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Fluoride release from model glass ionomer cements

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Glass ionomer cements (GICs) are an important class of biomedical material used extensively for color matched mercury free, dental restorations. GICs can release clinically beneficial amounts of fluoride and have acceptable handling properties which make them suitable as dental restoratives. The fluoride release of model GICs produced from specially synthesized fluoro-alumino-silicate glasses was studied. Nine glasses of varying fluoride content based on $4.5SiO_2$–$3Al_2O_3$–$1.5P_2O_5$–$(5–Z)CaO$–$ZCaF_2$ were synthesized and cement disks were prepared from them. The glass transition temperature reduced with increasing fluorine content of the glass. Fluoride ion release was measured into distilled water as a function of time for up to 140 days using a fluoride ion selective electrode. The quantity of fluoride released was found to be proportional to the fluorine content of the glass at all intervals time. The cumulative fluoride release was proportional to square root time. Substituting strontium for calcium in the glass had little influence on the fluoride release behavior of the cements.

Introduction

Glass ionomer cements (GICs) developed in the late 1960s at the Laboratory of the Government Chemist in London, UK [1] are now used extensively in dental applications as luting cements and as color matched alternatives to amalgam restoratives. Subsequent research resulted in the release to market of the first commercial GICs in the 1970s [2]. While the GICs now available to the dentist are far superior to these early materials, they work on similar chemical principles. GICs are formed by the reaction of an ion leachable alumino-silicate glass with an aqueous solution of poly(alkenoic) acid. Water is used as the reaction medium. This acid–base reaction, whereby the acid attacks and degrades the glass structure, results in the formation of a hydrogel polysalt matrix [3] and hence a rigid solid.

GICs can release clinically beneficial amounts of fluoride [4, 5] and have acceptable handling properties and aesthetics [6, 7] which make them suitable as dental restoratives. The fluoride ion is readily exchanged for the hydroxyl ion of hydroxyapatite. Fluorapatite is more stable than the hydroxyapatite mineral phase of tooth, since the fluoride ion is smaller than the hydroxyl ion and packs more readily into the apatite crystal lattice. Fluoride release and its cariostatic effect will become more important with the increasing use of tooth saving preparation methods, such as tunnel techniques. In these techniques because of the limited visibility there is a greater risk of leaving carious dentine behind than with conventional box cavities. Enamel and softened dentine can be remineralized in the presence of fluoride [8].

In restorative dentistry, fluoride plays a significant role in the prevention of secondary caries. In the 1940s, Volker *et al*. [9] observed that secondary caries rarely developed adjacent to silicate cement restorative fillings. This phenomenon was associated with the soluble nature of silicate cements in oral liquids, which allowed fluoride dissolution to occur. The leached fluoride was subsequently taken up by the adjacent enamel, imparting greater acid resistance and reducing secondary caries formation. While the arrival of dental composite technology led to a reduction in the use of silicate cements, as the composite materials had improved

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properties, silicates still had one major advantage over these new materials, namely their fluoride releasing capabilities and their observed cariostatic nature. In an effort to introduce a cariostatic ability to dental composites and amalgams, fluoride containing compounds, notably NaF and SnF_2, were included in material formulations. In the 1970s and 1980s greater emphasis has been placed on the use of dental materials for preventative purposes. GICs, the modern version of silicate cements, play such a ''bioactive'' role by not only chemically bonding to dentine and enamel but also by having caries inhibiting and anti-bactericidal properties.

There is extensive literature on fluoride ion release from GIC cements [10–12]. The majority of studies concern release from commercial materials where the glass component is frequently multiphase. The experiments have been performed using different procedures and the results were expressed in different forms and so consequently it is difficult to draw firm conclusions from the literature. Furthermore, there is very little in the literature discussing the possible mechanisms of fluoride ion release, or the relationship between glass composition and fluoride ion release [13, 14].

The glass, G200, developed by Wilson and his coworkers at the Laboratory of the Government Chemist in London for use in the first GIC contained a number of components including silica (SiO_2), alumina (Al_2O_3), aluminum fluoride (AlF_3), calcium fluoride (CaF_2), sodium fluoride (NaF), and aluminum phosphate ($AlPO_4$). Most of the early glasses were based on the system SiO_2–Al_2O_3–CaO–$AlPO_4$–$NaAlF_6$. All present commercial compositions are still based on the aluminosilicate network, although individual compositional ingredients may have changed. Many present glasses contain as their starting raw materials, SiO_2, Al_2O_3, CaO, CaF_2, Na_2O, and P_2O_5. Generally, fluoride is added in the form of CaF_2.

