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Ion release from $SrO–CaO–TiO_2–P_2O_5$ glasses in Tris buffer solution

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SrO-containing calcium phosphate invert glasses, $(60–x)CaO·xSrO·30P_2O_5·7Na_2O·3TiO_2$ (mol%, x = 0–60), which are expected to inhibit bone resorption by osteoclast and enhance bone formation, were prepared and their ion release behaviors in Tris buffer solution were estimated. The glass containing 20 mol% of SrO showed the smallest amount of the dissolved ions in the present work. Laser Raman spectra showed that the peaks of phosphate groups and TiO_y polyhedral groups red-shifted with increasing the SrO content in the glasses. The shift was suggested to be due to decrease in bonding strength between cations and phosphate groups or TiO_y polyhedral groups in the glasses. In the case of the glasses containing SrO over 20 mol%, no shifts of Raman peaks due to the TiO_y polyhedra were observed. The TiO_y (y = 4 or 6) polyhedra in the glasses can coordinate with cations up to 18 mol% since they contain 3 mol% of TiO_2. Sr^{2+} ions are supposed from the shift behavior of the Raman peaks to preferentially coordinate with the TiO_y polyhedra; the formation of this structure would induce decrease in the ion amounts released from the glasses containing 0–20 mol% of SrO.

Key-words : Calcium phosphate glass, Strontium, Structure, Ion release, Biomaterial

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1. Introduction

Titanium and its alloy are clinically used as artificial implant materials, since they show high strength and good biocompatibility, but they make no chemical bond to living bone. Calcium phosphate coating is one of the useful methods for improving the bioactivity of the metals. Our group have focused on bioactive glasses and glass-ceramics in the calcium-phosphate-based system and successfully prepared invert glasses of $60CaO·30P_2O_5·(10–z)Na_2O·zTiO_2$ (mol%, z = 0–10), containing ortho- and pyro-phosphate groups, by a conventional melting method.[1] Hydroxyapatite deposits on the glass surfaces after soaking in simulated body fluid (SBF).[2] Powders of the glasses have good sinterability, when heated at 850°C, and the resulting glass-ceramics also show the hydroxyapatite-forming ability in SBF.[3] The glass-ceramics can be successfully coated on a Ti–29Nb–13Ta–4.6Zr alloy (TNTZ)[4),5] having lower Young's modulus in comparison with the conventional alloys.[6),7]

Small amounts of ions, such as Si^{4+}, Sr^{2+}, Zn^{2+} and so on, were reported to enhance bone formation.[8)–11] Sr^{2+} ion was reported to show two specific effects on cell functions, the inhibition of bone resorption and the enhancement of bone formation.[9),12),13] Strontium ranelate (S129112–2, PROTELOS®) was invented for controlling the bone fracture of osteoporosis patients.[14),15] The ion inhibits osteoclasts differentiation and stimulate preoteoblasts and osteoblasts to replicate and differentiate.[12),16)–18] Several research groups reported strontium-containing biomaterials.[19),20] Xue et al. prepared a strontium-containing apatite and evaluated its abilities for the cell adhesion, proliferation and differentiation; the strontium-containing apatite was superior in the ability of cell adhesion in comparison with a conventional apatite. The numbers of the cells on the strontium-containing apatite and the conventional one, after 14 d of culturing were 15 and 9 times higher than those on each sample after 3 d of culturing, respectively. The cells cultured on the strontium-containing apatite more expressed alkaline phosphatase (ALP) and osteopontin (OPN) in comparison with that cultured on the conventional one.[19] Qiu et al. developed calcium polyphosphate substituted with strontium. The proliferation of osteoblast-like clonal cell line (ROS17/2.8) and ALP expression were much better on the calcium polyphosphate substituted with < 20 mol% strontium than on the unsubstituted one.[20]

Strontium-containing biodegradable materials, which can release Sr^{2+} ions slowly, may enhance bone formation through the stimulation of cell functions by the ions. Glasses and glass-ceramics are expected to be useful in the preparation of the materials.

The present work was performed as a fundamental study for developing a new type of glass with strontium-ion releasability; calcium phosphate invert glasses containing SrO were prepared by a conventional melting method and evaluated in their solubilities in Tris buffer solution (pH 7.40), assuming to the body system. Tris buffer solution was used to evaluate the solubilities of the glasses clearly because the solution contains no ions which were included in the glasses. The relationship between their ion-releasing behaviors and glass structures was discussed.

