Change in Microstructure and Solubility Improvement of HAp Ceramics by Heat-Treatment in a Vacuum

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HAp and the related calcium phosphates have been of great interest as biological materials for regenerating hard tissues, but their solubility should be improved to fit the remodeling cycle of hard tissues *in vivo* before their practical use for bone grafts. Control of the grain size of hydroxyapatite (HAp) matrix and change in constituent phase of the surface layer were examined to improve the dissolution rate in HAp ceramics. Surface and boundary layers composed of calcium phosphate phases with high solubility were formed by annealing at 1350°C in a vacuum, and the apparent mass transfer coefficient in the initial stage of the solubility experiment remarkably increased in an acetate buffer solution at pH of 4.0. The soluble surface and boundary layers are composed of tetracalcium diphosphate monoxide (TTCP), α -tricalcium phosphates (α -TCP) and amorphous calcium oxide (CaO) with high solubility, and their formation mechanism was discussed. Refinement of the grain size of HAp matrix also contributed to a slight increase in the apparent solubility.

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1. Introduction

Recent remarkable developments in medical science are promising for modest and high quality clinical treatment for patients. Titanium and other suitable metallic alloys have been used as successful implant materials which show good corrosion resistance, adequate mechanical properties and are bio-inert for bone grafting,¹⁻⁴ but they are not completely absorbed and often behave as an alien substance in the body. Hydroxyapatite (HAp) and its related calcium phosphates, which are the primary constituent of inorganic matrix of human bone and show biocompatibility, are thus of interest as substantial implant materials.^{5,6}

Synthetic HAp ceramics are the most promising candidates for bone substance, but rapid substitution of human hard tissue is not expected by the sintered ceramics because of the low solubility of HAp.⁷ Some other calcium phosphates of α - and β -tricalcium phosphates (α - and β -TCP) and tetracalcium diphosphate monoxide (TTCP), however, are known to show greater dissolution and degradation than HAp, so that the dissolution rate of each single phase is sometimes too fast to repair a bone defect.⁶

Biological hard tissues of bone, dentin and cementum undergo constant remodeling to destroy and reconstruct their organic and inorganic matrices in response to the action of osteoblasts and osteoclasts, respectively.⁸ Complete repair of bone defects requires development of implant materials suitable for the remodeling cycle. Control of solubility on synthesized HAp ceramics, in particular, is essential. In our previous study,^{9,10} the crystallinity of HAp and the related calcium phosphate for regenerating hard tissues *in vivo* was controlled by a mechanical grinding (MG) method and subsequent heat

treatment in order to improve their apparent solubility. The MG and the subsequent treatment were an effective process for controlling the crystallinity and changing the crystal structure in calcium powders but not in bulk materials.

In this study, therefore, an alternative approach to improve the apparent solubility of HAp was taken using heat-treatment in a vacuum focusing on the control of grain size and phase transformation of the surface layer of HAp ceramics *in vitro* with highly sintered density. The dissolution ratio of the heat-treated calcium phosphate ceramics was determined in an acetate solution.

2. Experimental Procedure

The HAp (HAP-200) powder supplied by Taihei Chemical Industrial Co., Ltd was synthesized by mixing slurries in the wet process at 90°C as the following chemical reaction:

Details can be seen in the references.^{11,12} It should be noted that the HAp used in this study was partially replaced by CO_3^{2-} ions to improve biological compatibility. Since the primary particles showed a small columnar shape along the c-axis about 1 μm long and 100 nm wide, second-stage products were formed by a van der Waals force operating between the primary particles. Therefore, the HAp slurry was prepared by the colloidal process using 35 vol% HAp powder and 65 vol% aqueous solution with a small amount of polycarboxylic acetate ammonium as an anion dispersant; this assured homogeneous distribution of the powder.¹³ The slurry was poured into a plaster mould and dried at 50°C for 24h. The dried specimens were sintered at 1050°C or 1200°C under one-

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axial compression stress below 40 MPa and hot-pressed to 60% reduction in height by holding for an hour in a vacuum. The sintered specimens were cut into a rectangular shape $3 \times 3 \times 2 \text{ mm}^3$ by a circular saw with a diamond wheel 0.15 mm thick and 75 mm in diameter. The specimens were abraded by emery paper and finally using diamond paste with 1 μm powder to remove surface damage. Some specimens previously sintered at 1200°C were sintered again at 1350°C for 1 h or 10 h in a vacuum. The rectangular specimens with $3.4 \times 3.4 \times 2.4 \text{ mm}^3$ were also prepared after sintering at 1200°C and subsequently sintered at 1350°C for 1 h. They were then ground to the size of $3 \times 3 \times 2 \text{ mm}^3$ to remove surface products.