Several authors, notably Forsten [15], Tveit and Gjerdet [16], Hatibovic-Kofman and Koch [17], have attempted to relate the fluoride content of the glass or cement to the materials' fluoride releasing capabilities. Generally no correlation was found.

Walls [18] suggested that GICs might take up fluoride when exposed to it in appreciable concentrations, and subsequently re-release it when the external fluoride level was low. Although Forsten *in vitro* [15] and Hatbovic-Kofman and Koch [17] *in vitro* and *in vivo* demonstrated enhanced release for GIC after exposure to fluoride this did not in fact demonstrate uptake of F, followed by re-release. As the GICs that these authors used contained intrinsic fluoride, the enhanced release rate might result from faster release of this rather than uptake followed by re-release. In a study by Thevadas *et al*. [19] the addition of NaF to a fluoride containing GIC resulted in enhanced release which can be calculated to represent approximately three times the actual quantity of F added as NaF. In 1996, Williams *et al*. [20] reported that a fluoride free GIC, after immersion in alkali metal fluoride solution, released large amounts of fluoride which it must obviously have taken up. It was also shown that the quantity released was far greater than if the water component in the cement was replaced by a solution of the same F concentration as that used for immersion. This study, while showing F uptake and re-release was possible, did not demonstrate that this happened with F-containing GICs, nor did it determine if all the F uptake of a F free GIC was available for re-release. Hadley *et al*. [21] confirmed that the enhanced release found from F-containing GICs was wholly attributable to uptake with no cement releasing more F than the amount taken up over the period over which the enhanced release was detected (in this case, 97 days or less). Cements in which F was a glass component took up more F ion from solution than F-free cements and also tended not to release all of the uptaken F ion.

Crisp and Wilson [3] postulated that fluorine is released from the cement not only as the free fluoride ion, but also when complexed to aluminum.

Kuhn and Wilson [22] hypothesized that fluoride release occurs principally by a counter ion mechanism where a fluoride ion is released along with a positively charged counter ion. Hill *et al*. [23] have shown by measuring all the ions released from glass polyalkenoate cements into distilled water that the major mechanism of fluoride ion release is by an ion exchange process, with a fluoride ion being exchanged for a hydroxyl ion. They also showed that in cements based on sodium containing glasses that exhibited much greater fluoride ion release, the major effect of sodium was to disrupt the cross-linking in the polysalt matrix, thereby facilitating diffusion and exchange of fluoride ions for hydroxyl ions. Hill *et al*. [23] also demonstrated that negligible amounts of fluoride were released as complexed species. One of the glasses studied by Hill *et al*. is identical in composition to one studied in the present paper.

GICs are now being developed for use as *in situ* cements for medical applications [24]. In these new applications, the biocompatibility of the cement is important. Fluoride ion release is known to stimulate apatite deposition in bone [25] as well as osteoblast mitosis. However excessive fluoride ion release has been associated with a cytotoxic response in cell culture [26–29]. The ability to both control and understand fluoride release are critical for optimizing the biocompatibility of glass polyalkenoate cements and their clinical performance.

Materials and methods

The glass compositions employed for this study were designed so as to prevent fluorine loss, as silicon tetrafluoride, from the melt during firing [30]. The glasses were based on the generic composition

$$4.5SiO_2–3Al_2O_3–1.5P_2O_5–(5–Z)CaO–ZCaF_2$$

and were synthesized by a high temperature melt quench route. The cross-link density of each glass was calculated according to the method outlined by Ray [31].

In this series of glasses an oxygen atom is being replaced by two fluorine atoms. In two of these glasses, calcium oxide (CaO) was substituted by strontium oxide (SrO) on a molar basis. The purpose of this was to investigate the influence of SrO on fluoride release when strontium is added to glass polyalkenoate cements

primarily to confer radiopacity, but studies indicate that it may also have a caries inhibitory role like fluoride [32]. Unlike in previous studies [33], the Al : (Si + P) ratio is always less than one and there are sufficient charge balancing cations in the form of Ca^{2+} and P^{5+} to charge balance Al^{3+} which should maintain the aluminum in a four co-ordinate tetrahedral state.

The glasses differ from conventional ionomer glasses used to form cements in that they contain no alkali metal cations, which are known to cause early hydrolytic stability and to result in some cement dissolution, as well as increased fluoride ion release [30].

