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Fluoride containing bioactive glass composite for orthodontic adhesives — Apatite formation properties

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ABSTRACT

Objectives. Dental materials that can form apatite offer the potential to not only prevent demineralisation but enhance remineralisation of the enamel. The objective of this study was to investigate the ability of a novel BAG-resin adhesive to form apatite in 3 immersion media.

Methods. A novel fluoride containing BAG-resin adhesive described previously, with 80% by weight filler load, was used to fabricate 90 disks. Each disk was immersed in 10 ml of either tris buffer (TB), or artificial saliva at pH = 7 (AS7) or pH = 4 (AS4). At ten time points (from 6 h to 6 months), three disks were taken from each of the solutions and investigated by ATR-FTIR, XRD and SEM.

Results. The BAG-resin formed apatite on the disk surface, which increased with time, especially in AS4 and AS7. The apatite crystals formed in AS7 were highly orientated and the orientation increased with time.

Significance. This novel BAG-resin adhesive differs from the currently used adhesives by prompting apatite formation, particularly under acidic conditions. Thus, applied in the clinical situation to bond orthodontic brackets, it may discourage the frequent occurrence of white spot lesion formation around the brackets.

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1. Introduction

Bioactive glasses (BAGs) were first used in dentistry for the treatment of bony defects [1]. This material was further developed as a commercial dentifrice to treat teeth with dentine hypersensitivity and enamel demineralisation [2].

The reduction of dentine hypersensitivity occurs by occluding exposed dentinal tubules with apatite formation using a calcium-sodium-phospho-silicate glass. Remineralisation of small enamel defects caused by acid erosion or caries is enhanced through the release of calcium and phosphate ions [3,4]. More recent research has focused on incorporating BAGs in dental composites and adhesives [5] to prevent and/or

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treat demineralisation of teeth through beneficial long term ion release and their acid neutralising characteristics [6,7]. Depending upon the glass composition, restorative materials containing BAG can release locally, and more continually, a range of therapeutic ions such as Ca^{2+} , Sr^{2+} , PO_4^{3-} and F^- at the site of demand, rather than less specifically through toothpaste or remineralising gel.

The mechanism of enamel demineralisation and remineralisation has been extensively studied over several decades. Hydroxyapatite crystals in enamel are in quasi dynamic equilibrium with the aqueous phases of saliva and plaque fluids [8]. The amount of dissolution of enamel is directly related to both the pH and the concentration of calcium and phosphate ions in the solution [2,9]. On the other hand the rate of apatite formation of the BAG has been shown to increase dramatically upon increasing the phosphate content, whilst maintaining the network connectivity (NC) at a low value [10,11]. Another factor that increases the rate of apatite formation is the addition of a small amount of fluoride, whilst again maintaining the NC [11–14]. The composition of the immersion solution can also affect the apatite formation process depending on the presence or absence of ions necessary for apatite crystal formation and on the pH of the solution. In our previous study [15], we manufactured and tested a novel fluoride containing BAG resin adhesive for its potential on ion release and acid neutralising effect. It was found that F^- , Ca^{2+} , PO_4^{3-} were released substantially over a six-month period and the release was higher and faster in acidic media at pH4 compared to pH7. The BAG resin was also shown to have a long term neutralising effect [15].

Very few studies exist evaluating the ability of the BAG adhesives or composites to form apatite, particularly with regards to the effect of the immersion media on apatite formation. The aim of the present study was to investigate the potential of the previously reported BAG resin adhesive [15] to form apatite in three different solutions: artificial saliva at pH4 (AS4), and pH7 (AS7), and tris buffer (TB) at pH7.35, simulating the extreme range of conditions present in the mouth. The characterisation of the apatite would also be investigated.

2. Materials and methods

The detailed composition of the novel BAG resin adhesive was described in the previous study [15]. The BAG was composed of 35.25% SiO_2 , 6% Na_2O , 43% CaO , 5.75% P_2O_5 , and 10% CaF_2 and was prepared via the melt quench technique. The resin was composed of 42.25% BisEMA, 55% TEGDMA, 0.25% DMAEM, 0.5% camphorquinone and 2% 4-Meta.