2. Experimental procedure

$(60–x)CaO·xSrO·30P_2O_5·7Na_2O·3TiO_2$ (mol%, x = 0–60, nominal composition) were prepared. Glass batches were prepared using $CaCO_3$ (99.5%), $SrCO_3$ (98%), H_3PO_4 (85% liquid), Na_2CO_3 (99.5%) and TiO_2 (99.5%). All reagents were purchased from Kishida Chemical Co., Ltd. The reagents were mixed with distilled water, to make a slurry. The slurry was dried at 140°C overnight. The resulting product was melted at 1400°C for 30 min

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and then quenched on a stainless steel, resulting in the formation of the glasses. The glasses were pulverized into 125–300 μm in size using an alumina mortar. Tris buffer solution was prepared using 6.118 g of Tris hydroxymethyl aminomethene ($NH_2C(CH_2OH)_3$, Kishida Chemical Co., Ltd.) and 1 liter of distilled water and its pH was adjusted to 7.40 at 37°C using hydrochloric acid. A 15 mg of the glass powders was soaked in 15 ml of Tris buffer solution at 37°C for 1 to 5 d. The amounts of the ions (Ca^{2+}, Sr^{2+}, P^{5+}, Na^{+}, Ti^{4+}) dissolved from the glasses in Tris buffer solution were evaluated by inductively coupled plasma atomic emission spectroscopy (ICP–AES, Shimadzu Co., ICPS–7000). Glass transition temperature (T_g) and crystallization temperature (T_c) of the resulting glasses were estimated from differential thermal analysis (DTA, Rigaku Co., Thermo plus, TG8120), which was performed until 1000°C at a heating rate of 5°C/min. Glass structure was examined by laser Raman spectroscopy (JASCO Co., NRS–2000, 514.4 nm).

3. Results

Figure 1 shows ion amounts dissolved from the glasses in Tris buffer solution. The ratios of the dissolved ion-amount to the total ion-amount in the various glasses were plotted against the SrO contents. In the case of Ca^{2+} and Sr^{2+} ions, the ratio was shown as the sum of their dissolved amounts since CaO was substituted with SrO in the glasses. The ion amounts dissolved from the glass containing 60 mol% of SrO were larger than those from the glasses containing no SrO. The amounts dissolved from the glasses containing 10–20 mol% of SrO showed smaller than those from the others.

Figure 2 shows glass transition temperature (T_g), crystallization temperature (T_c) and $(T_c–T_g)/T_g$. $(T_c–T_g)/T_g$ indicates a degree of glassification.[21] The large values are related to the easy glassification. The values of the glasses containing 10–30 mol% of SrO were relatively large and decrease with increasing the SrO content. The clear glasses with the 10–30 mol% of SrO could be much easily prepared.

Figure 3(a) shows laser Raman spectra of the glasses. The peaks corresponding to phosphate groups are as follows; 1040 cm^{-1}:P–O stretching due to non-bridging oxygen Q^1 species, 950 cm^{-1}:P–O stretching due to non-bridging oxygen Q^0 species and 740 cm^{-1}:P–O–P stretching due to bridging oxygen Q^1 species[22], where Q^0 and Q^1 indicate orthophosphate (PO_4^{3-}) and pyrophosphate ($P_2O_7^{4-}$), respectively. The peaks corresponding to TiO_y polyhedra are as follows; 880 cm^{-1}:TiO_4 tetrahedra and 650 cm^{-1}:TiO_6 octahedra.[23] The peaks due to Q^0, Q^1, TiO_4 and TiO_6 appeared in the all of the spectra. Figure 3(b) shows the relationship between Raman shift of the phosphate groups and the SrO content in the glasses. The wavenumbers at

