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Randomized controlled trial to study plaque inhibition in calcium sodium phosphosilicate dentifrices

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ABSTRACT

Objectives: To evaluate the effect of three calcium sodium phosphosilicate (CSPS)/sodium monofluorophosphate containing dentifrices, compared to positive and negative controls on plaque re-growth in a non-brushing model, after 4 days of twice daily use, as determined by plaque area and Turesky plaque index (TPI).

Methods: This was an exploratory, single-centre, examiner-blind, randomised, controlled, five treatment period, crossover, plaque re-growth study, with supervised use of study products. Twenty-three healthy adult volunteers were randomized to receive experimental 5% CSPS dentifrice; two marketed 5% CSPS dentifrices; active comparator mouthrinse and negative control dentifrice. At the start of each treatment period, zero plaque was established by dental prophylaxis and study products were dispensed as either dentifrice slurries or mouthrinse, twice daily for the next 4 days. No other forms of oral hygiene were permitted. After 96 h, supra-gingival plaque was determined by plaque area (direct entry, planimetric method) and TPI. Changes from zero plaque were analysed.

Results: For both measures, plaque re-growth at 96 h was significantly lower following treatment with active comparator mouthrinse and significantly higher following treatment with the experimental 5% CSPS dentifrice, compared to all other treatments. There were no statistically significant differences between the three other treatments, except between the marketed 5% CSPS dentifrices, for overall plaque area.

Conclusions: The comparator mouthwash was significantly more effective at preventing plaque accumulation than the dentifrice slurries. The three marketed dentifrices contained sodium lauryl sulphate and were more effective at reducing plaque re-growth than the experimental dentifrice formulated with a tegobetaine/adinol surfactant system.

Clinical relevance: The CSPS containing dentifrices tested in this study showed no significant chemical-therapeutic anti-plaque benefits compared to a negative control dentifrice. However, sodium lauryl sulphate-containing dentifrices controlled plaque more effectively than a tegobetaine/adinol-containing CSPS dentifrice suggesting that the impact of surfactant selection on anti-plaque activity of formulations warrants further investigation.

1. Introduction

Dental plaque is a soft, sticky deposit of bacteria that collects on the teeth and along the gingival margin. Bacterial by-products from dental plaque can affect the health of the gingiva by causing inflammation of the gingival tissue (gingivitis). Whilst gingivitis is reversible, if untreated it can progress to periodontitis in susceptible individuals, which can result in bone loss and ultimately tooth loss [1]. Gingivitis and periodontal disease can develop when dental plaque accumulates above levels compatible with oral health [2–4], management of gingivitis therefore being both a primary prevention strategy for periodontitis and a secondary prevention strategy for recurrent periodontitis. The maintenance of gingival health and the prevention of gingivitis are predominantly determined by the control of dental plaque [5]. The

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mechanical action of tooth brushing alone is often insufficient for most individuals to achieve adequate plaque control [6–8]; in a recent systematic review it was demonstrated that an average of only 42% of plaque is removed in a single brushing [9]. As tooth-brushing with dentifrice is the most common oral hygiene regime, dentifrices are an obvious choice for the delivery of anti-plaque agents and many have been developed to chemically inhibit plaque deposition or augment its removal [3].

Active ingredients (such as metal salts, triclosan, cetylpyridinium chloride and chlorhexidine) have been incorporated into dentifrices for many years with a view to delivering plaque control and oral health benefits [10]. While some efficacy has been demonstrated for metal salts, a meta-analysis of stannous fluoride demonstrated significant heterogeneity in the findings of clinical studies [11] and most studies have shown zinc salts to be effective only when used in combination with other agents such as triclosan or chlorhexidine [10]. Triclosan has been shown to be effective against plaque and gingivitis in two systematic reviews [12,13]; however, a second systematic review with different inclusion/exclusion criteria failed to demonstrate the same efficacy [11]. Furthermore, while triclosan is known to be safe for use in toothpaste formulations [14], its use in a wide range of healthcare products has resulted in an accumulation of it and its breakdown products in the environment [15]. Triclosan is not readily decontaminated, and concerns about its long term impact on health and bacterial resistance are now being raised [15]. To date, chlorhexidine is the most effective active ingredient tested. It has been shown to reduce plaque and improve gingival health [16]; however, the side effects of tooth-staining and altered taste sensation have resulted in the continued quest for other ingredients with similar efficacy.

