

Synthesis and dissolution behavior of β -TCP and HA/ β -TCP composite powders

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Abstract

Calcium phosphate powders, β -TCP and biphasic HA/ β -TCP, were synthesized by calcining the powders obtained from the coprecipitation method using $\text{Ca}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$ and $(\text{NH}_4)_2\text{HPO}_4$. The effects of the initial Ca/P ratio and pH of the solution on the phase evolution and in vitro dissolution behavior of the powders in a Ringer's solution were investigated. The Ca/P ratio of the resulting powders was strongly dependent on the pH of the solution and weakly dependent on the initial Ca/P ratio. Single phase TCP powder was obtained at pH = 7.4 and the initial Ca/P ratio had a little effect on the resulting Ca/P ratio. Biphasic composite powders were prepared at pH = 8.0 and the Ca/P ratio of resulting powder was controllable by adjusting the initial Ca/P ratio. TCP powder showed the highest dissolution rate in the Ringer's solution and biphasic composite powder exhibited an intermediate dissolution behavior between that of HA and TCP.

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1. Introduction

Calcium phosphate-based bioceramics have received much attention as bone graft substitutes primarily because of their excellent biocompatibility, bioactivity, and osteoconduction characteristics.^{1–5} The most widely used calcium phosphate-based bioceramics are hydroxyapatite [HA, $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$] and β -tricalcium phosphate [β -TCP, $\text{Ca}_3(\text{PO}_4)_2$]. HA is stable in a body fluid, while TCP is rather soluble.⁴ The in vivo and in vitro dissolution of calcium phosphate ceramics was found to be dependent on the composition, crystallinity, and pH of the solution.^{6–10} However, many studies have indicated that the dissolution of HA in the human body after implantation is too low to achieve the optimal results. On the other hand, the dissolution rate of β -TCP ceramics is too fast for bone bonding. To achieve an optimum resorbability of the material, studies have mainly focused on the biphasic calcium phosphate ceramics composed of HA and TCP.^{11–16} Several

results suggest that the resorbability of biphasic ceramics is largely determined by the HA/TCP ratio. Therefore, it is necessary to produce the biphasic ceramics with various HA/TCP ratios in a simple and systematic way.

The synthesis of HA powder has been extensively studied but that of a TCP or biphasic HA/TCP powder is still under investigation. TCP powders were generally prepared by solid-state reaction or thermal decomposition.^{15,17,18} In thermal decomposition, amorphous calcium phosphate (ACP) or calcium deficient HA, which is obtained under neutral or acid conditions, was used for the preparation. TCP is not formed in an aqueous system at normal laboratory conditions, but it (precisely, whitlockite) can only be precipitated when some of the Ca^{2+} ions are substituted by Mg^{2+} or Mn^{2+} ions.¹⁷

Biphasic HA/TCP composite powders are commonly produced as by-products during the synthesis of pure HA or pure TCP. However, recent demands for the controlled bioactivity require the biphasic composite powders with varying HA/TCP ratios. Biphasic powders can be prepared either by mechanical mixing of HA and TCP powders or by calcining the calcium deficient HA (Ca/P = 1.5~1.67) above 700 °C.^{19–22} A calcium deficient HA was synthesized by using wet chemical

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methods such as co-precipitation or hydrolysis of a dicalcium phosphate dihydrate (DCPA).¹⁷

In this study, TCP and biphasic HA/TCP composite powders were synthesized using a co-precipitation method. The purpose of this study is to determine the influence of initial Ca/P ratio and pH on the phase evolution, and to investigate the dissolution behavior of TCP and biphasic HA/TCP powders in Ringer's solution compared to HA.

2. Experimental procedures

TCP and biphasic HA/TCP powders were synthesized by calcining the powders obtained from the co-precipitation method with $\text{Ca}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$ and $(\text{NH}_4)_2\text{HPO}_4$. The initial Ca/P ratio was varied from 0.67 to 1.55 and the pH of the solution was maintained at 6.0, 7.4, and 8.0 during precipitation by adding either NH_4OH or HNO_3 . After the precipitation, the solution was aged in the water bath of 40 °C for 24 h. The precipitates were filtered and then dried at 100 °C for 24 h.

