MECHANICAL PROPERTIES OF β-TRICALCIUM PHOSPHATE CERAMICS DOPED WITH VANADATE IONS

Naoyuki Matsumoto1, Ayana Yokokawa2, Kenta Ohashi2, Katsumi Yoshida3, Kazuaki Hashimoto2*, Yoshitomo Toda2
(*Corresponding author: kazuaki.hashimoto@it-chiba.ac.jp)

1 Department and Faculty of Engineering, Graduate School, Chiba Institute of Technology, 2-17-1 Tsudanuma, Narashino-shi, Chiba 275-0016, Japan.
2 Department of Life and Environmental Sciences, Faculty of Engineering, Graduate School, Chiba Institute of Technology, 2-17-1 Tsudanuma, Narashino-shi, Chiba 275-0016, Japan.
3 Mass Transmutation Engineering Division, Research Laboratory for Nuclear Reactors, Tokyo Institute of Technology, 2-12-1 Ookayama, Meguro-ku, Tokyo 152-8550, Japan.

Keywords: Beta-tricalcium phosphate, Vanadate ions, Solid solution, Sintering, Mechanical properties

Abstract: Beta-tricalcium phosphate (β-TCP) powders and ceramics doped with vanadate (VO43-) ions were prepared, and the substitution mode of VO43- ions for the β-TCP structure and the mechanical properties were investigated. The synthesized powders consisted of a single β-TCP (0–80 mol%) or Ca3(VO4)2 (100 mol%) phase, and the a and c lattice constants increased linearly up to 100 mol%. These results indicate that the VO43- ions were homogeneously doped at all PO4 sites in β-TCP. The bending strength increased with the VO43- ion content up to 2.0 mol% because of the improvement in sinterability. However, when the VO43- ion content was above 2.0 mol%, the bending strength decreased because of crack formation and porosity due to excess grain growth. The bending strength of β-TCP ceramics was higher when doped with VO43- ions than with other metal ions; thus, β-TCP ceramics with excellent mechanical properties can be fabricated by substituting a small amount of VO43- ions.

(Received January 2, 2010; Accepted May 27, 2010)

INTRODUCTION

Vanadium is an essential trace element in vivo, and similar to insulin; vanadium (IV) ions decrease the blood sugar levels1-5. Furthermore, vanadium specifically inhibits Na+K-ATPase and intensifies the activation of Ca channels, Ca exchangers, and Ca-Mg pumps; this increases the concentration of Ca2+ ions in cells and releases the resultant extracellular Ca2+ ions6. On the other hand, insulin-like growth factors (IGFs), which enhance the growth of osteoblasts, are mainly produced by osteoblasts and are linked by the IGF receptors on osteoblast surfaces7. Insulin receptor substrates (IRS) are important molecules for transmitting IGF signals to IGF receptors in cells8. The signaling of IGFs via an IRS has been reported to be activated by vanadium9. Therefore, vanadium (ions) may accelerate bone formation.

Tricalcium phosphate [Ca3(PO4)2; TCP] and hydroxyapatite [Ca10(PO4)6(OH)2; HAp] have excellent biocompatibilities and osteointegration properties because their chemical compositions resemble those of the mineral phase of bones and teeth. Among these calcium phosphates, β-tricalcium phosphate (β-TCP) is a well-known biodegradable bioceramics, i.e., it is bioreabsorbed in vivo with new bone tissue growth. In contrast, HAp remains in vivo for a long time10-14.

We have reported substituting monovalent (Li, Na, K), divalent (Mg), and trivalent (Al) metal ions for Ca sites in the β-TCP structure; the substitution improves its following properties: the thermal stability of the β-phase of TCP, mechanical properties (sinterability), solubility (bioresorbability), and biological responses in vitro and in vivo15-18.

In light of these points, we first synthesized β-TCP doped with vanadium (V5+) ions and showed that the substitution of V5+ ions for Ca sites in β-TCP structure enhances the differentiation of osteoblasts (MC3T3-E1 cells)19; however, the substitution induced a decrease in sinterability (densification) for β-TCP ceramics and the formation of a secondary (glass) phase. Therefore, we focused on vanadate (VO43-) ions because it has been reported that VO43- ions could be substituted for PO4 sites in the HAp structure20-22.

In this study, we prepared β-TCP powders and ceramics doped with VO43- ions, and the substitution mode of VO43- ions for the β-TCP structure and investigated their mechanical properties. Furthermore,
we discuss the effect of substituting $\text{VO}_4^{3-}$ ions on the mechanical properties and sinterability.

