

# A STUDY OF PHOSPHATE ION RELEASE FROM GLASS-IONOMER DENTAL CEMENTS

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Submitted June 24, 2014; accepted October 26, 2014

**Keywords:** Glass-ionomer; Phosphate release; Ion chromatography

*Phosphorus elution from four commercial brands of glass-ionomer dental cement has been studied. Release was found to be linear with time up to 14 days in both neutral and acid conditions, indicating that release occurs by dissolution rather than by diffusion. Release was substantially greater in acidic conditions than neutral ones. The species released were studied by ion chromatography, and all brands showed clear release of the monomeric species orthophosphate  $PO_4^{3-}$ . Attempts to confirm this using  $^{31}P$  NMR spectroscopy were generally unsuccessful due to the relatively high detection limit in NMR, but for the neutral solution derived from the brand Chemflex, a weak signal was observed at 1.64 ppm, which confirmed the occurrence of orthophosphate. In addition, an unidentified species was released by all brands except Fuji IX, and this has been tentatively identified as mono-fluorophosphate  $PO_3F^{2-}$ . It is suggested that the release of these phosphate species may be beneficial in promoting remineralization when these cements are used clinically.*

## INTRODUCTION

Glass-ionomer cements are widely used in clinical dentistry. They are employed as restorative materials, both as liners and bases, and as permanent restorations, especially in children's dentistry [1]. They are formed by the reaction of special basic glass powders with aqueous solutions of polymeric acid. The most widely used acid is polyacrylic acid [1], though acrylic/maleic copolymers are used in certain commercial formulations [2].

The glass is a complex material. Initial formulations were based on  $CaO-SiO_2-Al_2O_3$  compositions, with some inclusion of  $CaF_2$  [3]. Modern formulations may substitute calcium salts with SrO (and  $SrF_2$ ) to form strontium glasses [4], and also replace aluminium compounds with, for example, zinc ones [5]. Many commercial glasses also include phosphate compounds, typically included at the fabrication stage as  $AlPO_4$  [3].

There have been numerous structural studies on these glasses and the changes that take place when these glasses undergo reaction as glass-ionomers set [6-8]. Solid state NMR with magic angle spinning has been widely used, with emphasis on the co-ordination state of aluminium. The principal finding from these studies is that aluminium exists in the glass mainly in 4-co-ordination, with some 5-co-ordinate sites [6-8]. On setting, aluminium becomes predominantly 6-co-ordinate [4, 6], and in discrete locations.

Although it is possible to prepare glasses of the desired basicity from oxide and oxy-fluoride systems, commercial glasses typically include phosphate, as we have seen [2, 3]. These glasses have improved translucency compared with the non-phosphate ones, and hence give rise to cements with improved aesthetics [3]. The phosphate units appear to exist in the glass as discrete units, albeit connected to up to four aluminium ions [8]. In a study using  $^{31}P$  solid state NMR spectroscopy, Stamboulis et al [8] showed that commercial ionomer glasses typically have chemical shifts in the range -8 to -23 ppm, which indicates the presence of  $PO_4$  tetrahedra surrounded by between 1 and 4 aluminium ions. The one exception was the glass from Ketac Molar, which had a chemical shift at 2-3 ppm, which indicates the presence of isolated orthophosphate tetrahedra that were not co-ordinated to aluminium ions,

During the setting of glass-ionomers there is transfer of ions from the glass to the matrix. It has long been known that calcium and aluminium are transferred in this way, because both calcium and aluminium polyacrylate bands can be observed in the infrared spectrum of set cements [9, 10]. Fluoride is also assumed to move into the matrix from the glass powder, since it is so readily released from the set cement [11] and the kinetics of this process is consistent with diffusion through the matrix [12]. Some years ago, the fact that water-insoluble cements of a sort could be made from ionomer glasses and aqueous

ethanoic (acetic) acid was reported [13], and because calcium and aluminium ethanoate salts are water-soluble, this was taken to indicate the formation of an inorganic matrix in addition to the matrix of metal polyacrylate salts. More recently, it has been shown that such pseudo-cements can only be prepared from phosphate-containing glasses [14] and that similar materials made from phosphate-free glasses do not become insoluble in water. Thus, it appears that phosphate is able to have a structural role in the matrix of glass-ionomer cements. It is known that this phosphate is at least slightly soluble in water, and also in acidic solutions, because phosphorus has been detected in the storage media of commercial glass-ionomers [15]. However, the nature of this soluble species is not known.

