Effectiveness of a Baking Soda Toothpaste Delivering Calcium and Phosphate in Reducing Dentinal Hypersensitivity

A. Ghassemi W. Hooper

Church & Dwight Co., Inc.
Princeton, NJ, USA

A.E. Winston

R&D for Hire
East Brunswick, NJ, USA

J. Sowinski J Bowman

Hill Top Research
Miamiville, OH, USA

N. Sharma

BioSci Research Canada, Ltd.
Mississauga, Canada

Abstract

- **Objective:** The purpose of this controlled clinical trial was to determine the effectiveness and safety of a single-phase dentifrice that delivers calcium, phosphate, and fluoride to the tooth surface (Arm & Hammer® Enamel Care® for Sensitive Teeth toothpaste, United Kingdom) in reducing dentinal hypersensitivity.
- **Methods:** Two-hundred and eight qualifying subjects were randomly assigned to either the Enamel Care dentifrice group or a control dentifrice group, and brushed twice daily with their assigned dentifrice for eight weeks. Pain/discomfort in response to a thermal stimulus was assessed at baseline, week 4, and week 8 using a Visual Analogue Scale (VAS; primary outcome variable) and the Schiff Thermal Sensitivity Scale (STSS; secondary outcome variable). After eight weeks, volunteers from the Enamel Care group were switched to the control dentifrice and participated in a second eight-week study to determine the degree of persistence of pain reduction.
- **Results:** Both groups had statistically significant VAS score reductions from baseline at weeks 4 and 8, with mean VAS scores in the Enamel Care group decreasing by 45.6% at week 4 and 61.1% at week 8 ($p < 0.0001$). Enamel Care was statistically significantly more effective than the control at weeks 4 and 8, with respective mean VAS reductions of 63% ($p < 0.0001$) and 33% ($p = 0.0004$) greater than the control. Consistent with the VAS score results, the Enamel Care group had respective statistically significant STSS score reductions of 77% and 58% greater than the control group ($p < 0.0001$). The reductions in dentinal hypersensitivity seen in the Enamel Care group at week 8 persisted for an additional eight weeks, during which the subjects discontinued use of Enamel Care and brushed with the control dentifrice.
- **Conclusion:** Enamel Care for Sensitive Teeth toothpaste (United Kingdom) is an effective dentifrice for the management of dentinal hypersensitivity, and its efficacy persists for a least eight weeks following discontinued product use.

(J Clin Dent 20:203–210, 2009)

Introduction

Dentinal hypersensitivity is a clinical problem, "characterized by short, sharp pain arising from exposed dentine in response to stimuli (typically thermal, evaporative, tactile, osmotic or chemical), and which cannot be ascribed to any other form of dental defect or pathology."[1] It typically involves the facial-cervical region of permanent teeth in instances in which dentine has been exposed as a result of the attrition, abrasion, or erosion of the covering enamel or cementum, or as the result of a developmental anomaly in the region of the cemento-enamel junction,[2-6] and is often associated with root surfaces that have been exposed by gingival recession secondary to mechanical trauma and/or periodontal disease.[5]

Reviews summarizing epidemiologic studies reveal the prevalence of dentinal hypersensitivity to have a wide range, from a low of 3 percent of the population up to 74 percent.[5,6] No doubt the marked variation reflects such factors as differences in the populations surveyed, and whether the hypersensitivity was self-reported or determined by a clinical examination that excluded other causes. In any event, it is generally accepted that dentinal hypersensitivity has a prevalence of 10 to 30 percent in the general population, and is found most frequently in individuals 20 to 50 years of age.[3,5]

While many theories for the mechanism responsible for dentinal hypersensitivity have been proposed over the years, the "hydrodynamic theory" has received the greatest amount of scientific support and general acceptance.[1-9] This theory posits that fluid movement within dentinal tubules, resulting from thermal, evaporative, or osmotic stimuli, is ultimately responsible for a hypersensitive reaction by triggering nerve fibers responsible for

pain. Since not all exposed dentine is sensitive, whether or not a given region of exposed dentine will have a painful response and the intensity of that response will be dependent upon the number of tubes in a given region of the dentine and the degree to which the tubules are present. In particular, it might be expected that tubules open to the external tooth surface, as well as to the pulp, would more likely be associated with a painful response than occluded tubules and, moreover, the magnitude of fluid shift within the tubules would be directly related to tubule diameter. This has been borne out by a scanning electron microscopic study that compared cervical dentine from caries-free teeth that were determined to be either sensitive or non-sensitive prior to extraction.[10] The morphologic findings of this study were confirmed by a second ultrastructural study.[11] In addition to morphologic studies, the hydrodynamic theory is supported by *in vitro* studies demonstrating actual fluid flow through patent dentinal tubules in response to various stimuli known to elicit pain *in vivo*.[12-14]

An understanding of the pathophysiologic basis for dentine hypersensitivity has led to the development of scientifically based treatment methods. These have resulted in effective consumer and professionally administered products, with the most widely used directed at either reducing nerve excitation secondary to fluid movement or occluding patent dentinal tubules.[5,6,9,15] Dentifrices containing potassium salts, and in particular potassium nitrate, have been shown in numerous clinical trials to have significant effectiveness in reducing tooth hypersensitivity when compared to placebo controls.[16-22] Although the mechanism of action of these products has often been attributed to a blockage of nerve conduction from exposure to potassium ions based on *in vitro* studies, it has not been definitively established that a sufficient concentration of potassium ions, in fact, penetrates into the dentinal tubules during actual clinical use to sustain intradental nerve inactivation.[20,23,24] Nevertheless, although the precise mechanism of action may need to be elucidated, a United States Food and Drug Administration (FDA) Advisory Panel, after reviewing supporting clinical data, has confirmed the safety and effectiveness of dentifrices containing 5% potassium nitrate in controlling dentinal hypersensitivity.[25]

An early *in vitro* study of desensitizing dentifrices provided evidence for the feasibility of managing dentinal hypersensitivity by occluding dentinal tubules, and thereby reducing dentine permeability.[26] Subsequent *in vitro*[27] and clinical studies[28,29] have confirmed the effectiveness of a professionally applied ferric oxalate sealant in reducing dentinal hypersensitivity.