Solubility measurement was performed in 50 ml of 0.5 M acetate buffer solution at pH of 4.0 and 37°C. Calcium concentration was determined by atomic absorption spectrophotometry (Shimadzu AA-6800F). Details of the method can be found in the Ref. 14).

Constituent phase of the sintered specimens was analyzed by an X-ray diffractometer (Shimadzu XD-5A) with monochromatic $\text{CuK}\alpha$ radiation at 40 kV, a scanning electron microscope (JEOL, JEM-840A) and electron probe microanalysis (EPMA) (JEOL JXA-8800R) operated at 20 kV and 40 kV, respectively.

3. Results

3.1 Constituent phase and microstructure in HAp ceramics sintered at different temperatures in a vacuum

Figure 1 shows variation in the microstructure of HAp ceramics sintered at different final temperatures for 1 h in a vacuum. Specimens finally sintered at 1350°C had previously been sintered at 1200°C for 1 h under the compressive stress. The microstructures were taken at the center of the specimens at a depth of 1 mm. The highly dense microstructure consisting of equi-axed grains was independent of final sintering

Fig. 1 Scanning electron micrographs of HAp ceramics finally sintered under compressive stress in a vacuum at 1050°C (a), 1200°C (b), 1350°C (c) and (d). Figure (d) corresponds to an enlarged photograph of fig. (c).

temperature, but the grain size depended strongly on this temperature as shown in Fig. 2. The grain size increased rapidly with increasing temperature, roughly obeying the Arrhenius equation. Moreover, the secondary phase with a white contrast different from HAp was observed especially at triple points in the specimen finally sintered at 1350°C as shown in Figs. 1(c) and (d).

Figure 3 shows variation in XRD profiles corresponding to the microstructures in Fig. 1. The powder was collected homogeneously from the entire specimen including the surface layer in each specimen. Diffraction peaks corresponding to the HAp phase were observed only in the HAp ceramics sintered at 1050°C and 1200°C, while diffractions from α -TCP and TTCP, which are known to show relatively high solubility,⁶⁾ slightly appeared in the ceramic sintered at 1350°C in addition to the dominant peaks of HAp. This suggests that

Fig. 2 Variation in HAp grain size (linear intercept length) with sintering temperature in HAp ceramics.

Fig. 3 Variation in XRD profiles as a function of sintering temperature in HAp ceramics. Ideal diffraction positions of HAp, α -TCP and TTCP are given for references.

Fig. 4 Variation in scanning electron microstructure at different depths in HAp sintered finally at 1350°C for 1 h at a depth of 0 μm (a), 25 μm (b), 200 μm (c) or 1000 μm (d) from the surface.

Table 1 Chemical composition, P/Ca ratio and Ca/P ratio in various representative calcium phosphates.

Type	Chemical formular	Ca	P	O	P/Ca	Ca/P
Mono calcium phosphate monohydrate (MCPM)	$\text{Ca}(\text{HPO}_4)_2 \cdot \text{H}_2\text{O}$	1	2	9	2.00	0.50
Meatacalcium phosphate (MTCP)	$\text{Ca}(\text{PO}_3)_2$	1	2	6	2.00	0.50
Dicalcium phosphate dihydrate (DCPD)	$\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$	1	1	6	1.00	1.00
Dicalcium phosphate anhydrous (DCPA)	CaHPO_4	1	1	4	1.00	1.00
Calcium pyrophosphate (CPP)	$\text{Ca}_2\text{P}_2\text{O}_7$	2	2	7	1.00	1.00
Octacalcium phosphate (OCP)	$\text{Ca}_8\text{H}_2(\text{PO}_4)_6 \cdot 5\text{H}_2\text{O}$	8	6	29	0.75	1.33
Tricalcium phosphate (TCP)	$\text{Ca}_3(\text{PO}_4)_2$	3	2	8	0.67	1.50
Hydroxyapatite (HAp)	$\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$	10	6	26	0.60	1.67
Tetracalcium diphosphate monooxide (TTCP)	$\text{Ca}_4\text{P}_2\text{O}_9$	4	2	9	0.50	2.00
Calcium oxide (CaO)	CaO	1	0	1	0.00	—

