J MATER SCI **41** (2006) 1341–1344

Hydrothermal preparation of tailored hydroxyapatite

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Hydrothermal vapor treatment method was applied for preparation of ceramic biomaterials. Hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$; HA) ceramics prepared by sintering with random crystal surface have already been used as bone-repairing materials which can directly bond to natural bones. If materials of HA could have the tailored specific crystal surface, they should have the advantage of adsorptive activity and osteoconductivity in comparison with the sintered HA. In the present study, porous HA sheets of about 50 μm to 1 mm in thickness and porous HA granules of about 50 μm to 1 mm in size with tailored crystal surface were prepared by the hydrothermal vapor exposure method at temperatures below 200°C. Porous sheets and porous granules of HA with controlled crystal surface should be suitable for scaffold of cultured bone, for bone graft material and for drug delivery system (DDS).

1. Introduction

Hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$; HA) is known as major component of human hard tissue such as bones and teeth. Sintered HA has already been used as a bone-repairing material which can directly bond to natural bones in bony defect. It has been known to be biocompatible and osteoconductive [1], but newly bone formation on HA is not quick in comparison with the autograft. If materials of HA could have the tailored specific crystal surface, they should have the quick bone formation because of the advantage of adsorptive activity.

The authors reported various kinds of HA materials prepared by the unique hydrothermal methods [2–8]. In the present investigation, porous HA sheets of about 50 μm to 1 mm in thickness and porous HA granules of about 50 μm to 1 mm in size with tailored crystal surface were prepared by the hydrothermal vapor exposure method [9–12]. This hydrothermal method is the strong technique for control the crystal surface.

The sheets and granules of HA must be suitable as scaffold for cultured bone, for bone graft material and for drug delivery system (DDS).

2. Experimental methods

2.1. Preparation of HA sheets

Commercial powders of α-tricalcium phosphate (α-$Ca_3(PO_4)_2$: α-TCP, Taihei Chemical Industrial Co., Ltd., Japan) and polyvinyl alcohol (PVA, Wako Pure Chemical Industries Ltd., Japan) were used as the starting materials. The slurry of α-TCP with PVA was prepared by using 10 mass% PVA aqueous solution at room temperature. To remove bubbles, the slurry was kept under vacuum condition. Films of α-TCP with PVA were prepared from this slurry by spin overcoat method. This method is very popular technique to preparing polymer film [13]. The glass dish was set on a turntable, and then the slurry was cast in the glass dish and twiddled. Films of α-TCP with PVA were dried at room temperature for 12 h. In order to control the thickness of films, rotation speed of the turntable was controlled. After heating at 1200°C for 5 min in air, the samples were set in a 105 cm^3 autoclave with 30 cm^3 of pure water, and then they were exposed to vapor of the pure water at the temperatures from 105 to 200°C under the saturated vapor pressure for 1–20 h.

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0022-2461 © *2006 Springer Science + Business Media, Inc.*
DOI: 10.1007/s10853-006-7338-5

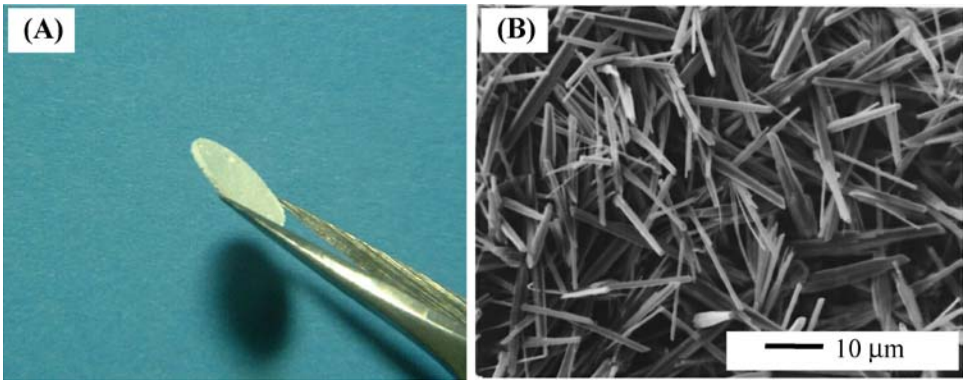

Figure 1 Sheet of HA prepared by hydrothermal method at 120°C under saturated vapor pressure for 3 h (A). Rod shaped crystals were observed by SEM (B).

