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PHYSICOMECHANICAL PROPERTIES OF STRONTIUM AND FLUORIDE MODIFIED BIODENTINE™
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PHYSICOMECHANICAL PROPERTIES OF STRONTIUM AND FLUORIDE MODIFIED BIODENTINE™

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ABSTRACT

Objectives: **To investigate the effect of bioactive glass addition on the physicomechanical properties of Biodentine™. The study compares the setting time, compressive strength and radiopacity of Biodentine™ modified by three different compositions of bioactive glasses**

Design: **This was an exploratory lab based quasi-experimental study**

Setting: **The study was conducted in the laboratory at Queen Mary, University of London Dental Physical Sciences Unit.**

Materials and methods: **Dental cements based on Biodentine™ and its modifications were used in the study. Original unmodified Biodentine™ cement was coded BO. Three bioactive glasses based on high fluoride (Q), high strontium (I) and high fluoride + strontium (H)were synthesized and 0.07g of each of the bioactive glasses added to Biodentine™ powder to yield 3 additional types of cements which were coded BQ, BI and BH respectively. A set mass of each cement type was prepared by adding 5 drops of the liquid supplied with Biodentine™ to the powders and triturating for 30 seconds in a 4000rpm electric amalgamator. These cements were subjected to setting time determination, compressive strength testing and radiopacity testing according to ISO 9917-1: 2007.Setting time and compressive strength were statistically analysed using T-test at 95% confidence level at a significance level of 0.05.**

Results: **Bioactive glass addition resulted in initial setting times of11.31+0.18, 12:22+ 0.11, 11:59+ 0.15 and 13:35+0.23 minutes for BO, BQ, BI and BH respectively. The increased setting time of BQ and BH were statistically significant. Student t-test analysis of compressive strength demonstrated statistically higher 14 day compressive strengths for BI(p=0.036) and BH (p=0004). BH cement had the highest grey scale value equivalent to 2.9mm of aluminium, which was consistent with the best radiopacity among the 4 Biodentine™ based cements.**

Conclusion: **Bioactive glass addition to Biodentine™ improved the radiographic detectability and compressive strength of the cement. This is important since current use of Biodentine™ is limited owing to inadequate strength and detection on radiographs.**

However, further studies are needed to explore alternative modifications that could shorten the setting time of this cement.

INTRODUCTION

The aim of biomaterials science has been to develop materials that are ideal mechanically, physically and biologically. In the past, most research effort was directed at the physico-mechanical properties of materials with less attention to biological properties. Only recently has focus shifted towards developing the bioactive aspect of biomaterials due to growing interest in minimally invasive procedures (1). One material borne of this research focus is Biodentine™.

Biodentine™ contains; tri calcium silicate (C3S), di-calcium silicate (C2S), calcium carbonate, oxide filler, iron oxide shade, zirconium oxide radiopacifier, calcium chloride accelerator and a hydrosoluble polymer /modified polycarboxylate/water (2)(3)(4)(5). This cement's stated setting time by the manufacturer is 12 minutes. It is applied for pulp therapy, while being able to act as a temporary coronal dentine replacement (4). Since its launch in 2009, considerable research on the product has been done and this is thoroughly reviewed by Malkondu et al., (2).

Although it has an impressive biological property profile, its use has been limited owing to less than optimum physico-mechanical properties. Comparative studies of the radiopacity of Biodentine™, various mineral trioxide aggregate (MTA) brands, Fuji II and Fuji IX agree that though the radiopacity of Biodentine™ matches that of GIC cements, it is still less than adequate (6). In MTA, this could be attributed to the presence of heavy metals (7).

It has been reported that though the setting time of Biodentine™ is shorter than MTA and thus presents a good alternative to the latter (8), this is still long for an ideal dental cement (7). The compressive strength of this product has been found to range between 73.8MPa and 300MPa in various studies (7)(9)(10).

Therefore, Biodentine™ does not seem to satisfy the requirements of most clinicians with regard to; setting time (7); radiographic detectability (11)(5); compressive strength(7); and the absence of the caries inhibiting fluoride and strontium species (12). Strontium is a species that has been shown to upregulate odontoblasts (13), improve radiopacity(14)(15)(16); manage dentine hypersensitivity(17); and leads to caries inhibition(18). Investigation of strontium's role in caries prevention and its synergistic effect with fluoride has also been explored (19).

