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Basic properties of novel S-PRG filler-containing cement

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This study was aimed to evaluate the effect of a novel surface pre-reacted glass-ionomer (S-PRG) filler-containing cement for root caries. We prepared the cements using five different S-PRG filler amounts (0, 10, 20, 30, and 40 wt%). Compressive strength, ion release, acid buffering capacity, and microstructure of the as-prepared cements were evaluated. The compressive strength was statistically significant; it was highest for 0 wt% S-PRG cement. Ion release in 0 wt% S-PRG was highest for F^- and Al, whereas in 40 wt% S-PRG it was highest for B. For 20, 30, and 40 wt% S-PRG cements, Na and Sr release was higher compared to the other ions. The acid buffering capacity was significantly higher in the 40 wt% S-PRG cement than in the others. In the microstructural analysis, no difference of surface structure was observed among each of the S-PRG filler contents (0–40 wt% S-PRG).

Keywords: S-PRG filler, Root caries, Compressive strength, Ion release, Acid buffering capacity

INTRODUCTION

The oral health of elderly people has improved over the past several decades, which has resulted in decreased tooth loss. However, caries and periodontitis remain problems for elderly people, since they tend to have more teeth than before. In particular, root caries are one of the biggest issues for the oral health of elderly people[1]. Gregory and Hyde reported that untreated root caries were present in 12% of the population aged 65–74 years old and 17% of people over 75[2]. Souza *et al.* reported that the majority of the elderly population has at least one root caries[3]. There has long been worldwide consensus that contraction of root caries clearly increases in elderly populations[4,5]. Thus, root caries is a serious global concern.

The following three materials are normally used to restore root caries: glass ionomer cement (GIC), resin modified glass ionomer cement (RMGIC), and composite resin[4,6]. However, these materials require more evidence to support their clinical effectiveness. Currently, dentists need to make choices which match the needs of each patient, considering the position of the caries, esthetic requirements of the patient, moisture of the environment, and caries risk[7]. In addition, elderly patients easily contract secondary caries due to many complex factors such as reduced production of saliva, genetics, bacterial flora, oral hygiene, and systemic disease. Hence, a combination of knowledge and skills gained through experience are necessary to treat root caries[4,8,9]. Moreover, for some patients, dentists cannot use rotary cutting devices and need to choose atraumatic restorative treatment (ART). ART is a minimally invasive technique that removes caries using only hand excavation[10]. Therefore, it is necessary to develop restorative materials for root caries which can be used with ART.

A surface pre-reacted glass-ionomer (S-PRG) filler can release several kinds of ions. Some papers have reported bacterial inhibition[11-13], tooth remineralization[11,14], and acid buffering capacity[15,16] associated with S-PRG filler-containing materials. When we consider materials compatible with ART, these properties make S-PRG fillers promising as effective restorative materials for root caries. At the moment, however, the application of S-PRG fillers in restorative materials for root caries has not yet been studied.

In the present study, we aimed to assess S-PRG filler-containing cement (0, 10, 20, 30, and 40 wt% S-PRG) for treatment of root caries. We evaluated the properties of these materials, including the compressive strength (a mechanical property), ion release, acid buffering capacity, and microstructure. The hypothesis tested was that increasing S-PRG filler content has positive effects on their properties.

MATERIALS AND METHODS

The study design is schematically explained in Fig. 1.

Preparation of specimens

From a mixture of S-PRG filler and fluoroaluminosilicate

Color figures can be viewed in the online issue, which is available at J-STAGE.

