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The role of Sr^{2+} on the structure and reactivity of $SrO–CaO–ZnO–SiO_2$ ionomer glasses

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Abstract The suitability of Glass Polyalkenoate Cements (GPCs) for use in orthopaedics is retarded by the presence in the glass phase of aluminium, a neurotoxin. Unfortunately, the aluminium ion plays an integral role in the setting process of GPCs and its absence is likely to hinder cement formation. However, the authors have previously shown that aluminium free GPCs may be formulated based on calcium zinc silicate glasses and these novel materials exhibit significant potential as hard tissue biomaterials. To further improve their potential, and given that Strontium (Sr) based drugs have had success in the treatment of osteoporosis, the authors have substituted Calcium (Ca) with Sr in the glass phase of a series of aluminium free GPCs. However to date little data exists on the effect SrO has on the structure and reactivity of $SrO–CaO–ZnO–SiO_2$ glasses. The objective of this work was to characterise the effect of the Ca/Sr substitution on the structure of such glasses, and evaluate the subsequent reactivity of these glasses with an aqueous solution of Polyacrylic acid (PAA). To this end ^{29}Si MAS-NMR, differential scanning calorimetry (DSC), X-ray diffraction, and network connectivity calculations, were used to characterize the structure of four strontium calcium zinc silicate glasses. Following glass characterization, GPCs were produced from each glass using a 40 wt% solution of PAA (powder:liquid = 2:1.5). The working times and setting times of the GPCs were recorded as per International standard ISO9917. The results acquired as part of this research indicate that the substitution of Ca for Sr in the glasses examined did not appear to significantly affect the structure of the glasses investigated. However it was noted that increasing the amount of Ca substituted for Sr did result in a concomitant increase in setting times, a feature that may be attributable to the higher basicity of SrO over CaO.

Introduction

Glass polyalkenoate cements (GPCs), used in dentistry for restorative purposes [1, 2], are usually formed by the reaction of a fluoro-aluminosilicate glass with an aqueous solution of polyalkenoic acid, usually polyacrylic acid (PAA). The acid attacks and degrades the glass structure, releasing metal cations into the aqueous phase of the setting cement. Once in the aqueous phase, these cations are cross-linked by the carboxylate groups on the PAA chains and form a cement with a microstructure consisting of reacted and unreacted glass particles embedded in a hydrated polysalt matrix [3, 4].

Commercial GPCs are conventionally based on aluminium glass chemistry [4]. Aluminium is present because it can isomorphically replace SiO_4 tetrahedra within the glass structure, causing local charge imbalances within the structure, thus increasing the acid degradability of the glass [5]. However, aluminium has been identified as a potent

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neuro-toxin due to its ability to disrupt both cellular calcium homeostasis [6–8] and promote cellular oxidation [9]. It has been implicated in degenerative brain disorders like Parkinson's and Alzheimer's disease [10–15]. Further to these issues, the use of aluminium containing GPCs for reconstructive otoneurosurgery [16] and total hip replacement [17] has produced negative results; in one case patient death [18]. The removal of aluminium within the glass phase of a GPC is critical if such materials are to be employed for skeletal applications.

The authors have previously shown that bioactive GPCs can be formulated using glasses from the ZnO–CaO–SiO_2 ternary system, because zinc has the ability to work as both a network modifier and an intermediate oxide in a similar way to alumina [19, 20]. Far from acting as a neurotoxin like aluminium, the release of zinc from such cements is likely to have positive effects in vivo as it can increase the DNA of osteoblasts [21], resulting in increased bone mass [22]. Zinc is required for the correct functioning of the immune system, and has also been shown to impart anti-bacterial properties to GPCs. Zn-GPCs therefore have considerable potential as hard tissue replacement materials.

It is possible to incorporate strontium (Sr^{2+}) into the glass structure on a substitutional basis for Ca^{2+}, as their respective ionic radii are similar [23]. The beneficial effect of Sr^{2+} on both diseased and healthy osseous tissue is well documented. Nielsen [24] noted that strontium shares some of the same physiological pathways as calcium. For example, Sr sustains secretion of insulin as a response to glucose and is also effective in mediating cell uptake of glucose, roles usually performed by calcium.

