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continuing the care that starts in your chair

SCIENTIFIC EVIDENCE BEHIND
ADVANCED STANNOUS CONTAINING SODIUM FLUORIDE DENTIFRICE TECHNOLOGY
Introduction

Procter & Gamble has a long history of innovation. The first Oral-B® toothbrush was created in 1950 and was named Oral-B®, implying that it was more than a toothbrush; it was a “mouth” brush for complete oral care. In 1978, the first mass-produced electrical brush was launched and since then its design has been continuously improved so as to achieve outstanding performance in plaque removal, combined with high compliance by patients. Triumph™ with SmartGuide™ being our latest innovation in power toothbrush design.

Since 1955 when Crest® was launched as the first clinically proven anticaries dentifrice, P&G’s researchers have continued to develop advanced technologies to provide patients with meaningful benefits. To note that P&G’s Crest® was the first dentifrice to be granted the ADA Seal of Acceptance and that P&G was the first company to develop an effective tartar control toothpaste in 1985.

Most recently, Crest® Pro-Health™, a ground-breaking dentifrice that combines the benefits of stabilized stannous fluoride with those of the polyphosphate, has been introduced in the US. Crest® Pro-Health™ received the ADA’s Seal of Acceptance in 2006, based on its own body of research.

Crest® Pro-Health™ dentifrice is now introduced in Europe as Oral-B® Pro-Expert® and delivers on the same benefits, whilst its formulation has been adapted to European standards, with a total content of Fluorides at 1450 ppm level. The product provides a comprehensive range of benefits, including protection against cavities, plaque, gum problems, sensitivity, erosion and extrinsic stains. In addition, it inhibits calculus and freshens breath.

Numerous laboratory and clinical studies have been conducted during its decade-long development. These studies demonstrated the safety and efficacy of stabilized stannous fluoride, the polyphosphate sodium hexametaphosphate, and dentifrice formulations containing these ingredients. These studies led to the development of this unique and patented formula, now available for your patients as Oral-B® Pro-Expert®.

Publications and research presentations related to dentifrice formulations with the ingredients the polyphosphate sodium hexametaphosphate and/or stannous fluoride have been summarized in this booklet. We do believe that this compilation will assist in making evidence-based recommendations for your patients’ daily oral hygiene.

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Global Research & Development

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Ass. Director
WE Oral Care
Professional & Scientific Relations

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LEGEND

Symbols appearing in summaries indicate the research was conducted on:

- Dentifrice formulation containing stabilized stannous fluoride
- Dentifrice formulation containing the polyphosphate sodium hexametaphosphate
- Dentifrice formulation containing stabilized stannous fluoride polyphosphate
Gingival Health

**Gingivitis:** 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.

**STANNOUS FLUORIDE AND GINGIVAL HEALTH**

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


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**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**

**Conclusion**

- Over a 6-month period a stabilized 0.454% stannous fluoride/sodium hexametaphosphate dentifrice (Crest® Pro-Health™) 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 (Crest® Pro-Health™) 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 re-examined.

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

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 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 stannous fluoride/sodium hexametaphosphate dentifrice as compared to control.
- No adverse reactions or tooth staining was reported.

<table>
<thead>
<tr>
<th>Dentifrice</th>
<th>Baseline N</th>
<th>Score (Adjusted Mean ± SD)</th>
<th>Mean * ± SE</th>
<th>% Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gingival Index Scores</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Month 3 Control</td>
<td>96</td>
<td>0.50 ± 0.25</td>
<td>0.31 ± 0.01</td>
<td>-</td>
</tr>
<tr>
<td>Month 3 SnF2/SHMP</td>
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<td>0.51 ± 0.26</td>
<td>0.37 ± 0.02</td>
<td>42.6</td>
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<tr>
<td>Month 6 Control</td>
<td>91</td>
<td>0.51 ± 0.26</td>
<td>0.37 ± 0.02</td>
<td>-</td>
</tr>
<tr>
<td>Month 6 SnF2/SHMP</td>
<td>95</td>
<td>0.52 ± 0.32</td>
<td>0.27 ± 0.02</td>
<td>25.8</td>
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<tr>
<td><strong>Number of Gingival Bleeding Sites</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Month 3 Control</td>
<td>96</td>
<td>39.8 ± 20.3</td>
<td>24.6 ± 1.07</td>
<td>-</td>
</tr>
<tr>
<td>Month 3 SnF2/SHMP</td>
<td>100</td>
<td>40.1 ± 20.4</td>
<td>28.9 ± 1.49</td>
<td>-</td>
</tr>
<tr>
<td>Month 6 Control</td>
<td>91</td>
<td>40.1 ± 20.4</td>
<td>28.9 ± 1.49</td>
<td>-</td>
</tr>
<tr>
<td>Month 6 SnF2/SHMP</td>
<td>95</td>
<td>40.6 ± 20.2</td>
<td>21.0 ± 1.46</td>
<td>27.4</td>
</tr>
</tbody>
</table>

* Adjusted means and standard errors (SE) from analysis of covariance with baseline score as covariate.
\( \text{Percent reduction} = 100\% \times (\text{control}-\text{experimental mean})/\text{control mean} \). 
\( \text{Stannous fluoride/sodium hexametaphosphate} \).

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Antigingivitis Efficacy of a Stabilized Stannous Fluoride/Sodium Hexametaphosphate Dentifrice in Subjects Previously Nonresponsive to a Triclosan/Copolymer Dentifrice

FULL TEXT AVAILABLE IN THE RESEARCH DATABASE AT WWW.DENTALCARE.COM


CONCLUSION

- Over a 12-week period Crest® Pro-Health™ showed a clinically and statistically significant effect on the control of gingivitis in subjects who were previously nonresponsive or minimally responsive to 6 months of use of a triclosan/copolymer dentifrice.

OBJECTIVE

To assess the antigingivitis efficacy of Crest® Pro-Health™ in subjects previously nonresponsive or minimally responsive to a triclosan/copolymer dentifrice.

MATERIALS AND METHODS

- Dentifrice was Crest® Pro-Health™ (0.454% stabilized stannous fluoride/sodium.
- Study subjects were 41 adult participants with 6-month gingivitis levels similar to their baseline scores in a separate 6-month efficacy trial in which they used a 0.243% sodium fluoride/0.30% triclosan/2% Gantrez copolymer dentifrice.*
- Subjects were provided with Crest® Pro-Health™ to use over 12 weeks and were instructed to brush twice daily with a manual soft toothbrush. Their toothbrushing was supervised on 3 days of each week.
- At Weeks 6 and 12, oral soft tissue was examined and the Löe-Silness Gingival Index (GI) was used to measure gingivitis; baseline gingivitis scores were the 6-month scores from the previous study.

RESULTS

- Data were analyzed for 38 subjects who had complete data.
- The average 6-week and 12-week GI scores were statistically significantly better (i.e. lower) than scores at baseline (p<0.001, <0.001, respectively).
- The average 6-week and 12-week number of gingival bleeding sites were statistically significantly better (i.e. lower) than scores at baseline (p<0.001, <0.001, respectively).
- No adverse events were reported.

**Stannous Fluoride Effects on Plaque Vitality**


**CONCLUSION**
- Stannous fluoride dentifrice is effective in reducing viability of dental plaque. These results also support the modeling of antimicrobial activity with plaque vitality assessments in this panel design.

**OBJECTIVE**
Stannous fluoride is an effective decay preventive ingredient which has unique antibacterial properties. The biofilm mode of dental plaque growth in the oral cavity offers protection against chemotherapeutic control. The degree of effectiveness provided by topical antimicrobials can be assessed in part by assessments in bacterial vitality changes in treated biofilms enabled by Confocal Scanning Laser Microscopy (CSLM). The aim of this study is to assess effects of stannous fluoride dentifrice on the average viability of plaque in vivo.

**MATERIALS AND METHODS**
- Subjects carried out standard oral hygiene with Crest® Cavity Protection Regular dentifrice to establish a treatment and washout baseline and then continued hygiene using Crest® Pro-Health™ (stannous fluoride - hexametaphosphate) dentifrice.
- After one week applications, the four dentition quadrants were sampled for plaque after refraining from all oral hygiene during 24h.
- Plaque was dispersed by sonication and immediately analyzed after Baclight® fluorescent staining with specialized dispersion and CSLM analysis.*

**RESULTS**
- During use of standard ‘non-antimicrobial’ dentifrice, the percentage of non-vital plaque averaged 57 ± 7%. Use of stannous fluoride increased non-vital plaque levels to 71 ±7.1%. (sig. vs. Crest® Cavity Protection Regular p < 0.05) respectively.


**Stannous Fluoride Effects on Plaque Vitality**

**Comparative Clinical Effectiveness of Stannous Fluoride Dentifrice in Treating Gingivitis**


**CONCLUSION**
- In a general population, 3-month use of 0.454% stannous fluoride/sodium hexametaphosphate dentifrice for the treatment of gingivitis resulted in significant reductions in gingival bleeding relative to baseline and a regular dentifrice control.

**OBJECTIVE**
A randomized, double-blind, controlled clinical trial was conducted to evaluate the clinical effectiveness and tolerability of 0.454% stannous fluoride/sodium hexametaphosphate dentifrice on established gingivitis.

**MATERIALS AND METHODS**
- 80 healthy adults with mild-to-moderate gingivitis were randomized to a 0.454% stannous fluoride/sodium hexametaphosphate dentifrice (Crest® ProHealth™) or a regular anticavity control (Crest® Cavity Protection).
- Treatment was unsupervised, and outcomes were measured over a 3-month period. Efficacy was measured clinically via whole mouth gingival bleeding sites, while safety was assessed from examination and interview.

**RESULTS**
- Mean (SD) age was 44.3 (9.2) years, 69% were female, and the study population averaged 17 bleeding sites, with groups balanced on pertinent demographic, behavioral characteristics and disease.
- The 0.454% stannous fluoride group had 13.3, 14.0 and 13.3 bleeding sites at months 1, 2 and 3, respectively, compared to 15.4, 17.2 and 16.4 for the control. Relative to baseline, the stannous fluoride group exhibited significant (p<0.05) reductions in bleeding at all timepoints.

*van der Mei et al. J Dent Res. 2007;86 (Spec Iss): Abstract 1191.

**Comparative Clinical Effectiveness of Stannous Fluoride Dentifrice in Treating Gingivitis**
Comparative Clinical Effectiveness of Stannous Fluoride Dentifrice in Treating Gingivitis

RESULTS (continued)

- Between-group comparisons showed significant (p < 0.05) end-of-treatment reductions in bleeding for the stannous fluoride dentifrice.
- Both dentifrices were well-tolerated, and no subject discontinued dentifrice use early because of a treatment-related adverse event.

![Whole Mouth Gingival Bleeding Sites](chart)

- **% Reduction Between-Group**
  - Control
  - Stannous fluoride

Objective

This clinical trial evaluated the incremental effects of therapeutic mouthrinses used in combination with therapeutic dentifrices.

Materials and Methods

- Four groups in a multi-leg clinical trial evaluated the effects of post-prophylaxis daily oral hygiene with or without a therapeutic rinse.
  - The groups were 0.3% triclosan copolymer dentifrice (Colgate® Total®) and a manual brush (Colgate® Wave) with or without an essential oils rinse (Listerine®), or 0.454% stannous fluoride sodium hexametaphosphate dentifrice (Crest® Pro-Health™) and a different manual brush (Oral-B® CrossAction®) with or without a 0.07% cetylpyridinium chloride rinse (Crest® Pro-Health™ Rinse).
  - Disclosed plaque was measured on 9 surfaces using a standard index (Navy) over an 8 week treatment period, while safety was assessed from interview and clinical examination.

RESULTS

- A total of 115 subjects completed the 8 week study. Groups were balanced (p > 0.38) on pre-prophylaxis plaque, with mean scores ranging from 0.39 to 0.41.
  - End-of-treatment mean plaque scores were 0.26 in the triclosan group, 0.21 in the triclosan + rinse group, 0.21 in the stannous fluoride group, and 0.17 in the stannous fluoride + rinse group.
Meta-Analysis of Gingivitis Effects with a 0.454% Stannous Fluoride Dentifrice


CONCLUSION
• Use of a 0.454% stannous fluoride dentifrice yielded significant reductions in gingivitis throughout the oral cavity.

OBJECTIVE
This meta-analysis was conducted to evaluate the gingivitis response and map intraoral distribution seen with a 0.454% stannous fluoride/sodium hexametaphosphate dentifrice.

MATERIALS AND METHODS
• Subjects from two 6-month gingivitis prevention clinical trials were included in the pooled analysis to allow for analysis of site-based responses.
• In each study, a prophylaxis was administered and qualifying subjects were randomized to 0.454% stannous fluoride sodium hexametaphosphate (Crest® Pro-Health™) or a regular anticavity dentifrice control. Toothbrushing was unsupervised, and clinical outcomes were measured over a 6-month period using the Modified Gingivitis Index (MGI).
• Intraoral distribution of gingivitis was mapped by site and region.
• Treatment comparisons were made using analysis of covariance.
• The meta-analysis included 265 subjects, with a mean (SD) age of 37.5 (11.25) years.
• Subjects assigned to the 0.454% stannous fluoride group had adjusted mean (SE) MGI scores of 2.02 (0.010) at baseline, 1.79 (0.012) at month 3 and 1.58 (0.019) at month 6, differing significantly from control at all postbaseline timepoints (p<0.001).

RESULTS (continued)
• Both rinse groups exhibited significant (p < 0.05) reductions in plaque relative to the respective no rinse controls.
• All treatments were well-tolerated, and no subject discontinued use early because of a product-related adverse event.

6-Week Plaque Results

<table>
<thead>
<tr>
<th>Rinse</th>
<th>Adjusted Mean Plaque Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wave/Total</td>
<td>0.256</td>
</tr>
<tr>
<td>Wave/Total Listerine</td>
<td>0.206</td>
</tr>
<tr>
<td>CrossAction/ProHealth</td>
<td>0.214</td>
</tr>
<tr>
<td>CrossAction/ProHealth/Rinse</td>
<td>0.172</td>
</tr>
</tbody>
</table>

Incremental Clinical Plaque Effects with CPC and Essential Oils Rinses

RESULTS (continued)
• Both rinse groups exhibited significant (p < 0.05) reductions in plaque relative to the respective no rinse controls.
• All treatments were well-tolerated, and no subject discontinued use early because of a product-related adverse event.

Colgate® and Total® are registered trademarks of the Colgate-Palmolive Company. Listerine® is a registered trademark of the Warner-Lambert Company.
Meta-Analysis of Gingivitis Effects with a 0.454% Stannous Fluoride Dentifrice

RESULTS
- Highly significant (p<0.001) effects were also found for the 0.454% stannous fluoride group versus control at Month 6 in each of the following regions: anterior (20.2% vs. control), posterior (18.3%), maxillary (18.3%), mandibular (20.5%), facial (21.9%) and lingual (17.1%).

Antiplaque Efficacy of Stannous Fluoride Dentifrice in Power Brush Users

CONCLUSION
- Despite the significant clinical antiplaque benefits of Oral-B® Triumph™ power toothbrush, the application of clinically proven antibacterial stannous fluoride further improved hygiene effectiveness by primarily controlling plaque regrowth between hygiene interventions. Crest® Pro-Health™ paste provides additive therapeutic effectiveness in power brush users.

OBJECTIVE
Numerous studies have demonstrated that power toothbrushes and antibacterial dentifrices (stabilized stannous fluoride) can separately provide improvements in plaque control and oral health. In this study, we assessed the additive effectiveness of stannous fluoride hexametaphosphate dentifrice (Crest® Pro-Health™ - CPH) in subjects using an Oral-B® Triumph™ power toothbrush in an intervention based Digital Plaque Image Analysis methodology.

MATERIALS AND METHODS
- Sixteen subjects were assigned commercial tubes of Crest® Cavity Protection dentifrice and an Oral-B® Triumph™ toothbrush (CCP-OBT) with instructions for bid brushing morning and evening.
- Subjects remained on CCP-OBT dentifrice for two weeks. During week 2 – subjects were evaluated for diurnal plaque levels 3 separate grading days each including assessments of pre brush a.m; post brush a.m. and p.m. plaque regrowth respectively (mid afternoon) using standardized UV imaging techniques as described previously.*
- At week 3, subjects replaced CCP dentifrice with stannous fluoride dentifrice and subjects continued brushing for two additional weeks with plaque re-evaluated during week 4.

