ION RELEASE BEHAVIOR OF SILICOPHOSPHATE GLASSES CONTAINING SIX-FOLD COORDINATED SILICON STRUCTURE

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Abstract: To facilitate the efficient use of phosphate-based glasses in various biomedical applications, it is essential to understand the effects of ion-releasing in the living body. In this work, the ion-releasing behavior of silicophosphate glass, designed as a supply source of silicate and phosphate ions that are effective for bone formation, was investigated. Two types of P2O5-SiO2-CaO-Na2O glasses containing 45-50 mol% of P2O5 with both four- and six-fold coordinated silicon structures were prepared. The glass with ~50 mol% of P2O5 content had a higher proportion of six-fold coordinated silicon structure, and it showed a lower ionic release to a simulated body fluid than that with ~45 mol% P2O5 content. The release of the therapeutic ions from the silicophosphate glass can be effectively controlled by choosing their composition.

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INTRODUCTION

Phosphate glass, which shows high solubility in water, is a promising candidate as a drug for supplying inorganic ions essential for enhancing the bone formation.1, 2 Several studies on the compositional dependence of the glass on its solubility have been reported.3, 4 Döhler et al. reported that when the P2O5 content was increased from 35 to 50 mol%, while fixing the CaO/Na2O ratio in P2O5-CaO-Na2O glasses at unity, their ion-releasing rates increased.5 Therapeutic ions, such as phosphate and silicate ions, are known to genetically stimulate osteoblasts and improve the bone-forming ability.6 The P2O5-SiO2-CaO-Na2O silicophosphate glass may be used effectively in continuous ion-releasing systems. However, excessive dissolution of phosphate ions into the living body results in the acidification of tissues around the glass and shows an inhibitory effect on cell viability, proliferation, etc.7 Therefore, to use phosphate glasses as biomaterials, a design to control their ion-releasing rate is required.

Dupree et al. showed that a six-fold coordinated silicon structure (hereafter denoted as [6]Si) was easily formed in silicophosphate glasses containing > 40 mol% of P2O5.8 Nogami et al. reported that, in SrO-P2O5-SiO2 glasses with high P2O5 content, the amount of [6]Si increased with increasing ([P2O5]+[SrO])/[SiO2] ratio.9 Miyabe et al. proposed that sodium ultraphosphate glasses containing < 10 mol% of SiO2 would include Si-O-P bonds (deduced from magic angle spinning nuclear magnetic resonance (MAS-NMR) spectra), and they have a structure with two Na+ ions restricted as charge compensation for SiO45− (based on the density functional theory (DFT) calculations) for clusters around [6]Si.10

The [6]Si formation in phosphate glasses changes their thermal, mechanical, and optical properties, such as the glass transition temperature, Vickers hardness, and refractive index.6, 11-13 Incorporation of [6]Si within the glass is an effective structural design method to control their properties. Therefore, information on the chemical durability of silicophosphate glasses, especially their solubility in water, is important for considering their applications as biomaterials. However, to the best of our knowledge, there are almost no reports on the solubility of silicophosphate glasses containing [6]Si.

In this work, we prepared two types of silicophosphate glasses by fixing the SiO2/Na2O/CaO ratio and examined their ion-releasing behaviors.

MATERIALS AND METHODS

Preparation of glasses: The composition of the two glass samples (glass codes: P45 and P50) prepared in this work are given in Table 1. A glass batch mixture was prepared using the reagents 85.0% H3PO4 liquid (Kishida Chemical, Osaka), 99.0% SiO2 (Kishida Chemical, Osaka), 99.0% NaH2PO4 (Kishida Chemical, Osaka), and 98.0% CaHPO4·2H2O (Wako Pure Chemical, Tokyo). The
mixture was placed in a Teflon® beaker with distilled water (DW) and stirred to form a slurry. It was then dried overnight under an infrared lamp. The resulting powder was melted in a platinum crucible at 1200 °C for 30 min in an electric furnace in air, which was then cast on a stainless-steel plate. This was subsequently quenched using an iron press method to obtain the plate-like glass pieces. This composition of the samples analyzed using an energy dispersive X-ray spectrometer (EDS: JED-2300, JEOL, Tokyo) are shown in Table 1. These values were close to those of the nominal compositions. The powder X-ray diffraction (XRD) pattern of each sample showed a broad halo peak indicating that the samples were amorphous with no evidence of devitrification.

