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SUBSTITUTION OF STRONTIUM FOR CALCIUM IN GLASS IONOMER CEMENTS (PART 1): GLASS SYNTHESIS AND CHARACTERISATION, AND THE EFFECTS ON THE CEMENT HANDLING VARIABLES AND SETTING REACTION

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ABSTRACT

Objectives: To investigate the effects of substituting strontium for calcium in fluoro-aluminosilicate glass on the handling variables and setting reaction of high-viscosity glass ionomer cements.
Design: An exploratory, laboratory-based study.
Setting: Dental biomaterials research laboratory, Dental Physical Sciences Unit, Barts and the London School of Medicine and Dentistry, Queen Mary, University of London.
Subjects: A series of five glasses in which strontium substitutes for calcium and based on the general formula: $4.5SiO_2 - 3Al_2O_3 – 1.25P_2O_5 – xSrO - ySrF_2 – zCaO - yCaF_2$, where x = 0, 0.5, 1.5 or 3; y = 0, 1 or 2; and, z = 0, 1.5, 2.5 or 3 were synthesized, ground, sieved and the powders characterised by X-Ray Diffraction (XRD), particle size analysis and thermal analysis. Thereafter, they were mixed with poly (acrylic acid) (PAA) and aqueous tartaric acid to form glass ionomer cements, whose properties were investigated at different time points: working and setting times were determined by rheometry; and, the setting reaction was studied by Fourier transform infra-red (FT-IR) spectroscopy.
Results: XRD confirmed the amorphous nature of the glasses, while thermal analysis showed a mixed alkaline/entropic effect on the glass transition temperature. Working and setting times did not vary significantly with strontium content but the shortest times were recorded for the cement with the smallest particle size.
Conclusion: The results suggest that substitution of strontium for calcium has insignificant effects on the manipulation and setting reaction of the cement; therefore, substitution can be optimised to produce restorative materials with beneficial anti-cariogenic properties.

INTRODUCTION

The concept of minimally invasive dentistry advocates for preservation of natural dental tissues by employing less destructive cavity preparation techniques and adhesive restorative materials (1). High viscosity glass ionomer cements are an example of such materials. Developed for use in atraumatic restorative treatment, these materials have several advantages which include chemical adhesion to dental hard tissues as well as anti-cariogenic properties through leaching of fluoride (2).

Strontium is another element that has generated considerable interest in dentistry; while its role in bone metabolism is well established as prevention of resorption and promotion of deposition (3), Strontium is also thought to be anti-cariogenic (4). Furthermore, there is evidence that there is a synergistic remineralising property of strontium in combination with fluoride (5). The anti-bacterial capabilities of strontium have also been demonstrated (6).

Strontium has been substituted for calcium in several commercial glass ionomers in order to confer radiopacity; however, its effects on the material properties as well as its release from these materials have hardly been studied. Substitution of strontium for calcium is possible due to the similarity in size between the two ions: the ionic radius of calcium is 0.94nm while that of strontium is 1.16nm. Therefore, replacing calcium with strontium in a glass results in a relative network expansion but insignificant structural effects (7,8).

This study was motivated by the potential remineralising, anti-bacterial and anti-cariogenic properties of strontium and how these properties may be harnessed by optimising the design of glasses used in high viscosity glass ionomer cements.

MATERIALS AND METHODS

1. Glass synthesis
The glasses studied were based on the following molar ratios: $4.5SiO_2 - 3Al_2O_3 – 1.25P_2O_5 – xSrO - ySrF_2 – zCaO- yCaF_2$, where x = 0, 0.5, 1.5 or 3; y = 0, 1 or 2; and, z = 0, 1.5, 2.5 or 3 (Table 1). Analytical grade SiO_2 (Prince Minerals Ltd, Stoke-on-Trent, UK), Al_2O_3, P_2O_5, SrF_2, $SrCO_3$, CaO_3 and CaF_2 (all Sigma Aldrich, Gillingham, UK) were weighed out using an electronic precision balance (Mettler Toledo, Beaumont Ley, Leicestershire, UK) to give a 200gm batch of powder. The reagents were mixed manually in a glass jar, transferred to a platinum-rhodium crucible and fired in an electric furnace (EHF 17/3, Lenton, Hope Valley, UK) at temperatures ranging from 1440-1450°C for 1hour 30 minutes. Thereafter, the crucible was removed from the furnace and the glass melt rapidly quenched in a tank of cold de-ionized water to produce an optically clear glass frit. The frit was dried in a vacuum oven (Thermo Scientific, Loughborough, Leicestershire, UK) for at least two hours, and subsequently, quantities of 100g were ground to powder in a Gyro mill (Glen Creston, Wembley, London, UK) in a 120mm diameter grinding pot for two cycles, each lasting seven minutes. The glass powder was then sieved through a 45μm analytical sieve (Endecotts Ltd, London, UK) to control the particle size; only the sieved glass powder was used in the experiments.

