SCIENTIFIC EVIDENCE BEHIND

ADVANCED STABILIZED STANNOUS FLUORIDE DENTIFRICE TECHNOLOGIES

Crest + Oral-B

Introduction

Procter & Gamble has a long history of innovation in dentifrice. Since 1955 when Crest was launched as the first clinically proven anticaries dentifrice, our researchers have continued to develop advanced technologies to provide patients with therapeutic and cosmetic benefits. Crest introduced the first tartar control dentifrice in 1985, which was also the first tartar control product to receive the ADA Seal, and the first whitening dentifrice to receive the ADA Seal in 1999.

More recently, our researchers have introduced a series of groundbreaking formulas that combine the therapeutic benefits of stabilized stannous fluoride with cosmetic benefits, such as extrinsic whitening. These products include Crest® PRO-HEALTH™ [HD]™, Crest® PRO-HEALTH™ Advanced Gum Protection, and Crest® PRO-HEALTH™ Clean Mint (Smooth Formula). Collectively, they provide a unique range of benefits, including protection against caries, plaque, gingivitis, sensitivity, extrinsic stains, calculus, and oral malodor. Numerous laboratory and clinical studies have demonstrated their safety and efficacy.

Key publications and research presentations related to these dentifrice formulations with stabilized stannous fluoride have been summarized in this booklet. We hope this compilation assists you in making evidence-based recommendations for your patients.

J. Leslie Winston, DDS, PhD
Director, Global Oral Care Professional & Clinical Operations

Table of Contents for Research Summaries

A Randomized Clinical Trial to Assess Gingivitis, Plaque, and Tooth Color after Use of a Daily Two-Step Dentifrice and Gel System versus Chlorhexidine Rinse

Reference: Terézhalmy GT[1], Archila LR[1], Gerlach RW[2], Walanski A[2], Cheng R[2], Anastasia MK[2]. Data on file.
[1]University of Texas Health Science Center at San Antonio, TX, USA. [2]Procter & Gamble, Mason, OH, USA.

KEY CLINICAL FINDINGS

Overall

- Use of a daily 2-step dentifrice and gel system resulted in plaque and gingivitis reductions comparable to chlorhexidine (with regular brushing) plus provided tooth whitening benefits. Step 1 is a 0.454% stannous fluoride dentifrice and Step 2 is a whitening gel.

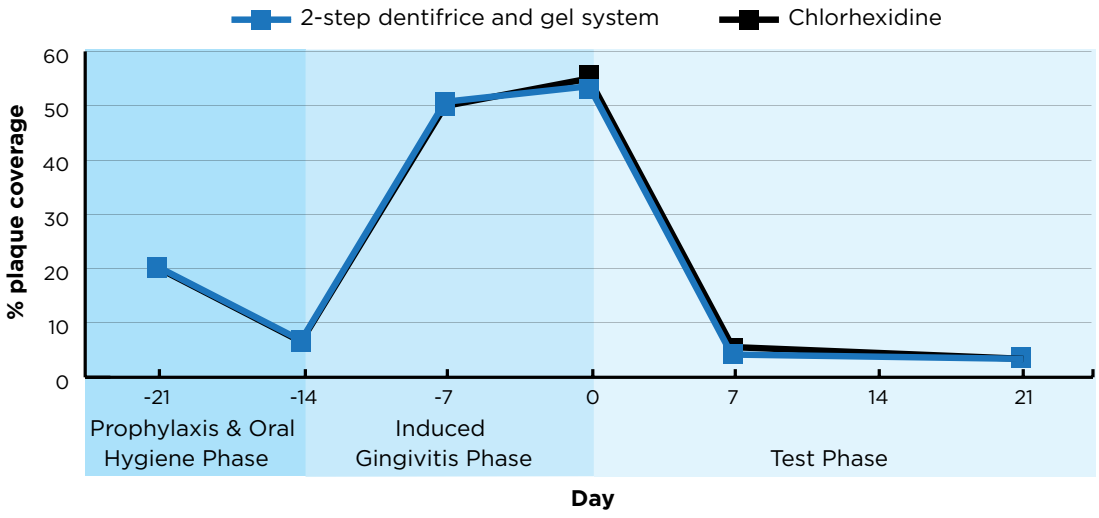
Plaque and Gingivitis

- The daily 2-step dentifrice and gel system group and the chlorhexidine group had statistically significant (P<0.01) improvements in plaque area and gingivitis color measurements at both Day 7 and Day 21 from Day 0. See Figures 1 and 2.
- There were no statistically significant differences between the 2-step dentifrice and gel system group and the chlorhexidine group in plaque and gingivitis reduction at Day 7 and Day 21.

Tooth Color

- The 2-step dentifrice and gel system group demonstrated statistically significantly (P<0.03) greater improvement in tooth color lightness (L*) values compared to the chlorhexidine group at Day 7 and 21. See Figure 3.

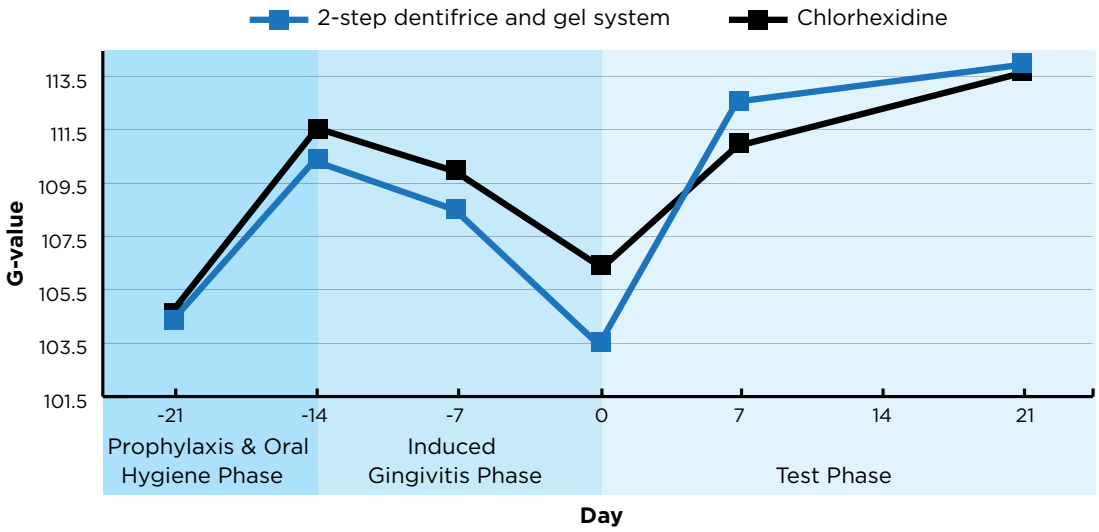
Figure 1. Percent Plaque Coverage



*Day 7 and Day 21 are Means adjusted for Day 0.
For both groups, Day 7 and Day 21 scores were statistically significantly different (P<0.0001) from Day 0.