Structural analysis of glasses: The MAS-31P NMR (HNM-ECA A600, JEOL, Tokyo) analysis was performed to examine the local structure around the phosphorous and silicon atoms in the glasses. The 31P MAS-NMR was performed using a 3.2 mm rotor spinning at 20 kHz. A Larmor frequency of 242.96 MHz, a pulse width of 1.1 μs, a recycle delay of 5.02 s, and a cumulated number of 256 scans were used for the experiment. Ammonium dihydrogen phosphate (NH4H2PO4, Kishida Chemical, Osaka) was used as a reference at 1 ppm. For 29Si MAS-NMR analysis, a resonance frequency of 119.24 MHz, a rotation speed of 4 kHz, a pulse width of 5.0 μs, and a recycle delay of 120.0 s were used. The cumulated number of scans were set to 120 to 360 times depending on the signal-to-noise (S/N) ratio of the signal using an 8.0 mm probe. The chemical shift was adjusted using 4-dimethyl 4-silapentane sulfonate sodium to 0 ppm. In the 29Si MAS-NMR measurement, glasses containing 0.1 wt.% of MnCO3, which is a magnetic substance, were prepared and used as samples to shorten the relaxation time.

Measurement of ion release amounts: Inductively coupled plasma atomic emission spectrometry (ICP-AES: ICPS-7000, Shimadzu, Kyoto) was used to examine the released amounts of therapeutic ions, namely phosphate and silicate ions, from the glasses into a simulated body fluid (SBF) proposed by Koko14. Seventy-five milligrams of glass powders, sieved to get particles of sizes ranging from 125 to 250 μm, were immersed in 50 mL of SBF (n = 3) and stirred at 125 rpm in an incubator shaker (KS4000i, IKA, Osaka) at 37 °C for 3 days. The phosphate and silicate ion concentrations in the supernatant after the predetermined periods were measured (n = 3). The phosphate and silicate ions were measured as P5+ and Si4+ ions, respectively, for the convenience of standard reagents.

RESULTS AND DISCUSSION

Figure 1 depicts the 31P MAS-NMR spectra of the glasses and their deconvoluted peaks using a Gaussian function. The peaks due to QP2 and QP3 structures were observed; the glasses were considered to include almost no ortho-(QP0) and pyro-(QP1) phosphate structures. The ratios of the integrated peaks are listed in Table 2. Although the difference in the P2O5 content between the P45 and P50 glasses was only approximately 5%, the former predominantly consisted of QP2 structure, whereas the latter contained a large amount of QP3 structure.

TABLE 1. Nominal and analyzed glass compositions (mol%). Analyzed compositions are shown in round brackets with the standard deviation (n = 5).

| Glass code | P2O5  | SiO2  | Na2O  | CaO  |
|------------|-------|-------|-------|------|
| P45        | 45.0  | 26.0  | 13.8  | 15.2 |
|            | (45.6±0.5) | (21.4±0.7) | (15.6±0.8) | (17.4±0.4) |
| P50        | 50.0  | 23.7  | 12.5  | 13.8 |
|            | (51.0±1.2) | (20.5±1.0) | (14.6±0.7) | (13.9±0.3) |