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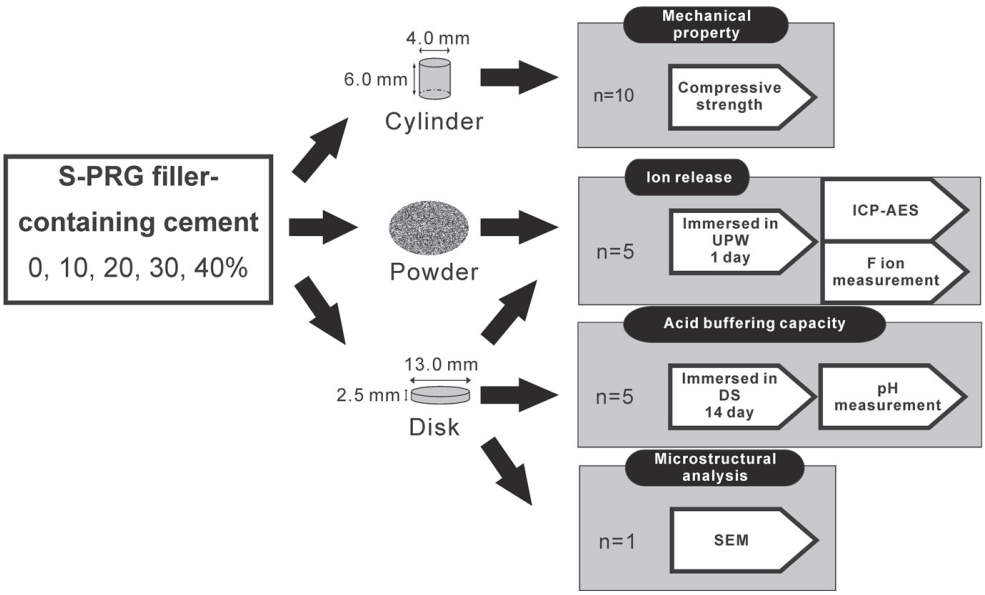

Fig. 1 Flow chart detailing the study setup.

Table 1 S-PRG filler contained cement for root caries

Material		Lot. No.	Composition
Powder	0 wt% S-PRG	RSP00	GIC Filler (8 μm)[1] 100 wt%
	10 wt% S-PRG	RSP01	S-PRG filler (3 μm)[2] 10 wt%, GIC Filler (8 μm) 90 wt%
	20 wt% S-PRG	RSP02	S-PRG filler (3 μm) 20 wt%, GIC Filler (8 μm) 80 wt%
	30 wt% S-PRG	RSP03	S-PRG filler (3 μm) 30 wt%, GIC Filler (8 μm) 70 wt%
	40 wt% S-PRG	RSP04	S-PRG filler (3 μm) 40 wt%, GIC Filler (8 μm) 60 wt%
Liquid		RSL01	Copolymer of Acrylic acid and Tricarboxylic acid Sodium Salt, Water, Others (pH=3.7)

[1] GIC filler: fluoroaluminosilicate glass; [2] S-PRG filler: filler having a three-layered structure, developed by applying PRG technology (forming a glass-ionomer phase only on the surface of a glass filler by means of an acid-base reaction between special surface-treated fluoroboroaluminosilicate glass filler and polyacrylic acid solution)

glass (Shofu, Kyoto, Japan) were prepared (Table 1). The powder and liquid were mixed in the powder/liquid ratio of 2.2 by weight at 23±2°C. The specimens were kept at 37°C in 100% humidity for 24 h.

Compressive strength

Cylinder shaped specimens (6.0 mm thickness, 4.0 mm diameter) were prepared for each S-PRG filler-containing cement (n=10). Compressive strength was measured using a universal testing machine (EZ-LX, Shimadzu, Kyoto, Japan). Specimens were loaded at a crosshead speed of 1 mm/min. The results were statistically analyzed using Weibull analysis (pivotal confidence bounds were calculated using Monte Carlo simulation)[17]. Each specimen was statistically compared to the 95% confidence interval at the B63.2 reliability level. Software packages (R3.4.3 and abrem, R Foundation for Statistical Computing, Vienna, Austria) were used for statistical analysis (α=0.05).

Ion release

To clarify the ion release from S-PRG filler-containing cements, we prepared two different kinds of specimens for each S-PRG filler-containing cement (n=5): disk shaped specimens (2.5 mm thickness, 13.0 mm diameter) and powder. Specimens were immersed in 20 mL of ultrapure water and incubated in conical tubes for 24 h at 37°C. F^- was measured using an ion meter (ORION 4STAR, Thermo Fisher Scientific, Waltham, MA, USA) equipped with a fluoride ion electrode (ORION 9609BN, Thermo Fisher Scientific). In addition, 0.5 mL of ionic strength adjuster (TISAB III, Thermo Fisher Scientific) was added to each solution. Calibration curves for the F^- ion electrode were prepared using NaF solutions (0.4,

1, 10, and 100 ppm). Al, B, Na, and Sr were measured using inductively coupled plasma atomic emission spectroscopy (ICP-AES; Spectro Arcos, Hitachi High-technologies, Tokyo, Japan). Calibration curves for ICP-AES were prepared using a standard solution (XSTC-22, Seishin Trading, Kobe, Japan). The ion measurements were statistically analyzed using the R software package and Shapiro-Wilk test followed by either one-way ANOVA with Tukey's *post hoc* test or Kruskal-Wallis test.