2.2. Preparation of HA granules

Commercial powders of α-tricalcium phosphate (α-$Ca_3(PO_4)_2$: α-TCP, Taihei Chemical Industrial Co., Ltd., Japan) were used as the starting material. After the addition of 10 mass% gelatin (Wako Chemical Co., Japan) aqueous solution, the obtained slurry was dispersed in the vegetable oil at 70°C, and then stirred at the rate of 0–900 r.p.m. because of controlling of granules size. The samples were filtered off to recover, washed with ethanol, and dried at 105°C in air. After heating at 1200°C for 5 min in air to remove organic matter and to keep crystal phase, the samples were set in a 105 cm^3 autoclave with 30 cm^3 of pure water, and then they were exposed to vapor of the pure water at the temperatures from 105 to 200°C under the saturated vapor pressure for 1–20 h.

2.3. Characterization

The produced phases were identified by powder X-ray diffractometry with graphite-monochromatized CuKα radiation, operating at 40 kV and 20 mA (XRD; Rigaku, Geiger flex 2027, Japan). The samples prepared were dissolved in 0.1 mol/dm^3 nitric acid, and then the chemical composition of them was analyzed by inductively coupled plasma spectrometer (ICP-MS; Seiko Instruments, SPQ 9000S, Japan). The microstructure of specimens was observed by electron microscopes (SEM; JEOL, JSM-T300, Japan and TEM; Hitachi, H800, Japan). Pore volume and distribution of pore diameter were measured by mercury intrusion porosimetry (MIP; Carlo Elba, Porosimeter 2000, Italy). Specific surface area of samples was measured by BET method.

3. Results and discussion

3.1. HA sheets

The thickness of α-TCP film was controlled from about 50 μm to about 1 mm by controlling of rotation speed of the turntable. The mixture film of α-TCP and PVA could be made into a convenient form. To remove PVA and keep crystal phase as α-TCP, the mixture of α-TCP and PVA film was heated at 1200°C for 5 min in air. Shrinkage of the sample was about 15%, but the shape of sheets was not changed and handling of the sample was not difficult. From X-ray diffraction, there were no phases other than α-TCP.

Using hydrothermal vapor exposure method [9–12], α-TCP changes into HA and the sample is hardened because of hydration of α-TCP [14]. Fig. 1A shows the HA sheet prepared by hydrothermal treatment at 120°C for 3 h under saturated vapor pressure. The porosity of HA sheet was about 75% and specific surface area was about 15 m^2/g. HA sheet prepared by hydrothermal treatment at 120°C for over 30 min was composed of rod-shaped crystals elongated along the c-axis by TEM analysis. Fig. 1B shows SEM image of rod-shaped crystals. The aspect ratio of crystals increased with increasing period of hydrothermal treatment. The rod-shaped crystals were about 20 μm in length with aspect ratio of about 10 and locked together to make micro-pores. The size of micro-pores increased gradually with the hydrothermal treatment period. The sheet of α-TCP completely changed into HA at 120°C under saturated vapor pressure for the period over 3 h. From X-ray diffraction, the HA sheet after heating at 900°C for 3 h in air contained HA and β-TCP. The relative intensity of XRD lines for HA and for β-TCP was used in order to determine the HA and β-TCP contents and then the Ca/P molar ratio of samples was estimated [15, 16]. The value of Ca/P of the HA sheet prepared by hydrothermal treatment at 120°C for 3 h was 1.51 and prepared at 120°C for 5 h was 1.57, these were lower than Ca/P of stoichiometric HA ($Ca/P = 1.67$). The value of Ca/P of samples treated hydrothermally at 120 to 200°C for 5 h was shown in Fig. 2. Chemical analysis by ICP-MS gave almost same value of Ca/P. This HA was calcium deficient hydroxyapatite.

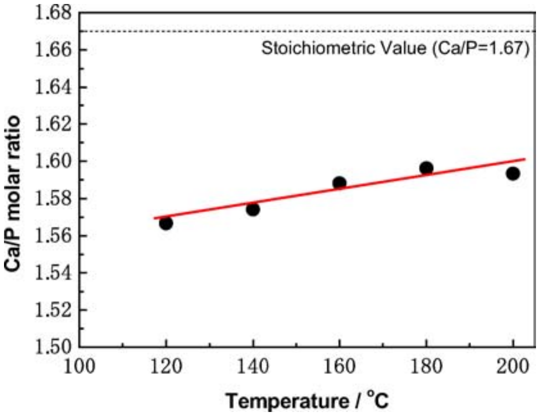

Figure 2 Ca/P molar ratio of rod-shaped HA particles prepared by hydrothermal vapor exposure method at the indicated temperature for 5 h.

3.2. HA granules

Spherical mixture of α-TCP and gelatin were obtained after dropping slurry into the vegetable oil. Gelatin was observed among the particles of α-TCP. The size of spherical particles could be controlled by the control of stirring rate of the vegetable oil. The size of particles decreased with increasing stirring rate. After heating at 1200°C for 5 min, gelatin was burned out and no other phases than α-TCP were revealed by XRD. The XRD pattern of the sample after hydrothermal treatment is showing high crystallinity of HA and the non-existence of phases other than HA.