**MATERIALS AND METHODS**

Beta-TCP powders doped with $\text{VO}_4^{3-}$ ions were synthesized by a conventional solid state reaction. $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ (Kishida Chemical, Osaka, Japan), $\text{CaCO}_3$ (Kishida Chemical), and $V_2\text{O}_5$ (Kishida Chemical) were used as starting materials. $V_2\text{O}_5$ was added to substitute 0–100 mol% of $\text{VO}_4^{3-}$ ions for all $\text{PO}_4$ sites in the $\beta$-TCP structure with a molar ratio of $\text{Ca}/(\text{PO}_4 + \text{VO}_4) = 1.50$, which is the stoichiometric ratio for $\beta$-TCP. These materials were mixed using an agate mortar for 60 min; the mixtures were then heated at 1000°C for 12 h in air. To achieve a high degree of crystallinity and a complete solid state reaction, the powder was remixed and reheated under the same previous conditions.

After the obtained powders were crushed, the crystalline phases were investigated using an X-ray powder diffractometer (XRD) with a rotating anode X-ray tube (RINT-1500, Rigaku, Tokyo, Japan). The lattice constants for the rhombohedral unit cell in the hexagonal setting were also determined using an XRD. They were refined by the least-squares method using silicon powder as an external standard and using a software (RINT/DMAX-2000 Ver.4.000, Rigaku); the reflection planes $(1\,1\,1)$, $(2\,2\,0)$, $(3\,1\,1)$, and $(4\,0\,0)$ of silicon and $(2\,0\,10)$, $(2\,1\,8)$, $(2\,2\,0)$, $(3\,2\,8)$, and $(2\,0\,20)$ of $\beta$-TCP were used to calculate the lattice constants. The ionic states of vanadium in the $\beta$-TCP structure were investigated by the diffuse reflectance method using KBr (Kishida Chemical) and with a Fourier transform infrared spectroscopy (FT-IR) spectrophotometer (FT/IR-230, JASCO, Tokyo, Japan).

To fabricate $\beta$-TCP ceramics doped with $\text{VO}_4^{3-}$ ions, the amounts of $\text{VO}_4^{3-}$ ions used were 0, 1.0, 2.0, 2.5, 3.0, 4.0, and 5.0 mol% for $\text{PO}_4$ sites in $\beta$-TCP. The same starting materials as described above were ball-milled in polyethylene bottles with alumina balls for 48 h using ethanol as a solvent. After removing the ethanol, the mixtures were calcined at 900°C for 12 h in air; we did so because $\beta$-TCP ceramics fabricated using powders synthesized under this condition were found to be densest. The calcined powder formed into a green compact ($5.0 \times 20.0 \times 45.0$ mm$^3$) under uniaxial pressure (32 MPa); this was then isostatically cold-pressed (200 MPa). The compact was pressureless-sintered at 1100°C for 24 h in air, which is a common sintering condition for $\beta$-TCP ceramics.

Bending strength measurement of the sintered bodies was taken using a testing machine (AG-I, Shimadzu, Kyoto, Japan). The three-point bending strength was measured at room temperature in air with a crosshead speed of 0.5 mm/min and lower span of 30 mm. Prior to the measurement, each sintered body was cut and polished to dimensions of $3.0 \times 4.0 \times 34$ mm$^3$. Five specimens were used for the bending test. The bulk density and porosity were measured using Archimedes’ method in ethanol as the dispersive medium. The microstructure of the

---

**Fig. 1** XRD patterns of synthesized powders containing various amounts of $\text{VO}_4^{3-}$ ions: (a) 0 mol%, (b) 20 mol%, (c) 40 mol%, (d) 60 mol%, (e) 80 mol%, and (f) 100 mol%.

**Fig. 2** FT-IR spectra of synthesized powders containing various amounts of $\text{VO}_4^{3-}$ ions: (a) 0 mol%, (b) 20 mol%, (c) 40 mol%, (d) 60 mol%, (e) 80 mol%, and (f) 100 mol%.
fabricated ceramics was observed using a scanning electron microscope (SEM, VE-7800, KEYENCE, Osaka, Japan). Before the SEM observation, the sintered bodies were mirror-polished and then thermal-etched at 1000°C for 5 h. The average particle size of the sintered bodies was determined by the intercept method using SEM photographs of the microstructure. The number of grains used for calculating the average particle size was 200.

