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DISSOLUTION BEHAVIOR OF MgO-CaO-P2O5-TiO2 INVERT GLASSES

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Abstract: Magnesium is an essential element to the human body, and Mg2+ ion can work to enhance cell adhesion, proliferation, differentiation, and mineralization. From the viewpoint of inorganic glass formation, MgO can be classified as an intermediate, that improves the glass-forming and ion-releasing abilities. The present work reports fundamental data for designing MgO-containing bioactive phosphate glasses with manipulated ion-releasability. MgO-CaO-P2O5-TiO2 invert glasses were prepared, in which TiO2 was substituted by MgO, and their structure and dissolution behavior were examined. Magnesium in the glasses were preferentially bonded to orthophosphate groups. The glass-forming ability and chemical durability of the glasses decreased with increasing MgO content, since P-O-Mg bonds are weaker than P-O-Ti bonds. In contrast, the ion-releasing ability of the glasses improved with increasing MgO content, and the released amount of Mg2+ ion was expected to be within the range suitable to stimulate cell adhesion and proliferation.

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INTRODUCTION

Calcium phosphate invert glasses (PIGs), containing intermediate oxides, have been the object of focus by our group in the past1-3. PIGs are composed of short phosphate groups, such as ortho-(Q10) and pyro-phosphate (Q20), that make bonds with intermediates, like P-O-Ti. These bonds support the formation of the glass network4,4. TiO2-containing PIG, 60CaO-30P2O5-10TiO2, and its crystallized one exhibited apatite-forming ability in a simulated body fluid (SBF)5,6. This glass-ceramic, which was coated on a titanium alloy, indicated direct bond to natural bone in animal tests2.

Magnesium is an essential element to the human body, where Mg2+ ion concentration influences bone strength7. In our previous work, the Mg2+ ion was shown to enhance cell adhesion and upregulate proliferation, differentiation, and mineralization of osteoblasts8-11. In general, MgO in glass can be classified as an intermediate, that acts both as a glass network former and/or a modifier12. The role of MgO in phosphate glasses can be determined by the structure of phosphate groups13. Recently, we reported MgO-containing phosphate invert glasses, composed of Q10 and/or Q20 groups14,15. MgO in PIGs preferentially bonds to Q20 groups to form a P-O-Mg bond, resulting in the improvement of their glass-forming ability16-18. In contrast, a P-O-Mg bond, due to its easier hydrolysis compared to other similar bonds19, decreases the chemical durability of PIGs16-17. Hence, including MgO in PIGs is an important concept for designing bioactive phosphate glasses with the invert composition.

In this work, MgO was included to ternary CaO-P2O5-TiO2 invert glasses, substituting TiO2, as we report fundamental data for designing MgO-containing bioactive phosphate glasses with manipulated ion-releasability. The structure and ion-releasing behavior of the prepared MgO-CaO-P2O5-TiO2 glasses were evaluated.

MATERIALS AND METHODS

MgO-containing PIGs with nominal compositions of xMgO-60CaO-30P2O5-(10-x)TiO2 (mol%, x = 0, 5, 10), denoted as PIG-xMg glasses, were prepared. MgO, CaCO3, H3PO4 (liquid), and TiO2 were used for preparing the batches. All the reagents were purchased from Kishida Chemical Co., Japan. The reagents were mixed with distilled water to make a slurry and subsequently dried at 140 °C. The each prepared batch was melted in a platinum crucible at 1500 °C for 30 min, and the melt was quenched by being pressed using stainless steel plates to obtain a glass.

The thermal properties of PIG-xMg glasses were examined using differential thermal analysis (DTA; Thermo plus TG8120, 5 K/min, Rigaku Co., Japan). Their glass transition and onset of crystallization temperatures (Tg and Tx, respectively) were obtained from the DTA trace.

Their glass structures were analyzed by laser Raman spectroscopy (XploRa; HORIBA Ltd., Japan).
PIG-\(x\)Mg glasses were excited at 532 nm by a Nd:YAG laser; exposure time was 10 s with a cumulative number of 8. The spectra were obtained in a region of 500 ~ 1400 cm\(^{-1}\).