The obtained powders were calcined at 800, 1000, 1150, and 1200 °C for 2 h. The Ca/P ratio of the dried powder was measured by inductively coupled plasma atomic emission spectroscopy (ICP-AES, Model ICPS-7500, Shimadzu, Japan). No differences were observed in the Ca/P values between the as-dried and calcined powders. X-ray diffraction (XRD, Model M18XHF-SRA, MAC Science Co., Japan) and Fourier transform infrared (FT-IR, Model DA-8, Bomem, Canada) spectroscopy were used for phase analysis and scanning electron microscopy (SEM) was used to observe the morphology. The specific surface area was measured by Brunauer-Emmett-Teller (BET, Model ASAP2010, Micromeritics Instrument Corp., Norcross, USA) method and the phase transitions were determined by differential thermal analysis and thermogravimetric analysis (DTA/TG, Model 2000, Du Pont Instruments, USA).

The dissolution behavior of the powders was estimated by immersing them in a Ringer's solution (Hartmann solution, Cheil Jedang, Korea) for up to 30 days. After immersing for a pre-determined period of time, the solution was separated by filtration and analyzed with ICP-AES. The filtered precipitates were dried and analyzed by XRD and FT-IR. The ion concentrations of Ringer's solution used in this study was compared with the human blood plasma in Table 1.⁴

3. Results and discussion

The effects of the initial Ca/P molar ratio and the pH of the solution on the composition of the precipitates were given in Fig. 1. The chemical analyses were performed on the precipitates after drying at 100 °C for 24 h, and

Table 1
Ion concentration (mM/l) of human plasma⁴ and Ringer's solution

| | Na^+ | K^+ | Mg^{2+} | Ca^{2+} | Cl^- | HCO_3^- | HPO_4^{2-} | SO_4^{2-} |
|-------------------|---------------|--------------|------------------|------------------|---------------|------------------|---------------------|--------------------|
| Human plasma | 142 | 5 | 1.5 | 2.5 | 103 | 13.5 | 1 | 0.5 |
| Ringer's solution | 132 | 5.4 | – | 2.4 | 113 | 28.7 | – | – |

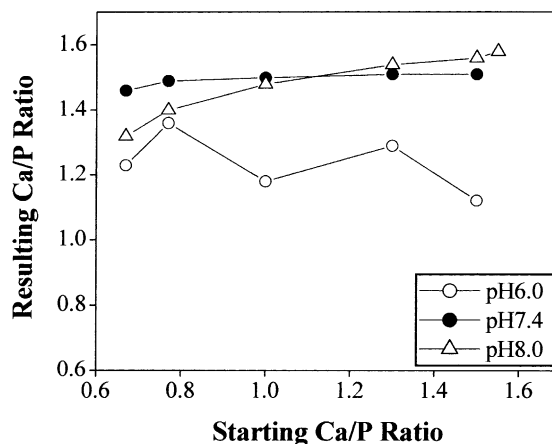


Fig. 1. The Ca/P molar ratio of the precipitates measured by ICP-AES analysis as a function of initial Ca/P ratio and pH of the solution.

further heat treatment did not show any composition change. When the pH of the solution was 6.0, the Ca/P values were lower than 1.5 for the entire initial compositions. As the pH increased to 7.4, the obtained Ca/P values were very close to 1.5 irrespective of the initial compositions. At pH=8.0, the resultant Ca/P ratio increased from 1.3 to 1.6 with increasing the initial Ca/P ratio, but the dependence was non-linear. The unreacted precursors are believed to be washed out during filtering process. Although no systematic correlation could be drawn from the chemical analysis results, the proper pH values for single phase TCP and biphasic HA/TCP powder syntheses are 7.4 and 8.0, respectively. The Ca/P ratio of the precipitates obtained at pH=6.0 was varied from 1.12 to 1.36 and was not the ranges for TCP or biphasic HA/TCP formation. Indeed, XRD patterns indicated that as-dried powder consisted of a dicalcium phosphate anhydrate (CaHPO_4 , DCPA) and a poor crystalline HA. When heated to 800 °C, DCPA and HA transformed into $\beta\text{-Ca}_2\text{P}_2\text{O}_7$ and $\beta\text{-TCP}$. Thus, the researches in this study were mainly focused on the powders precipitated at pH=7.4 and 8.0.

The phase evolution of the TCP precursors precipitated at pH 7.4 was shown in Fig. 2. The effect of the initial Ca/P ratio on the phase evolution was insignificant and the XRD patterns were obtained from the samples with the initial Ca/P ratio of 1.5. XRD pattern revealed that as-dried powder was a poorly crystallized HA [Fig. 2(A)]. The poorly crystallized HA is believed to

