Bioactivity of MgO–CaO–SiO₂ Porous Glass-Ceramics

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Porous glass-ceramics with bone-bonding ability, i.e. bioactivity, have been attractive as scaffold materials for bone regeneration, since their bioactivity and bioresorbability can be easily controlled by varying their composition. The prerequisite for artificial materials to show bioactivity is formation of a bone-like apatite layer on their surfaces in the body environment. This type of apatite formation can be observed in a simulated body fluid (Kokubo solution) which mimics the composition of human extracellular fluid. Previous studies revealed that the CaO–SiO₂ system is quite effective for the deposition of apatite in the body environment. Magnesium is one of the major inorganic elements existing in body fluid, and has already been used in bioactive glass-ceramics. Dissolution of glasses in the system CaO–SiO₂ could be controlled by addition of MgO. In this study, we synthesized porous glass-ceramics by heat treatment of glass powder with composition of 10MgO–40CaO–50SiO₂ mol% at various temperatures. Porous bodies with continuous pores about 500 μm in diameter were obtained after sintering and crystallization. Precipitation of para-wollastonite and diopside appeared after heat treatment at 900°C and more. The amount of precipitated diopside increased with increasing temperature of the heat treatment. The synthesized specimens formed apatite on their surfaces after soaking in Kokubo solution. Consequently, glasses in the system MgO–CaO–SiO₂ give easy production of porous glass-ceramics with bioactivity and bioresorption by a conventional sintering process.

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1. Introduction

Several kinds of ceramics such as Bioglass®, sintered hydroxyapatite and glass-ceramic A–W are known to exhibit specific biological affinity. Namely, they have the ability to make a direct bond to living bone when implanted into bony defects.¹,² They are called bioactive ceramics and are subjected to clinical applications as bone substitutes in orthopedic and dental fields. Porous bodies made of bioactive ceramics are also clinically utilized as bone fillers, since they can be easily handled and shaped in clinical usage. They have been attracting much attention as scaffold materials for bone regeneration in the field of tissue engineering, if they are incorporated with drugs or osteoinductive factors.³ As a skeleton of the porous bioactive materials, glasses and glass-ceramics are quite useful since their bioactivity and thermal properties can be easily controlled by varying composition of the mother glass.

It has been revealed that the essential requirement for artificial materials to exhibit bioactivity is formation of a low-crystalline apatite layer with a composition and structure similar to those of bone mineral on their surfaces in body environment.⁴,⁵ This apatite formation can be observed on the surfaces of bioactive materials even in an acellular simulated body fluid with inorganic ion concentrations similar to those of human extracellular fluid, as proposed by Kokubo and his colleagues.⁶–⁹ The solution is hereafter denoted as “Kokubo solution”. We can therefore say that materials which form apatite in Kokubo solution have a potential to show bioactivity.

Previous studies on the mechanism of apatite deposition on bioactive glasses and glass-ceramics in Kokubo solution showed that formation of the surface apatite layer is induced both by calcium ions dissolved from the bioactive materials, and by hydrated silica gel formed on the surfaces of the materials.¹⁰,¹¹ This means that glasses and glass-ceramics in the simple binary system CaO–SiO₂ play a role as essential constituent for apatite deposition in body environment. On the basis of these findings, the effect of additives on the bioactivity of glasses was investigated in ternary systems such as CaO–Al₂O₃–SiO₂,¹² CaO–SiO₂–TiO₂,¹³ Na₂O–CaO–SiO₂,¹⁴ CaO–B₂O₃–SiO₂.¹⁵ Magnesium is one of the major inorganic elements existing in body fluid, and has already been used in bioactive glass-ceramic. Tsuru et al. examined the ability of apatite deposition on various MgO–CaO–SiO₂ glasses in Kokubo solution, and showed that the glass with composition of 10MgO–40CaO–50SiO₂ in mol% forms the apatite within 3 d (=days).¹⁶ They also documented that the formed apatite layer was observed to be directly in contact with the glass substrates without formation of a thick silica gel layer between the apatite and the glass. This means that tight bonding of the apatite to the glass substrates is expected. Therefore, MgO is an important component for design of novel bioactive materials from glasses and glass-ceramics. In the present study, we examined the potential to obtain bioactive porous glass-ceramics in the system MgO–CaO–SiO₂ through conventional sintering. Their bioactivity was estimated from the ability of dense glass-ceramics to deposit apatite in Kokubo solution which is a model to precisely assume surface reaction of the porous glass-ceramics.