Dissolution behavior of each PIG-\(x\)Mg glass was evaluated using glass particles with the sizes of 125 ~ 250 \(\mu\)m in Tris-HCl buffer solution (TBS). TBS was prepared by dissolving 6.118 g of NH\(_4\)C(CH\(_2\)OH)\(_2\) (Kishida Chemical Co., Japan) in 1 L of distilled water and adjusting pH 7.4 at 37 °C. Fifteen mg of the glass particles were soaked in 15 mL of TBS for 5 d at 37 °C. Ion concentrations of the resulting solutions were measured by inductively coupled plasma atomic emission spectroscopy (ICP-AES; ICPS-7000, Shimadzu Co., Japan) for Mg, Ca, P, and Ti elements. The molar-releasing fraction for each element was obtained by the following equation\(^{17,18}\):

\[
\text{Release percentage} (\%) = \left( \frac{C_{\text{ion}}}{M_{\text{element}} \times \text{Frac}_{\text{mol}}} \right) \times \left( \frac{m_{\text{glass}} \times V_{\text{solution}}}{v_{\text{atom}} \times \text{Nom}} \right) \times 10^5
\]  

where \(C_{\text{ion}}\) is the concentration of the element of interest in mg·L\(^{-1}\), \(M_{\text{element}} (g)\) is the atomic weight of the respective element, \(\text{Frac}_{\text{mol}}\) is the nominal molar fraction of the element in the glass, \(m_{\text{glass}} (g)\) is the molar weight of the glass, \(v_{\text{atom}} (g)\) is the mass of the soaked glass sample, and \(V_{\text{solution}} (L)\) is the volume of the soaking solution.

RESULTS

Figure 1 shows \(T_g\) and \(T_c\) for the three types of PIG-\(x\)Mg glasses. The properties exhibited decreasing tendency with increasing MgO content in PIG-\(x\)Mg. The \(T_g\) and \(T_c\) decreased from 646 to 625 °C, and 703 to 672 °C, respectively.

![Figure 1](image1.png)

**FIGURE 1.** \(T_g\) and \(T_c\) of PIG-\(x\)Mg glasses.

Laser Raman spectra of the three PIG-\(x\)Mg glasses are shown in Figure 2. The phosphate groups showed Raman bands corresponding to \(Q^0_p\) and \(Q^4_p\) groups\(^{13,20}\), including POP symmetric stretching mode of bridging oxygen in \(Q^0_p\) (742 cm\(^{-1}\)), PO\(_3\) symmetric stretching mode of non-bridging oxygen in \(Q^4_p\) (948 cm\(^{-1}\)), PO\(_2\) symmetric stretching mode of non-bridging oxygen in \(Q^4_p\) (1038 cm\(^{-1}\)), and P-O stretching of \(Q^4_p\) chain terminator (1120 cm\(^{-1}\)). Ti-O groups\(^{12,21}\) showed bands corresponding to Ti-O stretching mode of TiO\(_6\) octahedron (643 cm\(^{-1}\)), Ti-O stretching mode of TiO\(_4\) tetrahedron (880 cm\(^{-1}\)), and P-O-Ti bonds (990 cm\(^{-1}\)).

![Figure 2](image2.png)

**FIGURE 2.** Laser Raman spectra of PIG-\(x\)Mg glasses.

The Raman spectra of PIG-\(x\)Mg glasses were simulated by assuming Gaussian lines in the range of 600 ~ 1400 cm\(^{-1}\) for quantitative analysis. Figure 3

![Figure 3](image3.png)

