FULL PAPER

Fabrication of an interconnected porous $\beta$-tricalcium phosphate structure by polyacrylic acid-mediated setting reaction and sintering

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ABSTRACT. Although the sintering process of ceramics is maintained the interconnectivity of pores (see Graphical Abstract). Although the sintering process of ceramics is suitable for fusing of granules, the low setting ability of $\beta$-TCP at high temperatures is a limitation of such a method.14)–16) For facilitating smooth sintering, methods for binding $\beta$-TCP granules are urgently needed.

Previously, we fabricated $\beta$-TCP with an interconnected porous structure from $\beta$-TCP granules using an HNO$_3$-mediated setting reaction with loading.16) When the granules were exposed to HNO$_3$, $\beta$-TCP partially dissolved and released Ca$^{2+}$ and PO$_4^{3-}$, as indicated in the following equation:

$$\text{Ca}_3(\text{PO}_4)_2 \rightarrow 3\text{Ca}^{2+} + \text{PO}_4^{3-}$$  \hspace{1cm} (1)

$$\text{PO}_4^{3-} + \text{H}^+ \rightarrow \text{HPO}_4^{2-}$$  \hspace{1cm} (2)

The dissolution of $\beta$-TCP increases the pH of the solution, which becomes supersaturated with dicalcium hydrogen phosphate dihydrate (DCPD, $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$), causing precipitation of DCPD crystals, as shown in the following equation:

$$\text{Ca}^{2+} + \text{HPO}_4^{2-} + 2\text{H}_2\text{O} \rightarrow \text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$$  \hspace{1cm} (3)

The DCPD crystals bridge $\beta$-TCP granules and trigger the setting reaction. Heat treatment causes evaporation of

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1. Introduction

$\beta$-tricalcium phosphate ($\beta$-TCP) with interconnected pores is an attractive substitute for bone because it shows excellent tissue response and osteoconductivity. An interconnected porous structure is a key factor for fast osteoconductivity, because it facilitates tissue and cell penetration. However, it is challenging to attach interconnected porous structure to $\beta$-TCP blocks. In this study, a new, simple, and safe method for fabricating interconnected porous $\beta$-TCP was developed, based on an analogous dental glass ionomer cement setting reaction. $\beta$-TCP granules were mixed with polyacrylic acid (PAA) by loading; PAA got bound to these granules and got set to form an interconnected porous structure; the sintering process decomposed PAA and yielded the interconnected porous $\beta$-TCP structure. Diametral tensile strength and porosity of the fabricated samples were 1.3 ± 0.2 MPa and 57.6 ± 1.1%, respectively. These values of samples were enough value for applying bone substitute. $\beta$-TCP with interconnected pores synthesized using the novel method described, herein, would be a suitable bone substitute in clinical settings.

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HNO$_3$ and transformation of DCPD and Ca$^{2+}$ in the solution to $\beta$-TCP, leading to the fabrication of $\beta$-TCP with interconnected pores. Although the setting reaction of $\beta$-TCP granules is an attractive step for imparting porosity, the use of HNO$_3$ might not be ideal because of its harmful chemical nature. Therefore, it is necessary to develop a safer method for the synthesis of $\beta$-TCP blocks with interconnected porous structure.

Polyacrylic acid (PAA) may be used in the setting reaction of $\beta$-TCP granules. PAA is a soluble acidic polymer with numerous −COOH groups and is used as a component of dental cement [i.e., glass ionomer cement (GIC)].$^{17-19}$ GIC sets as a result of a chelating reaction between the −COOH group of PAA and Ca$^{2+}$ from the filler surface. By a similar mechanism, $\beta$-TCP granules may also set when mixed with PAA (see Graphical Abstract). In this study, therefore, the feasibility of fabricating $\beta$-TCP with an interconnected porous structure based on the PAA-mediated setting reaction and a subsequent heat treatment was evaluated.

2. Experimental procedure

2.1 Preparation of $\beta$-TCP granules

$\beta$-TCP granules were prepared from commercial $\beta$-TCP powder (β-TCP-100, Taihei Chemical Industry Co., Japan). The powder was pressed under a 20 MPa loading pressure in a 30-mm diameter mold and sintered at 1100 °C for 6 h. The block was then crushed and sieved to generate granules, 200–300 μm in diameter.