The development of products for the treatment of dentinal hypersensitivity was advanced by discoveries of methods and technologies that could precipitate calcium and phosphate-containing minerals analogous to hydroxyapatite directly onto exposed dentine. For example, it was shown that high concentrations of calcium and phosphate ions could be delivered to the tooth surface to rapidly form amorphous calcium phosphates (ACP) that are quickly hydrolyzed to form apatite, a process that could enhance tooth remineralization and result in dentinal tubule occlusion.[30] Fluoride toothpastes that deliver calcium and phosphate have been shown to occlude dentinal tubules.[31,32] The effectiveness of ACP in reducing dentinal hypersensitivity has been demonstrated clinically in placebo-controlled studies using sequentially applied solutions in the dental office,[33] and by subjects using a two-phase fluoride toothpaste containing calcium and phosphate salts in their usual oral care regimen.[34] A recent clinical study of a dentifrice containing calcium sodium phosphosilicate has provided additional evidence that a dentifrice can deliver mineral to the tooth surface to occlude dentinal tubules and reduce dentinal hypersensitivity.[35]

Recent technological advances have enabled the ACP technology to be incorporated in a single-phase fluoride dentifrice that simultaneously delivers calcium and phosphate to the tooth surface (Arm & Hammer® Enamel Care® for Sensitive Teeth, Church & Dwight UK Ltd., Kent, UK). The aim of this controlled clinical trial was to determine the effectiveness and safety of this new single-phase ACP dentifrice in reducing dentinal hypersensitivity over an eight-week period, and the degree of persistence of any reduction in hypersensitivity over the subsequent eight weeks.

Materials and Methods

Study Design

This was a randomized, controlled, double-blind, parallel-group clinical trial conducted at two clinical sites, Hill Top Research, Miamiville, OH, USA and BioSci Research Canada, Ltd, Mississauga, Ontario, Canada. The study protocol was reviewed and approved by the respective Institutional Review Boards at each of these sites, and all subjects provided informed consent prior to entering into the study.

The study design consisted of two phases (Figure 1): Phase I, evaluation of efficacy; and Phase II, evaluation of efficacy persistence. Qualifying subjects were randomly assigned to either the test group, Arm & Hammer Enamel Care for Sensitive Teeth (Enamel Care) or the control group, Crest® Cavity Protection Regular toothpaste, (Procter & Gamble Co., Cincinnati, OH, USA). Both products contain 0.24% sodium fluoride. After the initial eight-week efficacy evaluation phase, the persistence of any reduced hypersensitivity effect over an eight-week period following discontinuation of Enamel Care use was evaluated by having the subjects in the Enamel Care group switch to the control dentifrice for an additional eight weeks.

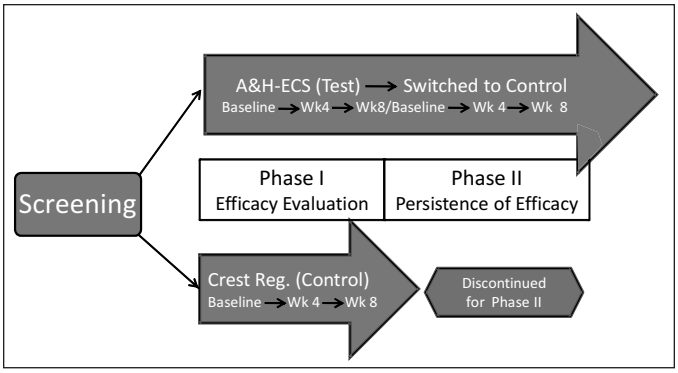

Figure 1. *Study design.*

Study Population

Two-hundred and eight qualifying male and female subjects between the ages of 18 and 64 were enrolled into the study so that

at least 100 subjects in each group could be expected to complete the study. Subjects were required to be in good general health and to have between two and eight accessible teeth (anterior teeth and bicuspids) sensitive to thermal stimulation, and generating a score of between 40 and 90 mm on a 100 mm VAS pain scale following a one-second air blast directed at exposed dentine. The VAS score served as the basis for tooth/subject inclusion and as the primary outcome variable. Subjects were also to have at least one accessible tooth not sensitive to thermal stimulation, and the qualifying teeth could not have extensive restorations and must be restoration-free on the facial surface. The qualifying teeth could also have no greater than mild inflammation (Löe-Silness Gingival Score < 2) of the facial marginal gingiva. Subjects with advanced periodontal disease or gross oral neglect, periodontal, orthodontic, or restorative treatment within the previous three months, or a dental prophylaxis within two weeks prior to the baseline assessment were excluded from the study, as were those with tooth sensitivity subsequent to tooth bleaching or whitening procedures, and oral mucosal symptoms, such as burning or tingling, and/or signs of sloughing or irritation of at least moderate intensity. Any subjects having daily use of medications that could interfere with pain perception, such as analgesics, sedatives, anticonvulsants, antihistamines, mood-altering drugs, or anti-inflammatory agents, having the need for antibiotic prophylaxis prior to invasive dental procedures, or a history of allergic reaction to ingredients in oral hygiene products, were also excluded. Finally, subjects were excluded if there was self-reported pregnancy or breast feeding, participation in a tooth desensitizing study within the previous 90 days, the use of a desensitizing toothpaste within six weeks of the screening evaluation, or any other product for reduction of dentinal sensitivity within the previous six months, and finally the inability to comply with protocol requirements.

