\theta = 28.04^\circ$, (2 1 0) plane at 2θ

= 28.91°, (2 1 1) plane at $2\theta = 31.75^\circ$, (3 0 0) plane at $2\theta = 32.84^\circ$, (2 0 2) plane at $2\theta = 33.99^\circ$, (1 3 0) plane at $2\theta = 39.75^\circ$, (2 2 2) plane at $2\theta = 46.75^\circ$, (2 1 3) plane at $2\theta = 49.44^\circ$, and (0 0 4) plane at $2\theta = 53.07^\circ$. This suggests that Al doping not only favors the HA:Al³⁺ formation, but also assists to stabilize it at room temperature. It should be mentioned that the nonexistence of any characteristic peaks for Al, or Al compounds such as gibbsite and a strong similarity of the XRD patterns recorded for the undoped and doped samples corroborate the substitution of Ca²⁺ by Al³⁺ in the apatite lattice. With an increase in the dopant content to 10% (S6), substantial changes were observed in the XRD reflection. In this case, the high intensity of the strongest peak attributed to gibbsite [(0 0 2) plane at $2\theta = 18.29^\circ$] serves as proof that there is an imperfect substitution due to the intrinsic structural constraints of HA. With increased dopant loading, the sharpness and intensity of the apatite-derived XRD peaks decreased. This behavior can be explained on the basis of the mechanically induced amorphization, which is associated with a significant increase in the lattice imperfections. Accordingly, the crystallinity degree of the milled samples declined drastically from 63±6 to 24±2 % with the increase of the Al content from 0 to 10% (Fig. 3). This result is consistent with the findings of Kandori *et al* [30], showing that the crystallinity of the substituted HA materials decreases with the increase of trivalent metal ions such as Al(III), La(III), and Fe(III).

3.2. Rietveld refinement results

HA is in the space group $P6_3/m$ and its unit cell parameters are $a = b = 9.4347 \text{ \AA}$ and $c = 6.8893 \text{ \AA}$ [36]. HA have two different binding sites (**C** and **P** sites) on the particle surface. After the dispersion of HA particles in aqueous media, the calcium atoms (Ca(2)) are exposed on the HA surface by the dissolution of OH⁻ ions, to produce calcium ions or positively charged sites on the particle surface, so-called **C** sites which are arranged on the ac or bc particle face. On the contrary, the **P** sites, negatively charged adsorbing sites, each formed by six oxygen atoms corresponding to three crystal phosphate ions, are arranged hexagonally on the ab particle face with a minimal interdistance, in both the a and b directions [30]. Therefore, it is quite clear that the HA structure presents two nonequivalent Ca²⁺ sites, where the smallest distance between a cation and a

coordinated oxygen is observed at site (2) and the smallest Ca–Ca distances are found between Ca^{2+} ions at site (1) [14]. This suggests that small ions are preferentially substituted at Ca (1), while large cations are preferably exchanged at site (2). Consequently, in the present case, Al^{3+} ions would first replace Ca^{2+} at site (1) as the ionic radius of Al^{3+} (0.535 Å) is smaller than that of Ca^{2+} (0.99 Å).

To authenticate the crystallographic data, the standard XRD patterns of nanostructured materials do not provide the necessary sufficient intensity data, and so further actions are needed to complete the structural analysis. In the present case, the structural refinements were done by the Rietveld method using the Fullprof program as well as the Crystallography Open Database of all possible occurring phases. The peak shapes were modeled on a pseudo-Voigt distribution, and an asymmetry parameter was refined. At first, all the parameters were fixed according to the literature values and subsequently they were all refined during the successive refinement cycles. Fig. 4a shows the Rietveld refinement plots of the 1 h milled specimens in the absence (S1) and presence of different amounts of dopant including S2 (2%), S3 (4%), S4 (6%), and S5 (8%). From these reflections, the refined XRD patterns demonstrate that all the specimens are in single phase form. In addition, these plots confirm the achievement of the Rietveld refinement, as reflected by small difference between calculated and observed. As the refinement progressed, the relative percentage of the hexagonal phase remained stable as the dopant content increased to 8%. However, with the increase of the dopant loading to 10% (S6), the percentage of the hexagonal structure corresponding to HA decreased severely to 77.5% while that of the monoclinic structure belonging to gibbsite increased to 22.5%. As can be seen in the magnified XRD profiles ($2\theta = 30\text{--}35^\circ$) (Fig. 4b), by increasing the dopant content, the apatite-derived XRD peaks declined in both sharpness and intensity which can be linked to the mechanically induced amorphization. The various R factors obtained from the Rietveld refinements are summarized in Table 2. The values of R factors like R_p , R_{wp} , and R_{exp} are found to be large. Similar high values of R factors for the nanostructured materials have been reported by the previous studies [37,38]. It can be derived from the poor counting statistics with a XRD fast scan. However, the goodness of fit ($G.O.F.$) values given by R_{wp}/R_{exp} were relatively