sintering at 1350°C in a vacuum induces the thermal decomposition from HAp to α -TCP and TTCP. When HAp ceramics are sintered in air, components are known to change little even at high temperatures around 1350°C.¹⁵⁾ This suggests that sintering in a vacuum accelerates the phase transformation. The constituent phase at 1350°C therefore depends on the depth from the surface. Remarkable texture of HAp was not observed depending on annealing temperature, while the *c*-axis of biological Ap in typical calcified tissues preferentially aligns depending on the shape and stress condition *in vivo*.¹⁶⁾

3.2 Variation in constituent phase of HAp ceramic sintered at 1350°C

Figures 4 and 5 show variations in microstructure and X-ray profiles, respectively, as a function of depth from the specimen surface. The typical microstructure and the corresponding X-ray profile were examined after a specimen was polished at each depth from the surface. They varied remarkably depending on the depth, especially up to 200 μm from the surface. According to the simple calculation of absorption of the incident X-ray using the absorption factors for constitution of HAp, more than 99% of the X-ray is absorbed at the depth of 20 μm at a Bragg angle of 20°. Thus, the microstructures in Fig. 4 roughly correspond to the XRD profiles in Fig. 5; these profiles in representative depth are enlarged in Fig. 6. In the surface layer, TTCP and α -TCP were clearly analyzed by the XRD profiles, and the additional HAp matrix was de-

tected at a depth of around 25 μm and more. Moreover, at 200 μm depth where the boundary phase with the white contrast appeared, the TTCP phase in addition to the dominant HAp phase was detected from the XRD profile in Fig. 6(c). Thus, the boundary phase was determined to be the TTCP precipitate. It should be noted that the relative intensity ratio of α -TCP to TTCP is the highest at the depth of around 25 μm.

As shown in Figs. 4(a) and (b), the surface microstructure at a depth less than 25 μm from the surface corresponds to the morphology of HAp grains before the phase transformation. On the surface after removing the surface layer to a depth of 25 μm, for example, very small particles composed of α -TCP and TTCP existed on the new surface.

Figure 7 shows variation in P/Ca ratio by EPMA analysis in the grain inside and at the grain boundary with the depth from the surface. Phosphorus was clearly lacking and little was detected on the surface. Representative calcium phosphates contain more than 0.5 P/Ca ratio as summarized in Table 1. Thus, the surface region showing negligible P/Ca ratio corresponds to the CaO phase; this phase often appears in synthesized and sprayed HAp at high temperatures.¹⁷⁾ Since no diffraction peaks from the CaO phase were detected, this phase must exist in an amorphous state. The P/Ca ratio at the grain boundary is smaller than 0.6 in the matrix HAp because the dominant boundary phase is TTCP with the stoichiometric P/Ca ratio of 0.5.

Fig. 5 Variation in XRD profiles of HAp ceramics sintered finally at 1350°C at different depths from the surface.

Fig. 6 Typical XRD profiles at Bragg angles between 20 and 40° of HAp sintered finally at 1350°C at different depths.

3.3 Dissolution property of HAp ceramics sintered at various temperatures in a vacuum

Control of HAp grain size and constituent phase near the surface and at the boundary was achieved by sintering between 1050°C and 1350°C in a vacuum. Since grain boundary of HAp and the transformed phases of CaO, α -TCP and

Fig. 7 Variation in P/Ca ratio analyzed by EPMA with depth from the surface in HAp ceramics sintered at 1350°C for 1 h.

Fig. 8 Variation in total calcium concentration in the acetate buffer solution during dissolution test for HAp ceramics sintered at different final temperatures. The surface layer of HAp ceramics sintered at 1350°C for 1 h was polished or not polished in order to examine the effect of this layer on dissolution.

TTCP can be preferentially dissolved, improvement of solubility for HAp ceramics is expected *in vivo* and *in vitro*.