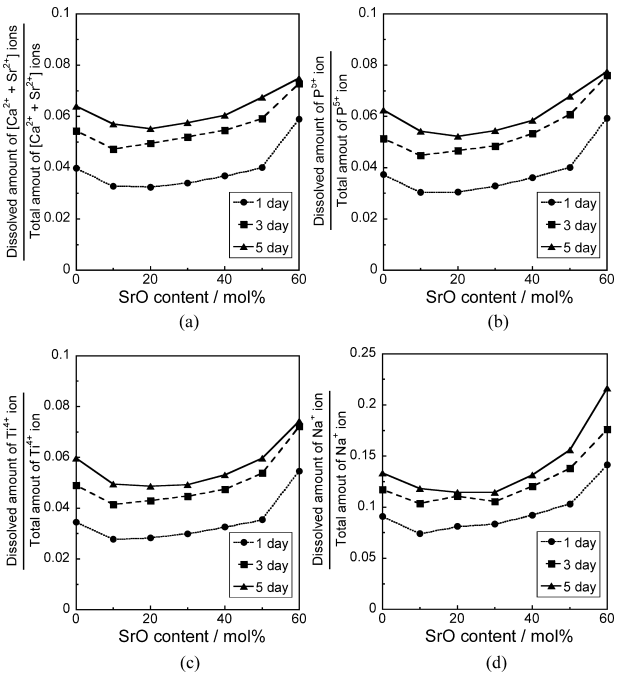

Fig. 1. Ion amounts dissolved from the glasses in Tris buffer solution after soaking for 1–5 d. (a) Ca^{2+}+Sr^{2+}, (b) P^{5+}, (c) Ti^{4+} and (d) Na^{+}.

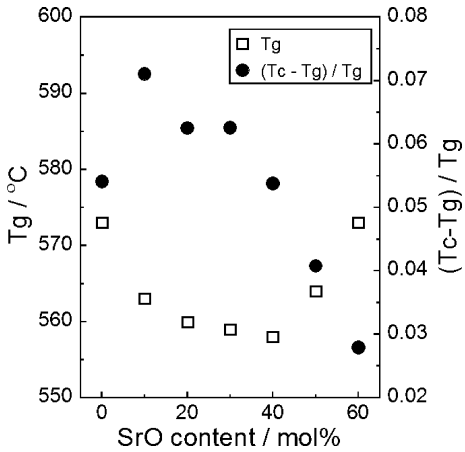

Fig. 2. $(T_c–T_g)/T_g$ values of the glasses.

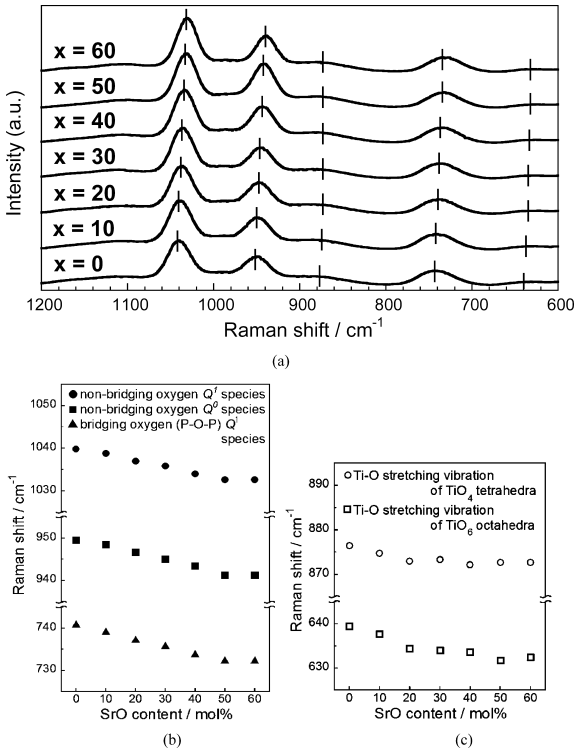

Fig. 3. Laser Raman spectra of the glasses. (a) The spectra of the glasses, (b) the wavenumbers of the peaks due to Q^0 and Q^1 groups of the glasses as a function of the SrO content and (c) the wavenumbers of the peaks due to Ti–O groups of the glasses as a function of the SrO content.

the tops of Q^0 and Q^1 peaks were plotted. All peaks due to Q^0 and Q^1 groups red-shift with increasing the SrO content. Figure 3(c) shows the relationship between Raman shift of TiO_y polyhedral groups and the SrO content in the glasses. The peaks due to the TiO_4 tetrahedra and the TiO_6 octahedra red-shift by 4 cm^{-1} in the range of 0 and 20 mol% of the SrO content, while they do not shift over 20 mol%.