REFERENCE:
**RESULTS**

- **Pre brushing/Overnight (mean plaque % ±SD):**
  - CCP: 8.8±4.9; CPH = 6.3±4.2
  - 29.1% relative reduction p < 0.05

- **Post brushing/Immediate (mean plaque % ±SD):**
  - CCP: 2.6±1.8; CPH = 2.1±1.3
  - 17.9% relative reduction, not significant

- **P.M. regrowth/Daytime (mean plaque % ±SD):**
  - CCP: 5.6±3.0; CPH = 4.1±2.5
  - 26.8% relative reduction p < 0.05

---

**ANTIPLAQUE EFFICACY OF STANNOUS FLUORIDE DENTIFRICE IN POWER BRUSH USERS**

Average % Plaque Coverage** at each Measurement Point

<table>
<thead>
<tr>
<th>% Reduction</th>
<th>17.9%</th>
<th>26.8%*</th>
<th>29.1%*</th>
</tr>
</thead>
</table>

**Plaque Area (%)**

- Immediate (Post)
- Daytime (PM)
- Overnight (Pre)

* Regular

**Pro-Health**

* **p < 0.05** Anova

** % Plaque Coverage =**

\[
\frac{\text{Total pixels classified as plaque}}{\text{Total pixels classified as plaque and tooth}} \times 100
\]


---

**CONCLUSION**

- Over a 6-month period a stabilized 0.454% 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).

**OJECTIVE**

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

**MATERIALS AND METHODS**

- 0.454% 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 ≥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 re-assessed.

**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) (P<0.001; 21.7%), for bleeding (Gingival Bleeding Index) (P<0.001; 57.1%), and for plaque (Plaque Index) (P=0.01; 6.9%).
- No adverse oral soft-hard-tissue effects or extrinsic tooth staining were observed.
Anti-Gingivitis Efficacy of a Stabilized 0.454% Stannous Fluoride/Sodium Hexametaphosphate Dentifrice: A Controlled 6-Month Clinical Trial

RESULTS (continued)

6-month results

<table>
<thead>
<tr>
<th>Dentifrice</th>
<th>Baseline score N</th>
<th>Adjusted (mean ± SD)</th>
<th>mean ± SE</th>
<th>% Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Modified Gingival index</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>66</td>
<td>2.04 ± 0.10</td>
<td>2.01 ± 0.03</td>
<td>21.7%</td>
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<tr>
<td>Experimental</td>
<td>64</td>
<td>2.03 ± 0.10</td>
<td>1.57 ± 0.03</td>
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<tr>
<td></td>
<td></td>
<td>Gingival Bleeding Index</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>66</td>
<td>9.38 ± 3.22</td>
<td>3.81 ± 0.40</td>
<td>57.1%</td>
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<tr>
<td>Experimental</td>
<td>64</td>
<td>9.38 ± 3.22</td>
<td>3.81 ± 0.40</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>Plaque Index</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>66</td>
<td>2.91 ± 0.35</td>
<td>2.30 ± 0.05</td>
<td>6.9%</td>
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<tr>
<td>Experimental</td>
<td>64</td>
<td>2.16 ± 0.41</td>
<td>2.14 ± 0.05</td>
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</tr>
</tbody>
</table>

\[ a \] Adjusted means and standard errors from analysis of covariance with baseline score as covariate.

\[ b \] Percent reduction = 100\% x (control-experimental mean)/control mean.


CONCLUSION

- This study demonstrates that use of 0.454% stannous fluoride dentifrices over a 5-week period provided a statistically significant effect in the control of gingivitis among subjects who were regular users of a triclosan/copolymer dentifrice.

OBJECTIVE

Gingivitis has been reported to have a high prevalence worldwide. Chemotherapeutic agents such as stannous fluoride and triclosan have been shown to be effective in the control of gingivitis. However, not all subjects respond to treatment.

This study assessed anti-gingivitis efficacy of 0.454% stannous fluoride dentifrices among subjects who were regular users of a 0.3% triclosan/copolymer dentifrice (Colgate® Total®).

MATERIALS AND METHODS

- This was a 5-week, double-blind, parallel-group, randomized clinical trial. Fifty-eight subjects who self-reported as regular users (≥2 months) of a triclosan/copolymer dentifrice and exhibited sufficient gingivitis (≥10% bleeding sites) were enrolled.

- Gender, baseline gingivitis, and baseline gingival bleeding were used to assign subjects randomly into two treatment groups. Subjects were instructed to brush twice daily with an experimental dual-phase 0.454% SnF₂ dentifrice and a marketed 0.454% SnF₂ dentifrice (Crest® Pro-Health™) for 5 weeks.

- Oral soft tissue and clinical assessments using the Modified Gingival Index (MGI) and Gingival Bleeding Index were performed at baseline and after 2 and 5 weeks of treatment. Longitudinal comparisons were performed for each group using matched-pair t-tests, and between-group comparisons were performed by analysis of covariance using baseline values as covariates.

Colgate® is a registered trademark of Colgate-Palmolive.
Anti-Gingivitis Efficacy of Stannous Fluoride Dentifrices Among Triclosan Regular Users

RESULTS
• All subjects completed the study. Both treatment groups had statistically significant decreases from baseline to final exams in mean MGI scores (>29% reductions) and in percentage of bleeding sites (>21% reductions).
• There were no statistically significant differences between the two test products for both MGI and Gingival Bleeding Index.
• Only minor adverse oral soft tissue effects were reported in the study.

Long-lasting Antibacterial Action of a Novel Stannous Fluoride Dentifrice

Full text available in the Research Database at www.dentalcare.com


CONCLUSION
• Four independent assays demonstrated the sustained antibacterial activities of a new stannous fluoride dentifrice technology (Crest® Pro-Health™).

OBJECTIVE
Four assays were conducted to assess the antimicrobial activity of stannous fluoride in dentifrice technology that combines 0.454% stabilized stannous fluoride and sodium hexametaphosphate.
The assays were as follows:
• (a) In vitro Live/Dead assay to assess viability of salivary bacteria to stannous fluoride/sodium hexametaphosphate dentifrice.
• (b) In vivo Plaque Glycolysis and Regrowth Model (PGRM) to assess inhibition of bacterial metabolic and regrowth activity.
• (c) In vitro evaluation of minimum concentration of tin needed for inhibition of bacterial metabolic activity.
• (d) In vivo 12-hour posttreatment measurement of total soluble tin levels (marker for active stannous fluoride).

MATERIALS AND METHODS
• Assay (a): Susceptibility of salivary bacteria to a stannous fluoride/ sodium hexametaphosphate dentifrice (Crest® Pro-Health™) relative to a water control was assessed using an in vitro Live/Dead fluorescence-staining technique for assessing bacterial viability.
• Assay (b): The PGRM assay evaluates an antimicrobial formulation (Crest® Pro-Health™) by comparing metabolic and regrowth activity of plaque treated in situ relative to control plaque samples from non-treated areas of the oral cavity from the same subject.
• Assay (c): Minimum level of stannous fluoride for inhibition of bacterial metabolic activity was assessed using a rapid assay that involved in vitro dosing of pooled human saliva containing 0.5% sucrose with stannous fluoride of varying concentrations followed by incubation, and measurement of percent reduction in acid production.
• Assay (d): 16 subjects rinsed with stannous fluoride/sodium hexametaphosphate (Crest® Pro-Health™) slurry and 12-hour plaque samples were analyzed for total tin by graphite furnace atomic absorption spectrometry.

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**Antiplaque Efficacy of Combined Chemotherapeutics**

**RESULTS**

- **Assay (a):** 16 hours after exposure to the dentifrice, approximately 90-99% of the salivary microbes were killed.
- **Assay (b):** 15 and 45 minutes after exposure, stannous fluoride dentifrice produced statistically significant reductions in plaque acid production and plaque regrowth activity compared to sodium fluoride control dentifrice.
- **Assay (c):** Stannous fluoride was shown to be a strong inhibitor of bacterial metabolism; 99% of metabolic activity inhibition occurred at tin levels as low as 20 ppm.
- **Assay (d):** Soluble tin was present at levels above the minimum metabolic inhibition level of 20 ppm 12 hours posttreatment. Median tin levels at 12 hours posttreatment were statistically significantly greater (P<0.01) than the baseline level.

**CONCLUSION**

- Stannous fluoride dentifrice provided significant improvements in plaque control vs. standard fluoridated dentifrice. Plaque levels were further significantly decreased by addition of cetylpyridinium chloride mouthrinse. This data provides professionals with a clinical basis for the advantages of chemotherapeutic regimens for patients.

**OBJECTIVE**

To assess the cumulative effectiveness of stannous fluoride/ hexametaphosphate dentifrice (Crest® Pro Health™ - CPHD) and cetylpyridinium chloride mouthrinse (Crest® Pro Health™ Rinse - CPHR) in an intervention based Digital Plaque Image Analysis methodology.

**MATERIALS AND METHODS**

- Nine subjects were assigned commercial tubes of Crest® Cavity Protection dentifrice and an Oral-B® P35 toothbrush (CCP-OBT) with instructions for bid brushing morning and evening.
- Subjects remained on CCP dentifrice for one week during which they were evaluated for diurnal plaque levels on 3 days including assessments of pre brush a.m; post brush a.m. and p.m. plaque regrowth respectively.*
- At week 2, subjects replaced CCP dentifrice with stannous fluoride dentifrice (CPHD) and subjects were evaluated in three replicates for an additional week.
- At week 3 subjects received an additional supply of CPHR with instructions to use bid following brushing and subjects carried out plaque evaluations for an additional three weeks.

**RESULTS**

**Mean±SD for Pre brushing:**
- CCP 13.8±6.7 vs. CPHD 11.3±4.7
  18% relative reduction, p < 0.02
- CPHD + CPHR (week 3 use) 5.0±1.6
  56% additional reduction, p < 0.003

**Mean±SD for Post brushing:**
- CCP 6.9±3.4 vs. CPHD 6.5±3.2
  6% relative reduction, NS
- CPHD + CPHR (week 3 use) 4.2±1.1
  36% additional reduction, p < 0.04
**RESULTS** (continued)

Mean ± SD P.M. regrowth:

- CCP 14.2±7.8 vs. CPHD 10.3±5.2
  27% relative reduction, p < 0.004
- CPHD + CPHR (week 3 use) 4.3±0.9
  58% additional reduction, p < 0.02

---

**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 stannous fluoride and sodium hexametaphosphate, extended to 24 hours post use.

**MATERIALS AND METHODS**

- The study design comprised 3 phases:
  1. An initial 1-week treatment period with a regimen that included toothbrushing with standard sodium fluoride dentifrice (Cavity Protection Regular) in conventional b.i.d. brushing;
  2. A second 1-week treatment period regimen where a modified hygiene regimen was applied using Cavity Protection Regular. A non-brushing period of 24 hours was included.
  3. A third 1-week treatment period which was identical to the second treatment period except subjects used Crest® Pro-Health™ instead of Cavity Protection Regular.

- A digital plaque image analysis (DPIA) technique was used to quantify in situ 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). Post-brushing plaque measurements were also taken in each treatment regimen.

- Study subjects were adults with sufficient plaque levels in pilot pre-screening to warrant participation.

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* White et al. J Clin Dent. 2006;17:22-26
A 24-Hour Dental Plaque Prevention Study with a Stannous Fluoride Dentifrice Containing Hexametaphosphate

RESULTS
• Sixteen subjects completed all three 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 pre-bedtime brushing was discontinued, with 24-hour growth covering 18.4% of the dentition.
• Treatment period 3:
  Intervention of the antimicrobial stannous fluoride/ 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 pre-brushing treatment comparisons

<table>
<thead>
<tr>
<th>Dentifrice Treatment</th>
<th>Number of Subjects</th>
<th>Plaque % Coverage Mean (SD)</th>
<th>Treatment Comparison p-value* vs. Sodium Fluoride 24 Hour Protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Period 1 - Standard Protocol</td>
<td>Sodium Fluoride</td>
<td>16</td>
<td>13.3 (4.27)</td>
</tr>
<tr>
<td>Period 2 - 24 Hour Protocol</td>
<td>Sodium Fluoride</td>
<td>16</td>
<td>18.4 (5.97)</td>
</tr>
<tr>
<td>Period 3 - 24 Hour Protocol</td>
<td>Stannous Fluoride/Hexametaphosphate</td>
<td>16</td>
<td>15.2 (6.87)</td>
</tr>
</tbody>
</table>

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

Two Year RCT of Two Dentifrices for Prevention of Periodontitis

CONCLUSION
• The study results establish the comparable therapeutic benefits for the stabilized 0.454% stannous fluoride/sodium hexametaphosphate (SHMP) dentifrice in the prevention of periodontal attachment loss when compared to the triclosan/copolymer control.

OBJECTIVE
To compare the efficacy of a 0.454% stannous fluoride/SHMP dentifrice relative to a positive control triclosan/copolymer dentifrice for the prevention of periodontal attachment loss.

MATERIALS AND METHODS
• This was a two-year, randomized, double-blind, parallel-group study.
• A 0.454% stannous fluoride/SHMP dentifrice was tested relative to a commercially available positive control dentifrice (0.30% triclosan/2.0% Gantrez copolymer) in medication induced xerostomic adults who were previously identified in a one-year run-in phase.
• Among 685 40-80 yr old subjects who received one-year examination, 440 demonstrated active progression of periodontitis with at least one tooth having a site with equal to or greater than 3mm attachment loss.
• Following baseline measurements subjects were stratified based on gender and baseline attachment level into two groups. Subjects were instructed to brush twice daily for 60 seconds using their assigned product.
• Clinical examinations including probing pocket depth, attachment level, and bleeding upon probing were performed at baseline, 1 and 2 years post baseline.
Two Year RCT of Two Dentifrices for Prevention of Periodontitis

RESULTS

- Of the 440 subjects with active progression of periodontitis, 392 of them completed the study. 334 subjects were determined evaluable across all visits.
- During the run-in phase, the average periodontal attachment loss was 1.33 mm and the periodontal pocket depth increased 0.95 mm.
- Over the course of the 2 year active treatment phase, attachment gain observed was 0.77 mm for the treatment group and 0.79 mm for the positive control group (not significant).
- The pocket depth decreased 0.57 mm for the test group and 0.53 mm for the positive control group.
- The change of the attachment level and pocket depth versus baseline was statistically significant (p<0.01) for each individual test group.

A Comparison of Intraoral Antimicrobial Effects of Stabilized Stannous Fluoride Dentifrice, Baking Soda/Peroxide Dentifrice, Conventional NaF Dentifrice and Essential Oil Mouthrinse


CONCLUSION

- These regimens show the value of developing new intraoral test protocols and provide the rationale for the efficacy of a stabilized stannous fluoride dentifrice in reducing gingivitis.

OBJECTIVE

To compare the antimicrobial activity of four commercial oral products in three test regimens.

MATERIALS AND METHODS

- The four following products were tested: 1) stabilized stannous fluoride dentifrice (SnF₂), 2) baking soda/peroxide/sodium fluoride (NaF) dentifrice, 3) essential oils mouthrinse, and 4) conventional NaF dentifrice.
- Products were tested for their ability to suppress:
  - regrowth and apical extension of plaque (30-hour plaque regrowth model)
  - facultative anaerobic (FA) bacteria from buccal gingival surfaces (Gingival Surface Microbial Index - GSMI model)
  - the glycolytic metabolic and regrowth activity of in-vivo-treated dental plaque (Plaque Glycolysis and Regrowth - PGRM model)
- 30-hour plaque regrowth model: 43 subjects used one of six treatments, 3x during each of 6, 30-hour cycles over a period of 7 weeks. Treatments included the 3 test products, the NaF comparator, purified water and an experimental dentifrice. Plaque assessments (Turesky et al Modification of the Quigley-Hein Plaque Index) were made at baseline and on day 2 of each of the 6 cycles.
- GSMI model: in two separate randomized crossover studies, 15 to 20 subjects brushed with their assigned dentifrice for 60 seconds. Facultative anaerobic bacteria counts were determined at baseline and 15, 60 and 120 minutes post-treatment.
- PGRM model: 8 subjects (two x 4) participated in a cross-over evaluation of the 3 test products. Self-sampled baseline plaque samples were taken. Subjects brushed with their assigned dentifrices for 30 seconds, and further samples were taken at 15 and 45 minutes post-treatment.
A Comparison of Intraoral Antimicrobial Effects of Stabilized Stannous Fluoride Dentifrice, Baking Soda/Peroxide Dentifrice, Conventional NaF Dentifrice and Essential Oil Mouthrinse

RESULTS

• 30-hour plaque regrowth model: the SnF₂ dentifrice was superior to all other treatments; the essential oils rinse was superior to water and the baking soda/peroxide/NaF dentifrice, and there was no difference between the NaF dentifrice, the baking soda/peroxide/NaF dentifrice, and water.
• GSMI model: the SnF₂ dentifrice produced statistically significant reductions in gingival FA bacteria compared to both the NaF and baking soda/peroxide dentifrices (P<0.001).
• PGRM model: the SnF₂ dentifrice produced significant inhibition of plaque regrowth compared to both the NaF and baking soda/peroxide/NaF dentifrices.