Calcium sodium phosphosilicate (CSPS) (Novamin®; GSK Consumer Healthcare, Brentford, UK) is a particulate bioactive material that upon exposure to the aqueous oral environment undergoes degradation at the tooth surface, releasing calcium and phosphate ions. This reaction is accompanied by a localized rise in pH and results in the formation of a hydroxycarbonate apatite-like material [17–19]. Studies have shown that particles of CSPS and associated silicas within the dentifrice formulation can bind to the dentine surface and within the tubules to physically occlude the dentinal tubules *in vitro* [17,18,20] and *in situ* [21], giving rise to its use as an occlusion agent in desensitizing dentifrices [22].

In addition to its de-sensitizing effects, CSPS has been reported to act as an anti-bacterial agent *in vitro* [23] and, in two clinical studies, to reduce supra-gingival plaque and gingival bleeding compared to a placebo dentifrice [24,25]. It is postulated that the high rate of ionic exchange when bioglasses such as CSPS come into contact with water, the release of large quantities of calcium and the localized increases in pH described above, may affect the dental plaque and be responsible for these effects [24,26]. However, evidence for this is not conclusive and further studies to confirm the mode of action and clinical efficacy of CSPS as an anti-plaque, anti-gingivitis agent are needed.

A number of plaque indices have been developed to assess the control of supra-gingival dental plaque. These can be objective (such as plaque weight) or subjective (such as plaque area). Subjective measures require a degree of examiner judgement during data collection [27]. The validity and credibility of subjective indices are increased by using more than one index to score plaque or by repeating the same subjective index, then assessing the variability of repeated measurements [27].

The Turesky modification of the Quigley and Hein [28] plaque index (TPI [29]) is a subjective index commonly used to assess disclosed plaque. It focuses initially on plaque in contact with the gingival margin and gives an ordinal plaque score. By contrast, the assessment of plaque area by planimetric means, developed by Addy et al. [30] as an adaptation of the Shaw and Murray [31] stain index, is based upon the subjective drawing of the outline of the area of disclosed plaque covering the entire scorable surface on a standard tooth chart. Planimetric data have been shown to be accurate [32] and provide an additional level of detail regarding plaque levels and distribution, but determining plaque areas from tooth charts on which they have been hand drawn is time consuming.

The objective of this study was to evaluate the effect of three 5.0% w/w CSPS/sodium-monofluorophosphate (SMFP) containing dentifrices, an active comparator mouthwash and a negative control dentifrice (with no CSPS) on plaque re-growth in a non-brushing model after four days of twice daily use, as measured by plaque area [30] and the TPI. The efficacy data generated by the study was used to evaluate and compare results from a new computer-based, direct data entry, planimetric methodology for recording and calculating plaque area, with the data derived using the TPI.

2. Materials and methods

2.1. Study design and methodology

This study was an exploratory, single centre, examiner blind, randomized, controlled, five way crossover *in vivo* study to investigate the effect of CSPS-containing dentifrices on plaque re-growth over four days twice-daily treatment in the absence of tooth brushing. Ethical approval for the study was awarded by a UK research ethics committee (NHS Research Ethics Committee Reference 12/SW/0294) and the study was conducted to Good Clinical Practice guidelines [33]. Volunteer recruitment, screening, treatment and clinical assessments were carried out at the study site, a UK Dental School. Potential subjects who had expressed an interest in the study were invited to screening and allocated a unique screening number assigned in ascending numerical order as they gave written informed consent to take part in the study. Eligible subjects were aged 18 years or over, and in the investigator's opinion, based on medical history, in good general health. Volunteers who were pregnant or breast feeding, had known allergies or intolerances to study materials, or who were on (or had been on) antibiotic or antimicrobial treatment within 14 days of the first treatment visit were excluded. Volunteers with diabetes mellitus (Type 1 or 2) or other diseases that could impact study outcomes were also excluded. Following an oral examination, participants were included if they had at least 20 natural, uncrowned teeth with at least 40 facial/buccal and lingual/palatal surfaces gradable for plaque area and TPI. If caries, severe gingivitis or periodontal disease was detected participants were excluded. Similarly subjects with orthodontics bands or oral lesions that could impact the study outcome were not included. Any volunteer with a dental condition requiring immediate treatment or that could worsen as a result of suspending normal oral hygiene procedures during the five treatment periods was also excluded.

Volunteers who satisfied the inclusion and exclusion criteria were randomized to the order in which they would receive each of the five treatments according to the randomization schedule provided by the sponsor. Randomization numbers were assigned by study staff at the study site in ascending numerical order as subjects were determined to be fully eligible to participate in the study. Following randomization subjects were given sub- and supra-gingival prophylaxis with flossing, followed by disclosure and removal of any residual plaque, to ensure all stain, calculus and plaque had been removed from the teeth. A second clinician confirmed that there was no visible plaque on the participants' teeth. All subjects were given a standard fluoride (washout) dentifrice (UK Colgate Cavity Protection; Colgate-Palmolive Ltd.,