

# SCIENTIFIC EVIDENCE BEHIND ADVANCED DENTIFRICE TECHNOLOGIES

- STABILIZED STANNOUS FLUORIDE
- SODIUM HEXAMETAPHOSPHATE

For more information about Crest PRO-HEALTH  
toothpaste, visit: [www.dentalcare.com](http://www.dentalcare.com)

## 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, as well as the first whitening dentifrice to receive the ADA Seal in 1999.

More recently, our researchers have introduced a groundbreaking formula that combines the therapeutic benefits of stabilized stannous fluoride and the cosmetic benefits of sodium hexametaphosphate. Crest® PRO-HEALTH® toothpaste, which took more than a decade to develop, provides 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 its safety efficacy.

Publications and research presentations related to dentifrice formulations with the ingredients stabilized stannous fluoride and sodium hexametaphosphate have been summarized in this booklet. We hope this compilation assists you in making evidence-based recommendations for your patients.

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# Gingival Health

**gin·gi·vi·tis:** inflammation of the gums

- Gingivitis, the mildest form of periodontal disease, affects more than 50% of the US adult population.\* If left untreated, gingivitis can progress to periodontitis, which may eventually lead to tooth loss. Recent findings also suggest that periodontal disease may be related to certain systemic conditions.
- Removing and inhibiting plaque biofilm reduces gingival inflammation and bleeding, helping to prevent the progression of gingivitis.
- Incorporating chemotherapeutic dentifrices into patients' home care routine is a convenient way to provide protection against plaque and gingivitis.



## GINGIVITIS

Mild inflammation of the gums due to plaque build-up  
Gums are red and/or sore and bleed when probed

## Stabilized stannous fluoride and gingival health

- Stabilized stannous fluoride is the only fluoride agent that helps protect against plaque and gingivitis in addition to its anticaries and desensitizing benefits.
- Research shows stabilized stannous fluoride has bacteriostatic and bactericidal properties.
- The benefits of stabilized stannous fluoride for the reduction of gingival inflammation and bleeding are supported by an extensive body of clinical research.

\* The Third National Health and Nutrition Examination: Survey (NHANES III) 1988-1994, National Center for Health Statistics, Centers for Disease Control and Prevention.

# The Comparative Efficacy of Stabilized Stannous Fluoride/ Sodium Hexametaphosphate Dentifrice and Sodium Fluoride/ Triclosan/Copolymer Dentifrice for the Control of Gingivitis: A 6-Month Randomized Clinical Study

**Reference:** Archila L, Bartizek RD, Winston JL, et al. *J Periodontol.* 2004;75(12):1592-1599.

## CONCLUSION

Over a 6-month period a 0.454% stabilized stannous fluoride/sodium hexametaphosphate dentifrice showed a statistically significant benefit in reducing gingivitis compared to a positive control triclosan/copolymer dentifrice.

## OBJECTIVE

To investigate the long-term antigingivitis efficacy of a stabilized 0.454% stannous fluoride/sodium hexametaphosphate dentifrice versus a positive control dentifrice.

## MATERIALS AND METHODS

- A 0.454% stabilized stannous fluoride/sodium hexametaphosphate dentifrice was compared to a positive control dentifrice with 0.243% sodium fluoride/0.30% triclosan/2.0% Gantrez copolymer (Colgate® Total®).
- Study subjects were 199 generally healthy adult subjects with a minimum of 16 natural teeth excluding third molars.
- At baseline, oral soft tissue was examined. The Löe and Silness Gingival Index (GI) was used to measure gingivitis and this was followed by a dental prophylaxis.
- Subjects were randomly assigned to either the stannous fluoride/sodium hexametaphosphate dentifrice or the triclosan/copolymer control dentifrice to use over 6 months and were instructed to brush twice daily for one minute with a manual soft toothbrush and assigned dentifrice. Their toothbrushing was supervised on 3 days of each week.
- At months 3 and 6 gingivitis and safety were reexamined.

## RESULTS

- Data were analyzed for 186 subjects who completed the study.
- At 6 months both groups showed highly significant reductions in GI scores compared to baseline ( $p < 0.001$ ) and group differences were statistically significant ( $p = 0.001$ ). Adjusted mean GI scores were 42.6% lower at 3 months and 25.8% lower at 6 months for the stabilized stannous fluoride/sodium hexametaphosphate dentifrice.
- At 6 months both groups showed highly significant reductions in the average number of gingival bleeding sites (sites graded as 2 or 3 based on GI scoring) compared to baseline ( $p < 0.001$ ) and group differences were highly statistically significant ( $p < 0.001$ ). Adjusted mean number of gingival bleeding sites was 43.4% lower at 3 months and 27.4% lower at 6 months for the stabilized stannous fluoride/sodium hexametaphosphate dentifrice as compared to control.
- No adverse reactions or tooth staining was reported.

Treatment	N	Baseline Score (Mean ± SD)	Treatment Score (Adjusted Mean <sup>a</sup> ± SE)	% Reduction <sup>b</sup>
<b>Gingival Index Scores</b>				
Month 3 Control	96	0.50±0.25	0.31±0.01	-
Month 3 SnF <sub>2</sub> /SHMP	100	0.51±0.32	0.18±0.01	42.6
Month 6 Control	91	0.51±0.26	0.37±0.02	-
Month 6 SnF <sub>2</sub> /SHMP	95	0.52±0.32	0.27±0.02	25.8
<b>Number of Gingival Bleeding Sites</b>				
Month 3 Control	96	39.8±20.3	24.6±1.07	-
Month 3 SnF <sub>2</sub> /SHMP	100	40.0±25.7	13.9±1.05	43.4
Month 6 Control	91	40.1±20.4	28.9±1.49	-
Month 6 SnF <sub>2</sub> /SHMP	95	40.6±26.2	21.0±1.46	27.4
<sup>a</sup> Adjusted means and standard errors (SE) from analysis of covariance with baseline score as covariate. <sup>b</sup> Percent reduction = 100% x (control-experimental mean)/control mean. SHMP = sodium hexametaphosphate; SnF <sub>2</sub> = stabilized stannous fluoride.				

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# Anti-Gingivitis Efficacy of a Stabilized 0.454% Stannous Fluoride/Sodium Hexametaphosphate Dentifrice: A Controlled 6-Month Clinical Trial

**Reference:** Mankodi S, Bartizek RD, Winston JL, et al. *J Clin Periodontol.* 2005;32(1):75-80.

## CONCLUSION

Over a 6-month period a 0.454% stabilized stannous fluoride/sodium hexametaphosphate (Crest PRO-HEALTH) dentifrice showed a statistically significant and clinically relevant effect on the control and prevention of gingivitis compared to a negative control dentifrice (Colgate® Cavity Protection).

## OBJECTIVE

To investigate the long-term anti-gingivitis efficacy of a 0.454% stabilized stannous fluoride/sodium hexametaphosphate dentifrice compared to a negative control dentifrice.

## MATERIALS AND METHODS

- 0.454% stabilized stannous fluoride/sodium hexametaphosphate experimental dentifrice (Crest PRO-HEALTH) was compared to a negative control dentifrice (Colgate® Cavity Protection).
- Study subjects were 143 generally healthy adults with a minimum of 18 natural teeth, a baseline Modified Gingival Index score of 1.75-2.3, and a Turesky Plaque Index score of  $\geq 1.5$ .
- Subjects were randomly assigned to either the experimental stannous fluoride/sodium hexametaphosphate dentifrice or the negative control dentifrice to use over 6 months and were instructed to brush twice daily for 1 minute with a manual soft toothbrush.
- At baseline, oral soft tissue was examined, subjects were scored for gingivitis (Modified Gingival Index), plaque (Turesky Plaque Index), gingival bleeding (Gingival Bleeding Index) and received a dental prophylaxis.
- At Months 3 and 6 plaque, gingivitis, gingival bleeding, and safety were reassessed.

## RESULTS

- 130 subjects completed the 6-month study.
- At 6 months, scores for the experimental group compared to the negative control group were significantly reduced for gingivitis (Modified Gingival Index) (21.7%;  $p < 0.001$ ), for bleeding (Gingival Bleeding Index) (57.1%;  $p < 0.001$ ), and for plaque (Plaque Index) (6.9%;  $p = 0.01$ ).
- No adverse oral soft-hard-tissue effects or extrinsic tooth staining were observed.

