



ELSEVIER

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.intl.elsevierhealth.com/journals/dema

Bioactive glass composite for orthodontic adhesives — Formation and characterisation of apatites using MAS-NMR and SEM

N.A. Al-eesa^{a,b,*}, N. Karpukhina^a, R.G. Hill^a, A. Johal^a, F.S.L. Wong^a

^a Queen Mary University of London, Barts & The London School of Medicine and Dentistry, Institute of Dentistry, Centre for Oral Bioengineering, Mile End Road, London, E1 4NS, UK

^b University of Anbar, Colledge of Dentistry, Department of Paediatric, Orthodontic and Preventive Dentistry, P.O. Box 55, Ramadi, Iraq

ARTICLE INFO

Article history:

Received 6 September 2018

Received in revised form

23 January 2019

Accepted 7 February 2019

Keywords:

Bioactive glass

Fluorapatite

White spot lesions

Orthodontic adhesives

MAS-NMR

SEM

ABSTRACT

Objectives. To study the dissolution and fluoroapatite (FAP) formation of a new bioactive glass (BAG)-resin adhesive in an acidic solution in reference to neutral solutions, using the magic angle spinning-nuclear magnetic resonance (MAS-NMR) and the scanning electron microscopy (SEM).

Methods. BAG composite disks (n = 90) were prepared from, novel fluoride-containing BAG-resin. Three sample groups (n = 30) of the disks were immersed in Tris buffer pH = 7.3 (TB), neutral artificial saliva pH = 7 (AS7) and acidic artificial saliva pH = 4 (AS4) at ten time points (from 6 h to 6 months). Half of the immersed disks at each time point were crushed into a powder and investigated by the solid state MAS-NMR. SEM studies were undertaken by embedding the other half of the immersed disk in a self-cure acrylic where the fracture surface was imaged.

Results. MAS-NMR results show that the BAG composite degraded significantly faster in AS4 compared to TB and AS7. At the end of the immersion period (6 months), around 80% of the glass particles in AS4 had reacted to form an apatite, evidenced by the sharp peak at 2.82 ppm in ³¹P signals compared to a broader peak in TB and AS7. It also shows evidence of fluorapatite (FAP) formation, indicated by ¹⁹F signal at -103 ppm, while signal around -108 ppm indicated the formation of calcium fluoride, from the excess Ca²⁺ and F⁻ especially on longer immersion. SEM images confirm higher degradation rate of the BAG composite in AS4 and reveal the impact of time on the dissolution of more glass particles. The images also indicate apatite formation around the glass particles in TB and AS4, while it forms predominantly over the disk surface in AS7.

Significance. BAG composite demonstrate smart reactivity in response to pH change which has a potential clinical benefit against demineralization and promoting remineralisation to form more stable fluorapatites.

© 2019 The Academy of Dental Materials. Published by Elsevier Inc. All rights reserved.

* Corresponding author at: 2nd Floor, Dental Physical Sciences Department, Francis Bancroft Building, Mile End, E1 4NS, UK.

E-mail address: n.a.r.aleesa@qmul.ac.uk (N.A. Al-eesa).

<https://doi.org/10.1016/j.dental.2019.02.010>

0109-5641/© 2019 The Academy of Dental Materials. Published by Elsevier Inc. All rights reserved.

1. Introduction

Fluoride has been shown to be an effective agent in the prevention of dental caries through its action on inhibiting demineralisation by forming more stable fluorapatite in enamel and promoting remineralisation in white spot lesions (WSLs). Therefore, reduction in caries incidence can be achieved by daily brushing of teeth with appropriately designed tooth pastes that contain fluoride [1]. Research shows that the presence of calcium and phosphate ions will further enhance the anti-cariogenic effects [2]. Patients who have orthodontic fixed appliances often have WSLs around the brackets, especially for those who have poor oral hygiene. Fluoride releasing adhesives, such as the resin modified glass ionomer cements (RMGICs), have been used in order to reduce the WSL formation, however, its effectiveness is uncertain [3,4]. This may be due to a lowering of the pH when GICs release F^- ions by ion exchange for OH^- ions in solution [5]. Furthermore there is a significant reduction in fluoride release after several days of the cement application which questions the long term benefit of the cement [6–8]. Bioactive glasses have been studied extensively as an artificial bone grafting material because of their characteristic formation of a calcium-phosphate layer [9–12]. Recently, a composite resin containing bioactive glass (BAG) has been developed [13]. Its bioactivity in terms of ion release [13] and apatite formation [14] have been reported, showing that Ca^{2+} , PO_4^{3-} and F^- continued to be released up to 6 months, and formed an apatite, even in acidic media. However, as only FTIR and XRD were used in these studies, the type of apatite formed could not be distinguished due to the overlap of the hydroxyapatite (HAP) and fluorapatite (FAP) peaks [15,16]. Hence, the aims of the present study were to use ^{31}P and ^{19}F MAS-NMR which are powerful techniques to (i) follow the degradation of the BAG (ii) to investigate the fluoride and phosphate compounds formed [15,17,18], and (iii) to determine the type of apatite (fluorapatite or hydroxyapatite) formed on the surface of the BAG composite disks after immersion. SEM was used to study the reaction of the micro sized BAG particles within these disks.

2. Materials and methods

A melt derived BAG composed of 35.25% SiO_2 , 5.75% P_2O_5 , 43% CaO , 6% Na_2O , and 10% CaF_2 was incorporated into a resin which was composed of 42.25% BisEMA, 55% TEGDMA, 0.25% DMAEM, 0.5% camphorquinone and 2% 4-Meta, to form an adhesive, with a BAG:resin weight ratio of 80:20. The adhesive was used to prepare 90 disks of 1.2 mm thickness and 10 mm diameter. The composition and synthesis of the novel BAG resin adhesive were described in detail in the previous study [13]. Three types of solutions; Tris buffer (TB) pH = 7.3, artificial saliva pH = 4 (AS7) and artificial saliva pH = 4 (AS4) [14] were prepared and the disks were divided into 3 groups ($n = 30$) and each disk was immersed in 10 ml of the solution inside a 15 ml polypropylene centrifuge tube (Fisher Scientific UK Ltd, Leicestershire, UK).

