Available online at www.sciencedirect.com

Journal of the European Ceramic Society 27 (2007) 1585–1588

www.elsevier.com/locate/jeurceramsoc

Fabrication of poly(vinyl alcohol)–apatite hybrids through biomimetic process

Caihong You[a], Toshiki Miyazaki[a,*], Eiichi Ishida[b], Masahiro Ashizuka[a],
Chikara Ohtsuki[c], Masao Tanihara[c]

[a] *Graduate School of Life Science and Systems Engineering, Kyushu Institute of Technology, 2-4 Hibikino, Wakamatsu-ku, Kitakyushu-shi, Fukuoka 808-0196, Japan*
[b] *Faculty of Engineering, Kyushu Institute of Technology, 1-1 Sensui-cho, Tobata-ku, Kitakyushu-shi, Fukuoka 804-8550, Japan*
[c] *Graduate School of Materials Science, Nara Institute of Science and Technology, 8916-5 Takayama-cho, Ikoma-shi, Nara 630-0192, Japan*

Abstract

Natural bone is a kind of organic–inorganic hybrid that is composed of collagen and apatite nanocrystals. Organic polymer–apatite hybrid is therefore expected as novel bone substitutes exhibiting both bone-bonding ability and mechanical performance analogous to natural bone. Biomimetic process has been paid much attention on fabrication of such hybrids, where bone-like apatite is deposited on material surfaces in a simulated body fluid (SBF, Kokubo solution) with ion concentrations nearly equal to those of human extracellular fluid at ambient conditions. Hydroxyl groups on several kinds of metal oxide gels effectively trigger heterogeneous nucleation of the apatite in body environment. This is significantly enhanced by release of calcium ions from the materials. In this study, we synthesized organic–inorganic hybrids from poly(vinyl alcohol) (PVA) by modification with silica as well as calcium nitrate. PVA has attractive features for bone substitutes such as high hydrophilicity and high flexibility. Ability of the apatite formation was examined in SBF. Apatite deposition was observed on the surfaces of the hybrids in SBF. The PVA–apatite hybrids obtained are expected as novel bone-repairing materials.

Keywords: Nanocomposites; Apatite; Silicate; Poly(vinyl alcohol) (PVA)

1. Introduction

Several kinds of ceramics have been found to bond directly to living bone after implantation in bony defects. They are called bioactive ceramics, meaning that they elicit and modulate specific biological activity. Sintered hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$),[1] Na_2O–CaO–SiO_2–P_2O_5 glass named Bioglass®,[2,3] and glass–ceramic A-W that contains apatite and β-wollastonite crystals in MgO–CaO–SiO_2 glassy matrix[4,5] are known as bioactive ceramics. Bone-bonding performance of bioactive ceramics is quite attractive, since tight fixation between the bone and the implanted material is achieved. However, there is limitation on clinical application, because of their inappropriate mechanical properties such as high Young's modulus, low toughness, and brittle character. In addition, medical doctors require development of novel bioactive materials that can be formed into desired shapes during operation.

It is well known that natural bone is a kind of organic–inorganic hybrid in which inorganic apatite nanocrystals are deposited on organic collagen woven into a three-dimensional structure. Therefore, the organic polymers deposited with the apatite are expected as novel artificial bone exhibiting not only bone-bonding ability, i.e. bioactivity, but also mechanical performance analogous to those of natural bone. Biomimetic process has been paid much attention on fabrication of such hybrids, where bone-like apatite is deposited on material surfaces in simulated body fluid (SBF, Kokubo solution) with ion concentrations nearly equal to those of human extracellular fluid at ambient conditions. Several functional groups such as Si–OH, Ti–OH, Zr–OH, Ta–OH, and Nb–OH groups are known to induce heterogeneous apatite nucleation in body environment.[6–10] In addition, release of calcium ions (Ca^{2+}) from the materials significantly enhances it. Among organic polymers, poly(vinyl alcohol) (PVA) has been studied inten-

---

[*] Corresponding author. Tel.: +81 93 695 6025; fax: +81 93 695 6025.
E-mail address: tmiya@life.kyutech.ac.jp (T. Miyazaki).