The present study has been undertaken to determine the nature and form of phosphate release from a range of commercial glass-ionomer cements. The techniques of ICP-OES, ion chromatography and NMR spectroscopy have been used to determine the amount of phosphorus and the nature of the phosphorus species occurring in the storage water around cements.

## EXPERIMENTAL

Four commercial hand-mixed glass-ionomer cements were used, namely AquaCem (Dentsply, Germany), Chemflex (Dentsply), Fuji IX (GC Corp., Japan) and IonoExpress (Kent Dental Ltd, UK). AquaCem is a water-activated cement, whereas the other three consist of separate glass powders and aqueous polymer solutions. Powder:liquid ratios employed were as recommended by manufacturers.

Cements were prepared by spatulation of powder into the liquid on a glass tile, with sufficient material being used to produce specimens of dimensions 4 mm diameter and 6 mm height in a split metal mould. Three specimens were prepared for each material, and were

stored in their moulds at 37°C for 1 hour, then removed and stored in individual 5 cm<sup>3</sup> volumes of deionised water at room temperature for 1 month.

After this storage period solutions were analysed ICP-OES (Perkin Elmer [UK] Optima 4300DV system) to determine the amount of phosphorus and by ion chromatography (using an ICS-2500 chromatograph, Dionex, UK) to determine the species of phosphorus. The chromatograph was fitted with 4 × 250 mm IonPac<sup>®</sup> AS16 columns mounted in an AS50 thermal compartment. The mobile phase comprised deionised water as carrier stream to which KOH could be added from an EG50 eluent generator (Dionex, UK). This system was used to produce the gradient elution scheme shown in Table 1. Detection employed an ASRS<sup>®</sup> suppressor at 242 mA (also Dionex, UK). The chromatograph was calibrated with the standards shown in Table 2. (For each standard, a 100 ppm working solution was prepared, from which calibration solutions at concentrations of 10 and 1 ppm were prepared by serial dilution).

Storage solutions were also examined by <sup>31</sup>P NMR spectroscopy using a 500 MHz FT NMR spectrometer incorporating an NM-50<sup>TM</sup>5AT/FG2 probe (JEOL ECA, Japan). Liquid samples were placed in a 5 mm o.d. borosilicate glass NMR tube. A coaxial insert containing D<sub>2</sub>O was placed inside the NMR tube to provide an external lock for the spectrometer. Samples were spun at 15 Hz. <sup>31</sup>P spectra were obtained using single pulse experiments with a relaxation delay of 1 second. A spectrum consisted of 22480 scans and the 90° pulse width was 9.6 μs. The data thus acquired was processed using Delta NMR Processing and Cotrol software (EOL USAInc).

## RESULTS

Release profiles for phosphorus into neutral and acidic conditions are shown in Figures 1 and 2. Final cumulative release data at 14 days are shown in Table 3. For all materials, substantially more phosphorus was released under acidic conditions than in neutral ones (p>0.01).

The calibration ion chromatogram is shown as Figure 3. Retention times for mono-phosphate (ortho-phosphate), di-phosphate, tri-polyphosphate and tri-metaphosphate were 4.9, 11.25, 12.4 and 15.7 minutes respectively.

Table 1. Gradient elution regime for ion chromatography (total gradient time = 20 min).

Aqueous phase	Time/min
30 mmol KOH	10
30-60 mmol KOH	5
60 mmol KOH	3
30 mmol KOH	2

Table 2. Ion chromatography standards employed.