Clinical Procedures

During the screening visit (seven to fourteen days prior to the study's baseline visit), qualifying subjects and teeth were identified. Teeth potentially qualifying as test teeth were required to have evidence of facial erosion, abrasion, or gingival recession. Tooth sensitivity was assessed using thermal stimulation, in which a one-second blast of room temperature air (40 ± 5 psi) from an air syringe was directed at the exposed facial dentinal surface from a distance of one centimeter. The examiner covered the adjacent teeth with his fingers or with cotton rolls in order to assure that any pain response could be attributed only to the tooth being tested. At each visit, the examiner first exposed a non-sensitive tooth to the thermal stimulus to provide the subject with a frame of reference with which to differentiate between sensitive and non-sensitive teeth. The subjects recorded the degree of dentinal hypersensitivity using a 100 mm VAS. After each tooth was tested, subjects indicated the intensity of the response by placing a mark on the 100 mm line for that tooth number, with the scale ranging from "no pain/no discomfort" to "severe pain/discomfort." With this scale, the distance from the "no pain/no discomfort" end provides an estimate of the severity of discomfort or pain perceived by the subject. In order to qualify for the study, subjects were required to have at least two teeth with a VAS score between 40 and 90 and one non-sensitive tooth. In addition, the marginal gingiva adjacent to the sensitive teeth was assessed at the screening and baseline visit using the Löe-Silness Gingival Score[36] of < 2 required for inclusion. Subjects entered into the study were provided with Aim® Cavity Protection dentifrice (Church & Dwight Co., Inc., Princeton, NJ, USA) and an Oral-B® 35 soft toothbrush (Procter & Gamble Co., Cincinnati, OH, USA) for use during the "washout" period between the screening and baseline visits.

Phase I—Efficacy Evaluation. During the baseline visit, the sensitive and non-sensitive teeth identified at the screening visit were assessed once again using thermal stimulation, and those teeth having a consistent VAS response at the screening visit were specified as test teeth for the study. At baseline, the degree of hypersensitivity was assessed using the VAS, which recorded the subject's response and served as the primary outcome variable, and the Schiff Scale,[17-19] which represented the examiner's assessment of the subject's response and served as the secondary outcome variable. Schiff Scale scores were determined as follows:

0 = The subject does not respond to the thermal stimulus
1 = The subject responds to the stimulus but does not request that it be discontinued
2 = The subject responds to the stimulus and requests that it be discontinued or moves away from it
3 = The subject responds to the stimulus, considers it to be painful, and requests that it be discontinued

Qualifying subjects were stratified according to VAS score, gender, and age, and were randomly assigned to either the test (Enamel Care) or control (Crest Regular) dentifrice groups. The dentifrices were dispensed in identical white coded tubes. The subjects were instructed to brush with their assigned dentifrice and the Oral-B 35 soft toothbrush provided to them in their usual manner for one minute, twice daily for the next eight weeks, using a ribbon of dentifrice that covered the length of the bristles. They were given a diary in which to document their twice-daily tooth brushing, and were instructed to time each brushing using a watch or clock to ensure that they brushed for a full minute. During the course of the study, subjects were instructed not to use any oral hygiene product other than their assigned dentifrice, and to report the use of any concomitant medications they may have taken after study initiation.

The clinical assessments were repeated at four and eight weeks. Compliance with dentifrice use was monitored by weighing the dentifrice tube at baseline and the week-4 and week-8 visits, and by monitoring subject diaries at the four- and eight-week visits. In addition, study personnel contacted the subjects by telephone approximately two weeks after the start of the study to reinforce product use instructions and study restrictions.

Phase II—Persistence of Efficacy Evaluation. At the conclusion of the eight-week Phase I efficacy study, subjects from the Enamel Care group were recruited for a second eight-week study to assess the persistence of any reduced hypersensitivity effect. Ninety of 103 subjects in the Enamel Care group agreed to participate for an additional eight weeks, and were entered into this second study after providing informed consent. The subjects brushed with the control dentifrice and a new Oral-B 35 soft

toothbrush twice daily for the additional eight weeks. For these subjects, their final (week 8) VAS and STSS mean scores in the first study served as the baselines (week 0) values for the second study. The clinical procedures for this study were the same as those used in the first study, with the exception that all subjects used the control dentifrice for this additional eight-week period.

Examiner and Site Calibration/Standardization

Prior to the screening, the study sites' personnel reviewed all clinical procedures and case report forms and data documentation, and the two examiners reviewed and calibrated their procedures for air stimulation and safety and efficacy evaluations to ensure consistency across the two study sites.

Statistical Analyses

Sample Size. A sample size of 200 completed subjects (100 per group) was based on the results of a pilot study, and was calculated to provide a power of 0.80 for detecting a statistically significant difference of 30-35% in between-group mean VAS scores.