Acid buffering capacity

Disk shaped specimens (2.5 mm thickness, 13.0 mm diameter) were prepared for each S-PRG filler-containing cement (n=5). Specimens were immersed in 5 mL of demineralized solution (DS; 2.2 mmol/L $CaCl_2$, 2.2 mmol/L NaH_2PO_4, 50 mmol/L acetic acid, 0.02% NaN_3, pH 4.5) and incubated in conical tubes for 14 days. The pH changes were measured by a pH meter (pH METER F-52, Horiba, Kyoto, Japan) connected to a pH electrode (9615S-10D, Horiba) at 23±2°C that was calibrated using pH 4.0 and pH 7.0 buffer solutions. The pH measurements were statistically analyzed using nonlinear regression according to equation (1) using the R software package[18].

$$pH=y_0+a(1-e^{-bt})+c(1-e^{-dt}) \quad (1)$$

where t is the time (h) and a, b, c, and d are constants.

Microstructural analysis

Disk shaped specimens (2.5 mm thickness, 13.0 mm diameter) were prepared for each S-PRG filler-containing cement (n=2). The specimens were polished using SiC paper of grit size 1500, followed by polishing with diamond slurries of particle size 0.25–6 μm. The specimens were sputter-coated with Pt and Pd nanoparticles (Quick Auto Coater sc-701AT, Sanyu Electron, Tokyo, Japan) and analyzed using scanning electron microscopy (SEM; Hitachi S-4500, Hitachi, Tokyo, Japan). Secondary electron microscopy (SEM) images were acquired using a voltage of 15 kV. The applied magnification was ×10,000 for each specimen.

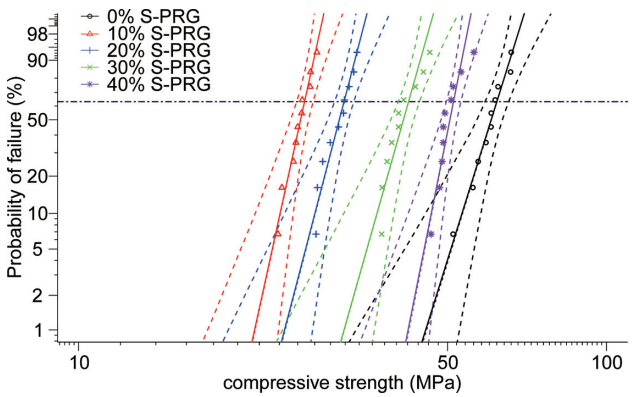

Fig. 2 Graph showing the Weibull analysis for the different S-PRG filler compositions.
Weibull analysis revealed the significantly highest compressive strength for the cements with 0 wt% S-PRG, whereas 10 wt% S-PRG showed the lowest. 20 and 30 wt% S-PRG showed higher compressive strength than 10 wt% S-PRG, although their compressive strengths were significantly lower than that of 40 wt% S-PRG.

RESULTS

Compressive strength

Figure 2 and Table 2 summarize the compressive strength results from the Weibull analysis. Overall, cements containing 0 and 40 wt% S-PRG filler resulted in higher compressive strength, whereas cement samples containing 10 and 20 wt% S-PRG filler showed significantly lower compressive strength. Interestingly, increasing the amount of S-PRG filler from 10 and 20 wt% to 30 and 40 wt% showed substantially higher compressive strength. Weibull analysis indicated significantly higher compressive strength for the cement with 0 wt% S-PRG (62.0 MPa). On the other hand, 40 wt% S-PRG showed the highest Weibull modulus (*i.e.*, the most consistent data).