**FIGURE 3.** (a) Raman peak top positions of phosphate groups and (b) normalized integrated intensities of phosphate groups in PIG-\(x\)Mg glasses.
(a) shows the peak top positions of phosphate $q_p^0$ and $q_p^1$ groups in the glasses. The positions of $(PO_4)_{sym}$ (948 cm$^{-1}$) and $Q_{p-term}^1$ (1120 cm$^{-1}$) were blue- and red-shifted, respectively, with increasing MgO content in the glasses, while the positions of POP$_{sym}$ (742 cm$^{-1}$) and $(PO_4)_{sym}$ (1038 cm$^{-1}$) displayed no significant difference after the introduction of MgO. The integrated intensities of the phosphate groups were normalized by the sum of $I(POP_{sym}) + I((PO_4)_{sym}) + I(POP^2_{term})$, as shown in Figure 3 (b), where $I$ denotes each peak’s amplitude. With increasing MgO content in PIG-xMg, integrated intensities of $(PO_4)_{sym}$ and $(PO_4)_{term}$ also increased, whereas those of POP$_{sym}$ and $Q_{p-term}$ decreased.

Figure 4 shows the percentages of calcium, phosphate, titanium, and magnesium ions released from PIG-xMg glasses, as a function of MgO content. Their released amounts increased with the soaking time. In particular, the amounts of Ca$^{2+}$ and phosphate ions increased linearly with increasing MgO content. The percentage of Ti ion from PIG-0Mg glass was similar to that measured for Ca$^{2+}$ and phosphate ions, whereas the (Ti + Mg) and Mg percentages for the PIG-5Mg and PIG-10Mg glasses, respectively, were smaller. The Mg$^{2+}$ ion amounts released from the PIG-5Mg and PIG-10Mg glasses at day 5 were approximately 0.02 and 0.04 mM, respectively.

**DISCUSSION**

According to Dietzel, MgO is classified as an intermediate. Karakassides et al. reported that MgO in phosphate glasses composed of $Q_p^0$ and/or $Q_{p-term}$ groups acts as a network former. Additionally, Mg in magnesium phosphate invert glasses acts as a network former to form P-O-Mg bonds and also improves the glass-forming ability, as reported in our previous work. $T_p$ and $T_{term}$ for PIG-xMg glasses decreased with increasing MgO content. PIG-0Mg and -5Mg glasses containing TiO$_2$ include P-O-Ti bonds (Figure 2). The bonding strength of cation-oxygen in the glass network structure can be discussed by field strength ($F$) as calculated with $F = Z_v / d^2 \ (valence / \text{Å}^2)$, where $Z_v$ is the valence of the cation and $d$ is the interatomic distance between the cation and oxygen ion. Mg-O and Ti-O is 0.53 and 1.17 for their four-coordinated structures, and 0.45 and 1.04 for their six-coordinated structures, respectively. Mg-O indicated smaller $F$ than Ti-O, and the strength of P-O-Mg bonds was smaller than that of P-O-Ti as well. Therefore, the glass network structure of PIG-xMg glasses loosened with increasing MgO content, due to substitution of the stronger P-O-Ti bond by the weaker P-O-Mg bond. As a result, $T_p$ and $T_{term}$ decreased with increasing MgO content in PIG-xMg glasses.

The Raman peak top positions of $(PO_4)_{sym}$ and $Q_{p-term}^1$ were shifted with increasing MgO content. When the substituting element has a smaller bonding strength than the existing one, around the bands of interest, the peak top position would red-shift. When the substituting element has a larger bonding strength than the existing one then the peak top position exhibits blue-shift. In our previous work, phosphate groups in PIGs were blue-shifted when CaO was substituted by MgO, and were red-shifted when CaO was substituted by SrO, where the $F$ of Mg, Ca, Sr were 0.45, 0.33, and 0.28, respectively. Additionally, Mg in PIGs preferentially bonds to $Q_p^0$ groups to form P-O-Mg bonds. Blue-shift of $(PO_4)_{sym}$ peak top positions with increasing MgO content in the glasses originates from magnesium preferentially bonding to $Q_p^0$ groups when replacing calcium. In contrast, $Q_{p-term}^1$ peak top positions were red-shifted with increasing the MgO content.Titanium in PIGs preferentially forms P-O-Ti bonds with terminal $Q_p^0$ groups. Thus, TiO$_2$ polyhedron in the glasses preferentially bonded to $Q_{p-term}^1$ groups to form P-O-Ti bonds. With increasing MgO content, the bonding structure of $Q_{p-term}^1$ groups was changed from P-O-Ti to P-O-Mg/Ca.