The samples were immersed up to 6 months and were investigated at 10 time points. At each time point (6, 12 and 24 h, 3, 7, 14, 30, 60, 90 and 180 days), 3 disks were removed

from each of the solutions, washed with deionised water and dried. Each disk was then investigated using solid state magic angle spinning-nuclear magnetic resonance (MAS-NMR) and scanning electron microscopy (SEM). All the remaining specimens were transferred to tubes containing fresh solution at each time point.

2.1. MAS-NMR experiments

Solid state NMR measurements were conducted on a Bruker (Germany) spectrometer which operates at 14.1T magnetic field. ^{31}P MAS-NMR measurements were carried out at a resonance frequency of 242.9 MHz and spinning rate of 12 kHz using a 4 mm rotor. The recycle delay time was 60 s and 16 scans were collected. The 85% H_3PO_4 was used as a reference and the chemical shift was adjusted to 0 ppm. ^{19}F MAS-NMR measurements were done at a resonance frequency of 564.7 MHz and spinning rate of 22 KHz using a 2.5 mm rotor. The recycle delay time was 60 s and 32 scans were acquired. The 1M aqueous solution of NaF was used as a reference for the chemical shift scale. The signal recorded for the solution was adjusted to -120 ppm. Data processing was carried out using TopSpin, the Bruker's standard acquisition and processing suite. The samples were turned into powder using mortar and pestle before conducting the measurements.

2.2. SEM experiments

For imaging using SEM, the immersed disk was halved by fracturing; one half was imbedded in a cold cure acrylic resin which was originally loaded inside a Teflon mould of 10.2 mm diameter and 5 mm height. The embedded disk was then polished at the fracture surface using silicon carbide grinding papers (CarbiMet™, BUEHLER, USA) at a sequence of P300, P1000 and P4000 in a Kent 4 Automatic Lapping and Polishing Unit (Kemet International Ltd, Maidstone UK). The samples were attached to SEM stubs and carbon coated to minimize charging and improve the imaging resolution. Silver dag was applied between the edge of the sample and edge of the stub. Samples were imaged using back scatter mode under a 10KeV beam voltage on scanning electron microscope (FEI Inspect F) equipped with energy dispersive x-ray detector (Oxford instruments). Images were taken at a working distance of approximately 10 mm.

3. Results

3.1. MAS-NMR

The ^{31}P NMR spectra of the BAG disks at different time points after immersion are shown in Fig. 1. At 0h, the spectra of the disk had a broad signal with a peak around 4 ppm. Up to the 1 week time point, the spectra in all the media had a slight left hand shoulder with the broad peaks shifting towards 3 ppm. This shoulder continued in the spectra at later time points for the disks in the TB and AS7 media (Fig. 1a–b). However, for the disk in AS4, a more symmetrical spectrum with a sharper peak started to emerge from 2 weeks onwards, progressively replacing the initial broad peak. Finally, at 6 months,

a single narrow signal with a sharp peak at 2.82 ppm was observed (Fig. 1c).

In the ^{19}F MAS-NMR spectra (Fig. 2), a broad spectrum with a maximum around -103 ppm were observed at 0 h. The spectra then skewed towards the left in the early time points. The broad peak remained for the disk immersed in TB and AS7 up to 6 months. For the disk in AS4, two peaks started to emerge after 2 weeks, progressively becoming more prominent and at 6 months, a more symmetrical spectrum with an intense sharp peak at -108 ppm and a less intense peak at -103 ppm were observed. For the disk in TB, the two peaks only started to emerge after 3 months but they were very broad and less distinctive.

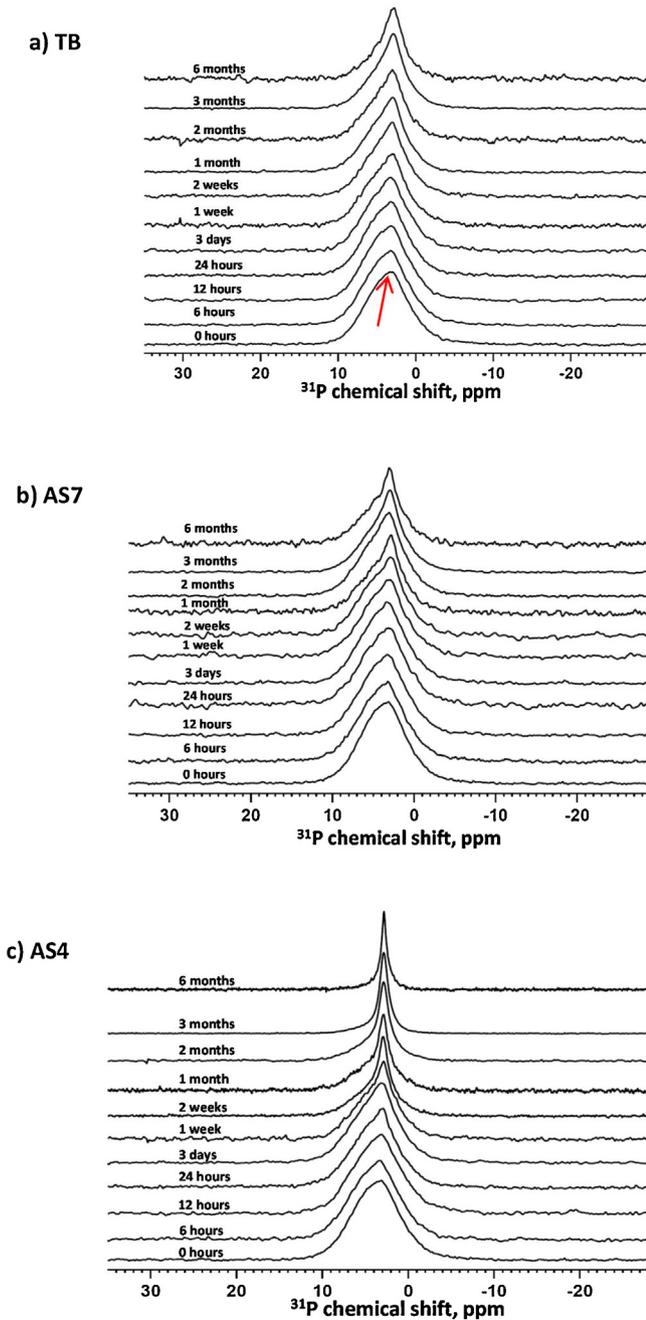


Fig. 1 – ^{31}P MAS-NMR spectra of the BAG-resin at 0 h–6 months for the (a)TB, (b)AS7 and (c)AS4 solutions.

