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Bioactivity and fluoride release of strontium and fluoride modified Biodentine

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ABSTRACT

Biodentine^{TM} is a novel tricalcium silicate based material used both as a coronal dentine replacement and in pulp therapy. Its multiple use in sealing perforations, pulp capping and as a temporary restoration arises from its ability to promote dentine formation and to confer an excellent marginal seal. However, there is still room for improvement of this cement as it lacks the anticariogenic effect typically conferred by fluoride ion release as seen in glass ionomer cement based dental materials. Therefore, this study was conducted to investigate the impact of bioactive glass addition to Biodentine^{TM}.

Objective. was to compare the apatite formation capacity, specificity of the apatite type formed and fluoride ion release by Biodentine^{TM} cements that have been modified by three different compositions of bioactive glasses.

Methods. High fluoride, high strontium and high fluoride plus strontium containing bioactive glasses were synthesized, incorporated into Biodentine^{TM} powder and four types of cements prepared. These cements were immersed in phosphate buffered saline solution and incubated for a period of 3 and 24 h, 3, 7 and 14 days. Fourier transform infra-red spectroscopy, X-ray diffraction, magic angle spinning nuclear magnetic resonance and fluoride ion release studies were performed.

Results. Bioactive glass addition to Biodentine^{TM} led to pronounced formation of apatite. Where the bioactive glass contained fluoride, fluorapatite and fluoride ion release were demonstrated.

Significance. Eliciting fluorapatite formation and fluoride ion release from Biodentine^{TM} is an important development as fluoride is known to have antibacterial and anticariogenic effects.

1. Introduction

Biomaterials science aims to develop materials that are ideal mechanically, physically and biologically. Previously, most research effort was directed at the physico-mechanical properties of materials with less attention to biological properties. However, recently that focus seems to be shifting towards developing the bioactive aspect of biomaterials due to interest in minimally invasive procedures [1].

Bioactivity is the induction of a favourable host response by a foreign implanted material leading to interfacial bond for-

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mation with biological tissues. This could be due to an effect on cells, hormones or other chemical signalling factors such as plasma proteins, the response thereof leading to reversal of disease process. A bioactive dental material should promote deposition of calcium hydroxyapatite crystals which promotes bonding with the remnant dental tissues [2]. Some bioactive dental materials include calcium hydroxide cements, glass ionomer cement, mineral trioxide aggregate (MTA), and other newer tricalcium silicate (TCS) based cements such as Biodentine^{TM}.

TCS based cements form a substantive mineral infiltration zone at their interface with the tooth and stimulate transforming growth factor (TGF) β1 production which is needed in inducing progenitor cell differentiation and dentine tissue deposition [3,4]. Therefore, despite these materials having inferior mechanical properties, they can reverse disease progression through multiple mechanisms [5]. These cements are superior to either calcium hydroxide or glass ionomer cements due to the extent of mineral uptake and infiltration [6,7]; superior sealing ability [8]; pronounced effect on TGF β1 [4]; speed with which they form a mineralized layer [9]; and the minimal inflammation that accompanies the process [10].

MTA, the prototype TCS cement was first discovered at Loma Linda University [11,12]. Although having desirable biological properties, MTA is a difficult cement to manipulate due to its grainy consistency and long setting time [13]. These limitations led to Septodont developing Biodentine^{TM}, using active Biosilicate technology [14]. Biodentine^{TM} sets in approximately 12 min and is effective in pulp therapy, while being able to act as a coronal dentine replacement. This cement is presented as a powder and liquid. The powder contains; tri-calcium silicate (C3S), di-calcium silicate (C2S), calcium carbonate filler, iron oxide shade, and zirconium oxide radiopacifier while the liquid has a calcium chloride accelerator and a hydrosoluble polymer [15].

Generally TCS cements promote formation of a thick dentine layer by initial production of calcium hydroxide cement during setting [6] and by ion infiltration into dentine [16]. Biodentine^{TM} also induces pulp cell differentiation into odontoblast like cells that facilitate tertiary dentine formation. It also increases alkaline phosphatase activity and secretion of TGF β1 [4] which is responsible for odontoblast differentiation during tooth morphogenesis [17].

Despite Biodentine^{TM}'s desirable properties, there is room for improvement by incorporation of the caries inhibiting fluoride and strontium species. Fluoride confers anticariogenic properties due to inhibition of plaque bacteria metabolism; impairing plaque bacteria adhesion and build up; and formation of acid resistant fluorapatite crystals [18]. Additionally, fluoride has a significant buffering effect that drives remineralization [19]. This caries inhibiting effect has led to extensive effort to incorporate and evaluate the fluoride release of various restorative materials [20].

Strontium on the other hand is a species that has been shown to manage dentine hypersensitivity [21] and lead to caries inhibition [22]. Moreover, its synergistic effect with fluoride in caries prevention is well documented by Lippert and Hara [23,24] who summarize earlier research by Curzon that demonstrated the caries inhibiting capability of strontium [25,26].

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 dissolution is dependent on the network connectivity of the bioactive glass, which in turn is influenced by its composition, thus, can be controlled [27]. The first bioactive material bearing the Bioglass trademark was first discovered by Larry Hench between 1969 and 1971 [28,29]. This material forms apatite when in the biophysiological environment and has been utilized in modifying other materials for dental applications [30,31]. Their apatite forming ability has been employed in nouvelle approaches to management of dentine hypersensitivity whereby apatite formed is useful in occluding open dentinal tubules [32,33].

The aim of this study was to incorporate fluoride and strontium containing bioactive glasses into Biodentine^{TM} and assess the impact on apatite formation and ion release of the modified cements. The cements' compressive strength, setting time and radiopacity were also evaluated and published separately [34]. The specific objectives were to;

(i) Synthesize three types of bioactive glasses; create three versions of modified Biodentine^{TM} cements in addition to unmodified cements by adding 10% by weight of high fluoride bioactive glass; 10% high strontium bioactive glass; or 10% fluoride plus strontium bioactive glass into Biodentine^{TM} powder before mixing with Biodentine^{TM} fluid
(ii) Use FTIR, XRD and NMR to characterize the structure of all the cements after immersion in PBS for 3 and 24 h, 3, 7 and 14 days
(iii) Determine the fluoride ion release profile of the two cements modified with fluoride containing bioactive glass.

2. Materials and methods

The bioactive glasses were prepared using a melt quench route. Mixtures of analytical grade SiO_2 (Prince Minerals Ltd., Stoke-on-Trent, UK), P_2O_5, $CaCO_3$, Na_2CO_3 and CaF_2 (all Sigma-Aldrich, Gillingham, UK) were prepared according to the compositions in Table 1. The weight percentages were correlated to the molar weight to maintain a desirable degree of network connectivity, important for bioactivity. 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 quenched in water to prevent crystallization and the frit retrieved using a large sieve. The frit was dried overnight in an oven at 50 °C. Later, the glass was ground using a Gyro-mill (Glen Creston, London, UK) for 3 min and thereafter sieved using a 90 μm mesh analytical sieve. XRD confirmed the amorphous nature of the two bioactive glass compositions, however, the third glass ($F^- + Sr = H$) partially crystallized to strontium fluoride SrF_2. The XRD patterns are provided in the supporting material (Fig. S1).

2.1. Cement preparation

Four different types of cements were manipulated. Plain Biodentine^{TM} cement coded 'BO', was prepared by adding

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