2.1. Preparation of the BAG-resin disks

Ninety disks were prepared using Teflon moulds measuring 10 mm in diameter and 1.2 mm in thickness. The BAG-resin:weight ratio was 80:20%. The disks were divided into three groups ($n=30$) to be immersed individually in three types of solutions. Each disk was immersed in a 15 ml polypropylene centrifuge tube (Fisher Scientific UK Ltd, Leicestershire, UK) containing 10 ml of the solution.

2.2. Preparation of the immersion media

2.2.1. Tris buffer (TB)

The preparation of TB solution was by dissolving 15.09 g tris-(hydroxymethyl)aminomethane (Sigma-Aldrich) in 800 ml deionized water, adding 44.2 ml 1 M hydrochloric acid (Sigma-Aldrich) and overnight heating to 37 °C. The pH was adjusted to 7.3 the next day, using 1 M hydrochloric acid and a pH meter (Oakton Instruments, Nijkerk, the Netherlands). Deionized water was then added to make up a total volume of 2.0 l. The solution was kept at 37 °C [11].

2.2.2. Artificial saliva

Artificial saliva (demineralising and remineralising buffers) were prepared according to Ten Cate et al. [16]:

1. Demineralising buffer (AS4): 2.0 l AS4 was prepared by dissolving 0.4411 g of $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$, 0.245 g KH_2PO_4 (all Sigma-Aldrich) in 800 ml of deionized water, and adding 5.72 ml acetic acid (Sigma-Aldrich). The pH was adjusted to 4, by adding 0.5 M KOH (Sigma-Aldrich), and deionized water was then added to make up a total volume of 2.0. The solution was stored in a fridge at 2 °C.
2. Remineralising buffer (AS7): 2.0 l AS7 was prepared by dissolving 0.4411 g $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$, 0.245 g KH_2PO_4 , 9.532 Hepes and 19.386 g KCL (all Sigma-Aldrich) in 800 ml of deionized water. The pH was adjusted to 7, by adding 0.5 M KOH (Sigma-Aldrich) and deionized water was then added to make up a total volume of 2.0 l. The solution was stored in a fridge at 2 °C.

2.3. Investigations for apatite formation

For the characterisation, the samples were investigated by the following techniques

(1) Attenuated total reflection-Fourier transform infrared spectroscopy (ATR-FTIR) using a Spectrum GX (Perkin-Elmer, Waltham, MA, USA) — The disk was pressed against the ATIR-FTIR lens to attain maximum signal intensity. Data collected from 1800 to 500 cm^{-1} in absorbance mode.

(2) X-ray diffraction (XRD) using an X'pert Pro Diffractometer (Panalytical, Netherlands) with $\text{Cu-K}\alpha$ alpha radiation. The samples were analysed using a 2θ range of 3–70°, with a step size of 0.03 and a step time of 200 s.

(3) Scanning electron microscope (SEM) — The immersed disk was halved and one half was imbedded in a cold cure acrylic resin in a Teflon mould of 10.2 mm diameter and 5 mm depth. The embedded disk was polished at the fracture surface using a sequence of silicon carbide grinding papers (P300, P1000 and P4000 respectively) 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.

2.3.1. Bioactivity of BAG — 24 h study

In order to investigate the bioactivity and its potential of the BAG, an initial 24 h study was carried out. A sample of the BAG powder (75 mg) was immersed in 50 ml of TB in a 250 ml polypropylene container and one BAG-resin disk was immersed in 10 ml of TB in a 15 ml polypropylene centrifuge

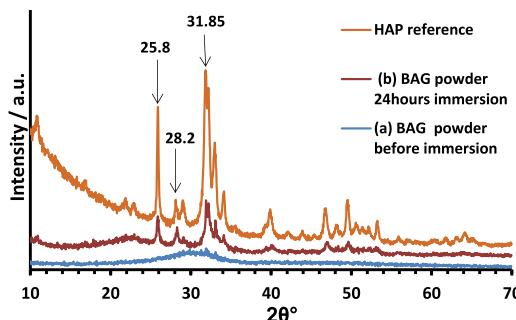


Fig. 1 – XRD of the original glass (a) and the glass after 24 h of immersion in the TB (b), with HAP reference. Apatite formed after immersion in TB.

tube. Both containers were stored in an incubator (KS 4000i control, IKA) at 37 °C with a 60 rpm agitation. After 24 h, the BAG powder was collected by passing the solution through a filter paper, and dried overnight at 37 °C. The disk was removed, washed using deionised water and dried. The samples were investigated using ATR-FTIR and XRD.