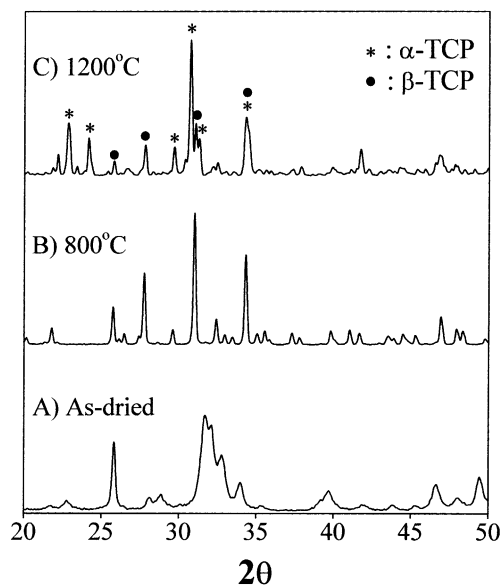


Fig. 2. XRD patterns of the TCP precipitates obtained at pH = 7.4; (A) as-dried, (B) calcined at 800 °C, and (C) calcined at 1200 °C.

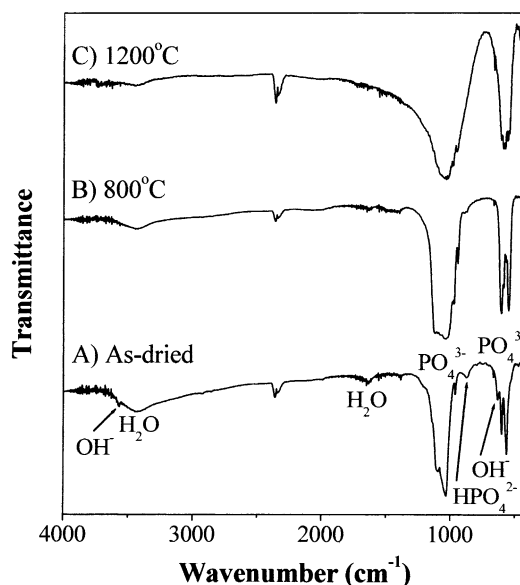


Fig. 3. FT-IR spectra of the TCP precipitates obtained at pH = 7.4; (A) as-dried, (B) calcined at 800 °C, and (C) calcined at 1200 °C.

be a non-stoichiometric calcium deficient HA ($\text{Ca}_{10-x}(\text{HPO}_4)_x(\text{PO}_4)_{6-x}(\text{OH})_{2-x}n\text{H}_2\text{O}$, $x=0\sim 1$, $n=0\sim 2$), which is supported by the Ca/P ratio of 1.5. The β -TCP appeared in the sample calcined at 800 °C and kept existing as the stable phase at higher temperatures [Fig. 2(B)]. That is, single phase β -TCP was successfully synthesized at temperatures between 800 and 1100 °C. However, further heat treatment resulted in the β - α transformation of TCP. Therefore, intense α -TCP peaks were observed along with the weak β -TCP peaks in the powder calcined at 1200 °C [Fig. 2(C)].

The corresponding FT-IR absorption spectra of the TCP precursors were presented in Fig. 3. The characteristic PO_4^{3-} and OH^- absorption bands of HA were observed in the as-dried sample along with the additional broad bands at 1640 cm^{-1} and 3430 cm^{-1} from the adsorbed H_2O [Fig. 3(A)]. The weak absorption peak at 880 cm^{-1} was assigned to the P–O–H vibration in the HPO_4^{2-} group,²³ which exists in non-stoichiometric HA. The C–O vibration in CO_3^{2-} group can also contribute to this absorption band. In the sample calcined at 800 °C, the OH^- absorption band disappeared and the spectrum obtained was characteristic of β -TCP [Fig. 3(B)]. With increasing the calcination temperature, the PO_4^{3-} vibration peaks at 603 and 568 cm^{-1} gradually merged. The FT-IR spectrum of the powders calcined at 1200 °C became similar to that of α -TCP, which consistent with the previous XRD result [Fig. 3(C)].¹⁷

Fig. 4 illustrates the results of thermal analysis for the TCP precursors precipitated at pH = 7.4. One exothermic peak at 214 °C and two endothermic peaks at 790 and 1185 °C were observed in the DTA. TG showed that all the volatiles were removed by 850 °C and the total weight loss measured upon heating to 1000 °C was

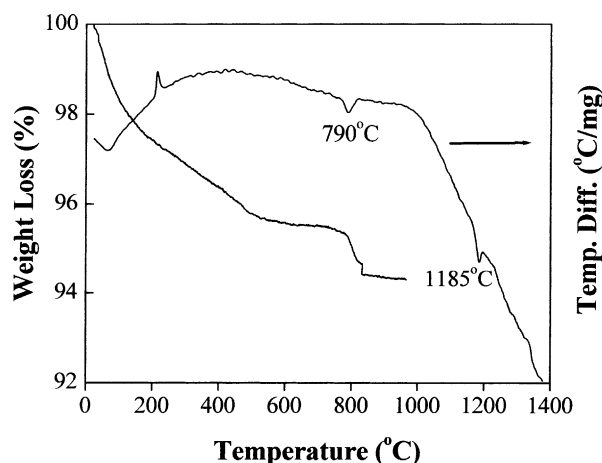


Fig. 4. Thermal analyses of the TCP precipitates obtained at pH = 7.4.