2.2 Fabrication of porous $\beta$-TCP using PAA treatment and sintering

PAA (M$_W$: 25000; Wako Pure Chemical Inc., Japan) was mixed with water to form a slurry with a liquid/powder (L/P) ratio of 1:1 as weight ratio. The pH value of PAA slurry was measured with a pH electrode (LAQUA ToupH 961SS-10D with pH meter D-72, Horiba Co., Kyoto, Japan). This was then mixed with PAA (1:1 L/P ratio) and pressed under 5, 10, and 15 MPa loading pressures in a 6-mm diameter acrylic resin mold. The obtained cylindrical bodies of the set $\beta$-TCP/PAA were 6 mm in diameter and 3 mm in height. Thereafter, the set samples were sintered in a tubular furnace (Electric furnace TMF-300N, AS ONE Co., Japan) at 1100 °C with a heating rate of 5 °C/min and maintained at 1100 °C for 6 h before cooling in the furnace.

2.3 Characterization

X-ray diffraction (XRD; D08 Advance, Bruker AXS Co., Tokyo, Japan) measurements were made at an acceleration voltage of 40 kV and a current of 40 mA using a copper target to characterize the materials. The measured 2θ step was 0.021, 2θ ranged from 20 to 70°, and the time per step was 20 s/θ. The specimens were mixed using an agate mortar and pestle to avoid a preferred orientation effect. The chemical shifts of the mixed specimens were also measured using attenuated total reflection (ATR)-type Fourier-transform infrared spectroscopy (ATR-FT-IR; FT/IR-6200, Jasco Co., Tokyo, Japan; 32 scans, resolution = 2 cm$^{-1}$).

The morphology of the specimens was examined by scanning electron microscopy (SEM; S-3400N, Hitachi Co., Tokyo, Japan) performed at an acceleration voltage of 5 kV after coating with Au.

The diametral tensile strength (DTS: $\sigma_s$) of the specimens was measured using a universal testing machine (AGS-J; Shimadzu Co., Kyoto, Japan) at a crosshead speed of 1 mm/min. The $\sigma_s$ of the foams (cylinder shape, ranging approximately 6 × 3 mm, was calculated from the compressive load (P) and specimen diameter (d) and length (l) using Eq. (4):

$$\sigma_s = \frac{2P}{\pi dl} \quad \text{(4)}$$

The interior structures of the specimens were measured using micro-computed tomography analysis (micro-CT; SkyScan 1076, Toyo Technica Co., Tokyo, Japan) at an acceleration voltage of 60 kV and a current of 170 μA using a 0.5-mm Al filter. Porosity was calculated from the bulk density of each sample and theoretical density of $\beta$-TCP (3.07 g/cm$^3$).$^{11,12}$ Bulk density was determined from the weight and external volume of each sample.

3. Results

Figure 1 shows photographs of typical $\beta$-TCP granules [Fig. 1(a)], set $\beta$-TCP/PAA granules pressed under a 10 MPa loading pressure, compacted before [Fig. 1(b)] and after sintering at 1100 °C [Fig. 1(c)]. The set $\beta$-TCP/PAA granules became pellet-like compact and a bit transparent compared to the granules before mixing with PAA. After heating, the set $\beta$-TCP/PAA granules showed a whitish color, typical of $\beta$-TCP, and their shape was
The microCT image of the set β-TCP sample [Fig. 1(d)] showed that the microstructure of the set β-TCP/PAA granules was maintained during sintering. Thus, the interconnected porous structure was formed because of sintering. We also estimated the effect loading pressure on the shape and inner structure of the set β-TCP/PAA granules. However, the structure was essentially the same.

The XRD patterns of β-TCP granules, set β-TCP/PAA granules compacted under 10 MPa loading pressure before and after sintering at 1100 °C, are shown in Fig. 2. The XRD patterns of β-TCP, DCPD, and PAA were also included to facilitate comparisons. XRD patterns of all the samples indicated that no crystalline phase other than that of β-TCP was present. Although treated PAA slurry was acidic solution and its pH value was 2.40, we could not detect any crystalline phases such as DCPD. Therefore, it was suggested that the non-crystalline phase might be a key factor in this setting reaction.