Table 1
Molar ratios of the constituents of the glasses studied

SiO_2	Al_2O_3	P_2O_5	SrF_2	SrO	CaO	CaF_2	Sr to Ca	% Sr substitution
4.5	3	1.25	0	0	3	2	0Sr 5Ca	0
4.5	3	1.25	1	0	3	1	1Sr 4Ca	20
4.5	3	1.25	2	0.5	2.5	0	2.5Sr2.5Ca	50
4.5	3	1.25	2	1.5	1.5	0	3.5Sr1.5Ca	70
4.5	3	1.25	2	3	0	0	5Sr 0Ca	100

Table 2
Powder/Liquid ratios used to prepare the cements

Glass formulation	Powder (gm)	PAA (gm)	Aqueous solution of 10% tartaric acid (ml)
0Sr 5Ca	0.5	0.1	0.1
1Sr 4Ca	0.52	0.1	0.1
2.5Sr 2.5Ca	0.55	0.1	0.1
3.5Sr 1.5Ca	0.58	0.1	0.1
5Sr 0Ca	0.61	0.1	0.1

Table 3
Average particle sizes of the glass powders

Glass formulation (% Sr substitution)	D10(μm)	D50(μm)	D90(μm)
0Sr 5Ca (0%)	0.88	7.98	32.58
1Sr 4Ca (20%)	0.78	5.15	34.14
2.5Sr 2.5Ca (50%)	0.83	6.06	46.04
3.5Sr 1.5Ca (70%)	0.62	2.82	24.07
5Sr 0Ca (100%)	0.81	6.64	39.11

2. Characterisation of the glass powder
Powder X-ray diffraction: X-ray diffraction (XRD) is a non-destructive technique commonly used for structural and chemical analysis of crystalline substances (9). Powder X-ray Diffraction (XRD; X'Pert PRO MPD, PANalytical, Cambridge, UK) was used to confirm the non-crystalline nature of the glasses by their amorphous diffraction pattern as well as to study the influence of substituting strontium for calcium on the diffraction pattern, observable by a shift in the two theta angle.

Particle size analysis by laser diffraction: Laser diffraction is a fast and simple technique for particle size analysis, based on the fact that spatial distribution of a monochromatic beam of scattered light is a function of the particle size within a sample (10). Laser diffraction (Malvern 2000, Malvern Instruments, Worcestershire, UK) was used to determine the particle size of the glass powders; the powders were dispersed in de-ionised water, with three runs performed for each glass sample.

Differential scanning calorimetry (DSC): Differential scanning calorimetry (DSC) is a quick and easy thermal analysis technique used to study how a material's heat capacity is changed by temperature (11). DSC (Stanton Redcroft DSC 1500, Rheometric Scientific, Epsom, UK) was used to determine the glass transition (Tg) of the glass powders; 50 mg of the glass powder was compared against analytical grade Al_2O_3 reference in platinum-rhodium crucibles. DSC runs were conducted in air at a heating rate of 20°C per minute.

3. Preparation and characterisation of the cements
Cement preparation: The cements were prepared by mixing the glass powders with high molecular weight (80 KDa) freeze-dried poly (acrylic acid) (S & C Polymer GmbH, Elmshorn, Germany) and an aqueous solution of 10% tartaric acid (Sigma Aldrich), in predetermined powder/liquid ratios that

corresponded to 50% molar mass of poly (acrylic acid). Adjustments were made for the higher density with increasing amounts of strontium in the glass (Table 2). To ensure homogeneity, 50 gms of each glass powder was pre-mixed with the appropriate quantity of poly (acrylic acid) in a glass jar and the adjusted amount of the mixture was weighed out using an electronic analytical balance (Mettler Toledo, Beaumont Ley, Leicestershire, UK) as required for each experiment.

Determination of working and setting times: Working time (WT) is the duration from the start of mixing until there is a change in viscosity of the material such that it can no longer be manipulated, while setting time (ST) is the duration from the start of mixing until the material attains some degree of rigidity. In practical sense this means that after mixing, the material should remain in a soft, pliable state to facilitate its placement and contouring within a cavity during the working time; shortly thereafter, it should become rigid (or set) within its setting time.