5.7%. There was a sharp weight loss around 790 °C. Based on the previous XRD and FT-IR results, the endothermic peak at ~ 790 °C on the DTA curve, which was accompanied by a 1% weight loss on the TG curve, was attributed to the decomposition of nonstoichiometric HA to β -TCP and H_2O . The endothermic peak at 1185 °C can be assigned to the β - α transformation of TCP. From the phase diagram, β -TCP is stable up to 1125 °C, and above this and up to 1430 °C, α -TCP becomes the stable phase.²⁴ The determined transformation temperature in this study was higher than that predicted from the phase diagram. However, it has been reported that this transformation temperature varied depending on the synthesis conditions and substitution ions.¹⁷ In particular, Mg ions are known to strongly influence the transformation temperature.¹⁷

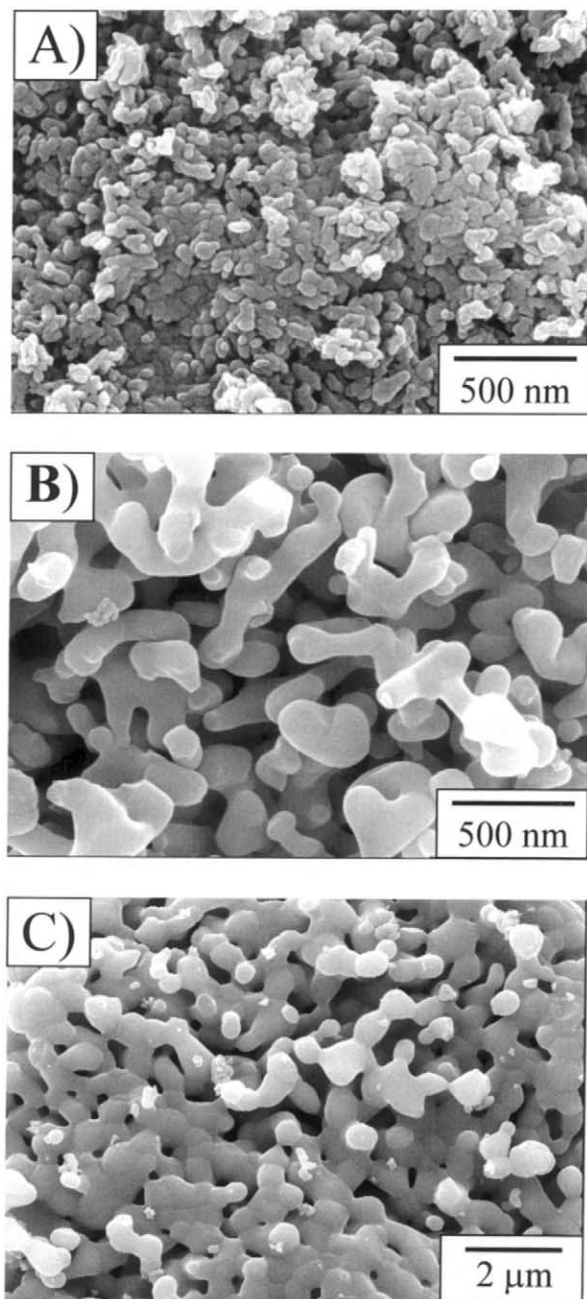


Fig. 5. SEM micrographs of the TCP precipitates obtained at pH=7.4; (A) as-dried, (B) calcined at 800 °C, and (C) calcined at 1000 °C.

The morphologies of the TCP powders precipitated at pH=7.4 were shown in Fig. 5. The as-dried TCP precursors were almost spherical and highly agglomerated, and the observed particle size was ~ 50 nm [Fig. 5(A)]. The specific surface area determined by BET was $85 \text{ m}^2/\text{g}$. The particle coarsening occurred significantly with calcination. The particle size was ~ 300 nm at 800 °C and increased up to $\sim 1 \mu\text{m}$ at 1000 °C. The necking among the particles was apparent due to localized sintering at 1000 °C.