2.3.2. BAG-resin disks — long term study

For the long term study, the disks, after immersion in the solutions, 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 by ATR-FTIR, XRD and SEM. The rest of the disks were washed in deionised water and reimmersed in a fresh solution.

3. Results

3.1. Characterisation of the BAG bioactivity in tris buffer

The XRD pattern and ATR-FTIR spectra for BAG powder before and after immersion are shown as a reference in Figs. 1 and 2, respectively. It can be observed that the BAG powder changed from an amorphous pattern (Figs. 1a and 2a) to form apatite, similar to that of HAP after 24 h of TB immersion (Figs. 1b and 2b). For the BAG-resin disk before immersion (Fig. 3b), the ATR-FTIR spectra have a broad band between

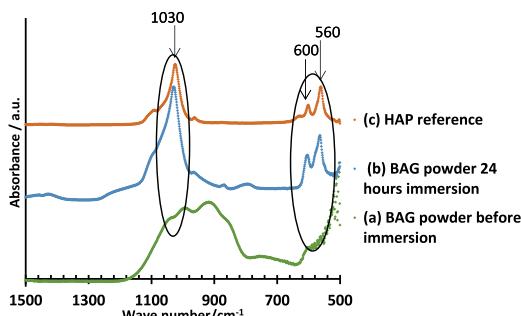


Fig. 2 – ATR-FTIR spectra of the original glass (a), glass powder after 24 h immersion in the TB (b) and the HAP reference (c).

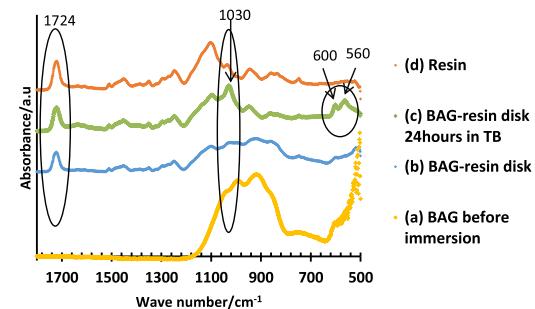


Fig. 3 – ATR-FTIR spectra of the BAG powder before immersion (a), BAG-resin disk, before (b) and after (c) immersion and the resin alone (d).

1200–800 cm⁻³ representing the amorphous BAG (Fig. 3a) and peaks at 1724 cm⁻¹ representing the resin [17] (Fig. 3d). After 24 h immersion in TB, new peaks at 560, 600 and 1030 cm⁻¹ were found in the BAG-resin spectra (Fig. 3c), similar to that for the BAG powder after immersion (Fig. 2b). On the other hand, the resin component of the spectrum at 1724 cm⁻¹ did not show any change.

3.2. Bioactivities of BAG-resin disks after long term immersion

After long term immersion, 6 h–6 months, the change of the ATR-FTIR spectra and XRD pattern with time for the BAG-resin in TB was similar to that in AS4 (Figs. 4a and b, and 5a and b, respectively), but the ATR-FTIR bands around 560, 600 and 1030 cm⁻¹ are more defined and the XRD peaks at 25.8° and 31.8° 2θ are sharper for AS4. It was also noted that the bands at 1724 cm⁻¹ diminished after 3 months and furthermore disappeared after 6 months of AS4 immersion. After immersion in AS7, the 1724 cm⁻¹ peak in the ATR-FTIR spectra was lost and the bands around 560, 600 and 1030 cm⁻¹ were formed at 6 h. There was little change of the spectra after 6 h (Fig. 4c). In the corresponding XRD, the patterns were similar to that of HAP from 6 h to 3 months. At 6 months, the peak 25.8° became very intense (Fig. 5c).

The SEM images of the disks show that the BAG particles had reacted in the surface layer of the BAG-resin disk after both TB and AS4 immersion (Fig. 6a and b). For AS7, a very thin reacted layer was found in the BAG-resin disk but a distinct fairly thick precipitated layer was formed on the surface of the disk (Fig. 6c). A precipitated layer was also seen on the AS4 disk at 6 months.