CONCLUSION

• The use of stabilized 0.454% stannous fluoride dentifrices showed a statistically significant reduction in gingivitis relative to a control fluoride-containing dentifrice over a 6-month period.

OBJECTIVE

To assess the clinical effects on gingivitis, gingival bleeding, plaque and stain of 0.454% stannous fluoride (SnF₂) products stabilized in conventional dentifrice formulations.

MATERIALS AND METHODS

• The following dentifrice treatment groups were used: 1) 0.243% sodium fluoride (control); 2) 0.454% SnF₂ stabilized with 1.5% SnCl₂ and 2.08% sodium gluconate; 3) 0.454% SnF₂ stabilized with 1.5% SnCl₂ and 4.16% sodium gluconate; 4) experimental dentifrice.
• Study subjects were 620 healthy adults with at least 5 gingival bleeding sites and 16 natural teeth, including 4 molars.
• At baseline, oral soft tissue health was examined and subjects were assessed for gingivitis and gingival bleeding (Löe and Silness Gingival Index), plaque accumulation (Silness and Löe PII index), and extrinsic dental stain.
• Following an oral prophylaxis, subjects were randomly assigned to one of the four dentifrice groups and were instructed to use their assigned dentifrice as per their normal oral hygiene habits over 6 months.
• At Month 3 and 6, gingivitis, gingival bleeding, plaque and stain, and oral tissue were re-assessed.

The Clinical Effect of Dentifrices Containing Stabilized Stannous Fluoride on Plaque Formation and Gingivitis – A Six-Month Study with Ad Libitum Brushing

The Clinical Effect of Dentifrices Containing Stabilized Stannous Fluoride on Plaque Formation and Gingivitis - A Six-Month Study with Ad Libitum Brushing

RESULTS

- 549 subjects completed the 6-month study.
- Gingivitis: stannous fluoride dentifrices stabilized with 2.08% or 4.16% sodium gluconate statistically significantly (α=0.05) reduced gingivitis compared to the control group by 14.6% and 16.7%, respectively, at Month 3, and 18.8% and 18.0%, respectively, at Month 6.
- Gingival bleeding: stannous fluoride dentifrices stabilized with 2.08% or 4.16% sodium gluconate showed reductions in gingival bleeding compared to the control group of 27.9% and 20.2%, respectively, at Month 3, and 30.5% and 23.1%, respectively, at Month 6.
- Plaque: stannous fluoride dentifrices stabilized with 2.08% or 4.16% sodium gluconate showed reductions in plaque compared to the control group of 6.5% and 7.7%, respectively, at Month 3, and 2.6% and 1.6%, respectively, at Month 6.
- Stain: At both Months 3 and 6 extrinsic tooth stain was significantly greater (α=0.05) in both of the stabilized stannous fluoride groups than the control group. (This early stabilized SnF₂ dentifrice did not contain a whitening agent. The latest stabilized SnF₂ dentifrice from Crest®, Crest® Pro-Health™, does contain a whitening agent.)
- No significant differences in adverse oral soft tissue effects were observed between the test and control groups.

Covariance-adjusted 3- and 6-month results

<table>
<thead>
<tr>
<th>Exam Time</th>
<th>Treatment</th>
<th>N</th>
<th>Mean score</th>
<th>Percent reduction vs. control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Gingivitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Month 3</td>
<td>Control</td>
<td>135</td>
<td>0.4809</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>2.08% gluconate</td>
<td>141</td>
<td>0.4108</td>
<td>14.6</td>
</tr>
<tr>
<td></td>
<td>4.16% gluconate</td>
<td>136</td>
<td>0.4005</td>
<td>16.7</td>
</tr>
<tr>
<td>Month 6</td>
<td>Control</td>
<td>136</td>
<td>0.4523</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>2.08% gluconate</td>
<td>140</td>
<td>0.362/2</td>
<td>18.1</td>
</tr>
<tr>
<td></td>
<td>4.16% gluconate</td>
<td>140</td>
<td>0.3707</td>
<td>18.0</td>
</tr>
<tr>
<td></td>
<td>Gingival Bleeding</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Month 3</td>
<td>Control</td>
<td>135</td>
<td>6.59</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>2.08% gluconate</td>
<td>141</td>
<td>4.75</td>
<td>21.9</td>
</tr>
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<td></td>
<td>4.16% gluconate</td>
<td>136</td>
<td>5.26</td>
<td>20.2</td>
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<tr>
<td>Month 6</td>
<td>Control</td>
<td>136</td>
<td>6.04</td>
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<td>2.08% gluconate</td>
<td>140</td>
<td>4.21</td>
<td>30.5</td>
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<tr>
<td></td>
<td>4.16% gluconate</td>
<td>140</td>
<td>4.66</td>
<td>23.1</td>
</tr>
</tbody>
</table>

The Comparative Efficacy of Stabilized Stannous Fluoride Dentifrice, Peroxide/Baking Soda Dentifrice, and Essential Oil Mouthrinse for the Prevention of Gingivitis

CONCLUSION

- Stabilized stannous fluoride dentifrice showed superior efficacy against gingivitis and gingival bleeding compared to a combination of sodium fluoride dentifrice and essential oils mouthrinse.

OBJECTIVE

To compare the effectiveness of a stabilized stannous fluoride (SnF₂) dentifrice, a baking soda and peroxide dentifrice and an essential oils mouthrinse compared to a conventional sodium fluoride (NaF) dentifrice for the control of plaque, gingivitis, and gingival bleeding over 6 months.

MATERIALS AND METHODS

- The following products were tested: 1) stabilized 0.454% SnF₂, 2) baking soda/peroxide/0.243% NaF dentifrice (BSP), 3) a commercially available dentifrice combined with an essential oils mouthrinse (NaF + PHEN), 4) a conventional 0.243% NaF dentifrice.
- 918 subjects with 20 natural teeth, including 4 molars, and at least 5 gingival bleeding sites participated (Löe and Silness Gingival Index [GI] 0-3).
- Subjects received an oral prophylaxis at baseline, and were then randomly assigned one of the 4 treatment groups and instructed to brush with their assigned product at least twice a day.
- Assessments were made at 3 and 6 months for gingivitis (Löe and Silness GI grades 0-3), gingival bleeding (GI grades 2 or 3), supragingival plaque (Silness and Löe plaque index 0-3), extrinsic tooth stain (0-4 point scoring, where 0 = no stain and 4 = 75% coverage) and oral soft tissue health.

REFERENCE

The Comparative Efficacy of Stabilized Stannous Fluoride Dentifrice, Peroxide/Baking Soda Dentifrice, and Essential Oil Mouthrinse for the Prevention of Gingivitis

RESULTS

- **835 subjects** were included in the final analyses.
- **Gingivitis**: at both 3 and 6 months the SnF₂ dentifrice was significantly (Fisher Least Significant Difference [LSD] p≤0.0167) more effective than the NaF (9.2% and 17.5%, respectively) and BSP dentifrices (6.5% and 13.8%, respectively), and also at 6 months the SnF₂ dentifrice was significantly (LSD p≤0.0167) more effective than NaF+PHEN (10.8%).
- **Gingival bleeding**: at both 3 and 6 months the SnF₂ dentifrice was significantly (LSD p≤0.0167) more effective than all other treatments: compared to NaF, 18% and 27.5%, respectively; BSP, 15.3% and 26.1%, respectively; NaF + PHEN, 11.2% and 23%, respectively.
- **Plaque**: at both 3 and 6 months, there were no statistically significant differences amongst the treatment groups.
- **Stain**: at 6 months both the SnF₂ and the NaF + PHEN groups had significantly more staining than the NaF and BSP groups. (This early stabilized SnF₂ dentifrice from Crest®, Crest® Pro-Health™, contains a whitening agent.)

Covariance-adjusted 3- and 6-month results

<table>
<thead>
<tr>
<th>Exam Time</th>
<th>Dentifrice</th>
<th>N</th>
<th>Mean score</th>
<th>% benefit of SnF₂ over treatment</th>
<th>Mean score</th>
<th>% benefit of SnF₂ over treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 months</td>
<td>NaF</td>
<td>143</td>
<td>0.79</td>
<td>19.2</td>
<td>22.02</td>
<td>18.0</td>
</tr>
<tr>
<td></td>
<td>BSP</td>
<td>148</td>
<td>0.76</td>
<td>16.5</td>
<td>21.31</td>
<td>15.3</td>
</tr>
<tr>
<td></td>
<td>NaF + PHEN</td>
<td>284</td>
<td>0.73</td>
<td>11.6</td>
<td>20.35</td>
<td>1.12</td>
</tr>
<tr>
<td>6 months</td>
<td>SnF₂</td>
<td>272</td>
<td>0.72</td>
<td>12.7</td>
<td>18.05</td>
<td>18.05</td>
</tr>
<tr>
<td></td>
<td>NaF</td>
<td>140</td>
<td>0.78</td>
<td>17.5</td>
<td>22.25</td>
<td>27.5</td>
</tr>
<tr>
<td></td>
<td>BSP</td>
<td>14/</td>
<td>0.74</td>
<td>16.8</td>
<td>21.82</td>
<td>26.1</td>
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<tr>
<td></td>
<td>NaF + PHEN</td>
<td>281</td>
<td>0.72</td>
<td>10.8</td>
<td>20.19</td>
<td>26.1</td>
</tr>
<tr>
<td></td>
<td>SnF₂</td>
<td>26/</td>
<td>0.64</td>
<td>16.1</td>
<td>16.13</td>
<td>16.1</td>
</tr>
</tbody>
</table>

CONCLUSION

- These findings indicate that stannous fluoride demonstrates direct anti-inflammatory activity and prevention of tissue destruction in addition to its well established anti-bacterial activity against gingivitis.

OBJECTIVE

Stannous fluoride (SnF₂) is a broad spectrum anti-bacterial agent which has been clinically proven in dentifrice to help control supragingival plaque and gingivitis. The purpose of this study was to evaluate the potential anti-inflammatory action of SnF₂, independent of the anti-bacterial action.

MATERIALS AND METHODS

- The inhibition of several host and bacterial pro-inflammatory enzymes by SnF₂ was tested in vitro.
- The inhibition of purified human mammalian matrix metalloproteinases (MMPs) and IL-1 beta converting enzyme (ICE) were measured by the cleavage of the fluorogenic substrates Mca-Pro-Leu-Gly-Leu-Dpa-Ala-Arg- NH₂ and N-acetyl-Trp-Glu-His-Asp-AMC, respectively.
- The activity of Porphyromonas gingivalis R-gingipain was tested on the fluorogenic substrate Z-Phe-Arg-AMC•HCl.

**Sn retained post use**

<table>
<thead>
<tr>
<th>% Control Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 h immediate</td>
</tr>
<tr>
<td>(33 ppm)</td>
</tr>
<tr>
<td>(900 ppm)</td>
</tr>
</tbody>
</table>

Activities of MMP1, MMP2, MMP3, MMP9, MMP13, gingipain and ICE.
Anti-inflammatory Action of Stannous Fluoride

RESULTS

- SnF₂ demonstrated inhibition of several mammalian matrix metalloproteinase subtypes and other pro-inflammatory enzymes, with a rank order of potency of gingipain > MMP13 > MMP3 > MMP2 > ICE > MMP9 > MMP1.

CONCLUSION

- Results of a 9-week study show strong in vivo antimicrobial actions of stabilized stannous fluoride. No development of resistance of plaque to stannous fluoride was seen with 9 weeks of toothbrushing with a stabilized stannous fluoride dentifrice.

OBJECTIVE

To evaluate (i) the effects of continuous exposure to toothbrushing with a stabilized stannous fluoride (SnF₂) dentifrice on intrinsic plaque virulence as measured by acidogenicity and regrowth activity of in vivo treated plaque and (ii) the potential development of plaque resistance to (SnF₂) antimicrobial activity over time.

MATERIALS AND METHODS

- Dentifrices used were: 1) active 0.454% stabilized SnF₂; 2) control placebo dentifrice; 3) sodium fluoride tartar control dentifrice.
- 70 individuals in good general oral health were pre-screened to evaluate their potential to develop sufficient levels of dental plaque with minimum levels of plaque acidogenicity under Plaque Glycolysis and Regrowth Method (PGRM) assay conditions.
- 30 subjects satisfied baseline screening and were divided into 3 study groups of 10 each:
  - Group I: Effects of 3x per day toothbrushing with SnF₂ dentifrice on plaque virulence.
  - Group II: Effects of combined 3x per day toothbrushing with SnF₂ dentifrice (2x) and tartar control dentifrice (1x) on plaque virulence.
  - Group III: Effects of 1x per day toothbrushing with SnF₂ dentifrice on plaque virulence.
- Subjects brushed their teeth for 1 minute with stabilized stannous fluoride or placebo dentifrice once, twice or three times a day for 9 weeks and plaque was sampled on the morning of Weeks 3, 6 and 9. Subjects were crossed over after 9 weeks and repeated the study with the alternative product.
- PGRM was used to evaluate dental plaque samples for standardized glycolysis and regrowth activity in Weeks 3, 6, 7, 8 and 9.
- At Week 18, following the second 9-week treatment period, subjects participated in a single-treatment PGRM assessment using stabilized SnF₂ dentifrice.

Effects of Nine Weeks’ Use of a New Stabilized Stannous Fluoride Dentifrice on Intrinsic Plaque Virulence Expressed as Acidogenicity and Regrowth: A Modified PGRM Study

RESULTS

- **Group I:** 9 subjects completed both crossover portions of the test. Subjects using active SnF₂ dentifrice showed 3x/day decreased plaque glycolysis and regrowth throughout the 9 weeks of toothbrushing.

- **Group II:** 8 subjects completed both crossover portions of the test. Subjects using active SnF₂ dentifrice 2x/day coupled with tartar control dentifrice 1x/day showed reductions in intrinsic plaque acid production and regrowth (relative to placebo) throughout the 9 weeks of toothbrushing.

- **Group III:** 10 subjects completed both crossover portions of the test. Subjects using active SnF₂ dentifrice 1x/day showed reductions in plaque acidogenicity and regrowth (relative to placebo) over the 9 weeks of toothbrushing.

### Change in Intrinsic Plaque Glycolysis Activity and Plaque Regrowth Activity in Subjects Brushing for 9 weeks

<table>
<thead>
<tr>
<th>Treatment</th>
<th>N</th>
<th>Plaque Glycolysis Activity</th>
<th>Plaque Regrowth Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>least square mean pH change initial-final (SEM)*</td>
<td>p-value placebo vs. active Treatment/ Carryover</td>
</tr>
<tr>
<td>Placebo 1x/day**</td>
<td>10</td>
<td>1.81 (0.03)</td>
<td>8.44 (0.51)</td>
</tr>
<tr>
<td>SnF₂ 3x/day**</td>
<td>10</td>
<td>1.66 (0.05)</td>
<td>7.97 (0.55)</td>
</tr>
<tr>
<td>Placebo 2x/day**</td>
<td>8</td>
<td>1.77 (0.03)</td>
<td>7.29 (0.49)</td>
</tr>
<tr>
<td>SnF₂ 2x/day**</td>
<td>8</td>
<td>1.39 (0.06)</td>
<td>6.41 (0.52)</td>
</tr>
<tr>
<td>Placebo 3x/day**</td>
<td>9</td>
<td>1.91 (0.04)</td>
<td>9.61 (0.56)</td>
</tr>
<tr>
<td>SnF₂ 3x/day**</td>
<td>9</td>
<td>1.69 (0.03)</td>
<td>9.04 (0.56)</td>
</tr>
</tbody>
</table>

* Includes 2x/day brushing with placebo dentifrice.
** Includes 3x/day brushing with tartar control dentifrice.

