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ORIGINAL ARTICLE

Comparison of different bioglass applications on root caries – A laboratory-based study

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KEYWORDS

Root caries;
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Profilometry;
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Scanning Electron Microscopy

Abstract The aim of this *in-vitro* study was to assess the effect of bioglass with different concentrations on root caries.

Ninety freshly-extracted teeth with root caries were randomly assigned to a single-use prophylaxis paste containing 15 % bioglass for 30 s with 1,450 ppmF toothpaste (15 % bioglass, n = 30), 1,450 ppmF toothpaste with 5 % bioglass (5 % bioglass, n = 30), and toothpaste containing 1,450 ppmF (Control, n = 30). Each sample received a standard brushing procedure for 10 s twice a day using the toothpastes. Teeth were immersed in remineralising solution with pH of 7 at 37 °C for 720 h. Surface roughness (Ra) was measured at baseline and after the application of the products at 0.5, 1, 4, 12, 24, 48, 168, 336 and 720 h. Subsequently, three samples from each group were randomly selected to measure calcium ion release over 15 h immersion in deionised water. These samples were then analysed using the SEM for the qualitative assessment of lesion topography. Repeated measures ANOVA, Wilcoxon paired tests and percentage changes were carried out to assess Ra. Calcium ion release data was analysed using one-way ANOVA and Tukey post-hoc tests.

After 720 h, 15 % bioglass had the highest decrease in Ra (Mean-difference = 1.502 µm, $p = 0.001$), then 5 % bioglass (Mean-difference = 0.723 µm, $p = 0.09$) whereas the control had the lowest Ra decrease (Mean-difference = 0.518 µm, $p = 0.55$). The differences in Ra between the groups were highly significant ($p < 0.001$). The cumulative calcium ion release was significantly high for the

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5 % bioglass in comparison to the 15 % bioglass, whilst the control had the lowest release ($p < 0.001$). SEM analysis showed the presence of bioglass particles only on 15 % bioglass samples.

The use of prophylaxis paste with 15 % bioglass and 1,450 ppmF toothpaste was promising to reverse/arrest root caries when compared to the toothpaste containing 1,450 ppmF with 5 % bioglass for a period of 30 days.

1. Introduction

The number of people worldwide aged 60 years or older will rise from 900 million to 2 billion between 2015 and 2050 which makes 22 % of the total global population (WHO, 2018). The incidence of root caries is also increasing in older patients (Hariyani et al., 2017). However, Hayes et al (2014) reported that there is lack of adequate evidence to recommend any tailored management strategies for root caries.

Early detection and remineralisation are the key management concepts for root carious lesions (Frencken et al., 2012), since the arrested lesions are more resistant to bacterial attack than the sound dentine (Hamilton, 1990). In this respect, management of root caries using different fluoridated, and non-fluoridated topical agents, such as sodium fluoride, silver diamine fluoride, calcium-phosphate based agents and chlorhexidine has been considered (Wierichs and Meyer-Lueckel, 2015).

Calcium sodium phosphosilicate (NovaMin) is a bioactive glass (bioglass) system that can initiate ion exchange (including calcium and phosphate ions) in an aqueous solution to form carbonated hydroxyapatite, which is similar to tooth mineral (Wefel, 2009). Sodium ions present in the formulation are replaced with hydrogen ions which in turn increases the pH. Calcium and phosphate ions may be released over several days and this complex is able to crystallise into hydroxycarbonate apatite by forming the superficial layer saturated with calcium phosphate on tooth surfaces. Bioactive glass materials are popular in clinical dentistry, although the understanding of the term of "bioactivity" needs to be clarified. Bioactive dental materials have a biological effect or are biologically active to form a mechanical and/or chemical bond with the hard tissues i.e., dentine/enamel (Vallittu et al., 2018). To date, there is limited evidence to support any type of fluoride delivery system with different concentrations of bioglass for the management of root caries.