3.2. SEM

Negligible surface changes were observed on the BAG disks immersed in TB at the early time points (Fig. 3a and b). After 3 days, the surface BAG layer started to react, and this became clearer at 2 months (appearing as a darker layer at the disk surface, denoted by an arrow in Fig. 3c, with a thickness just less than $100\ \mu\text{m}$). At 6 months, about $40\ \mu\text{m}$ of the disk has reacted with the solution (Fig. 3d).

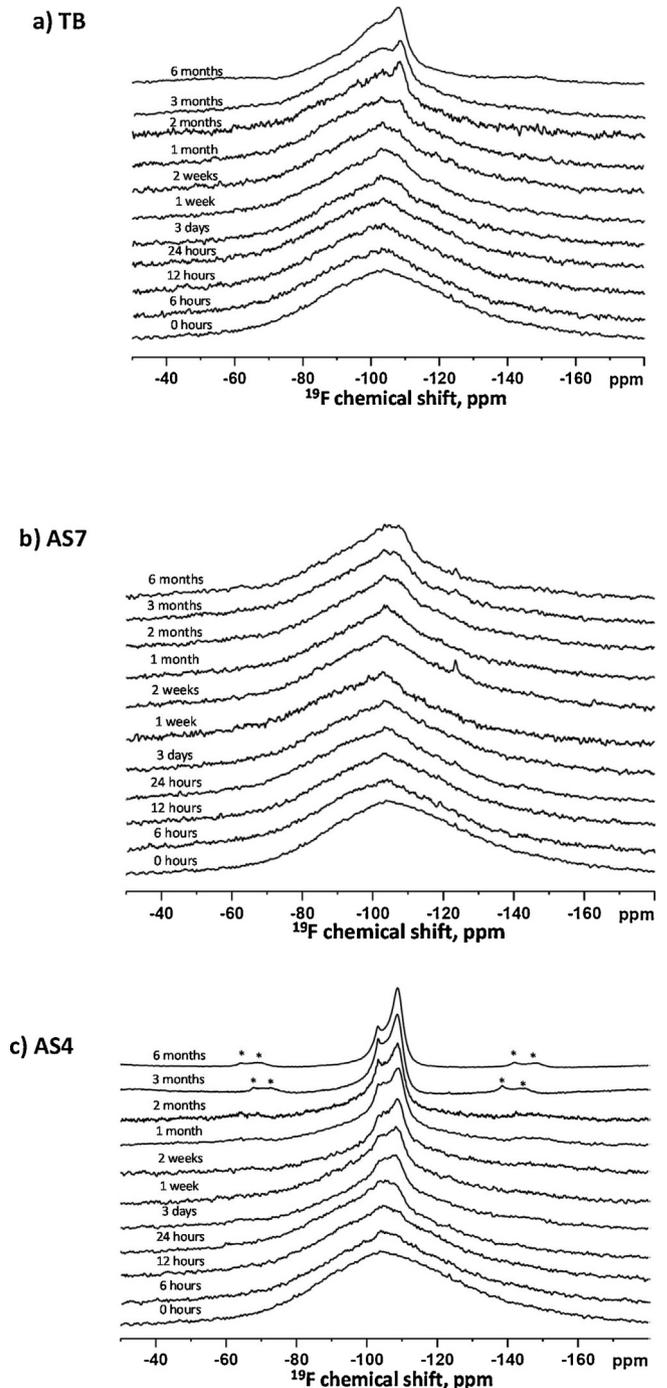


Fig. 2 – ^{19}F MAS-NMR spectra of the BAG-resin at 0 h–6 months (bottom to top) for (a)TB, (b)AS7 and (c)AS4 solutions.

For the disks immersed in AS7, the reacted BAG layer was thinner and only the surface $\sim 100\ \mu\text{m}$ was reacted after 6 months (Fig. 4e). However, a thin precipitated layer over the disk surface was observed after 6 h immersion. This layer became thicker over time and achieved a thickness of $\sim 10\ \mu\text{m}$ at 2 months and become thicker on longer immersion to reach about $20\ \mu\text{m}$ at 6 months (Fig. 4a–e). Higher magnification shows that the precipitated layer had a thick white base with a brush like surface structure, which resembled highly organised orientated needle like crystals (Fig. 4f and g). This is consistent with previous XRD studies [14] that have shown a layer of apatite forms that grows preferentially in the 002 direction.

After 6 h of immersion in AS4, the BAG disks started to have a reacted surface layer of few microns, which increased in thickness rapidly with time (Fig. 5). At 6 months, most of the disk thickness has reacted with the solution (Fig. 5d). The BAG showed partial degradation around the core of the particle at all time points (Fig. 6). A very thin precipitated layer was also seen on the AS4 disk at 6 months (Fig. 7).

4. Discussion

4.1. MAS-NMR

In order to understand how the BAG reacted with the media, the ^{31}P MAS-NMR was used to investigate possible formation of new phosphate compounds, by measuring the changes in

the chemical shift of the original form of phosphate in the glass compared to new phosphate compounds formed such as apatite. The results also gave an indication how the glass degraded in the media. Before immersion, the centre of gravity of the broad signal was around 4 ppm, corresponding to an amorphous orthophosphate charge balanced by the cations available in the glass composition. The glass also showed a small peak at 3.1 ppm (red arrow), which indicated the formation of small amount of apatite in the original glass because of slight crystallisation during quenching, which is consistent with the XRD data shown previously [14]. Following immersion, the peak of crystalline apatite between 2.8 and 3 ppm [18] was seen in all the spectra for all the media types. This agrees with the characterisation data by ATR-FTIR and XRD reported previously [14]. After 2 weeks, the broad signals in TB and AS7 immersed samples started to become narrower and skewed. This is more noticeable at 6 months, indicating that the spectrum was a combination of two components, a broad amorphous orthophosphate peak from the original unreacted glass and a sharper peak from the crystalline apatite that forms. The asymmetry of the spectra might also be due to the preferential loss of a small amount of sodium from the original glass that charge balanced the orthophosphate. In contrast, for the BAG disks immersed in AS4, the loss of the broad amorphous signal and the development of a narrow and sharp peak at 2.8 ppm at 6 months indicated that most of the BAG particles have reacted to form apatite. Faster degradation of the BAG disk in acidic media compared to TB and AS7 is in agree-