Microstructure designed HA granules from about 50 μm to 1 mm in size could be prepared by hydrothermal vapor exposure method at the temperatures from 105 to 200°C under saturated vapor pressure of pure water. Spherical HA granules prepared hydrothermally at 160°C for 3 h were shown in Fig. 3. The size of HA granules (A), (B) and (C) was different because the stirring rate of the vegetable oil was different. The size of granules could be controlled by the control of stirring rate (Fig. 4). The granular HA was composed of rod-shaped crystals of about 20 μm in length with the mean aspect ratio of 30 (Fig. 5). Rod-shaped HA crystals were not obtained below 70°C. These crystals were elongated along the c-axis according to TEM analysis. Rod-shaped HA crystals were locked together to make micro-pores of about 0.1 μm in size. Specific surface area of granules did not depend on their size and the values were about 20 m^2/g. These granules were non-stoichiometric HA with calcium deficient composition of $Ca/P < 1.60$ according to ICP-MS analysis.

These granular HA must have the advantage of adsorptive activity in comparison with the reported materials [17, 18], because the HA has large specific crystal surface and micro-pores. Microstructure designed HA granules with controlled surface must be suitable for drug delivery

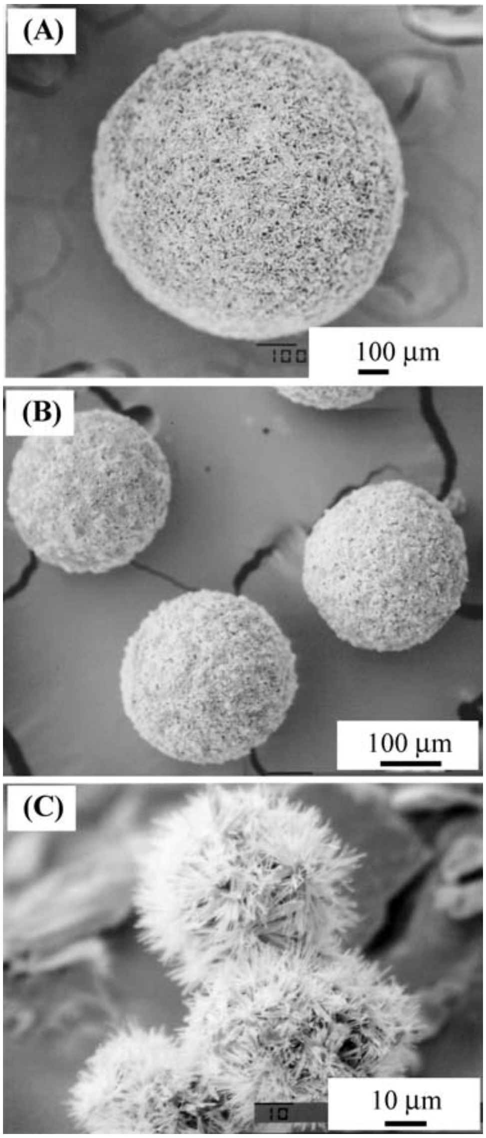

Figure 3 Scanning electron micrographs of HA granules prepared by hydrothermal vapor exposere method at 160°C for 3 h. The stirring rate was (A) 0 r.p.m., (B) 300 r.p.m. and (C) 900 r.p.m.

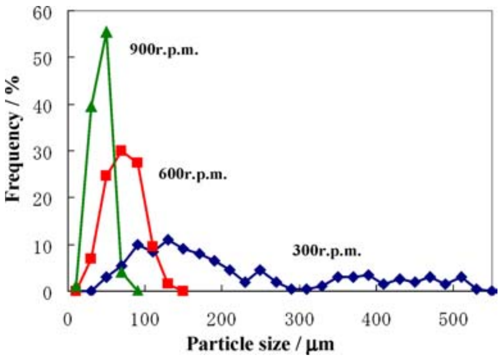

Figure 4 Particle size distribution of HA granules prepared at the indicated stirring rate.