4. Discussion

4.1. Characterisation of the bioactivity of BAG

The 24 h experiment shows that BAG is bioactive, forming apatite when it is immersed in a neutral solution (TB) which contains no Ca or PO₄ ions. The XRD patterns were compared to the reference patterns of hydroxyapatite (JCPDS 09-432), fluorapatite, FAP (15-876), carbonated hydroxyapatite (JCPD 19-272) and carbonated fluorapatite (JCPDS 31-267). However, due

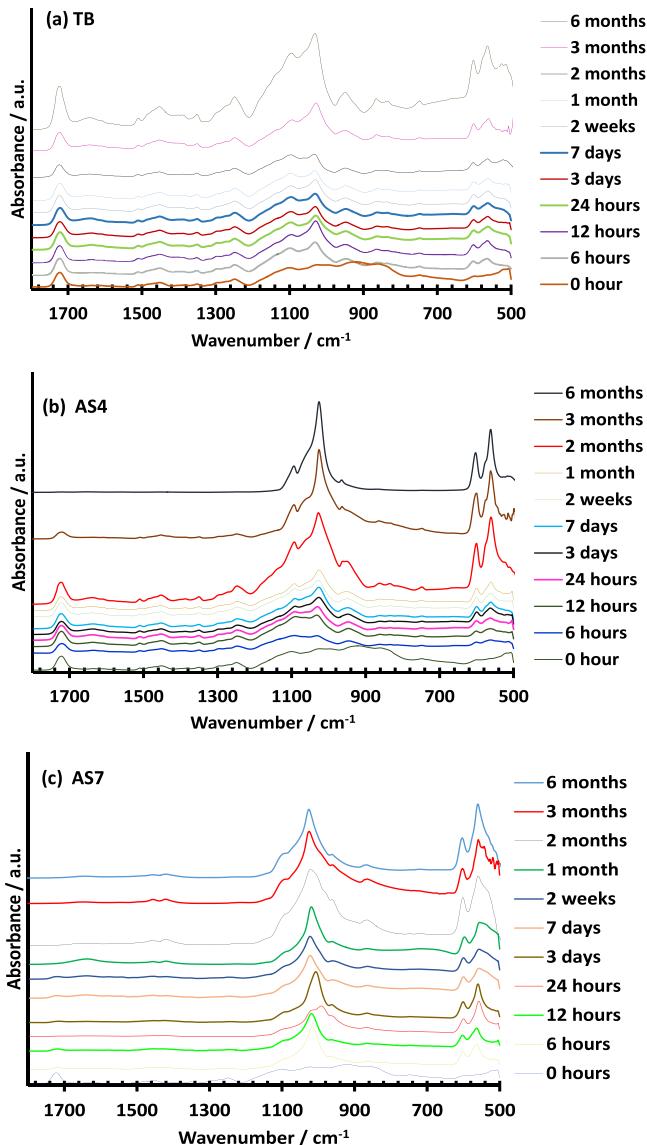


Fig. 4 – ATR-FTIR spectra of the BAG-resin disks after immersion in (a) TB, (b) AS4 and (c) AS7 for up to 6 months.

to the overlap of these diffraction patterns, they are indistinguishable and will be referred to as HAP pattern. It was shown by the XRD that the BAG was mainly amorphous (with a halo centred around 30° 2θ) before immersion (Fig. 1a). There was a very small amount (<5%) of the BAG revealing a crystalline structure as indicated by the small peaks at 31.8° and 33.9° 2θ. However, the amount was so small that it was not detected by the ATR-FTIR technique which spectra showed wide bands of the non-bridging oxygen at 1012–935 cm⁻¹ (Fig. 2a). Following 24 h TB immersion, the XRD pattern showed peaks emerging at 25.8°, 28.2° and 31.8° 2θ, and small peaks at 39° 2θ and 46–49° 2θ corresponding to apatite (Fig. 1b). The ATR-FTIR spectra (Fig. 2b) are characterised by the disappearance of the non-bridging oxygen vibrations, changes in the Si–O stretches at 770 cm⁻¹, 935 cm⁻¹ and 1012 cm⁻¹, emergence of a peak at 1030 cm⁻¹ and the split peaks of the P–O vibrations at 560 and 600 cm⁻¹. As these spectra pattern are similar to those