Figure 8 shows variations in total calcium concentration of the solution as a function of immersion time. Although rectangular specimens $3 \times 3 \times 2 \text{ mm}^3$ were used for the solubility experiment, total calcium concentration was normalized by the total surface area of 42 mm^2 of the ideal specimen size to avoid the effect of size change during the fabrication and polishing. Since the specimen sintered at 1350°C for 1 h in a vacuum has the surface phase composed of HAp and other phases with high solubility, a specimen surface was polished to 200 μm depth and the solubility was examined in comparison. Remarkable differences in solubility-time curves were observed depending on the sintering condition and the surface treatment with and without polishing. As no remarkable surface layer existed in the specimens sintered at 1050°C and 1200°C or at 1350°C after removal of the surface phase, the calcium concentration linearly increased with time, while the slope slightly decreased accompanied by increase in total Ca concentration of the solution. The slope decreased with increasing sintering temperature in spite of the existence of the TTCP highly soluble boundary phase in the specimen sintered at 1350°C and in which the surface layer was subsequently polished to a depth of 200 μm . This suggests that the grain boundary predominantly affects the solubility of HAp ceramics and that the solubility is improved with finer grain; this is

Fig. 9 Scanning electron micrographs of HAp ceramics after dissolution tests for 5 h in the acetate buffer solution at pH of 4.0 at 37°C. The specimens were sintered at 1050°C (a), 1200°C (b) 1350°C with polishing (c) and 1350°C without polishing (d) for 1 h before the test.

true because the grain boundary with extra boundary energy is preferentially soluble. In contrast, a rapid increase in total calcium concentration was observed at the beginning of the solubility experiment in the specimen sintered at 1350°C without surface polishing. The high solubility would be due to the existence and dissolution of the transformed phases of CaO, α -TCP and TTCP formed in the surface layer.⁶⁾ Since thickness of the surface layer composed of the transformed phases increases with increasing the sintering period at 1350°C, the dissolution rate of Ca depends on the period as shown in Fig. 8. The simple heat-treatment in a vacuum produced more soluble calcium phosphates than HAp, and improved the initial dissolution rate. After the rapid dissolution of Ca from the surface layer, the dissolution rate decreased with immersion time showing a parabolic curve, and finally was saturated because of increase in Ca concentration in the acetate buffer solution. Following immersion of the specimen sintered at 1350°C for 1 h in the solution for 5 h and removal of most of the soluble surface, the solubility curve of the specimen in the new acetate solution looked similar to that of the specimen without the surface phases.

Figure 9 shows SEM micrographs of the surface of the specimens after the solubility experiment in the acetate solution at 37°C for 5 h. Grain boundaries were preferentially dissolved and etched deeply independent of the sintering temperature, confirming that the grain boundary acts as a preferential site for the dissolution. The XRD profile from the surface in the specimens sintered at 1350°C followed by the solubility experiment for 5 h, is described in Fig. 10(c). The XRD profiles for depths of 35 μ m and 50 μ m show HAp matrix, α -TCP and TTCP. The diffraction peaks from the transformed surface layers including α -TCP and TTCP disappeared after the 5 h dissolution. This result is in good accordance with the surface layer preferentially dissolving and contributes to the rapid dissolution rate as shown in Fig. 8.

4. Discussion

4.1 Constituent phase and the formation mechanism of HAp ceramics sintered at 1350°C

The phase transformation from HAp to other high-soluble phases gradually proceeded on the specimen surface and im-

Fig. 10 Variation in XRD profiles from the surface in HAp ceramics sintered at 1350°C for 1 h and subsequently dissolved for 5 h in the acetate buffer solution.

proved the initial dissolution rate in HAp ceramics sintered at a final temperature of 1350°C. Moreover, the initial dissolution rate of Ca could be controlled by the thickness of the transformed surface layer depending on the sintering time. Details of the constituent phase and the formation mechanism of the surface layer are discussed in this section.

Figure 11 shows a detailed schematic illustration of the constituent phase in HAp ceramics finally sintered at a final temperature of 1350°C for 1 h on the basis of analysis by XRD and EPMA. The transformed phase-layer near the surface was classified into several layers. The top-surface layer was composed of amorphous CaO and TTCP. As the distance from the surface deepened, α -TCP appeared in addition to TTCP and CaO, and subsequently CaO must disappear. The

Fig. 11 Schematic illustration of surface layers on cross section in HAp ceramics sintered at 1350°C for 1 h.

second layer including CaO was believed to be between the top-surface layer and the third layer composed of three phases (TTCP+ α -TCP+HAp) because the P/Ca ratio was lower than 0.6 for HAp at 25 μ m depth.