2. Experimental

2.1 Preparation of MgO–CaO–SiO₂ glass powder

A powder mixture of the nominal composition of 10MgO–40CaO–50SiO₂ in mol% was prepared by using reagent grade chemicals of MgO, CaCO₃ and SiO₂. The chemical of SiO₂ was calcined at 1000°C for 3 h (= hours), while those of MgO and CaCO₃ were used without calcination. The mixture was
melted at 1500°C for 2 h in a platinum crucible, poured on a stainless steel plate to be formed into plates about 1 mm thick. Thus obtained glass plates were pulverized by a planetary type zirconia ball mill (P-7, Fritsch, Germany), and sieved to obtain the grains less than 44 μm in size.

2.2 Preparation of the glass-ceramics

For the porous specimens, the prepared glass powder was dispersed into ultrapure water to form a slurry. A polyurethane sponge 15 × 15 × 15 mm³ in size was dipped in the slurry and dried at 60°C for 1 h. For dense specimens, the glass powder was pressed into rectangular specimens 20 × 20 × 2.5 mm³ in size under a uniaxial pressure of 196 MPa.

The specimens were then heated up to 770°C at a rate of 1°C/min and kept at 770°C for 3 h in order to sinter the glass. After cooling to room temperature, it was then heated up to various temperatures ranging from 770 to 1200°C at a rate of 5°C/min and kept at the given temperature for 6 h, followed by natural cooling in the furnace.

2.3 Soaking in Kokubo solution

The prepared porous and dense glass-ceramics were immersed in 35 mL of Kokubo solution (Na⁺ 142.0, K⁺ 5.0, Mg²⁺ 1.5, Ca²⁺ 2.5, Cl⁻ 147.8, HCO₃⁻ 4.2, HPO₄²⁻ 1.0, and SO₄²⁻ 0.5 mol/m³) for various periods up to 14 d. The solution was buffered at pH 7.25 with 50 mol/m³ trishydroxymethyl-aminomethane (© (CH₃OH)₃CNH₂) and appropriate amounts of hydrochloric acid (HCl), and its temperature was kept at 36.5°C. After given periods, the specimens were removed from the fluid, washed gently with ultrapure water, and then dried at room temperature.

2.4 Analysis of specimens

Thermal properties of the as-prepared glass powder were examined by differential thermal analysis (DTA, 2000S, MAC Science Co., Ltd., Japan). Thermal expansion of the compact of the glass powder was also measured with a thermal dilatometer (TDS-200, MAC Science Co., Ltd., Japan). Changes in surface structure of the specimen before and after soaking in Kokubo solution were characterized by X-ray diffraction (XRD, M18XHF22-SRA, MAC Science Co., Ltd., Japan) and scanning electron microscopy (SEM, S-3500N, Hitachi, Ltd., Japan) attached with energy dispersive X-ray micro-analysis (EDX, EMAX ENERGY EX-400, Horiba, Ltd., Japan). The XRD measurement was performed by 2θ/θ scanning with CuKα radiation. In SEM observation, a thin film of gold was coated on the surfaces of the specimens by a sputtering method.

3. Results

Figure 1 shows DTA and thermal expansion profiles of the glass powder with the composition of 10MgO-40CaO-50SiO₂ in mol%. Glass-transition temperature is determined at about 729°C. An exothermic peak on the DTA profile was observed at about 854°C, which is attributed to crystallization of the glass. The thermal expansion profile of the compact of the glass powder showed that a decrease in volume of the glass started at about 764°C, and finished at about 851°C. In this temperature range, sintering of the glass powder occurred. On the basis of these results, the temperature of sintering was hereafter determined at 770°C, where the glass powder was sintered with little crystallization.

Figure 2 shows SEM photographs of the inside of the porous specimens heat-treated at various temperatures. Continuous pores of more than 500 μm in diameter were observed for all the specimens. Figure 3 shows powder XRD patterns of the porous specimens heat-treated at various temperatures. A broad halo pattern was mainly observed for the specimen heat-treated at 770°C, while there appears a little peak assigned to para-wollastonite (JCPDS #43-1460). Peaks assigned to para-wollastonite and diopside (JCPDS #19-239) were observed for the specimen heat-treated at 900°C or more. The peak intensity of para-wollastonite was large even for the specimens heat-treated at 900°C, while that of diopside was small at 900°C and increased with increasing temperature of the heat treatment.