Sr has been used in the treatment of osteoporosis for the last 40 years [25], and has numerous beneficial effects on bone [26]. Studies have shown that Sr^{2+} enhances the replication of pre-osteoblastic cells, and stimulates bone formation in cells and calvarial cultures in vitro [27]. Furthermore, clinical trials have shown that the administration of strontium ranelate enhances cell replication and bone formation in vivo [24]. Dahl et al. [26] also note that the administration of Sr to rats (as strontium ranelate or strontium chloride) is associated with increased osteoid and osteoblast surfaces, resulting in increased bone-forming sites. Consequently, strontium administration reduces the incidence of hip fractures and vertebral compression fractures in postmenopausal osteoporosis patients [28]. Further to increased bone formation, evidence has been presented to indicate that Sr also acts as an uncoupling agent in the bone remodelling cycle, apparently diminishing osteoclastic turnover, while maintaining or enhancing osteoblastic activity [26]. It is likely therefore that the release of Sr from hard tissue biomaterials will have a positive effect on bone formation. Indeed, Johal et al. [29] who examined the in vivo response of Sr^{2+} and Zn^{2+} containing, aluminium-based GPCs showed that the cements containing a high mole fraction of Sr were the most osteoconductive of all cements. However, the effect of substituting calcium with strontium ions in ionomer glasses has not been fully investigated; in terms of both glass structure, and reactivity.

Nicholson [30] has previously shown that SrO added as dry powder to a GPC formulation resulted in decreased setting times at low levels (5 wt%), and increased compressive strengths. However, at higher levels SrO decreased compressive strengths. Unfortunately the study did not investigate SrO as a glass component—which is an imperative point for consideration.

The purpose of this research was to fully characterize a series of ionomeric glasses where SrO incrementally replaces CaO within the glass network, and then to evaluate the reactivity of these glasses when mixed with an aqueous solution of PAA.

Materials and methods

Glass preparation

Appropriate amounts of analytical grade silica, zinc oxide, strontium carbonate and calcium carbonate were weighed out and mixed in a ball mill (1 h), then dried in an oven (100 °C, 1 h). Each batch was then transferred to a mullite crucible for firing (1480 °C, 1 h). The glass melts were shock quenched into water, and the resulting frit was dried, then ground and sieved to retrieve <45 μm glass powder. Glass powders were then annealed at 650 °C for 3 h, and subsequently used for glass characterization and production of cements. Table 1 shows the chemical composition (mole fraction) of the glasses used.

Thermal characterisation of glasses

A combined differential thermal analyser-thermal gravimetric analyser (DTA-TGA, Stanton Redcroft STA 1640, Rheometric Scientific, Epsom, England) was used to measure the glass transition temperature (T_g) of each glass. A heating rate of 10 °C min^{-1} (up to 1,000 °C) was used. Materials were tested in an air atmosphere with alumina as a reference in a matched platinum crucible.

Structural characterisation of glasses

Network connectivity

The network connectivity (NC) of the glasses was calculated with Eq. 1 using the molar compositions of the glass.

Table 1 Glass compositions (mole fraction)

Glass code	SrO	CaO	ZnO	SiO_2
BT 100	0	0.16	0.36	0.48
BT 101	0.04	0.12	0.36	0.48
BT 102	0.08	0.08	0.36	0.48
BT 103	0.12	0.04	0.36	0.48

$$NC = \frac{No.\ BOs - No.\ NBOs}{Total\ No.\ Bridging\ species} \quad (1)$$

Where:

NC = Network Connectivity
BO = Bridging Oxygens
NBO = Non-Bridging Oxygens

X-ray diffraction

Powdered samples of each glass were pressed to form discs (32 mm ∅ × 3 mm). Ethyl cellulose was used as a backing material. Samples were analysed using $CuK_{\alpha 1}$ radiation emitted from an Xpert MPD Pro 3040/60 X-ray diffraction unit (Philips, Eindhoven, Netherlands).

Magic Angle Spinning Nuclear Magnetic Resonance (MAS-NMR) Spectroscopy

Powdered samples of each glass were examined by ^{29}Si MAS-NMR. The measurements were conducted at a resonance frequency of 39.77 MHz using an FT-NMR spectrometer (DSX-200, Bruker, Germany). The spinning rate of the samples at the magic angle was 5 kHz for ^{29}Si. The recycle time was 2.0 s. The reference material used to measure the chemical shift was tetramethylsilane.

Cement preparation and evaluation

Ciba speciality polymers (Bradford, UK) supplied PAA, coded E9, in aqueous solution (25%m/w). E9, with a number average molar mass M_n of 26,100 [31], was freeze-dried, ground and sieved to retrieve a <90 µm powder. Cements were prepared by thoroughly mixing the 2 g of glass powder (<45 µm) with 0.6 g PAA powder and 0.9 ml distilled water on a glass plate. This yielded a cement based on a P:L ratio of 2:1.5, and a PAA concentration of 40 wt%. Complete mixing of cements was undertaken within 30 s. Working times were defined as “the period of time, measured from the start of mixing, during which it is possible to manipulate a dental material without an adverse effect on its properties”. [32]. The net setting time was measured in accordance with ISO9917E [32].