The working and setting times of the cements were determined using Wilson's oscillating rheometer (12). The rheometer consists of two plates, approximately 2 mm apart, one of which is fixed while the other oscillates under the action of an eccentrically driven spring. The fixed plate is connected to a water bath thus enabling measurements at 37°C. The oscillations are noted as a voltage induced by a rod moving in and out of the transducer and are plotted to produce a rheogram.

The rheometer operates on the following principle: while the cement is in its unset state between the plates, the rod can move freely; however, as the cement sets, the amplitude of oscillation is progressively dampened, restricting the movement of the rod within the transducer, and resulting in decreased output voltage. Once the cement is fully set, the voltage drops to zero. This can be deduced by the tapering off observed on the rheogram (Figure 1).

Figure 1
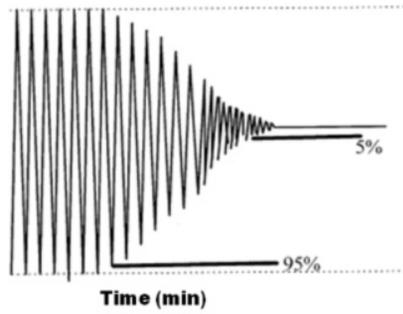*Rheogram and derivation of points corresponding to WT (95% of oscillation amplitude) and ST (5% of oscillation amplitude)12*
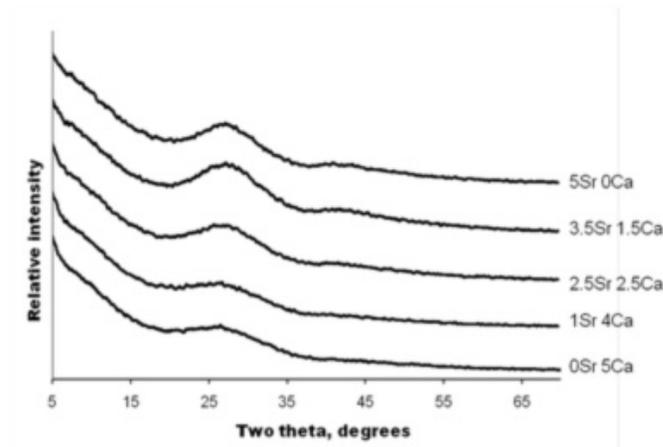

Figure 2
XRD patterns of the glasses

Figure 3
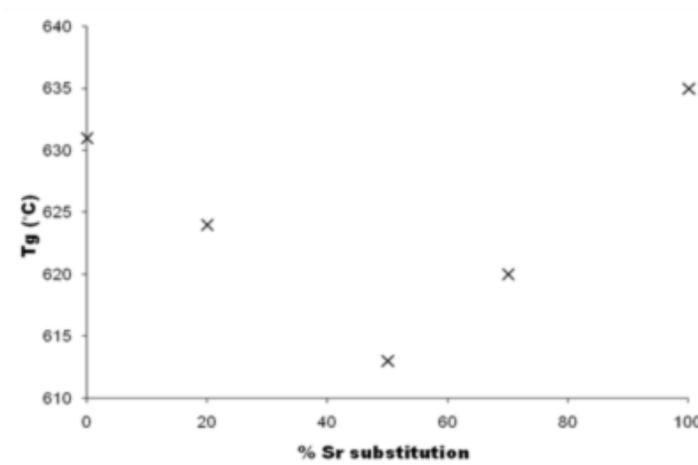*Percentage Sr substitution against Tg*