0955-2219/$ – see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.jeurceramsoc.2006.04.055

sively because of its attractive features for medical applications such as high hydrophilicity, good film forming and processability. Furthermore, PVA is paid much attention for reconstruction of articular cartilage.[11,12] Although preparation of hybrids from alkoxysilane and PVA has been reported, optimization of the composition of the hybrids for bone repair has not been examined.[13]

In this study, we synthesized organic–inorganic hybrids from PVA by chemical modification with alkoxysilane that gives Si–OH groups as well as water-soluble calcium salts. Ability of apatite formation on the hybrids was examined in SBF.

2. Materials and methods

PVA with molecular weight of 86,000 (Wako Pure Chemical Industries Ltd., Japan) was dissolved in mixed solvent of ultra-pure water and ethanol to form 5 mass% solution at 80 °C. Tetraethoxysilane (TEOS, $Si(OC_2H_5)_4$, Nacalai Tesque Inc., Japan) was added to the solution under vigorous stirring. After mixing for 30 min, HCl aqueous solution and calcium nitrate tetrahydrate ($Ca(NO_3)_2 \cdot 4H_2O$, Wako Pure Chemical Industries Ltd.) were added. The mass proportion of TEOS to the total of PVA and TEOS was ranged from 20% to 60%, with TEOS:HCl:$Ca(NO_3)_2$ = 10:1:1 (molar ratio). The obtained solutions were then poured into the Telflon® dish and dried at 36.5 °C for 7 days. The specimen with TEOS/(TEOS + PVA) = x (mass%) and $Ca(NO_3)_2$/TEOS = 0.1 (molar ratio) is hereafter denoted as "SixCa01".

The obtained films of TEOS–PVA hybrid were cut into 1.5 mm × 1.5 mm in size and then soaked in SBF (Na^+ 142.0 mmol/dm^3, K^+ 5.0 mmol/dm^3, Mg^{2+} 1.5 mmol/dm^3, Ca^{2+} 2.5 mmol/dm^3, Cl^- 147.8 mmol/dm^3, $HCO_3{}^-$ 4.2 mmol/dm^3, $HPO_4{}^{2-}$ 1.0 mmol/dm^3 and $SO_4{}^{2-}$ 0.5 mmol/dm^3).[7] The solution was buffered at pH 7.40 with tris(hydroxymethyl) aminomethane ($(CH_2OH)_3CNH_2$) and 1 mol/dm^3 hydrochloric acid at 36.5 °C. After soaking in SBF, the specimens were removed from the fluid, washed gently with ultra-pure water and dried at ambient temperature.

Their surface structures were examined by thin-film X-ray diffraction (TF-XRD; MXP3V, Mac Science Ltd., Japan) and scanning electron microscopic (SEM; S-3500N, Hitachi Co., Japan) observation. Tensile mechanical properties of the hybrids were evaluated using a universal testing machine (AG-1, Shimadzu Co., Japan) under ambient conditions according to JIS K7161. Dumbbell-shaped specimens more than 115 mm in length, 25 ± 1 mm in width at center and 6 ± 0.4 mm in width at edge were subjected to the tensile test. Three specimens were prepared for each composition.

3. Results

For all the compositions, crack-free, homogeneous and transparent monolithic films were obtained. Fig. 1 shows SEM photographs of the surfaces of TEOS–PVA hybrids, which were soaked in SBF for 20 h. A lot of fine particles were observed to cover whole surfaces of all the hybrids after soaking in SBF for as short time as 20 h. Morphology of the fine particles was quite similar to that of the apatite layer formed on bioactive glasses and glass–ceramics in SBF.[14,15] Fig. 2 shows TF-XRD patterns of the surfaces of TEOS–PVA hybrids, which were soaked in SBF for 20 h. Broad peaks assigned to poorly crystalline apatite were detected at 26° and 32° in 2θ for all the examined hybrids. The JCPDS card (#09-0432) showed that the peak at 26° is due to (0 0 2) diffraction of apatite while a broader one at about 32° is an envelope of (2 1 1), (1 1 2), and (3 0 0) diffractions of apatite. These results indicate that the prepared TEOS–PVA hybrids can induce the apatite deposition on their surfaces in SBF.