### Summary

- **Group I:** Subjects using active SnF₂ dentifrice showed 3x/day decreased plaque glycolysis and regrowth throughout the 9 weeks of toothbrushing.
- **Group II:** Subjects using active SnF₂ dentifrice 2x/day coupled with tartar control dentifrice 1x/day showed reductions in intrinsic plaque acid production and regrowth (relative to placebo) throughout the 9 weeks of toothbrushing.
- **Group III:** Subjects using active SnF₂ dentifrice 1x/day showed reductions in plaque acidogenicity and regrowth (relative to placebo) over the 9 weeks of toothbrushing.

Comparative Antimicrobial Effects of SnF₂ and Baking Soda/Peroxide NaF Dentifrices

**Reference:** Lanzalaco AC, Bacca LA, Becus MS, Leusch MS. Research presented at the ADA/FDI World Dental Congress, 1996.

**CONCLUSION**

- Results show that at all post-brushing time points, gum surfaces treated with the stannous fluoride paste and stannous fluoride gel had significantly less (p<0.01) total facultative anaerobic bacteria than surfaces treated with either the baking soda/peroxide or standard sodium fluoride dentifrice.

**OBJECTIVE**

To compare the antibacterial activity of three commercially available dentifrices containing either stannous fluoride (SnF₂) or baking soda/peroxide to a commercially available sodium fluoride (NaF) dentifrice.

**MATERIALS AND METHODS**

- The study utilized 20 subjects in a 4x4 Latin Square crossover that was balanced for first order carryover effects. In this design, each subject served as his/her own control.

- Subjects brushed with each of the four dentifrices with at least a 48-hour washout period between the use of test products:
  1. Advanced Formula Crest®, 0.243% NaF
  2. Crest® Gum Care Paste, 0.454% SnF₂
  3. Crest® Gum Care Gel, 0.454% SnF₂
  4. Mentadent® Baking Soda/Peroxide, 0.243% NaF

Subjects refrained from all oral hygiene for approximately 12 hours before baseline samples were taken.

- Following a baseline sampling, subjects brushed with the test dentifrice as they normally would for 1 minute, followed by a brief water rinse. Additional bacterial samples were taken from the gingival tissue with a sterile cotton swab at 15, 60, and 120 minutes post-brushing. Total facultative anaerobic bacteria counts were evaluated.

- An ANOVA for a 4 period, 4 treatment crossover study was performed on the data generated. Reductions in total mean log bacteria counts from baseline at 15, 60 and 120 minutes post-treatment are shown in chart.
Inhibition of Plaque Activity After Using a Chlorhexidine Rinse and SnF2 Dentifrice

CONCLUSION

- Results indicate the sequential use of a stannous fluoride dentifrice and chlorhexidine rinse provides increased inhibition of plaque glycolytic activity relative to use of a chlorhexidine rinse alone.

OBJECTIVE

To evaluate the effects on plaque glycolysis and regrowth of a combined usage regimen of a stannous fluoride (SnF2) dentifrice and chlorhexidine mouthrinse.

MATERIALS AND METHODS

- The standard plaque glycolysis and growth model* was used to assess glycolytic and regrowth activity of plaque following use of a chlorhexidine rinse (Peridex® Oral Rinse, 0.12% chlorhexidine) either alone or preceded by brushing with a SnF2 dentifrice (Crest® Gum Care, 0.454% SnF2).
- On the morning of the test, subjects presented to the site having refrained from oral hygiene the previous 12 hours. Baseline plaque samples were collected from the upper dentition.
- Subjects were then divided into two groups with one group (n=4) rinsing with chlorhexidine (Chx) for 10 seconds, while the second group (n=7) first brushed their upper dentition for 30 seconds with the SnF2 dentifrice then rinsed for 10 seconds with chlorhexidine. Plaque samples were collected from the lower left and lower right quadrants, 15 and 45 minutes post-product use.
- Normalized plaque biomass, incubated in 0.03% TSB buffers, was then assayed for plaque glycolytic and regrowth activities as described by White.*

RESULTS

- Results are presented as area under the curve (AUC) over time.
  - or glycolysis
    - SnF2 + Chx: 65.67a
    - Chx alone: 45.67b (a>b: ANOVA, p=0.007)
  - or regrowth
    - SnF2 + Chx: 233.23a
    - Chx alone: 181.72a (NSD, ANOVA, p=0.437


Comparative Antimicrobial Effects of SnF2 and Baking Soda/Peroxide NaF Dentifrices

- Reductions for the SnF2 paste and SnF2 gel were statistically significantly different from reductions for the BS/P dentifrice and the NaF control (p<0.01).
- No differences were seen between the SnF2 treatments or between the BS/P dentifrice and NaF control.

Mean log Reduction in Total Facultative Anaerobic Bacteria Counts on the Gum Surfaces

**Stannous Fluoride Reduces EPS Production by Oral Biofilm Bacteria**

CONCLUSION

- Stannous fluoride dentifrice is effective in reducing bacterial EPS production in dental plaque.

OBJECTIVE

- Extracellular Polymeric Substance (EPS), excreted by biofilm bacteria, constitutes the glue that holds a biofilm together and moreover protects biofilm organisms against antimicrobial attacks. Interference in EPS production would therefore be a valuable tool in preventing dental plaque formation.

- The aim of this study is to assess effects of a stannous fluoride dentifrice on EPS production in vivo.

MATERIALS AND METHODS

- Eight volunteers carried out standard oral hygiene with Crest® Regular dentifrice to establish a treatment and washout baseline (2 weeks) and then continued hygiene using Crest® Pro-Health™ (stannous fluoride – sodium hexametaphosphate) dentifrice.

- After one week application, the entire dentition was sampled for plaque after refraining from all oral hygiene during 24h. Plaque was dispersed by sonication and immediately analyzed after Baclight live/dead staining and EPS was quantified using a phenol-sulfuric acid reaction according to Dubois.

RESULTS

- During use of a standard dentifrice, the amount of EPS produced per mouth (430±248_g/mouth) as well as per biofilm bacterium (156±85x10^-9_g/bacterium) was significantly (p<0.01, Student t-test) higher than during the use of a stannous fluoride containing dentifrice (163±56_g/mouth and 67±30x10^-9_g/bacterium, respectively).

**Comparative 12-Hour Antibacterial Effectiveness of a 0.454% Stannous Fluoride Dentifrice**

CONCLUSION

- In a randomized controlled trial, 7-day use of 0.454% stannous fluoride resulted in a significant (p<0.05) reduction in 12-hour post-brushing total facultative anaerobic bacteria in dental plaque compared to a regular dentifrice control.

OBJECTIVE

A randomized controlled clinical trial was conducted to evaluate 12-hour, overnight antibacterial effectiveness of a stannous fluoride sodium hexametaphosphate dentifrice.

MATERIALS AND METHODS

- The clinical study was a randomized, double-blind, 2-treatment, 3-period, crossover with 40 adults.

- All subjects received a marketed anticavity dentifrice for a 7-day acclimation and for use during the 7-day washout between treatment periods.

- Subjects were randomly assigned to a three period treatment sequence with 0.454% stabilized stannous fluoride sodium hexametaphosphate dentifrice (Crest® Pro-Health™) or a regular dentifrice control without stannous fluoride (Crest® Cavity Protection). Brushing was unsupervised, at-home for 1 minute twice daily for 7 days.

- Supragingival plaque samples were collected 12-hour post-brushing, diluted, plated and incubated using standard methods, and then total facultative anaerobic bacteria were enumerated (CFU/mL). Treatments were compared (log10 CFU/mL) using analysis of variance for crossover studies with a 5% significance level.

RESULTS

- The study population ranged from 20-76 years of age, with females comprising 68%.

- At baseline, groups were balanced for 12-hour post-brushing total facultative anaerobic bacteria (p=0.855).

- After 7 days, the 0.454% stannous fluoride dentifrice group had significantly (p=0.015) lower mean 12-hour post-brushing total facultative anaerobic bacteria compared to the regular dentifrice control.
Clinical Study Evaluating 0.454% Stannous Fluoride Dentifrice on Established Gingivitis


CONCLUSION
• In a general population, 3-month use of 0.454% stannous fluoride sodium hexametaphosphate dentifrice for the treatment of gingivitis resulted in 23-24% reductions in gingivitis and bleeding relative to a regular dentifrice control.

OBJECTIVE
• A double-blind, randomized controlled 3-month clinical trial was conducted to evaluate the effects of a 0.454% stannous fluoride sodium hexametaphosphate dentifrice on established gingivitis.

MATERIALS AND METHODS
• Adults with mild gingivitis were randomized to a therapeutic dentifrice with 0.454% stannous fluoride sodium hexametaphosphate dentifrice (Crest® ProHealth™) or a negative dentifrice control (Crest® Cavity Protection).
• No prophylaxis was administered in this treatment study, subjects were simply dispensed assigned test products, and instructed on at-home unsupervised brushing.
• Efficacy was measured at baseline and Month 3 via a whole mouth clinical gingivitis index (Loe-Silness), while safety was assessed from examination and interview.

RESULTS
• 70 subjects (35 per group) were evaluated at Month 3. That population averaged 31 years of age, mean (SD) gingivitis scores were 0.27 (0.13), and groups were balanced with respect to demographics and gingivitis scores.
• At Month 3, the 0.454% stannous fluoride group had experienced a 54% reduction in gingivitis, and a 56% reduction in bleeding, differing significantly (p<0.001) from baseline on each endpoint.
• Between-group comparisons showed a 23% reduction in gingivitis and a 24% reduction in bleeding, with the 0.454% stannous fluoride dentifrice differing significantly from the negative control.
• Adverse events were limited to mild oral irritation (both groups), with no early “for cause” dropouts.
Gingivitis Treatment with 0.454% Stannous Fluoride Dentifrice: Clinical Meta-Analysis


CONCLUSION
- A 3-month treatment model in a general population showed significant 20% reductions in gingivitis and 23% reductions in bleeding with a 0.454% stannous fluoride dentifrice versus control.

OBJECTIVE
- This meta-analysis was conducted to evaluate effects of 0.454% stannous fluoride dentifrice on established gingivitis, and to assess the utility of a gingivitis treatment clinical model.

MATERIALS AND METHODS
- Subjects from two identical 3-month gingivitis treatment clinical trials were included in the pooled analysis.
- In each study, general subjects with mild gingivitis were randomized to Crest® ProHealth™ (0.454% stannous fluoride sodium hexametaphosphate) dentifrice or a regular anticavity dentifrice control (Crest® Cavity Protection).
- Brushing was unsupervised, and clinical outcomes were measured monthly using the whole mouth Gingivitis Index (GI). GI and bleeding data were analyzed separately using a general linear mixed model that included age and baseline, with treatment as a fixed effect and study as a random effect.

RESULTS
- The meta-analysis included 167 subjects, with mean (SD) age of 37.6 (11.6) years, and mean GI score of 0.26 (0.15).
- Adjusted mean (SE) GI scores in the 0.454% stannous fluoride group were 0.19 (0.014) at Month 1, 0.19 (0.028) at Month 2, and 0.16 (0.050) at Month 3. Adjusted mean (SE) GI scores in the regular dentifrice control were 0.22 (0.014) at Month 1, 0.22 (0.028) at Month 2, and 0.20 (0.050) at Month 3. Treatments differed significantly (p<0.05) beginning at Month 1.
- Both dentifrices were well tolerated.
Randomized Trial Evaluating 0.454% Stannous Fluoride Dentifrice with Restorative Dentistry


CONCLUSION
- This pilot study supports use of 0.454% stannous fluoride dentifrice to reduce gingivitis and bleeding during crown and bridge treatment.

OBJECTIVE
- A pilot clinical trial was conducted to evaluate the clinical response of 0.454% stannous fluoride dentifrice used during routine crown and bridge treatment.

MATERIALS AND METHODS
- After informed consent, healthy adults undergoing crown and bridge treatment at the dental school were randomized to a therapeutic dentifrice or normal oral hygiene, which served as the untreated control.
- Test products were distributed blind to treatment at the preparation visit, with subjects receiving either 0.454% stannous fluoride sodium hexametaphosphate (Crest® Pro-Health™) or control. Subjects were instructed to brush normally (unsupervised) at least twice daily.
- Gingivitis and bleeding were measured at the preparation, impression and cementation visits using a standard clinical index (Loe-Silness). Treatments were compared using non-parametric ANCOVA.

RESULTS
- 33 subjects with common gingivitis evaluators at all time points were included the analysis. Groups were balanced (p>0.33) on gingivitis and bleeding.
- At both the impression and cementation visits, the stannous fluoride dentifrice group had lower observed gingivitis and bleeding scores than control.
- In the crown preparation region, median gingivitis scores were 0.00 in the stannous fluoride group compared to 0.26 in the control, resulting into significantly lower gingivitis (p<0.01) and bleeding (p<0.05) with the therapeutic dentifrice at the impression visit.
- Outcomes were directionally similar at cementation, with median gingivitis scores of 0.11 in the stannous fluoride group and 0.33 in control.
- Treatment was generally well-tolerated.

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


CONCLUSION
- Over 6 months, twice daily use of the SnF₂/SHMP 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 SnF₂/sodium hexametaphosphate (SHMP) dentifrice relative to a negative control sodium fluoride dentifrice.

MATERIALS AND METHODS
- Randomized, 6-month, double-blind, parallel group, clinical study.
- Treatments included:
  - A stabilized 0.454% SnF₂/SHMP dentifrice
  - Commercially available negative control sodium fluoride dentifrice
- 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, 5 and 6 months post treatment using the Modified Gingival Index, Gingival Bleeding Index and the Turesky Modified Quigley-Hein Plaque Index.
- Oral tissue examinations were performed at all visits.
A Controlled 6-Month Clinical Trial to Study the Effects of a Stannous Fluoride Dentifrice on Gingivitis

RESULTS

- 140 subjects were enrolled. 128 completed the study.
- The SnF₂ dentifrice delivered a 16.9% reduction in gingivitis (p<0.001), a 40.8% reduction (p<0.001) in gingival bleeding, and an 8.5% reduction in plaque (p=0.001) versus the negative control after 6 months.
- Both treatments were well tolerated.

16.9% less gingivitis vs. control

40.8% less gingivitis vs. control

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

A Comparison of Stabilized Stannous Fluoride Dentifrice and a Triclosan/Copolymer Dentifrice for Efficacy in the Reduction of Gingivitis and Gingival Bleeding: Six-Month Clinical Results

CONCLUSION

- The stabilized stannous fluoride dentifrice showed superior efficacy for the control of gingivitis and gingival bleeding compared to the triclosan/copolymer dentifrice.

To compare two antimicrobial dentifrices for their effectiveness against plaque, gingivitis and gingival bleeding.

- The two products were: A stabilized stannous fluoride (SnF₂) dentifrice with 0.454% SnF₂ in a silica abrasive base and a triclosan/copolymer dentifrice with 0.30% triclosan, 2% co-polymer, and 0.243% sodium fluoride (NaF) in a silica abrasive base. The control was a conventional dentifrice with 0.243% NaF in a silica abrasive base.

- Subjects were 570 healthy adults with 5 gingival bleeding sites and 16 natural teeth, including 4 molars.

- All subjects had a prophylaxis at baseline and then brushed with 0.243% NaF twice a day for 1 minute for a 3 month pre-test period. Baseline levels were then taken for gingivitis, gingival bleeding, supragingival plaque, extrinsic tooth stain and oral soft tissue condition. This was followed by a further prophylaxis.

- Subjects were then assigned to their treatment groups and instructed as before.

- Assessments were made at 3 and 6 months for gingivitis, gingival bleeding, supragingival plaque, extrinsic tooth stain and oral soft tissue condition.

1. Crest® Pro-Health™, Procter & Gamble, Cincinnati, OH, USA
2. AquaFresh Triple Protection, GlaxoSmithKline Consumer Healthcare, Pittsburgh, PA, USA
A Comparison of Stabilized Stannous Fluoride Dentifrice and a Triclosan/Copolymer Dentifrice for Efficacy in the Reduction of Gingivitis and Gingival Bleeding: Six-Month Clinical Results

RESULTS

- Gingivitis: The SnF₂ dentifrice was significantly more effective than the NaF dentifrice at both 3 months (18.4%) and 6 months (20.3%), and the triclosan/copolymer dentifrice at both 3 and 6 months (P<0.05).
- Gingival bleeding: the SnF₂ dentifrice was significantly more effective than the NaF dentifrice at both 3 months (31.3%) and 6 months (33.4%) months and the triclosan/copolymer dentifrice at both 3 and 6 months (P<0.05).
- Plaque: compared to the NaF dentifrice, the SnF₂ dentifrice was more effective at both 3 months (5.9%) and 6 months (3.1%). The difference was statistically significant at 3 months only (P<0.05).
- Stain: There was significantly more stain in the SnF₂ dentifrice treatment group than in the other two groups (P<0.05). (This early stabilized SnF₂ dentifrice did not contain a whitening agent. The latest stabilized SnF₂ dentifrice from Crest®, Crest® Pro-Health™, contains a whitening agent.)
- Oral tissue examinations showed no differences between groups at either timepoint.