4. Discussion

The dissolved amounts of ions from the glasses are small in the range of 10–30 mol% of the SrO content, as shown in Fig. 1. The $(T_c–T_g)/T_g$ values of the glasses containing 10–30 mol% of SrO are high, as shown in Fig. 2. This may indicate that the glasses have larger bonding strength for the network formation in comparison with those containing > 40 mol% of SrO. In Fig. 3(c), the Raman peaks of TiO_y polyhedra red-shift with increasing the SrO content in the ragne of 0 to 20 mol%. These glasses contain 3 mol% of TiO_2, which has the 4- or 6-fold coordination. TiO_y polyhedral groups in the glasses would be able to coordinate with 12–18 mol% of cations. It is may be supposed that Sr^{2+} ions coordinate preferentially with TiO_y polyhedra in the glasses. Some of the Sr^{2+} ions are expected to be coordinated with Q^0 and Q^1 groups and make a network structure in the invert glasses containing SrO over 20 mol%.

Sr^{2+} and Ca^{2+} ions have the 8-fold coordination. Radius of Sr^{2+} and Ca^{2+} ions are 1.27 Å and 1.06 Å, respectively. Ditzel suggested the field strength that is the simplified Coulomb's force of ions in oxides.

$$F = \frac{Z}{a^2} \text{ (valance/Å}^2\text{)} \quad (1)$$

F is a field strength, Z is a cation valance and a is a distance between cation and anion. The field strengths of Sr^{2+} and Ca^{2+} ions in oxides are 0.28 and 0.33, respectively.[24] Sr^{2+} ion has the lower field strength than Ca^{2+} ion, which means Sr–O bond more weakly than Ca–O.

Nelson et al. reported that Raman peaks of phosphate groups in phosphate glasses containing alkaline earth metals red-shift with increasing the atomic number of the metals.[25] This is due to increase in the angle of O–P–O bonding in PO_4 tetrahedra with decrease in the field strength of the metals, which depend on their atomic numbers. When O–P–O angle increases, the peaks due to the bond red-shift, due to decrease in its bonding energy.[26] The bonding strength of Sr^{2+} ion with oxide is weaker than that of Ca^{2+} ion. Therefore, the peaks of phosphate groups red-shift with increasing SrO content, as shown in Fig. 3(b).

The dissolved amounts of ions from the glass containing no SrO is larger than those from the glasses containing 10–20 mol% of SrO. It is supposed that Sr^{2+} ions coordinate preferentially with TiO_y polyhedra. TiO_y polyhedra in phosphate glasses contributes to induce their high chemical durability.[27] As a result, the chemical durabilities of the glasses may be improved by including 10–20 mol% SrO. The dissolved ion amount from the glass containing 60 mol% of SrO is larger than that from the glass containing no SrO. This may indicate that Ca^{2+} ion, of which the field strength is larger than that of Sr^{2+} ion, bonds more strongly with phosphate groups to make an invert-type network structure.

The present work is important as a fundamental study for controlling the amount of strontium-ion release from the calcium phosphate invert glasses. Barbara et al. reported that 0.1–1 mM (8–80 ppm) of strontium ranelate inhibit bone resorption and enhance bone formation.[28] In the glasses prepared in the present work, > 0.1 mM of Sr^{2+} ions were released from the glasses containing more than 20 mol% of SrO, while < 1 mM of the ions were released from the glass containing of 60 mol% of SrO. Calcium is one of the important elements for bone formation. It may be possible to prepare calcium phosphate invert glasses for enhancing bone formation when they contain the both Ca^{2+} and Sr^{2+} ions.

5. Summary

SrO-containing calcium phosphate invert glasses were prepared and their ion releasing behaviors were evaluated. The dissolved amounts of the glasses containing 10–30 mol% of SrO were small, since Sr^{2+} ions were supposed to coordinated preferentially with TiO_y polyhedra in the glasses. The glass containing 60 mol% of SrO dissolved larger amounts of ions than that containing 0 mol%. The dissolution behavior may be influenced by the lower field strength of Sr^{2+} ion in the glasses than that of Ca^{2+} ion. Due to difference in the field strength between Ca^{2+} and Sr^{2+} ions, the Raman peaks due to phosphate groups red-shifted with increasing the SrO content, while those due to TiO_y polyhedral groups in the glasses containing 0–20 mol% of SrO red-shifted. The ion release from the glasses is suggested to be influenced by the coordination of Sr^{2+} ion with TiO_y group. These results are expected to give an effective guideline for designing glassy materials with the releasing ability of Sr^{2+} ion.

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