Figure 4

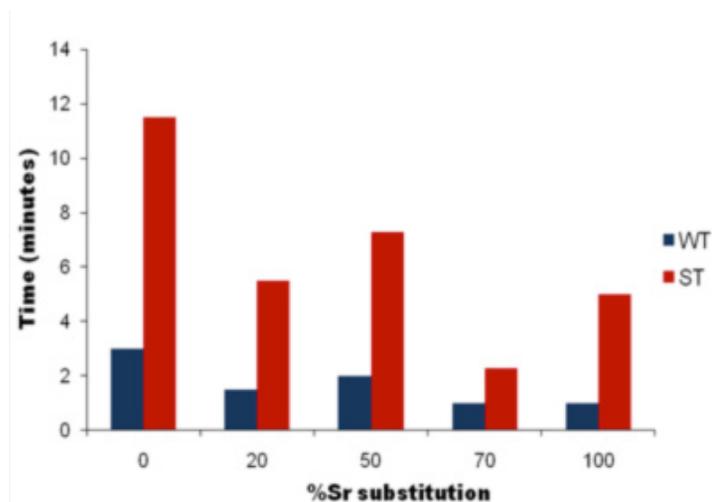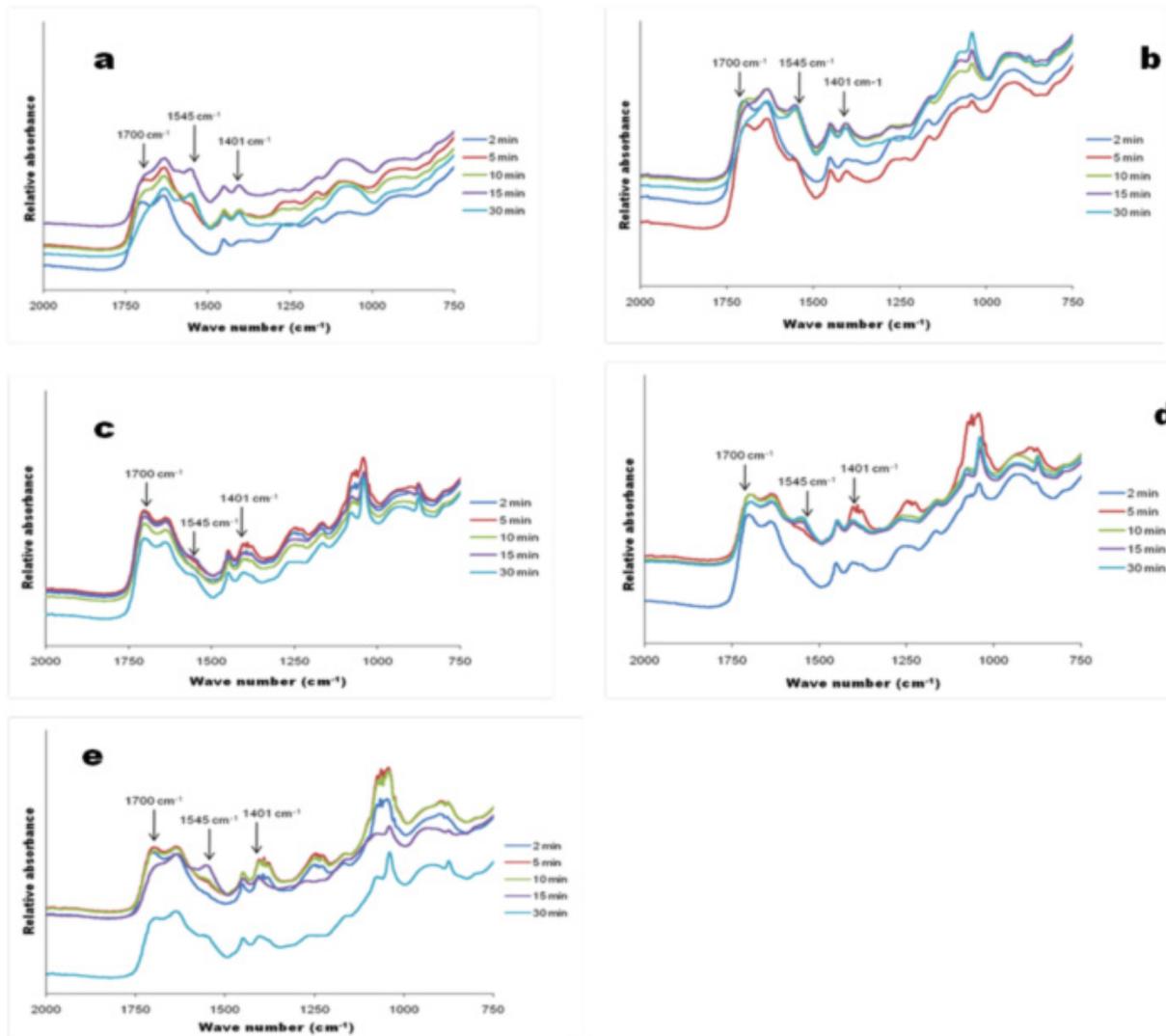*Percentage strontium substitution against cement working (WT) and setting times (ST)*

Figure 5

Real time FT-IR spectra of the cement pastes containing 0% (a), 20% (b), 50% (c), 70% (d) and 100% (e) strontium at different time points after mixing

The rheometer was switched on at the start of mixing; the powder and liquid were spatulated for 30 seconds to obtain cement pastes, which were then quickly transferred to the apparatus, set at 37°C. From the resultant rheogram, the working and setting times of the cement were taken as the time when the amplitude of the oscillation fell to 95% and 5% of its initial value, respectively (Figure 1).