Since the CaO phase was detected on the top-surface layer, the following reaction likely proceeded,^{17,18)}

In this reaction, the α -TCP phase in the surface layers is directly formed. The α -TCP phase possibly produces the TTCP phase by discharging P_2O_5 , but transformation of α -TCP powder under the same sintering condition did not proceed even on the powder surface in the preliminary experiment. Therefore, the surface layer is not formed in eq. (2).

HAp simultaneously changes into α -TCP and TTCP as the following reaction,¹⁹⁾

In this reaction, the CaO phase is not directly produced. Since CaO formed only a very thin layer, and TTCP and α -TCP were widely distributed near the surface, eq. (3) must be the dominant path in this study. This reaction is accompanied by discharge of H_2O , and thus it must be accelerated in a vacuum. In fact, the transformation from HAp to α -TCP and TTCP hardly proceeded during the heat treatment at 1350°C in air.

On the surface, the α -TCP phase transforms to CaO accom-

panied by discharge of P_2O_5 in the following reaction,

Since the vaporizing point of P_2O_5 is around 600°C,²⁰⁾ the produced P_2O_5 quickly evaporates from the surface leaving the CaO phase.

In contrast, since the boundary phase was largely composed of TTCP without α -TCP, the reaction at the boundary is as follows,

This reaction must also be accelerated in a vacuum due to the discharge of H_2O and P_2O_5 . Although the amount of the transformed TTCP boundary phase depends on the depth from the surface, the TTCP phase was formed at the boundary even in the center of the specimens as shown in Fig. 1(d). Therefore, diffusion of phosphorus at the HAp boundary may be relatively fast, while that in the HAp matrix was relatively late because the reaction (4) appeared only in the very thin part of the surface.

4.2 Apparent mass transfer coefficient in acetate buffer solution at pH 4.0

For quantitative evaluation of the dissolution rate in HAp ceramics synthesized in this study, apparent mass transfer coefficient, K (m/s), is calculated at the initial stage within 1 h;¹⁴⁾

$$V \cdot dC/dt = K \cdot A \cdot (C_s - C) \quad (6)$$

where V (m^3) is the volume of the closed system for the solubility test, t (s) is the time during dissolution test, A (m^2) is the total surface area of the specimen, C (M) is the concentration of HAp and C_s (M) is the solubility of HAp at the tested temperature and pH. At low pH, HAp dissolves as follows,

Since H^+ is fully provided at pH 4.0, only Ca concentration should be taken into account in calculating the apparent solubility of HAp in an acetate solution. C_s was determined to be 0.0257 M at pH 4.0 on the basis of the solubility product. Figure 12 shows K value in the initial stage within 1 h. This value basically decreases with increasing sintering temperature accompanied by an increase in HAp grain size. The surface layer transformed from HAp to TTCP, α -TCP and CaO increased the K value about 9 and 13 times larger than that after polishing in the specimen sintered at 1350°C for 1 h and 10 h, respectively.

In conclusion, heat treatment in a vacuum is one method to easily control and improve the apparent solubility of HAp ceramics because it accelerates the transformed reaction discharging H_2O or P_2O_5 .

5. Conclusion

Control of crystal structure and grain size in HAp ceramics was done by individual heat treatments at a temperature

Fig. 12 Apparent mass transfer coefficient, K , of HAP ceramics sintered at different final temperatures. Ceramics sintered at 1350°C for 1 h was also examined after polishing the surface layer to a depth of 200 μm .

of 1050, 1200 and 1350°C in a vacuum. The apparent solubility of the sintered ceramics was examined *in vitro* and the following conclusions were drawn:

(1) Highly dense HAP ceramics were obtained during sintering at temperatures between 1050 and 1350°C in a vacuum under hot-pressing by one loading axis. Surface and boundary layer products at 1350°C were different from HAP matrix.

(2) Apparent mass transfer coefficient, K , *in vitro* was improved by formation of a surface layer composed of TTCP, α -TCP and CaO in HAP ceramics sintered at 1350°C in a vacuum. Fine HAP grain also improved the dissolution rate.

(3) The transformed phase-layers composed of at least three regions appeared near the surface in addition to near the TTCP boundary phase in HAP ceramics sintered at 1350°C.

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