low, i.e., all approximately less than 2%, which is considered as acceptable in accordance with basic principle of *G.O.F.* less than 4% [39]. It has been reported that diffuse scattering in the diffraction pattern of the nanocrystalline materials is more prominent than that of bulk crystalline materials. This effect is due to the large ratio of surface to volume atoms. In fact, the diffuse scattering becomes significant at the nanoscale while Bragg scattering gets diminished, which leads to decline in crystallinity and large *R* factors [40].

Figure 5 illustrates the refined lattice constants and unit cell volume for samples S1, S2, S3, S4, and S5 based on the XRD-Rietveld analysis. Figure 5b shows the variation of the *a*-axis parameter of the HA phase with the dopant loading. For the undoped HA, the *a*-axis tends to decrease compared to the standard. A similar trend was observed in the case of the doped powders as dopant content increased to 6% (S4). In fact, for the doped powders, the *a*-axis was shorter than the standard HA, but with a further increase in the dopant content to 8%, the *a*-axis rose to 9.4335 Å. On the other hand, measurement of the *c*-axis (Fig. 5c) shows that the pure HA (S1) is increased slightly in length (6.8945 Å) as compared to the standard. This finding is contrary to the doped cases. It is obvious that the HA decreases faintly in length with the dopant loading and reached a minimum of 6.8835 Å in the case of S5 (8%). The change in the unit cell volume of the hexagonal phase as a function of the dopant content is shown in Fig. 5d. A decrease in the unit cell volume of the hexagonal phase with an increase in the dopant loading indicates the incorporation of Al³⁺ into the HA lattice. These findings reveal that only about 8% of the dopant (Al³⁺) probably incorporates into the HA lattice and the rest remains as the unwanted phase (see Fig. 2).

3.3. FTIR analysis

The FTIR spectra of the mechanosynthesized powders were recorded to assess the functional groups of the undoped and doped samples as shown in Fig. 6. Besides, the corresponding assignments of the 1 h milled specimens are listed in Table 3., The bands attributed to apatite are recognized from Fig. 6a and Table 3. It is obvious that the functional groups in the doped samples are very similar to the HA. However, some differences can be observed in the position and shape of

the bands in the short-range FTIR spectra (Fig. 6b and c). The characteristic bands for PO_4^{3-} groups appear at 1097, 1044, 961, 603, 569 and 471 cm^{-1} [6,7,13,14]. The asymmetrical stretching (ν_3) and bending (ν_4) modes of the PO_4 -derived bands are detected at around 1097 and 1044, and 603 and 569 cm^{-1} , respectively. The symmetric stretching modes (ν_1 and ν_2) of the PO_4^{3-} ions were also observed at around 961 and 471 cm^{-1} , respectively. In addition, the stretching and vibration modes of the OH^- ion are identified at around 3576 and 670 cm^{-1} , respectively [41]. The lower intensity of both the OH^- and PO_4 -derived bands in the doped samples could be explained on the basis of the carbonate content within the synthesized powders [14]. Lafon *et al.* [42] found that the intensity of the OH^- -derived bands decreased as the carbonate content increased in the HA lattice and these bands disappeared fully at high carbonate contents. In the present case, the level of carbonate substitution increased as the dopant content rose to 10% (S6), signifying the mechanically-induced substitution of Al can stimulate the solid-state amorphization in some bioceramics. As shown in Fig. 6c, the two regions of the carbonate vibrations in the HA:Al^{3+} powders are: (i) 1463–1423 cm^{-1} attributed to ν_3 (asymmetric stretch vibration) and (ii) CO_3 -derived bands at 874 cm^{-1} ascribed to ν_2 (out-of-plane bending vibration). The position of the CO_3 -derived bands implies that the CO_3^{2-} -for- PO_4^{3-} substitution (B-type) dominates in the HA:Al^{3+} powders. However, some fraction of the OH^- groups might be substituted by the CO_3^{2-} groups (A-type), which is usually observed in carbonated HAp powders. The increase in the concentration of dopant along with the carbonate (with x) in the HA:Al^{3+} powders, which raises the lattice disorder, can be partially justified by the broadening of the XRD reflections, with increasing x (see Fig. 4). It is important to note that the deficit in the negative charge, caused by the replacement of PO_4^{3-} by CO_3^{2-} , can be compensated by the loss of a positive charge through the removal of Ca^{2+} from the lattice [10]. This anionic complex can improve the mechanical properties, biological responses as well as the densification of HA and also reduces the sintering temperature required to achieve a near-full density compared to the stoichiometric HA [43]. It should be noted that all the experiments were done in an open atmosphere, therefore the