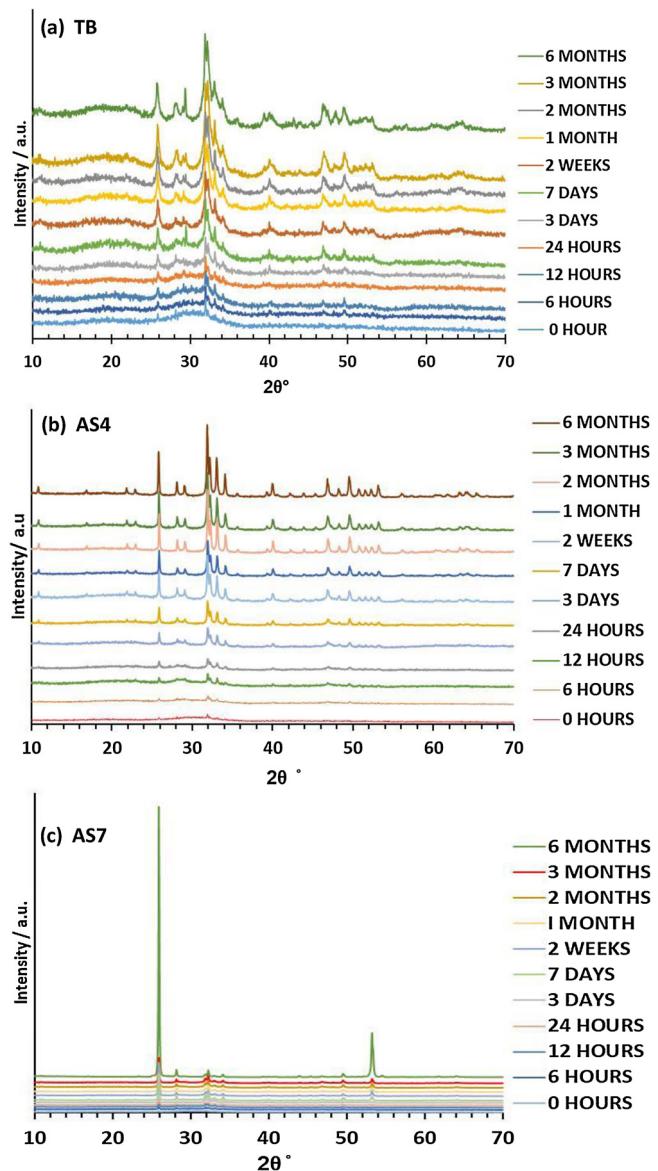


Fig. 5 – XRD patterns of the BAG-resin disks after immersion in (a) TB, (b) AS4 and (c) AS7 for up to 6 months.

for HAP, it indicates that the BAG powder bioactively changes from an amorphous structure to form crystalline HAP apatite [10,11,18,19].

4.2. Apatite formation of BAG-resin in 3 different media

The long term abilities of the BAG-resin to form apatite were investigated by 3 techniques. It is noted that the infra-red rays of the ATR-FTIR only scan the surface and only provide information on the surface of the sample; whilst the X-rays in XRD penetrate through the surface layer and react with atoms along their pathway, thus providing information at a deeper layer (~50 µm) including the sub-surface (Fig. 7). Hence SEM was used to ascertain what layer the spectra represented.

ATR-FTIR showed that apatite formed in TB (Fig. 4a) as early as six hours, but the intensity of apatite did not change signif-