Primary Outcome Variable. The primary outcome variable was thermal sensitivity, determined by using subject mean VAS scores calculated at each of the three exam times. The baseline mean VAS scores were compared using an analysis of variance (ANOVA) model. Within-group differences in mean VAS scores from baseline to four weeks and eight weeks were analyzed using the Student's t-test for paired data. Between-group differences in mean VAS scores at weeks 4 and 8 were analyzed using an analysis of covariance (ANCOVA) model, with the mean baseline scores included as a covariate and each of the study sites included as a blocking factor.

Secondary Outcome Variable. The secondary outcome variable was thermal sensitivity determined by using subject mean Schiff Scale scores calculated at each of the three exam times. The data used for this analysis were derived from the selected test teeth with baseline STSS scores > 1. Within-group differences in mean STSS scores from baseline to weeks 4 and 8 were analyzed using Wilcoxon's Signed Rank Test. Between-group comparisons at weeks 4 and 8 were analyzed using Wilcoxon's Rank Sum Test.

In addition, changes in the response of individual teeth from baseline to weeks four and eight were analyzed. Chi-square tests were used for between-group comparisons of the proportions in each category. The number of teeth with categorical percent reductions in VAS scores (*e.g.*, > 0%, ≥ 50%, ≥ 75%) at each examination period were tabulated. The same teeth included in the VAS analysis were also compared for categorical reductions in STSS scores (*i.e.*, number and percent of teeth with a baseline STSS score of 3 or 2 in each group that changed to a score of 0 or 1 at weeks 4 or 8). While these chi-square tests do not account for nesting of teeth with patients, they were included as supplemental and confirmatory to the other analyses conducted.

Results

The baseline demographic characteristics for the intent-to-treat (ITT) population are shown in Table I. Two-hundred and eight subjects were randomized into the study, of which two-hundred and three satisfied all the protocol requirements and constituted the evaluable subject population. The five subjects not completing the study were disqualified for either not returning for the four-week evaluation (four subjects) or for an adverse event unrelated to the study materials (one subject). The two groups were comparable with respect to gender, age, race, and smoking status, with the majority of subjects female, white, and non-smokers.

Table I
Baseline Demographic Characteristics (Phase I Study): Intent-To-Treat Population

	Enamel Care n = 106	Control n = 102
Gender		
Male	24 (23%)	24 (24%)
Female	82 (77%)	78 (76%)
Age		
Mean (SD)	42.21 (9.75)	42.24 (10.10)
Median	42	41
Range	20–59	20–64
Race		
Asian	10 (9%)	14 (14%)
Black (Non-Hispanic)	11 (10%)	14 (14%)
Hispanic	1 (1%)	3 (3%)
White (Non-Hispanic)	83 (78%)	71 (70%)
Other	1 (1%)	0
Smoking Status		
No	84 (79%)	88 (86%)
Yes	22 (21%)	14 (14%)

The oral mucosal examinations and subject comments revealed mild to moderate findings in 14 subjects that were judged to be possibly attributable to product use. These were divided equally between the two product groups and consisted primarily of dryness of the mouth or lips. None of these changes caused the subject to discontinue participation in the study.

Phase I—Efficacy Evaluation

Primary Outcome Variable. The VAS pain/discomfort scores at baseline, week 4, and week 8 are presented in Table II and summarized in Figure 2, where "A&H-ECS-All" refers to all subjects in the A&H Enamel Care group who completed the Phase I study, and "A&H-ECS-Continued" refers to those sub-

Table II
VAS Scores: Per Protocol Population

Visit	n	VAS Score Mean (SD)	Mean (SD) Change from Baseline	% Reduction vs. Control[1]	p-value[2]
Baseline					
Enamel Care	103	63.46 (11.1)	—	—	—
Control	100	63.30 (9.6)	—	—	—
Week 4					
Enamel Care	103	34.79 (22.5)	–28.68 (21.1)	63%	< 0.0001
Control	100	45.69 (18.2)	–17.61 (16.4)	—	—
Week 8					
Enamel Care	103	25.01 (22.8)	–38.45 (21.8)	33%	0.0004
Control	100	34.39 (20.2)	–28.91 (19.5)	—	—

[1]Calculation was based on the adjusted mean differences from baseline as follows: [(Enamel Care – Control) / Control] × 100.
[2]Statistically significant reductions from control (analysis of covariance).

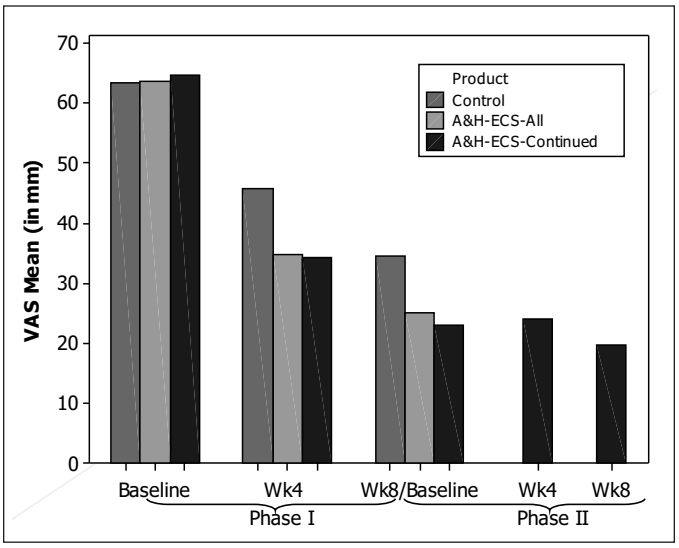

Figure 2. *Mean VAS score results.*

jects in the A&H Enamel Care group who continued on to the Phase II study and switched to the control dentifrice for the additional eight weeks. Within-group analyses indicated that both the Enamel Care and the control groups had statistically significant ($p < 0.0001$) VAS score reductions from baseline at four and eight weeks, with the Enamel Care group having larger absolute reductions at both examinations. The Enamel Care group showed 45.6% and 61.1% reductions in VAS scores at week 4 and 8 visits versus baseline, respectively. An ANCOVA revealed that Enamel Care was statistically significantly more effective than the control, producing a 63% greater reduction in adjusted mean VAS score at week 4 ($p < 0.0001$) and a 33% greater reduction at week 8 ($p = 0.0004$) compared to the control group.