Covariance-adjusted 3- and 6-month results

<table>
<thead>
<tr>
<th>Exam Time</th>
<th>Dentifrice</th>
<th>N</th>
<th>Mean gingivitis score</th>
<th>Percent reduction versus NaF control*</th>
<th>Mean gingival bleeding score</th>
<th>Percent reduction versus NaF control*</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 months</td>
<td>NaF</td>
<td>187</td>
<td>0.53</td>
<td>-10.52</td>
<td>10.69</td>
<td>-1.6</td>
</tr>
<tr>
<td></td>
<td>Triclosan/Copolymer</td>
<td>175</td>
<td>0.52</td>
<td>1.9</td>
<td>10.69</td>
<td>-1.6</td>
</tr>
<tr>
<td></td>
<td>Stannous Fluoride</td>
<td>184</td>
<td>0.45</td>
<td>18.4</td>
<td>-2.5</td>
<td>31.3</td>
</tr>
<tr>
<td>6 months</td>
<td>NaF</td>
<td>174</td>
<td>0.52</td>
<td>8.57</td>
<td>10.69</td>
<td>-1.6</td>
</tr>
<tr>
<td></td>
<td>Triclosan/Copolymer</td>
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<td>0.51</td>
<td>1.4</td>
<td>10.69</td>
<td>-1.6</td>
</tr>
<tr>
<td></td>
<td>Stannous Fluoride</td>
<td>154</td>
<td>0.41</td>
<td>20.5</td>
<td>5.71</td>
<td>33.4</td>
</tr>
</tbody>
</table>

* Percent reduction = 100% x (1-treatment mean/NaF control mean)

The Clinical Effect of a Stabilized Stannous Fluoride Dentifrice on Plaque Formation, Gingivitis and Gingival Bleeding: A Six-Month Study

CONCLUSION

- Twice-daily use for six months of a dentifrice containing 0.454% stabilized stannous fluoride significantly reduced gingivitis and gingival bleeding compared to a 0.243% sodium fluoride control dentifrice.

OBJECTIVE

To evaluate previous reports that a dentifrice containing 0.454% stabilized stannous fluoride (SnF₂) improves gingival health by relative reduction of gingivitis and gingival bleeding.

MATERIALS AND METHODS

- The following dentifrice treatment groups were used:
  1) 0.454% stabilized SnF₂;
  2) 0.243% sodium fluoride (control);
  3) one of three experimental dentifrices.
- Study subjects were healthy adults with at least 5 gingival bleeding sites and 16 natural teeth, including 4 molars.
- The study comprised two periods:
  3-month pre-test period: Following initial examination, subjects received an oral prophylaxis and were provided with a 0.243% sodium fluoride dentifrice (identity blinded) for use during the pre-test period. They were instructed to brush normally twice a day with their own toothbrushes for at least 1 minute. At the end of the pre-test period the following baseline assessments were made: gingivitis (Löe and Silness Gingival Index; GI grades 0-3), gingival bleeding (GI grades 2 and 3), supragingival plaque (Turesky modification of Quigley-Hein), extrinsic tooth stain (Meckel index; intensity score 0-3 and area to nearest 5%) and oral soft tissue health.
  6-month treatment period: Following baseline assessments, subjects received a further oral prophylaxis and were randomly assigned to one of five treatment groups, with the same brushing instructions as before. At 3 and 6 months subjects were again assessed for gingivitis, gingival bleeding, supragingival plaque, extrinsic tooth stain and oral soft tissue health.

**RESULTS**

- 328 subjects using the stabilized stannous fluoride (SnF$_2$) or sodium fluoride dentifrice (control) completed the 6-month study; results presented excluded the three experimental dentifrice groups.

- **Gingivitis**: the SnF$_2$ group statistically significantly ($\alpha=0.05$) reduced gingivitis compared to the control group by 18.4% and 20.5% at Months 3 and 6, respectively.

- **Gingival bleeding**: the SnF$_2$ group statistically significantly ($\alpha=0.05$) reduced gingival bleeding compared to the control group by 31.3% and 33.4% at Months 3 and 6, respectively.

- **Plaque**: the SnF$_2$ group significantly ($\alpha=0.05$) reduced plaque compared to the control group at Month 3.

- **Stain**: At both Months 3 and 6 extrinsic tooth stain was significantly greater ($\alpha=0.05$) in the SnF$_2$ group than the control group. (This early stabilized SnF$_2$ dentifrice did not contain a whitening agent. The latest stabilized SnF$_2$ dentifrice from Crest®, Crest® Pro-Health™, contains a whitening agent).

- No clinically significant oral soft-tissue-health effects were associated with use of the test dentifrice.

**Covariance-adjusted Month 3 and Month 6 Results**

<table>
<thead>
<tr>
<th>Exam Time</th>
<th>Treatment</th>
<th>N</th>
<th>Mean score</th>
<th>% Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gingivitis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Month 3</td>
<td>Control</td>
<td>187</td>
<td>0.3228</td>
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<tr>
<td></td>
<td>0.454% SnF$_2$</td>
<td>184</td>
<td>0.3345*</td>
<td>18.4</td>
</tr>
<tr>
<td>Month 6</td>
<td>Control</td>
<td>174</td>
<td>0.3168</td>
<td></td>
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<td></td>
<td>0.454% SnF$_2$</td>
<td>174</td>
<td>0.4107*</td>
<td>20.5</td>
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<tr>
<td><strong>Gingival Bleeding</strong></td>
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<td></td>
<td></td>
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<tr>
<td>Month 3</td>
<td>Control</td>
<td>187</td>
<td>10.52</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.454% SnF$_2$</td>
<td>184</td>
<td>9.24*</td>
<td>13.4</td>
</tr>
<tr>
<td>Month 6</td>
<td>Control</td>
<td>174</td>
<td>8.57</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.454% SnF$_2$</td>
<td>174</td>
<td>7.71*</td>
<td>33.4</td>
</tr>
</tbody>
</table>

* Significantly different from control at alpha = 0.05, 2-tailed test

**CONCLUSION**

- The overall reduction of gingivitis is a good way to improve oral health. The benefits of widespread use of topical antimicrobials in OTC antigingivitis products should not be underestimated.

**OBJECTIVE**

To review the role of gingivitis in the progression to periodontitis and to consider the management of gingival health.

**KEY MESSAGES**

- There is a high prevalence of gingivitis in Western populations suggesting mechanical hygiene practices are inadequate.

- Toothpastes and mouthrinses incorporating antimicrobial agents have been developed that reduce plaque and gingivitis; a stabilized stannous fluoride dentifrice is one such agent.

- The role of gingivitis in the progression of periodontitis is unclear. While the presence of gingivitis does not automatically predict future tooth loss it does indicate microbial virulence.

- The etiological events that arise in the progression from gingival health to gingivitis are associated with changes in the bacterial flora of the adjacent dental plaque.

- Differences between adults and children in the composition and levels of bacterial plaque associated with gingivitis largely mirror the epidemiological and histopathological data for these age groups, and show a significant difference in susceptibility to gingivitis between pre school children and adults.

- These data provide insight into the relationship between plaque and gingivitis, and the potential role of gingivitis in the development of periodontitis.
Gingivitis: A Prelude to Periodontitis?

KEY MESSAGES (continued)

- Although there is no direct evidence that childhood gingivitis leads to increased risk of periodontal disease in adulthood, an environment may be created in the gingival sulcus that paves the way for the development of periodontitis by, for example, favoring the establishment of more pathogenic flora, e.g. spirochetes.
- Plaque accumulation and repeated episodes of gingivitis throughout childhood could allow for destructive periodontal disease to develop.
- In contrast to children, the elderly have a heightened gingival response to plaque compared to young adults, which may be due to gingival recession.
- There appears to be a closer link between gingivitis progression and periodontitis in elderly adults than younger adults.
- Evidence suggests that intermittent episodes of gingivitis account for the progression of destructive disease over time.
- Gingivitis provides the necessary periodontal environment for pathogenic bacteria to grow and lead to attachment loss.
- The lack of gingival bleeding appears consistent with continued periodontal health.
- The development of products, such as a stabilized stannous fluoride dentifrice, with the potential to control gingivitis and gingival bleeding is important for helping to improve periodontal oral health.

Dentifrice Effects on Plaque Regrowth: Digital Plaque Image Analysis

CONCLUSION

- Stannous fluoride dentifrice was effective in preventing plaque regrowth between toothbrushings as well as in plaque removal during toothbrushing. Under these test conditions, the antimicrobial actions of stannous fluoride dentifrice were superior to those by Zinc Citrate/Baking Soda/Peroxide and sodium fluoride.

OBJECTIVE

An in vivo plaque removal/regrowth model was used to evaluate the anti-plaque effects of three dentifrices in a randomized cross-over design.

MATERIALS AND METHODS

- Dentifrices evaluated were:
  1. Crest® Gum Care (CGC), 0.454% stannous fluoride (SnF₂)
  2. Mentadent® Gum Care (MGC), 2.0 zinc citrate/0.76% SMFP
  3. Crest® Regular (CR), 0.243% sodium fluoride (CR)
- Nine subjects refrained from oral hygiene for 12 hours before baseline samples were taken via Digital Plaque Image Analysis (DPIA). Next, subjects brushed their entire dentition with 1.5 g of test product for 1 min followed by DPIA plaque measurement.
- Over the next 24 hours, subjects brushed lingual surfaces of their dentition twice more using 1.5 g of test product. Each brushing included 30 sec of brushing followed by 30 sec of swishing the developed slurry to the facial surfaces.
- Morning plaque levels on Day 2 were re-measured via DPIA. Washout period involved 48 hr of placebo (CR) dentifrice use.
Dentifrice Effects on Plaque Regrowth: Digital Plaque Image Analysis

RESULTS

- There were no significant differences between products in terms of plaque reduction (initial brushing) (p=0.753).
- In terms of plaque regrowth, CGC produced a significant 36.8% reduction in plaque level following 24 hour product use, while MGC (-7.7%) and CR (-12.9%) produced no reduction in plaque levels relative to baseline (ANOVA p=0.0027).

Effect of a Stannous Fluoride Dentifrice on Plaque Formation and Removal: A Digital Plaque Imaging Study

CONCLUSION

- Use of a 0.454% stannous fluoride dentifrice produced statistically significant reductions in dental plaque formation as compared to the similar use of a standard 0.243% sodium fluoride dentifrice.

OBJECTIVE

To evaluate the antiplaque effectiveness of a 0.454% stannous fluoride (SnF$_2$) dentifrice using a repeated measures digital imaging technique (Digital Plaque Image Analysis-DPIA).

MATERIALS AND METHODS

- Fourteen qualifying subjects (based on previous assessment) were entered into a cross-over study design. Dentifrice treatments included a standard 0.243% sodium fluoride (NaF) dentifrice or a 0.454% SnF$_2$ dentifrice.
- A one-week washout period separated the cross-over periods. While using the assigned treatments, subjects visited the imaging laboratory on six separate days over a two week period. On these days, they reported for three separate assessments of plaque accumulation using DPIA.
- On each “grading day,” plaque was assessed prior to morning tooth brushing, and without consumption of food or beverages. After the morning “pre-brushing” assessment, subjects brushed with the assigned dentifrice. Plaque was then immediately reassessed (morning post-brushing). Subjects also reported to the imaging clinic for an afternoon plaque regrowth assessment. Subjects were again required to avoid food and drink for one hour prior to this measurement.

Imaging System

Effect of a Stannous Fluoride Dentifrice on Plaque Formation and Removal: A Digital Plaque Imaging Study

RESULTS

- The SnF₂ dentifrice was observed to produce statistically significant reductions in dental plaque, measuring 24.4% in the morning pre-brushing, and 27.9% in the afternoon assessment.
- Tooth brushing was observed to significantly reduce plaque on the teeth in the morning post-brushing for subjects using either the standard NaF or the SnF₂ dentifrice.
- There were no statistically significant differences in plaque coverage on teeth following tooth brushing with the NaF (6.3% coverage) or SnF₂ (6.2% coverage) dentifrices.

Effect of a Stabilized Stannous Fluoride Dentifrice on Plaque Acid (Toxin) Production

CONCLUSION

- The stabilized stannous fluoride test dentifrice, (0.454% stannous fluoride stabilized in a silica abrasive with sodium gluconate/stannous chloride), showed superior efficacy in inhibiting plaque metabolic activity compared with a control dentifrice containing 0.243% sodium fluoride in a silica abrasive.
  
  The study demonstrated the usefulness of PGRM methodology for evaluating antimicrobial treatment effects.

OBJECTIVE

To determine the effects of stabilized stannous fluoride (SnF₂) dentifrice on plaque acid (toxin) production using a Plaque Glycolysis and Regrowth Model (PGRM).

MATERIALS AND METHODS

- The test dentifrice, SnF₂, was compared with a control sodium fluoride dentifrice (NaF), after a single brushing.
- Study subjects were 8 adults in good general and oral health.
- Subjects brushed with the test and control dentifrices in a crossover design.
- The PGRM method was used to evaluate antimicrobial treatments by comparing post-treatment plaque growth or metabolism in vivo with control plaque obtained pre-treatment from the same subject.
- Baseline plaque and plaque 45-minutes post-treatment were compared in terms of pH (acid production), and the composition and proportion of acid toxins were compared using capillary electrophoresis.
Effect of a Stabilized Stannous Fluoride Dentifrice on Plaque Acid (Toxin) Production

RESULTS

- pH responses after baseline- and treatment-plaque incubation showed less acid following toothbrushing with SnF$_2$. The control dentifrice had less effect on pH.
- Plaque samples following treatment with SnF$_2$ dentifrice showed significantly less total acid production than at baseline. Plaque samples following treatment with the control dentifrice did not significantly reduce total acid production compared with baseline.
- Both SnF$_2$ dentifrice and control dentifrice significantly reduced acetate production in treated plaques.
- SnF$_2$ dentifrice treated samples produced significantly less lactic acid, but control dentifrice did not significantly reduce lactic acid production.
- Analyses of combined and individual lactic and acetic acids produced during plaque incubation confirmed that SnF$_2$ dentifrice is superior to control dentifrice at inhibiting plaque metabolic activity.

PROPORTIONAL METABOLIC INHIBITION OF ACID PRODUCTION

<table>
<thead>
<tr>
<th>Plaque Treatment</th>
<th>% Reduction in Total Acid (± SD)</th>
<th>% Reduction in Lactic Acid (± SD)</th>
<th>% Reduction in Acetic Acid (± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NaF</td>
<td>29.5 (32.3)*</td>
<td>13.8 (30.2)*</td>
<td>38.5 (24.4)*</td>
</tr>
<tr>
<td>SnF$_2$</td>
<td>67.5 (21.9)</td>
<td>65.1 (25.1)</td>
<td>67.4 (24.2)</td>
</tr>
</tbody>
</table>

* Plaque treatment differences; p<0.05 (Student’s paired t-test)

A new Plaque Glycolysis and Regrowth Method (PGRM) for the In Vivo Determination of Antimicrobial Dentifrice/Rinse Efficacy Towards the Inhibition of Plaque Growth and Metabolism - Method Development, Validation and Initial Activity Screens


CONCLUSION

- This paper describes the development and preliminary validation of a method, the Plaque Glycolysis and Regrowth Method (PGRM), for the in vivo determination of antimicrobial dentifrice/rinse efficacy towards the inhibition of plaque growth and metabolism.

OBJECTIVE

To describe the development and preliminary validation of an in vivo method, PGRM, for the determination of antimicrobial dentifrice/rinse efficacy against bacterial growth/metabolism in plaque.

