PROPERTIES OF CALCIUM-PHOSPHATE PASTE WITH HOLLOW SPHERICAL β-CALCIUM-ORTHOPHOSPHATE AGGLOMERATES

Yoshiro Musha¹, Mari Abe², Tomohiro Umeda²*, Kiyoshi Itatani²

(*Corresponding author: umeda4993tomohiro@yahoo.co.jp)

¹ The 2nd Department of Orthopaedic Surgery, School of Medicine, Toho University, 2-17-6 Oohashi, Meguro-ku, Tokyo 153-8515 Japan

² Department of Chemistry, Faculty of Science and Engineering, Sophia University, 7-1 Kioi-cho, Chiyoda-ku, Tokyo 122-8554 Japan

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Abstract: The spherical β-calcium orthophosphate (β-Ca₃(PO₄)₂; β-TCP) agglomerates have been prepared by a spray-pyrolysis technique. The hollow spherical agglomerates were obtained by heating the spray-pyrolyzed powder at 900°C for 10 min. The cylindrical specimen was fabricated mixing the calcium-phosphate paste (CPP) with 10-50 mass% β-TCP agglomerates, using malaxation liquid. The setting time of CPP specimen increased from 8.5 to 17 min with increasing amount of β-TCP from 10 to 50 mass%. The CPP specimens with β-TCP addition were immersed into the simulated body fluid (SBF) at 37±0.2°C for various times. The compressive strengths of CPP specimens with β-TCP addition reached maxima, e.g., 42.8 MPa for 10 mass% β-TCP addition and 7.5 MPa for 50 mass% β-TCP addition, respectively, after the immersion of these specimens in SBF for 3-7 d. Crystalline phases of the CPP specimens after the immersion in SBF for 7 d were HAp and β-TCP. The total porosity of CPP specimen increased with increasing amount of β-TCP and attained 67.1% for 50 mass% β-TCP addition.

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INTRODUCTION

In the orthopedic surgery, calcium-phosphate ceramic is now being used for repairing bone defects formed by illness or surgical treatment, and a number of clinical researches on this type of ceramic bones have been reported.¹⁻² Such ceramic bones are commercially-available in the forms of block and granules. When a block-type ceramic is used for repairing bone defects, one must select either an as-fabricated ceramic bone that is implanted into the processed bone defects, or processed ceramic bones whose shapes are matched to those of bone defects. In both cases, however, it may be difficult to accommodate the shapes of ceramic bones to the complex-shaped bone defects. Although the granule-type ceramic bone is used for repairing complex-shaped bone defects, it has the problem on the poor mechanical strength during the resorption of bones and substitution with new osseous tissues. In order to overcome these problems, many researchers paid attention to the development of bone paste,³⁻⁴ whose advantages are: (1) injection via a small hole directly to the bone defects; (2) filling in the complex-shaped defects; (3) sufficient mechanical strength that is satisfied with the requirements; and (4) bioactivity comparable to that of apatite.

As a typical bone paste, calcium phosphate paste (CPP) for the injection through small holes has been developed and came onto the market in Japan.¹⁻² The setting of such CPP may be divided into two stages. The first stage of setting involves a rapid increase in compressive strength due to the chelating reaction between succinic acid (a component of the malaxation liquid) and calcium ions. The second stage of setting involves a slow increase in compressive strength through conversion of various types of calcium phosphates into hydroxyapatite (Ca₁₀(PO₄)₆(OH)₂; HAp). Since the hardening of CPP does not involve polymerization, unlike the utilization of organic cements, little heat is emitted when it hardens. Also, there is no problem on the residual monomers. Furthermore, because this cement changes structurally into apatite in vivo, it has excellent osteoconductivity and biocompatibility comparable to those of bone prostheses of apatite.

A problem on the utilization of CPP may be the long-term retention of cement in vivo,³⁻⁷ i.e. poor bioabsorbability, due to the formation of comparatively dense CPP after hardening. To date, the porous CPP⁸⁻¹⁰ and apatite cement (carbonate-apatite formed by combining cement with sodium hydrogen carbonate) have been fabricated in order to improve such bioabsorbability.¹¹⁻¹² The present authors
Table 1 Setting time of CPP with β-TCP fabricated using a malaxation liquid, together with P/L ratios.