FIGURE 1. 31P MAS-NMR spectra of P45 and P50 and their deconvoluted peaks using the Gaussian function.
Figure 2 shows the $^{29}$Si MAS-NMR spectra of P45 and P50. Peaks at approximately -120 ppm and -215 ppm were observed for both the glasses and are assigned to 4-fold and 6-fold coordinated silicon structures (denoted by $[^4]$Si and $[^6]$Si, respectively), respectively. The peak intensity of $[^6]$Si in P50 was stronger than that in P45. The MAS-NMR spectra showed that P45 was based on a $Q^{2}_P$ structure with a large amount of $[^4]$Si, while P50 was based on a $Q^{3}_P$ structure with a large amount of $[^6]$Si. Yamashita et al. explained the $[^6]$Si formation in terms of the electron donicity of oxygen (optical basicity). Since phosphorus has a higher electronegativity than silicon, the optical basicity ($\Lambda$) of glass decreases with increasing the P$_2$O$_5$ content. In P$_2$O$_5$-SiO$_2$-Na$_2$O glasses, $[^6]$Si formed in the glasses less than $\Lambda = 0.48$, which is the $\Lambda$ value of a pure SiO$_2$ glass. That is, the weakening of the electron donicity of oxygen originating from the existence of a large amount of P$_2$O$_5$ is considered to be one of the important factors in the $[^6]$Si formation.

The full widths at half maximum (FWHMs) of the $Q^{2}_P$ and $Q^{3}_P$ peaks are also shown in Table 2. The FWHMs of the $Q^{3}_P$ structures in the glasses are larger than those of the $Q^{2}_P$ structures, and the FWHM of the $Q^{3}_P$ peak in P50 is larger than that in P45. This increase in the FWHM indicates that the electron density distribution around the $Q^{3}_P$ structure has been diversified. Miyabe et al. reported that Si-O-P bonds may form when a small amount of SiO$_2$ was included in a phosphate glass with a large amount of P$_2$O$_5$.

### Table 2. The integrated percentages and FWHMs of deconvoluted $^{31}$P MAS-NMR spectra of P45 and P50.

| Glass code | $Q^{0}_P$ Area (%) | $Q^{1}_P$ Area (%) | FWHM (ppm) | $Q^{2}_P$ Area (%) | FWHM (ppm) | $Q^{3}_P$ Area (%) | FWHM (ppm) |
|------------|-------------------|-------------------|------------|-------------------|------------|-------------------|------------|
| P45        | N.D.              | N.D.              | -          | 64.5              | 10.2       | 35.5              | 14.5       |
| P50        | N.D.              | 0.2              | 2.2        | 21.9              | 9.6        | 77.9              | 18.8       |

N.D.: the structure could not be deconvoluted.

Figure 3 shows the relationship between the pH of the SBF and the immersion time when the glasses were immersed. Although the pH decreased after immersion, the decrease in pH in P50 was controlled better than that in P45. Figure 4 depicts the amount of silicate and phosphate ions released in the SBF after the immersion of the glasses. The amounts of the ions released in P50 were smaller than those in P45. In the case of phosphate glasses without SiO$_2$, such as the P$_2$O$_5$-CaO-Na$_2$O glasses, their solubility in aqueous solutions increase with increasing P$_2$O$_5$ content.

The $Q^{3}_P$ peaks are believed to give information not only on the P-O-P bonds but also on the Si-O-P bonds.
hydrolyzed due to an anti-branching rule.\textsuperscript{17} In the $P_2O_5$-$SiO_2$-$CaO$-$Na_2O$ glasses, it may be considered that $Q^3_P$ and $^{[6]}Si$ form a Si-O-P bond, thereby suppressing their hydrolysis.

**SUMMARY**

In this work, the structures of silicophosphate glasses and their solubilities in an SBF were examined. The MAS-NMR spectra of the glasses showed the wider FWHM of the $Q^3_P$ peak than the $Q^2_P$ peak and the $^{[6]}Si$ formation. Usually, in the case of phosphate glass without $SiO_2$, the ion-releasing rate increases with increasing $P_2O_5$ content. In contrast, in the case of the silicophosphate glasses in this work, the release amounts of ions were controlled by increasing $P_2O_5$ content by 5%. It is expected that the supply of therapeutic ions is adjusted by altering the composition of the silicophosphate glass used.

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