Compound	Structure	Grade	Supplier
Sodium phosphate tribasic	Na <sub>3</sub> PO <sub>4</sub>	ACS reagent, 98 %	Sigma Aldrich UK
Tetrasodium pyrophosphate decahydrate	Na <sub>2</sub> P <sub>2</sub> O <sub>7</sub> · 10H <sub>2</sub> O	99.5 %	Sigma Aldrich UK
Pentasodium tripolyphosphate	Na <sub>5</sub> P <sub>3</sub> O <sub>10</sub>	Technical grade, 85 %	Sigma Aldrich UK
Trisodium trimetaphosphate	Na <sub>3</sub> P <sub>3</sub> O <sub>9</sub>	Grade III, 98 %	Sigma Aldrich UK

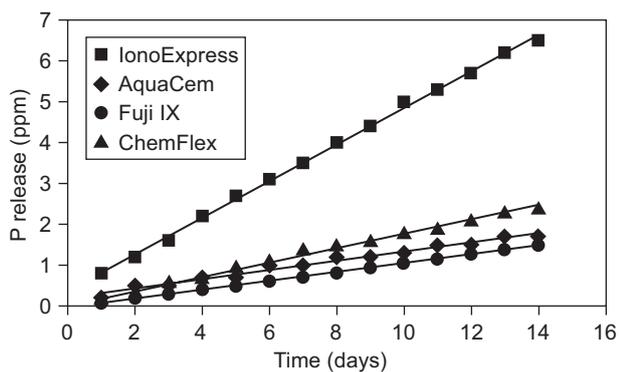


Figure 1. Phosphorus release (ppm) into water over 14 days.

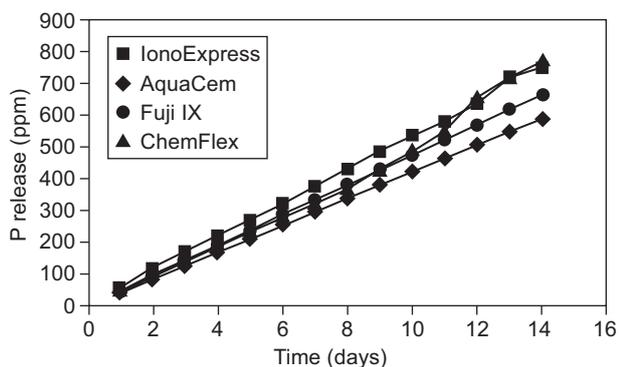


Figure 2. Phosphorus release (ppm) into lactic acid solution over 14 days.

Table 3. Cumulative phosphorus release (ppm) at 14 days (room temperature storage).

Cement	Water	Lactic acid
AquaCem	1.7	588.3
Chemflex	2.4	771.2
Fuji IX	1.5	664.3
IonoExpress	6.9	748.2

Table 4. Retention times of peaks in the ion chromatograms of neutral storage media.

Cement	Retention time (s)/min	
AquaCem	4.8	6.8
Chemflex	4.8	6.9
Fuji IX	4.8	–
IonoExpress	4.8	6.4

A typical ion chromatogram for one of the specimens (AquaCem) stored in water is shown as Figure 4 and complete data for the ion chromatograms are shown in Table 4. In all cases except Fuji IX, there was an unidentified peak in the chromatogram at a retention time of 6.4-6.9 minutes. The similarity of the retention time indicates that it was the same anionic species in all three cases, but it was not identified by reference to the standard compounds employed.

Finally, using NMR spectroscopy, there were no peaks detected in the <sup>31</sup>P spectra of the solutions in which various glass-ionomers had been stored, except for ChemFlex stored in pure water. This showed a very weak peak at 1.64 ppm, which was assigned to phosphorus as orthophosphate PO<sub>4</sub><sup>3-</sup>. The assignment was confirmed using H<sub>3</sub>PO<sub>4</sub> as reference standard, which showed a single peak in the same position. For the remaining samples, the sensitivity was too low to make any conclusive observations concerning precipitation of phosphors.