Table III presents the between-group analysis comparing categorical changes from baseline to four and eight weeks on an individual tooth basis. The results of this analysis parallel the results of the analyses based on subject mean VAS scores. While reductions in the magnitude of individual tooth VAS scores in both groups increased progressively between baseline and four and eight weeks, there was a statistically significant difference between the Enamel Care and control groups for each of the percent reduction categories, with the Enamel Care group having a statistically significantly larger number of teeth with high percent reductions at each evaluation. For example, at eight weeks, 175 of a total of 382 teeth (46%) in the Enamel Care group had VAS score reductions of 75% or greater compared to 114 of a total of 393 teeth (29%) in the control group.

Secondary Outcome Variable. The mean STSS scores at baseline, four, and eight weeks for teeth with a baseline score greater than 1 are presented in Table IV and summarized in Figure 3. Within-group analyses indicated that both the Enamel Care and control groups had statistically significant ($p < 0.0001$)

Table IV
Schiff Scale Scores: Per Protocol Population with Baseline Scores of Greater than 1

Visit	n	Schiff Score Mean (SD)	Mean (SD) Change from Baseline	% Reduction vs. Control[1]	p-value[2]
Baseline					
Enamel Care	90	2.30 (0.4)	—	—	—
Control	86	2.30 (0.3)	—	—	—
Week 4					
Enamel Care	90	1.08 (0.6)	–1.22 (0.7)	77%	< 0.0001
Control	86	1.61 (0.5)	–0.69 (0.5)	—	—
Week 8					
Enamel Care	89	0.71 (0.6)	–1.58 (0.7)	58%	< 0.0001
Control	86	1.29 (0.6)	–1.01 (0.6)	—	—

[1]Calculation was based on the adjusted mean differences from baseline as follows: [(Enamel Care – Control) / Control] × 100.
[2]Statistically significant reductions from control (Wilcoxon Rank Sum Test).

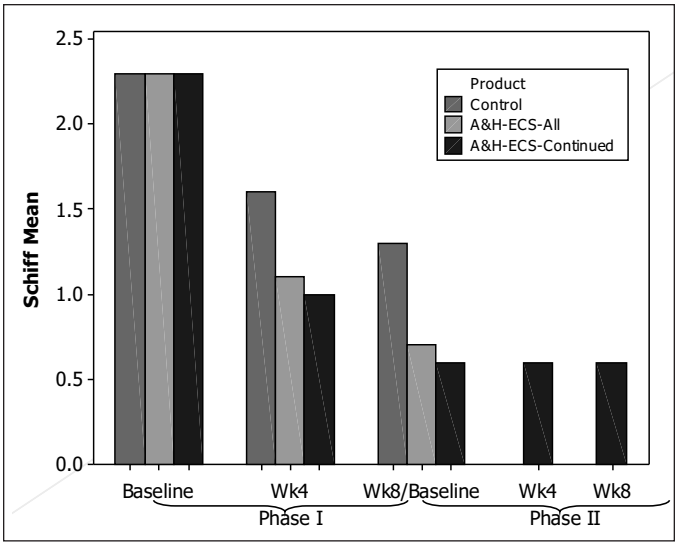

Figure 3. *Mean Schiff score results.*

Table III
Between-Group Comparison of Categorical Percent Reductions in Tooth VAS Scores from Baseline

Visit	Product Group	Number of Subjects	Total Number of Teeth	Percent Reduction Categories, Number of Teeth (Percent of Total) > 0%	≥ 50%	≥ 75%	≥ 90%	100%
Week 4	Enamel Care	103	382	329 (86%)	177 (46%)	114 (30%)	61 (16%)	14 (4%)
	Control	100	393	290 (74%)	107 (27%)	55 (14%)	12 (3%)	4 (1%)
		Chi-Square p-value		< 0.0001*	< 0.0001*	< 0.0001*	< 0.0001*	0.0144*
Week 8	Enamel Care	103	382	349 (91%)	229 (60%)	175 (46%)	125 (33%)	28 (7%)
	Control	100	393	339 (86%)	194 (49%)	114 (29%)	57 (15%)	10 (3%)
		Chi-Square p-value		0.0245*	0.0031*	< 0.0001*	< 0.0001*	0.0020*

*Statistically significant between-group difference in favor of Enamel Care.

mean STSS score reductions from baseline, with the Enamel Care group showing greater reductions than the control group. The Enamel Care group showed a 51.8% reduction at week 4 and 68.3% reduction in mean STSS score at week 8 versus baseline, respectively. At four and eight weeks, the Enamel Care group's respective mean reductions in STSS scores were 77% and 58% greater than those of the control group, with the differences being statistically significant ($p < 0.0001$).