Figure 4 shows SEM photographs and EDX profiles of the surfaces of porous specimens heat-treated at 770 and 1100°C, which were soaked in Kokubo solution for 7 d. Assemblies of fine particles were observed to be formed for both the specimens after the soaking. EDX spectra showed that the formed particles contained large amounts of Ca and P. The morphology of the particles was quite similar to those of the apatite layer which was formed on bioactive glasses and glass-ceramics in Kokubo solution. Figure 5 shows XRD patterns of the dense specimens heat-treated at various temperatures, which were soaked in Kokubo solution for 14 d. Broad peaks assigned to low-crystalline apatite were observed for all the specimens at 26° and 32° after the soaking. The peak at 26° is assigned to 002 diffraction of hydroxyapatite (JCPDS #09-0432) while that at about 32° is an envelope of 211, 112 and 300 diffractions of hydroxyapatite. These results indicate that low-crystalline apatite was deposited on the surface of the glass-ceramics within 14 days after exposure to Kokubo solution, irrespective of the temperature during heat treatment.

![Fig. 1. DTA and thermal expansion profiles of the glass powder with the composition of 10MgO-40CaO-50SiO₂ in mol%](image-url)
4. Discussion

The results from Figs. 2 and 3 indicate that glass-ceramics containing continuous pores of more than 500 μm in diameter can be synthesized through a simple sintering process of glass powders. It is documented that continuous pores more than 150 μm in diameter in materials are effective for inducing bone ingrowth. The porous glass-ceramics prepared in this study are therefore expected to make a morphological fixation to surrounding bony tissues in the living body.

Judging from the results in Fig. 4, we can see that the prepared porous glass-ceramics have the ability to deposit apatite in Kokubo solution. This is supported by the results indicating apatite formation on dense glass-ceramics with the same composition (see Fig. 5). Thus, the porous glass-ceramics would also form an apatite layer on their surfaces when implanted in the body, and make direct bonds to living bone through the formed apatite layer. The apatite formation on the glass-ceramics is governed by release of Ca$^{2+}$ and formation of a silanol (Si-OH) group that may induce heterogeneous nucleation of apatite in the physiological environment. Formation of a hydrated silica gel layer on the glass-ceramics may lead to benefits on increase in the number of nucleation sites. But a thick layer of silica hydrogel relates to a decrease in bonding strength between the glass-ceramics and bone after the direct bonding was constructed. Glass-ceramic A-W, in the system MgO–CaO–SiO$_2$–P$_2$O$_5$–CaF$_2$, may form a very thin layer of silanol groups, because the silica gel layer could not be observed at the interface between the glass-ceramic and apatite layer. We can therefore expect that MgO–containing glasses and glass-ceramics are useful to construct a controlled interface structure having a thin silica gel. This phenomena relates on the rate of dissolution of the glasses and glass-ceramics with an appropriate rate. Control of the dissolution may govern bioresorbability of the designed glass-ceramics. Glass-ceramics in the system MgO–CaO–SiO$_2$ therefore give bioactive and bioresorbable materials for bone substitutes and tissue engineering for bone regeneration utilizing the osteoconductivity and porous structure of the glass-ceramics. Optimization of their composition for clinical applications should be made in the further studies by quantitatively examining the rate of apatite deposition and dissolution of the glass-ceramics in body environment.

5. Conclusions

It was found that bioactive porous glass-ceramics in the system MgO–CaO–SiO$_2$ were fabricated through the sintering process of glass powders. The prepared glass-ceramics have para-wollastonite and diopside as crystalline phases. They are useful for novel bone-repairing materials, and have a high potential as scaffold materials for tissue engineering, because of their ability to form apatite in the body environment and easy fabrication of continuous pores of more than 500 μm in diameter.

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Fig. 4. SEM photographs and EDX profiles of the surfaces of porous specimens heat-treated at 770 (upper) and 1100°C (lower), which were soaked in Kokubo solution for 7 days.

Fig. 5. XRD patterns of the dense specimens heat-treated at various temperatures, which were soaked in Kokubo solution for 14 days.

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