<table>
<thead>
<tr>
<th>Amount of βTCP / mass %</th>
<th>10</th>
<th>30</th>
<th>50</th>
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<tbody>
<tr>
<td>Powder (P) / Liquid (L) / g/g</td>
<td>2.7</td>
<td>1.8</td>
<td>1.3</td>
</tr>
<tr>
<td>Setting time / min</td>
<td>8.5</td>
<td>16</td>
<td>17</td>
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Fig. 1 Typical SEM micrograph of the β-TCP agglomerates heat-treated at 900°C for 10 min.
accelerating voltage, 2 kV), after coating the specimen with Pt-Pd in order to avoid charging effect.

The compressive strength of the CPP specimen was measured using a testing machine (Auto Strain, Model: YZ-500-1-PC, Yasuda Seisakusyo, Nishinomiya, Japan) with a cross head speed of 0.5 mm·min	extsuperscript{-1}. The compressive strength of the CPP specimen was measured using a testing machine (Auto Strain, Model: YZ-500-1-PC, Yasuda Seisakusyo, Nishinomiya, Japan) with a cross head speed of 0.5 mm·min	extsuperscript{-1}.

16.17 after the immersion in SBF for 7 d was 77.8 MPa, whereas the compressive strengths of CPP with 10, 30 and 50 mass% \(\beta\)-TCP addition were 42.8, 21.4 and 7.5 MPa, respectively.

The compressive strength of CPP specimen decreases with increasing amount of \(\beta\)-TCP addition. This phenomenon may be attributed to the increase in porosity with increasing amount of \(\beta\)-TCP addition. A slight reduction of compressive strength after the immersion in SBF for 7 d or more seems to be ascribed to the dissolution of chemical components (e.g., \(\text{Ca}^{2+}\) and \(\text{PO}_4^{3-}\)) into the SBF. As the present data indicate, the compressive strengths of CPP specimens with and without \(\beta\)-TCP addition must be dependent on the porosities. Detail will be discussed later, together with the data on porosity.

RESULTS AND DISCUSSION

1. Properties of CPP specimen with \(\beta\)-TCP addition

In order to evaluate the handling of CPP with \(\beta\)-TCP addition, the setting times were measured, together with their P/L ratios. As shown in Table 1, the P/L ratio decreased and the setting time increased with increasing amount of \(\beta\)-TCP addition. The setting time of CPP specimen with 10 mass% \(\beta\)-TCP addition was 8.5 min, whereas that of CPP specimen with 50 mass% of \(\beta\)-TCP was 17 min. Such increase in setting time is attributed to the decrease in P/L ratio, i.e., the increase in the amount of malaxation liquid. Thus a larger amount of malaxation liquid seems to be needed for the setting of CPP with increasing amount of \(\beta\)-TCP, which also contributes to increasing the setting time.

Fig. 2 shows the compressive strengths of CPP specimens with \(\beta\)-TCP addition. The overall trend reveals that the compressive strengths increased with immersion time and reached maxima after the immersion in SBF for 3 to 7 d. The compressive strength of CPP specimen without \(\beta\)-TCP addition after the immersion in SBF for 7 d was 77.8 MPa, whereas the compressive strengths of CPP with 10, 30 and 50 mass% \(\beta\)-TCP addition were 42.8, 21.4 and 7.5 MPa, respectively.

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Fig. 3 shows the phase changes of CPP with 50 mass% \(\beta\)-TCP addition during the immersion in SBF. After the immersion in SBF for 3 h, the resulting CPP contained HAp, together with \(\alpha\)-TCP, \(\beta\)-TCP and TECP. X-ray intensities of the \(\alpha\)-TCP and TECP decreased but HAp increased with increasing immersion time (Fig. 3 (a) and (b)). After the immersion in SBF for 7 and 14 d, the resulting CPP contained HAp and \(\beta\)-TCP (Fig. 3 (c) and (d)). X-ray intensities of the \(\beta\)-TCP were higher, compared to those of CPP with 10 and 30 mass % \(\beta\)-TCP addition (not shown in the figure).