Table V presents between-group comparison of the number of teeth with baseline STSS scores of 2 or 3 that decreased to 0 (complete resolution of hypersensitivity) or decreased to 0 or 1 by week 8. The Enamel Care group had a statistically significantly ($p = 0.0005$) greater number of teeth with a STSS score that decreased from 3 or 2 to 0 or 1 than the control group. In the Enamel Care group, 109 of a total of 380 teeth (29%) with baseline STSS scores of 3 or 2 showed complete reversal of sensitivity (STSS score of 0) by week 8, as compared to only 34 of a total of 393 teeth (9%) in the control group showing complete reversal of sensitivity at week 8.

Table V
Between-Group Comparison of Reduction of Individual Tooth Schiff Scores from Baseline to Week 8: Teeth with Baseline Scores of Greater Than 1

		Number of Teeth (Percent of Total)	
Group	Total No. of Teeth	Change from 3 or 2 to 0	Change from 3 or 2 to 0 or 1
Enamel Care	380	109 (29%)	227 (60%)
Control	393	34 (9%)	186 (47%)
Chi-Square p-value		< 0.0001*	0.0005*

*Statistically significant between-group differences in favor of Enamel Care.

Phase II—Persistence of Efficacy

All subjects who were willing to continue with the second phase and had at least one post-baseline exam were considered evaluable for the ITT population. The subjects switched to using the control dentifrice during the Phase II study. The eight-week VAS and STSS scores for the participating subjects from the Phase I study served as the baseline scores for the second phase of evaluation of persistence of efficacy. The demographic characteristics and baseline scores of the ITT subject population are presented in Table VI. The VAS and STSS scores at baseline, week 4, and week 8 are presented in Table VII. The results indicate that the improvement observed in the Enamel Care group by the eighth week of the effectiveness study was maintained throughout the subsequent eight weeks, during which the subjects discontinued use of Enamel Care and switched to the control dentifrice.

Table VI
Persistence of Efficacy Evaluation Study (Phase II): Demographic Characteristics and Baseline Scores, Intent-To-Treat Subject Population

Gender	
Male	20 (23%)
Female	67 (77%)
Age	
Mean (SD)	41.98 (10)
Median	42
Range	20–59
Race	
Asian	10 (11.5%)
Black (Non-Hispanic)	10 (11.5%)
Hispanic	1 (1%)
White (Non-Hispanic)	66 (76%)
Smoking Status	
No	68 (78%)
Yes	19 (22%)

Table VII
Phase II—Persistence of Efficacy Evaluation: VAS and Schiff Scores

Visit	n[1]	Mean Score (SD)[1]	Mean Change from Baseline (SD)[2]
VAS Scale			
Baseline	85	23.23 (22.09)	—
Week 4	85	24.10 (23.70)	0.86 (13.32)
Baseline	85	23.05 (22.16)	—
Week 8	85	19.61 (22.95)	–3.44 (11.95)
Schiff Scale			
Baseline	75	0.59 (0.49)	—
Week 4	75	0.60 (0.59)	0.01 (0.40)
Baseline	74	0.58 (0.49)	—
Week 8	74	0.60 (0.69)	0.02 (0.53)

[1]Values for n and mean scores represent data for 85 subjects who completed both baseline (*i.e.*, week 8 of Phase I study) and applicable exam time point of Phase II study. Of the 85 subjects in the VAS group, 75 had at least one tooth with a Schiff score greater than 1.

[2]The lasting effect of Enamel Care in reduced sensitivity persisted for an additional 8 weeks, as there was minimal change in reduced tooth sensitivity observed with EC treatment.

Discussion

Dentinal hypersensitivity is found to a relatively large extent in the general population, and can have a significant impact on the oral health quality of life.[37] The results of this study demonstrate that Enamel Care is both effective and safe for reducing dentinal hypersensitivity. The assessment using the primary outcome variable, mean VAS scores, showed this toothpaste produced statistically significant reductions from baseline of 45.6% and 61.1% at weeks 4 and 8, respectively. At both evaluations, Enamel Care was also statistically significantly more effective than the control, with respective week 4 and week 8 reductions of 63% and 33% greater than the control. The results obtained using VAS scores were confirmed by reductions in the corresponding STSS scores which paralleled the VAS findings at each of the evaluation periods. The desensitizing mechanism of action of Enamel Care is consistent with the hydrodynamic theory; that is, its effectiveness is due to its ability to deliver calcium and phosphate to the dentin surface to form amorphous calcium phosphate that is hydrolyzed to apatite that occludes dentinal tubules to prevent fluid displacement in response to painful stimuli. Since sensitivity to cold is reported to be the most frequent complaint of individuals suffering from dentinal hypersensitivity,[2,3,9,38] the use of a cold air stimulus in this study reinforces the clinical relevance of the results. In addition, an air blast stimulus has been shown to be more reproducible than other types of stimuli, including tactile stimuli, with reproducibility consistent with that of pain assessments in other fields.[39]

The conventional fluoride-containing dentifrice used in this study served as a control, as it is not generally thought to have desensitizing activity.[1] Nevertheless, the group using the control dentifrice also experienced significant reductions in sensitivity from baseline at the week 4 and week 8 assessments. It is, however, often the case that control dentifrices in dentinal hypersensitivity trials will themselves produce sizable reductions from baseline, whether they are marketed products or placebos specifically formulated for a given study.[16,17,21,35,40-42] The marked reduction of hypersensitivity in the control group typically seen in these trials has been ascribed to two possible causes:[9] First, to a true placebo response in subjects whose pain perception might change over time, especially since they know they are participating in a trial of an anti-hypersensitivity product but are unaware that they have been randomized to the control group; Second, to the Hawthorne effect by which subjects may unconsciously change their behavior and brush more thoroughly and effectively with the knowledge that they are participating in an oral product clinical trial. This is not unique to studies on dentinal hypersensitivity but is characteristic, as well, of studies of other types of oral care products, such as antiplaque and antigingivitis mouthrinses.[43] It has been suggested that more thorough brushing with a conventional dentifrice might lead to a reduction in sensitivity by the temporary and/or incomplete occlusion of dentinal tubules by, for example, abrasive agents in the formulation.[9,44] Given the apparent effectiveness of the control dentifrice in this and other studies, the fact that Enamel Care for Sensitive Teeth had substantially greater desensitization effectiveness than the control is especially notable, and confirms the clinical value of the Enamel Care product.