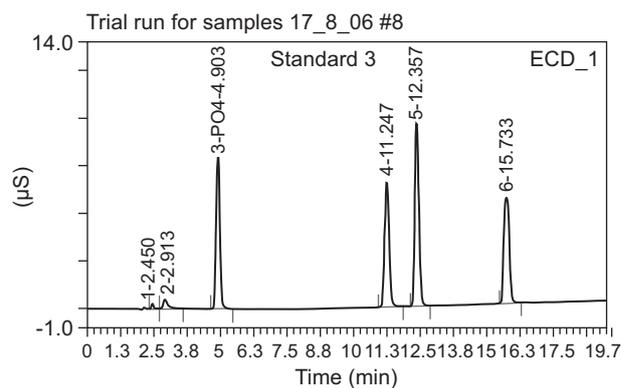


Figure 3. Calibration chromatogram for phosphate species.

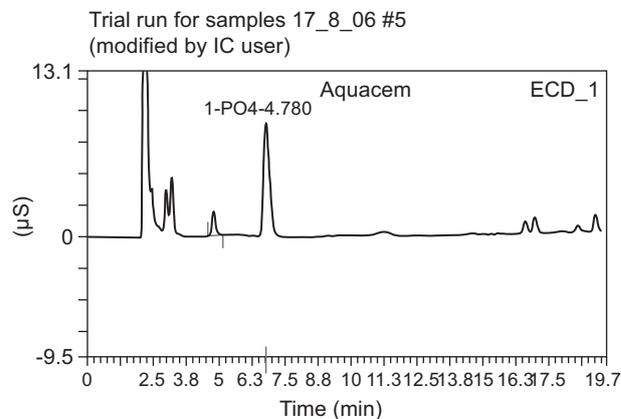


Figure 4. Example ion chromatogram for AquaCem stored in water.

## DISCUSSION

Results for phosphorus release for all four brands of glass-ionomer cement are similar to those reported previously [15] in that more phosphorus was released in acidic conditions than in neutral ones. Release kinetics have not previously been reported, and our results for cumulative release showed that the amount released increased linearly with time up to 14 days in both acidic and neutral conditions. Data for the release plots are shown in Tables 5 and 6.

Table 5. Values of  $k$  and intercept,  $c$ , for cements stored in neutral conditions.

Cement	$k$ (ppm/day)	Intercept (ppm)
AquaCem	0.09	0.25
Chemflex	0.17	0.00
Fuji IX	0.09	0.00
IonoExpress	0.45	0.50

Table 6. Values of  $k$  and intercept,  $c$ , for cements stored in acidic conditions.

Cement	$k$ (ppm/day)	Intercept (ppm)
AquaCem	41.8	20.0
Chemflex	46.5	10.0
Fuji IX	46.5	10.0
IonoExpress	52.5	37.5

Linear release means that, in all cases, plots of cumulative release against time were of the form:

$$M = kt + c$$

where  $M$  = amount released,  $k$  = the dissolution rate and  $x$  = time. Values of  $k$ , the dissolution rate, varied between 0.09 and 0.45 ppm/day in neutral conditions and between 41.8 and 52.5 ppm/day in acidic conditions, demonstrating that an acidic storage medium enhances the rate of dissolution. In most cases, the value of  $c$  was positive, though very small compared with overall amounts released at daily intervals. This may suggest the instantaneous dissolution of a very small amount of phosphate, or may represent a small margin of uncertainty in the extrapolation of the graphs. Either way, this amount is negligible and the majority of the phosphate dissolved according to well-defined linear kinetics.

A linear release pattern of this type has been previously observed for fluoride from glass-ionomers stored in acidic conditions [16]. In that case, it was attributed to release predominantly by dissolution. Dissolution consists of two steps, namely a loss of surface material from the solid and diffusion of this material into the bulk solution. If the solution is well below saturation, the diffusion process will be essentially unhindered, and loss of material from the surface controls the rate of dissolution. This seems likely to be the mechanism for phosphorus release from glass-ionomer cements stored under static conditions in aqueous media. Release thus appears to occur mainly by dissolution of limited amounts of soluble phosphate species at the surface of the cement rather than by a specific diffusion and release mechanism of the type that predominates for fluoride in neutral conditions [12].