### 6-Month Results

Treatment	N	Baseline Mean $\pm$ SD	Adjusted Mean <sup>a</sup> $\pm$ SE	% Reduction <sup>b</sup>
<b>Modified Gingival Index</b>				
Control	66	2.04 $\pm$ 0.10	2.01 $\pm$ 0.03	
Experimental	64	2.03 $\pm$ 0.10	1.57 $\pm$ 0.03	21.7%
<b>Gingival Bleeding index</b>				
Control	66	8.68 $\pm$ 3.40	8.88 $\pm$ 0.39	
Experimental	64	9.39 $\pm$ 3.22	3.81 $\pm$ 0.40	57.1%
<b>Plaque index</b>				
Control	66	2.91 $\pm$ 0.35	2.30 $\pm$ 0.05	
Experimental	64	2.73 $\pm$ 0.41	2.14 $\pm$ 0.05	6.9%
<sup>a</sup> Adjusted means and standard errors from analysis of covariance with baseline score as covariate. <sup>b</sup> Percent reduction = 100% x (control-experimental mean)/control mean.				

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# A 24-Hour Dental Plaque Prevention Study with a Stannous Fluoride Dentifrice Containing Hexametaphosphate

Full text available in the Research Database at [www.dentalcare.com](http://www.dentalcare.com)

**Reference:** White DJ, Kozak KM, Gibb RD, et al. *J Contemp Dent Pract.* 2006;7(3):1-11.

## CONCLUSION

Crest PRO-HEALTH produced a statistically significant reduction in dental plaque coverage 24 hours following last use.

## OBJECTIVE

To determine whether the antiplaque efficacy of Crest PRO-HEALTH, an antibacterial fluoride dentifrice containing stabilized stannous fluoride and sodium hexametaphosphate, extended to 24 hours postuse.

## MATERIALS AND METHODS

- The study design comprised 3 phases:
  - An initial 1-week treatment period with a regimen that included toothbrushing with standard sodium fluoride dentifrice (Crest® Cavity Protection Regular) in conventional BID brushing.
  - A second 1-week treatment period regimen where a modified hygiene regimen was applied using Crest Cavity Protection Regular. A nonbrushing period of 24 hours was included.
  - A third 1-week treatment period which was identical to the second treatment period except subjects used Crest PRO-HEALTH instead of Crest Cavity Protection Regular.
- A digital plaque image analysis (DPIA) technique was used to quantify plaque formation. Plaque formation was assessed in morning measurements following either standard evening hygiene (treatment period 1) or 24 hours since brushing (treatment periods 2 and 3). Postbrushing plaque measurements were also taken in each treatment regimen.
- Study subjects were adults with sufficient plaque levels in pilot pre-screening to warrant participation.



Imaging System

## RESULTS

- Sixteen subjects completed all 3 treatment regimens with no side effects or oral complaints.
- Treatment period 1: Morning plaque coverage was 13.3%.
- Treatment period 2: Plaque coverage significantly increased when prebedtime brushing was discontinued, with 24-hour growth covering 18.4% of the dentition.
- Treatment period 3: Intervention of the antimicrobial stabilized stannous fluoride/sodium hexametaphosphate dentifrice provided significant inhibition of plaque regrowth over 24 hours (15.2% coverage, a 17.4% reduction vs sodium fluoride dentifrice control).
- These results support the strong retention and lasting antimicrobial efficacy of Crest PRO-HEALTH dentifrice.

### Morning Prebrushing Treatment Comparisons

Dentifrice Treatment	Number of Subjects	Plaque % Coverage Mean (SD)	Treatment Comparison $p$ -value* vs Sodium Fluoride 24-Hour Protocol
<b>Period 1 - Standard Protocol</b>			
Sodium Fluoride	16	13.3 (4.27)	<0.0001
<b>Period 2 - 24-Hour Protocol</b>			
Sodium Fluoride	16	18.4 (5.97)	
<b>Period 3 - 24-Hour Protocol</b>			
Stabilized Stannous Fluoride/ Sodium Hexametaphosphate	16	15.2 (6.87)	0.0002

\* Two-sided  $p$ -values from a paired-difference t-test.

# A Controlled 6-Month Clinical Trial to Study the Effects of a Stannous Fluoride Dentifrice on Gingivitis

**Reference:** Mallatt M, Mankodi S, Bauroth K, et al. *J Clin Periodontol.* 2007;34(9):762-767.

## CONCLUSION

Over 6 months, twice daily use of the stabilized stannous fluoride/sodium hexmetaphosphate dentifrice provided statistically significant anti-plaque and anti-gingivitis benefits relative to the negative control dentifrice.

## OBJECTIVE

To assess anti-plaque and anti-gingivitis benefits of a stabilized stannous fluoride/sodium hexametaphosphate, dentifrice relative to a negative control sodium fluoride dentifrice.

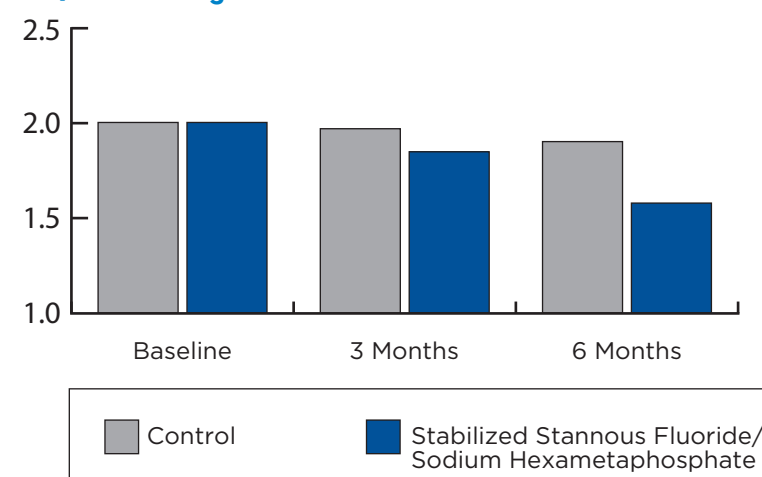
## MATERIALS AND METHODS

- Randomized, 6-month, double-blind, parallel group, clinical study.
- Treatments included:
  - A 0.454% stabilized stannous fluoride/sodium hexametaphosphate dentifrice<sup>1</sup>
  - Commercially available negative control sodium fluoride dentifrice<sup>2</sup>
- Subjects received a dental prophylaxis after baseline measurements. They were instructed to brush twice daily for 60 seconds using their assigned product.
- Efficacy measurements were obtained at baseline, and 3 and 6 months using the Modified Gingival Index, Gingival Bleeding Index, and the Turesky Modified Quigley-Hein Plaque Index.
- Oral tissue examinations were performed at all visits.

## RESULTS

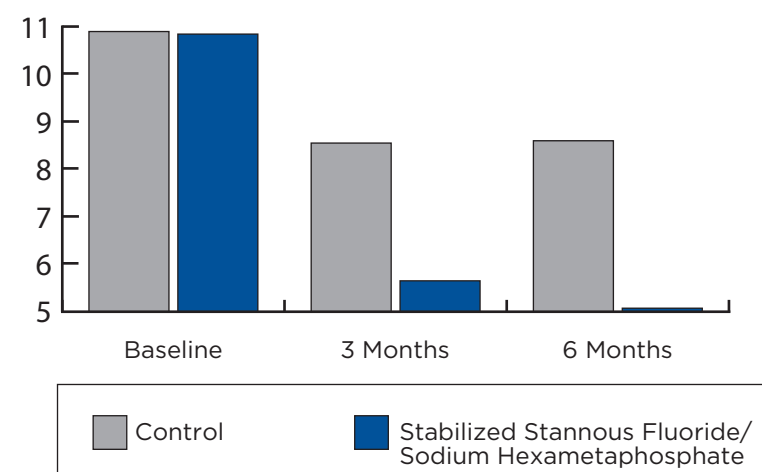
- 140 subjects were enrolled; 128 completed the study.
- The stabilized stannous fluoride dentifrice delivered a 16.9% reduction in gingivitis ( $P < 0.001$ ), a 40.8% reduction in gingival bleeding ( $p < 0.001$ ), and an 8.5% reduction in plaque ( $p = 0.001$ ) vs the negative control after 6 months.
- Both treatments were well tolerated.