For the above reasons, strontium is increasingly being incorporated into various dental materials (15) (20). Bioactive glass can be used as a carrier for mineral species due to its dissolution leading to release of ions and independent apatite forming ability. This bioactive material was first discovered and marketed as Bioglass by Larry Hench who described it as a rapid cooled non crystalline material capable of forming apatite when in the bio-physiological environment (21)(22). It has been used in modifying the biological properties of several dental materials (23) (24)(25).

The aim of this study therefore was to incorporate fluoride and strontium containing bioactive glasses into Biodentine™ and assess the effect on the setting time, compressive strength and radiopacity of the modified cement. The specific objectives were to (i) synthesize 3 types of bioactive glasses, (ii) to create three versions of modified Biodentine™ cements in addition to unmodified Biodentine™ by adding 10% by weight of high fluoride bioactive glass; 10% high strontium bioactive glass; or 10% fluoride + strontium bioactive glass into Biodentine™ powder before mixing with Biodentine™ fluid, (iii) to evaluate the setting time , compressive strength and radiographic detectability of the original Biodentine™ and its modified versions.

MATERIALS AND METHODS

Bioactive glass synthesis

The bioactive glasses were prepared using a melt quench route. Mixtures of analytical grade SiO2 (Prince Minerals Ltd, Stoke-on-Trent, UK), P2O5, CaCO3, Na2CO3 and CaF2 (Sigma-Aldrich, Gillingham, UK) were prepared according to the compositions in Table1.

Table 1

Molar percentage of bioactive glass compositions used

Bioactive glass	SiO_2	P_2O_5	SrO	Na_2O	CaO	CaF_2		SrF_2
High F^- - Q	36.8	0.8	-	19.6	17.2	25.5		-
High Sr - I	38.1	6.3	25.9	29.6	-	-		-
F^- + Sr– H	36.8	0.8	17.2	19.6	-	-		25.5

Each composition was melted in a platinum–rhodium crucible for 1 h at 1430 °C in an electric furnace(EHF 17/3, Lenton, Hope Valley, UK). After melting, the glasses were rapidly quenched into water and a large size sieve was placed at the bottom of the water containing bucket to simplify the frit retrieval process.

The frit was dried overnight in an oven (Thermo Scientific, Loughborough, Leiceistershire, UK) at 50°C. Later, the glass was ground using a Gyro mill (Glen Creston, Wembley, London, UK) for 3 minutes and thereafter sieved using a 90 μm mesh analytical sieve (Endecotts Ltd, London, UK).

Cement Preparation

Four different types of cements were manipulated. Plain Biodentine™ cement coded 'BO', was prepared by adding five drops of fluid to the powder and triturating for 30 seconds in a 4000rpm electric amalgamator. All modified Biodentine™ samples were prepared by adding 0.07g of the specific bioactive glass into the Biodentine™ containing capsule. This amount was approximately 10% of the Biodentine™ content. The first modification involved addition of 0.07g of high F- (Q) bioactive glass into a Biodentine™ powder containing capsule. This was mixed in the 4000rpm amalgamator used for Biodentine™ manipulation for 10 seconds.

To this mix, five drops of Biodentine™ fluid were added and amalgamated for 30seconds. This cement sample was coded BQ. Similar steps were followed to produce cement sample BI and BH, using high Sr (I) bioactive glass and high F- + Sr (H) bioactive glass respectively. All three modified cements for testing contained bioactive glass: Biodentine™ in the ratio of 1:10. The unmodified Biodentine™ cement acted as a control.

Setting time determination

Prepared cement was packed into stainless steel moulds of 10 mm diameter and 2 mm height. The disks, together with a Gilmore needle apparatus were transferred to a water bath assembly maintained at 37^{oC} and covered by plastic cling film to provide relative humidity. Initial setting was determined with the initial Gilmore needle measuring 2.12mmin diameter and weighing 113g, while for the final setting time, the Gilmore needle measuring 1.06mm in diameter and weighing 453.6g was used. The initial and final setting time of each cement was obtained by arithmetic mean of three repetitions of the test for each cement sample. The cement samples were kept within the sheltered water bath set up throughout the test procedure.