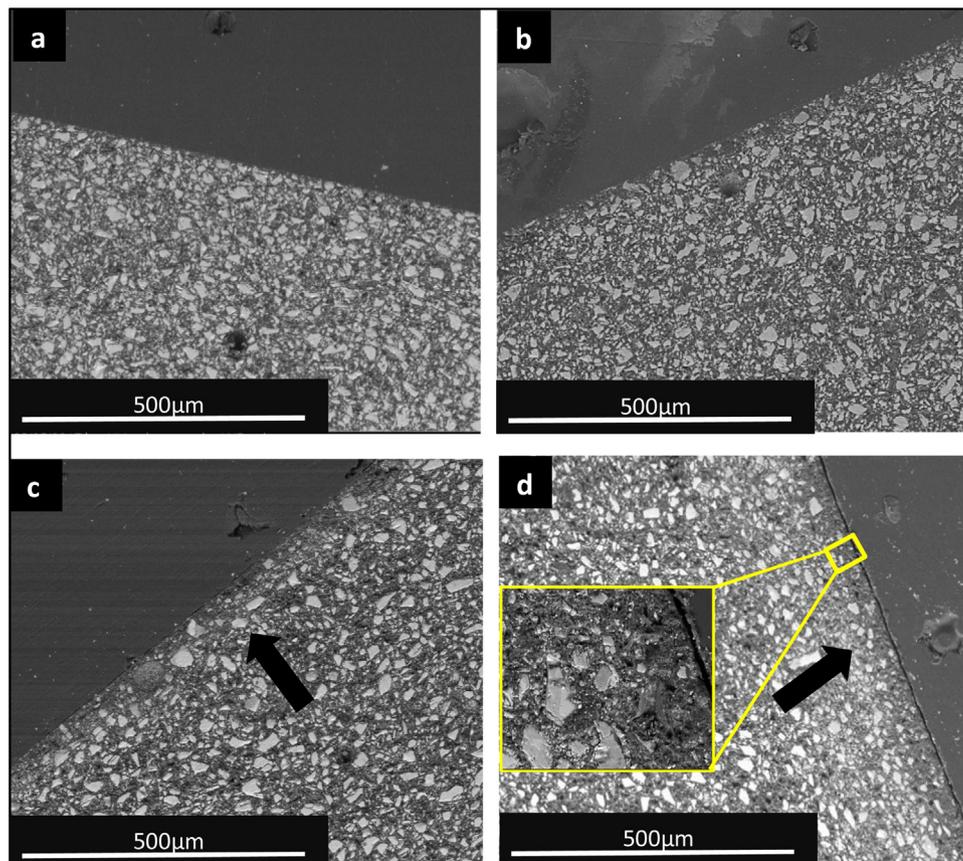


Fig. 3 – SEM images of the BAG disks following immersion in TB solution for four selected time points; (a) 24 h, (b) 2 weeks, (c) 2 months and (d) 6 months. The black arrows point to the reacted layer.