Figure 2. Gingivitis

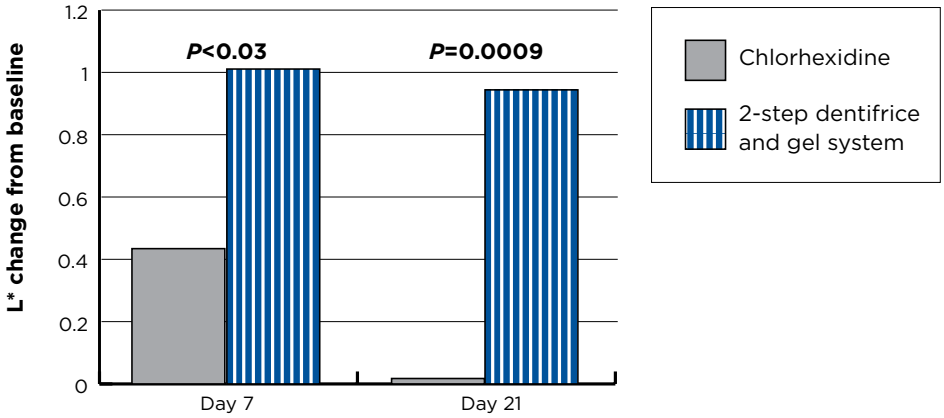
(Digital Gingival Imaging, a higher G-value indicates less gingivitis)



*Day 7 and Day 21 are Means adjusted for Day 0
For both groups, Day 7 and Day 21 scores were statistically significantly different ($P<0.007$) from Day 0.

Figure 3. Tooth color lightness (L*) change from baseline

(Combined Arches, Analysis of Covariance)



OBJECTIVE

To assess the effect of a daily 2-step dentifrice and gel system versus chlorhexidine (with regular brushing) using imaging of plaque, gingivitis and tooth color in an induced gingivitis model.

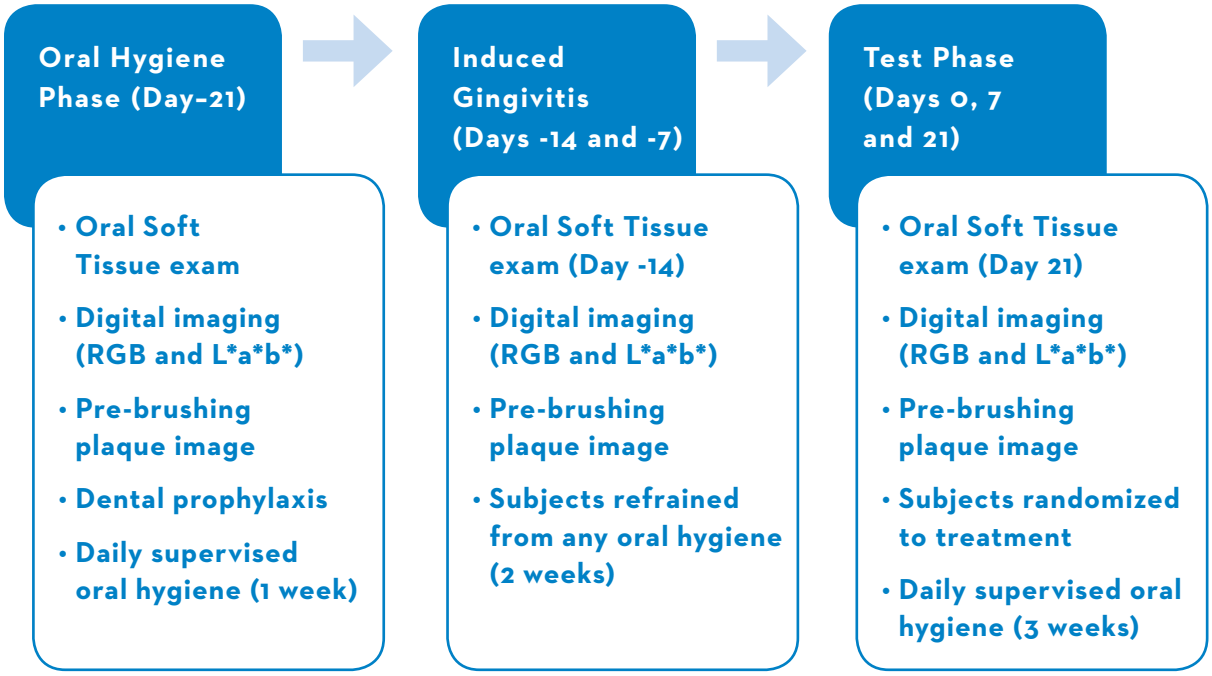
METHODS

- This was a single-blind, supervised-use, randomized, parallel-group, positive-controlled clinical trial.

—Continued on next page

- During the Oral Hygiene Phase, up to 40 healthy volunteers received a dental prophylaxis and used regular oral hygiene products under supervision for one week. During the Induced Gingivitis Phase, subjects refrained from oral hygiene for two weeks. After gingivitis induction, subjects were randomized into 2 treatment groups for the test phase: 2-step dentifrice and gel system or chlorhexidine mouth rinse plus regular brushing. Gingivitis (RGB*), plaque (area %) and tooth color (L*a*b*) were measured by digital image analysis after one and three weeks of product us. See Figure 4.
- During the test phase, subjects were randomly assigned to one of the following treatment groups based on average gingival redness (G) score and pre-brush percent plaque coverage:
    1. Daily 2-Step System (Crest® PRO-HEALTH™ [HD]™, Procter & Gamble): Step 1, 0.454% stannous fluoride dentifrice; Step 2, 3% hydrogen peroxide whitening gel and a soft, regular manual toothbrush (Oral-B® Indicator).
    2. 0.12% chlorhexidine gluconate oral rinse (Oral-B®) and 0.76% sodium monofluorophosphate dentifrice (Colgate® Cavity Protection toothpaste) and a soft, regular manual toothbrush (Oral-B® Indicator).
- Subjects were instructed on product use. Study personnel supervised product use twice daily at least 5 and up to 7 days a week until the end of the study.

Figure 4. Study Design



* Standard Test Method for Objective Measurement of Gingival Color Using Digital Still Cameras. ASTM E2545 - 07(2012). http://www.astm.org/Standards/E2545.htm

A 3-Week Randomized Clinical Trial to Assess the Effect of a Daily Two-Step Dentifrice and Gel System on Tooth Color and Gingivitis using Digital Image Analysis

Reference: Archila LR[1], Terézhalmy GT[1], Gerlach RW[2], Walanski A[2], Barker ML[2], Anastasia MK[2]. Data on file.
[1]University of Texas Health Science Center at San Antonio, TX, USA. [2]Procter & Gamble, Mason, OH, USA.

KEY CLINICAL FINDINGS

Overall

- Use of a daily 2-step dentifrice and gel system demonstrated a significant reduction in gingivitis and improvement in tooth color compared to regular oral hygiene. Step 1 is a 0.454% stannous fluoride dentifrice and Step 2 is a 3% hydrogen peroxide gel.

Gingival Color

- The 2-step dentifrice and gel system group demonstrated a statistically significant (P<0.001) improvement in gingivitis at Weeks 1, 2 and 3, as indicated by the mean change from Baseline for Digital Gingival Imaging* G-value.
- There was a statistically significant difference (P≤0.009) between the 2-step dentifrice and gel system group and the control group in adjusted mean change from Baseline for G-value at Weeks 1, 2, and 3 (Figure 1).

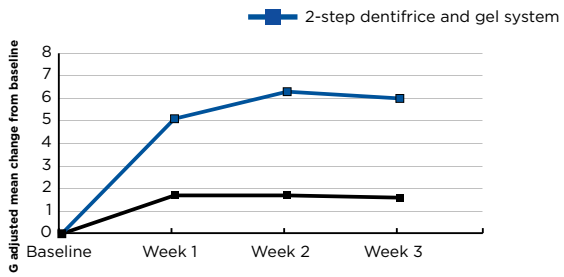
Tooth Color

- The daily 2-step dentifrice and gel system group demonstrated a statistically significant (P<0.001) color improvement at Weeks 1, 2 and 3, as indicated by mean change from Baseline for yellowness (b*) and lightness (L*).
- There was a statistically significant difference between the 2-step dentifrice and gel system group and the control group in adjusted mean change from Baseline for b* (P<0.001, Figure 2) and L* (P≤0.04) at Weeks 1, 2, and 3.