Compressive strength testing

Cylindrical moulds measuring 4mm by 6mm were cleaned, dried using ethanol, coated with silicone

spray and allowed to dry for 15 minutes. A mixture of each cement was packed into the steel moulds. Eight cylinders for each time point of 24 hours and 14 days were cast. These were clamped with polyethylene sheets and placed in an incubator at 37^{0C} for one hour. Afterwards, the cylinder bases were polished with 600A grit silicone carbide paper disks to achieve a smooth finish before being carefully detached from the moulds.

Each cylindrical specimen was placed into 10ml deionized water, labelled and stored at 37^{0C}. At the end of the 24 hour and 14-day immersion periods, the cylinders were retrieved and their diameter measured. They were compressed using a universal testing machine (Instron, High Wycombe, UK) with a crosshead speed of 1 mm/min. A 30kN load was used and load at fracture was recorded.

The final strength value for each cement group was arrived at by averaging the values from the 8 cylinders. The results were plotted on a graph to compare the strengths of the 4 cements with each other, and the strength at the 24hr and 14day time points.

Radiopacity testing

Radiopacity measurements were performed by comparison to an aluminium 6step wedge, measuring 0.5,1, 2, 3, 4 and 5mm thickness. The test specimen disks measured 10 mm wide and 1mm thickness, and were prepared from Teflon moulds. After mixing and packing, the BiodentineTM based cements were protected with polyethylene sheets, clamped and incubated at 37o C for 1hour. FUJI IX (GC Corp, Tokyo, Japan) and Pro Root MTA (Dentsply Sirona, Pennsylvania, USA) were introduced in radiopacity testing in order to offer a better comparison.

This is especially so because studies have confirmed MTA to be the most radiopaque tricalcium silicate based cements while GIC's radiopacity tends to be comparable to Biodentine™(6). These two cements were manipulated according to the manufacturer's instructions and packed into moulds. On extraction, they were hand polished to achieve an even thickness of 1.0± 0.1mm. All the above-mentioned samples were stored dry in air tight plastic bags until 24 hours later when radiographs were taken.

An aluminium wedge was placed against the three test samples at a time and the set up was irradiated with a digital X-ray machine (Dentsply Gendex 765 DC) at 30cm focal length, 65 KV, 7 mA, aluminium filtration of 2mm Al, Focal spot size 0.4 mm with an F speed film with a 0.2 sec. exposure. The digital radiograph images were analysed using Image J software (http://rsbweb.nih.gov/ij/) to determine the grey scale values of each material specimen relative to that of the aluminium wedge. The step wedge grey scale values were recorded in Microsoft Excel and a calibration graph was plotted against the thickness of aluminium step.

Statistical analysis

The setting time and compressive strength were statistically analysed (3 repeats for setting time; 8 repeats for compressive strength) using T-test at 95% confidence level at a significance level of 0.05.