The aim of this laboratory-based study was to assess the effect of different applications of bioglass with fluoride on the surface roughness of root caries using non-contact optical profilometry (NCOP), 'free' calcium ion release using a real-time ion selective electrode system (ISEs), and on the surface topography of root caries using Scanning Electron Microscopy (SEM).

2. Materials and methods

2.1. Study design

Fig. 1 shows the flow chart that describes each stage in this study.

2.2. Selection of root carious lesions

A total of 275 freshly extracted teeth with primary root caries were collected from the Dental Emergency Clinics. Ethical approval was obtained from the Office for Research Ethics Committees Northern Ireland (ORECNI, 16/NI/0101). Subsequently, 90 teeth with leathery type of root caries were chosen. An Ash No.6 blunt probe with a pressure of around 100 g was used to assess these lesions (Beighton et al., 1993).

2.3. Sample preparation

Each tooth was cut to the full depth from the labial/buccal to palatal/lingual surfaces ensuring that the surface contained the root carious lesion using a diamond cutter saw under water lubrication (Struers, Germany). Samples were then embedded onto a customised NCOP tray using a regular set putty (Elite HD+, Zhermack). During the study period, these samples were stored in the remineralisation solution and kept in an incubator at 37°C.

2.4. Application of test materials

Each group (n = 30) received one of the allocated treatments (Table 1). In 15 % bioglass, the single-use prophylaxis paste

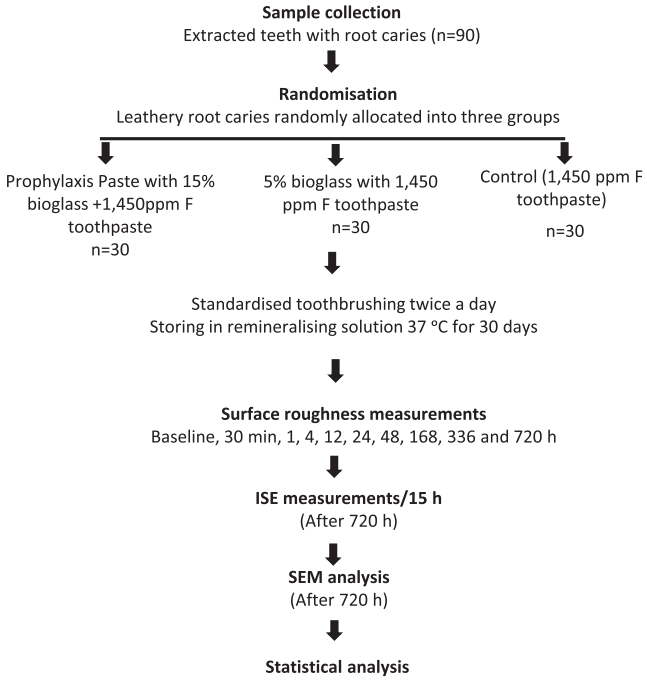

Fig. 1 Study flow chart.

Table 1 Oral care products used for the study.

Code	Groups	Product name Company	Active ingredients	Other ingredients	Additional treatment (standard toothpaste)
15 % bioglass	**Prophylaxis Paste and Standard toothpaste containing 1,450 ppm fluoride**	NUPRO Sensodyne Prophylaxis Paste, Dentsply Sirona, USA	15 % bioglass, 2.72 % Sodium Fluoride (1.23 % fluoride ion)	Glycerol,pumice, frits chemicals, lead containing sodium metasilicate, titanium dioxide, sodium fluoride, silica crystalline–quartz	1,450 ppm Sodium Fluoride/ Aqua Fresh Toothpaste, GSK, UK (Water, Hydrated Silica, Sorbitol, Glycerin, PEG-8, Flavor, Sodium Lauryl Sulfate, Xanthan Gum, Titanium Dioxide, Cocamidopropyl Betaine, Sodium Saccharin, Synthetic Iron Oxide, D&C Red 30)
5 % bioglass	**Toothpaste containing bioglass**	Repair and Protect Sensodyne Toothpaste, GSK, UK	5 % bioglass (Calcium Sodium Phosphosilicate, NOVAMIN), and 1,450 ppm Sodium Fluoride	Glycerin, PEG-8, Hydrated Silica, Cocamidopropyl Betaine, Sodium Methyl Cocoyl Taurate, Aroma, Titanium Dioxide, Carbomer, Sodium Saccharin	–
Control	**Standard toothpaste containing 1,450 ppm fluoride**	Aqua Fresh, GSK, UK	1,450 ppm Sodium Fluoride	Water, Hydrated Silica, Sorbitol, Glycerin, PEG-8, Flavor, Sodium Lauryl Sulfate, Xanthan Gum, Titanium Dioxide, Cocamidopropyl Betaine, Sodium Saccharin, Synthetic Iron Oxide, D&C Red 30	–