### 16.9% Less Gingivitis vs Control



N=128. 3- and 6-month means are adjusted means from ANCOVA. Modified Gingival Index. Control = AquaFresh® Triple Protection®.

### 40.8% Less Bleeding vs Control



N=128. 3- and 6-month means are adjusted means from ANCOVA. Gingival Bleeding Index. Control = AquaFresh Triple Protection.

Crest PRO-HEALTH, Procter & Gamble, Cincinnati, OH, USA  
 AquaFresh Triple Protection, GlaxoSmithKline Consumer Healthcare, Pittsburgh, PA, USA

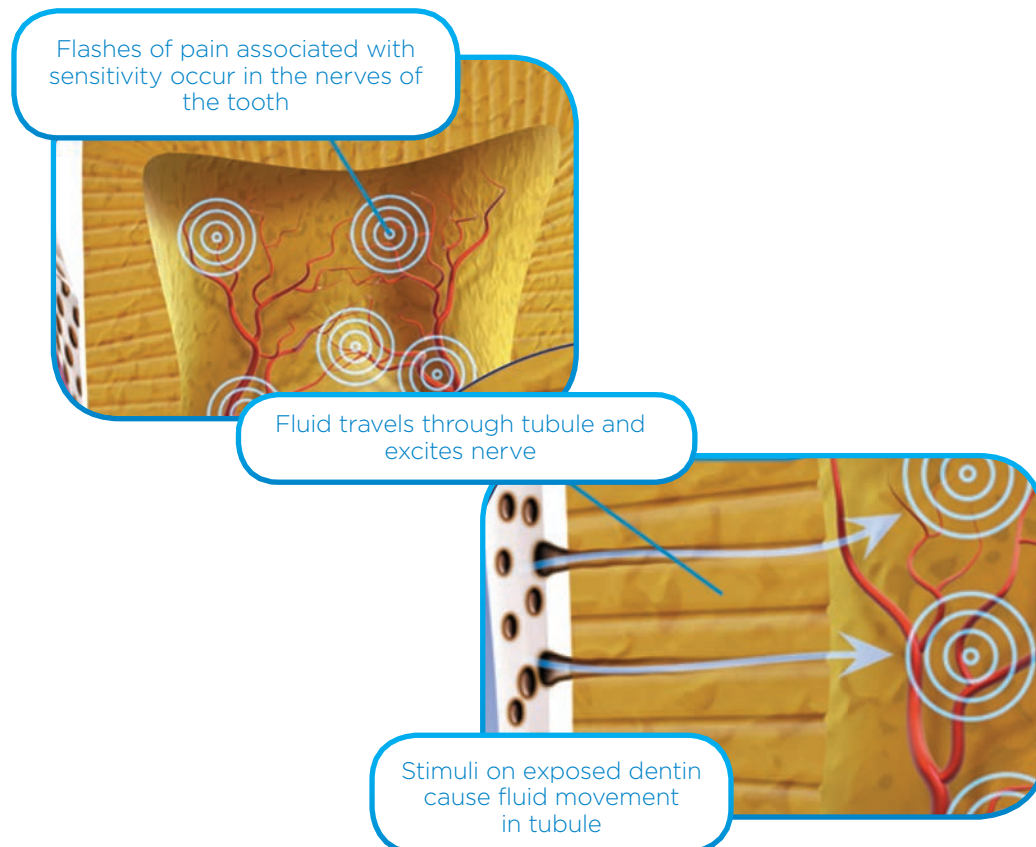
# Dentinal Hypersensitivity

**sen·si·tiv·i·ty:** short or transient sharp pain of a rapid onset that arises from exposed dentin

- Approximately one-third of the dentate adult population in North America report having experienced dentinal hypersensitivity. Sensitivity is reported to be even more prevalent among periodontal patients, with figures ranging from 72-98%.<sup>1</sup>
- Sensitivity results from exposed dentinal tubules, most often due to gingival recession and loss of cementum through erosion, abrasion, or other factors.
- Brännström's hydrodynamic theory is broadly accepted as explaining the mechanism of tooth sensitivity. Pain occurs when the dentin surface is exposed to stimuli (eg, thermal, tactile) that provoke fluid movement in the tubules.
- Fluid flow stimulates nerve terminals, triggering the sensation of pain. Routine activities like drinking cold beverages can elicit this type of sharp, transient pain.
- Desensitizing dentifrices are commonly used to treat and prevent sensitivity.

## Stannous fluoride and dentinal hypersensitivity

- Stannous fluoride occludes tubules, reducing fluid movement and nerve stimulation.
- Rigorous laboratory and clinical research supports the benefits of a stabilized stannous fluoride dentifrice in controlling dentinal hypersensitivity.





# Efficacy and Safety of a Novel Stabilized Stannous Fluoride and Sodium Hexametaphosphate Dentifrice for Dentinal Hypersensitivity

**Reference:** Schiff T, He T, Sagel L, et al. *J Contemp Dent Pract.* 2006;7(2):1-8.

## CONCLUSION

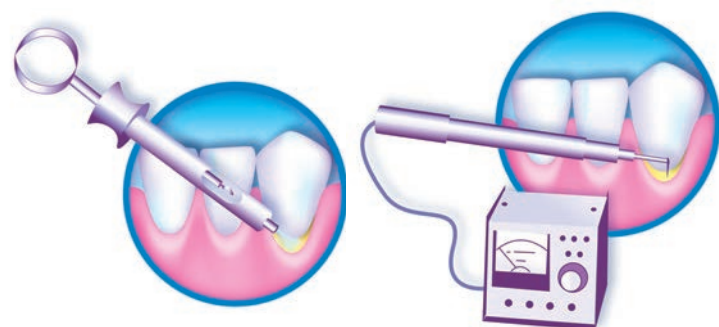
Crest PRO-HEALTH provided statistically significant reductions in dentinal hypersensitivity at 4 and 8 weeks compared to the sodium fluoride control dentifrice.

## OBJECTIVE

To compare the efficacy of Crest PRO-HEALTH vs a negative control dentifrice in the reduction of dentinal hypersensitivity over an 8-week period.

## MATERIALS AND METHODS

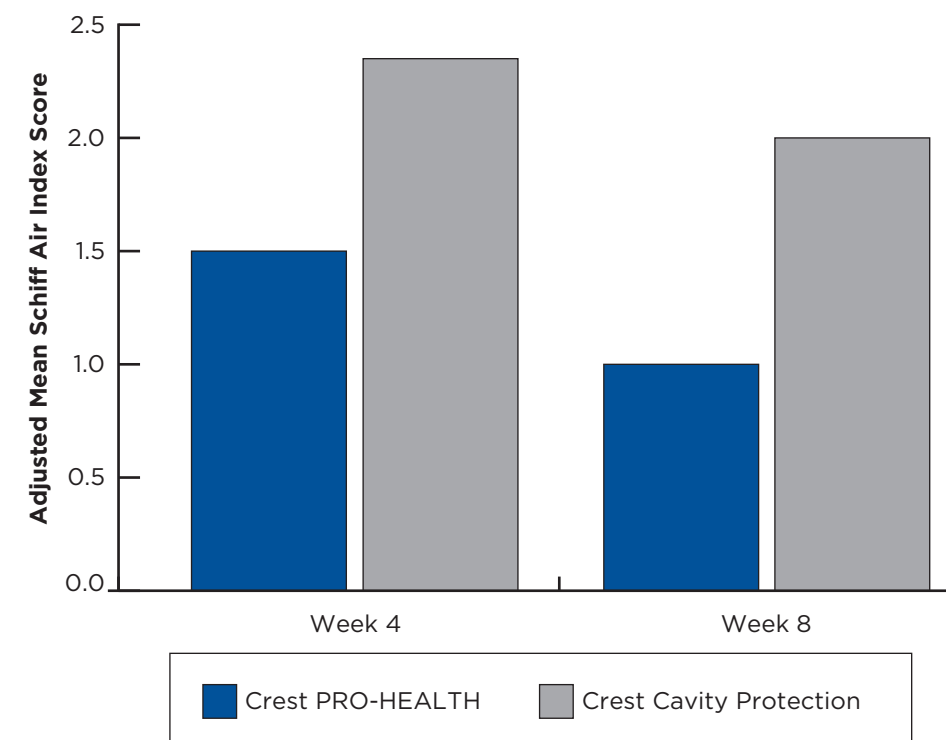
- Crest PRO-HEALTH (a novel 0.454% stabilized stannous fluoride plus sodium hexametaphosphate dentifrice) was compared to a negative control dentifrice containing 0.243% sodium fluoride (Crest Cavity Protection).
- Study subjects were 90 generally healthy adults with moderate dentinal hypersensitivity: minimum of 2 bicuspid or cuspid teeth with sensitivity criteria of Yeaple Probe Index score = 10 g and Schiff Air Sensitivity Scale score of >1.
- Tooth sensitivity was measured by tactile examination using the Yeaple probe (only teeth responding positively to 10 g and rechallenge at 10 g were evaluated) and cold air using the Schiff Air Index (teeth responding to air stimulus were evaluated).
- Oral soft tissue examinations were performed.
- Subjects were randomized to either the stabilized stannous fluoride/sodium hexametaphosphate dentifrice or the control dentifrice.
- Subjects brushed twice daily with their assigned dentifrice using a manual soft toothbrush for 8 weeks.
- Subjects were assessed again for sensitivity and safety at weeks 4 and 8.