RESULTS AND DISCUSSION

Substitution mode of vanadate ions for β-TCP structure

Figure 1 shows the XRD patterns of the synthesized powders. Their crystal phases were recognized as a single β-TCP (ICDD: 09-0164) phase up to 80 mol%. Furthermore, the diffraction peaks shifted toward a low angle with an increasing amount of VO$_4^{3-}$ ions, and the crystal phase at 100 mol% was a single Ca$_3$(VO$_4$)$_2$ (ICDD: 46-0756) phase, which has the isotypic structure with β-TCP.$^{23}$

FT-IR spectra of β-TCP powder containing various amounts of VO$_4^{3-}$ ions are shown in Figure 2. The bands at 1100–960 and 600–570 cm$^{-1}$, which were attributed to the phosphate (PO$_4$) stretching vibrations and PO$_4$ bending vibrations, respectively, appeared in FT-IR spectra of powders containing 0–80 mol% VO$_4^{3-}$ ions. In contrast, the band at 800–900 cm$^{-1}$, which was attributed to the vanadate (VO$_4$) vibration, was observed in FT-IR spectra of samples containing 20–100 mol% of VO$_4^{3-}$ ions. The absorption intensity of the VO$_4$ group increased and that of the PO$_4$ group decreased when the amount of VO$_4^{3-}$ ions increased. In addition, the band for the VO$_4$ group broadened and that of the PO$_4$ group sharpened with an increase in the amount of VO$_4^{3-}$ ions. The same tendency was observed in FT-IR spectra of HAp doped with VO$_4^{3-}$ ions,$^{20}$ this should be attributed to the change in symmetry of the VO$_4$ and PO$_4$ tetrahedrons with the change in the β-TCP structure due to substitution of the VO$_4^{3-}$ ions. In case of β-TCP doped with V$^{3+}$ ions, the band of the VO$_4$ group in FT-IR spectra could not be observed because V$^{3+}$ ions could replace Ca(5) sites in β-TCP.$^{15}$ These results indicate that VO$_4^{3-}$ ions were substituted for PO$_4$ sites in the β-TCP structure.

Figure 3 shows the change in the $a$ and $c$ lattice constants for the synthesized powders with the amount of VO$_4^{3-}$ ions. The $a$ and $c$ lattice constants linearly increased with VO$_4^{3-}$ ion content up to 100 mol%. The increase in lattice constants should be caused by the difference in dimensions between the PO$_4$ and VO$_4$ tetrahedrons; the VO$_4$ tetrahedron is bigger. In addition, the lattice constant changes have the same tendency as VO$_4^{3-}$ ions substituting for PO$_4$ sites in HAp; here, VO$_4^{3-}$ ions replace the PO$_4$ sites, and the maximum substitution is 100 mol%.$^{20-22}$ The crystal structure of pure β-TCP was first determined by Dickens et al.$^{24}$ Yashima et al. also refined the pure β-TCP structure using high-temperature neutron powder diffraction and the Rietveld method. They reported that β-TCP crystallizes into rhombohedral
structures (space group $R\overline{3}c$, $Z = 21$) with unit cell parameters of $a = b = 1.0435(2)$ nm, $c = 3.74029(5)$ nm, $\alpha = \beta = 90^\circ$, and $\gamma = 120^\circ$ in the hexagonal setting; the crystal structure consists of columns A and B located independently along the $c$-axis. Columns A and B are composed of $-P(1)O_4-\square-Ca(5)O_6-P(1)O_4-$ (where $\square$ is a vacancy) and $-P(3)O_4-Ca(1)O_7-Ca(3)O_8-Ca(2)O_8-P(2)O_4-P(3)O_4-$, respectively\(^{25}\). When $V^{3+}$ ions are substituted into $\beta$-TCP, the $a$ lattice constant linearly decreased with an increase in the amount of $V^{3+}$ ions up to 9.09 mol\%, whereas $c$ constants initially increased up to 2.0 mol\% and then decreased up to 9.09 mol\%; therefore, $V^{3+}$ ions are substituted for Ca(5) sites in $\beta$-TCP as described above. We can infer from these results that $VO_4^{3-}$ ions were homogeneously doped into all PO$_4$ sites [P(1), P(2), and P(3)] in $\beta$-TCP structure up to 100 mol\%.

Mechanical properties of $\beta$-TCP ceramics doped with vanadate ions

When we fabricated $\beta$-TCP ceramics doped with $VO_4^{3-}$ ions using the powders calcined at 900°C, the change in the $VO_4^{3-}$ ion content was over a small range (0–5.0 mol\%) because excess vanadium are considered to be toxic activity in vivo\(^{22}\). The change in bending strength of the sintered bodies containing various amounts of $VO_4^{3-}$ ions is shown in Figure 4. The bending strength increased with increasing $VO_4^{3-}$ ion content up to 2.0 mol\%, after which it decreased gradually; the bending strength of $\beta$-TCP ceramics doped with 2.0 mol\% $VO_4^{3-}$ ions was 120 MPa.