(15 % bioglass, 1 ml) was applied onto the root carious lesions and gently polished using a rubber cup with slow speed handpiece for a period of 30 s. Subsequently, these samples were left for one min *prior* to rinsing with deionised water for 30 s (Milleman et al., 2012). Following the single application of the prophylaxis paste, samples were brushed regularly using 1,450 ppm fluoridated toothpaste during the study period. In 5 % bioglass, the samples received fluoridated toothpaste containing 1,450 ppm fluoridated toothpaste with 5 % bioglass whilst control group had toothpaste containing 1,450 ppm alone as a control group.

2.5. Toothbrushing procedure

Mechanical brushing procedure used with a standard brushing time of 10 s with force of 150 g for each sample (McCracken et al. 2003, George, 2016, Sleibi et al., 2018). A medium bristle toothbrush (Oral-B, UK) with 1,450 ppm fluoridated toothpaste (Aquafresh GSK, UK) was used twice a day for 30 days both in the 15 % bioglass and control groups, whilst the 5 % bioglass had the same brushing procedure using 1,450 ppm fluoridated toothpaste with 5 % bioglass (Sensodyne Repair and Protect, GSK, UK). The brushing process was performed using 1 ml of a 1:3 slurry of each toothpaste and deionised water for 10 s (Carvalho and Lussi, 2014). Each sample was then left for two minutes to simulate *in vivo* condition (George, 2016, Sleibi et al., 2018) before washing with deionised water.

2.6. Remineralisation buffer solution

A remineralisation solution was prepared using 1.5 mmol/L $CaCl_2$, 0.9 mmol/L KH_2PO^4, 20 mmol/ L HEPES and 130 mmol/L KCl. 1.5 mmol/L NaN_3 was added to prevent microbial growth (Ten Cate, 2008). The pH was adjusted to 7.0 using 0.5 M KOH.

2.7. Non-contact optical profilometry

NCOP was carried out using a Proscan 2000 (Scantron, UK) with a S13/1.2 sensor to measure the surface roughness (Ra). At baseline, three lines of 1.5 mm (each: 1500 points, 1.0 μm apart) on each lesion was selected and scanned with the NCOP. NCOP line scans with operational parameters (step size: 0.001 mm, number of steps: 1500) were carried out. A sampling rate of 30 Hz was used (Baysan et al., 2018). Ra measurements of all samples were carried out in μm at baseline before treatment, and then repeated after 30 min, 1, 4, 12, 24, 48, 168, 336 and 720 h.

2.8. Real-time ISE methodology

This part of the study aimed to measure continuously 'free' calcium ions released into deionised water from the test and control samples (n = 3 each) using the computer interfaced Ca^{2+}-ISEs [Nico 2000 Ltd, UK] (Huang et al., 2018). The results were presented in mmol/L.

2.9. Scanning Electron Microscopy (SEM)

At the end of the study, these three samples were visualised using SEM (Oxford Instruments, Oxford, UK) for the assessment of lesion topography at different magnifications (2000–10.000X).