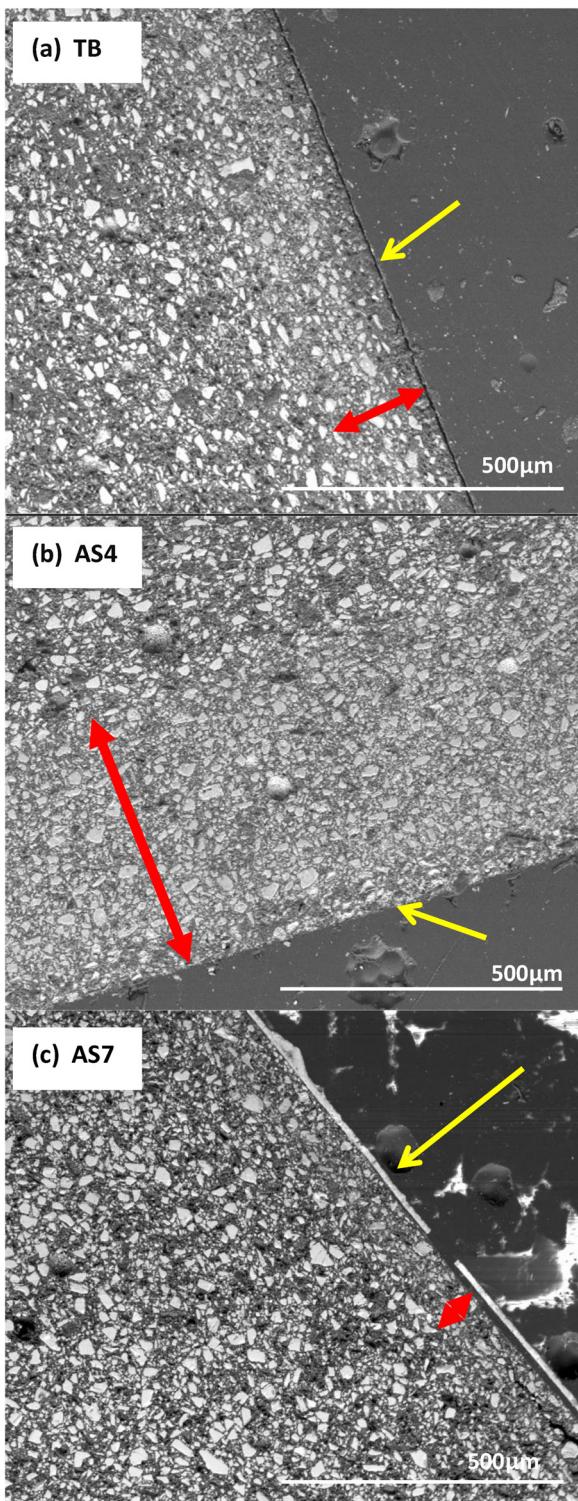


Fig. 6 – SEM images of cross sections of the BAG-resin disks after 6 months immersion in (a) TB, (b) AS4 and (c) AS7. The yellow arrows point to the surface apatite precipitate. The red arrows indicate BAG-resin reactive layers. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.).

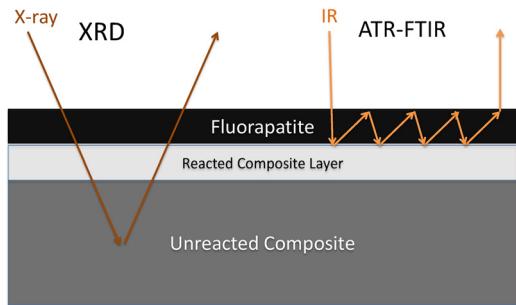


Fig. 7 – Schematic illustration of probed depths with XRD and ATR-FTIR. X-ray Diffraction probes about the first 50 μm of sample surface whilst ATR-FTIR probes the first few microns.

icantly upon longer immersion, while in AS4 (Fig. 4b), apatite formed after 6 h of immersion and the intensity increased throughout the immersion period. However, the XRD patterns reveal an increase in intensity upon immersion in both solutions (Fig. 5a and b). This would suggest that in AS4, the particles at the surface of the disk did not react completely because of the rapid diffusion of the solution to react with the deeper layer to form apatite incrementally. On the other hand, in the TB, the BAG particles on the surface were degraded before the solution moved deeper to react with more particles. This interpretation is supported by the SEM images which reveal the layer of reactive BAG-resin was thinner after TB, than that after AS4 immersions (Fig. 6a and b respectively). This might also explain the presence of diffraction peaks of the non-reacted glass particles in the TB samples. In AS7 ATR-FTIR spectra, the resin peak at 1724 cm^{-1} disappeared after 6 h (Fig. 4c). As the SEM image shows the very thin BAG-resin reactive layer and a distinct precipitated layer on the surface (Fig. 6c). This precipitated layer could be regarded as a de novo layer formed from the components (Ca and PO_4) in the AS7 solution and from the BAG-resin disk. This observation is also noted on the BAG-resin disk after 6 months of AS4 immersion.

