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# Preliminary Work on the Antibacterial Effect of Strontium in Glass Ionomer Cements

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# Preliminary work on the antibacterial effect of strontium in glass ionomer cements

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Major problems associated with glass ionomer cement (GIC) dental materials are pulpal damage and the development of recurrent caries [1], which are caused by bacterial infection and not by the restorative material itself [2]. Bacteria can enter through the tooth/restoration interface by micro-leakage or it can multiply from single microbes remaining within the smear layer. Secondary caries is a result of these bacteria. Any antibacterial activity imparted by the restorative material will reduce pulpal damage and increase the restoration's longevity. Although the population of micro-organisms is known to reduce around GIC restorations [3], the available information about the antibacterial effects of GICs is limited in both the number of materials evaluated and the bacteria tested [4].

GICs are being developed for use as *in situ* medical cements and in these applications the biocompatibility of the cement is important. Fluoride release is known to stimulate apatite deposition in bone [5], but excessive release has been associated with a cytotoxic response in cell culture [6, 7]. While the antibacterial activity of GICs has generally been attributed to fluoride, obtaining a correlation between fluoride release and antibacterial activity is complicated because cements may release other caries inhibitory species such as strontium, zinc and silver ions. The cements studied in this work have been shown to represent model materials of defined chemical composition, which are free of such complications [8]. Fluoride release from these cements is directly proportional to the fluorine content of the glass; fluoride being released principally by an ion exchange process [8, 9]. The purpose of this study was to undertake preliminary analysis of the antibacterial properties of these GICs and then to reevaluate these properties when strontium ions were added.

The glasses employed were based on the generic composition:

$$4.5SiO_2\text{-}3Al_2O_3\text{-}1.5P_2O_5\text{-}(5\text{-}Z)CaO\text{-}ZCaF_2$$

In these glasses one oxygen atom is replaced by two fluorine atoms. In two of the glasses calcium oxide was substituted by strontium oxide on a molar basis (Table I). Strontium is added to GICs to confer radiopacity, but studies indicate that it may have a caries inhibitory role [10].

The glass production method has been reported elsewhere [9]. The poly(acrylic acid) (Advanced Healthcare Ltd., Tonbridge, UK) has a number average molar mass of $2.29 \times 10^4$ and a weight average molar mass of $1.68 \times 10^5$. Cement discs (5 mmØ, 4 mm thick) were prepared by mixing the glass powder (<45 $\mu$m) with the acid and distilled water containing 10% m/m (+) tartaric acid solution in the weight ratio 10:2:3. The cements were allowed to set (37 $\pm$ 2 °C, 24 h) then de-molded prior to testing.

The glass transition temperatures ($T_g$) of these glasses are shown in Table I. $T_g$, a measure of the degree of disruption of the glass network, decreases with increasing fluorine content consistent with fluorine replacing bridging oxygens by non-bridging fluorines. The $Sr^{2+}$ ion has a similar charge to size ratio as $Ca^{2+}$ and consequently substitution of strontium for calcium has little influence on glass structure or mechanical properties of the cements.

The fluoride release of these cements has been reported previously [9], but is reproduced here (Fig. 1) for completeness. The release was directly proportional to the fluorine content of the glass from which the cement is formed. The substitution of strontium for calcium had little influence on fluoride release.

Antibacterial activity was evaluated by the agar plate diffusion method, which has been employed previously [11, 12]. Studies on bacteria invading the cavity floor under restorations have identified the facultative anaerobes *Streptococcus* and *Actinomyces* as the predominant bacteria involved [13]; thus *Streptococcus mutans* (ATCC 25175) and *Actinomyces viscosus* (ATCC 19246) were chosen for this work. These bacteria (American Type Culture Collection Rockville, MD, USA) were grown from freshly isolated colonies in 2.5 ml brain heart infusion (BHI) broth (Oxoid). Incubation was for 16 h at 37 °C with shaking at 200 rpm. Following dilution in fresh BHI broth to give an $OD_{600}$

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TABLE I Glass compositions studied in molar proportions based on (4.5SiO2-3A1203-1.5P205-(5-Z-X)CaO-ZCaF2 XSrO), melting temperatures and glass transition temperatures ($T_g$), compared with the mean inhibition zone produced by the cements

| Glass code | Z | Sr:Ca | Melting temperature (°C) | $T_g$ (°C) | *F* release 20 weeks $\mu$moles/g cm cement | *S. mutans* (mm) | *A. viscosus* (mm) |
|---|---|---|---|---|---|---|---|
| LG99 | 3.0 | 0 | 1380 | 606 | 21.1 | 0.4 | –[a] |
| LG97 | 2.6 | 0 | 1390 | 616 | 19.0 | 0.7 | –[a] |
| LG96 | 2.4 | 0 | 1400 | 621 | 17.6 | 0.4 | –[a] |
| LG26 | 2.0 | 0 | 1420 | 640 | 17.0 | 0.9 | –[a] |
| LG119 | 2.0 | 1.5:3.5 | 1420 | 616 | 15.4 | 2.3 | 1.2 |
| LG125 | 2.0 | 3:2 | 1420 | 606 | 16.6 | 2.5 | 0.7 |
| LG115 | 1.0 | 0 | 1450 | 680 | 7.7 | 2.2 | 0.4 |
| LG120 | 0.5 | 0 | 1465 | 725 | 2.7 | 1.7 | 0.3 |
| LG116 | 0 | 0 | 1475 | 796 | 0.0 | 0.1 | –[a] |

[a]No detectable inhibition.