Schiff Air Index and Yeaple Probe Images courtesy of *The Journal of Contemporary Dental Practice.*

## RESULTS

- Data were analyzed for all 90 subjects (45 in each treatment group).
- Schiff Air Index scores were statistically significantly lower for the stabilized stannous fluoride/sodium hexametaphosphate group than the sodium fluoride control group at both weeks 4 and 8 ( $p < 0.0001$ ).
- Compared to the sodium fluoride control group, the stannous fluoride/sodium hexametaphosphate group showed a 33% lower Schiff Air Index score (adjusted mean) than the sodium fluoride control group at week 4 and a 44% lower score at week 8.
- Yeaple Probe Index scores were statistically significantly higher for the stabilized stannous fluoride/sodium hexametaphosphate group than the sodium fluoride control group at both weeks 4 and 8 ( $p < 0.0001$ ).
- Compared to the sodium fluoride control group, the stabilized stannous fluoride/sodium hexametaphosphate group had a mean Yeaple Probe Index score 14 units higher (representing a mean desensitizing improvement of 114% greater) than that of the sodium fluoride control group at week 4, and 11 units higher (representing a mean desensitizing improvement of 71% greater) at week 8.
- No adverse events were reported or observed.



Lower Schiff Air Index scores indicate less tooth sensitivity.

# Desensitizing Effect of a Stabilized Stannous Fluoride/Sodium Hexametaphosphate Dentifrice

Full text available in the Research Database at [www.dentalcare.com](http://www.dentalcare.com)

**Reference:** Schiff T, Saletta L, Baker RA, et al. *Compend Contin Educ Dent.* 2005;26(suppl 1):35-40.

## CONCLUSION

Crest PRO-HEALTH showed a clinically and statistically significant decrease in hypersensitivity compared to a negative control dentifrice.

## OBJECTIVE

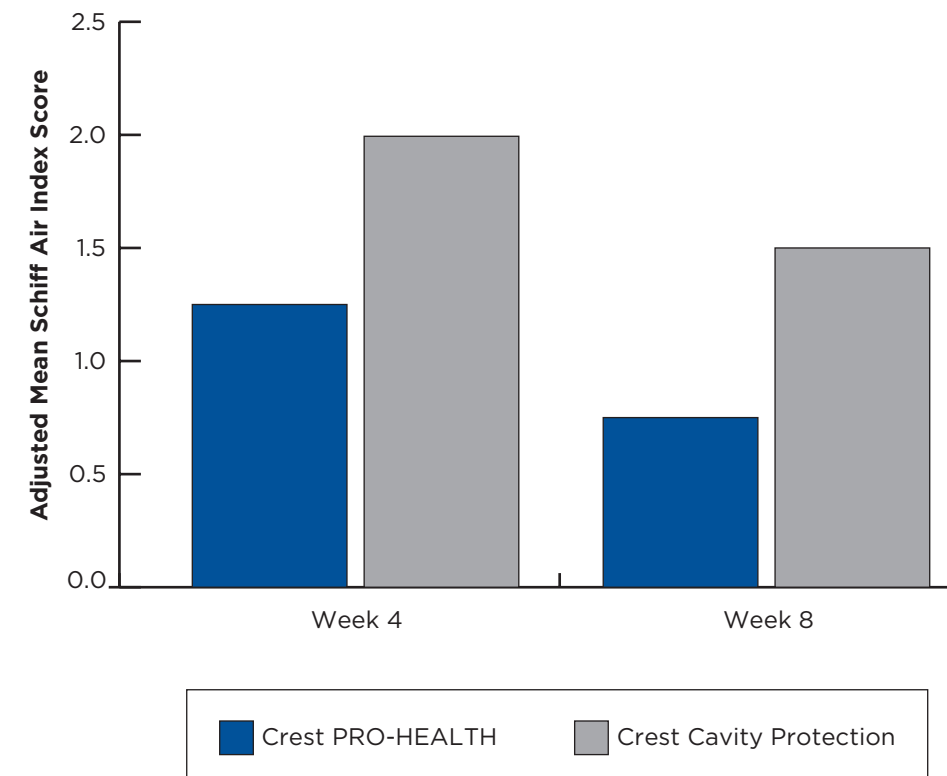
To evaluate the desensitizing properties of Crest PRO-HEALTH compared to a negative control dentifrice.

## MATERIALS AND METHODS

- Crest PRO-HEALTH (0.454% stabilized stannous fluoride/sodium hexametaphosphate dentifrice) was compared to a marketed negative control dentifrice containing 0.243% sodium fluoride (Crest Cavity Protection).
- Study subjects were adults with a minimum of 2 bicuspid/cuspid teeth with sensitivity criteria of Yeaple Probe Index = 10 g and Schiff Air Sensitivity Scale score of >1.
- Tooth sensitivity was measured by tactile examination using the Yeaple probe and thermal examination using the Schiff Air Index.
- Oral soft tissue examinations were conducted and adverse events recorded.
- Subjects were randomized to either the stabilized stannous fluoride/sodium hexametaphosphate dentifrice or the control dentifrice.
- Subjects brushed twice daily with their assigned dentifrice using a manual soft toothbrush for 8 weeks.
- Subjects were examined again for tooth sensitivity and safety at weeks 4 and 8.

## RESULTS

- Data were analyzed for 77 subjects who had complete data.
- Yeaple Probe Index scores were statistically significantly higher for the stabilized stannous fluoride/sodium hexametaphosphate group than the sodium fluoride control group at both weeks 4 and 8 ( $p < 0.0001$ ). Higher Yeaple Probe Index scores indicate less tooth sensitivity.
- Compared to the sodium fluoride control group, the stabilized stannous fluoride/sodium hexametaphosphate group had a mean Yeaple Probe Index score 1.6 times that of the sodium fluoride group at week 4 and 2 times at week 8.
- Schiff Air Index scores were statistically significantly lower for the stabilized stannous fluoride/sodium hexametaphosphate group than the sodium fluoride control group at both weeks 4 and 8 ( $p < 0.0001$ ). Lower Schiff Air Index scores indicate less tooth sensitivity.
- Compared to the sodium fluoride control group, the stabilized stannous fluoride/sodium hexametaphosphate group showed a 36% lower Schiff Air Index score (adjusted mean) than the sodium fluoride group at week 4 and a 44% lower score at week 8.
- No adverse events were reported or observed.

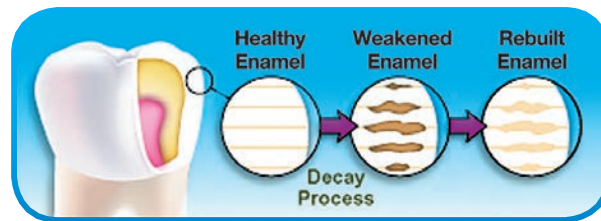


Lower Schiff Air Index scores indicate less tooth sensitivity.

# Caries Protection

dental caries: a progressive destruction of tooth

- Dental caries result when acids produced by bacteria (eg, *S. mutans*) demineralize tooth structure below the tooth surface.
- Fluoride is commonly used to protect against caries by inhibiting demineralization and enhancing remineralization of partially demineralized enamel.
- When fluoride is incorporated into the tooth structure, it results in a stronger mineral that is less soluble than the original mineral.
- Incorporating chemotherapeutic dentifrices into patients' home care routine is a convenient way to provide anticaries protection.