2.10. Statistical analyses

Repeated measures ANOVA test was applied to assess the differences in Ra between the test and control groups. Wilcoxon paired test was also used to analyse the differences between time points of each group. In addition, percentage of change was applied to present any differences between groups at the end of study. The cumulative calcium ion release data between samples were analysed with one-way ANOVA and Tukey post-hoc tests at a significant level of 0.05. All statistical analyses were carried out using IBM SPSS Statistics 25.0 (SPSS, Chicago, IL, USA).?>

3. Results

3.1. Surface roughness (Ra)

The lesions in 15 % bioglass showed a steady decrease in Ra during the first 168 h after treatment ($p = 0.12$). This was followed by a decrease in Ra at about 350 h ($p = 0.01$). Furthermore, there was an increase at the end of the study (30 days) ($p = 0.30$). Overall, there was a significant decrease in Ra for the 15 % bioglass between the baseline and after the product application for a period of 30 days (Mean-difference = 1.502 µm, $p = 0.001$). In 5 % bioglass, there was an irregular change in Ra with a very slight decrease in the first 48 h ($p > 0.05$). This was followed by a steady decrease in Ra that continued for a period of 720 h (Mean-difference = 0.723 µm, $p = 0.09$). However, the control group had the most irregular tendency in Ra during the first 48 h ($p < 0.05$). Following this, there was a decrease in Ra up to 168 h ($p = 0.01$), however the Ra then increased at the end of study for this group (Mean-difference = 0.518 µm, $p = 0.55$) (Fig. 2).

The changes towards the lower Ra (smooth surfaces) were approximately doubled in 15 % bioglass compared to the 5 % bioglass (48 %), whereas the lowest shift was for the control group (34 %). The differences in Ra between the groups were significant ($p < 0.001$) (Fig. 3).

3.2. Calcium ion release

The carious dentine lesions in 15 % bioglass demonstrated a continuous and linear release of calcium ions throughout the immersion period (Fig. 4). The mean of calcium ions release for this group was 0.00224 ± 0.00053 mmol/L. Root carious lesions in 5 % bioglass released approximately double the amount of calcium compared to the 15 % bioglass (0.00383 ± 0.00103 mmol/L). Whereas only 0.00078 ± 0.00016 mmol/L of calcium ions were released for the control group. The overall differences between the groups were significant ($p < 0.001$).

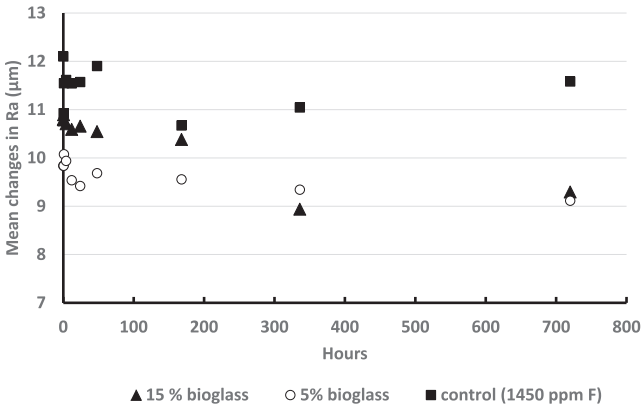

Fig. 2 Mean changes in Ra of the test and control groups over 720 h (30 days). At baseline, the control group had Ra values of 12.10 ± 5.95 µm compared to the 15 % bioglass values (10.79 ± 5.88), whilst 5 % bioglass presented with Ra values of. 9.83 ± 5.22.

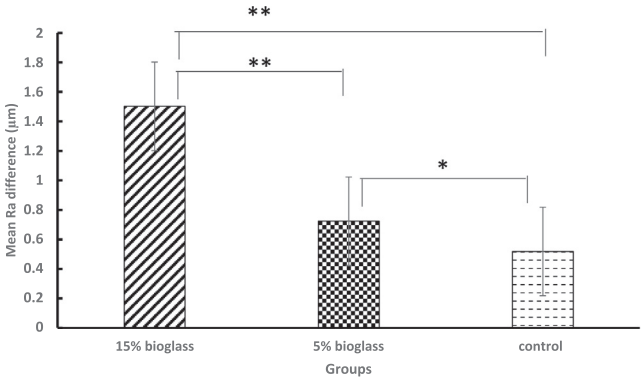

Fig. 3 Mean ± SD of Ra differences (baseline-final scan) of test and control groups, at the end of the study. The maximum decrease in Ra is for the 15 % bioglass, compared to the 5 % bioglass, whereas the control shows the minimum decrease in Ra, ($p < 0.001$).