Table 2 Summary of the compressive strength Weibull analysis results

S-PRG Content (wt%)	n	Weibull modulus m[1]	Characteristic strength σ_0[2] (B63.2)	95% Confidence level at σ_0[3] (B63.2)
0	10	14.8	62.0	56.1–65.3 (a)
10	10	21.1	26.8	25.9–27.8 (e)
20	10	17.7	31.8	30.5–33.2 (d)
30	10	16.3	42.2	40.3–44.3 (c)
40	10	23.2	51.3	49.7–53.0 (b)

[1] The higher the Weibull shape, the more reliable the treatment; [2] the higher the Weibull scale, the higher the compressive strength; [3]different letters within brackets indicate statistical significance at B63.2.

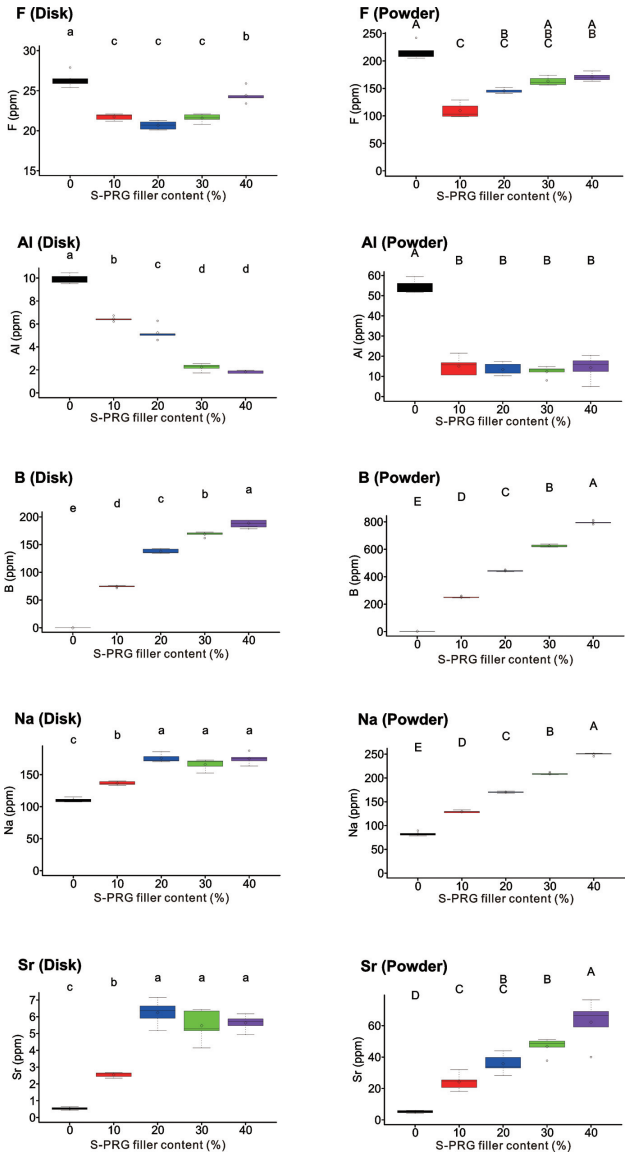

Fig. 3 Graph showing the F^-, Al, B, Na, and Sr release from S-PRG filler-containing cement (disk and powder) in ultrapure water.
One-way ANOVA followed by Tukey's *post hoc* test revealed that F^- and Al resulted in the statistically significantly highest values for 0 wt% S-PRG ($p<0.01$). B, Na, and Sr were the statistically significantly highest for 40 wt% S-PRG ($p<0.01$). Na and Sr (disk) were saturated at 20, 30, and 40 wt% S-PRG.

Ion release

Figure 3 shows the results of F^-, Al, B, Na, and Sr release from S-PRG filler-containing cement in ultrapure water. The trends in ion release are peculiar and obviously differ for each ion. Cement containing 0 wt% S-PRG was highest in F^- (for both the disk and powder samples). Al release from the disk decreased in proportion to the amount of S-PRG filler, whereas Al release from the powder was highest from cement containing no S-PRG (0 wt% S-PRG). On the other hand, B, Na, and Sr (both disk and powder) increased in proportion to the amount of S-PRG filler present in the cement. Both Na and Sr release from the disk saturated at 20 wt% S-PRG.