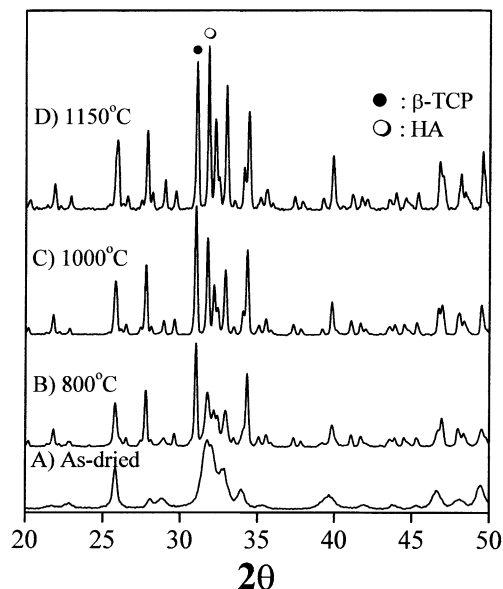


Fig. 6. XRD patterns of the biphasic precipitates obtained at pH=8.0; (A) as-dried, (B) calcined at 800 °C, (C) calcined at 1000 °C, and (D) calcined at 1150 °C.

According to the chemical analysis, the resulting Ca/P ratio of the precursors precipitated at pH=8.0 varied from 1.35 to 1.58 depending on the initial Ca/P ratio. In order to synthesize the biphasic HA/TCP composite powders, the Ca/P ratio should be larger than 1.5. Therefore, the phase evolution was considered in the sample with the starting Ca/P ratio of 1.55 (resulting Ca/P ratio of 1.58). XRD showed that the as-dried precursor was the poorly crystallized HA similar to the case at pH=7.4 [Fig. 6(A)]. When heated to 800 °C, β -TCP was observed along with HA [Fig. 6(B)] and the FT-IR spectrum showed an OH^- absorption band, which was different from the case at pH=7.4. The HA peaks were not well resolved at this stage suggesting the poor crystallinity. However, further heating increased the HA peak intensities and HA peaks became well resolved [Fig. 6(C)]. At 1150 °C, the peak intensities of β -TCP and HA were comparable [Fig. 6(D)]. Considering the Ca/P ratio of 1.58, β -TCP and HA phase concentration in these sample was believed to be 1:1. One thing to note is that the XRD intensities of β -TCP and HA peaks changed with the calcination temperature although the chemical compositions were constant. The transformation mechanism from calcium deficient HA into biphasic HA/TCP is not well understood although a solid-state ionic diffusion mechanism has been proposed.²² In addition, the precipitates obtained at pH=8.0 with the initial Ca/P ratio of ≤ 1.0 (resulting Ca/P ratio of < 1.5) were β -TCP mixed with $\beta\text{-Ca}_2\text{P}_2\text{O}_7$ after calcining above 800 °C. The precipitates with the starting Ca/P ratio of ≥ 1.3 was composed of β -TCP and HA, and the amount of HA in

the calcined powder increased with the initial Ca/P ratio. Therefore, HA or TCP phase concentration in biphasic composite powders was controlled by adjusting the Ca/P ratio of the precursors.

The morphologies of the biphasic powders were shown in Fig. 7. As-dried precursors were nearly spherical and slightly smaller than TCP precursors. The specific surface area determined by BET was 90 m²/g. After calcining at 1000 °C, the particle size increased to ~0.5 μm but was smaller than TCP powders. From the morphology, it was hard to distinguish between β-TCP and HA powders.

The dissolution behavior of the synthesized powders in the Ringer's solution was shown in Fig. 8. The TCP and biphasic HA/TCP powders correspond to those described in Figs. 2 and 6, respectively and they were calcined at 1150 °C to avoid the β-α transformation of TCP. The HA powder was prepared by calcining the precursors at 1250 °C, which were precipitated at pH = 11.0 and aged at 80 °C. When HA was immersed in the solution, the Ca²⁺ concentration increased initially but stabilized after 1 day. However, the overall amount of HA dissolution was minimal. The dissolution of PO₄³⁻ was even lower as shown in the figure [Fig. 8(B)].