Results & discussion

The glasses synthesized in this work were designed using network connectivity calculations, where, the determination of NC for each glass assumes (based on previous research by the authors [33]) that Zn^{2+} predominantly plays a network-modifying role in CaO–ZnO–SiO_2 glasses. The series was designed such that glasses would be structurally identical to one another (NC = 1.83), and thus facilitate investigating the effect Sr^{2+} on the rheology of resultant cements.

XRD & DTA results

X-ray diffraction patterns obtained from each glass (Fig. 1) indicate that all glasses are amorphous, with the exception of glass BT101 which exhibits a small degree of crystallinity. The diffractogram for BT101 indicates the presence of hardystonite, the only ternary compound on the relevant Ca–Zn–Si phase diagram. The phase separation of this glass is likely due to processing conditions, which vary slightly during glass production. However, irrespective of the partial crystallinity evident in Glass BT101, all glasses exhibit T_g values within 5 °C of each other (mean T_g = 674 °C; deviation from mean = 2 °C). These results indicate that the glasses in the series are structurally similar.

^{29}Si MAS-NMR results

^{29}Si MAS-NMR was performed to probe the local environment of the ^{29}Si isotope in each glass. The ^{29}Si MAS-NMR results (Fig. 2/Table 2) indicate that the glasses in the series are structurally similar, save for the decreased peak width associated with BT101, a feature attributable to

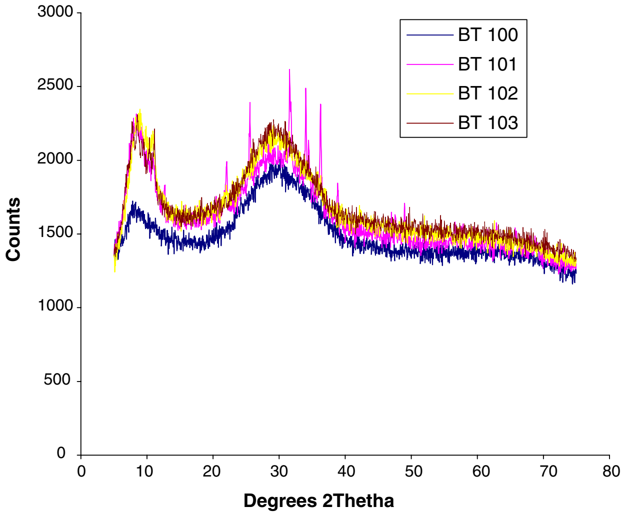

Fig. 1 X-ray diffraction patterns for glasses BT100–BT103

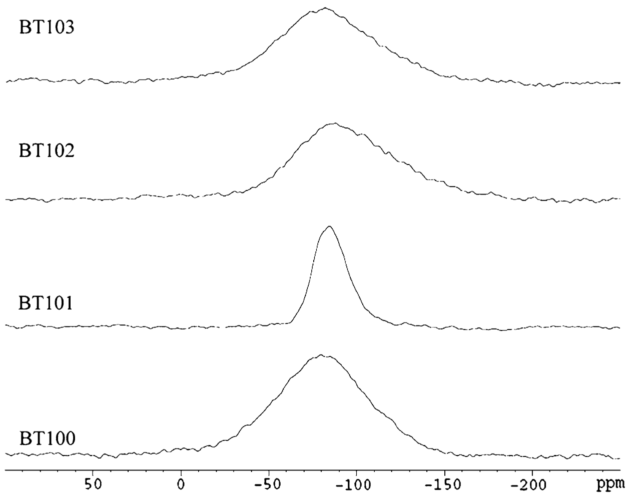

Fig. 2 ^{29}Si MAS-NMR spectra for glasses BT100–BT103

the partial crystallinity of the glass. The ^{29}Si MAS-NMR spectra for each glass (Fig. 2) exhibit a large broad peak at around –70 to –100 ppm for each glass. The chemical shift observed for silicon in a four co-ordinate state is between –60 and –100 ppm [34] indicating that the Si in each glass examined is in a tetrahedral configuration. The chemical shift however depends on the number of NBOs present in the glass. Increasing the number of NBOs moves the peak in a positive direction, whilst increasing the number of next nearest neighbour Si atoms moves the peak in a negative direction. It is accepted that Si resonance's occurring at ~86 ppm are associated with Q^3 species, and resonances at ~78 ppm are associated with Q^2 structures [35] Oliveira et al. [36] have indicated that ^{29}Si resonances between –60 and –83 ppm have also been associated with the $Q^{0/1}$ structural unit. In the literature Q^2 structures are known to resonate at –78.9 ppm [35], This shows that the substitution of Ca^{2+} with Sr^{2+} in the glass network does not affect the glass structure, presumably due to their similar ionic radii [23].