Fourier transform infra-red (FT-IR) spectroscopy of setting reaction: Infra-red spectroscopy is the 'absorption measurement of different infrared (IR) frequencies by a sample positioned in the path of an IR beam' (13). IR spectroscopy identifies compounds by their unique absorption frequency which is dependent on the chemical functional groups present in the sample; it is based on the principle that all atoms in a molecule are in continuous vibration with respect to each other, producing a net change in the dipole moments. When the frequency of a specific vibration is equal to the frequency of the IR radiation directed on the molecule, the molecule absorbs the radiation. The major types of molecular vibrations are stretching and bending. On absorption of the IR radiation, the associated energy is converted into these types of motions which lead to the characteristic absorption bands observed on the spectrum.

FT-IR spectroscopy (Spectrum GX, Perkin-Elmer, Waltham, MA, USA) was used to identify the cross-linked poly-salt matrices associated with the setting reaction of glass ionomer cements. This was done in two ways: firstly, real time absorption was recorded by scanning the setting cement pastes 2, 5, 10, 15 and 30minutes after mixing; secondly, following the compressive strength tests (described in Part 2 of this paper), the first three cylinders of each group within the three time points of 24 hours, 7 days and 28 days were ground in ethanol to stop the setting reaction and the powder samples subjected to IR spectroscopy.

The glass powders, freeze-dried poly (acrylic acid) and tartaric acid powders were also scanned as reference materials. The spectra for the different glasses, cement pastes and cement powders at various time points were super-imposed in order to visualize the shifts in the peaks corresponding to the neutralization of the acids and formation of the cross-linked salts. Data was collected in the mid IR region, from 2000 to 750 cm-1.

RESULTS

1. Glass characterisation

X-ray diffraction confirmed the non-crystalline nature of the glasses by their amorphous diffraction patterns (Figure 2). There was a slight shift of the amorphous halo towards a lower two theta angle with increasing strontium substitution. The glasses had similar particle sizes, all within the range for restorative cements; however, the glass containing 70% strontium had comparatively smaller particles (Table 3). The Tg of the glasses ranged from 613°C to 635°C. From 630°C for the glass containing 0% strontium, the Tg dropped steadily to the lowest value of 613°C for the glass containing 50% strontium. Thereafter, it rose again, with the highest value of 635°C recorded for the glass containing 100% strontium (Figure 3).

2. Cement working and setting times

The longest working and setting times were recorded for the cements containing no strontium, while comparatively shorter working and setting times were recorded for the strontium containing cements, as shown in figure 4.

3. FT-IR spectroscopy of setting reaction

Figure 5 (a to e) shows the real time spectra at different time points after mixing the cement pastes. The spectra appeared similar with subtle differences observable in the peaks 1545 cm-1 and 1401 cm-1 which corresponded to the COO- asymmetric and symmetric stretches respectively. These peaks rose with time while the 1700 cm-1 peak diminished as the acids were neutralised by the glasses. However, it was observed that the 1700 cm-1 peak diminished earlier for the cements containing 0% and 20% strontium (Figure 5a and 5b) as compared to 50%, 70% and 100% strontium (Figure 5c, 5d and 5e); this was associated with an earlier appearance of the 1545 cm-1 and 1401 cm-1 peaks for the former. These peaks appeared later for the cements containing 50%, 70% and 100% strontium.

DISCUSSION

A series of fluoro-aluminosilicate glasses in which strontium substitutes for calcium on a molar basis from 0% to 100% was synthesised and thereafter subjected to various laboratory experiments aimed at determining the effect of the substitution on the glasses, and cement handling and setting reaction. This was essentially an in-vitro study which formed part of preliminary testing of a nouvelle dental biomaterial. One of the greatest disadvantages of in-vitro studies is questionable relevance to actual usage of the materials. Although test conditions often try to simulate body functions, they are a poor predictor of a material's performance under the real physiological conditions. Nevertheless, in-vitro tests are useful for standardized and less expensive large scale screening during the initial stages of biomaterial development (14).