3.3. SEM

All samples showed non-uniform, rough and irregular surfaces at the lesion sites. In all cases, there was an evidence of dentinal tubules being either partially or completely closed. However, sharp, angular and irregular particles with various shapes resembling the bioglass particles (Baysan et al., 2018) was detected in the 15 % bioglass only (Fig. 5).

4. Discussion

This laboratory-based study aimed to investigate the effects of two different concentrations of bioglass-containing products compared to a non-bioglass toothpaste on root caries. A greater decrease in Ra for the 15 % bioglass group suggests that remineralisation has occurred resulting from the deposition of mineral within the root carious lesions. Therefore, the single-use prophylaxis paste with 15 % bioglass and standard

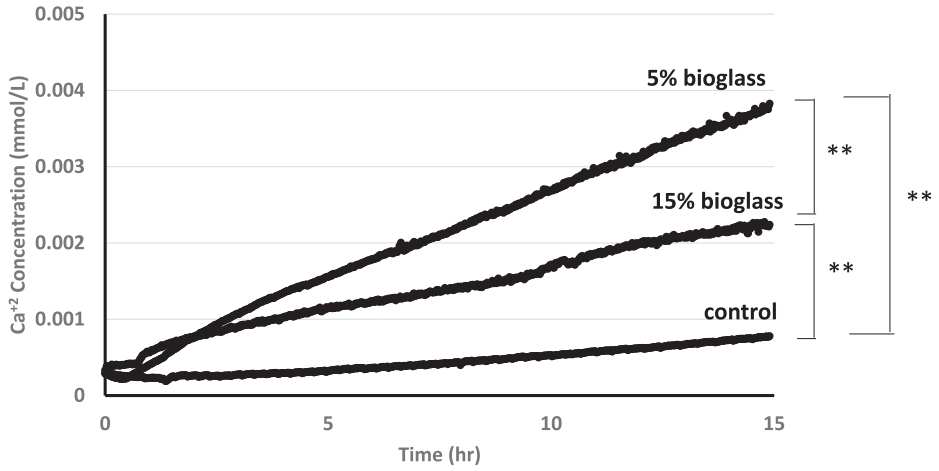

Fig. 4 Mean Ca + 2 release after prophylaxis paste with 15 % bioglass (middle line), 5 % bioglass toothpaste (top line), and toothpaste, 1,450 ppm F (control, bottom line) treatments on carious dentine. The Ca 2 + -ISEs were calibrated using the CaCl2 solution. A calibration, curve is obtained by plotting the logarithm of calcium concentration against ISE readings in millivolts. The calibration was performed at 23.0, ± 1.0 °C using a temperature-stabilised stirre.