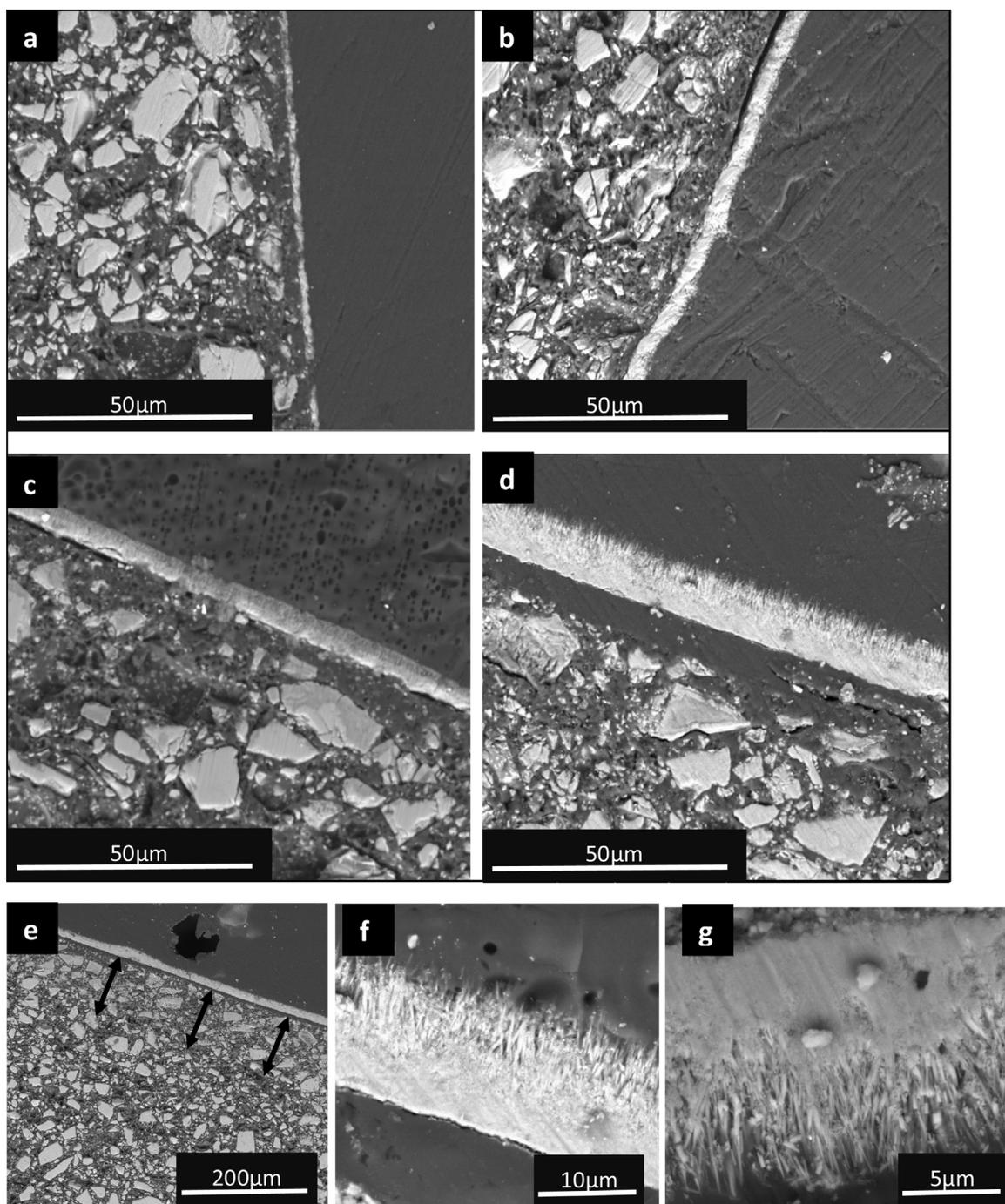


Fig. 4 – SEM images of the BAG disks following immersion in AS7 solution for four selected time points; (a) 24 h, (b) 2 weeks, (c) 2 months and (d) 6 months. (e) The arrows indicate the thickness of the reacted layer of the disk following immersion for 6 months. (f) and (g) Layer of apatite formed over the disk surface in magnified views.

ment with the results of ion release, pH changes, ATR-FTIR, XRD obtained previously [13,14], and the SEM micrographs presented later.

Further analysis of the NMR spectra of the BAG disks immersed in the three immersion media was implemented. This was undertaken by deconvolution of the spectra (Fig. 8) at all the time points using line fitting software (Dmfit, [19]). The results obtained indicated that the percentage of the phosphorus transformed into apatite phase from the phosphorus

in the original glass (before immersion) was increasing linearly with time upon immersion in AS4 and TB. Furthermore, it indicated that approximately 76% of the glass was reacted and converted into apatite after 6 months of immersion in AS4, and just below 40% of phosphate from the glass was converted into apatite in TB. The trend of apatite contribution in AS7 is different and did not fit the linear trend well, though at the initial stages the amount of apatite formed in AS7 was close to the values seen in TB. It indicates that the

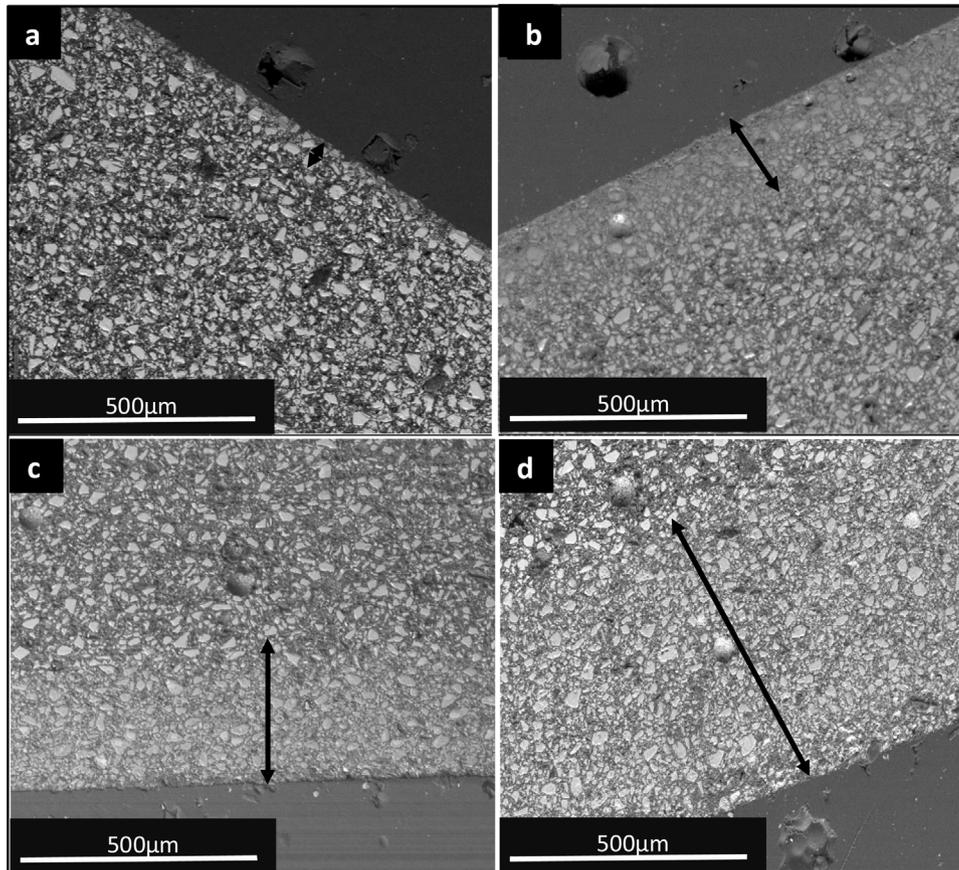


Fig. 5 – SEM images of the BAG disks following immersion in AS4 solution for four selected time points; (a) 24 h, (b) 2 weeks, (c) 2 months and (d) 6 months. The arrows indicate the thickness of the reacted layer of the disk.

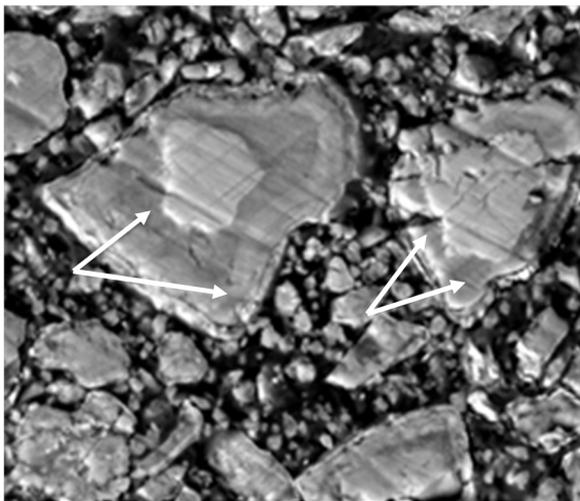


Fig. 6 – SEM images showing partially degraded (white arrows) glass particles.

amount of apatite did not progressively increase over the six month time period and remained nearly constant after two weeks of immersion in AS7 compared to AS4 and TB. This implies that formation of apatite in AS4 and TB is diffusion controlled, whereas it is different from the processes driving

apatite formation in AS7. These results are in agreement with the ion release data, particularly for the PO_4 which showed a reduction in the concentration throughout the experiment [13], indicating phosphate ions in the AS7 solutions were consumed in the process of apatite formation leaving the solution with less free phosphate ions to be detected.