The melt and quench technique is a straight-forward and reproducible way of synthesising glasses, by simply fusing various oxide ceramics at high temperatures then quenching the melt rapidly in cold de-ionised water to obtain a glass frit (15). The glass

frit or powder can then be easily characterised using reliable structural, chemical and thermal analytical techniques such as those employed in this study. Laboratory-based studies tend to be both technique-sensitive as well as labour-intensive; this may be challenging particularly with regards to eliminating errors and ensuring that results are valid. Despite the limited time available to conduct the study, each experiment was repeated at least twice to minimize errors and ensure validity.

While the diffraction pattern confirmed the amorphous nature of the glasses, there was an apparent slight shift of the amorphous halo towards the lower two theta angle with increasing strontium substitution. Such findings are expected given the expansion of the glass network due to the larger ionic radius of strontium when compared to calcium, and was similarly observed in bioactive glasses (7,16). Nevertheless, the effect was not as obvious in the glass containing 0% strontium and was probably due to masking by the background scattering.

The DSC results for Tg of the glasses suggest both a mixed alkaline earth effect as well as an entropic effect. A mixed alkaline earth effect manifests as a non-linear behaviour of properties such as the glass transition and is dependent on the mobility of the modifier cations; the said property acquires a maximum or minimum value at a certain level of substitution of one alkali ion for another. An entropic effect manifests as dependence of certain properties, including glass transition, on the composition of the system. The findings differ from those observed in bioactive glasses (16); however, a mixed alkaline earth effect as well as entropic effects on the Tg of fluoro-apatite glasses and glass ceramics have been recorded (8). In the latter study, while the decreasing Tg with increasing strontium substitution was attributed to the expansion of the glass network by the larger strontium ion, the researchers could not explain why the highest Tg was observed in the glass containing 100% strontium, which was also the case in the current study.

While the glass particle sizes were similar and fell within the range for restorative cements (17), the results suggest that the slight variation in size influenced the cement working and setting times. The shortest working and setting times were recorded for the cement with 70% strontium substitution, whose glass had the smallest D10 and D50 particle sizes. The influence of the D50 was probably less, as suggested by the observation that the cement containing 100% strontium set faster than that containing 50% strontium despite the latter having a smaller D50 value. It is expected that a smaller particle size presents a larger surface area which accelerates the chemical setting reaction. Therefore, the smaller particles directly influence the cement working and setting times, as was observed in the experiment.

There was no obvious effect of substituting strontium for calcium on the working and setting times of the cements studied.

The results of the FT-IR scans for real time setting reaction of the cements coincided with 1700 cm-1 for COOH, 1545 cm-1 for COO- asymmetric stretch and 1401 cm-1 for COO- symmetric stretch and are consistent with those proposed in other studies (18-20). Slight variations of these peaks may occur depending on the test conditions (19). While there were only slight variations among the spectra for the real time setting reactions, the results suggest that the strontium based glasses neutralise the acids at a slower rate than the strontium free glasses. This is based on the observation of a steeper slope formed by the peak ratios of COO-/COOH for the strontium free cement as compared to that observed for the cements with increasing strontium substitution. The COO-/COOH peak ratios of the strontium free cements and the cements containing 20% strontium were also higher after 30 minutes; conversely the peak ratios of the glasses and COOH are highest for the cement containing 100% strontium after 30 minutes.

Furthermore, the peaks corresponding to the poly-salts appeared earlier in the real time scans for the strontium free cement and the cement containing 20% strontium as compared to the cements containing higher levels of strontium. The FT-IR scans of the set cements at 24 hours and 7days showed higher salt peaks for the strontium containing cements; however, at 28 days, the salt peaks for all the cements are nearly the same. The suggestion that calcium based glasses would neutralise the acids faster than the strontium containing glasses may be explained by the difference in the ionic radii of the two thus calcium would be expected to diffuse faster than strontium on dissolution. Nevertheless, this observation differs from that made on strontium containing bioactive glasses which dissolved faster than calcium based glasses (21); this finding was attributed to expansion of the glass network by strontium due to its larger ionic radius.

In conclusion, the results suggest that substitution of strontium for calcium in the glass neither affects the glass structure nor the cement handling properties and setting reaction significantly, a finding that is attributed to the similarity between the ionic sizes of the two elements. Therefore, further research should aim at designing glasses containing optimum ratios of strontium which can be utilized to produce superior preventive and restorative dental materials that harness the benefits of strontium.

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