MATERIALS AND METHODS

- The PGRM is based on the observation that natural fasted dental plaque samples collected from different quadrants of the dentition show similar metabolic and regrowth properties when similarly dispersed and normalized in standardized incubation media.
- Subjects collected overnight fasting plaque from the gingival margin of one quadrant of their dentition as baseline untreated plaque for PGRM assessments. This was followed by use of the test products (toothpastes or mouthrinses) after which dental plaque was self-collected from the remaining three quadrants in specified order and at specified time intervals, thereby allowing for various natural processes within the oral cavity (back diffusion, clearance, deactivation of formulation components).
- Non-treated and treated plaque samples were dispersed into standardized media with adjustment of biomass to a constant level and tested for metabolic and regrowth activity.
- Validation measurements of PGRM are described. Pilot PGRM screens of test products are presented:
  - conventional dentifrice versus chlorhexidine
  - stannous fluoride antimicrobial dentifrice versus conventional dentifrice
  - comparison of antimicrobial mouthwashes
A new Plaque Glycolysis and Regrowth Method (PGRM) for the In Vivo Determination of Antimicrobial Dentifrice/Rinse Efficacy Towards the Inhibition of Plaque Growth and Metabolism - Method Development, Validation and Initial Activity Screens

RESULTS

- Technique validation: studies on non-treated dental plaques showed excellent reproducibility of plaque/regrowth characteristics based on sites (quadrants) and over extended time periods.
- Pilot PGRM screens:
  - chlorhexidine provided superior antimicrobial activity relative to a conventional fluoride dentifrice
  - stannous fluoride antimicrobial dentifrice showed superior antimicrobial actions relative to a conventional fluoride dentifrice

Retention of Tin in Dental Plaque: Pharmacokinetic Modeling


CONCLUSION

- Tin is cleared from saliva rapidly but very well retained in dental plaque. The prolonged retention of tin in dental plaque offers the basis for its anti-plaque and anti-gingivitis benefits.

OBJECTIVE

Stannous ion is a divalent metal cation with antimicrobial properties. It has been used in the oral cavity, most commonly delivered in the form of a dentifrice, for treatment and prevention of plaque and gingivitis. The objective of this research is to evaluate the time-course fate of total tin in saliva and dental plaque.

MATERIALS AND METHODS

- 20 generally healthy subjects were enrolled in the study.
- Baseline saliva and plaque samples were taken after one week of acclimation using a sodium fluoride dentifrice. Subjects then rinsed with an experimental 0.454% stannous fluoride/sodium hexametaphosphate dentifrice slurry for 60 seconds.
- Saliva samples were collected at 5, 15, 30, 45, 60, 90 minutes, 2, 3, 4.5, and 6 hours post rinsing. Supragingival plaque samples were collected using a sterile plastic curette at 15, 30, 60 minutes, 2, 3, 4.5, and 6 hours post rinsing.
- Sample times and quadrants were evenly distributed across the subjects to ensure proper statistical representation of these parameters. Samples were assayed for total tin content and simultaneously modeled using an unusual two compartment model.

RESULTS

- The concentration of tin in saliva dropped rapidly immediately after dentifrice slurry administration. The plaque tin profile indicated that the oral surfaces were readily charged with tin during administration. There was a small additional accumulation after administration.
- The plaque tin levels changed very little over the course of 6 hours. Modeling indicates that there is an obvious kinetic relationship between saliva and plaque compartments and that tin is very well retained in and slowly released from plaque into saliva. Additionally, both compartments were simultaneously loaded during administration.

* Terminal pH following 2 hours incubation - initial pH = 7.10
A Randomized Clinical Trial to Compare Plaque Inhibition of a Sodium Fluoride/Potassium Nitrate Dentifrice Versus a Stabilized Stannous Fluoride/Sodium Hexametaphosphate Dentifrice.


CONCLUSION
• The SnF<sub>2</sub>/SHMP dentifrice (blend-a-med Pro-Expert® GUM PROTECTION) inhibits plaque regrowth both overnight and during the day to a significantly greater degree than the NaF/KNO<sub>3</sub> dentifrice (Sensodyne ProNamel, GlaxoSmithKline).

OBJECTIVE
To compare the plaque inhibition efficacy of a sodium fluoride/potassium nitrate (NaF/KNO<sub>3</sub> with 1450 ppm F) test dentifrice to a 0.454% stannous fluoride/sodium hexametaphosphate/sodium fluoride positive control dentifrice (SnF<sub>2</sub>/SHMP with 1450 ppm F).

MATERIALS AND METHODS
• Twenty-five subjects were randomized to a two-period, two-treatment, double blind crossover sequence using NaF/KNO<sub>3</sub> (Sensodyne ProNamel dentifrice) and SnF<sub>2</sub>/SHMP (blend-a-med Pro-Expert® GUM PROTECTION dentifrice).
• Each treatment was conducted with a standard manual toothbrush (Oral-B® P35 Indicator). Digital plaque image analysis (DPIA) was used on three consecutive days to evaluate:
  (a) overnight plaque formation (A.M. pre-brushing);
  (b) following 40 seconds of brushing with the test product (A.M. post-brushing);
  and
  (c) mid-afternoon (P.M.).
• Images were analysed using an objective computer algorithm to calculate the total area of visible plaque. A four-day washout period was instituted for the crossover phase.

RESULTS
• All 25 subjects completed the study.
• The SnF<sub>2</sub>/SHMP positive control dentifrice provided statistically significantly lower levels of plaque area coverage versus the NaF/KNO<sub>3</sub> test dentifrice at each time point.
• For the SnF<sub>2</sub>/SHMP dentifrice, plaque coverage was 23.0% lower (p<0.0001) at A.M. pre-brushing, 17.3% (p=0.0163) lower at A.M. post-brushing, and 22.6% (p=0.0004) lower at the P.M. measure relative to the NaF/KNO<sub>3</sub> dentifrice. See Figure.

FIGURE. Percent benefit for SnF<sub>2</sub>/SHMP dentifrice vs. NaF/KNO<sub>3</sub> dentifrice.
CONCLUSION

- The blend-a-med EXPERT GUMS PROTECTION toothpaste inhibits plaque regrowth both overnight and during the day to a significantly greater degree than Lacalut Aktiv. Additionally, immediately after brushing with blend-a-med EXPERT GUMS PROTECTION, subjects had significantly less plaque than after brushing with Lacalut Aktiv.

OBJECTIVE

To compare the plaque inhibition benefits of a control 0.454% stannous fluoride/sodium hexametaphosphate/sodium fluoride dentifrice (SnF<sub>2</sub>/SHMP with 1450ppm F) to a chlorhexidine digluconate (0.05%), aluminum lactate (0.8%) and aluminum fluoride (AlF<sub>3</sub>/Chx with 1400ppm F) dentifrice.

MATERIALS AND METHODS

- 29 subjects were randomised to a two-period, two-treatment, double blind crossover sequence using blend-a-med® EXPERT GUMS PROTECTION (Procter & Gamble, Gross Gerau, Germany) toothpaste (SnF<sub>2</sub>/SHMP) and Lacalut® Aktiv (Arcam GmBH, Homburg, Germany) toothpaste (AlF<sub>3</sub>/Chx).
- Each treatment was used along with a standard manual toothbrush (Oral-B® P35 Indicator, Procter & Gamble, Gross Gerau, Germany) for 17 days.
- Digital plaque image analysis (DPIA) was used at the end of each period for three consecutive days to evaluate plaque levels: a) overnight (A.M. pre-brush); b) following 40 seconds of brushing with the test product (A.M. post-brush); and c) mid-afternoon (P.M.). Images were analysed using an objective computer algorithm to calculate the total area of visible plaque.
- A four day washout period was instituted for the crossover phase.

RESULTS

- 27 subjects completed the study.
- The SnF<sub>2</sub>/SHMP dentifrice provided a statistically significant lower level of plaque area coverage compared to the AlF<sub>3</sub>/Chx dentifrice at all timepoints. See Table.
- For the SnF<sub>2</sub>/SHMP dentifrice, plaque coverage was 19.4% lower (p=0.0043) at A.M. pre-brush, 25.6% lower (p=0.0014) at A.M. Post-brush, and 19.8% lower (p= 0.0057) at the P.M. measure versus the AlF<sub>3</sub>/Chx dentifrice. See Figure.

FIGURE. Percent benefit for SnF<sub>2</sub>/SHMP dentifrice vs. AlF<sub>3</sub>/Chx.
Dentinal Hypersensitivity

sensitivity: 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%.*
- 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 (e.g., 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, inhibiting fluid movement and nerve stimulation.
- Rigorous laboratory and clinical research supports the benefits of stabilized stannous fluoride dentifrice in controlling dentinal hypersensitivity.

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

Full text available at www.thejcdp.com


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™ versus 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 ≥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 stannous fluoride/sodium hexametaphosphate dentifrice or the control dentifrice.
- Subjects brushed twice daily with their assigned dentifrice and manual soft toothbrush for 8 weeks.
- Subjects were assessed again for sensitivity and safety at Weeks 4 and 8.

RESULTS

- Data were analyzed for all 90 subjects (45 in each treatment group).
- Schiff Air Index scores were statistically significantly lower for the 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 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 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


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™ (stabilized 0.454% stannous fluoride/sodium hexametaphosphate dentifrice) was compared to a marketed negative control dentifrice containing 0.243% sodium fluoride (Crest® Cavity Protection Regular Paste).
• 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 stannous fluoride/sodium hexametaphosphate dentifrice or the control dentifrice.
• Subjects brushed twice daily with their assigned dentifrice and 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 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 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 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 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.

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™ (stabilized 0.454% stannous fluoride/sodium hexametaphosphate dentifrice) was compared to a marketed negative control dentifrice containing 0.243% sodium fluoride (Crest® Cavity Protection Regular Paste).
• 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 stannous fluoride/sodium hexametaphosphate dentifrice or the control dentifrice.
• Subjects brushed twice daily with their assigned dentifrice and 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 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 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 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 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.
Stannous Fluoride/Sodium Hexametaphosphate Dentifrice Increases Dentin Resistance to Tubule Exposure In Vitro

CONCLUSION
• A stannous fluoride dentifrice with sodium hexametaphosphate (Crest® Pro-Health™) prevents tubule exposure of smear layer dentin surfaces and dietary acid softening.

OBJECTIVE
To evaluate: 1) reactivity of three dentifrice formulations on smear layer-covered root dentin surfaces, and 2) effects of the treatments on resistance to acid softening and dentinal tubuli disclosure.

MATERIALS AND METHODS
• Three commercial dentifrices were tested:
  1. Crest® Cavity Protection with sodium fluoride (NaF)
  2. Crest® Pro-Health™ with stannous fluoride and sodium hexametaphosphate (SnF₂/SHMP)
  3. Colgate® Total® with sodium fluoride and triclosan/copolymer
• Dentifrices were cycled through a pre-treatment period on smear layer-covered dentin surfaces. This involved intermittent soaking in dentifrice slurries and whole human saliva immersion.
• After pre-treatments, the cycling treatments were adjusted to include dietary acid exposure, including soaks in an acidic soft drink.
• Dentin reactivity and smear layer protection were assessed using Vickers surface microhardness, variable pressure scanning electron microscopy (VP-SEM), and confocal laser scanning microscopy in reflection mode (CLSM).

RESULTS
• CLSM and SEM analyses showed specimens treated with SnF₂/SHMP appeared to resist acid solubilization, evidenced by the absence of disclosed dentinal tubuli. The histo-tomographic observations in this study were in agreement with the hardness measurements.

RESULTS (continued)
• The superior surface protection of dentin with SnF₂/SHMP would suggest potential benefits in ameliorating dentinal hypersensitivity in the clinical situation.

Microhardness Values for Dentin Specimens Before and After Treatment

Colgate® and Colgate® Total® are registered trademarks of the Colgate-Palmolive Company.
**Stannous Fluoride Effects on Dentinal Tubules**


**CONCLUSION**

- Stannous fluoride shows efficacy in the blocking of patent dentinal tubuli through chemical precipitation which resists future acid solubilized tubule disclosure. These effects help explain clinical benefits of stannous fluoride in the relief of dentinal hypersensitivity.

**OBJECTIVE**

This study examined the ability of concentrated stannous fluoride (SnF$_2$) gel (Gel-Kam® 0.454% SnF$_2$ in a glycerin carbopol base) to occlude patent tubuli in vitro and to resist solubilization with dietary acids.

**MATERIALS AND METHODS**

- Human root dentin blocks were mounted in methacrylate, ground to form smear layers and then acid etched (phosphoric) to produce surfaces with patent tubuli.
- Specimens were soaked 24 hours in pooled human saliva and then cycled for 3 days with 4x/day soaks (2-min.) in slurries of standard sodium fluoride dentifrice (Crest® Regular) or stannous fluoride gel (Gel-Kam) interspersed with saliva incubation.
- Before and after cycling, specimens were evaluated for surface hardness and profilometry. Following cycling specimens were 1/2 coated in parafilm and cycled through an additional 3 day acid challenge protocol including saliva soaks, standard F dentifrice soaks and dietary acid challenges including bid 3 min. soaking of specimens in Coca-Cola® soft drink.
- Hardness and profilometry were repeated following which treated and acid challenged sides were compared by SEM and CLSM microscopy.

**RESULTS**

- Dentin hardness did not change on treatment cycling but roughness decreased with NaF dentifrice and with SnF$_2$ gel (R$_a$ controls 0.35 - 0.40 sig. NaF 0.18 sig. SnF$_2$ 0.28).
- Post acid cycling surface roughness increased (R$_a$ NaF 0.25 sig. SnF$_2$ 0.33). SEM revealed superior tubule obturation with SnF$_2$ gel and EDAX and XPS showed high surface stannous and fluoride concentrations.
- SnF$_2$ treated dentin also strongly resisted acid solubilization.

**SnF$_2$ Effects on Acid Resistance of HAP Mineral in Vitro**


**CONCLUSION**

- These results provide a more detailed mechanism rationale for the actions of stannous fluoride hexametaphosphate dentifrice in providing smear layer acid resistance previously documented (J Clin Dent 2007;18,55-9) and may explain clinical actions in reducing hypersensitivity for this dentifrice (Compend Contin Educ Dent 2005;26(Suppl-1),35-40; J Contemp Dent Pract 2006;7,1-8).
- HAP solubilization kinetics may provide a rapid screening method to assess potential for desensitizing technologies to provide environmental resistance to dentin surfaces.

**OBJECTIVE**

The efficacy of stannous fluoride for the treatment of dentinal hypersensitivity may include protection of exposed root surfaces against oral environmental conditions including dietary acids. This study describes a method to compare effects of Stannous Fluoride Hexametaphosphate dentifrice (SF-HMP) to NaF dentifrice (NaF) on kinetics of mineral solubilization in vitro.

**MATERIALS AND METHODS**

- 500 mg of HAP mineral standard (BioRad HTP) was pretreated with 25% dentifrice supernatant and washed 3x with water through centrifugation cycles. HAP was re-dispersed into water (10 ml) and a 1 ml (50 mg HAP suspension) aliquot was added into 50 ml of citric acid solution containing 50mM citric acid adjusted to initial pH 2.5 or 3.5 then diluted to 10mM concentration. During dissolution the pH was monitored de novo by potentiostat.
- Kinetics of dissolution were modeled under controlled hydrodynamics with pH change during dissolution monitored by ion selective electrode. Non treated HAP produced a kinetic profile permitting development of rate parameters for quantitative comparison of mineral protection against dietary acids. Results are standardized as % protection vs. Crest® NaF regular paste control.
- Kinetics of dissolution were modeled under controlled hydrodynamics with pH change during dissolution monitored by ion selective electrode. Non treated HAP produced a kinetic profile permitting development of rate parameters for quantitative comparison of mineral protection against dietary acids. Results are standardized as % protection vs. Crest® NaF regular paste control.

**RESULTS**

- Stannous fluoride hexametaphosphate dentifrice produced reductions in HAP demineralization averaging 40% over Crest® NaF regular paste at pH 2.5 (sig. p < 0.05) and 42% over Crest® NaF regular paste at pH 3.5 (sig. p < 0.05).
Dentinal Hypersensitivity: A Review

CONCLUSION
- This paper reviews the prevalence, diagnosis, and treatment of dentinal hypersensitivity.

OBJECTIVE
To review the prevalence, theories, diagnosis, treatments and the clinical evidence for home care recommendations of the condition commonly referred to as “dentinal hypersensitivity" or “tooth sensitivity”.

MATERIALS AND METHODS
- **Prevalence:** Patients most often report dental hypersensitivity after feeling a sharp pain caused by one of several different stimuli. Up to 30% of adults experience dental hypersensitivity at some time during their lifetime, but it may be under-reported by the dental patient population or misdiagnosed. The pain response varies substantially from one person to another. The condition generally involves the facial surfaces of teeth near the cervical aspect and is very common in premolars and canines.