Fig. 3 shows representative stress–strain curves of the specimens before soaking in SBF. The tensile strength increased in the order Si20Ca01 (20.84 ± 0.09 MPa) < Si40Ca01 (37.44 ± 1.2 MPa) < Si60Ca01 (46.82 ± 0.07 MPa). The Young's modulus of the specimens increased in the order Si20Ca01 (32.8 ± 1.1 MPa) < Si40Ca01 (55.8 ± 2.1 MPa) < Si60Ca01 (96.1 ± 3.6 MPa).

4. Discussion

The results obtained in this study show that essentially crack-free films of TEOS–PVA hybrid can be obtained by modification of PVA with TEOS and calcium nitrate. The Young's modu-

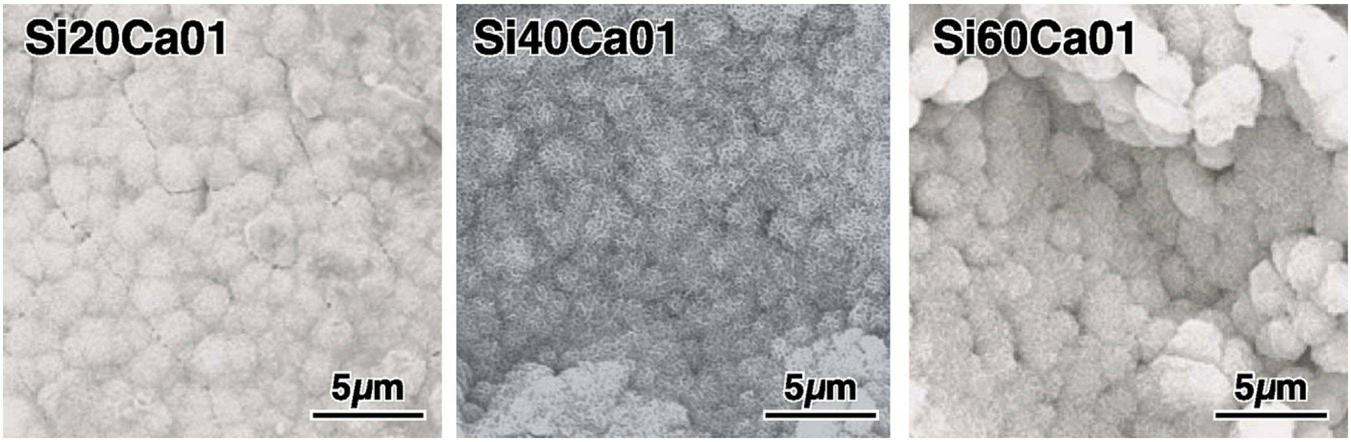

Fig. 1. SEM photographs of the surfaces of TEOS–PVA hybrids, which were soaked in SBF for 20 h.