The glass was produced by mixing the appropriate amounts of $> 99.99\%$ pure silica (Tilcon Industrial Minerals, Stoke-on-Trent, UK) with GPR grade alumina (BDH, Poole, UK), calcium carbonate (Merck, Darmstadt, Germany) and CaF_2 (Aldrich Chemical Co., Milwaukee, USA). The mixture was then ball milled for one hour, whereupon the appropriate amount of GPR grade phosphorus pentoxide (BDH, Poole, UK) was added and mixed in. The batch was then placed in a high density sintered mullite crucible (Zedmark Refractories, Dewsbury, UK) and fired at the appropriate temperature for 2 h. The resulting glass melt was poured directly into de-mineralized water to produce granular glass frit. The glass batch was weighed after drying (24 h, 30 °C). The crucible was also weighed before and after firing. After allowing for the loss of carbon dioxide, weight losses were less than 0.9 wt %, thus the pre-fired composition and the final glass composition can be assumed to be identical.

The frit was subsequently ground in a Gyro mill (Glen Greston, London, UK) with a 120 mm diameter grinding pot, for two periods of 7 min. Batch quantities of 100 g were ground at a time. The resulting glass powders were sieved through a 45 μm mesh sieve.

The glasses produced were characterized by X-ray powder diffraction (XRD) and differential scanning calorimetry (DSC), using a Phillips powder diffractometer (Phillips Eindhoven, NL) employing CuK_α X-rays and a Stanton Redcroft DSC 1500 (Rheometrics, Epsom, UK), repectively. The DSC crucibles used were matched pairs made of platinum–rhodium alloy. Alumina was used as the reference material. Runs were performed in dry nitrogen at a heating rate of $10\,^{\circ}C\,min^{-1}$.

The poly(acrylic acid) for this study was a medical grade polymer supplied by Advanced Healthcare Limited, (AHL, Tonbridge, UK). Gel permeation chromatography showed this polymer to have a number average molar mass of 2.29×10^4 and a weight average molar mass of 1.68×10^5.

Cements were prepared by thoroughly mixing the glass powder (< 45 μm) with the poly(acrylic acid), the latter incorporating 10% m/m (+) tartaric acid solution. The cements were allowed to set in the appropriate mold for 1 h at $37 \pm 2\,^{\circ}C$ then removed from the mold and stored in distilled water at $37 \pm 2\,^{\circ}C$, prior to testing. The specimen preparation techniques are based on ''ISO 7489: 1986 Dental Glass Polyalkenoate Cements'' [34].

Cement disks, 20 mm in diameter × 2 mm thick were prepared by mixing the appropriate glass powder with 40% poly(acrylic acid) in distilled water in a weight ratio of 1 : 0.5. All the samples were stored at $37 \pm 2\,^{\circ}C$ for 24 h, then put into 50 ml of distilled water at $37 \pm 2\,^{\circ}C$, which corresponds to sink conditions. During the equilibration period, the water was renewed. This occurred daily for the first week, then at 4, 8, 12, and 20 weeks. The fluoride ion content of the water after each elution period was determined using a fluoride ion selective electrode, ''Orion Fluoride Standard Ion Plus'' (Orion Research, USA). The amount of fluoride released was expressed in terms of $\mu g/cm^2$ cement surface.

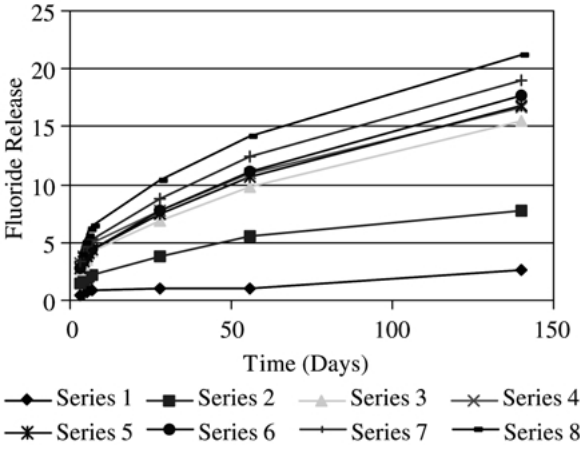

Figure 1 Fluoride release against time for the model glass ionomer cements.

Results and discussion

All the glass frits were optically clear, prior to grinding and XRD analysis confirmed that they were completely amorphous. This indicates that the glasses produced were homogenous and single phase. The glass compositions are shown in Table 1. The glass transition temperature is a measure of the degree of disruption of the glass network and hence the fluorine content. The glass transition temperature decreased with increasing fluorine content consistent with fluorine replacing bridging oxygens by non-bridging fluorines in the glass network. The Sr^{2+} ion has a similar charge to size ratio as Ca^{2+} and consequently substitution of calcium for strontium has little influence on the glass transition temperature,

TABLE I Glass Compositions Molar Proportions for ($4.5SiO_2$–$3Al_2O_3$–$1.5P_2O_5$–(5–ZCaO–$ZCaF_2$)