- **Theories:** The most widely accepted explanation of how the pain occurs is Brännström’s hydrodynamic theory. Fluid movement within the dentinal tubules, resulting from temperature changes or physical osmotic changes, stimulates a nerve receptor sensitive to pressure. This leads to the transmission of the stimuli: cold, hot, osmotic, electrical, dehydration and chemical. In order to exhibit a response to the stimuli, the tubules would have to be open at the dentin surface as well as the pulpal surface of the tooth.

- **Diagnosis:** The dental professional, using a variety of diagnostic techniques, will discern the condition from others that may cause sensitive teeth. Diagnostic tools include air/water syringe (thermal), dental explorer (touch), percussion, and bite stress tests. The most commonly cited reason for exposed dentinal tubules is gingival recession. Recessed areas may become sensitive due to the loss of cementum, ultimately exposing dentin.

- **Treatments:** Treatment of the condition can be invasive or noninvasive in nature. The most inexpensive and efficacious first line of treatment for most patients is a dentifrice containing a desensitizing active ingredient such as potassium nitrate and/or stannous fluoride. The potassium ions in potassium nitrate are thought to work by blocking the synapse between nerve cells, reducing nerve excitation, and the associated pain. Efficacy data from clinical trials provide evidence that potassium nitrate is effective in reducing pain due to tooth sensitivity. Stannous fluoride occludes the tubules so that stimulation of the mechanoreceptors does not occur, thus, preventing the pain response. Efficacy data from clinical trials provide evidence that 0.4% stannous fluoride gel and cavity wash are effective in reducing pain and sensitivity.

RESULTS OF REVIEW
- This review considered the prevalence, theories, diagnosis, and treatments of tooth sensitivity.
- The initial cause is generally recessed gingiva, the tubules are exposed and the patient experiences pain. Treatment is aimed at covering up the tubules to desensitize the nerves (eg. stannous fluoride) or interfering with the transmission of pain signal at the synapse (eg. potassium nitrate).
- The patient should be informed of the treatment options and daily habits that could contribute to the problem. The chosen product needs to fit into the patient’s oral hygiene regimen.
- The most effective active ingredients available in toothpaste today to treat dentinal hypersensitivity may be potassium nitrate and stannous fluoride.
Erosion

*erosion: enamel loss through extrinsic or intrinsic acids or chelators acting on plaque-free tooth surfaces*

- Up to 82% of the adult population show signs of erosion*.
- Frequent acid attacks by acidic drinks (e.g., orange juice, sports drinks) or low saliva amount can contribute to permanent enamel loss.
- Acid softens and demineralizes enamel.
- Saliva neutralizes acid and provides a source of minerals to remineralize softened enamel.
- Can lead to exposed dentin causing hypersensitivity with pain sensation to hot, cold, osmotic or tactile stimuli.

\[
\text{NaF} \quad \text{SNF}_2
\]

Slabs of human enamel treated with \( \text{SnF}_2 \) or \( \text{NaF} \), and challenged with repeated acid treatments

**STANNOUS FLUORIDE AND EROSION**

- Creates acid resistant smear layer on enamel surface.
- Protective shield helps to defend enamel against acid attacks thereby protecting it against acid erosion.

*Jaeggi T, Lussi A. Monogr Oral Sci 2006; 20: 44-65*
The Protective Effects of Toothpaste Against Erosion By Orange Juice: Studies in Situ and in Vitro

CONCLUSION

• The results of this study provide further support for tooth brushing before meals. Results further suggest the stannous fluoride dentifrice with sodium hexametaphosphate could be used to provide significant erosion protection in susceptible patients versus that provided by conventional fluoride products.

OBJECTIVE

Consumption of soft drinks, fruit juices and sport drinks has increased dramatically in the UK, the US, and elsewhere. Previous studies have demonstrated the erosive nature of these acidic soft drinks. The objective of this study was to determine the protective effects of experimental stannous fluoride-based toothpaste, containing sodium hexametaphosphate, against an erosive challenge (orange juice) on tooth enamel.

MATERIALS AND METHODS

• This research included a 15-day challenge in vitro study and a 15-day in situ single blind, 3-way, crossover clinical trial.
• The following formulations were tested:
  1) experimental stannous fluoride-sodium hexametaphosphate dentifrice (P&G);
  2) a benchmark sodium fluoride dentifrice (Crest® Cavity Protection, P&G); and
  3) negative control, water.
• Flat, polished human enamel samples with a surface profile of +/-0.1μm, were exposed to the three regimens.
• The orange juice used as erosion challenge had a pH 3.8.
• 15 volunteers wore an intra-oral appliance with 2 specimens of enamel embedded in the mid-palatal region from 9:00 to 17:00 (removed for 1 hour at lunchtime). Whilst appliances were in place, no food or drink other than water and the designated orange juice were consumed. Volunteers were asked to rinse with a toothpaste slurry or water at 9:00 and 13:00 followed by consumption of 250 ml orange juice 1 and 3 h later.
• Subjects were treated with one study formulation for 5 days followed by two non-treatment days.
• A profilometer was used to measure depths of the resulting eroded areas at days 5, 10 and 15.

RESULTS

• There was significantly more erosive damage on the specimens exposed to the benchmark paste (NaF) and negative control (water) compared to the test stannous fluoride-sodium hexametaphosphate toothpaste in both the in situ (Fig. 1) and in vitro (Fig 2) studies.

FIG 1. In situ loss of material*

FIG 2. In vitro loss of material*

*mean value based on duplicate determinations of two enamel specimens
The Enamel Protection of a Stabilized Stannous Fluoride Sodium Hexametaphosphate Dentifrice

P&G data on file, 2007

CONCLUSION

- An in vitro research study demonstrated Crest® ProHealth™ dentifrice provides protection against erosive dietary acids. Results confirmed Crest ProHealth™ provided significantly more protection than Elmex® (GABA), Total® (Colgate®) or Sensodyne Pronamel® (GlaxoSmithKline).

OBJECTIVE

To evaluate the ability of dentifrice products to protect enamel surfaces against erosive dietary acids.

MATERIALS AND METHODS

- The in vitro erosion cycling method tests the relative ability of oral care products to protect enamel surfaces against erosive dietary acid challenges.

Dentifrices compared in this study were:
- Crest® Pro-Health™ (1100 ppm fluoride as stannous fluoride)
- Colgate® Total® (1450 ppm fluoride as sodium fluoride)
- Elmex® (1450 ppm fluoride as amine fluoride)
- Sensodyne Pronamel® (1450 ppm fluoride as sodium fluoride)
- Control (1100ppm fluoride as sodium fluoride)

Erosion Cycling

- Enamel specimens were prepared from extracted human teeth
- Each side of the specimen is controlled leaving an exposed treatment area in the center of the specimen
- Specimens were exposed to a cycling regimen of:
  - toothpaste slurry (2 min) _ saliva (1 hour) _ erosive acid challenge (10 min.) _ saliva (50min)
- Specimens receive 20 treatment cycles over a 5 day period

Specimen Analysis

Thin sections were cut from each specimen using a hard tissue sectioning saw to allow the control and treated portions to be analyzed together. These sections were X-rayed and the radiographic images analyzed using a computer based imaging system. The controlled (untreated) surface was compared to the treated surface, enabling the depth of the eroded area to be measured (µm surface lost).

The Enamel Protection of a Stabilized Stannous Fluoride Sodium Hexametaphosphate Dentifrice

RESULTS

- Crest® Pro-Health™ dentifrice was shown to provide significantly more protection from dietary acids than three marketed dentifrices containing higher levels of fluoride.

<table>
<thead>
<tr>
<th>Product</th>
<th>Mean Surface Loss* (µm (SEM))</th>
</tr>
</thead>
<tbody>
<tr>
<td>ProHealth</td>
<td>7.75 (1.84)a</td>
</tr>
<tr>
<td>Elmex</td>
<td>40.50 (1.19)b</td>
</tr>
<tr>
<td>Total</td>
<td>41.25 (5.51)b</td>
</tr>
<tr>
<td>Control</td>
<td>46.75 (1.80)b</td>
</tr>
<tr>
<td>Pronamel</td>
<td>49.75 (3.50)b</td>
</tr>
</tbody>
</table>

* Mean (n=4) values with different letter designations are significantly different (P<.05) by the least significant difference test.

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Enamel Protection Superiority of SnF₂ vs. Prescription Level Fluorides

CONCLUSION

• Results from this study demonstrated 1100ppm F as SnF₂ provides superior protection against common acid attack compared to some of the most popular prescription level fluoride treatments.

OBJECTIVE

Some researchers believe that since F in general provides a low level of benefit to the enamel against external acid attack, more F likely works even better. The purpose of this study was to determine the relative ability of various F-containing products to protect enamel against the initiation and progression of enamel surface damage due to acid challenges.

MATERIALS AND METHODS

• Cores of enamel were removed from extracted human teeth, cleaned, lightly ground and polished to provide an essentially virgin enamel surface, soaked in pooled human saliva (pellicle formation), then treated in a 1:3 slurry (product:saliva) of product representing both OTC level (1100ppm) and prescription level (5000ppm) of F.

• Products compared included:
  a) 1100ppm F as NaF;
  b) 1100ppm F as SnF₂;
  c) 5000ppm F as NaF; and
  d) 5000ppm F as NaF + acidulated phosphate.

• Specimens were subjected to pH cycling conditions in which the specimens were exposed to a 1% citric acid solution (pH 2.4) over the course of 5 days of treatment, representing challenges to the enamel by a common food based acid.

RESULTS

• Specimens treated with 1100ppm F (SnF₂) toothpaste demonstrated significantly less damage (p>0.05, ANOVA) as a result of this citric acid challenge, losing, on average, only 8.0μm of enamel.

• The 1100ppm F as NaF treated specimens suffered 22.8μm of enamel loss, the 5000ppm F as NaF lost 20.9μm of enamel and the 5000ppm F as NaF + acidulated phosphate lost an average of 24.0μm enamel.
**Enamel Protection vs. Abrasivity - A Study of Relevance**

**CONCLUSION**

- These results indicate
  1) the primary driver for enamel protection benefits is more likely the particular F salt, rather than RDA of the formulation.
  
  and
  
  2) this model is reproducible.

- Under the conditions of these studies, SnF$_2$ provided superior protection against acid mediated enamel tooth surface loss.

**OBJECTIVE**

Dentifrices with RDA< 250 are considered safe for daily use. Some researchers believe products with low RDA may be less aggressive on erosively softened enamel. Others believe that once softened, erosively challenged enamel will be removed by any friction, even by the tongue. This research was conducted to determine the primary driver of enamel protection benefits: is abrasivity or fluoride (F) salt the more important factor?

**MATERIALS AND METHODS**

- Cores of extracted, human enamel were cleaned, ground and polished to provide a virgin enamel surface, soaked in human saliva (pellicle formation), and treated in a 1:3 (product:saliva) slurry of toothpaste representing a range of actives/RDA values [SnF$_2$(RDA-150), NaF #1(RDA-100), NaF #2(RDA-50)].
  
- Specimens were subjected to dynamic pH cycling conditions including exposure to multiple 1% citric acid challenges over a 5-day period.
  
- Treatment slurries and saliva baths were constantly stirred to ensure a steady flow, representing repetitive challenges to the enamel by a combination of common dietary acid and abrasive elements.
  
- The study was run in duplicate to test model reproducibility.

  Results were averaged.

**RESULTS**

- The product with RDA-150 provided significant (p=0.05, ANOVA) protection against damage (8.0μm of surface loss), with lower RDA products (RDA-50 or 100) showing no significant differences between them in their ability to protect enamel against damage (27.3 and 25.4μm of surface loss, respectively). See Table and Figure.
  
- It is important to note the active F species in the RDA-150 formulation was SnF$_2$. SnF$_2$ provides significant protection against erosive acid damage by forming a protective barrier layer on the enamel surface, protecting against external challenges.
  
- The model is reproducible.

**TABLE. Results**

<table>
<thead>
<tr>
<th>Product Tested</th>
<th>RDA</th>
<th>Depth of Total Mineral Loss (μm)</th>
<th>Depth of Total Mineral Loss (μm)</th>
<th>Depth of Total Mineral Loss (μm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>STUDY 1</td>
<td>STUDY 2</td>
<td>AVERAGE</td>
</tr>
<tr>
<td>SnF$_2$</td>
<td>-150</td>
<td>8.0</td>
<td>8.0</td>
<td>8.0</td>
</tr>
<tr>
<td>NaF #1</td>
<td>-100</td>
<td>28.0</td>
<td>22.8</td>
<td>25.4</td>
</tr>
<tr>
<td>NaF #2</td>
<td>-50</td>
<td>271</td>
<td>27.5</td>
<td>27.3</td>
</tr>
</tbody>
</table>

**FIGURE.** Average % Reduction in Total Mineral Loss*  

* (vs. NaF product)
Surface Protective Mechanism of SnF<sub>2</sub> Against Irreversible Acid Damage

**CONCLUSION**

- This study confirms the deposition of an invisible stannous containing layer into/onto the pellicle coated enamel surface as a result of treatment with a stannous fluoride containing dentifrice.
- These results, coupled with in vitro and in situ demonstrations of effective protection against dietary acid challenges, support the superiority of stannous fluoride for its potential to protect enamel against the emerging trend of irreversible tooth surface loss.

**OBJECTIVE**

Deposition of an invisible barrier layer onto the enamel surface has been proposed as a potentially superior means for protecting enamel against an ever increasing level of acid based challenges from both dietary and food sources. The purpose of this study was to demonstrate the barrier layer deposited onto pellicle coated enamel surfaces from stannous fluoride (SnF<sub>2</sub>) containing toothpaste using laser ablation ICP-MS.

**MATERIALS AND METHODS**

- Squares of bovine enamel (5x5x1mm) were exposed overnight to pooled human saliva, resulting in the deposition of a reasonably mature pellicle layer on the enamel specimens.
- Specimens were treated with the supernatant of a 1:3 slurry of toothpaste: Water for 2 minutes (SnF<sub>2</sub>, NaF, or Water control), then rinsed with deionized, distilled water.
- Surface analysis of specimens was done using laser ablation ICP-MS, with a field of view for all images being 790mm x 590mm. The intensity of all isotopes was corrected pixel by pixel using <sup>13</sup>C as the internal standard.

**FIGURE 1.** Measurement Technique: Laser Ablation Inductively Coupled Plasma

**RESULTS**

- Figure 2a shows bovine enamel chip with pellicle showing no stannous deposition. Figure 2b shows bovine pellicle coated enamel chip treated with the sodium fluoride dentifrice showing no stannous deposition. Figure 2c shows the bovine pellicle coated enamel chip treated with the Crest® Pro-Health™ dentifrice showing a protective stannous layer.
- Deposition of a relatively continuous stannous layer onto the pellicle coated enamel surface was clearly demonstrated, with significant deposition of stannous (using isotopes <sup>117</sup>Sn + <sup>120</sup>Sn) measured, incorporated into or onto the pellicle coated enamel surface.

**FIGURE 2.**

- Field of view for all images is 790 mm x 590 mm.
- Colormaps for all zinc images have the same scale.
- Colormaps for all tin images have the same scale.
- Only first pass data is shown.
CONCLUSION

- These results clearly demonstrate SnF$_2$ provides superior protection to the tooth enamel against common dietary acid attacks. Due to the potentially irreversible nature of erosive acid damage, development of products designed to help prevent damage initiation and progression is key to providing meaningful tooth health benefits.

OBJECTIVE

Tooth health can be measured not only by prevention against subsurface damage (caries) but also by assessing the ability of products to strengthen and protect enamel against the initial enamel softening that can lead to irreversible damage. The purpose of this study was to determine the relative ability of various fluoride (F) salts to protect enamel against the initiation and progression of damage due to dietary acids.

MATERIALS AND METHODS

- Cores of extracted, human enamel were cleaned, ground and polished, providing a virgin enamel surface, soaked in pooled saliva (pellicle formation), and treated with a 1:3 slurry (product:saliva) of toothpaste representing three F salts commonly used in toothpastes (a:NaF; b:NaMFP; c:SnF$_2$).
- Specimens were subjected to pH cycling conditions (5 day model) that included:
  - Study 1: 1% citric acid challenges;
  - Study 2: marketed cola (phosphoric acid) challenges.