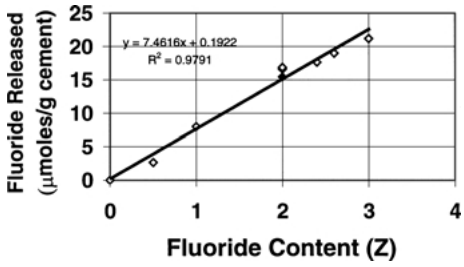


*Figure 1* Cumulative fluoride release at 20 weeks plotted against the fluorine content of the cements. The dark points indicate the strontium glasses.

of 0.05, the cultures were streaked in 2 directions on 15 cm BHI agar plates containing agar of 4 mm height. Inoculation was carried out using clinical swabs, giving an inoculum density of approximately $5 \times 10^3$ bacterial cells per plate. Following inoculation, plates were incubated at 37 °C for 10 min prior to application of discs. No more than 5 discs were analyzed on a single plate. Aerobic incubation was allowed to continue for 48 h at 37 °C, after which diameters of haloes of inhibition were measured using calipers. Disc diameters were measured at the same point and the size of inhibition zones was calculated as follows:

$$\text{size of inhibition zone (mm)} = (\text{diameter of zone of inhibition} - \text{diameter of disc}) \times \frac{1}{2}$$

Assays were carried out in triplicate and the mean zone of inhibition of the experiments was calculated. Table I shows the sizes of inhibition zones measured for the GICs studied.

Sample LG116, containing no fluoride, was included as a control. Each of the cements, with the exception of LG116, exhibited some degree of antibacterial activity against *S. mutans*. Antimicrobial activity was greatest in the case of cements that contained strontium, while the zones of inhibition were larger in all cases than the corresponding zones observed with *A. viscosus*. Several of the cements tested showed no detectable antibacterial activity against *A. viscosus*, with the presence of strontium apparently making a considerable contribution to antibacterial activity against this particular species.

This study found no significant correlation between fluoride release and antibacterial activity. The cements did have an antibacterial effect at low fluoride concentrations, but this could be due to the influence of pH. This cannot be separated entirely from fluoride release as this is mostly by an ion exchange process where a fluoride ion is exchanged for a hydroxyl ion in the external solution leaving a proton behind and acidifying the external medium [9]. Local pH effects are known to contribute to antibacterial activity, but other work has indicated that the reduction in pH in the region of GICs is due to acidification of the growth medium as a result of bacterial growth, with only minimal reductions in pH being observed with control cements or when inhibition of bacterial growth occurs [14]. This implies that the antibacterial activity of these materials is related to an ability of the materials to interfere with bacterial metabolism and growth directly rather than via a pH effect [15]. Furthermore, in an apparent conflict with the relative antibacterial effects presented in this work, Harper and Loesche [16] reported *S. mutans* to exhibit a greater acid tolerance than *A. viscosus*, indicating again that the antibacterial activities seen in our study are unlikely to be related to pH effects.

The results of this study agree with previous observations that GICs antibacterial, but differ as to how this effect occurs. Indeed, there is little agreement throughout the literature as to the nature of such effects, with support for an antimicrobial effect of fluoride ions [17], a synergistic effect of zinc and fluoride [14] or, increasingly, recognition that there is a lack of definitive evidence to link any of a variety of components to the antimicrobial effects of these GICs [15, 18]. This study indicates that the antibacterial effect is associated more with strontium release than fluoride release, or with a synergistic process involving strontium and fluoride ions. The results indicate a contribution of fluoride to antibacterial activity at low fluoride release with a greatly enhanced effect when strontium is added (LG119 and LG125; Table I). Significant bacteriocidal activity is seen against *A. viscosus* only in the presence of strontium, indicating the importance of using strontium containing cements to prevent post-operative complications resulting from residual or contaminating bacteria.

It is not possible to fully explain the mechanism by which GICs exhibit antibacterial properties, but this research suggests that the bacteriocidal action of strontium is more significant than that of fluoride. The role of fluoride in caries inhibition is probably associated

with re-mineralization of the enamel and dentine under the restorations and the reduced solubility of fluorapatite compared to hydroxyapatite in acidic solution [9], rather than its antibacterial activity.

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