## Stannous fluoride and caries

- Stannous fluoride is an antibacterial fluoride that protects against caries by inhibiting demineralization and promoting remineralization.

# A Stabilized Stannous Fluoride/Sodium Hexametaphosphate Dentifrice: In Vitro Studies of Anticaries Potential

Full text available in the Research Database at [www.dentalcare.com](http://www.dentalcare.com)

**Reference:** Pfarrer AM, McQueen CM, Lawless MA, et al. *Compend Contin Educ Dent.* 2005;26(9 suppl 1):41-46.

## CONCLUSION

*In vitro* studies demonstrated the anticaries potential of the stabilized stannous fluoride/sodium hexametaphosphate dentifrice.

## OBJECTIVE

To examine the anticaries potential of the stabilized stannous fluoride/sodium hexametaphosphate dentifrice.

## MATERIALS AND METHODS

*In vitro* anticaries profile methods were:

- Fluoride uptake into demineralized enamel: single-treatment, mechanism-of-action study.
- Remineralization/inhibition of demineralization: multiple-treatment study under lesion progression pH-cycling conditions. Dentifrices compared in the respective profile methods were:
  - Stabilized stannous fluoride/sodium hexametaphosphate (1100 ppm fluoride as stannous fluoride, sodium hexametaphosphate, and silica)
  - United States Pharmacopeia (USP) Reference Standard (1100 ppm fluoride as stannous fluoride and silica)
  - Dose-response control USP Reference Standard (diluted to 250 ppm fluoride as stannous fluoride and silica)
  - Placebo negative control (<1ppm fluoride and silica)
- **Fluoride uptake**
  - Stabilized stannous fluoride/sodium hexametaphosphate (1100 ppm fluoride as stannous fluoride, sodium hexametaphosphate, and silica)
  - United States Pharmacopeia (USP) Reference Standard (1100 ppm fluoride as stannous fluoride and silica)
  - Dose-response control USP Reference Standard (diluted to 250 ppm fluoride as stannous fluoride and silica)
  - Placebo negative control (<1ppm fluoride and silica)
- **Remineralization/inhibition of demineralization**
  - Stabilized stannous fluoride/sodium hexametaphosphate
  - Sodium fluoride/sodium hexametaphosphate (1100 ppm fluoride as sodium fluoride, sodium hexametaphosphate, and silica)
  - Stannous fluoride USP Reference Standard (1100 ppm fluoride as stannous fluoride and silica)
  - Sodium fluoride USP Reference Standard (1100 ppm fluoride as sodium fluoride and silica)
  - Dose-response sodium fluoride control
  - Placebo negative control (<1ppm fluoride)

## MATERIALS AND METHODS (continued)

### • Fluoride uptake

Human enamel samples from extracted teeth—3 mm diameter cores—were decalcified for 24 hours to produce early caries lesions 20-30 µm deep. Samples were taken from the cores by the microdrill biopsy technique and measured for fluoride levels pre-dentifrice treatment. Groups of specimens were treated with dentifrice/saliva slurries. Samples were taken to determine post-treatment fluoride levels. The difference between pre and post levels determined fluoride uptake.

### • Remineralization/inhibition of demineralization

Caries-free human molar or premolar crowns were each treated with acid-resistant varnish to produce a 3 x 2 mm window on one surface as the entry point for demineralization. 24-hour test cycles—6 hours demineralization, 1 minute dentifrice treatment, 16 hours remineralization, 1 minute treatment—were repeated for 14 days. Cycles were designed to model normal demineralization and remineralization. The resulting lesions were measured for progression into the enamel, and mineral loss from each lesion calculated.

## RESULTS

### • Fluoride uptake

There was no statistically significant difference between the stannous fluoride/sodium hexametaphosphate toothpaste and the stannous fluoride USP Reference Standard toothpaste.

### • Remineralization/inhibition of demineralization

The stannous fluoride/sodium hexametaphosphate toothpaste was at least as good as the clinically proven stannous fluoride and sodium fluoride USP Reference Standard toothpastes.

Product	Mean Fluoride Uptake* µgF/cm <sup>2</sup> (SD)	Mean Mineral Loss: ΔZ <sup>†</sup> µm x Vol % min (SD)
Stannous Fluoride/SHMP	8.09 (0.25) <sup>a</sup>	36 (260) <sup>a</sup>
Sodium Fluoride/SHMP	— — —	85 (257) <sup>a</sup>
Stannous Fluoride USP Reference Standard	7.44 (0.98) <sup>a</sup>	281 (139) <sup>a</sup>
Sodium Fluoride USP Reference Standard	— — —	298 (401) <sup>a</sup>
Dose-Response Control	5.48 (0.25) <sup>b</sup>	738 (642) <sup>b</sup>
Placebo	2.76 (0.84) <sup>c</sup>	2,567 (870) <sup>c</sup>

\* Mean (n=4) values with different letter designations are significantly different (p<0.05) by the least significant difference test.  
 † Mean (n=10) values with different letter designations are significantly different (p<0.05) by the least significant difference test.  
 SD = standard deviation; SHMP=sodium hexametaphosphate; USP = United States Pharmacopeia.

# The Relative Anticaries Effectiveness of Three Fluoride-Containing Dentifrices in Puerto Rico

Full text available in the Research Database at [www.dentalcare.com](http://www.dentalcare.com)

**Reference:** Stookey GK, Mau MS, Isaacs RL, et al. *Caries Res.* 2004;38(6):542-550.

## CONCLUSION

Subjects in both the high-dose sodium fluoride dentifrice (2800 ppm F) group and the 0.454% stabilized stannous fluoride/sodium hexametaphosphate dentifrice (1,100 ppm F) group showed significantly fewer caries increments than subjects in the sodium fluoride positive control dentifrice group (1100 ppm F). The low-NaF group (550 ppm F) and the control group did not differ.

## OBJECTIVE

To compare the anticaries effectiveness of a low-dose (500 ppm F) and high-dose (2800 ppm F) sodium fluoride dentifrice (low-NaF and high NaF) and an experimental dentifrice (stabilized stannous fluoride/sodium hexametaphosphate; 1100 ppm F) with a sodium fluoride positive control dentifrice (1100 ppm F) over 2 years. (Note: This was an early prototype of the eventual marketed stannous fluoride/sodium hexametaphosphate product.)

## MATERIALS AND METHODS

- The 4 dentifrices compared were as follows: an experimental dentifrice (0.454% stabilized stannous fluoride/sodium hexametaphosphate), low-NaF, high-NaF, positive control.
- Study subjects were 955 school children (-9-12 years) from an urban area in Puerto Rico.
- Subjects were randomly assigned to the 4 treatments and were supplied with their dentifrice and toothbrushes, which were replaced every 3 months. Their 1-minute toothbrushing was supervised twice a day by teachers in the classroom; brushing was ad libitum outside school hours.
- Caries were assessed by visual-tactile examinations (with aid of fiberoptic illumination and artificial light, mouth mirror, compressed air, dental explorer) as DMFS (decayed, missing, and filled surfaces) by 2 examiners and supplemented with a radiographic examination at baseline and after 12 and 24 months.
- Both examiners examined all subjects. Examiners were tested for the sensitivity and specificity of their examinations and repeatability of their results prior to the study.

## RESULTS

- 799 subjects completed the year 1 assessment; 683 subjects were re-examined at year 2.
- Considering evaluable subjects (ie, those who attended at least 60% of the supervised brushing sessions over the 2-year study period):
  - Both examiners showed that caries increments were lower in the high-NaF group than the control group.
  - Both examiners showed statistically significantly less caries in the stabilized stannous fluoride/sodium hexametaphosphate group than the control group.
  - Neither examiner showed statistically significant differences in caries increments between low-NaF and control groups.