Glass code	Z	Sr : Ca	Melting temperature (°C)
LG99	3.0	0	1380
LG98	2.8	0	1390
LG97	2.6	0	1390
LG96	2.4	0	1400
LG95	2.2	0	1410
LG26	2.0	0	1420
LG119	2.0	1.5/2.0	1420
LG125	2.0	3.0/2.0	1420
LG134	1.5	0	1430
LG115	1.0	0	1450
LG120	0.5	0	1465
LG116	0	0	1475

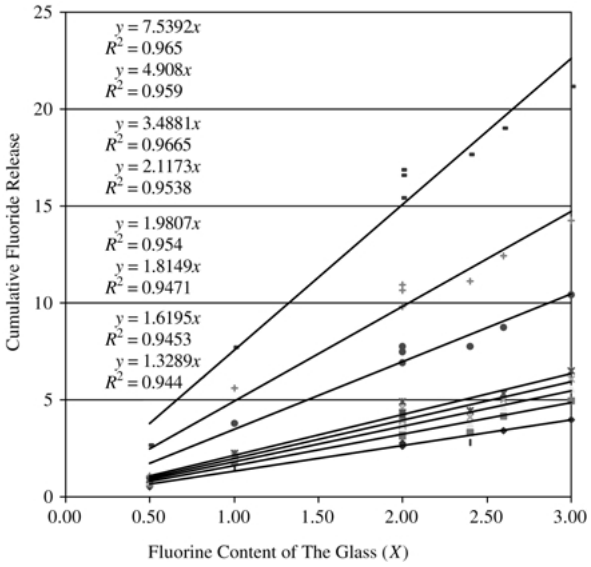

Figure 2 Cumulative fluoride release of the glass ionomer cements plotted against fluorine content of the glass phase.

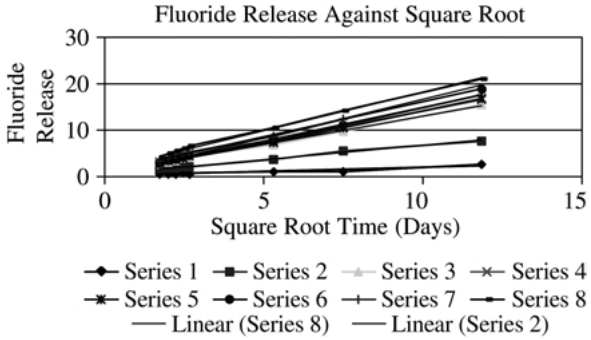

Figure 3 Cumulative fluoride release against square root time for the model glass ionomer cements.

glass structure degradability, or on the mechanical properties of the cements.

The results for the fluoride release are plotted in Fig. 1. No fluoride was released from the cement based on the fluorine free LG116 glass so the results are not shown. The glasses where strontium was substituted for calcium show a very slightly higher fluoride release at all times and the higher strontium content glass shows the greater fluoride release. The slightly increased fluoride release is probably a result of the greater density of the strontium containing glasses resulting in a slight reduction in the volume fraction of glass being used in the manufacture of the cements, which were produced using weight ratios.

Fig. 2 shows the cumulative fluoride release plotted against the fluorine content of the glass. There is strong correlation between the fluorine content of the glass and the cumulative fluoride released at all time intervals studied. Linear regression analysis of the data gave correlation coefficients between 0.94 and 0.97. This result is to be expected and agrees with a study by Hill *et al*. [23] on a related series, but it contrasts with a previous study that indicated no correlation between fluoride release and fluorine content of the glass for commercially available cements [11]. The lack of direct correlation may be a result of some of the fluorine in the commercial glasses being in the form of crystalline inclusions of fluorite and therefore being unavailable during the cement setting reaction.

Fig. 3 shows the cumulative fluoride release plotted against square root time. The plots are very linear. There is often a ''burst effect'' at early times with increased fluoride ion release. The burst effect, thought to be due to dissolution of the cement surface, was not observed in the present study. This may be due to it being suppressed by the low monovalent cation content of the present cements and their reduced solubility, plus the fact that the earliest fluoride release measurements are being taken at three days.

Conclusions

1. The glass transition temperature of the glass decreases with fluorine content. The substitution of calcium with strontium has little influence on T_g.
2. The measured fluoride release from these cements is directly proportional to the fluoride content of the glass that the cement is formed from.
3. Substituting strontium for calcium has little influence on the fluoride release. The small increase observed is due to the increased density of strontium affecting the measured powder : liquid mixing ratio.
4. Measured fluoride release is directly proportional to $(t)^{1/2}$.

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