On the basis of the above XRD data, the reaction routes of CPP with \(\beta\)-TCP addition in the SBF solution are considered as follows:
immersed in SBF for 14 days shown in immersed in SBF for 14 days shown in
conversion of various types of calcium phosphates conversion of various types of calcium phosphates
direction of the centers of agglomerates. Such \( \beta \)-TCP agglomerates, which were grown in the direction of the centers of agglomerates. Such needle-like particles may be formed during the conversion of various types of calcium phosphates into HAp in the presence of SBF.

\[
2 \text{Ca}_3(\text{PO}_4)_2 + \text{Ca}_9(\text{PO}_4)_2 \cdot \text{H}_2\text{O} \rightarrow \text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2 \quad (3)
\]

\[
2 \text{Ca}_3(\text{PO}_4)_2 \cdot 2\text{CaHPO}_4 \cdot 2\text{H}_2\text{O} \rightarrow \text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2 + 4\text{H}_2\text{O} \quad (4)
\]

\[2 \text{Ca}_3(\text{PO}_4)_2 + \text{Ca}_9(\text{PO}_4)_2 \cdot \text{H}_2\text{O} \rightarrow \text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2 \]

Fig. 4 shows the typical SEM micrographs of surfaces and cross sections of CPP specimen with 50 mass% \( \beta \)-TCP addition after the immersion in SBF for various times at 37±0.2°C.

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Fig. 6 shows the relationship between total porosities and compressive strengths of CPP specimens with and without \( \beta \)-TCP addition. Note that all of the data were obtained after the immersion in SBF at 37±0.2°C for 7 d. The compressive strength of CPP specimen without \( \beta \)-TCP addition decreased with increasing total porosity. The relationship between total porosity and compressive strength CPP specimen with \( \beta \)-TCP addition fits on the plots of CPP specimens without \( \beta \)-TCP addition. Total porosities of CPP specimens with 10, 30 and 50 mass% \( \beta \)-TCP addition were 48.6, 60.2 and 67.1%, respectively.

The total porosity of CPP specimen increases with increasing amount of \( \beta \)-TCP addition. As the present

<table>
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<th>Surfaces</th>
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<tr>
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<td>1 d</td>
<td><img src="image5.png" alt="Image" /></td>
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Fig. 5 Typical SEM micrograph after the immersion of CPP specimen with 10 mass% \( \beta \)-TCP addition in SBF at 37±0.2°C for 14 d.

Fig. 6 Relationship between total porosity and compressive strength of CPP specimen with \( \beta \)-TCP addition after the immersion in SBF at 37±0.2°C for 7 d.

The amount of \( \beta \)-TCP addition:

(a) 0 mass%  (b) 10 mass% (c) 30 mass%
(d) 50 mass%
data indicate, the hollow spherical β-TCP agglomerates contribute to increasing the total porosity. Moreover, the increase in P/L ratio for the fabrication of CPP specimen with increasing amount of β-TCP addition must also contribute to increasing the total porosity, because the excess amount of malaxation liquid over the stoichiometry tends to form the pores after the elimination of it.

2. Porosity of CPP specimen with β-TCP addition
The total porosity is composed of open and closed porosities. The open porosity plays an important role in the introduction of osteoblast into the CPP specimen. Fig. 7 shows the results on the porosities of both open and closed porosities of CPP specimens with and without β-TCP addition, as well as the total porosity. Total, open and closed porosities of CPP specimen without β-TCP addition were 42.8%, 25.7 and 17.2%, respectively. The total porosity of CPP specimen increased with increasing amount of β-TCP addition. Open and closed porosities also increased with increasing amount of β-TCP addition and became 35.1% and 32.0%, respectively, for 50 mass% β-TCP addition. This fact suggests that more than one half of the pores are regarded as open pores in the CPP specimen and that these pores may contribute to enhancing the bioabsorbability. On the other hand, the closed porosities of CPP specimens with β-TCP addition do not contribute to enhancing the bioabsorbability. The bioabsorbability of CPP specimen may be further improved if the open porosity is enhanced, e.g., by (i) the strict controlling of the fabrication conditions of CPP specimens and (ii) the increase in porosities of hollow spherical β-TCP agglomerates. Further research is, therefore, needed in order to improve the bioabsorbability of CPP specimen.