The potential of the BAG adhesive to form apatite which was demonstrated by this FTIR and XRD study is consistent with the pattern of ion release presented by the authors previously [15]. Despite the BAG used was deliberately designed with low soda content to minimise loss of the mechanical properties of the adhesive upon water storage, there was a significant cumulative release of Ca^{+2} and PO_4^{-3} indicated the ability of the material to deliver these ions especially when required during acidic attack. The PO_4^{-3} concentration was subsequently started to level off especially in TB and AS7 solution suggesting that the released phosphate was consumed in apatite formation which is consistent with the apatite formation potential found with the three solutions.

4.2.1. BAG-resin in TB

The ATR-FTIR spectra show that apatite started to form on the surface of the disk as early as 6 h after TB immersion (Fig. 4a), evidenced by the emergence of the split bands at 560 and 600 cm^{-1} (vibration of the P–O bond) and the Si–O–Si band around 1030 cm^{-1} , but the intensity of these bands did not change significantly upon longer immersion until after 3

months. However, the XRD pattern show further increase in intensity of the diffraction peaks at 25.8° and 31.8° 2θ from 7 days (Fig. 5a) suggesting a difference in depth of detection between the two techniques. In addition, the halo found around $18-25^\circ$ 2θ indicates that there was a degradation of the BAG to form amorphous silica gel on the surface layer. In the SEM image (Fig. 6a), no distinctive layer of precipitation was found. Therefore, it can be concluded that the reaction of the BAG-resin in TB is a surface phenomenon, affecting only a few microns on the surface of the disk.

4.2.2. BAG-resin in AS4

The ATR-FTIR spectra also show apatite started to form after AS4 immersion by the emergence of very shallow peaks at 560 and 600 cm^{-1} at 6 h onwards (Fig. 4b). The Si—O—Si band around 1030 cm^{-1} also has similar pattern of increase intensity with time. The XRD peaks show more crystalline apatite were formed after AS4 immersion than TB, evidenced from the sharper and more intense peak at 25.8° and 31.8° 2θ (Fig. 5b). As these sharper peaks are also found earlier after AS4 than TB immersion, it confirms that BAG dissolves faster in acidic than in a neutral media [20]. This also indicates that the rapid and high releases of ions from BAG in acidic solution, as reported in our previous study [15], do not only have a neutralising effect, but are also used to form thicker apatite layer on the surface of the disk. This can be confirmed by the disappearance of the resin peak at 1724 cm^{-1} in the ATR-FTIR spectra at 6 months time point, and the thin layer of deposit in SEM image (Fig. 6b). In addition, the high release of F ion from the BAG-resin in acidic condition [15] might enhance the formation of apatite.

4.2.3. BAG adhesive disks in AS7

Although both the ATR-FTIR and XRD show apatite formation on the disk surface after AS7 immersion (Figs. 4c and 5c), a very thin surface reactive layer was observed in the SEM image (Fig. 6c). A layer of precipitate appeared as a chalky white layer, on the disk surface. In addition, the resin peak at 1724 cm^{-1} in the ATR-FTIR spectra was not found at all the time points from 6 h of AS7 immersion. These features indicate that the apatite was precipitated using the Ca and PO_4 ions from the AS7 solution. It is also noted that the relative intensity in the XRD peaks at 25.8° (002 plane) to 31.8° (121 plane) after AS7 immersion, is about 20 times that of HAP. This indicates that the apatite crystals are more orientated, similar to that of human enamel when they are formed in a neutral solution saturated with Ca and PO_4 ions. Also, this preferential orientation increased with time as shown by the increase of the relative intensities (Fig. 8). This preferential orientation of apatite crystals formed on BAG was found previously by Rehman et al. [21] on solid disks of Bioglass® immersed in simulated body fluid. However, they found a reduction of preferential orientation of these crystals with time and the orientation was much less marked compared to the present study. The variance in the findings is probably attributed to the difference in the composition of the BAG used. In the present study the glass has a lower Na and higher Ca content and it also contains fluoride. The higher Ca concentration on the disk surface might affect the concentration gradient and lead to a more preferential crystal orientation. In addition, the fluoride content