Consequently, the peak top position of $Q_{p-term}^1$ groups was red-shifted with increasing MgO content, since the strength of P-O-Mg/Ca bonds is smaller than that of P-O-Ti bonds. On the contrary, there were no
significant changes in the peak top positions of (PO)_{3 sym} and POP_{sym} groups, since magnesium preferentially bonded to Q_{p}^{0} groups.

The integrated intensities of POP_{sym} and (PO)_{3 sym} groups decreased and increased, respectively, with increasing MgO content in PIG-xMg glasses. This would indicate that the substitution of CaO by MgO in PIGs induced the breaking of phosphate chains.\(^16\) Thus, introduction of magnesium into PIGs breaks Q_{p} groups, resulting in the formation of Q_{p}^{0} groups through P-O-Mg bonds. Raman intensities of Ti-O groups, such as TiO_{4} polyhedron and P-O-Ti bonds in the glasses decreased with increasing MgO content. Thus, the Raman intensity of the Q_{p}^{0} group is related to the amount of P-O-Ti bonds in the glasses. In contrast, the integrated intensity of the (PO)_{3 sym} group increased with increasing MgO content, and the peak top position did not change. This would be represented by the fact that P-O-Ca bonds, in PIG-xMg glasses increased with increasing MgO content. Consequently, Q_{p}^{0} and (PO)_{3 sym} groups in the glasses decreased and increased, respectively, with increasing MgO content, since the bonding structure of Q_{p} groups is changed from P-O-Ti to P-O-Ca bonds.

Chemical durability of PIG-xMg glasses was decreased with increasing MgO content, since P-O-Ti bonds were replaced with weaker P-O-Mg/Ca bonds, as discussed above. The released amounts of (Ti + Mg) ions from PIG-5Mg and PIG-10Mg were smaller compared to those of calcium and phosphate ions. With increasing MgO content in the glasses, Q_{p}^{0} and Q_{p} groups preferentially bonded through P-O-Mg and P-O-Ca bonds, respectively, as discussed above. The strength of the P-O-Mg bond is larger than that of P-O-Ca, due to the larger F value of Mg compared to that of Ca. P-O-Ca bonds in aqueous solution would be more easily hydrolyzed than P-O-Mg bonds. Thus, Mg\(^{2+}\) ion percentage released from PIG-10Mg glass exhibited smaller compared to those of Ca\(^{2+}\) and phosphate ions. The ion percentages of Ti and Mg released from PIG-5Mg glass at day 5 were 3.82% and 3.28%, respectively. The ion percentage of Ti was comparable to that of calcium and phosphate ions, since Ti bonded with Q_{p} groups and Ca preferentially coordinated with that structure. By contrast, the ion percentage of Mg released from PIG-5Mg glass exhibited smaller, due to the larger strength of the P-O-Mg bond compared to that of P-O-Ca. In our previous work, Mg\(^{2+}\) ion amounts of 0.02 to 0.03 mM were suitable to enhance cell adhesion and proliferation for mouse osteoblastic-like cell\(^1\). PIG-5Mg and PIG-10Mg glasses released Mg\(^{2+}\) ion of 0.02 and 0.04 mM in 5 days, respectively, which would be expected to stimulate cell adhesion and proliferation.

CONCLUSIONS

MgO-containing calcium phosphate invert glasses were prepared, and their structure and dissolution behaviors were evaluated. Magnesium was preferentially bonded to Q_{p}^{0} groups to form P-O-Mg bonds. The chemical durability of the glasses decreased with increasing MgO content, since the strength of P-O-Mg bonds was less than that of the P-O-Ti bonds. The ion-releasing amount from the PIG-xMg glasses increased with increasing MgO content, and the amount of released Mg\(^{2+}\) ion was expected to be in suitable amounts to stimulate cell adhesion and proliferation.

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