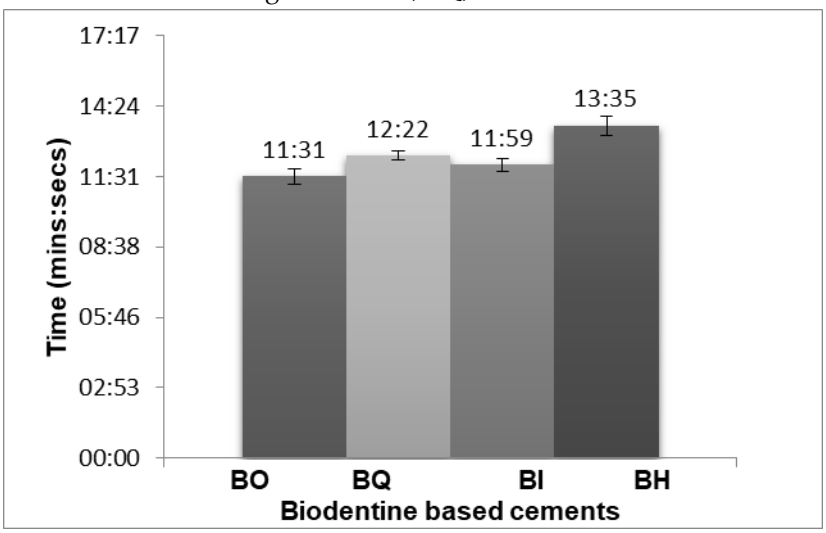
RESULTS

Setting Time

The initial setting times of BO, BQ, BI and BH were found to be 11.31+0.18, 12:22 + 0.11, 11:59+ 0.15 and 13:35+0.23 minutes respectively (Figure1).

Figure 1

Initial setting time of BO, BQ, BI and BH cements



Although BI had a lower initial setting time than BO, this is not statistically significant. However, the higher initial setting time of BQ (p= 0.02) and BH (p = 0.001) were found to be significant (Table 2).

Table 2

Summarized student t-test statistical analysis of setting time findings

	BO: BQ		BO: BI		BO: BH	
	Initial	Final	Initial	Final	Initial	Final
P-value	0.022**	0.017**	0.252*	0.010**	0.002**	0.001***

Where * = not significant; ** = significant; ***= highly significant

The final setting times of the bioactive glass modified Biodentine™ were also higher. Thus, BQ = 13.56+0.12, BI = 13.59+0.17and BH = 18.12+0.08 minutes, compared to BO = 12.14+0.15.

Compressive strength. At both 24 hours (Figure 2) and 14 day (Figure 3) time points, the bioactive glass modified cements had better strength than plain Biodentine™. Fourteen-day strength improved significantly for BH (197.9+47.7) and marginally for BI (164.5+31). However, 14-day strength was lower for BO (124.4+37.9) and BQ (145.4+34.2).

Figure 2
24-hour compressive strength

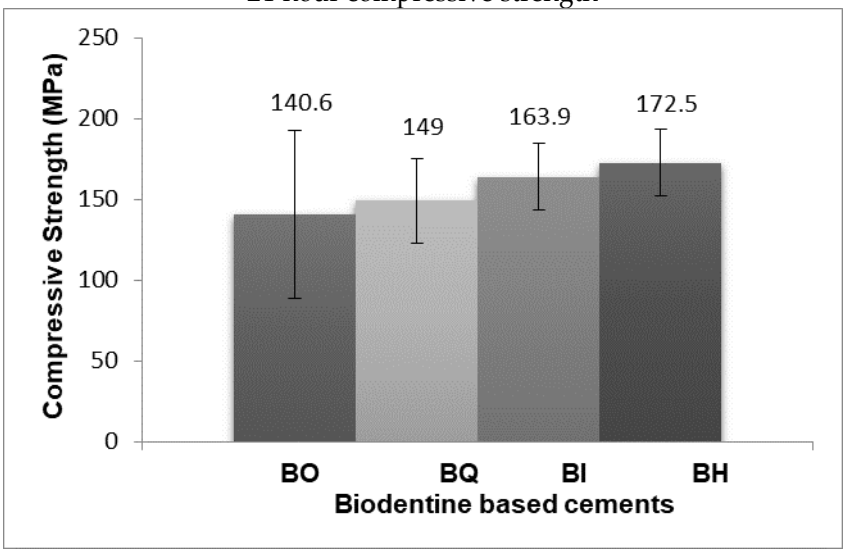
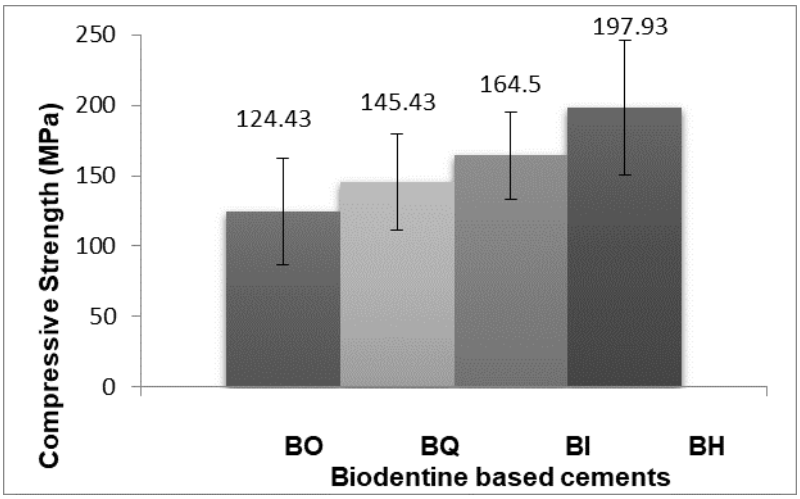