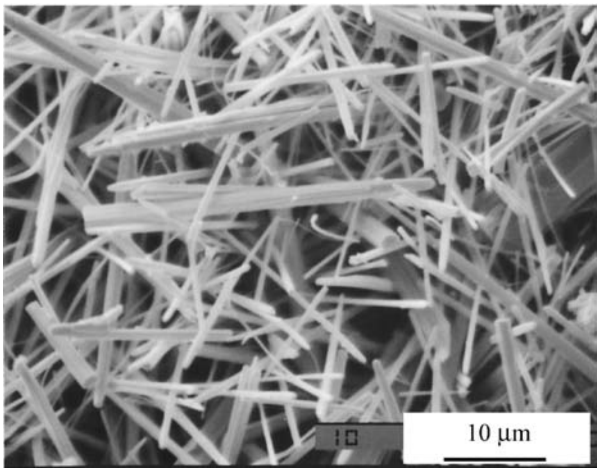

Figure 5 Scanning electron micrograph of the HA granule (Fig. 3(A)) prepared by hydrothermal vapor exposure method.

system (DDS), for scaffold of cultured bone and for bone graft material.

4. Conclusions

The results described in this paper allow to drawing the following summary.

1. Hydrothermal vapor treatment method is the strong technique for control the crystal surface.

2. Rod-shaped crystals of HA with Ca deficient composition with Ca/P < 1.67 could be synthesized under hydrothermal conditions.

3. Porous HA sheets with about 50 μm to 1 mm in thickness composed of rod-shaped crystals were prepared by the hydrothermal vapor exposure method.

4. Porous HA granules of about 50 μm to 1 mm in size composed of rod-shaped crystals were prepared by the hydrothermal vapor exposure method.

5. These HA materials must have the advantage of adsorptive activity, because they had large specific crystal surface of a-face and micro-pores.

Acknowledgments

The authors wish to thank Mr. T. Tsujimoto and Mr. Y. Kamae of Yamaguchi University in Japan for their experimental helping and also wish to thank Mr. M. Watanabe of Konoshima Chemical Ind. Co., Japan for his helping of BET measurement and chemical analysis. The present research was supported in part by the Grant-in-Aid for Scientific Research ((C)16560592) from the Japan Society for the Promotion of Science.

References

1. H. OHGUSHI and A. I. CAPLAN, *J. Biomed. Mater. Res. (Applied Biomaterials)* **48** (1999) 913.
2. K. IOKU, M. YOSHIMURA and S. SOMIYA, in "Bioceramics **1**" (Ishiyaku EuroAmerica, Tokyo and St. Louis, 1989) p. 62.
3. idem., *Biomaterials*, **11** (1990) 57.
4. idem., *Phosphorus Res. Bull.*, **1** (1991) 15.
5. M. YOSHIMURA, H. SUDA, K. OKAMOTO and K. IOKU, *J. Mater. Sci.* **29** (1994) 3399.
6. K. IOKU, K. YAMAMOTO, K. YANAGISAWA and N. YAMASAKI, *Phosphorus Res. Bull.* **4** (1994) 65.
7. K. IOKU, A. OSHITA, H. FUJIMORI, S. GOTO and M. YOSHIMURA, *Trans. Mater. Res. Soc. Japan* **26** (2001) 1243.
8. K. IOKU, S. YAMAUCHI, H. FUJIMORI, S. GOTO and M. YOSHIMURA, *Solid State Ionics* **151** (2002) 147.
9. K. IOKU, S. NISHIMURA, Y. EGUCHI and S. GOTO, *Rev. High Pressure Sci. Technol.* **7** (1998) 1398.
10. K. IOKU, M. FUKUHARA, H. FUJIMORI and S. GOTO, *Korean J. Ceram.* **5** (1999) 115.
11. K. IOKU, H. MISUMI, H. FUJIMORI, S. GOTO and M. YOSHIMURA, in Proc. 5th Int. Conf. Solvo-Thermal Reactions, NJ, USA, July 2002, edited by R. E. Riman (Rutgers, The State Univ. of NJ, USA, 2002), p. 233.
12. K. IOKU, M. TODA, H. FUJIMORI, S. GOTO and M. YOSHIMURA, *Key Engineering Materials* **254–256** (2004) 19.
13. E. TENGROTENHUIS, W. J. M. VAN DER KEMP, J.G. BLOK, J.C. VAN MILTENBURG and J. P. VAN DEREERDEN, *Colloids and Surfaces B. Biointerfaces* **6** (1996) 209.
14. H. MONMA and T. KANAZAWA, *J. Ceram. Soc. Japan* **84** (1976) 209.
15. K. IOKU, T. MURAKAMI, Y. IKUMA and M. YOSHIMURA, *J. Ceram. Soc. Japan Int. Edition* **100** (1992) 1015.
16. K. ISHIKAWA, P. DUCHEYNE and S. RADIN, *J. Mater. Sci.: Mater. Med.* **4** (1993) 165.
17. W. PAUL and C. P. SHARMA, *ibid.* **10** (1999) 383.
18. V. S. KOMLEV and S. M. BARINOV, *ibid.* **13** (2002) 295.

Received 19 August 2004
and accepted 10 April 2005