### Two-Year Caries Increment Results for Evaluable Subjects (Attended 60% of Supervised Visits)

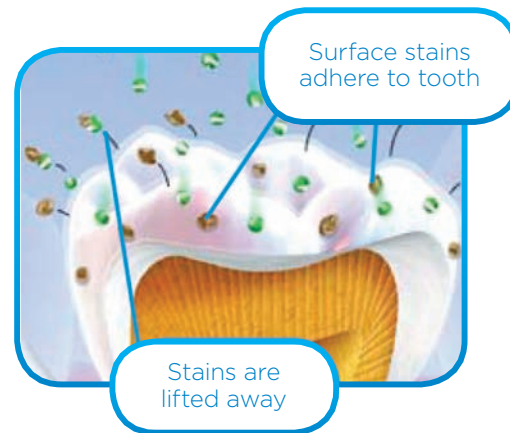
Dentifrice	N	Adjusted Mean DMFS <sup>a</sup>	SEM	% Reduction <sup>b</sup>	p-value
<b>Examiner A</b>					
500 ppm F	161	6.05	0.355	2.7	0.631
1100 ppm F	168	6.21	0.347	-	-
2800 ppm F	176	5.38	0.339	13.4	0.043
Experimental	159	5.16	0.369	17.0	0.019 <sup>c</sup>
<b>Examiner B</b>					
500 ppm F	161	4.30	0.308	12.2	0.916
1100 ppm F	168	4.89	0.300	-	-
2800 ppm F	176	3.76	0.294	23.2	0.004
Experimental	150	3.64	0.319	25.5	0.002 <sup>d</sup>

<sup>a</sup>Adjusted means from analysis of covariance.  
<sup>b</sup>Percent reduction = 100% (1100 ppm mean minus treatment mean) divided by 1100 ppm mean.  
<sup>c</sup>Two-sided p-value is 0.038.  
<sup>d</sup>Two-sided p-value is 0.005.

# Extrinsic Whitening

## Stain Removal and Stain Prevention

- Demand for whiter teeth has grown dramatically in the past decade. A multitude of oral care products on the market today claim to provide a whitening benefit.
- Extrinsic stains, those forming on the surface of the tooth, are caused by factors such as diet, poor hygiene, and smoking.
- Dentifrice formulations with whitening agents provide an efficient way to help remove and prevent extrinsic stains. Common ingredients include those that work by physical stain removal (eg, silica) and those that work by chemical stain control (eg, sodium hexametaphosphate).



## Sodium hexametaphosphate and extrinsic whitening

- Sodium hexametaphosphate provides a chemical whitening benefit due to its:
  - Strong attraction to calcium hydroxyapatite
  - Ability to disrupt the pellicle to remove extrinsic stain
  - Retention on tooth surface to prevent new extrinsic stain
- *In vitro* and *in vivo* data demonstrate the extrinsic whitening benefits of sodium hexametaphosphate in various oral care product formulations.

# Extrinsic Stain Removal Efficacy of a Stannous Fluoride Dentifrice with Sodium Hexametaphosphate

Reference: He T, Baker R, Bartizek RD, et al. *J Clin Dent.* 2007;18(1):7-11.

## CONCLUSION

In 2 studies, Crest PRO-HEALTH demonstrated significant extrinsic stain removal vs baseline and comparable stain removal to the positive control dentifrice.

## OBJECTIVE

To compare stain removal of a dentifrice containing stabilized stannous fluoride and sodium hexametaphosphate to a positive control dentifrice in 2 independent, double-blind, randomized 6-week trials.

The following dentifrices were tested in each study:

- Crest PRO-HEALTH (0.454% stabilized stannous fluoride + sodium hexametaphosphate).
- Positive control dentifrice (Colgate Total Plus Whitening with sodium fluoride).

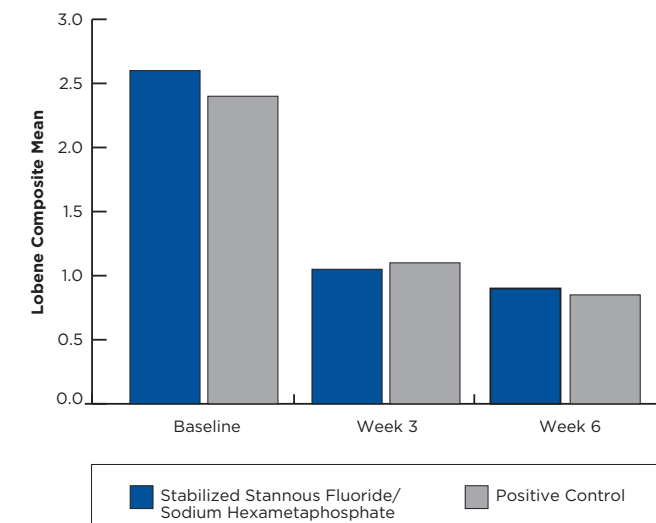
## MATERIALS AND METHODS

- Both studies followed the same protocol.
- Study subjects were healthy adults with visible extrinsic tooth stain.
- The modified Lobene Stain Index was used to measure stain on the facial surfaces of the 8 central and lateral incisors at baseline.
- Oral soft and hard tissue examinations were also conducted.
- Subjects were randomized to either the stabilized stannous fluoride + sodium hexametaphosphate toothpaste or positive control toothpaste.
- Subjects used their assigned dentifrice twice a day for 6 weeks.
- Patients were examined again for stain and safety at weeks 3 & 6.

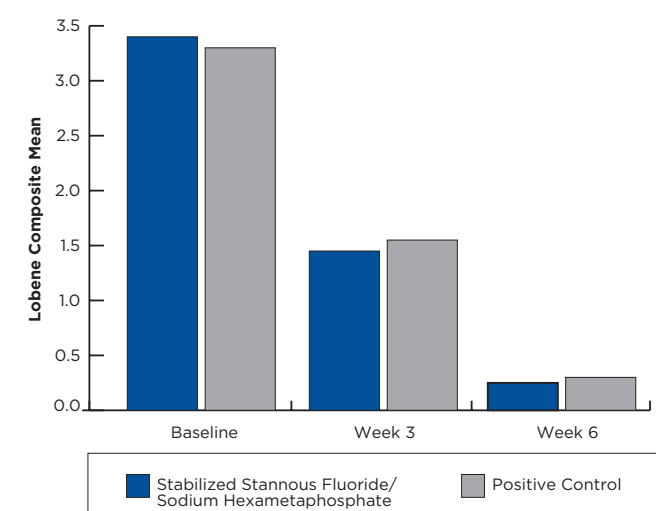
## RESULTS

- 52 subjects completed Study 1; 58 subjects completed Study 2.
- Lobene composite stain scores were not statistically significantly different between the 2 dentifrice groups at all 3 time points (baseline, week 3, and week 6) in each study.
- Relative to baseline scores, both dentifrice groups showed statistically significant reductions in Lobene composite stain scores at week 3 ( $p < 0.0001$ ) and week 6 ( $p < 0.0001$ ).

### STUDY 1. Lobene Composite Stain Score, Evaluable Subjects



### STUDY 2. Lobene Composite Stain Score, Evaluable Subjects



Weeks 3 and 6 are adjusted mean values.

# Clinical Evaluation of the Stain Removal Efficacy of a Novel Stannous Fluoride and Sodium Hexametaphosphate Dentifrice

**Reference:** Terézhalmy G, Chaves E, Bsoul S, et al. *Am J Dent.* 2007;20(1):53-58.

## CONCLUSION

In 2 independent clinical trials, a novel 0.454% stabilized stannous fluoride/sodium hexametaphosphate dentifrice (Crest PRO-HEALTH) showed comparable extrinsic stain removal compared to a positive control whitening dentifrice (Colgate Total Plus Whitening) over a 2-week period.

## OBJECTIVE

To evaluate the stain removal efficacy of Crest PRO-HEALTH relative to a positive control whitening dentifrice over a 2-week period in subjects with preexisting natural extrinsic stain.

## MATERIALS AND METHODS

- Crest PRO-HEALTH (0.454% stabilized stannous fluoride/sodium hexametaphosphate) was compared to a positive control whitening dentifrice (Colgate Total Plus Whitening), in 2 independent studies.
- Study subjects in each of the two treatment groups in each study were 15 generally healthy adults with visible stain of the facial surfaces of the 12 anterior teeth (modified Lobene score >1.0 at baseline).
- Subjects were randomly assigned to either the experimental stabilized stannous fluoride/sodium hexametaphosphate dentifrice or the positive control dentifrice to use over 2 weeks and were instructed to brush twice daily as normal.
- At baseline, oral soft tissue was examined, subjects received a modified Lobene stain examination on the 12 facial surfaces of the anterior teeth, and intraoral photographs of the surfaces of these teeth were taken. At week 2, stain and safety were reexamined.