Figure 3
14-day compressive strength of BO, BQ, BI and BH cements



Overall, at both 1 day and 14 days, the bioactive glass modified cements yield better strength than the plain Biodentine. However, statistical analysis in (**Table 3**) shows that the strengths of the cements were comparable. The 14 days' strength for BI

was significantly higher than that of BO (p= 0.036), while that of BH was much more so (p=0.04).

Table 3

Summarized student t-test statistical analysis of compressive strength findings

	BO: BQ		BO: BI		BO: BH	
	1 day	14 days	1 day	14 days	1 day	14 days
P-value	0.692*	0.264*	0.257*	0.036**	0.129**	0.004***

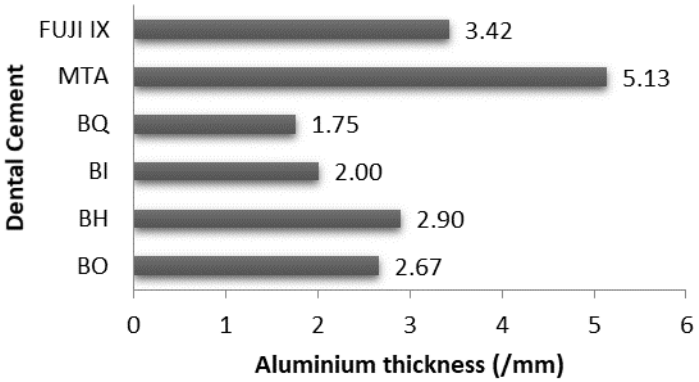
Where * = not significant; ** = significant; ***= highly significant

Radiopacity testing

The effect of bioactive glass addition on the radiopacity of Biodentine™ was seen to decrease with both BQ and BI and increased with the strontium containing bioactive glass -BH cement. Calculated grey scale values of the four cements are lower than those of MTA and FUJI IX (Figure 4). The aluminum thickness values for Biodentine™ were lower than the 3.5mm claimed by the manufacturer.

Figure 4

The comparative radiopacities of the 6 cements, represented as aluminum thickness equivalents



DISCUSSION

The BH cement seems to rank best with regard to most of the properties (Table 4).

Table 4
Arbitrary ranking of the results from this study; where 1 is best and 4 is worst.

Cement	Radiopacity	Final compressive strength	Setting time
Plain Biodentine™ BO	2	4	1
Biodentine™ + F bioactive glass BQ	4	3	3
Biodentine™ + Sr bioactive glass BI	3	2	2
Biodentine™ + F & Sr bioactive glass BH	1	1	4

A higher grey scale value, equivalent to 2.9 mm thickness of aluminium was recorded for the BH samples which may arise from the presence of the radiodense strontium (26). Although having strontium too, BI yielded lower radiopacity values than Biodentine™ which could be attributed to porosities and the lower molar percentage of strontium in this cement. Suffice to add, BH also had the best compressive strength.

Perhaps, the presence of crystallized bioactive glass in the BH group could have a role in its higher recorded strength. The crystalline compounds may act as stable fillers, with less susceptibility to dissolution compared to their amorphous counterparts in the BI and BQ cements. Stable fillers can contribute to strengthening silicate cements by making the cement more compact. (27)(28). Other known radio pacifying agents exist such as zirconium oxide, titanium, tantalum, platinum, tungsten, barium sulphate and zirconium oxide (15), but in this specific study, strontium was chosen since it is a known substitute for calcium in bioactive glasses and is known to confer cariostasis (23) and may also stimulate odontoblasts(13).The BQ specimen, which had no additional opacifying agent showed less opacity than unmodified Biodentine™.