The bulk density and open porosity of $\beta$-TCP ceramics doped with $VO_4^{3-}$ ions are shown in Figure 5. The bulk density increased and open porosity decreased with increasing $VO_4^{3-}$ ion content up to 2.0 mol\%. However, above 2.0 mol\%, the bulk density
decreased, and the open porosity increased.

SEM photographs of microstructure of \( \beta \)-TCP ceramics doped with VO\(_4\)\(^{3-}\) ions are shown in Figure 6. In addition, the particle average size, which was determined by an intercept method using SEM photographs of the microstructure, is shown in Figure 7. SEM observations showed that densification of the sintered bodies was enhanced by increasing the VO\(_4\)\(^{3-}\) ion content up to 2.0 mol%; this also increased the average particle size, as shown in Fig. 7. These results correspond to the increase in bulk density and the decrease in open porosity, indicating that the substitution of VO\(_4\)\(^{3-}\) ions should improve the sinterability and bending strength of sintered bodies; the improvements can be attributed to the increase in the diffusion coefficient (mass-transfer coefficient) due to the substitution of VO\(_4\)\(^{3-}\) ions. More detailed studies are underway to clarify the mechanism for sinterability promotion caused by doping with VO\(_4\)\(^{3-}\) ions. In contrast, cracks formed and micropores increased in \( \beta \)-TCP ceramics doped with over 2.0 mol% VO\(_4\)\(^{3-}\) ions; these agree with the changes in bulk density and open porosity, while the average particle size increased with VO\(_4\)\(^{3-}\) ion content. These results show that excess substitution of VO\(_4\)\(^{3-}\) ions should induce the formation of cracks and micropores due to excess grain growth. Furthermore, the cracks and micropores precipitate the destruction of the sintered bodies because destruction mainly occurred from micropores in grain boundaries and cracks (data not shown), resulting in a decrease in bending strength, as shown in Fig. 4.

Figure 8 shows the bending strength of \( \beta \)-TCP ceramics doped with VO\(_4\)\(^{3-}\) ions or other metal ions (Na\(^{+}\), Mg\(^{2+}\), and Na\(^{+}\) + 9.09 mol% Mg\(^{2+}\) ions); these are reported in this paper and our previous paper\(^{18}\), respectively. Beta-TCP ceramics doped with VO\(_4\)\(^{3-}\) ions had higher bending strength than \( \beta \)-TCP ceramics doped with other metal ions, and the high bending strength was possible due to substituting a smaller amount of VO\(_4\)\(^{3-}\) ions.

These results show that the substitution of a small amount of VO\(_4\)\(^{3-}\) ions into \( \beta \)-TCP ceramics is effective for improving sinterability and mechanical properties (bending strength); i.e., it should be possible to fabricate \( \beta \)-TCP bioabsorbable ceramics with high bending strength and bulk density by doping VO\(_4\)\(^{3-}\) ions.

**CONCLUSIONS**

Beta-TCP powders doped with VO\(_4\)\(^{3-}\) ions were synthesized, and the substitution mode of VO\(_4\)\(^{3-}\) ions for \( \beta \)-TCP was determined. In addition, \( \beta \)-TCP ceramics containing VO\(_4\)\(^{3-}\) ions were fabricated, and their mechanical properties were investigated. The crystal phase of \( \beta \)-TCP powders containing VO\(_4\)\(^{3-}\) ions was a single \( \beta \)-TCP phase up to 80 mol% and a single Ca\(_3\)(VO\(_4\))\(_2\) phase at 100 mol%. The \( a \) and \( c \)
lattice constants increased linearly with the VO$_3^-$ ion content up to 100 mol%. These results indicate that VO$_3^-$ ions can be homogeneously substituted for all PO$_4$ sites in the $\beta$-TCP structure. The bending strength of $\beta$-TCP ceramics containing up to 2.0 mol% VO$_3^-$ ions increased because the substitution of VO$_3^-$ ions improves the sinterability. However, more than 2.0 mol%, the bending strength decreased by the formation of cracks and micropores due to excess grain growth. Further studies are planned on $\beta$-TCP ceramics containing VO$_3^-$ ions for clinical applications involving the dissolution test, in vitro cytotoxicity test, in vitro cell evaluations using osteoblasts and osteoclasts, and in vivo test.

REFERENCES