## RESULTS

- 29 subjects (15 in the stabilized stannous fluoride/sodium hexametaphosphate group; 14 in the positive control group) completed Study 1; 30 subjects completed Study 2 (15 in each group).
- At week 2 composite (intensity x extent) Lobene stain scores were reduced by 61.8% and 61.9% for the stabilized stannous fluoride/sodium hexametaphosphate group and the control group, respectively, in Study 1; and 96.6% and 94.4% for the stabilized stannous fluoride/sodium hexametaphosphate group and the control group, respectively, in Study 2.
- No significant group differences were found in either study.
- Both dentifrices were well tolerated.

### Composite Lobene Stain Reduction Results

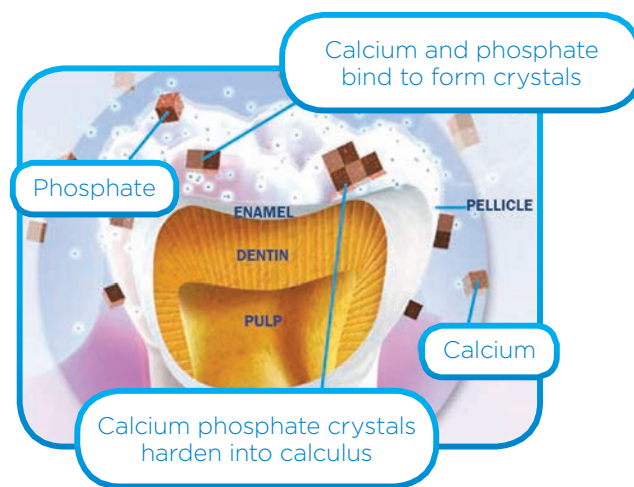
Treatment	Baseline Mean (SD)	2-Week Adjusted Change Mean (SE)	Comparison to Baseline p-values	2-Week Between Treatment p-values	Median % Stain Removal
<b>Study 1</b>					
Positive Control	1.65 (0.538)	0.94 (0.090)	<0.0001	0.929	61.9
Stabilized Stannous Fluoride/Sodium Hexametaphosphate	1.56 (0.406)	0.95 (0.087)	<0.0001		61.8
<b>Study 2</b>					
Positive Control	2.64 (1.000)	2.60 (0.044)	<0.0001	0.761	94.4
Stabilized Stannous Fluoride/Sodium Hexametaphosphate	2.95 (0.786)	2.61 (0.044)	<0.0001		96.6



# Calculus

**cal·cu·lus:** an incrustation on the teeth consisting of plaque that has become hardened by the deposition of mineral salts (such as calcium carbonate)

- Supragingival calculus results from calcium phosphate mineralization in dental plaque above the gum line. It often forms along the gingival margin, particularly on lingual surfaces.
- Due to its hardness and tenacity, calculus must be removed by dental professionals at the time of routine dental treatment.
- Dentifrice formulations with anticalculus ingredients are routinely used to inhibit its formation between dental visits, resulting in improved oral hygiene and easier dental cleanings.



## Sodium hexametaphosphate and calculus inhibition

- Sodium hexametaphosphate is an advanced mineralization inhibitor. It chemically slows the rate of calcium-phosphate mineralization within dental plaque. It has multiple binding sites to resist inactivation by salivary enzymes.
- Published research demonstrates sodium hexametaphosphate's anticalculus benefits in dentifrice formulations with stannous fluoride.

# Anticalculus Efficacy and Safety of a Stabilized Stannous Fluoride/Sodium Hexametaphosphate Dentifrice

Full text available in the Research Database at [www.dentalcare.com](http://www.dentalcare.com)

**Reference:** Schiff T, Saletta L, et al. *Compend Contin Educ Dent*. 2005;26(suppl 1):29-34.

## CONCLUSION

Over a 6-month period a stabilized stannous fluoride/sodium hexametaphosphate dentifrice showed superior anticalculus efficacy compared with a marketed tartar control triclosan/copolymer control.

## OBJECTIVE

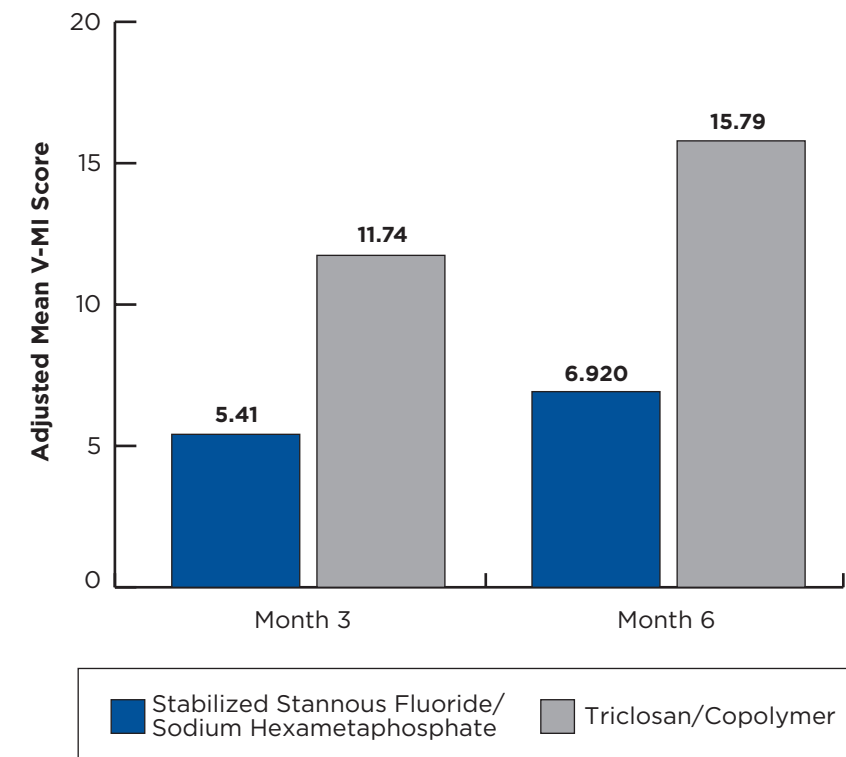
To assess the anticalculus efficacy of a 0.454% stabilized stannous fluoride/sodium hexametaphosphate dentifrice vs a positive control dentifrice.

## MATERIALS AND METHODS

- A 0.454% stabilized stannous fluoride/sodium hexametaphosphate dentifrice was compared to a marketed tartar control (0.30% triclosan/0.243% sodium fluoride/2% Gantrez copolymer) dentifrice.
- Study subjects were 81 adult participants with the ability to form at least 1.5 mm of calculus on anterior mandibular teeth (lingual surfaces) in an 8-week pretest phase following dental prophylaxis.
- The Volpe-Manhold Index was used to measure calculus on the lingual surfaces of the lower 6 anterior teeth.
- Oral soft and hard tissue examinations were also conducted.
- The Lobene Index was used to measure stain on the facial surfaces of 12 anterior teeth.
- Subjects were randomized to either the stabilized stannous fluoride/sodium hexametaphosphate dentifrice or the control dentifrice.
- Subjects used their assigned dentifrice twice a day for 6 months.
- Subjects were examined again for calculus, stain, and soft tissue safety at months 3 and 6.

## RESULTS

- Data were analyzed for 80 subjects who had complete data.
- Volpe-Manhold Index scores were statistically significantly lower for the stabilized stannous fluoride/sodium hexametaphosphate group than the triclosan/sodium fluoride copolymer group at both months 3 and 6 ( $p < 0.0001$ ).
- Compared to the triclosan/sodium fluoride copolymer group, the stabilized stannous fluoride/sodium hexametaphosphate group showed a 54% reduction (adjusted means) in calculus accumulation at month 3 and a 56% reduction at month 6.
- Neither group of subjects showed any appreciable extrinsic stain accumulation.
- No adverse events were reported.



Lower V-MI scores indicate less calculus.

# Malodor

**hal·i·to·sis:** a condition of having breath with a heavy, offensive smell

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- Breath malodor is a common social concern. Most breath odor results from gram-negative anaerobic bacteria in the oral cavities, primarily on the tongue. These bacteria break down amino acids, producing volatile sulfur compounds (VSC).
- While the tongue is considered the primary source of VSC production, other dental problems can generate these offensive gases.
- Meticulous oral hygiene, including tongue brushing, is commonly recommended to improve breath odor.