The peaks recorded for the glasses in this work are broad, a feature commonly associated with ^{29}Si MAS-NMR spectra. Lockyer et al. [37] have shown that two resonances corresponding to different Q structures can overlap and merge into one peak. Furthermore, Stamboulis et al. [38] have reported peaks widths of –80 to –120 ppm for commercial ionomeric glasses, while Jones et al. [39] report peak widths between –80 and –110 ppm. Given the width of the peaks for each glass and the precedence for peak merging in the literature, it is assumed that this feature is the result of an assortment of Q^n structures present within each glass network.

Accepting that the ^{29}Si peaks for each glass implicate the presence of a variety of Q^n structures in the network it is fair to conclude, based on the NC calculations and the corroborating chemical shift data that Q^2 structures are pervasive in the glass network. This data is important for three reasons; in the first instance it demonstrates that all the glasses produced in this study are similar, and so a fair analysis of the effect of Sr^{2+} can be made when analysing the rheology of cements produced from each glass. In the second instance, it can be stated that the replacement of CaO with SrO in the glass formulation does not affect the resultant glass network up to additions of 0.12 mole fraction in the glasses examined. This is evinced by the fact that there is no appreciable change in the ^{29}Si chemical shift data or T_g values across the series. Finally, the data herein indicates that the Zn^{2+} ion is predominantly a network-modifying ion in CaO/SrO–ZnO–SiO_2 glasses; and as such substantiates previous reports by the authors [33], which have indicated similarly.

Cement working times and setting times

At this stage it must be emphasized that all glasses are structurally very similar, and that the only variable present is the increasing SrO:CaO ratio across the series. Figure 3 illustrates the working time and setting time of cements produced from each glass, each data point being the average of three tests.

It can be seen that the working times and net setting times of cements produced from respective glasses decreases with increasing substitution of SrO for CaO in the glass, and that this decrease is not due to increased disruption of the glass network. Therefore the decreased working/setting times must be due to some feature independent of the network structure. A possible explanation for the decreased working/setting times might be found in the decreased electronegativity of Sr when compared to Ca. Elements with lower electronegativity tend to form oxides

Table 2 Illustrates decreasing working/setting time for the glass series, irrespective of the structural similarity between the glass networks

Glass designation	Working time (s) (SD)	Net setting time (s)	NC	T_g (°C)	Mean chemical shift (ppm)	Predominant Q^n Distribution
BT100	48 (2.5)	103 (2.8)	1.83	672	–80	Q^2
BT101	42 (1.1)	114 (5.29)	1.83	675	–84	Q^2
BT102	32 (0.6)	78 (6.8)	1.83	674	–81	Q^2
BT103	24 (2.6)	60 (9.81)	1.83	677	–81	Q^2

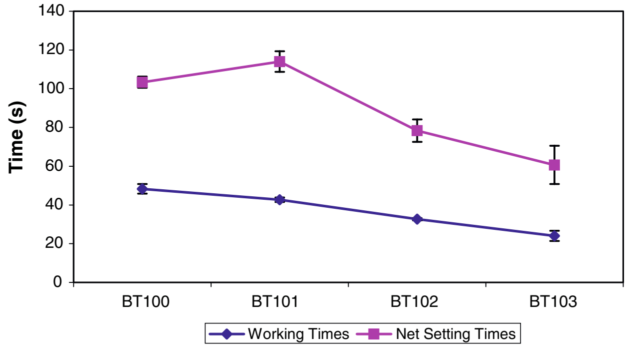

Fig. 3 Effect of SrO/CaO substitution on working times and net setting times

which are more basic than elements with higher electronegativity values. In support of this point the literature indicates that CaO is a moderate base while SrO should be considered a strong base [40]. It is accepted that the reactivity of a glass towards acid depends on its acid base properties [3], and that increased basicity of the glass increases its reactivity with the acid component of GPC formulation. It is the contention of the authors that the mechanism behind the decreased working/setting times associated with Sr substituted Ca–Zn–Si glasses is due to increased basicity of the glass network due to Sr inclusion.

Conclusions

The substitution of Sr for Ca in the $CaO–ZnO–SiO_2$ glasses examined did not appear to have any effect on the connectivity of the network, as illustrated by the negligible effect the substitution has on T_g's and Q^n distributions of each glass. Furthermore, the likely reason for concomitant decreases in working/setting times with increased SrO substitution is likely attributable to increased basicity of the Sr containing glasses. Further work is under way to evaluate the effect of the Sr substitution on the mechanical and biological properties of GPCs derived from these glasses.

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