The increased release of phosphorus under acidic conditions may be clinically beneficial. Previous studies have shown that low concentrations of fluoride adjacent to the mineral surface enhance the precipitation of calcium phosphate, thus promoting mineralization [16]. Consequently, enhanced release of phosphate from a glass-ionomer restoration may improve local availability of this ion adjacent to a region in which remineralization is beneficial. This possibility finds support in experimental studies, in which an *in vitro* model was used and showed that enhancing ion release, including phosphate, from a glass-ionomer cement by the addition of bioactive glass particles gave observable improvements in the mineralization of adjacent dentine surfaces [17]. It is also supported by evidence that bovine teeth can be mineralized by the ions released from glass-ionomer restorations without any additions [18].

In the present study, all four cements showed clearly that the monomeric species  $\text{PO}_4^{3-}$  (orthophosphate) was released. Ion chromatography is a sensitive technique capable of detecting anions at the parts per billion level [19], so that the absence of peaks at retention times found for the other phosphate species is an indication that they are not present at reasonable levels. However, in addition to orthophosphate, three out of four brands also showed an unidentified species that eluted close to  $\text{PO}_4^{3-}$ , the one exception being Fuji IX. Ion chromatography owes part of its selectivity to the nature of the guard columns employed, which suggests that in this case the unknown species is unlikely to be fluoride as  $\text{F}^-$ . This is supported by the fact that the peak was absent in the chromatograms for Fuji IX, yet this cement, like the others, is known to release fluoride at reasonable and sustained levels [20].

A possible identity of this unknown species is mono-fluorophosphate,  $\text{PO}_3\text{F}^{2-}$ . In previous studies of the analysis of phosphate species this has been found to elute close to  $\text{PO}_4^{3-}$  in ion chromatography [21], and it is a plausible species to occur in glass-ionomer cements. Indeed, one study has suggested that it is a possible means by which fluoride is released from glass-ionomer cements [22]. How this species might originate is not clear, as it has not been detected in  $^{31}\text{P}$  NMR spectroscopy studies of the cement-forming glasses [6-8]. Also, it is not apparent why it should not occur in cements formed from the Fuji IX glass. However, this glass has previously been found to behave differently from other ionomer glasses [8, 23], for example crystallising to strontium fluorapatite on heating, whereas other glasses crystallize to apatite [23]. Strontium in association with fluoride is known to alter the nature of apatite mineralisation [24], which suggests that it is the presence of strontium in the Fuji IX glass that alters the interaction of phosphate and fluoride within the cement.

Whether or not the unknown species is mono-fluorophosphate, where it is released, it occurs in greater amounts than  $\text{PO}_4^{3-}$ . Further work is necessary to characterise this species and to determine how it might be produced during the cement-forming reactions.

## CONCLUSIONS

Cumulative phosphate release from glass-ionomer cements has been shown to be linear with time in both neutral and acidic conditions, from which it is concluded that release occurs due to dissolution rather than diffusion. This is a relatively slow process in both types of condition, but occurs to a greater extent under acidic conditions than neutral ones.

All four cement brands studied showed a peak at 4.9 minutes in the ion chromatogram, attributable to orthophosphate,  $\text{PO}_4^{3-}$ . Three of the brands also showed a second species at higher concentration than  $\text{PO}_4^{3-}$ , at 6.8 minutes in all three cases. This has been tentatively proposed to be mono-fluorophosphate,  $\text{PO}_3\text{F}^{2-}$ . It is suggested that release of these phosphate species may be clinically beneficial in assisting enamel remineralization *in vivo*.

## Acknowledgement

*We thank Professor Jonathan Knowles (Department of Biomaterials, Eastman Dental Institute, University College, London) for generous permission to use the ion chromatograph in his department.*

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