atmospheric CO₂ absorption was unavoidable. Based on the FTIR spectra, the position and shape of the characteristics bands of apatite may be locally controlled by the dopant loading.

3.4. SEM/TEM observations and EDS analysis

Given that the morphological features, chemical composition and spatial distribution of elements in nanostructured bioceramics play an important role in biomedical functionality, the size and morphology, as well as the chemical constituents of the mechanosynthesized powders were analyzed by SEM, TEM/HRTEM and EDS techniques. Figure 7 shows the SEM images and the edge mode of the SEM micrographs of the 1 h milled HA:Al³⁺ powder. As shown in Fig. 7a, the doped nanoparticles exhibit a high tendency to agglomerate due to their large surface to volume ratio. A closer examination at higher magnification illustrates that each agglomerates comprises of many fine round particles (Fig. 7b). Generally, the deformation of the smaller particles and convection processes can control the coalescence of liquid nanoparticles. On the other hand, solid state diffusion dominates the coalescence of solid-like particles [44]. Accordingly, in the present case, the coalescence of the milled particles is due to the solid state diffusion. Figure 7c and d shows a high level of the volume fraction of grain boundary in the doped case. This feature suggests an ultrafine microstructure formed in the presence of the dopant. In fact, the incorporation of Al in the HA lattice led to a grain refinement and a decrease of particle size during the mechanical activation. It is likely that the doped particles in grain boundaries led to an intensive work hardening as well as an increase in the lattice imperfections and subgrain boundaries, and therefore resulted in a decrease in the grain size.

Figure 8 demonstrates the TEM micrographs accompanied by the HRTEM image of the 1 h milled HA:Al³⁺ powder. From the TEM images in Fig. 8a–c, the doped powder consists of nanospheroids with an average size of 44±20 nm and so it is very promising for bone tissue regeneration. As can be seen in Fig. 8b and c, the coalescence of nanospheroids during the milling influences the formation of cluster-like agglomerates. It is quite evident that the milled sample has a high tendency to agglomerate, as shown in SEM images. As soon as two adjacent primary particles

collide, the coalescence may happen on the basis that these two particles share a common crystallographic orientation. Accordingly, the two primary particles are connected and combined to generate a secondary one. Given that the sizes of the secondary particles are still very small, it is reasonable that they will continue to collide and interact, which may ultimately lead to the agglomeration. The HRTEM image in Fig. 8d reveals a distance of 0.28 nm between the adjacent lattice fringe, which implies the growth control along the (100) crystallographic plane. Based on the SEM/TEM observations, the agglomeration mechanism is proposed as shown in Fig. 9. It is most likely that the agglomeration occurs in three certain stages as follows [45]: (1) *Rittinger stage*, where the particles interaction can be neglected and the energy input is nearly proportional to the new surface area formation; (2) *aggregation stage*, wherein the formed new surface area is not congruent to the energy input. Nonetheless, the dispersion degree is still rising considerably. In this stage, the particles stick to each other without any chemical reaction and therefore the resultant aggregates can be separated by slight mechanical intervention; (3) *agglomeration stage*, where a rise in the dispersion first drops to a negligible value, then stops altogether; it may even give way to a decrease of the surface area due to the particle interaction (agglomeration). In this stage, the particles are grown together by chemical bonds and separation becomes impossible and thus it is most likely that the mechanochemical reaction and structural modifications mostly happen at this stage.