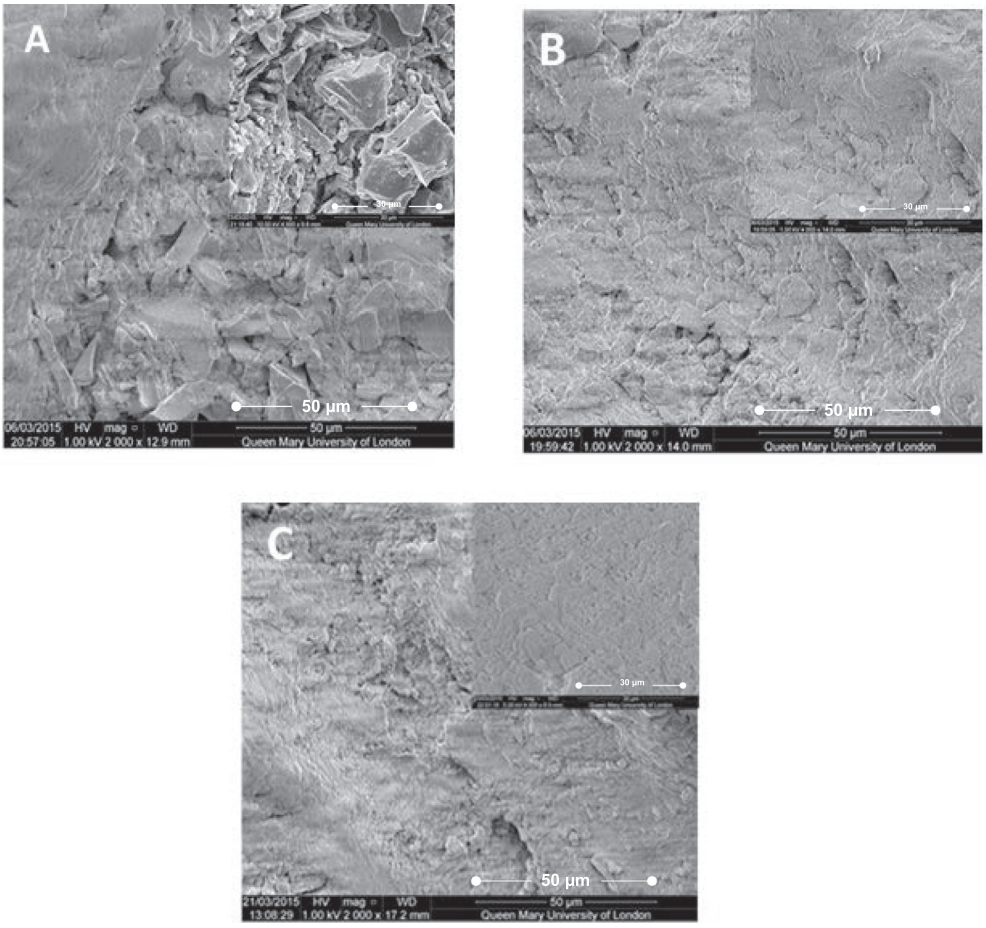

Fig. 5 Representative SEM images (2000 and 4000X) of each samples after 720 h (30 days) (A) a, sample treated with prophylaxis paste containing 15 % bioglass, (B) sample treated with toothpaste, containing 5 % bioglass, and (C) sample treated with standard toothpaste containing 1,450 ppm F (control).

fluoridated toothpaste group had the greatest ability to precipitate minerals in root carious lesions by smoothing irregularities and thereby reducing the surface roughness of these lesions. In previous studies, quantitative Ra analyses were successfully implemented to monitor surface mineral changes with regards to demineralisation and remineralisation process in

both enamel (Zhou et al., 2012) and dentine (ten Cate, 2008, Sleibi et al., 2018, Baysan et al., 2018) with promising results. Nevertheless, differentiation between the organic and the mineral components of dentine during the de/remineralisation process using the profilometry is questionable (Klont and ten Cate, 1991, Ganss et al., 2009).

The decreasing trends in Ra for both bioglass groups were different from that in the control group, where there was an increase in Ra by the end of the study. This might be due to both remineralisation and demineralisation occurring throughout the duration of the study, since clinically root caries tends to shift from rough to smooth texture when a lesion changes from active to inactive. This result may also be due to the short study period (720 h) which is insufficient to achieve the optimal desired smoothness with standard toothbrushing using a toothpaste containing 1,450 ppm fluoride alone (Sleibi et al., 2018). In this respect, Tezvergil-Mutluay et al., (2017) reported that precipitation of calcium phosphates onto the exposed dentine fibrils restricts the activity of endogenous proteases to dissolve dentine collagen. This ultimately plays an important role in the remin/demineralisation process. In this current study, it can be speculated that the changes in surface roughness could be related to the effect of bioglass. Interestingly, Sleibi et al., (2018) reported that dental varnish containing 5 % fluoride with bioglass (45S5) had a superior effect on root caries remineralisation compared to the dental varnish with 5 % fluoride alone.