Safety

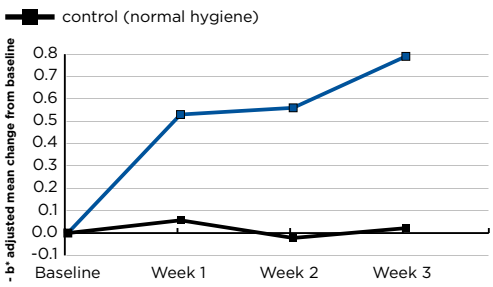
- There were no serious adverse events observed or reported that were deemed related to the study.

Figure 1. Gingivitis (DGIA: G Adjusted mean change from Baseline)
Larger value indicates less gingivitis



P≤0.009 at all time points, 2-sided tests of no treatment difference

Figure 2. Tooth Color (-b* Adjusted mean change from Baseline)
Larger value indicates less yellowness



P<0.001 at all time points, 2-sided tests of no treatment difference.

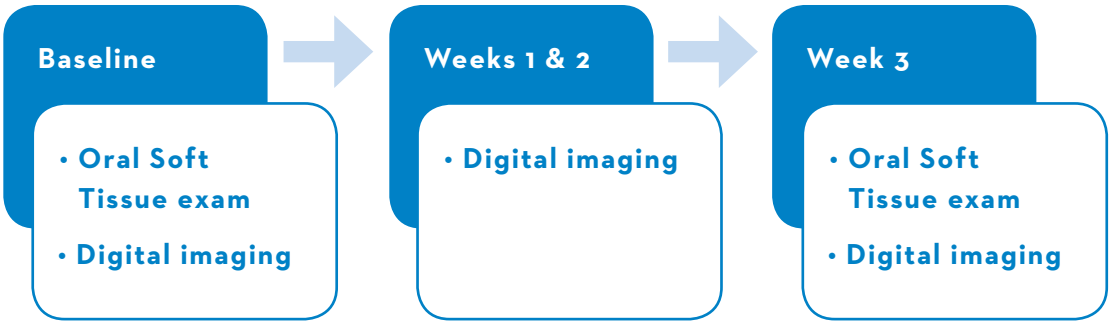
OBJECTIVE

To assess the effect of a daily 2-step dentifrice and gel system relative to a normal hygiene control on gingivitis and tooth color.

METHODS

- This was a single-blind, supervised-use, randomized, two-treatment, parallel group clinical trial.
- 58 healthy adult volunteers who had never whitened their teeth and who had at least 4 gradable maxillary anterior teeth and 4 gradable mandibular anterior teeth with a Vita shade score of A2 or darker were enrolled. Clinical response was measured after 1, 2 and 3 weeks using digital imaging methods for gingival color (RGB) and tooth color (L*a*b*). See Figure 3.
- Subjects were randomly assigned to one of the following groups balancing for baseline L*, b* and G values:
    1. Subjects in the control group performed their normal oral hygiene routine using their regular products, under supervision.
    2. Daily 2-step system used per manufacturer's instructions (Crest® PRO-HEALTH™ [HD]™, Procter & Gamble): Step 1, 0.454% stannous fluoride dentifrice; Step 2, 3% hydrogen peroxide whitening gel. The system was used with an extra soft manual toothbrush (Oral-B® Sensitive Advantage®, Procter & Gamble)

Figure 3. Study Design



* Standard Test Method for Objective Measurement of Gingival Color Using Digital Still Cameras. ASTM E2545 - 07(2012). http://www.astm.org/Standards/E2545.htm

A Clinical Trial to Assess Plaque Prevention with Use of a Daily Two-Step Dentifrice and Gel System

Reference: García-Godoy C[1], Gerlach RW[2], Walanski A[2], Cheng R[2], Anastasia MK[2].
[1]Nova Southeastern University, Ft. Lauderdale, FL,USA. [2]Procter & Gamble, Mason, OH, USA.
Data on file.

KEY CLINICAL FINDING

The two-step dentifrice and gel system group had significantly (*P*≤0.011) less overnight (pre-brush) percent plaque area than the control group at Week 1 (52.9%) and Week 2 (45%). See Figures 1 & 2. Step 1 is a 0.454% stannous fluoride dentifrice and Step 2 is a 3% hydrogen peroxide whitening gel.

Figure 1. Mean Overnight (Pre-Brush) Percent Plaque Area

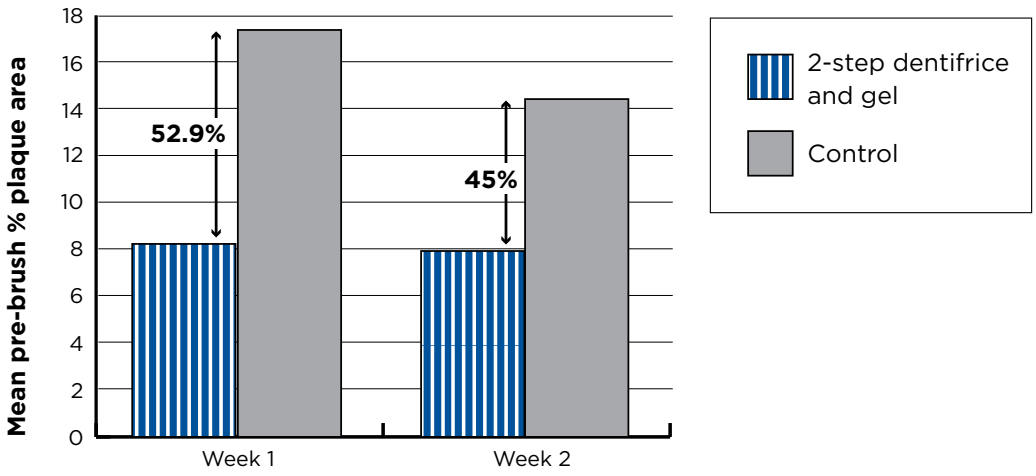
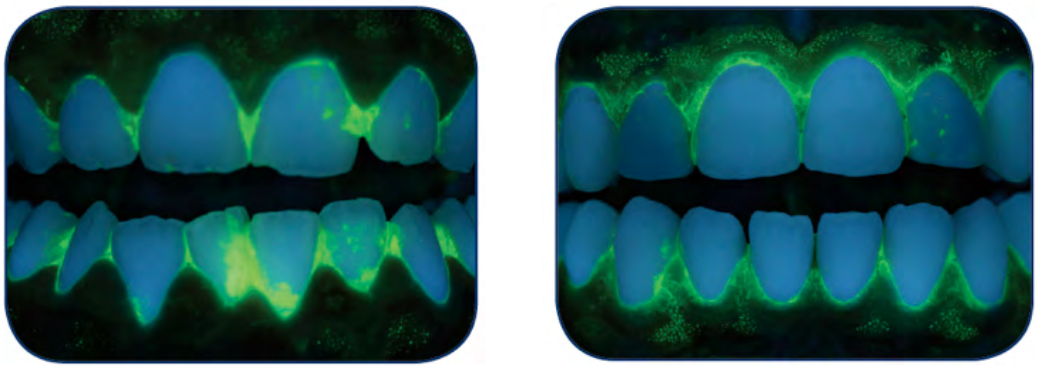


Figure 2. Representative response of overnight plaque coverage at Week 1



Standard oral hygiene control
19.4%

2-step dentifrice and gel system
6.8%

OBJECTIVE

To assess plaque area following a dental prophylaxis and twice daily use of a 2-step dentifrice and gel system versus a standard oral hygiene control.