In summary, this controlled clinical trial has shown that Enamel Care for Sensitive Teeth dentifrice is effective in reducing dentinal hypersensitivity compared to a conventional fluoride dentifrice and, moreover, the improvement is maintained for at least an eight-week period following discontinuation of Enamel Care use.

Acknowledgment: The authors thank clinical study coordinators (Linda Vorwerk, Jimmy Qaqish, and Kathy Barrett), Dr. Howard Proskin for statistical guidance, and Drs. Michael Barnett and Sebastian Ciancio for review and editorial assistance. This study was supported by Church & Dwight Co., Inc.

For further correspondence with the author(s) of this paper, contact Dr. Annahita Ghassemi—annahita.ghassemi@churchdwight.com.

References

1. Holland GR, Narhi MN, Addy M, Gangarosa L, Orchardson R: Guidelines for the design and conduct of clinical trials on dentine hypersensitivity. *J Clin Periodontol* 24:808–813, 1997.
2. Dababneh RH, Khouri AT, Addy A: Dentine hypersensitivity—An enigma? A review of terminology, epidemiology, mechanisms, aetiology and management. *Br Dent J* 187:606–611, 1999.
3. Addy M: Dentine hypersensitivity: New perspectives on an old problem. *Int Dent J* 52:376–375, 2002.
4. Canadian Advisory Board on Dentin Hypersensitivity: Consensus-based recommendations for the diagnosis and management of dentin hypersensitivity. *J Can Dent Assoc* 69:221–226, 2003.
5. Bartold PM: Dentinal hypersensitivity: A review. *Aust Dent J* 51:212–218, 2006.
6. West NX. Dentine hypersensitivity: Preventive and therapeutic approaches to treatment. *Periodontol 2000* 48:31–41, 2008.
7. Brännström M: A hydrodynamic mechanism in the transmission of pain-producing stimuli through the dentine. In: *Sensory Mechanisms in Dentine.* Anderson DJ, ed., The Macmillan Co., New York, pp. 73–79, 1963.
8. Brännström M: The hydrodynamic theory of dentinal pain: Sensation in preparations, caries, and the dentinal crack syndrome. *J Endod* 12:453–457, 1986.
9. Markowitz K, Pashley DH: Discovering new treatments for sensitive teeth: The long path from biology to therapy. *J Oral Rehabil* 35:300–315, 2008.
10. Absi EG, Addy M, Adams D: Dentine hypersensitivity. A study of the patency of dentinal tubules in sensitive and non-sensitive cervical dentine. *J Clin Periodontol* 14:280–284, 1987.
11. Rimondini L, Baroni C, Carrassi A: Ultrastructure of hypersensitive and non-sensitive dentine. A study on replica models. *J Clin Periodontol* 22:899–902, 1995.
12. Pashley DH, Matthews WG, Zhang Y, Johnson M: Fluid shifts across human dentine *in vitro* in response to hydrodynamic stimuli. *Arch Oral Biol* 11: 1065–1072, 1996.
13. Kawabata M, Hector MP, Davis GR, Parkinson CR, Rees GD, Anderson P: Diffusive transport within dentinal tubules: An x-ray microtomographic study. *Arch Oral Biol* 53:736–743, 2008.
14. Williams CG, Macpherson JV, Unwin PR, Parkinson C: Laser scanning confocal microscopy coupled with hydraulic permeability measurements for elucidating fluid flow across porous materials: Application to human dentine. *Anal Sci* 24:437–442, 2008.
15. Orchardson R, Gillam DG: Managing dentin hypersensitivity. *JADA* 137: 990–998, 2006.
16. Tarbet WJ, Silverman G, Stolman JM, Fratarcangelo PA: Clinical evaluation of a new treatment for dentinal hypersensitivity. *J Periodontol* 51:535–540, 1980.
17. Schiff T, Dotson M, Cohen S, DeVizio W, McCool J, Volpe A: Efficacy of a dentifrice containing potassium nitrate, soluble pyrophosphate, PVM/MA copolymer, and sodium fluoride on dentinal hypersensitivity: A twelve-week clinical study. *J Clin Dent* 5 (Spec Iss):87–92, 1994.
18. Schiff T, Dos Santos M, Laffi S, Yoshioka M, Baines E, McCool JJ, DeVizio W: Efficacy of a dentifrice containing 5% potassium nitrate and 1500 ppm sodium monofluorophosphate in a precipitated calcium carbonate base on dentinal hypersensitivity. *J Clin Dent* 9:22–25, 1998.
19. Schiff T, Zhang YP, DeVizio W, Stewart B, Chaknis P, Petrone ME, Volpe AR, Proskin HM: A randomized clinical trial of the desensitizing efficacy of three dentifrices. *Compend Contin Educ Dent* 21 (Suppl):4–10, 2000.
20. Orchardson R, Gillam DG: The efficacy of potassium salts as agents for treating dentin hypersensitivity. *J Orofac Pain* 14:9–19, 2000.
21. Wara-aswapati N, Krongnawakul D, Jiraviboon D, Adulyanon S, Karimbux N, Pitiphat W: The effect of a new toothpaste containing potassium nitrate and triclosan on gingival health, plaque formation and dentine hypersensitivity. *J Clin Periodontol* 32:53–58, 2005.
22. Tzanova S, Ivanova Z, Velinova S: Clinical evaluation of dentinal hypersensitivity treatment with 5% potassium nitrate dentifrice. *Folia Med* 47: 65–69, 2005.
23. Markowitz K, Kim S: The role of selected cations in the desensitization of intradental nerves. *Proc Finn Dent Soc* 88 (Suppl):39–54, 1992.
24. Peacock JM, Orchardson R: Effects of potassium ions on action potential conduction in A- and C-fibers of rat spinal nerves. *J Dent Res* 74:634–641, 1995.
25. Department of Health and Human Services: Oral health care drug products for over-the-counter human use; Amendment to tentative final monograph to include OTC relief of oral discomfort drug products. *Fed Register* 56: 48302, September 24, 1991.
26. Pashley DH, O'Meara JA, Kepler EE, Galloway SE, Thompson SM, Stewart FP: Dentin permeability. Effects of desensitizing dentifrices *in vitro*. *J Periodontol* 55:522–525, 1984.
27. Dragolich WE, Pashley DH, Brennan WA, O'Neal RB, Horner JA, Van Dyke TE: An *in vitro* study of dentinal tubule occlusion by ferric oxalate. *J Periodontol* 64:1045–1051, 1993.
28. Wang HL, Yeh CT, Smith F, Burgett FG, Richards P, Shyr Y, O'Neal R: Evaluation of ferric oxalate as an agent for use during surgery to prevent postoperative root hypersensitivity. *J Periodontol* 64:1040–1044, 1993.
29. Gillam DG, Newman HN, Davies EH, Bulman JS, Troullos ES, Curro FA: Clinical evaluation of ferric oxalate in relieving dentine hypersensitivity.