The broad ^{19}F signal of the BAG before immersion reveal overlapping of multiple fluoride species, consisting of amorphous F-Ca(n) at around -90 ppm and a mixed F-Ca(n)Na(m) at about -130 ppm [20]. The left skewed asymmetry of the signals following immersion is probably due to the degradation of the glass where the F-Ca(n)Na(m) containing species were lost preferentially on dissolution. The fluorapatite signal at around -103 ppm [20] appeared at 6 h onwards for all immersion solutions. This signal was most pronounced for disks in the AS4 media, especially at the end of the treatment period, indicating more conversion of the glass to fluorapatite in acidic media. For AS7, it is important to note that the calcium and phosphate contribution to apatite formation is probably mainly from the immersion solution, rather than from reaction of the glass, therefore, the signals continued to be generally broad along the treatment time points indicating that the initial fluoride species in the glass remained largely unchanged, because much less glass degradation took place. The signal for the TB, at 1 month and thereafter, demonstrated a peak at around -108 ppm assigned to crystalline CaF_2 (flu-

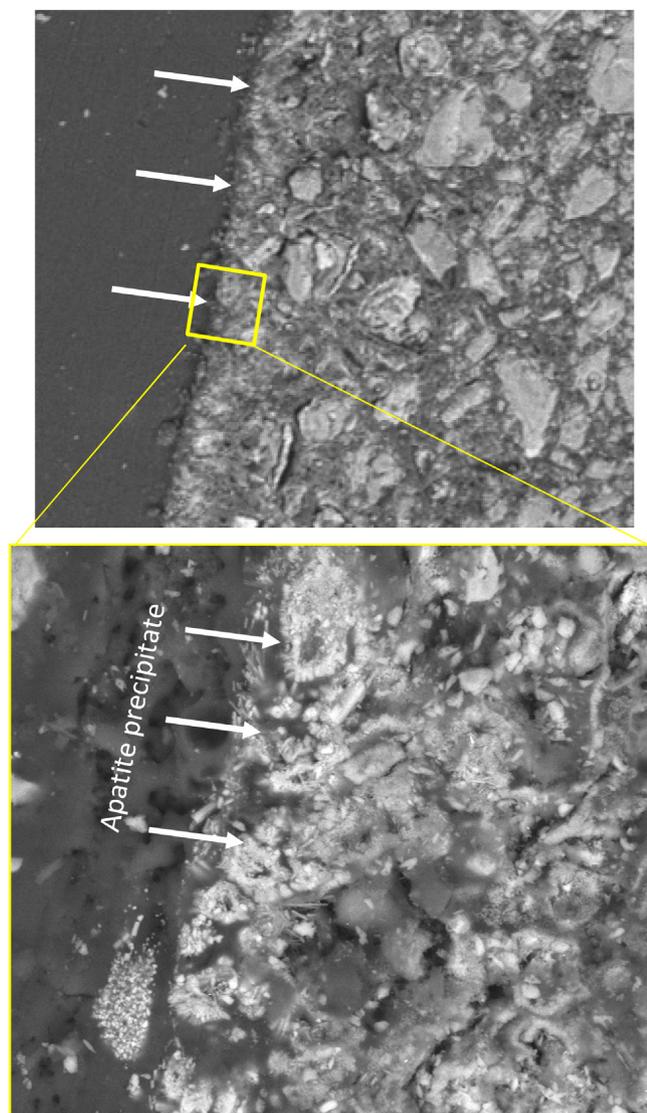


Fig. 7 – SEM images showing the apatite layer (White arrows) precipitated inside the disk immersed for 6 months in AS4.

orite) [20] in addition to the peak of fluorapatite at -103 ppm, but the former was slightly sharper and more intense than the latter. In contrast, AS4 samples showed a relatively broad peak at -108 ppm as early as 3 days in addition to the fluorapatite peak at -103 ppm. The signal continued to narrow with increasing time, indicating transformation of more fluorine species in the glass to either fluorapatite or fluorite, and the peaks became sharper on longer immersion. At 6 months the signal at -108 ppm was enhanced significantly above the fluorapatite peak suggesting more fluorite has formed. The formation of fluorite in the TB and AS4 solutions especially at the longest time points indicates the presence of excess calcium and fluoride released from the glass. However, the demonstration of sharper and more intense peaks in AS4 seems to be related to both the higher degradation of the glass at pH4 where more H^+ ions are available in the solution, and to the contribution from calcium ions originally present in

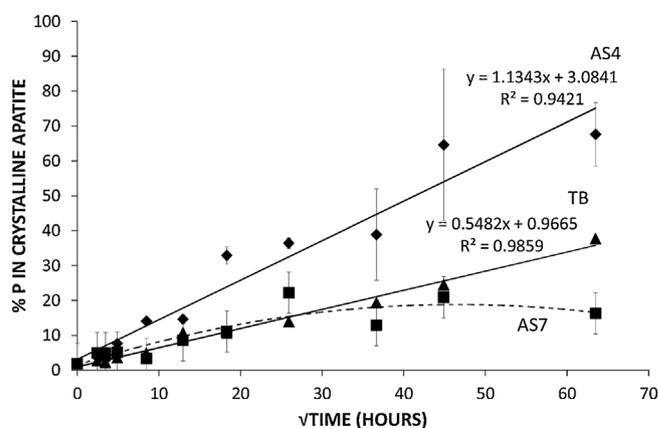


Fig. 8 – Concentration of phosphorus (in apatite) quantified by deconvolution of the ^{31}P NMR spectra of the BAG adhesive immersed in TB, AS7 and AS4 solutions.

the solution. The ion release, data from the previous study [13], showed the continuous release of high concentrations of calcium ions with a drop in the phosphorus concentration, especially at the longer time points, which favours fluorite formation at the expense of FAP. The tendency of BAGs to form fluorite upon immersion was previously shown by Brauer et al. [20] who found that the fraction of fluorite increases with increasing CaF_2 content in the glass.