In addition to the amount of open pores in CPP specimen, the pore diameters should also be noted for the introduction of osteoblast. Fig. 8 shows the pore diameter distributions of CPP specimens with and without β-TCP addition measured by the mercury porosimetry. Pore diameters of CPP without β-TCP addition were distributed over the range of 0.006 to 0.01 µm (Fig. 8(a)). On the other hand, pore diameters of CPP specimens with 10 and 30 mass% β-TCP addition were distributed in the ranges of 0.009 and 0.02 µm and 0.006 and 0.05 µm, respectively; the amount of pores with sizes below 0.01 µm increased with increasing amount of β-TCP from 10 to 30 mass% (Fig. 8(b) and (c)). Furthermore, most of the pore diameters of CPP specimen with 50 mass% β-TCP addition were distributed in the range of 0.075 to 0.9 µm; small amounts of pores with diameters in the range of 1 to 10 µm were also present in the specimen (Fig. 8(d)).

Pore diameters below 0.01 µm, which are found in the CPP specimens with 10 and 30 mass% β-TCP addition, seem to be attributed to those of hollow spherical β-TCP agglomerates, because the amount of such pores increased with increasing amount of β-TCP addition. Such small pores are not found but the pores with diameters of 0.1 to 10 µm are observed in the CPP specimen with 50 mass% β-TCP addition.
According to the SEM micrographs of CPP specimens with β-TCP addition (Figs. 4 and 5), pores with diameters of around 5 μm are observed in the original β-TCP agglomerates. Such pores cannot be detected by mercury porosimetry but are actually found by SEM observation. This fact indicates that the needle-like particles grown in the direction of the centers of spherical β-TCP agglomerates hinder the intrusion of mercury into the β-TCP agglomerates. The pores in the β-TCP agglomerates, therefore, do not seem to be detected by mercury porosimetry until the amount of such needle-like particles may be reduced with increasing amount of β-TCP addition (i.e., with decreasing amount of CPP).

CONCLUSIONS

We investigated the properties of calcium-phosphate paste (CPP) specimens with hollow spherical β-calcium orthophosphate (β-Ca₉(PO₄)₂: β-TCP) agglomerates. The starting β-TCP agglomerates were obtained by the spray-pyrolysis technique. The hollow spherical agglomerates were obtained by heating the spray-pyrolysed powder at 900°C for 10 min. The results obtained were summarized as follows:

1. The cylindrical specimens were fabricated mixing the CPP with 10-50 mass% β-TCP agglomerates, using malaxation liquid. The setting time of the CPP specimen increased with increasing amount of β-TCP: the setting time of CPP containing 10 mass% of β-TCP was 8.5 min, whereas that of CPP containing 50 mass% of β-TCP increased to 17 min.

2. The chemical and mechanical properties of CPP specimens with β-TCP addition were examined by immersing these specimens into a simulated body fluid (SBF). The compressive strength of CPP specimen reached maximum values, e.g., 42.8 MPa for 10 mass% β-TCP addition and 7.5 MPa for 50 mass% β-TCP addition, respectively, after the immersion in SBF for 3-7 d; however, it decreased with a further increase in the amount of β-TCP. Crystalline phases of the CPP specimens after the immersion in SBF for 7 d were hydroxyapatite (Ca₁₀(PO₄)₆(OH)₂; HAp) and β-TCP. The total porosity of CPP specimen increased with increasing amount of β-TCP addition and attained 67.1% for 50 mass% of β-TCP addition. Open and closed porosities of the CPP specimen with 50 mass% β-TCP addition were 35.1% and 32.0%, respectively.

Acknowledgements

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