J Oral Rehabil 31:245–250, 2004.
30. Tung MS, Eichmiller FC: Dental applications of amorphous calcium phosphates. *J Clin Dent* 10 (Spec Iss):1–6, 1999.
31. Charig AJ, Xu Y, Thong S, Winston AE: Comparison of mechanism of action of desensitizing treatments. *J Dent Res* 87 (Spec Iss):3160, 2008.
32. Buelo A, Charig AJ, Winston AE, Xu Y, Thong S, Major E: Assessment of desensitizing ingredients in a tubule occluding toothpaste. *J Dent Res* 87 (Spec Iss):3158, 2008.
33. Geiger S, Matalon S, Blasbalg J, Tung MS, Eichmiller FC: The clinical effect of amorphous calcium phosphate (ACP) on root surface hypersensitivity. *Oper Dent* 28:496–500, 2003.
34. Kaufman HW, Wolff MS, Winston AE, Triol CW: Clinical evaluation of the effect of a remineralizing toothpaste on dentinal sensitivity. *J Clin Dent* 10 (Spec Iss):50–54, 1999.
35. Du Min Q, Bian Z, Jiang H, Greenspan DC, Burwell AK, Zhong J, Tai BJ: Clinical evaluation of a dentifrice containing sodium phosphosilicate (Novamin) for the treatment of dentin hypersensitivity. *Am J Dent* 21:2 10–214, 2008.
36. Löe H, Silness J: Periodontal disease in pregnancy. I. Prevalence and severity. *Acta Odontol Scand* 21:533–551, 1963.
37. Bekes K, John MT, Schaller HG, Hirsch C: Oral health-related quality of life in patients seeking care for dentin hypersensitivity. *J Oral Rehabil* 36:45–51, 2009.
38. Gillam DG, Seo HS, Bulman JS, Newman HN: Perception of dentine hypersensitivity in a general practice population. *J Oral Rehabil* 26:710–714, 1999.
39. Ide M, Wilson RF, Ashley FP: The reproducibility of methods of assessment of cervical dentine hypersensitivity. *J Clin Periodontol* 28:16–22, 2001.
40. Pearce NX, Addy M, Newcombe RG: Dentine hypersensitivity: A clinical trial to compare 2 strontium desensitizing toothpastes with a conventional fluoride toothpaste. *J Periodontol* 65:113–119, 1994.
41. Silverman G, Berman E, Hanna CB, Salvato A, Fratarcangelo P, Bartizek RD, Bollmer BW, Campbell SL, Lanzalaco AC, Mackay BJ, McClanahan SF, Perlich MA, Shaffer JB: Assessing the efficacy of three dentifrices in the treatment of dentinal hypersensitivity. *JADA* 127:191–201, 1996.
42. West NX, Addy M, Jackson RJ, Ridge DB: Dentine hypersensitivity and the placebo response. A comparison of the effect of strontium acetate, potassium nitrate and fluoride toothpastes. *J Clin Periodontol* 24:209–215, 1997.
43. Barnett ML: The role of therapeutic antimicrobial mouthrinses in clinical practice. Control of supragingival plaque and gingivitis. *JADA* 134:699–704, 2003.
44. Addy M, Mostafa P: Dentine hypersensitivity. II. Effects produced by the uptake *in vitro* of toothpastes onto dentine. *J Oral Rehabil* 16:35–48, 1989.