4.2. SEM

Generally, as the reacted BAG particles lose ions, like calcium, their ability to back scatter electrons reduces. The small change observed in the back scatter SEM (BSEM) images of the disk surface after immersion in TB confirms the FTIR and XRD results [14] that there was little degradation of the disks throughout all the time points. The resin peaks in the ATR-FTIR did not show any reduction in intensity caused by an apatite surface layer forming and the XRD peaks continued to demonstrate the amorphous phase of the glass. However, the fraction of apatite seen in the NMR spectra slowly but steadily increased with time, as seen in Fig. 8. This suggests that the ions released from the glass particles were preferentially released to the solution, rather than precipitating in or on the disk as apatite, as the solution is already deficient in ions. This trend probably mostly affects the smaller glass particles near the disk surface, and this might contribute to less back scattered contrast, found in the disk surface at 6 months (Fig. 3). The total thickness of the reacted disk found by BSEM, which indicates that less than 50% of the glass in the disk has reacted, correlates with the extent of glass degradation observed in the NMR data.

As discussed earlier, the behaviour of the BAG disk in AS7 is different from TB and AS4. The presence of Ca and P in the artificial saliva, plus the neutral pH result in the precipitation of apatite crystals over the surface of the disk. The calcium and phosphate ions come largely from the solution with only a small contribution from the reacted glass. As the thickness of this apatite layer increased with time without a significant increase in the thickness of the reacted glass layer (Fig. 4a–d),

this suggests that the degradation of the glass particles was much lower in AS7. Clinically, this means that the adhesive does not react rapidly when the media is saturated with ions and the pH is neutral.

The rapid increase in the reacted layer thickness in AS4 with immersion time indicates the fast degradation of the glass (Fig. 5), which is consistent with the previous ion release data that showed the highest cumulative ion release [13]. This is also in agreement with the NMR spectra, which indicated the transformation of around 80% of the phosphate species of the original glass into apatite. The precipitated apatite layer on the surface of the disk at 6 months indicates the effect of the pH at later time points which increased from 4 to approximately to 7 [13]. This increase in pH and the saturation of the solution with the ions favour the apatite precipitation process. However, the precipitation of this layer was inside the disk, rather than on the disk surface, which suggests that it was formed largely from calcium and phosphate from the BAG particles of the disk. It seems that due to the extreme acidity of the solution, there was less chance for the precipitation of apatite on the surface of the disk and therefore precipitated took place quickly around the glass particles within the bulk of the composite disk. It was apparent too that the glass particles in the disk were not completely reacted or completely dissolved. This could be explained by (i) insoluble silica gel forming and (ii) the formation of highly insoluble components such as FAP and CaF_2 on the glass particle surface that resist further acid degradation. This might be an advantage especially when applied as an orthodontic adhesive, because complete dissolution of the glass particles and formation of voids might cause weakening of the adhesive matrix and subsequent bond failure.

The study of the tendency of the BAG adhesive to react in the acidic environment is more relevant to the application requirements of this research since bacterial plaque that accumulates around the orthodontic bracket, releases acids, which degrade the glass more quickly. Therefore, knowing the relation between the degradation and time in acidic and neutral media is essential to anticipate the longevity of the adhesive in terms of its bioactivity. The reacted layer thickness within the composite, at one side, under the acidic (AS4) and neutral (AS7) condition was measured from the micrographs and are shown in Fig. 9. Both sets of the data show linear dependence on square root of time. The AS4 immersed samples showed greater changes in the reacted layer thickness throughout the experiment compared to the AS7 data. However, as we have pointed out before, the dissolution of the glass particles was not complete, especially in AS4 due to the rapid formation of FAP and/or CaF_2 phases, which are both resistant to acid dissolution. In vivo, the apatite formed from the adhesive is likely to form on the existing enamel apatite.

The linear increase in reacted layer with immersion time correlated well with the linear increase in apatite seen by the NMR (Fig. 8) for AS4. The NMR results in AS7 did not show a linear correlation and this is because NMR data deliver an average amount of apatite that can be found and identified in the sample regardless whether it originated from the reacted layer or a precipitated layer of highly orientated apatite seen in the SEM (Fig. 4).

The thickness of the apatite layer that formed on the surface of the disk immersed in AS7 was also measured and is

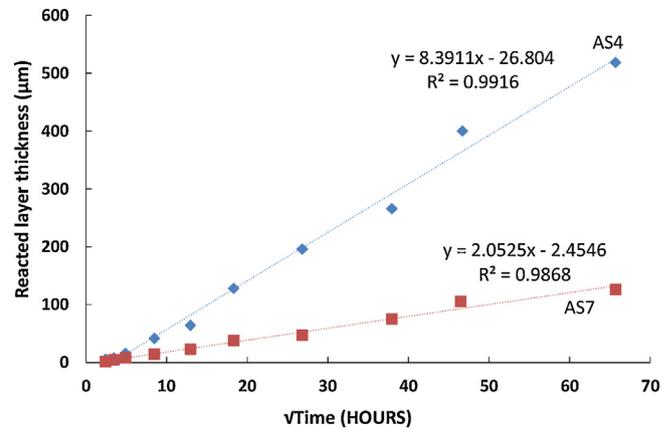


Fig. 9 – The relation between the reacted layer thickness of the composite in AS4, and time.

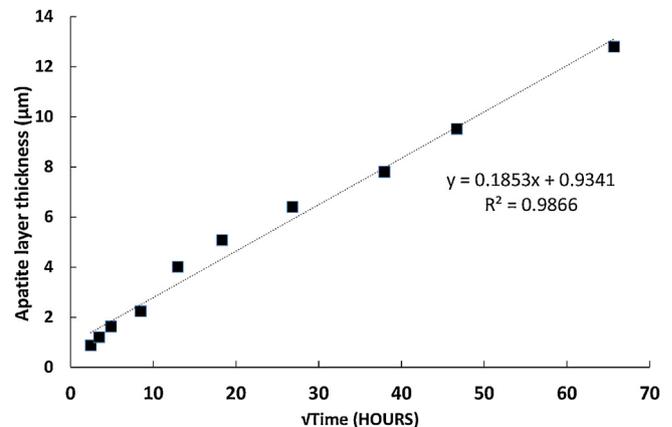


Fig. 10 – The relation between apatite layer thickness of the composite in AS7, and time.

shown in (Fig. 10). The result reveals that the thickness of the apatite is increased in a nearly linear relation to the square root of time. This suggests that the ions are precipitated accumulatively on the disk surface regardless of the thickness of apatite formed. We have pointed out previously that this layer is formed by contribution of ions from the glass (BAG) and from the solution (AS7), however, this accumulative precipitation indicates that the crystals are mostly produced by the ions coming from the solution, which is consistent with thin reacted layer thickness seen in SEM after 6 months of immersion, and the low rate of degradation seen in the NMR spectra.