METHODS

- This was a randomized, controlled, examiner-blind, 2-treatment parallel group plaque prevention study among healthy adult volunteers with plaque.
- Following a whole-mouth dental prophylaxis, subjects were randomized to one of two groups:
  - Standard oral hygiene control group: 0.76% sodium monofluorophosphate dentifrice (Colgate® Cavity Protection, Colgate-Palmolive) and a soft, regular manual toothbrush (Oral-B® Indicator®, Procter & Gamble)
  - 2-step dentifrice and gel system (Crest® PRO-HEALTH™ [HD]™, Procter & Gamble): Step 1, 0.454% stannous fluoride dentifrice; Step 2, 3% hydrogen peroxide whitening gel. The system was used with a soft, regular manual toothbrush (Oral-B® Indicator®).
- Overnight percent plaque area was assessed after 1 and 2 weeks of treatment by digital image analysis of fluorescein-disclosed plaque.

A Randomized Clinical Trial to Evaluate the Effects of a Novel 0.454% Stannous Fluoride Dentifrice on Gingivitis

Reference: Gerlach RW and Amini P. Randomized Controlled Trial of 0.454% Stannous Fluoride Dentifrice to Treat Gingival Bleeding. *Compend Contin Educ Dent* 2012; 33 (2):134-138.

KEY CLINICAL RESULTS

- Relative to baseline, the novel 0.454% stannous fluoride dentifrice demonstrated a statistically significant (P<0.001) improvement in gingival bleeding at Months 1, 2, and 3. (Fig. 1) The reduction ranged from 50% to 74%. (Fig. 2) Gingival bleeding for the control group was relatively unchanged versus baseline over the 3-month trial.
- The test group had a statistically significantly lower adjusted mean number of bleeding sites than the control group at all 3 time points (P<0.001).

Figure 1 - Number of bleeding sites at Months 1, 2 and 3.

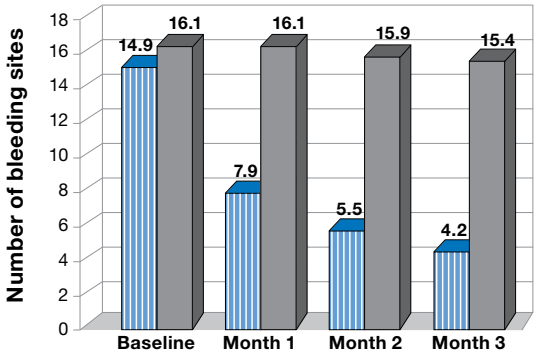
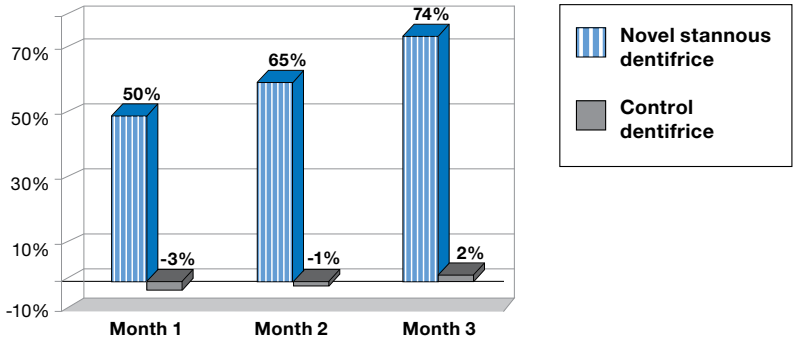


Figure 2 - Percent improvement in bleeding relative to baseline



OBJECTIVE

To evaluate the effects of a novel 0.454% stannous fluoride dentifrice versus a negative control dentifrice on gingivitis.

STUDY DESIGN

- This was a double-blind, randomized, negative-controlled, 2-treatment parallel group trial involving adult subjects with mild-to-moderate gingivitis.
- Qualifying subjects were randomized to either the novel 0.454% stannous fluoride dentifrice (Crest® PRO-HEALTH™ Advanced Gum Protection, Procter & Gamble) or a control toothpaste with 0.76% sodium monofluorophospate (Colgate® Cavity Protection, Colgate-Palmolive). Subjects brushed with their assigned dentifrice and a standard manual toothbrush (Oral-B® Indicator) twice a day over 3 months.
- Efficacy was assessed clinically using the Gingival Bleeding Index (GBI) at baseline and months 1, 2, and 3 of treatment.
- Comparisons of the number of bleeding sites (GBI) to baseline were made using a paired-difference t-test. The groups were compared using ANOVA with baseline as a covariate. Treatment comparisons utilized two-sided testing with a significance level of 0.05.

Assessment of the Effects of a 0.454% Stannous Fluoride Dentifrice on Gingivitis in a 2-Month Positive-Controlled Clinical Trial

Reference: He T, Barker ML, Goyal CR, Biesbrock AR. *Am J Dent* 2012;25:136-140

KEY CLINICAL RESULTS

- Baseline values were balanced across the treatment groups ($P>0.36$) with overall baseline means of 2.09 for gingivitis, 15.8 for gingival bleeding and 15.6 for number of bleeding sites. Relative to baseline, both the stannous fluoride dentifrice group and the positive control group demonstrated a statistically significant ($P<0.0001$) reduction in gingivitis, gingival bleeding, and number of bleeding sites at Month 2.
- Between-treatment group comparisons for change from baseline showed the improvement from baseline for the stannous fluoride group was 45% greater for gingivitis, 60% greater for gingival bleeding and 62% greater for number of bleeding sites versus that of the positive control group ($P<0.0001$).
  See Figs 1–3.
- At Month 2, the stannous fluoride dentifrice group demonstrated statistically significantly lower adjusted mean scores versus the positive control group for all 3 measures ($P<0.0001$).

Figure 1 - Analysis of Covariance Summary for gingivitis (MGI). Improvement from baseline at Month 2.

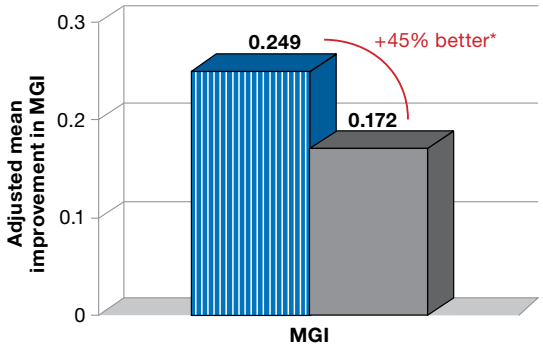


Figure 2 - Analysis of Covariance Summary for gingival bleeding (GBI). Improvement from baseline at Month 2.

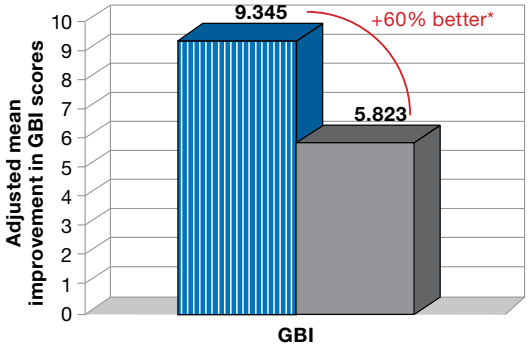
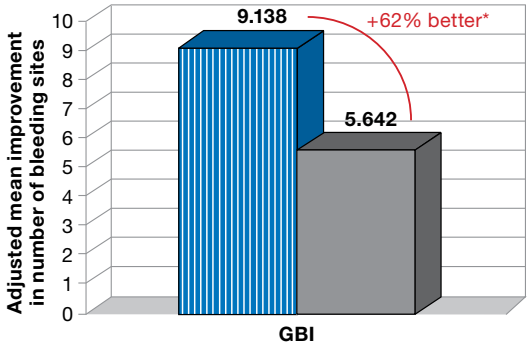
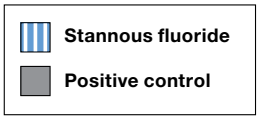


Figure 3 - Analysis of Covariance Summary for number of bleeding sites. Improvement from baseline at Month 2.