## Stannous fluoride and malodor

- Stannous fluoride is an antibacterial fluoride agent used in dentifrice formulations.
- Published research shows stannous fluoride dentifrice formulations can be effective in reducing breath odor as measured by halimeter and organoleptic graders.

# Effects of 0.454% SnF<sub>2</sub> Dentifrice on Daytime and Overnight Malodor

Reference: Farrell S, Gerlach RW, Barker ML, et al. *J Dent Res*. 2008;87 (spec issue B):Abstract 3161.

## CONCLUSION

The use of the 0.454% stabilized stannous fluoride dentifrice resulted in significant reduction in short-term and long-term daytime and overnight malodor relative to a control dentifrice.

## OBJECTIVE

A clinical study was conducted to evaluate daytime and overnight oral malodor reduction benefit of a 0.454% stabilized stannous fluoride therapeutic dentifrice with short-term and long-term use.

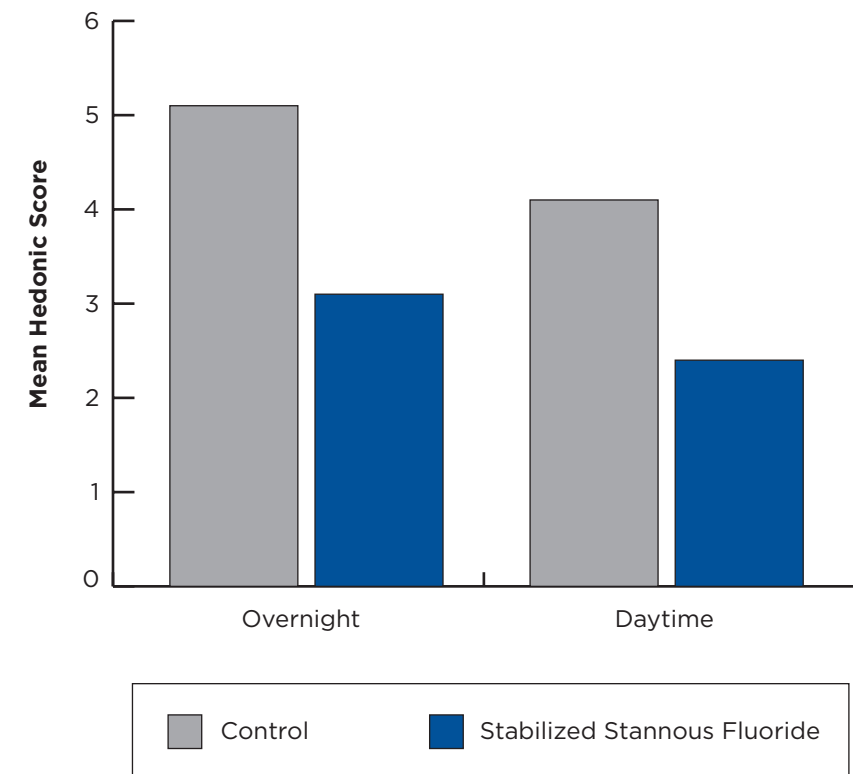
## MATERIALS AND METHODS

- The study was a randomized, double-blinded, 2-treatment, 3-period cross-over clinical trial.
- After completing an acclimation period, 45 subjects with existing oral malodor were randomly assigned to a cross-over treatment sequence consisting of Crest PRO-HEALTH® dentifrice (0.454% stabilized stannous fluoride dentifrice) and Crest Cavity Protection dentifrice (control).
- For each treatment period, subjects brushed with the assigned product twice a day for 7 days. Oral malodor was assessed on a 9-point hedonic scale at baseline, day 2-overnight, day 2-daytime (4 hours post morning brushing), day 8-overnight, day 8-daytime (4 hours post morning brushing). Treatment periods were separated by washout periods during which subjects brushed with the control dentifrice.

## RESULTS

- Subjects had a mean age of 39 years, 58% of the subjects were female and the mean baseline hedonic score was 7.4.
- Relative to the control, use of the stabilized stannous fluoride dentifrice resulted in significant ( $p < 0.002$ ) improvement of the overnight and daytime malodor both short-term at day 2 and long-term at day 8.
- The mean overnight hedonic scores were 3.2 and 5.1 at day 8 after 1 week of brushing for the stabilized stannous fluoride and the control dentifrices, respectively. The mean daytime hedonic scores were 2.4 and 4.1 at day 8 for the stabilized stannous fluoride and the control dentifrices, respectively.

Mean Hedonic Scores at Day 8



Lower score indicates less malodor.

# Oral Malodor Reduction with 3-Week Use of 0.454% SnF<sub>2</sub> Dentifrice

**Reference:** Nachnani S, La S, Lee S, et al. *J Dent Res* 2008;87(spec issue B):Abstract 2864.

## CONCLUSION

Three-week use of the 0.454% stabilized stannous fluoride dentifrice resulted in sustained significant improvement in oral malodor relative to a control dentifrice.

## OBJECTIVE

This clinical study evaluated the effects of the 3-week use of a 0.454% stabilized stannous fluoride therapeutic dentifrice on oral malodor.

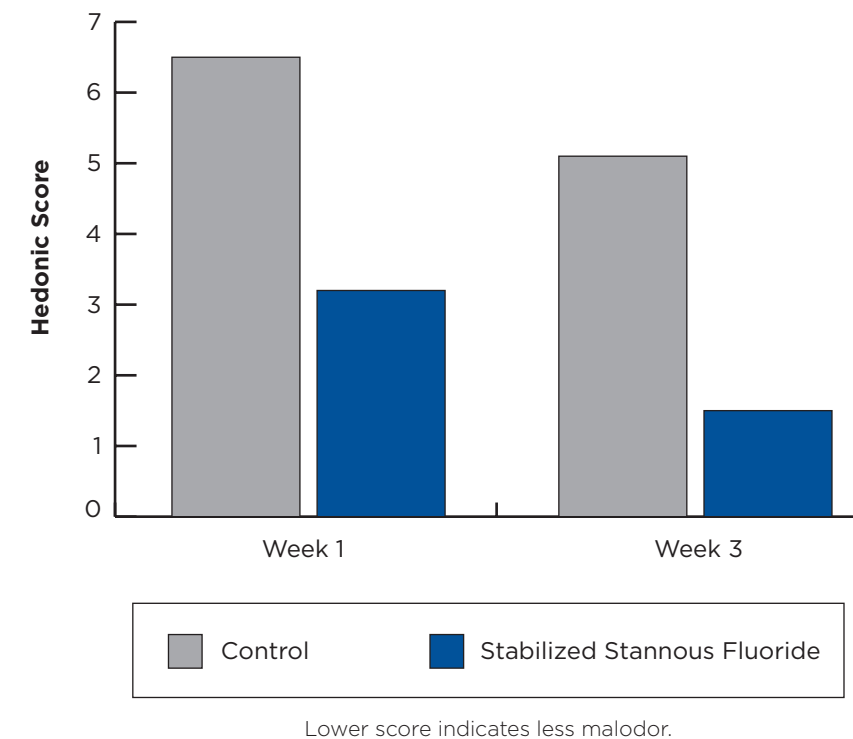
## MATERIALS AND METHODS

- The study was a randomized, double-blinded, 2-treatment, parallel design clinical trial.
- After completing an acclimation period, 71 subjects with existing oral malodor were randomized to 1 of the 2 treatments: 0.454% stabilized stannous fluoride Crest PRO-HEALTH dentifrice (stabilized stannous fluoride dentifrice) or Crest Cavity Protection dentifrice (control). Subjects brushed with the assigned product twice a day for 3 weeks.
- Oral malodor was assessed on a 9-point hedonic scale at baseline, week 1, and week 3.

## RESULTS

- The mean age of study participants was 37.8 and 59% were female. The baseline mean hedonic score was 8.19.
- At week 1, the mean hedonic scores (SE) were 3.40 (0.18) and 6.62 (0.18) for the stabilized stannous fluoride dentifrice and the control dentifrice, respectively.
- At week 3, the mean hedonic scores (SE) were 1.55 (0.18) and 5.28 (0.18) for the stabilized stannous fluoride dentifrice and the control dentifrice, respectively.
- Relative to the control, the use of the stabilized stannous fluoride dentifrice resulted in significantly ( $p < 0.0001$ ) greater reduction in oral malodor at both visits. Both treatments were well tolerated.

### Mean Hedonic Scores





## Notes

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