It should be noted that this is the first study to measure calcium ion release from bioglasses applied to the natural root caries. These findings demonstrate the ability of both 15 % and 5 % bioglass applications to release calcium. It was reported that bioglass can remineralise root dentine structure since bioglass precipitates both calcium and phosphate ions on the C-terminal telopeptide and C-terminal cross-linked telopeptide within the dentine structure, thereby becomes hard and stabilises these functioning proteases. This process has the degradation effect on dentine matrix (Tezvergil-Mutluay et al., 2017). In the current study, calcium release was also demonstrated following the application of products containing bioglass. In this respect, both bioglass treatments demonstrated continuous calcium ion release. The higher cumulative calcium release of the 5 % bioglass group compared to the 15 % bioglass might be related to cumulative effect from the continuous use of the 5 % bioglass containing toothpaste with 1,450 ppm F during the study, which might lead to precipitation of more bioglass on the carious dentine, and then releasing high quantity of calcium. However, this was in contrast with the Ra measurements where the maximum decrease in Ra was for the single application of 15 % bioglass. This might be related to the differences in the method of application, in which the 15 % bioglass was applied as a prophylaxis paste using a rotary instrument with a gentle pressure, which might assist in the implementation of these bioglasses into the exposed dentine fibrils and inside irregularities, reducing the lesion Ra. Therefore, bioglass particles could be more effective when applied as prophylaxis paste rather than as a toothpaste. This was supported by the SEM results which showed the presence of bioglass particles on carious dentine surface in the 15 % bioglass group compared to other groups. Likewise, profilometry analysis showed that the single application of 15 % bioglass resulted in lower Ra when compared to the 5 % bioglass. In this respect, Paolinelis et al., (2008) reported that bioglass particles can be retained on both sound and carious dentine surfaces following the air-abrasion using bioglass powder.

The calcium release from the 15 % bioglass after 720 h is in agreement with findings from a study investigating a novel orthodontic adhesive containing bioglass with a sustained calcium release both in Tris buffer and artificial saliva over 180 days (Al-Eesa et al., 2017). However, it should be noted that calcium ion release could also be the result of dentine demineralisation. Therefore, calcium ions might also come from other sources in addition to the bioglass. In this study, bioglass was the main source of calcium ions, since the amount of calcium ion released from the control group was very low compared to both the test groups ($p < 0.001$). Furthermore, the ISEs could only measure free ion concentration and failed to detect the bound calcium, such as CaF_2, calcium inorganic complexes, nor calcium protein complexes.

In addition, bioglass has the ability to provide both calcium and phosphate ions which are essential components to drive the formation of fluorapatite during the remineralisation (Reynold, 2008). However, the current study only analysed calcium ion release, which could be one of the study limitations. This is due to the percentage of phosphate in the bioglass (45S5: 46.1 SiO_2, 2.6 P_2O_5, 24.4 Na_2O and 26.9 CaO mol%) used in this study is much lower compared to calcium (Hill and Brauer, 2011), therefore the detection of phosphate ion in such limited amounts of applied bioglass was unlikely to be achieved. Regarding the immersion solution, the current study was carried out using remineralisation solution only to simulate the optimum clinical condition. However, investigation of bioglass products using remineralising/demineralising cycling is required.

This laboratory-based study demonstrated that there was a promising remineralisation effect following the use of dental products containing different concentrations of bioglass on root caries. Further controlled randomised triple blinded clinical studies are required to compare the effect of fluoride either with or without bioglass for patients with root caries.

5. Conclusion

This laboratory-based study showed that a single application prophylaxis paste with 15 % bioglass and 1,450 ppmF toothpaste was promising to reverse/arrest root caries when compared to the toothpaste containing 1,450 ppmF with 5 % bioglass for a period of 720 h (30 days).

6. Disclosure statement

There is no conflict of interests existing where an author has a personal or financial relationship that might introduce bias or affect their judgment.

7. Statement of Ethics

Ethical approval was obtained from the Office for Research Ethics Committees Northern Ireland (ORECNI, 16/NI/0101). Every patient signed an informed consent for their extracted teeth to be included in the study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sdentj.2022.07.002.

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