FT-IR spectroscopic analysis allowed us to evaluate the chemical bonding within the samples. The FT-IR spectra of β-TCP granules and set β-TCP/PAA granules, compacted under 10 MPa loading pressure before and after sintering at 1100 °C are shown in Fig. 3. The FT-IR spectra of β-TCP, DCPD, and PAA are also included to facilitate comparisons. The C=O stretching band of a –COOH group belonging to PAA molecules in set β-TCP/PAA granules was found to be slightly shifted, suggesting the formation of a bond or structure between PAA and β-TCP in set β-TCP/PAA granules.

Figure 4 shows SEM micrographs of β-TCP granules [Figs. 4(a) and 4(b)], set β-TCP/PAA granules, compacted under 10 MPa loading pressure before [Figs. 4(c) and 4(d)] and after [Figs. 4(e) and 4(f)] sintering at 1100 °C. The surface of β-TCP granules resembled the typical surface of sintered ceramics with a microporous structure. After mixing with PAA, an interconnected porous structure was formed among β-TCP granules. At a higher magnification, wide connections between granules and smooth film-like structures (with characteristics similar to that of a typical polymer surface) covering the microporous surface of β-TCP were observed [Fig. 4(d)]. After sintering, the smooth film disappeared whilst the bonds between the granules and the porous structure remained [Fig. 4(e)]. In addition, the typical microporous structure of β-TCP was also observed [Fig. 4(f)].

The DTS values of set β-TCP/PAA granules that were compacted and then sintered at 1100 °C are presented in Fig. 5; the DTS value increased along with the loading pressure applied during compaction. On the other hand,
the porosity of samples decreased slightly when the loading pressure was increased (Fig. 6).

4. Discussion

Our results clearly indicate that β-TCP with interconnected pores can be fabricated through the PAA reaction followed by a sintering process. The interaction between the –COOH group of PAA and Ca\(^{2+}\) of β-TCP establishes the bonding among β-TCP granules. Moreover, the PAA slurry has a viscous consistency and contributes to the adhesion of the granules. Loading pressure, applied to produce compacted samples, also increases the mechanical strength as it increases the contact area among the granules. Although the PAA phase was decomposed during sintering and the samples finally transformed to pure β-TCP (as confirmed by the XRD results), the bonds between β-TCP granules remained intact. As further evaluations, we also employed other polymers such as polyvinyl alcohol (PVA) for setting reactions. Although the β-TCP granules could be set and β-TCP with interconnected porous structures could be fabricated, the mechanical strength of materials were relatively lower than those of PAA treatment. Therefore, we considered that the –COOH group of PAA and Ca\(^{2+}\) of β-TCP establishes the bonding among β-TCP granules is the key for β-TCP interconnected porous structures fabrications.

The PAA-mediated production of β-TCP granules was considered a chelating process rather than an interlocking process of the formed DCPD crystals. Therefore, the setting reaction of β-TCP granules can be described as analogous to the GIC setting reaction (see Graphical Abstract). Even though the sample went through a sintering process, such a chelating structure of PAA maintained the granule binding. The novelty of this process is that it avoids the use of harmful chemicals, such as HNO\(_3\), needed for the setting reaction.

The fabricated β-TCP sample with interconnected pores has enough mechanical strength for implantation, and could, therefore, be safely used in clinical trials. Furthermore, the β-TCP structures with interconnected pores created in a PAA-mediated manner showed no significant differences in physical and chemical properties, compared to those that went through the HNO\(_3\) treatment.\(^{16}\) Therefore, it can be concluded that the PAA treatment is an effective approach to fabricate interconnected porous β-TCP structures from β-TCP granules. Furthermore, the fabricated β-TCP sample with interconnected pores has
suitable pore-sizes around several 100μm in diameter which tissues could penetrate its interiors and, enhances their bone remodeling cycles.

Our proposed method for synthesizing β-TCP structures with interconnected pores is highly controllable and easy-to-handle. The pore size and porosity of interconnected porous β-TCP can be controlled by changing the initial size of the granules.

5. Conclusion

β-TCP, with an interconnected porous structure, was fabricated by applying a PAA treatment to the β-TCP granules, followed by compaction under various loading conditions and sintering. The loading pressure applied for the compaction of PAA-treated β-TCP contributes to the increase in its mechanical strength. The bond between the granules remained intact after sintering, even though the PAA phase was decomposed. The fabricated β-TCP samples loading with 10 and 15 MPa exhibited enough values both mechanical strength and porosity for applying bone substitute as interconnected porous structures.

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