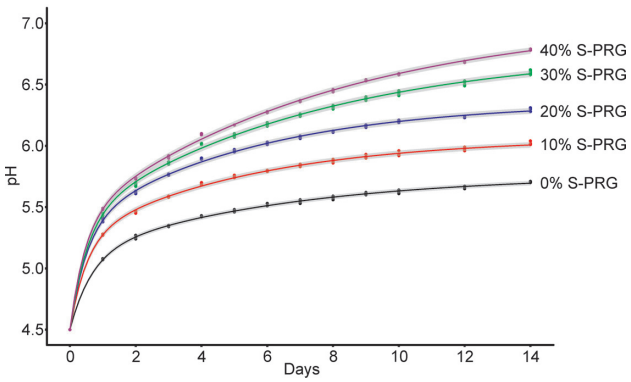

Fig. 4 Graphical summary of the results of pH changes for five S-PRG filler-containing cements immersed in DS over 14 days.
The gray bands around the curves show 95% confidence interval. The initial pH of the DS was 4.5, which increased to pH 6.8 after 14 days of cement immersion. For the 95 % confidence interval calculated with nonlinear regression analysis (gray bands around curves), 20, 30, and 40 wt% S-PRG resulted in significantly higher pH levels on day 1, and 30 and 40 wt% S-PRG resulted in significantly higher pH levels on day 2, as compared to the other grades. The 40 wt% S-PRG filler-containing cement resulted in the significantly highest pH after 4 days. The 0 wt% S-PRG sample was statistically significantly the lowest for all days.

Acid buffering capacity

Figure 4 summarizes the results of pH change for five S-PRG filler-containing cements immersed in DS over 14 days. The pH change as a function of time is described according to equation (1), with the constants summarized in Table 3. The initial pH of the DS was 4.5, which increased to pH 6.8 after 14 days of cement immersion. For the 95% confidence interval calculated with nonlinear regression analysis (gray bands around curves in Fig. 4), 20, 30, and 40 wt% S-PRG resulted in significantly higher pH levels on day 1, and 30 and 40 wt% S-PRG resulted in significantly higher pH on day 2, as compared to the other grade. The 40 wt% S-PRG filler-containing cement resulted in the significantly highest pH after 4 days. The 0 wt% S-PRG sample was statistically significantly the lowest for all days.

Microstructural analysis

Figure 5 shows the results from the microstructural analysis of the specimen surfaces. Several cracks were observed on the specimen surfaces. S-PRG fillers in the matrix were observed for each specimen. The filler

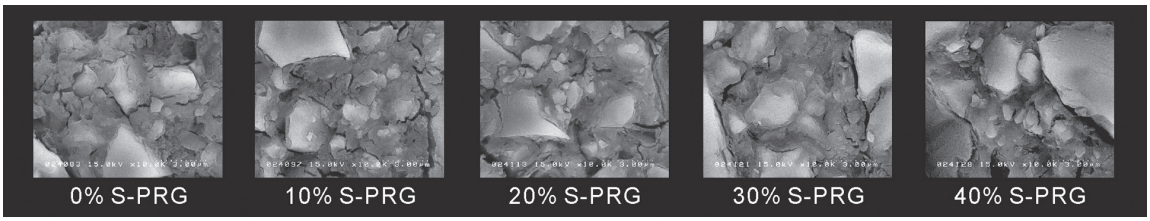

Fig. 5 Representative SEM photomicrographs of the five cements (one without S-PRG filler and four containing S-PGR filler).
Several cracks were observed on the specimen surfaces. The difference of the filler particle size was minimal for all five S-PRG filler contents. No difference of surface structure was observed among each of the S-PRG filler contents (0–40 wt% S-PRG).

Table 3 Summary of the non-linear regression analysis: constants corresponding to equation (1)

S-PRG Content (wt%)	y_0	a	b	c	d
0	4.5	0.6038	0.0634	0.6618	0.0066
10	4.5	0.7302	0.0829	0.8371	0.0078
20	4.5	0.8336	0.0824	1.0290	0.0076
30	4.5	0.8883	0.0806	1.4049	0.0057
40	4.5	0.8874	0.0894	1.6672	0.0053

particle size was comparable for all five cements (one without S-PRG and four containing S-PRG filler). No difference of surface structure was observed among each of the S-PRG filler contents (0–40 wt% S-PRG).