This could be due to the generally radiolucent nature of bioactive glasses (29). Generally, dental material radiopacity allows distinction from the dental hard tissues and helps identify and assess restorative margins and secondary caries. According to ISO 6876:2012 any dental cement's radiopacity should be at least 3mm Al (30). Clinically however, 2mm Al equivalent helps distinction from dentine which is equivalent to 1mm Al. Therefore, radiopacity

values matching or greater than those of enamel should be the target for dental materials (15). At 2.9mm of aluminium thickness, BH is well within this recommendation.

The superior 24 hour and 14 day compressive strengths of the bioactive glass modified cements may be correlated to the setting time. Given that BH had the longest setting time, perhaps this allowed for better hydration, which tends to lead to better compressive strength for water based cements. However, this is contrary to another study where a decrease in compressive strength was observed with glass ionomer cements modified with bioactive glass (31).

At the same time, any substitution of calcium for strontium would result in weakening of the glass structure network due to the expanding effect of the larger strontium ions (26). It would therefore be expected that the strontium containing bioactive glass modifications; BI and BH would record lower strengths than BQ, which was not the case. Perhaps this could be because the bioactive glass added was very low. A different experimental design may be required to assess this impact with relation to increasing Biodentine™: bioactive glass ratios.The lower 14 day strengths recorded for BQ and BO are puzzling since silicate cements should record higher strengths with time owing to the slow reaction of the dicalcium silicate phase which typically transforms into a calcium silicate hydrate, which confers strength. It is possible that manipulation variability arising from proportioning the Biodentine™ liquid as drops, rather than precisely measured volume could account for this.

Whenever the drops differed in size this could affect the powder; liquid ratio and porosity in the specimen, ultimately lowering the strength. Despite the need to improve Biodentine™ as discussed above, this should not be at the expense of unfavorably altering its handling profile. Calcium silicates undergo a 2 stage setting reaction. Stage one, is marked by formation of a metastable phase of calcium silicate hydrate and calcium hydroxide; followed by formation of semi crystalline calcium silicate hydrate and calcium hydroxide. There is an induction period during which the metastable calcium silicate hydrate phase coats the tricalcium silicate particles, and controls the rate at which precipitation of calcium silicate hydrate occurs. The solubility of the metastable phase is higher than the crystalline phase while that of tricalcium silicate is greater than metastable monomeric calcium silicate hydrate.

Therefore, in the presence of seeds of the final product, growth of these seeds can immediately take place even at the slightest super saturation (32). Biodentine™ has already achieved a lower setting time of 12minutes compared to its counterparts such as MTA which set in 3-4hrs(33). This is likely because of addition of calcium chloride Which has been used in modifying concrete setting(34). With this in mind, we could speculate that since Biodentine™ already contains calcium chloride for this purpose, bioactive glass addition may introduce unnecessary calcium which adsorbs onto the tricalcium silicate hence prolongs the induction phase.

Additionally, the prolonged setting of BH, could arise from the effect of strontium on alkalinity which is consistent with studies done on strontium substituted glass ionomer cements (35). Alkalinity in BH is bound to be pronounced, since Biodentine™ in itself is characterized by a very alkaline pH on setting. It is also possible that the bioactive glass that underwent crystallization present in BH remained predominantly as filler particles that may have interfered with matrix formation. Contrary to BH, strontium containing BI cement recorded the lowest initial setting time of the 3 modified cements. This could arise from the rapidity of the 1st stage of the setting reaction in this modification. However, due to the strontium connection to alkalinity (36) described above, the delay in final setting time is expected. This study provides an indication of the possible physicomechanical sequelae of incorporating bioactive glass into Biodentine™. Proof of the use of bioactive glass with strontium and fluoride to improve the compressive strength and radiopacity of Biodentine™ is obtained. The undesirable lengthening of the setting is also observed. These results should motivate efforts to not only understand the mechanisms by which

the above occurs, but to recognize and continue exploring the possible means by which Biodentine™ can be improved.

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