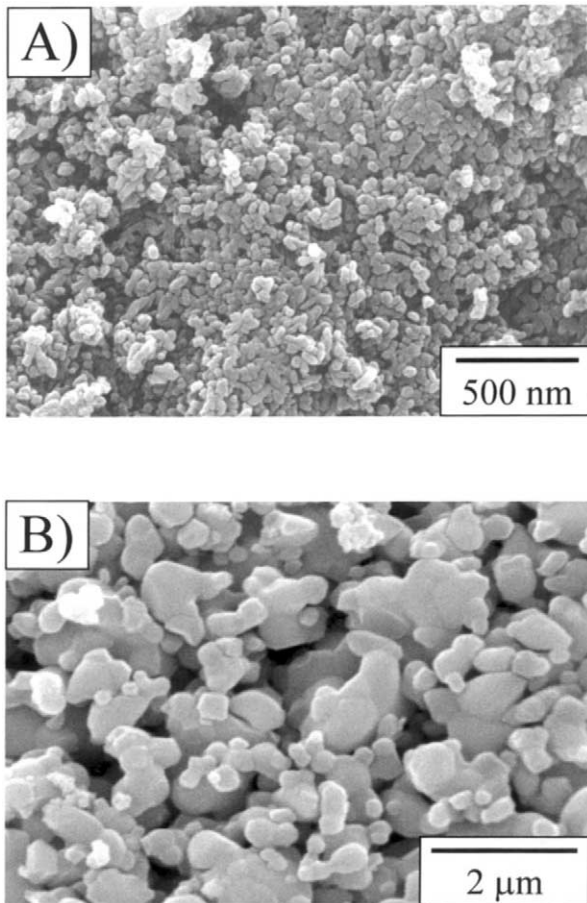


Fig. 7. SEM micrographs of biphasic precipitates obtained at pH = 8.0; (A) as-dried and (B) calcined at 1000 °C.

The pH of the solution increased rapidly up to ~7.5 and remained constant thereafter. XRD patterns of the immersed specimens revealed only HA phase. However, the FT-IR spectrum of the HA powders after 30 day immersion exhibited the carbonate bands at 1450 and 870 cm⁻¹ [Fig. 9], which are characteristic of carbonated hydroxyapatite.^{25,26} It has been reported that in-vitro dissolution of HA is affected by several factors such as composition, crystallinity, and pH of the solution, and that the CO₃-apatite was formed on the surface of HA in the biological fluid.⁴ Based on the previous reports, the possible explanation to above experimental results is that HA is dissolved initially releasing the Ca²⁺ and PO₄³⁻ ions into the solution. With increasing the ion

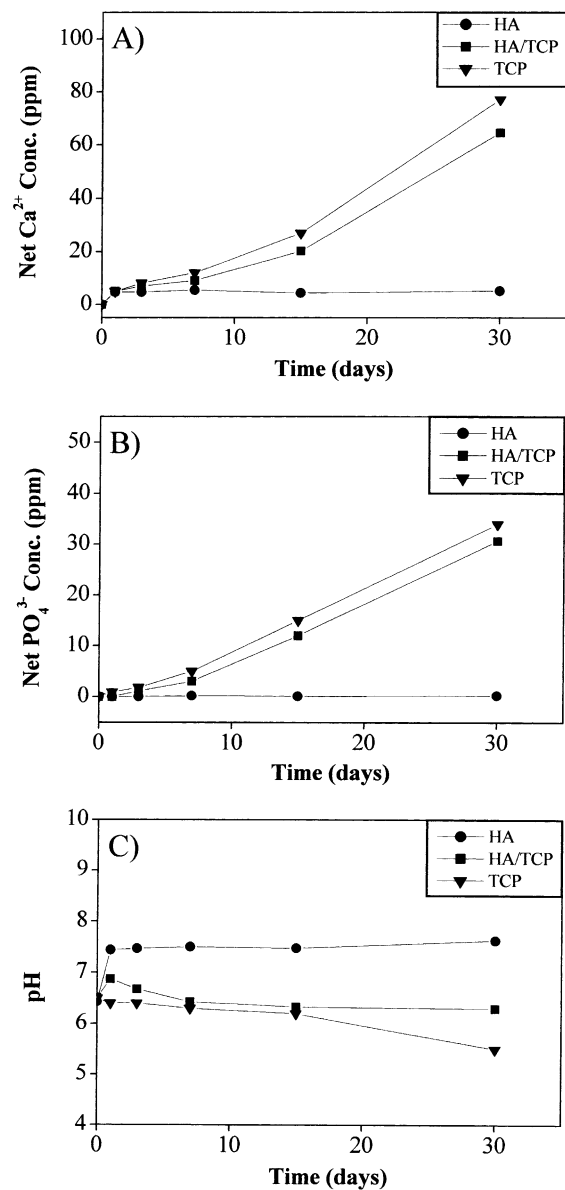


Fig. 8. (A) Net Ca²⁺ concentration, (B) net PO₄³⁻ concentration, and (C) pH variation in the HA, TCP, and biphasic HA/TCP powder immersed solutions.