*Statistically significant difference between groups, favoring the stannous fluoride group ($P<0.0001$)

OBJECTIVE

To assess the effects of a 0.454% stannous fluoride dentifrice on the treatment of gingivitis as compared to a positive control dentifrice in a 2-month clinical trial.

STUDY DESIGN

- This was a randomized, positive-controlled, double-blind, parallel-group, single-center study with two treatment groups composed of healthy adult volunteers.
- 200 qualified subjects were enrolled; each treatment group contained 100 subjects. 99 subjects in the stannous fluoride group and 97 in the positive control group completed the study.
- During the treatment phase, subjects performed their treatment routine unsupervised using their assigned dentifrice (Crest® PRO-HEALTH™ Advanced Gum Protection with 0.454% stannous fluoride, Procter & Gamble, or Colgate® Total with 0.3% triclosan and 0.32% sodium fluoride, Colgate-Palmolive) per manufacturers' instructions (twice daily for stannous fluoride dentifrice; three times daily for the control) for 2 months. Both groups used an ADA soft reference manual toothbrush.
- Efficacy measurements were obtained at Baseline and 2-months post-treatment. Anti-gingivitis efficacy was determined using mean Modified Gingival Index (MGI) and Gingival Bleeding Index (GBI).
- Oral soft tissue and hard tissue assessments were conducted at each examination interval.

 OMIS11658

A Randomized Clinical Trial to Measure the Erosion Protection Benefits of a Stannous Fluoride Dentifrice versus a Triclosan/ Copolymer Dentifrice

N. West[1], T. He[2], A. Wilberg[2], R. Eusebio[2]
[1]University of Bristol Dental School and Hospital, Bristol, UK. [2]Procter & Gamble, Mason, OH, USA

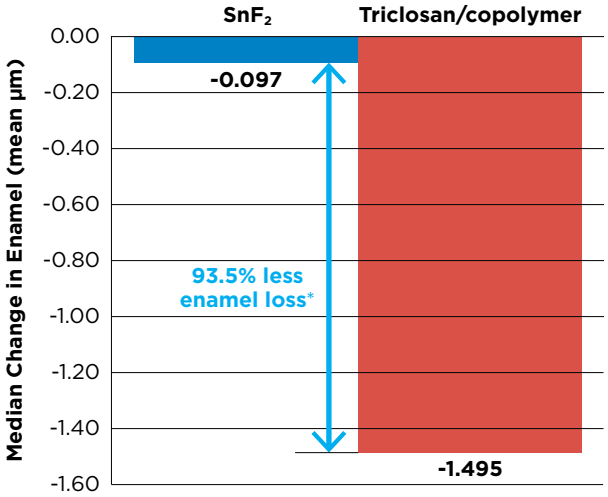
KEY CLINICAL FINDINGS

Crest® PRO-HEALTH™ Advanced dentifrice (SnF_2) demonstrated significantly greater protection against dental erosion relative to the Colgate® Total (triclosan/copolymer) dentifrice in a 10-day *in situ* clinical study.

At Day 10, the SnF_2 dentifrice demonstrated 93.5% lower enamel loss than the triclosan/copolymer dentifrice with median loss of 0.097 µm and 1.495 µm, respectively, which was statistically significant ($P<0.0001$). See Figure.

Both products were well tolerated.

Figure. Treatment comparison at Day 10: Median Change in Enamel (µm)



* Treatment difference at Day 10 was statistically significant. $P<0.0001$
N=34.

OBJECTIVE

To compare the enamel protection efficacy (loss of tooth enamel due to erosion as measured by surfometry) of a marketed stannous fluoride dentifrice and a marketed triclosan/copolymer sodium fluoride dentifrice in a 10-day *in situ* erosion model.

STUDY DESIGN

- A single center, double-blind, randomized, 2-treatment, and 4-period crossover clinical study was conducted involving healthy adults.
- Subjects presented for 4 study periods and were randomized to treatment sequences, receiving one of the two marketed dentifrice products each period:
  1. Crest® PRO-HEALTH™ Advanced Gum Protection — 0.454% Stannous fluoride (1100 ppm fluoride), The Procter & Gamble Company, Cincinnati, OH.
  2. Colgate® Total® Clean Mint — 0.24% Sodium fluoride with 0.3% Triclosan/ copolymer, Colgate-Palmolive Co., New York, NY.
- Each study period was comprised of 10 treatment days. On each treatment day, subjects brushed their teeth at home in their usual manner, using a non-treatment toothpaste (Crest® Decay Protection, 1450 ppm F as sodium fluoride, Procter & Gamble) and a manual toothbrush (Oral-B® 35, Procter & Gamble) supplied at the screening visit.
- Subjects then attended the clinical trials unit where they collected their upper palatal intra-oral appliance fitted with two enamel samples and placed it in their mouth. Subjects wore the appliance for approximately 6 hours total over the course of each study day. While wearing the appliance, subjects swished twice a day with their assigned treatment toothpaste slurry at the clinical site for 60 seconds.
- The erosive challenge occurred with the appliance in the mouth. The subjects were required to sip 25mL of orange juice over a timed minute, swishing it around their mouth, then spitting out. This was repeated 10 times so that a total of 250mL of orange juice was exposed to the enamel samples over a 10 minute period. The erosive challenge occurred a total of four times on each treatment day.
- On Day 10, the enamel samples were measured for tissue loss using a calibrated contact surface profilometer. Measurements were taken at baseline, prior to the start of the study, and at the end of treatment Day 10. Fresh enamel samples were placed in the intra-oral appliance at the beginning of each study period.

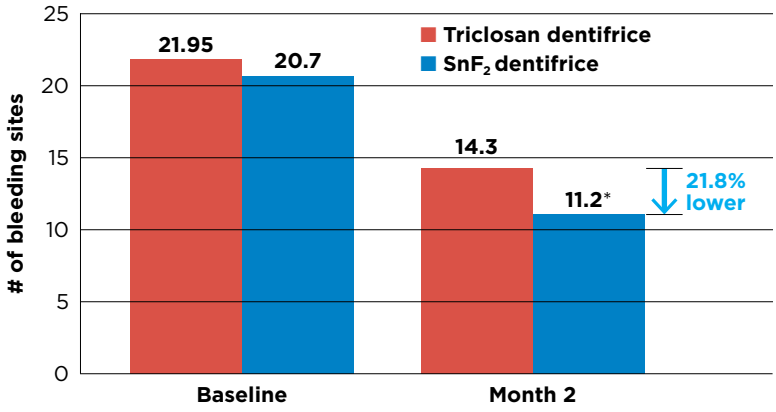
A Randomized 2-Month Clinical Trial Evaluating the Anti-Gingivitis Efficacy of a Stabilized Stannous Fluoride Dentifrice versus a Triclosan Dentifrice

CR Goyal,[1] JG Qaqish,[1] T He,[2] R Eusebio.[2]
[1]All Sum Research, Mississauga, Ontario, Canada. [2]Procter & Gamble, Mason, OH USA.

KEY CLINICAL FINDINGS

- After 2 months of use, the stabilized stannous fluoride (SnF_2) test dentifrice group had 21.8% fewer bleeding sites versus the triclosan positive control dentifrice group (*P*<0.001).
- Both groups showed statistically significant reductions in bleeding sites from Baseline (*P*<0.0001).