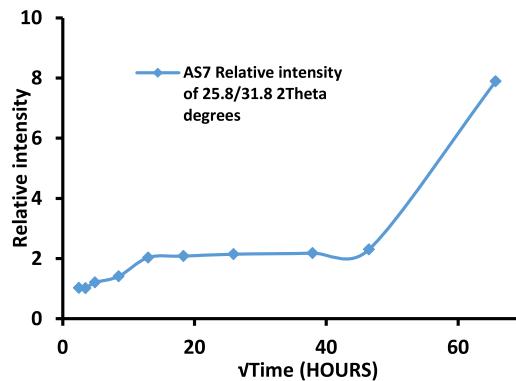


Fig. 8 – The relative intensity of apatite peaks at 25.8° (002 direction) to that at 31.8° (121 direction) for samples immersed in AS7 as a function of time.

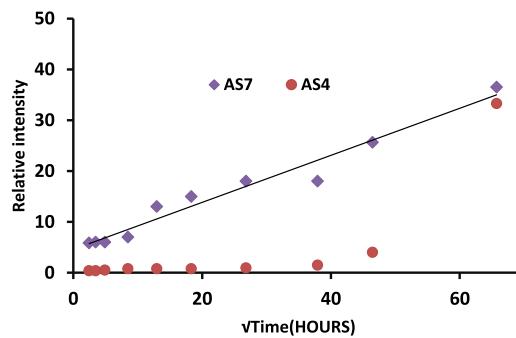


Fig. 9 – The relative intensity of the apatite ATR-FTIR spectra (at 600 cm^{-1} normalised to 1724 cm^{-1}) for AS4 and AS7 as a function of time.

could favour more needle like crystal formation by promoting growth in the c-direction.

The relative intensity of the apatite formed was observed to increase as a function of time which was confirmed by the ATR-FTIR results. Fig. 9 shows the band at 600 cm^{-1} for apatite normalised to the intensity of the band at 1724 cm^{-1} corresponding to the resin. The data indicates that apatite is forming in AS7 preferentially on the surface and the apatite that formed is becoming thicker with time. In the case of immersion in AS4, the apatite layer is only formed on the surface after 6 months which supports the SEM images.

4.2.4. Clinical application

The current study shows that when the BAG-resin is in a neutral solution, there is little reactivity except that it may promote orientated apatite formation if the solution is saturated with Ca and PO_4 ions, probably enhanced by its F release. This is likened to the resting phase of saliva and the precipitation of apatite may form a protective layer on enamel against future attack. Hence, the BAG-resin does not react until it is challenged in an acidic environment (e.g. acid produced by bacterial plaque) to release neutralising ions and F. As these ions also promote apatite formation, the BAG-resin does not only have a preventive effect through acid neutralisation, but also importantly a reparative effect on demineralised enamel. Because of the high F content of the BAG, FAP instead of HAP

may be formed. In the present study, it is not certain which type of apatite is formed due to the indistinguishable peaks of HAP and FAP in the FTIR spectra and XRD patterns. However, the water ligation band at 630 cm^{-1} in the FTIR associated with the O–H of hydroxyapatite [22] was not present, which could be due to structural disorder in the apatite lattice or be a result of a fluorapatite forming. Therefore, further study using ^{19}F magic angle spinning-nuclear magnetic resonance (MAS-NMR) spectroscopy is planned to establish if a fluorapatite forms. If FAP is formed, it will give an additional benefit as FAP is more stable and resistant to acid challenge than HAP.

Finally, as many studies have investigated the addition of bioactive components such as amorphous calcium phosphate and hydroxyapatite to dental composites to reduce the potential for demineralisation and caries [23–25], few of them have studied the effect of incorporating BAG as the active component [5,26,27]. It was found that the BAG composites neutralise acid pHs, release beneficial ions and have a potential demineralisation prevention effect, which is in agreement with the results of the current and the previously presented studies [15]. However, the current study provides additional information regarding the possible impact of the pH and the saturation of the immersion solution on apatite formation and demonstrated some correlations between the detected ion concentrations and the tendency to form apatite.

5. Conclusions

This novel BAG-resin has the potential to be developed into an orthodontic adhesive due to its long term protective and repairable effect to form apatite.

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