The EDS spectra and elemental mapping images of the 1 h milled HA:Al³⁺ powder is shown in Fig. 10. It is clear that the main elements are calcium, phosphorus, oxygen and aluminum. From the EDS results, the (Ca + Al) / P ratio of the doped sample is around 1.75, more than 1.67 as a result of a decrease in the Ca and P concentration. This increase in (Ca + Al) / P ratio can be linked to the CO₃²⁻-for-PO₄³⁻ substitution (B-type), which is in good agreement with the FTIR results. Moreover, contamination due to the excessive wearing of the vial and balls was absent, which confirmed the purity of the as-prepared powders. With regards to the elemental mapping images, an appropriate spatial distribution of the elements in the nanopowders was detected, indicating the formation of the HA:Al³⁺ powder with a homogenous microstructure during an efficient mechanochemical process.

4. Conclusions

In summary, HA:Al³⁺ nanopowders were successfully synthesized using a one-pot mechanochemical reaction. The resultant nanopowders were systematically treated by Rietveld refinement to extract the quantitative phase analysis and the structural parameters. Results showed that an increase in dopant loading induced the amorphization of HA and consequently the crystallinity degree of the milled samples decreased drastically from 63±6 to 24±2 % as the dopant content increased from 0 to 10%. Moreover, *a*- and *c*-axis directions and unit cell volume exhibited a decreasing mode with increasing dopant content owing to the smaller ionic size of Al³⁺ as compared to Ca²⁺. The structural refinements revealed that only about 8% of the dopant probably goes into the HA lattice and the rest stays as unwanted phase. The position of the CO₃-derived bands in FTIR spectra indicated that the CO₃²⁻-for-PO₄³⁻ substitution (B-type) was dominant in the HA:Al³⁺ powders. From the SEM and TEM observations, the doped nanoparticles had a high tendency to agglomerate and closer examination at higher magnification demonstrated that each agglomerate consisted of nanospheroids with an average size of 44±20 nm. According to the edges mode of the SEM micrographs, a high level of the volume fraction of grain boundary was detected, which showed the mechanically induced incorporation of Al in to the HA lattice may lead to a grain refinement and a decrease of particle size. The elemental mapping images confirmed the formation of the HA:Al³⁺ nanopowders with a homogenous microstructure. The proposed mechanochemical reaction offers an outline for the future design of nanocrystalline substituted apatites.

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Fig. 1 XRD profile of the dopant agent.

Fig. 2 XRD patterns of the 1 h milled specimens in the absence (S1) and presence of different amounts of dopant (S2–S6).

Fig. 3 Crystallinity degree of the 1 h milled samples as a function of the dopant loading.

Fig. 4 (a) Rietveld refinement plots of the 1 h milled specimens in the absence (S1) and presence of different amounts of dopant including S2 (2%), S3 (4%), S4 (6%), and S5 (8%); (b) magnified XRD-Rietveld refinement profiles ($2\theta = 30\text{--}35$).

Fig. 5 The refined (a-c) lattice constants and (d) unit cell volume of the 1 h milled samples as function of the dopant loading.

Fig. 6 (a) FTIR spectra of the 1 h milled samples as well as some changes in the position and shape of the bands in the short-range FTIR spectra (b) OH stretching band region and (b) OH libration band region.

Fig. 7 (a,b) SEM images and (c,d) the edges mode of the SEM micrographs of the 1 h milled HA:Al³⁺ powder.

Fig. 8 (a-c) TEM observations at different magnifications accompanied by (d) HRTEM image of the 1 h milled HA:Al³⁺ powder.

Fig. 9 The proposed agglomeration mechanism on the basis of SEM/TEM observations.

Fig. 10 EDS spectra and elemental mapping images of the 1 h milled HA:Al³⁺ powder.

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Table 1 Details of the substitution degree.

Table 2 *R* factors obtained from the Rietveld refinements of the Al substituted HA.

Table 3 The revealed bands and their assignments for FTIR spectra.

Fig. 1

Fig. 3

Fig. 4

Fig. 5

Fig. 6

Fig. 7

Fig. 8

Agglomeration Mechanism

Fig. 9

Fig. 10

Graphical Abstract