Figure 1. Number of bleeding sites per group



*Significant difference between groups at Month 2, *P*<0.001. Groups were not significantly different at Baseline (*P*>0.05).

OBJECTIVE

To compare the anti-gingivitis efficacy of a stabilized SnF_2 dentifrice versus a positive control triclosan dentifrice over a 2-month period.

METHODS

- This was a randomized, positive-controlled, double-blind, parallel-group clinical trial involving generally healthy adults with mild to moderate gingivitis.
- Qualifying subjects were randomized to one of two treatment groups:
  - 0.454% stabilized SnF_2 dentifrice (Crest® PRO-HEALTH™ Clean Mint [Smooth Formula], Procter & Gamble)
  - Positive control dentifrice with 0.3% triclosan and 0.243% sodium fluoride (Colgate® Total®, Colgate-Palmolive)
- Dentifrice was distributed over-labeled or over-tubed for blinding purposes, with a soft manual flat-trim toothbrush (Oral-B® Indicator®, Procter & Gamble). Subjects were instructed to brush with their respective dentifrice according to each manufacturer's instructions.

- The following efficacy and safety evaluations were conducted at Baseline and Month 2: Gingival Bleeding Index; Modified Gingival Index; and Oral Soft Tissue.
- Treatment groups were compared using analysis of covariance with Baseline value as covariate. All statistical tests were two-sided with a 5% level of significance.

CLINICAL COMMENT

Gingival bleeding is an important early sign of gingivitis, the initial stage of periodontal disease. Reducing gingival bleeding is the ultimate goal of treating gingivitis, since research indicates the absence of gingival bleeding is a reliable indicator for sustained periodontal health.* This clinical trial showed subjects using the SnF_2 dentifrice had significantly fewer (21.8%) bleeding sites than those using a positive control triclosan dentifrice after 2 months of use. Based on these findings, dental professionals should consider recommending the SnF_2 dentifrice to patients with gingivitis to reduce bleeding and improve periodontal health.

* Lang NP. et al. *J Clin Periodontol*. 1990 Nov;17(10):714-21.

 ORAL-21190

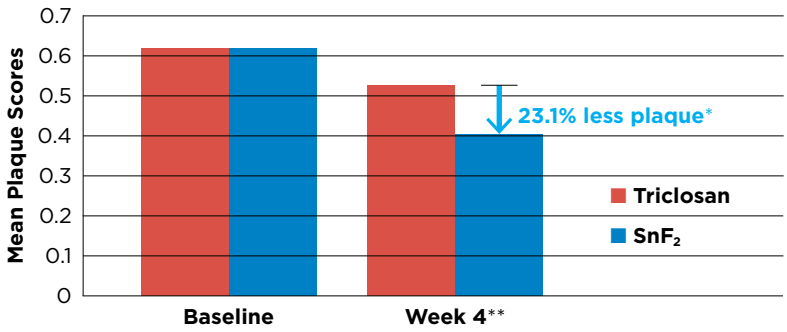
Comparative Anti-plaque Effect of Stabilized Stannous Fluoride and Triclosan Dentifrices

L Friesen,[1] CR Goyal,[2] JG Qaqish,[2] T. He,[3] R Eusebio.[3]
[1]The University of Missouri, School of Dentistry, Kansas, MO, USA. [2]All Sum Research Ltd, Mississauga, ON, Canada.
[3]Procter & Gamble, Mason, OH, USA

KEY CLINICAL FINDINGS

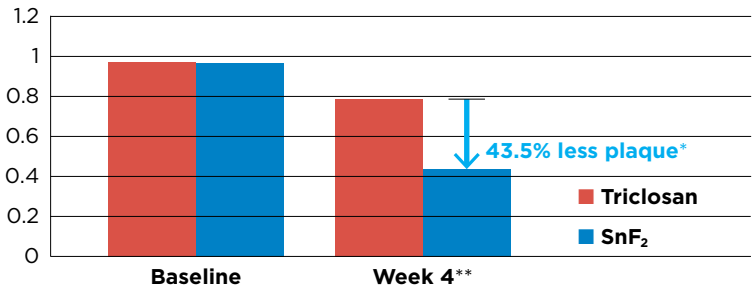
- After 4 weeks of use, the stabilized stannous fluoride (SnF_2) dentifrice group had 23.1% lower whole mouth plaque scores and 43.5% lower interproximal plaque scores than the triclosan positive control dentifrice group (*P*<0.0001). See Figures 1 and 2.
- Both the triclosan and SnF_2 dentifrice groups demonstrated statistically significant (*P*<0.0001) reductions in plaque levels at Week 4 versus Baseline.
- Both treatments were well tolerated.

Figure 1. Whole mouth plaque scores at Baseline and Week 4.



N=118. *Statistically significant difference between groups, *P*<0.0001.
**Week 4 values are adjusted means.

Figure 2. Interproximal plaque scores at Baseline and Week 4.



N=118. *Statistically significant difference between groups, *P*<0.0001.
**Week 4 values are adjusted means.

OBJECTIVE

To compare the effect of a SnF_2 dentifrice versus triclosan dentifrice on reduction of plaque over a 4-week period.

STUDY DESIGN

- This was a randomized, parallel, double-blind, 4-week clinical trial including subjects with evidence of plaque.

- Subjects were randomized to one of two treatment groups:
  - Experimental 0.454% stabilized SnF_2 dentifrice (Crest® PRO-HEALTH™ Clean Mint [Smooth Formula], Procter & Gamble) or
  - Triclosan positive control dentifrice with 0.243% sodium fluoride (Colgate® Total®, Colgate-Palmolive). Both groups used a soft, regular manual toothbrush (American Dental Association) and brushed with their respective product according to manufacturer's instructions at-home.
- Plaque was evaluated using the Rustogi Modification of the Navy Plaque Index (RMNPI) at Baseline and after 4 weeks of product use.
- Statistical analyses utilized analysis of covariance with baseline value as covariate.

CLINICAL COMMENT

Chemotherapeutic antimicrobial dentifrices play an important role in the control of plaque-induced oral diseases, such as gingivitis. Both SnF_2 and triclosan dentifrices have been shown to provide significant inhibition of plaque.[1,2] This study showed the new smooth formula SnF_2 dentifrice provided significantly greater plaque control than the triclosan dentifrice. These findings are consistent with other studies in the literature showing superior plaque protection for SnF_2 versus triclosan dentifrice.[3,4]

[1]White DJ, et al. *J Contemp Dent Pract*. 2006;July (7)3:001-011.
[2]Rover JA, et al. *Am J Dent*. 2014 Jun;27(3):167-70.
[3]He T, et al. *Am J Dent*. 2013;26: 303-306.
[4]Sharma NC et al. *J Clin Dent*. 2013;24:31-36.

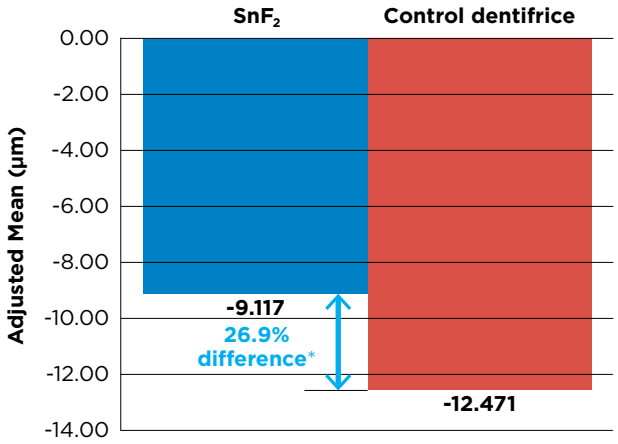
A Randomized Clinical Trial to Measure the Erosion Protection Benefits of a Stabilized Stannous Fluoride Dentifrice versus a Control Dentifrice

XY Zhao[1], T He[2], Y He[2], C Cheng[2], HJ Chen[2].
[1]Fourth Military Medical University, Xi'an, PR China; [2]Procter & Gamble.