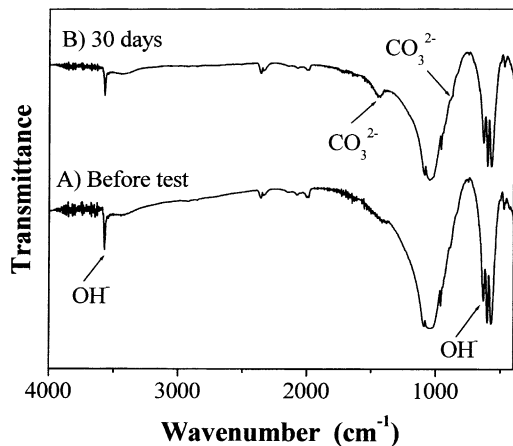


Fig. 9. FT-IR spectra of HA powders; (A) as-calcined and (B) immersed for 30 days in Ringer's solution.

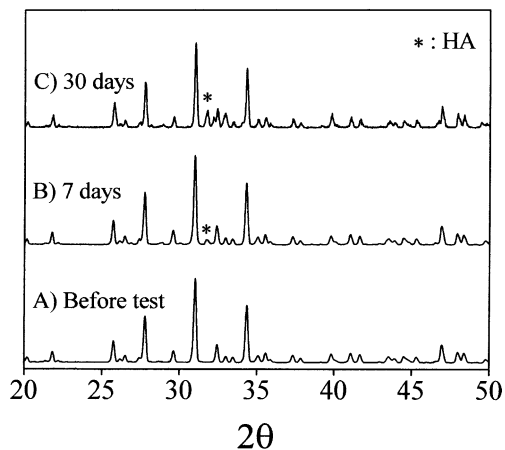


Fig. 10. XRD patterns of TCP powders; (A) as-calcined, (B) immersed for 7 days, and (C) immersed for 30 days in Ringer's solution.

concentrations, the solution becomes super-saturated with those ions resulting in the re-precipitation as CO_3 -apatite.

As expected, the dissolution rate of TCP was greater than that of HA. The concentrations of Ca^{2+} and PO_4^{3-} increased continuously and the solution's pH gradually decreased over 30 days. Similar results of pH variations have been reported previously.¹¹ XRD analyses indicate HA formation after immersion for more than 7 days [Fig. 10]. The dissolved Ca^{2+} and PO_4^{3-} ions are supposed to be precipitated as HA phase on the surface of TCP. However, OH^- and CO_3^{2-} absorption peaks were not observed in the FT-IR spectra. Like the other properties, the HA/TCP biphasic composite powder exhibited an intermediate dissolution behavior between that of HA and TCP powders. The concentrations of Ca^{2+} and PO_4^{3-} increased continuously with increasing immersion time, and the pH of the solution followed HA trends initially and then TCP trends. The intermediate dissolution behavior of biphasic composite powder is consistent with the previous results¹¹ but further

studies are required to quantify the dissolution rates depending on the compositions by using the biphasic powders of various Ca/P ratios.

4. Summary

Single-phase TCP and biphasic HA/TCP composite powders have been synthesized by controlling the starting Ca/P ratio of the precursors and the pH of the solution in co-precipitation method. β -TCP powder was successfully prepared by calcining the precipitates above 800 °C, which were obtained at pH=7.4. Biphasic composite powder was obtained from the poor crystalline HA precipitated at pH=8.0, and HA content of biphasic powder could be controlled by adjusting the initial Ca/P ratio. The dissolution rate of the calcium phosphate powders was strongly dependent on the TCP content and it was possible to control the bioresorbability of the calcium phosphate powders by adjusting the TCP concentration, i.e. the processing parameters in the co-precipitation method.