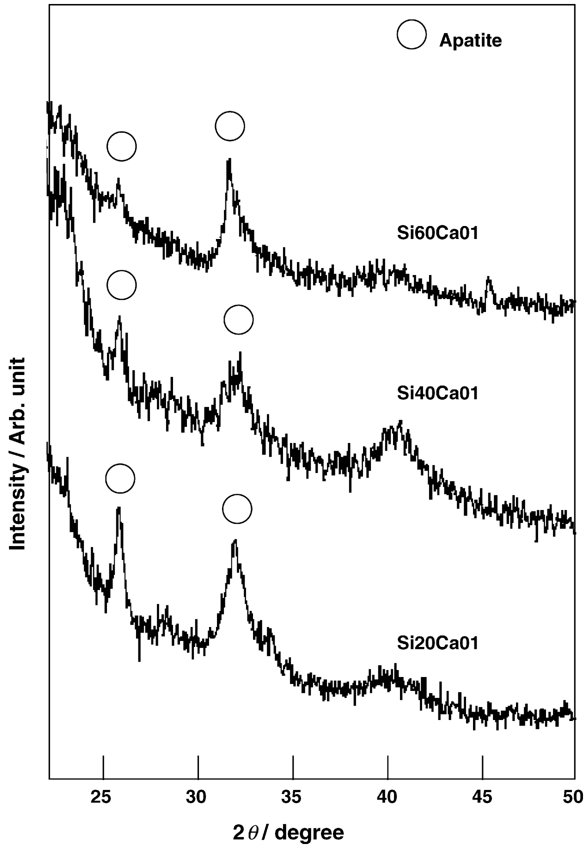

Fig. 2. TF-XRD patterns of the surfaces of TEOS–PVA hybrids, which were soaked in SBF for 20 h.

lus of the hybrids is quite similar to that of human cancellous bone (50–500 MPa). Such hybrids are expected to bring a novel material for reconstruction of cancellous bone. The hybrids were found to form the apatite after soaking in SBF. This means that PVA–apatite hybrids can be synthesized by simple soaking of the TEOS–PVA hybrids in SBF. The formed apatite showed a character of low crystallinity (see Fig. 2). This indicates that the hybrids are expected to exhibit ability of direct bone-bonding, since the structure of the formed apatite is quite similar to that of natural bone.[5]

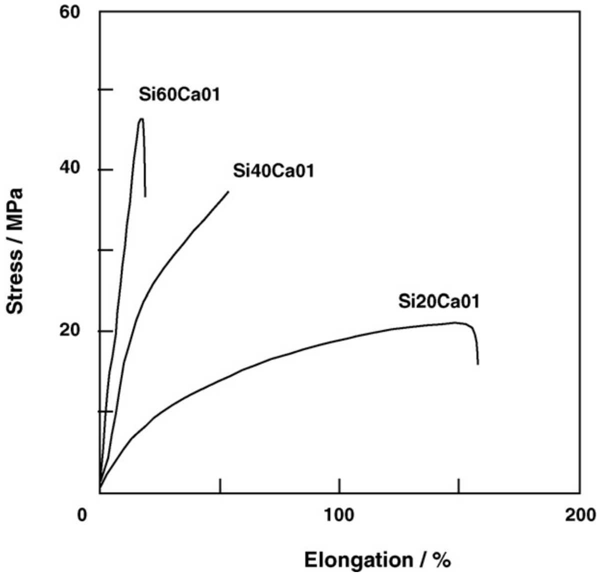

Fig. 3. Representative stress–strain curves of TEOS–PVA hybrids before soaking in SBF.

Mechanism of the apatite formation on the hybrids can be explained as follows. Si–OH groups would be formed on the surfaces of the specimens through hydrolysis of TEOS, similar to TEOS-containing organic–inorganic hybrids previously reported.[16] The Si–OH groups provide nucleation sites of the apatite, while Ca^{2+} ions are released from the surface layer of the specimens into SBF. The released Ca^{2+} ions simultaneously increase the ionic activity product of the surrounding fluid with respect to the apatite. Once the apatite nuclei are formed, they grow spontaneously by consuming Ca^{2+} and phosphate ions in SBF.

5. Conclusion

Organic–inorganic hybrids were successfully synthesized from PVA by modification with TEOS and calcium nitrate. The hybrids formed bone-like apatite on their surfaces after soaking in SBF. This type of PVA–apatite hybrid is expected as new kind of bone-repairing materials.

Acknowledgment

This study was supported by SHISEIDO Grant for Science Research.