KEY CLINICAL RESULTS

The experimental stabilized stannous fluoride (SnF_2) dentifrice provided 26.9% greater erosion protection relative to the control dentifrice at Day 10 (P<0.03).

Figure 1. Enamel loss at Day 10



*Treatment difference at Day 10 was statistically significant. (P=0.0227). N=12 subjects; 18 observations per product.

OBJECTIVE

To compare the enamel protection efficacy of a stabilized stannous fluoride dentifrice and a marketed control dentifrice in a 10-day *in situ* erosion model.

STUDY DESIGN

- A single center, double-blind, randomized, 2-treatment, and 3-period crossover clinical study was conducted involving healthy adults.
- Subjects presented for 3 study periods and were randomized to treatment sequences, receiving one of the two marketed dentifrice products each period:
  1) Experimental 0.454% stabilized SnF_2 dentifrice (Crest® PRO-HEALTH™ Clean Mint [Smooth Formula], Procter & Gamble)
  2) Sodium fluoride dentifrice with potassium nitrate marketed for erosion protection (Sensodyne® Pronamel®, GlaxoSmithKline)
- Each study period was comprised of 10 treatment days. On each treatment day, subjects brushed their teeth at home in their usual manner, using a non-treatment toothpaste and a regular, soft manual toothbrush supplied at the screening visit.
- Subjects then attended the clinical trials unit where they collected their lower palatal intra-oral appliance fitted with 8 enamel samples and placed it in their mouth. Subjects wore the appliance for approximately 6 hours total over the course

of each study day. While wearing the appliance, subjects brushed their lingual teeth for 30 seconds, and swished with their assigned treatment toothpaste slurry for 90 seconds twice a day under the supervision of clinic staff.

- The erosive challenge occurred with the appliance in the mouth. The subjects were required to sip 25mL of orange juice over a timed minute, swishing it around their mouth, then spitting out. This was repeated 10 times so that a total of 250mL of orange juice was exposed to the enamel samples over a 10 minute period. The erosive challenge occurred a total of four times on each treatment day.
- On Day 10, the enamel samples were measured for tissue loss using a calibrated contact surface profilometer. Measurements were taken at baseline, prior to the start of the study, and at the end of treatment Day 10. Fresh enamel samples were placed in the intra-oral appliance at the beginning of each treatment period.
- Statistical analyses utilized a general linear mixed model with period and treatment as fixed effects and subject as a random effect.

CLINICAL COMMENT

Stabilized SnF_2 dentifrice has been shown to provide significantly greater protection from acid erosion compared to other types of fluoride dentifrice.* In this trial, a novel stabilized stannous fluoride dentifrice showed a significant anti-erosion benefit over a sodium fluoride/potassium nitrate dentifrice which is marketed for protecting enamel against acid erosion. Dental professionals should consider recommending this SnF_2 dentifrice for its high level of protection against acid erosion as well as its benefits for reduction of gingivitis and plaque.

* Lussi A. *Int Dent J*2014;64 (Suppl 1):2-3.

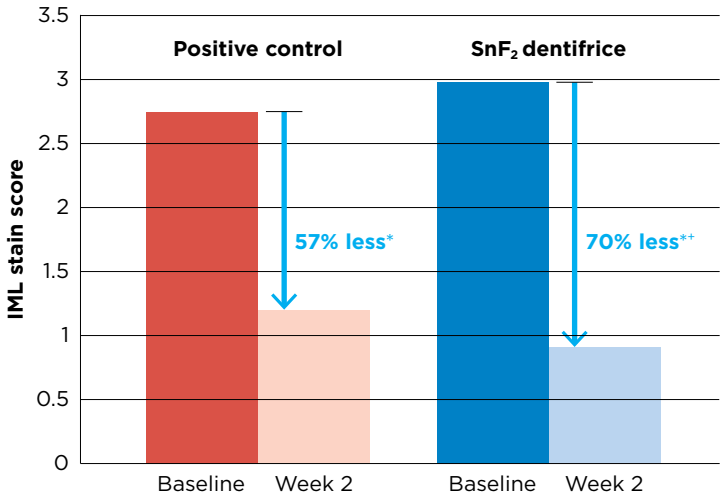
Extrinsic Stain Removal Efficacy of a Stabilized Stannous Fluoride Dentifrice

Lynn Friesen[1], T He[2], R. Eusebio[2].
[1]The University of Missouri, School of Dentistry, Kansas, MO, USA. [2]Procter & Gamble, Mason, OH, USA.

KEY CLINICAL FINDINGS

- After 2 week of use, the experimental stabilized stannous fluoride (SnF_2) group demonstrated significantly less Interproximal Modified Lobene (IML) stain overall (see Figure) and interproximal surface stain than the positive control dentifrice group (*P*<0.0012).
- Both groups showed statistically significant reductions in IML stain scores at Week 2 (*P*<0.0001) relative to Baseline. The median percent change reductions were 57% for the positive control and 70% for the SnF_2 dentifrice.

Figure. Interproximal Modified Lobene Stain Scores per Group.



N=25 per group.
* Both groups showed a statistically significant reduction versus Baseline, percents based on median percent change.
+ Statistically significant difference between groups at Week 2 (*P*<0.0012).

OBJECTIVE

To assess the extrinsic stain removal benefit delivered by a SnF_2 dentifrice and a positive control dentifrice over a two-week period.

METHODS

- This study utilized a randomized, two-week, double-blind, parallel group design.
- At Baseline, an IML examination[‡] was performed on the facial surfaces of the twelve anterior teeth. The two teeth with the highest IML composite scores were selected as the test teeth.

- Subjects were stratified on stain scores of the test teeth, and gender, and randomized to one of two treatment groups:
  - Experimental 0.454% stabilized stannous fluoride dentifrice (Crest® PRO-HEALTH® Clean Mint [Smooth Formula], Procter & Gamble); or
  - 0.243% sodium fluoride/0.3% triclosan positive control whitening dentifrice (Colgate® Total® Whitening, Colgate-Palmolive).
- Subjects were instructed to use their respective test product following the manufacturer's instructions at home over the two week study duration.
- Tooth color was reassessed at Week Two.
- Baseline to post-treatment change in stain score was tested using paired t-tests. Analysis of covariance (ANCOVA) with treatment as a factor and Baseline Lobene score as the covariate was used to assess treatment differences post-treatment. All comparisons were two-sided using a 5% level of significance.

CLINICAL COMMENT

Stabilized SnF_2 dentifrice has been shown to provide significant oral health benefits, including protection against caries, plaque, gingivitis and sensitivity.[§] SnF_2 formulations have also been developed to provide esthetic benefits consumers desire, including extrinsic stain removal. This high silica containing toothpaste is uniquely formulated to provide effective cleaning and surface stain removal.

[‡] Friesen L, et al. *Am J Dent* 2016; 29:20-24.
[§] Baig A and He T. *Compend Contin Educ Dent* 2005;26 (Suppl 1): 4-11.