Acknowledgements

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References

- de Groot, K., *Bioceramics of Calcium Phosphate*. CRC Press, Boca Raton, FL, 1983.
- Bucholz, R. W., Carlton, A. and Holmes, R. E., Hydroxyapatite and tricalcium phosphate bone graft substitutes. *Orthop. Clin. North Am.*, 1987, **18**, 323–334.
- Lavernia, C. and Schoenung, J. M., Calcium phosphate ceramics as bone substitutes. *Ceram. Bull.*, 1991, **70**, 95–100.
- Hench, L. L. and Wilson, J., *An Introduction to Bioceramics*. World Scientific, London, UK, 1993.
- Hench, L. L., *Bioceramics. J. Am. Ceram. Soc.*, 1998, **81**, 1705–1728.
- Klein, C. P. A. T., Driessen, A. A., Groot, K. and de Hooff, A., van den, biodegradation behavior of various calcium phosphate materials in bone tissue. *J. Biomed. Mater. Res.*, 1983, **17**, 769–784.
- Takeishi, A., Hayashi, H., Kamatsubara, H., Yokoyama, A., Kohri, M., Miki, K. and Kohgo, T., Implant of calcium phosphate ceramics altering Ca/P ratio in bone. *J. Dent. Res.*, 1989, **68**, 680.
- de Groot, K., Clinical applications of calcium phosphate biomaterials: a review. *Ceramics International*, 1993, **19**, 363–366.
- Ducheyne, P., Radin, S. R. and King, L., The effect of calcium phosphate ceramic composition and structure on in vitro behavior: I. *Dissolution. J. Biomed. Mater. Res.*, 1993, **27**, 25–34.
- Radin, S. R. and Ducheyne, P., The effect of calcium phosphate ceramic composition and structure on in vitro behavior: II. *Precipitation. J. Biomed. Mater. Res.*, 1993, **27**, 35–45.
- Kohri, M., Miki, K., Waite, D. E., Nakajima, H. and Okabe, T., In vitro stability of biphasic calcium phosphate ceramics. *Biomaterials*, 1993, **14**, 299–304.

12. Hollander, W., den, Patka, Klein, P. C. P. A. T. and Heidendal, G. A. K., Macroporous calcium phosphate ceramics for bone substitution: a tracer study on biodegradation with ^{45}Ca Tracer. *Biomaterials*, 1991, **12**, 569–573.
13. Nery, E. B., LeGeros, R. Z., Lynch, K. L. and Lee, K., Tissue response to biphasic calcium phosphate ceramics with different ratios of HA/ β -TCP in periodontal osseous defects. *J. Periodontol.*, 1992, **63**, 729–735.
14. Frayssinet, P., Trouillet, J. L., Rouquet, N., Azimus, E. and Autefage, A., Osseointegration of macroporous calcium phosphate ceramics having a different chemical composition. *Biomaterials*, 1993, **14**, 423–429.
15. Yang, X. and Wang, Z., Synthesis of biphasic ceramics of hydroxyapatite and β -tricalcium phosphate with controlled phase content and porosity. *J. Mater. Chem.*, 1998, **8**, 2233–2237.
16. Kivrak, N. and Tas, A. C., Synthesis of calcium hydroxyapatite-tricalcium phosphate (HA-TCP) composite bioceramic powders and their sintering behavior. *J. Am. Ceram. Soc.*, 1998, **81**, 2245–2252.
17. Elliott, J. C., *Structure and Chemistry of the Apatites and Other Calcium Orthophosphates*. Elsevier, Amsterdam, Netherlands, 1994.
18. Kanazawa, T., *Inorganic Phosphate Materials*. Kodansha Ltd, Tokyo, Japan, 1989.
19. LeGeros, R. Z., Variability of HAP/ β -TCP ratios in sintered apatites. *J. Dent. Res.*, 1986, **65**, 292.
20. LeGeros, R. Z. and Daculsi, G., In Vivo transformation of biphasic calcium phosphate ceramics: ultrastructural and physicochemical characterizations. Handbook of Bioactive Ceramics, C.R.C. Vol. II. In *Calcium Phosphate and Hydroxylapatite Ceramics*, ed. T. Yamamuro, L. L. Hench and J. Wilson. CRC Press, Boca Raton, FL, 1990, pp. 17–28.
21. LeGeros, R. Z., Calcium phosphate in oral biology and medicine. In *Monographs in Oral Sciences*, Vol. 15, ed. H. Myers. S. Karger, Basel, 1991.
22. Dorozhkin, S. V., Solid-state transformation of a non-stoichiometric calcium deficient apatite into the biphasic calcium phosphate. *Key Engineering Materials*, 2001, **192–195**, 155–158.
23. Yubao, L., Klein, C. P. A. T., Xingdong, Z. and de Groot, K., Formation of a bone apatite-like layer on the surface of porous hydroxyapatite ceramics. *Biomaterials*, 1994, **15**, 835–841.
24. Roth, R. S., Dennis, J. R. and McMurdie H. F., In *Phase Diagrams for Ceramists*, ed. M. K. Reser. American Ceramic Society, Columbus, OH, 1964.
25. Heughebaert, M., LeGeros, R. Z., Gineste, M., Guihem, A. and Bonel, G., Physicochemical characterization of deposits associated with HA ceramics implanted in nonosseous sites. *J. Biomed. Mater. Res.: Applied Biomaterials*, 1988, **22**, 257–268.
26. Apfelbaum, F., Diab, H., Mayer, I. and Featherstone, J. D. B., An FTIR study of carbonate in synthetic apatites. *J. Inorg. Biochem.*, 1992, **45**, 277–282.