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A randomised clinical trial investigating calcium sodium phosphosilicate as a dentine mineralising agent in the oral environment

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ABSTRACT

Objective: The ability of a dentifrice containing the bioactive material calcium sodium phosphosilicate (CSPS) to remineralise the surface of dentine and physically occlude patent tubules was investigated in a 20 day *in situ* randomised clinical study.

Methods: Changes in surface microhardness and surface topography of dentine specimens treated for 5, 10, 15 and 20 days, twice daily with either a dentifrice containing 5% CSPS or a fluoride-only containing placebo dentifrice were compared. The substantivity of any mineral deposits formed on the surface of dentine were investigated by the application of an intra-oral dietary acid challenge twice daily during the final 10 days of treatment.

Results: After 5 and 10 days of treatment, the dentine samples in both treatment groups demonstrated an increase in surface microhardness. After 10 days of treatment the increase in surface hardness was directionally greater for the specimens treated with 5% CSPS dentifrice. Introducing an intra-oral acid exposure resulted in a reduction in surface microhardness which was significantly greater for the specimens treated with the placebo dentifrice compared to the dentifrice containing 5% CSPS, at day 20. Occlusion of the patent tubules was evident at each time-point and was significantly greater for the 5% CSPS containing dentifrice on days 5 and 10. On day 15 both dentifrices demonstrated the same degree of occlusion.

Conclusion: This *in situ* study demonstrated that dentifrice containing 5% CSPS may have potential to mineralise and occlude the dentine in the oral environment.

Study Registered under NRES Committee South West – Exeter (11/SW/0163).

Clinical Significance: This work provides evidence of potential agents that can be used to reduce the pain of dentine hypersensitivity when formulated into dentifrice and applied as part of a normal oral hygiene routine.

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1. Introduction

Described as a sharp but transient pain arising in response to a stimuli, dentine hypersensitivity (DH) is a rather common condition affecting up to 42% of the population.[1] The origin of DH is generally agreed to result from the exposure of dentine, following either loss of the protective enamel layer or *via* gum recession, and the development of patent tubules. Currently, a number of inorganic materials are employed in a variety of dentifrice formulations with the aim of depositing material in or on dentine to physically occlude patent dentine tubules and provide relief from the pain of DH.

Calcium sodium phosphosilicate (CSPS) is an ingredient found in a number of professional use and over-the-counter dental products designed to provide relief from DH. CSPS is a bioactive glass ($CaO\text{-}Na_2O\text{-}P_2O_5\text{-}SiO_2$) and was originally developed as bone repair material in the early 1970s.[2] CSPS has been reported to form a direct bond with calcified tissue following exposure to an aqueous environment.[3] Once in an aqueous environment CSPS has been reported to undergo a series of chemical reactions that result in an increase of the local pH to approximately 9. This creates an environment suitable for silica release, formation of a porous silica gel surface and the formation of calcium apatite.[2,4] A reservoir of calcium and phosphate is formed beneath the silica gel and these ions are released into the aqueous environment through the porous surface. CSPS incorporated in dentifrice formulations has been reported to physically occlude dentine tubules,[5] increase dentine mineralization[6,7] and provide relief from the pain of DH. *In vitro*,[6,8] *in situ*[9] and clinical efficacy studies[10–14] have demonstrated significant levels of dentine occlusion and relief from dentine hypersensitivity, following treatment with CSPS containing dentifrices.

The primary objective of this exploratory *in situ* study was to evaluate the dentine mineralisation potential of a dentifrice, containing 5% (w/w) CSPS and 1450 ppm fluoride (as sodium monofluorophosphate) compared to baseline and to a CSPS-placebo dentifrice containing 0% CSPS and 1450 ppm fluoride (as sodium monofluorophosphate). Further exploratory objectives were to: (i) evaluate changes in surface topography conferred by the test dentifrices. The null hypothesis being tested was that the addition of 5% CSPS to the dentifrice would not provide an increase in remineralisation or an increase in tubular occlusion and, (ii) to evaluate for each treatment, the influence of acid challenge on dentine mineralisation (SMH), dentine tubule occlusion (SEM) and dentine tissue loss (noncontact profilometry) by comparing assessment results of Day 20 to those of Day 10 using an *in situ* model.

2. Materials and methods

2.1. Study design and methodology

This study was a single centre, single blind (persons responsible for sample analysis), randomised, two treatment, two period crossover design, exploratory *in situ* study in healthy participants.

During the treatment phase, each participant wore a lower right and left buccal appliance holding 4 dentine specimens each. Specimens in both appliances were treated with the same dentifrice for 20 days (non-consecutive days – Monday to Friday only) with a wash out period of 48 h preceding a second treatment phase with the alternative dentifrice.

For each study day, participants wore the appliances for a minimum of 60 min before application of their assigned dentifrice. All treatments were applied *ex vivo* using an Oral B Vitality Precision Clean Power toothbrush fitted with an EB17 precision clean head (Procter and Gamble, Surrey, UK). 1.1 ± 0.1 g of dentifrice was evenly applied to four specimens over a 10 s period. The appliances were rinsed with water to remove dentifrice residue and placed back in the participants' mouth. Post first treatment, the appliances were kept in the mouth for a minimum of 60 min prior to lunch and for a further 60 min post lunch before the second treatment and for a further 60 min following the second treatment. In total, the appliances were kept in the mouth for a minimum of 4 h each day. Following day 5, 10, 15 and 20 one dentine specimen was removed from the appliance for measurement. A blank resin block replaced the specimen that was removed.

On treatment days 11–20, specimens were also exposed to an intra-oral acid challenge consisting of orange juice. After a minimum of 60 min following the second treatment application the participants gently swished 250 mL of orange juice around the mouth at a rate of 25 mL/min over a 10 min period and then rinsed their mouth with water.

Ethical approval was awarded by a UK research committee for the study to be conducted and data collected in a single English Dental School. The study was registered under NRES Committee South West – Exeter, under the registration number 11/SW/0163 and ran from July to November 2011. Each participant gave oral and written consent to take part in the study which was conducted to Good Clinical Practice guidelines. Eligible participants were adults 18 years or over in good general health, who in the opinion of the investigator, presented clinical DH as defined by Holland.[15] Subjects presenting DH were part of the inclusion criteria as it was considered that individuals with DH may be less able to mineralise patent dentine from saliva alone, and CSPS is indicated for sufferers of DH. In total, 21 subjects were screened and 19 were randomised using a computer generated schedule and assigned by the study staff in ascending numerical order according to participant appearance at the study site on the first day. This was an exploratory study so there was no previous data available to justify the sample size.

2.2. Specimen preparation

Dentine specimens were sourced and sectioned following the same procedure as described by Seong et al.[16] Each section was cured in dental composite (Quixfil, Dentsply, Surrey, UK) and polished using silicon carbide discs to a finish with p1200 grit paper. Following polishing, each specimen was etched in a 0.5 M citric acid (Sigma, Dorset, UK) solution for 30 s to remove a smear layer that would have formed during the sectioning process and expose patent dentine tubules. All specimens were screened for levels of dentine patency using a non-destructive Phenom G2 pro desktop scanning electron

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