References

1. Jarcho, M., Hydroxyapatite synthesis and characterization in dense polycrystalline forms. *J. Mater. Sci.*, 1976, **11**, 2027–2035.
2. Hench, L. L., Bioceramics; from concept to clinic. *J. Am. Ceram. Soc.*, 1991, **74**, 1487–1510.
3. Hench, L. L., Bioceramics. *J. Am. Ceram. Soc.*, 1998, **81**, 1705–1728.
4. Kokubo, T., A/W glass–ceramic: processing and properties. In *An Introduction to Bioceramics*, ed. L. L. Hench and J. Wilson. World Sci., Singapore, 1993, pp. 75–88.
5. Kokubo, T., Kim, H.-M. and Kawashita, M., Novel bioactive materials with different mechanical properties. *Biomaterials*, 2003, **24**, 2161–2175.
6. Li, P., Ohtsuki, C., Kokubo, T., Nakanishi, K., Soga, N. and deGroot, K., The role of hydrated silica, titania and alumina in inducing apatite on implants. *J. Biomed. Mater. Res.*, 1994, **28**, 7–15.
7. Cho, S. B., Kokubo, T., Nakanishi, K., Soga, N., Ohtsuki, C., Nakamura, T. *et al.*, Dependence of apatite formation on silica gel on its structure: effect of heat treatment. *J. Am. Ceram. Soc.*, 1995, **78**, 1769–1774.
8. Uchida, M., Kim, H.-M., Kokubo, T., Miyaji, F. and Nakamura, T., Bonelike apatite formation induced on zirconia gel in a simulated body fluid and its modified solutions. *J. Am. Ceram. Soc.*, 2001, **84**, 2041–2044.
9. Miyazaki, T., Kim, H.-M., Kokubo, T., Kato, H. and Nakamura, T., Induction and acceleration of bonelike apatite formation on tantalum oxide gel in simulated body fluid. *J. Sol–Gel Sci. Technol.*, 2001, **21**, 83–88.
10. Miyazaki, T., Kim, H.-M., Kokubo, T., Ohtsuki, C. and Nakamura, T., Bonelike apatite formation induced on niobium oxide gels in simulated body fluid. *J. Ceram. Soc. Jpn.*, 2001, **109**, 934–938.
11. Huang, R. Y. M. and Rhim, J. W., Modification of poly(vinyl alcohol) using maleic-acid and its application to the separation of acetic-acid water mixtures by the pervaporation technique. *Polym. Int.*, 1993, **30**, 129–135.
12. Gimenez, V., Mantecon, A. and Cadiz, V., Modification of poly(vinyl alcohol) with acid chlorides and crosslinking with difunctional hardeners. *J. Polym. Sci., Polym. Chem.*, 1996, **34**, 925–934.

13. Ionescu, C., Simon, M., Ionascu, C. and Savii, C., Synthesis and characterization of sol–gel derived TEOS–PVA hybrid matrices. In *Proceedings of the 3rd International Symposium of the Multidisciplinary Research Association from Western Romania (ISIM 2000)*, 2000, pp. 282–290.
14. Kokubo, T., Ito, S., Huang, Z. T., Hayashi, T., Sakka, S., Kitsugi, T. *et al.*, Ca,P-rich layer formed on high-strength bioactive glass–ceramic A-W. *J. Biomed. Mater. Res.*, 1990, **24**, 331–343.
15. Ohtsuki, C., Kokubo, T. and Yamamuro, T., Mechanism of apatite formation on CaO–SiO_2–P_2O_5 glasses in a simulated body fluid. *J. Non-Cryst. Solids*, 1992, **143**, 84–92.
16. Kamitakahara, M., Kawashita, M., Miyata, N., Kokubo, T. and Nakamura, T., Bioactivity and mechanical properties of polydimethylsiloxane (PDMS)–CaO–SiO_2 hybrids with different PDMS contents. *J. Sol–Gel Sci. Technol.*, 2001, **21**, 75–81.