 ORAL-21195

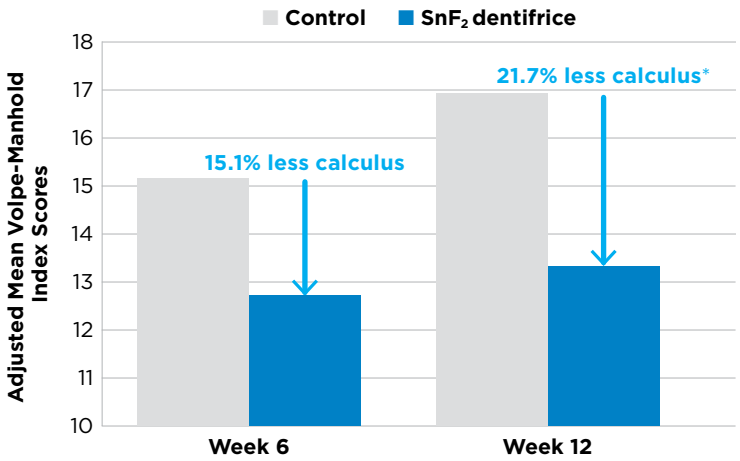
Anti-calculus Efficacy of a Stabilized Stannous Fluoride Dentifrice in a 3-month Clinical Trial

JL Milleman,[1] T He,[2] MK Anastasia.[2]
[1]Salus Research, Fort Wayne, IN, USA, [2]Procter & Gamble, Mason, OH, USA.

KEY CLINICAL FINDINGS

- Subjects using the stabilized stannous fluoride (SnF_2) dentifrice demonstrated 15.1% less calculus at Week 6 (P=0.05) and 21.7% less calculus at Month 3 (P<0.01) compared to subjects in the control group.
- Both test products were well tolerated.

Figure. Calculus scores (VMI) per group.



N=78. * Significant difference between groups (P<0.05) using analysis of covariance.

OBJECTIVE

To assess the calculus prevention benefit of an experimental stabilized SnF_2 dentifrice relative to a negative control dentifrice.

STUDY DESIGN

- This was a 3-month, parallel-group, double-blind, randomized and controlled clinical trial.
- Subjects received a dental prophylaxis and then entered a 2-month run-in phase. At the end of 2 months, subjects received a Volpe-Manhold Index (V-MI) calculus examination.
- Qualified subjects who formed a minimum of 9 mm of calculus on the lingual surfaces of the six mandibular anterior teeth received another prophylaxis and were randomly assigned to one of the two treatments:
  - Experimental 0.454% stabilized SnF_2 dentifrice (Crest® PRO-HEALTH™ Clean Mint [Smooth Formula], Procter & Gamble) with zinc to control calculus; or
  - Negative control dentifrice (Colgate® Cavity Protection, Colgate-Palmolive).
- Subjects brushed with their assigned product twice daily using a standard manual toothbrush, one minute per brushing, during the 3-month trial.

- Safety and calculus measurements were taken via Oral Soft Tissue and Volpe-Manhold Index examinations at Baseline, Week 6 and Month 3.
- Treatment groups were compared using analysis of covariance. All statistical tests were two-sided with a 5% level of significance.

CLINICAL COMMENT

Calculus build-up can lead to less efficient oral hygiene and tooth discoloration, as well as extending the time required for a dental prophylaxis. This research demonstrated a directional anti-calculus benefit for the SnF_2 dentifrice relative to the control dentifrice in as early as 6 weeks. The relative benefit for the SnF_2 dentifrice was even greater after 12 weeks of use. Dental professionals should consider recommending the SnF_2 dentifrice for patients who form calculus, as it also improves gingival health and strengthens enamel.

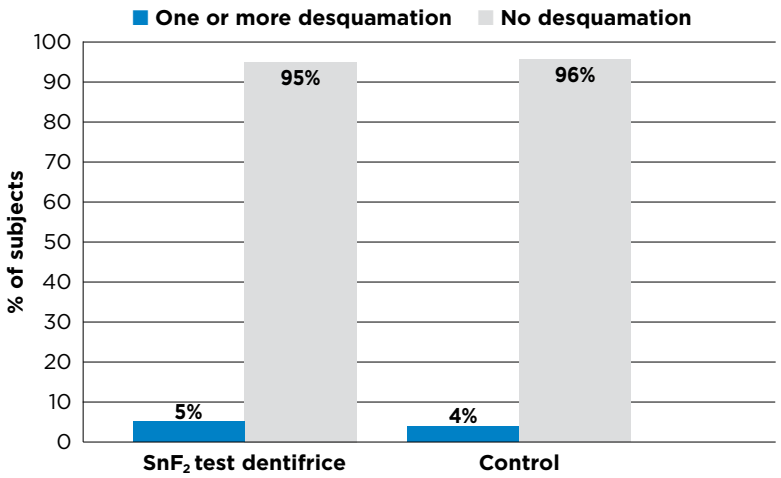
A Meta-Analysis of Stabilized Stannous Fluoride Dentifrice and Oral Tissue Safety

J. Grender, S. Farrell, T. He, M.K. Anastasia. Procter & Gamble, Mason, OH, USA.

KEY CLINICAL RESULTS

- Of the 243 subjects that tested the experimental stannous fluoride (SnF_2) dentifrice, 10 subjects (4.1%) had ≥ 1 Adverse Event (AE). Of the 235 subjects that tested the negative control, 6 subjects (2.6%) had ≥ 1 AE. All AEs were mild in nature, and no subjects discontinued use due to a treatment-related AE. Desquamation was the most frequent AE.
- In the short-term studies, the percent of subjects with ≥ 1 desquamation was 5% in the SnF_2 dentifrice test group and 4% in the negative control. The two treatments did not differ significantly from each other with respect to occurrence of desquamation (*P*=0.5429).
- No AEs were reported or observed in the long-term studies.
- Subjects in the meta-analysis ranged in age from 18 to 84 years and represented diverse ethnicity.

Figure. Percent (%) of subjects in short-term studies with > 1 desquamation versus no desquamation per group.



* There was no significant difference between groups (*P*=0.5429).

OBJECTIVE

To evaluate the oral tissue safety of an experimental stabilized SnF_2 dentifrice relative to a negative control.

STUDY DESIGN

- Seven randomized, controlled clinical trials were included in the analysis.
- One hundred-eighty subjects participated in two 12-week, long-term, parallel clinical studies, and 156 subjects participated in five short-term crossover studies with periods < 1 week in duration.

- In each parallel study, subjects were randomized to either the experimental 0.454% stabilized SnF_2 dentifrice (test group, Crest® PRO-HEALTH™ Clean Mint [Smooth Formula] prototypes, Procter & Gamble) or a 0.76% sodium monofluorophosphate dentifrice (negative control group, Colgate® Cavity Protection, Colgate-Palmolive) for daily use.
- In each crossover study, subjects were randomized to a sequence in which they received both products. Oral tissue safety was assessed via clinical examination or voluntary reports. Proportion of subjects with AEs was summarized by study and treatment. Treatments were compared using generalized linear mixed model.

CLINICAL COMMENT

Mild desquamation is a common AE reported with some dentifrice formulations, particularly those with a tartar control benefit. The SnF_2 dentifrice tested in these studies contains zinc to protect against calculus build-up. While desquamation is usually a harmless occurrence that subsides with continued use, some patients find it unpleasant. In this meta-analysis, only 5% of subjects using the test SnF_2 dentifrice in short-term trials reported one or more desquamation, which was not significantly different from subjects experiencing desquamation (4%) in the negative control group. No AEs were observed or reported in either group in the long-term trials. Dental professionals should consider recommending this SnF_2 dentifrice for patients who need a tartar control benefit, particularly those who have difficulty tolerating tartar control dentifrice. It also improves gingival health and strengthens enamel.

For more information about Crest® PRO-HEALTH™ toothpastes, visit www.dentalcare.com

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