DISCUSSION

Increased S-PRG content in the cements improved ion release and acid buffering capacity, whereas a small amount of S-PRG content tended to decrease compressive strength. Therefore, the hypothesis that increasing S-PRG filler content has positive effects on their properties was partially validated.

Regarding the S-PRG filler content in the cement, we investigated cements containing 0–40 wt% S-PRG filler. In a pilot study, we also prepared cements containing over 50 wt% S-PRG. However, it was quite difficult to control the mixing and handling time, because increased S-PRG content resulted in shorter setting time. For this reason, we used cements with S-PRG filler content up to 40 wt%.

We measured the compressive strength to evaluate a mechanical property of the S-PRG filler-containing cement. According to some recent studies, the reported compressive strength of conventional commercially available GIC was approximately 120–140 MPa[19,20]. In this study, no S-PRG filler (0 wt% S-PRG) resulted in the highest compressive strength. Compressive strength of 0 wt% S-PRG was 60 MPa, which is approximately half the compressive strength of conventional GICs. For conventional GICs, bonding between polycarboxylic acids and released ions results in better strength[21]. However, the pH of the liquid for the S-PRG filler-containing cements (pH=3.7) was higher than that of the conventional GIC (pH<2[22]). The higher pH in the liquid resulted in insufficient matrix formation, which may lead to lower acid attack on the glass during setting[21]. Lower content (10 wt%) of S-PRG filler-containing cements resulted in the lowest compressive strength. One reason for this may be due to competition between the conventional GIC filler and S-PRG filler. The pH increased when S-PRG filler-containing cements were immersed for days due to the acid buffering capacity of S-PRG filler[15]. This resulted in less ion release compared to conventional GICs, which may lead to incomplete setting and lower strength. On the other hand, S-PRG filler can release ions in distilled water[15]. Cements containing higher amount of S-PRG filler resulted in greater ion release, which may lead to more bonding to polycarboxylic acids. Therefore, we assume that the compressive strength of S-PRG filler-containing cements depends on the S-PRG filler content of the powder because of increased bonding to polycarboxylic acids as a result of the setting reaction from the S-PRG filler (S-PRG filler-acid base reaction).

Regarding ion release, S-PRG filler-containing cement released a significant amount of F^- and B. Fujimoto *et al.* reported that S-PRG filler released several ions, such as F^-, Al, B, Na, Sr, and Si[15]. In this study, to quantitatively analyze these ions, an ICP-AES and a fluoride electrode were employed. Moreover, to clarify the influence of S-PRG filler, we investigated both disk shaped specimens made from S-PRG filler-containing

cements and powders themselves. As we showed in Fig. 3, ion release from disks and powder samples differed. Cement that did not contain S-PRG filler (0 wt% S-PRG) was highest in F^- release for both the disk and powder. F^- ion release was low when 10 wt% S-PRG filler was present, and then gradually increased when the amount of S-PRG filler increased up to 40 wt%. This is likely due to F^- anions bonding to some cations present in the S-PRG filler-containing cements, which led to a decrease in F^- ion release (relative to no S-PRG present). As the amount of S-PRG filler increased, on the other hand, F^- ion release also increased due to excess F^- that were unable to bond to cations in the S-PRG. This is one possible explanation for the increasing F^- ion release as a function of increasing S-PRG filler content.

Al release from the disk gradually decreased as S-PRG filler content increased. For Al from powder, on the other hand, only 0 wt% S-PRG resulted in significant Al release. Similar to F^- ion, Al from the powder may bond to some ions from the S-PRG filler-containing cements, and precipitate during centrifugation. Al from the disk did not precipitate, because compounds were already formed. Regarding B release, increased amount of B resulted in higher B release for both the disk and powder. With regard to Na and Sr, increased amounts of Na and Sr resulted in higher Na and Sr release for both the disk and powder. However, both Na and Sr released from the disk showed saturated release at 20 wt% S-PRG. The saturation is probably due to facile elution of ions on the surface of the specimens, whereas ions inside the specimens are released more slowly.