More importantly, when the clinical situation is taken into account, the degradation profile could be much less, in other words, the time required for degradation of all glass particles of the BAG adhesive would be longer. As the diameter of the disk is 10 mm, it provided a large surface area for the solution to go through to the inside of the disk compared to the surface area of the disk thickness which is around 1.2 mm. The geometry of the adhesive film for bonding orthodontic bracket to the tooth surface is different. The thickness of the film is around 0.25 mm [21] and it is exposed to the saliva at one side only which is the border of the bracket. So according to this graph, if we assume that the bracket is square in shape and the

dimensions are 3×3 mm, the fluid needs to penetrate 1.5 mm from each side of the bracket to reach the centre of the adhesive. This process will take about 3 years and corresponds to the complete reaction of the adhesive. The typical time for a course of orthodontic treatment is around 2 years, therefore, it is unlikely that the BAG particles will be completely reacted and the anti-cariogenic properties of the adhesive is lost.

5. Conclusion

This novel BAG composite degrades faster under acidic condition releasing calcium, phosphate and fluoride ions. The increase in the pH from 4 to 5 and above favours FAP formation. The BAG composite promotes the surface precipitation of apatite in neutral saliva which acts as a protective layer against acid challenges. The apatite formed with the BAG composites is fluorapatite.

The lower pH values found previously [13] and the absence of calcium and phosphate in solution favour the formation of calcium fluoride at the expense of fluorapatite.

The BAG has a smart reactivity in response to pH changes reacting more rapidly at lower pH and this has a potential clinical benefit in preventing demineralisation and promoting remineralisation.

REFERENCES

- [1] Stamm JW. Multi-function toothpastes for better oral health: a behavioural perspective. *Int Dent J* 2007;57:351–63.
- [2] Shaw L, Murray J, Burchell C, Best J. Calcium and phosphorus content of plaque and saliva in relation to dental caries. *Caries Res* 1983;17:543–8.
- [3] Rogers S, Chadwick B, Treasure E. Fluoride-containing orthodontic adhesives and decalcification in patients with fixed appliances: a systematic review. *Am J Orthod Dentofac Orthop* 2010;138(390):e1–8.
- [4] Benson PE, Parkin N, Dyer F, Millett DT, Furness S, Germain P. Fluorides for the prevention of early tooth decay (demineralised white lesions) during fixed brace treatment. *Cochrane Database Syst Rev* 2013;12.
- [5] Hill RG, Barra DE, Griffin S, Henn G, Devlin J, Hatton P, et al. Fluoride release from glass polyalkenoate (ionomer) cements. In: *Key engineering materials*. Trans Tech Publ; 1995. p. 315–22.
- [6] Kuvvetli SS, Tuna EB, Cildir SK, Sandalli N, Gençay K. Evaluation of the fluoride release from orthodontic band cements. *Am J Dent* 2006;19:275–8.
- [7] Cacciafesta V, Sfondrini MF, Tagliani P, Klersy C. In-vitro fluoride release rates from 9 orthodontic bonding adhesives. *Am J Orthod Dentofac Orthop* 2007;132:656–62.
- [8] Santos RL, Pithon MM, Fernandes ABN, Carvalho FG, Cavalcanti AL, Vaitsman DS. Fluoride release/uptake from different orthodontic adhesives: a 30-month longitudinal study. *Braz Dent J* 2013;24:410–4.
- [9] Hench LL, Freiman SW. *Advances in nucleation and crystallization in glasses*. Columbus: The American Ceramic Society; 1971.
- [10] Hench LL, Andersson Ö. *Bioactive glass coatings. An introduction to bioceramics*. World Scientific; 1993. p. 239–59.
- [11] Hill RG, Brauer DS. Predicting the bioactivity of glasses using the network connectivity or split network models. *J Non Cryst Solids* 2011;357:3884–7.
- [12] Li X, Wang J, Joiner A, Chang J. The remineralisation of enamel: a review of the literature. *J Dent* 2014;42:S12–20.
- [13] Al-eesa NA, Wong FSL, Johal A, Hill RG. Fluoride containing bioactive glass composite for orthodontic adhesives — ion release properties. *Dent Mater* 2017;33:1324–9.
- [14] Al-eesa NA, Johal A, Hill RG, Wong FSL. Fluoride containing bioactive glass composite for orthodontic adhesives — apatite formation properties. *Dent Mater* 2018;34:1127–33.
- [15] Brauer DS, Mneimne M, Hill RG. Fluoride-containing bioactive glasses: fluoride loss during melting and ion release in tris buffer solution. *J Non Cryst Solids* 2011;357:3328–33.
- [16] Brauer DS. Bioactive glasses — structure and properties. *Angew Chemie Int Ed* 2015;54:4160–81.
- [17] Mneimne M, Hill RG, Bushby AJ, Brauer DS. High phosphate content significantly increases apatite formation of fluoride-containing bioactive glasses. *Acta Biomater* 2011;7:1827–34.
- [18] Fredholm YC, Karpukhina N, Brauer DS, Jones JR, Law RV, Hill RG. Influence of strontium for calcium substitution in bioactive glasses on degradation, ion release and apatite formation. *J R Soc Interface* 2012;9:880–9.
- [19] Massiot D, Fayon F, Capron M, King I, Le Calve S, Alonso B, et al. Modelling one- and two-dimensional solid-state NMR spectra. *Magn Reson Chem* 2002;40:70–6.
- [20] Brauer DS, Karpukhina N, O'Donnell MD, Law RV, Hill RG. Fluoride-containing bioactive glasses: effect of glass design and structure on degradation, pH and apatite formation in simulated body fluid. *Acta Biomater* 2010;6:3275–82.
- [21] Arici S, Caniklioglu CM, Arici N, Ozer M, Oguz B. Adhesive thickness effects on the bond strength of a light-cured resin-modified glass ionomer cement. *Angle Orthod* 2005;75:254–9.