Regarding the antibacterial effect of released ions from S-PRG filler, some studies have reported that F^- and B inhibited growth of *S. mutans*[23]. Kitagawa *et al.* concluded that concentration of F^- at 3.4–13.5 ppm and B at 67.8–271 ppm inhibited the metabolic activity of *S. mutans*, and consequently inhibited their growth[12]. In our study, the maximum concentration of F^- was observed in 40 wt% S-PRG filler-containing cement (24.40 ppm), whereas the maximum concentration of B was observed in 40 wt% S-PRG filler-containing cement (188.73 ppm) (Fig. 3). When we consider the results of the metabolic inhibition of *S. mutans* reported by Kitagawa *et al.*, the concentration of F^- and B in 40 wt% S-PRG filler-containing cement was higher than or equal to the concentration used for inhibiting metabolic activities of *S. mutans*. Hence, F^- and B released from S-PRG filler-containing cement may inhibit *S. mutans* metabolic activities. Further investigation is needed to confirm this hypothesis concerning the antibacterial effect of the S-PRG filler-containing cements.

The ICP-AES measurement also revealed that S-PRG filler-containing cement released Sr. Replacement of hydroxyapatite in teeth with fluoroapatite and strontiumapatite is known to increase the acid resistance of the tooth structure[24]. In a previous study, S-PRG filler was found to aid fluoride uptake and increase the acid resistance zone in dentin[25]. In caries-affected dentine, the penetration depth of F^- was 701 μm whereas that of B was 818 μm[26]. Thuy *et al.* reported that Sr with 1 ppm F^- resulted in a significant reduction in lesion depth, whereas 1 ppm F^- alone did not affect the lesion depth[27]. These results indicate that, in ART with S-PRG filler-containing cement, Sr ion release may contribute to the acid resistance capacity and improvement of demineralization. We are planning to investigate the effect of S-PRG filler-containing cement on the dentine of human teeth.

Regarding the acid buffering capacity, increased S-PRG filler content contributed to the higher acid buffering capacity. Previously, Ma *et al.* reported the influence of S-PRG in a coating resin on the buffering capacity of acid produced by *S. mutans*. They reported that the pH fell to 4.61 for the resin that did not contain S-PRG filler, while the pH increased to 5.13 when S-PRG filler was present in the resin[28]. Based on this result, we assessed the acid buffering capacity with DS (pH 4.5). Improved buffering capacity was observed when we increased the S-PRG filler content (Fig. 4). Comparing the results of the acid buffering capacity at day 1 and the ion release of Na and Sr, similar trends were observed. Thus, Na and Sr may contribute to the acid buffering capacity of cement containing S-PRG. Our results are in agreement with a previous study reported by Kaga *et al.*[29]. Therefore, it can be concluded that increased Sr and Na in S-PRG filler may contribute to improved acid buffering capacity of cement containing S-PRG filler.

With regard to the microstructural analysis by SEM, we could not recognize differences of surface structure in each of the S-PRG filler contents (Fig. 5). Moreover, several cracks were observed on the specimen surface. This could be caused by the pre-treatments for SEM analysis, mainly vacuum evacuation. SEM analysis revealed comparable microstructures for each of the S-PRG filler contents investigated (0–40 wt% S-PRG). Considering the setting characteristics of GIC, the first filler is dissolved by acid attack[30], followed by the degradation of the aluminosilicate network and hydrate formation with Ca^{2+} and Al^{3+} [31]. The cement-containing S-PRG filler released many ions compared with the conventional GIC[15]. Therefore, change in mechanical strength can be attributed to the formation of chemical band by ion release from the S-PRG filler, and not to the cement structure.

Cement containing S-PRG filler showed ion release and the acid buffering capacity. Furthermore, increased S-PRG filler content resulted in higher ion release and the acid buffering capacity. Our results indicate that 40 wt% S-PRG content was the most promising. However, as limitations of this study, it was difficult to investigate the setting mechanism and ion release mechanism of S-PRG filler-containing cement. In a future study, we plan to investigate the influence of S-PRG filler-containing cement on bacterial growth. Moreover, bonding efficacy of the S-PRG filler-containing cement to dentin should be investigated. We need to improve the mechanical properties of the cement containing S-PRG filler due to the high mechanical stress on the root surface cavity[32].

CONCLUSION

In summary, adding S-PRG filler into a glass ionomer-based cement decreased the compressive strength but improved its ion release capabilities and acid buffering capacity. The cement formulation containing 40 wt% S-PRG filler was the best composition of compressive strength and F^- and B release acid buffering capacity. It was found to be the most promising for use as a novel cement.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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