Together, these studies represent challenges to the enamel by common food based acids.

RESULTS

- SnF$_2$ treated specimens resulted in 10.3 and 2.0 microns of enamel lost (citric and phosphoric acid, respectively).
- NaF and NaMFP treated specimens resulted in 24.5/12.8um (citric/phosphoric) and 28.0/14.9um (citric/phosphoric) of total mineral loss, respectively.
- These studies suggest citric acid is more aggressive than phosphoric acid, and both studies demonstrate clearly superior protection against acid challenge attributed to the SnF$_2$ formulation tested, with SnF$_2$ providing a 58.2% reduction in acid mediated damage (vs. the NaF control) for citric acid, and a reduction of 84% (vs. NaF) when tested using a phosphoric acid challenge.
HAP Dissolution Study I: 
SnF$_2$ vs. NaF Solution Study


CONCLUSION

• These results confirm that SnF$_2$ was significantly stronger at attaching to HAP and inhibiting HAP dissolution than NaF solution. These results suggest the potential for SnF$_2$ superiority in protecting enamel against acid attack and dissolution.

OBJECTIVE

To compare the ability of 2 active ingredients normally used in dentifrice to inhibit HAP dissolution.

MATERIALS AND METHODS

• HAP powder, a synthetic analog of enamel and dentine, was pretreated with test solutions (10g solution/300mg HAP powder) for 1 minute followed by 3x washing with water, then dried. 50mg of pre-treated HAP was exposed to 25 ml of acid dissolution media containing 0.10M lactic acid + 0.15M NaCl. pH of the media was adjusted to and maintained at pH 4.5.

• Exposure of HAP to the media results in dissolution and release of hydroxide ion, increasing pH of the solution. The increase in pH is compensated for by automatic additions of lactic acid (0.05M) to maintain the original pH (4.5) of the reaction cell (Metrohm Titrino).

• Total volume of titrant added after 30 minutes was used to calculate % reductions vs. non-treated HAP control. In this study, results were compared between NaF and SnF$_2$ solutions to determine their relative ability to protect enamel against acid attack and dissolution.

RESULTS

• Results showed that both SnF$_2$ and NaF solutions have significant effect in slowing down the HAP powder dissolution compared with non-treated HAP under this experiment condition.

• The % reduction by SnF$_2$ is consistently higher than that by NaF treatment series.

• The % reduction of dissolution (30 min) is significantly correlated with Log [concentration] of each ingredient. At a given F concentration, e.g. 280ppm, reduction in HAP dissolution for NaF was 47.6%, while reduction for the SnF$_2$ treated sample was 75.7%.

% Reduction of HAP dissolution

| SnF (BLUE LINE) |
|-----------------|---|---|---|---|---|---|
| X-value         | 12.5 | 25 | 50 | 75 | 121 | 245 |
| Y-value         | 27.2 | 38.0 | 44.9 | 56.1 | 61.8 | 74.3 |

| NaF (GREY LINE) |
|-----------------|---|---|---|---|---|---|
| X-value         | 12.5 | 25 | 50 | 100 | 200 | 400 |
| Y-value         | 25.1 | 30.3 | 38.3 | 42.1 | 45.8 | 47.9 |
**CONCLUSION**

- These results confirm the ability of SnF$_2$, as delivered from a SnF$_2$ containing toothpaste, to:
  1) bind to hydroxyapatite, the primary component of human enamel; and
  2) inhibit dissolution of this key enamel component more efficiently than NaF.

- In terms of its relative ability to protect enamel against acid challenge, the 1100ppm F (SnF$_2$) formulation included in this study provides a significant advantage over other fluoride actives in its ability to protect enamel against irreversible acid wear and dissolution.

**OBJECTIVE**

Superior protection against acid dissolution is key to deliver enamel protection benefits. Hydroxyapatite (HAP), the main mineral component of human enamel, provides an efficient means to determine the ability of compounds to attach to and protect apatite against acid dissolution. The purpose of this research was to demonstrate the ability of SnF$_2$ to protect HAP against acid dissolution.

**MATERIALS AND METHODS**

- HAP powder was pretreated with dentifrice slurry supernatant (20g supernate/200mg HAP powder), followed by 3x washing with water, then freeze dried.
- 50mg of the pre-treated HAP was exposed to 25 ml of acid dissolution media (0.05M acetic acid, 0.05M sodium acetate and 0.109 M sodium chloride) adjusted to and maintained at pH 4.5. As exposure of HAP to the media results in dissolution and release of hydroxide ion, the increase in pH is compensated by automatic additions of dilute hydrochloric acid (0.1N) to maintain the pH (4.5) of the reaction cell (Brinkman Titrino).
- The total volume of titrant added after 30 minutes was used to calculate % reduction vs. control. Results were compared between NaF (1100ppm F) and SnF$_2$ (1100ppm F) dentifrice to determine their relative ability to protect enamel against acid challenge.

**RESULTS**

- Reduction in dissolution for NaF was 63.1%, while the reduction in HAP dissolution for the SnF$_2$ treated sample was 92.8%. Differences in % reduction were statistically significant (paired-T Test).
- SnF$_2$ binds to HAP surfaces more effectively than NaF.
- These results confirm the ability of SnF$_2$, delivered from a toothpaste, to protect the hydroxyapatite component of enamel more efficiently than NaF.
Fluoride Dentifrice Protection of Enamel Against Acid Challenge and Softening


CONCLUSION
- This study demonstrated clear differences in performance when comparing the surface protection ability of different F salts, with the 1100ppm F (SnF\(_2\)) dentifrice providing roughly double the level of protection against a wide range of acid challenges.

OBJECTIVE
To assess the ability of fluoride (F) containing dentifrices to protect human enamel against dietary acid challenges.

MATERIALS AND METHODS
- Enamel protection model (EPM) studies were based on method #33 described in the US FDA testing procedures, with modifications as reported by Newby et al., Abs.1777, New Orleans, 2007.
- Briefly, human molars were treated with centrifuged supernatants produced from 1 part dentifrice to 3 parts water (weight/weight) for 5 minutes with constant agitation. Pre and post treatment etchings were performed with 1% citric acid pH 3.8, 0.85% tartaric acid pH 3.1 or 6% acetic acid pH 2.4 for 12, 4 or 2 minutes respectively at 37°C with agitation. Etching times were designed to provide a similar pre-etch phosphate concentration for each acid tested.
- A marketed F dentifrice containing 1150ppm F (NaF) + KNO\(_3\) served as the reference control. Performance of two other F dentifrices (1100ppm F as NaF and 1100ppm F as SnF\(_2\)), were compared for their ability to protect enamel against these three acids that represent acids found in everyday foods and beverages. Results are expressed as a % reduction relative to pre-etch phosphate control values.

RESULTS
- The 1100ppm F (SnF\(_2\)) toothpaste resulted in an average % reduction in Enamel Solubility of 28.7%, while the 1100ppm F (NaF) product provided an average of 15.5% reduction, and the marketed, reference control product containing 1150ppm F (NaF) + KNO\(_3\), product delivered a 1.8% reduction in enamel solubility. All differences were significant (p=0.05).

Cavity Protection
dental caries: a progressive destruction of tooth

- Dental caries results when acids produced by bacteria (i.e., S. mutans) demineralize tooth structure below the tooth surface. Over 90% of dentate adults in the US have had dental caries.*
- Fluoride is commonly used to protect against caries by inhibiting demineralization and enhancing remineralization of partially demineralized enamel.
- When fluoride is incorporated in 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 in two ways.
- It strengthens enamel and dentin to inhibit demineralization and promote remineralization.
- Stannous fluoride also has the ability to reduce S. mutans.
- Thus, the anti-caries effect of stannous fluoride includes a combination of physical chemical effects and antimicrobial actions.

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

Full text available in the Research Database at www.dentalcare.com


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 anti-caries 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:

• Fluoride uptake
  - Stabilized stannous fluoride/sodium hexametaphosphate (1,100 ppm fluoride as stannous fluoride, sodium hexametaphosphate, and silica)
  - United States Pharmacopeia (USP) Reference Standard (1,100 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 (1,100 ppm fluoride as sodium fluoride, sodium hexametaphosphate, and silica)
  - Stannous fluoride USP Reference Standard (1,100 ppm fluoride as stannous fluoride and silica)
  - Sodium fluoride USP Reference Standard (1,100 ppm fluoride as sodium fluoride and silica)
  - Dose-response sodium fluoride control
  - Placebo negative control (<1ppm fluoride)

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.

<table>
<thead>
<tr>
<th>Product</th>
<th>Mean Fluoride Uptake µgF/cm² (SD)</th>
<th>Mean mineral loss. µm x Vol % min (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stannous fluoride/SHMP</td>
<td>8.09 (0.25)a</td>
<td>96 (241)b</td>
</tr>
<tr>
<td>Sodium fluoride/SHMP</td>
<td>85 (257)c</td>
<td></td>
</tr>
<tr>
<td>Stannous fluoride USP Reference Standard</td>
<td>7.44 (0.98)c</td>
<td>281 (139)a</td>
</tr>
<tr>
<td>Sodium fluoride USP Reference Standard</td>
<td>2.98 (4.01)c</td>
<td></td>
</tr>
<tr>
<td>Dose-response control</td>
<td>5.48 (0.25)c</td>
<td>738 (642)c</td>
</tr>
<tr>
<td>Placebo</td>
<td>2.76 (0.94)c</td>
<td>2.16 / (8/0)c</td>
</tr>
</tbody>
</table>

*Mean (n = 4) values with different letter designations are significantly different (P < .05) by the least significant difference test.

†Mean (n = 10) values with different letter designations are significantly different (P < .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

RESULTS

- 799 subjects completed the year 1 assessment; 683 subjects were re-examined at year 2.
- Considering evaluable subjects (i.e., 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 SnF₂-SHMP group than the control group.
  - Neither examiner showed statistically significant differences in caries increments between low-NaF and control groups.

<table>
<thead>
<tr>
<th>Dentifrice</th>
<th>n</th>
<th>mean#</th>
<th>Adjusted mean DMFS</th>
<th>% reduction</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>500 ppm F</td>
<td>161</td>
<td>6.05</td>
<td>0.355</td>
<td>2.7</td>
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<td>1,100 ppm F</td>
<td>168</td>
<td>6.21</td>
<td>0.347</td>
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<tr>
<td>2,800 ppm F</td>
<td>176</td>
<td>5.38</td>
<td>0.339</td>
<td>13.4</td>
<td>0.043</td>
</tr>
<tr>
<td>Experimental</td>
<td>159</td>
<td>5.76</td>
<td>0.369</td>
<td>13.0</td>
<td>0.019</td>
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- **Examiner A**

<table>
<thead>
<tr>
<th>Dentifrice</th>
<th>n</th>
<th>mean#</th>
<th>Adjusted mean DMFS</th>
<th>% reduction</th>
<th>p value</th>
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</thead>
<tbody>
<tr>
<td>500 ppm F</td>
<td>161</td>
<td>4.30</td>
<td>0.308</td>
<td>12.2</td>
<td>0.916</td>
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<tr>
<td>1,100 ppm F</td>
<td>168</td>
<td>4.89</td>
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<tr>
<td>2,800 ppm F</td>
<td>176</td>
<td>3.67</td>
<td>0.294</td>
<td>25.2</td>
<td>0.0014</td>
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<tr>
<td>Experimental</td>
<td>150</td>
<td>3.64</td>
<td>0.319</td>
<td>25.5</td>
<td>0.002</td>
</tr>
</tbody>
</table>

- **Examiner B**

- Adjusted means from analysis of covariance.
- Percent reduction = 100% (1,100 ppm mean minus treatment mean) divided by 1,100 ppm mean.
- Two-sided p-value is 0.0258.
- Two-sided p-value is 0.0016.
In Situ Evaluation Of Sodium Hexametaphosphate-Containing Dentifrices

Results suggested a clinical level of anticaries activity for the experimental SnF₂ and NaF dentifrice formulations that was as good as either of the positive controls, when evaluated using polarized light microscopy.

**RESULTS**

**Objective**

An investigator-blinded, in situ clinical study was conducted to evaluate the effects of two experimental dentifrice formulations containing sodium hexametaphosphate, an anticalculus/whitening agent, on demineralization-remineralization.

**Materials and Methods**

Experimental dentifrices were:

- Stannous fluoride (SnF₂) and sodium hexametaphosphate
- Sodium fluoride (NaF) and sodium hexametaphosphate

Both experimental dentifrices were packaged in a dual-phase tube.

Three controls were used to evaluate the experimental dentifrice formulations’ ability to alter demineralization-remineralization:

- SnF₂-positive control
- NaF-positive control
- No fluoride placebo-negative control

The single-section crown model, developed at the University of Iowa, was used to evaluate the fluoride efficacy of the treatments.

The crown slot held:

1) a sound root section;
2) a root surface lesion section; and
3) enamel surface lesion section.

Thirty subjects were randomized to one of 10 treatment sequences involving 5 dentifrice treatments. Each dentifrice was used twice per day for 1 month over the 5-month period. At the end of each leg, the gold crown was removed and replaced by a new crown with three new substrates.

**Conclusion**

Based on this research, sodium hexametaphosphate does not interfere with the normal fluoride activity of the toothpastes tested. Relative to the positive and negative controls, the experimental dentifrice with stannous fluoride was numerically better at inhibiting demineralization of sound root surfaces.

**Root Sections: Analysis of Variance**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>N</th>
<th>difference</th>
<th>Root lesion mean</th>
<th>SE</th>
<th>Ranking*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>27</td>
<td>-184.18</td>
<td>11.22</td>
<td></td>
<td>A</td>
</tr>
<tr>
<td>SnF₂-positive control</td>
<td>27</td>
<td>-80.91</td>
<td>11.23</td>
<td></td>
<td>B</td>
</tr>
<tr>
<td>NaF-positive control</td>
<td>27</td>
<td>-69.88</td>
<td>11.24</td>
<td></td>
<td>B</td>
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<tr>
<td>NaF-SHMP experimental</td>
<td>28</td>
<td>-61.13</td>
<td>10.97</td>
<td></td>
<td>B</td>
</tr>
<tr>
<td>SnF₂-SHMP experimental</td>
<td>28</td>
<td>-57.60</td>
<td>10.97</td>
<td></td>
<td>B</td>
</tr>
<tr>
<td>Sound root mean</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>26</td>
<td>260.82</td>
<td>22.48</td>
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<td>A</td>
</tr>
<tr>
<td>NaF-positive control</td>
<td>27</td>
<td>202.51</td>
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<td>NaF-SHMP experimental</td>
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<td>161.77</td>
<td>21.47</td>
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<tr>
<td>SnF₂-positive control</td>
<td>27</td>
<td>153.06</td>
<td>21.96</td>
<td></td>
<td>BC</td>
</tr>
<tr>
<td>SnF₂-SHMP experimental</td>
<td>28</td>
<td>118.91</td>
<td>21.47</td>
<td></td>
<td>C</td>
</tr>
</tbody>
</table>

* Based on pairwise comparisons (p < 0.05)

See publication for additional results.
Antiglycolytic Efficacy Against the Cariogenic Streptococcus Mutans Strain (ATCC 25175)

CONCLUSION
• Oral-B® Pro-Expert® dentifrice provides antiglycolytic efficacy against the cariogenic Streptococcus mutans strain (ATCC 25175) in an in-vitro test.

OBJECTIVE
The first stage of dental caries occurs when acid produced by bacteria, especially Streptococcus mutans, initiate dematerialization of the enamel. Inhibition of the acid production may therefore lead to less dematerialization and consequently to less risk of caries. The objective of this in-vitro study was to compare the acid inhibition efficacy of Oral-B® Pro-Expert® relative to various marketed dentifrice and no treatment controls.

MATERIALS AND METHODS
• Treatments tested: Oral-B® Pro-Expert® (SnF₂), Elmex Anti-Cavity (AmF), Zendium Classic (NaF) and Crest® Decay Prevention (NaF), no treatment controls with and without bacteria.
• Tryptone Soya Broth and glucose solution were mixed with pure culture of Strep.mutans and dentifrice slurry, which was incubated in a shaking waterbath at 37°C.
• pH was measured before and after incubation (2 hrs).
• Changes in pH were calculated and used as a measure of glycolytic inhibition (small pH change = more inhibition).

RESULTS
• Oral-B® Pro-Expert® showed statistically significantly greater inhibition of acid production than Zendium Classic and Crest® Decay Prevention. There was no statistically significant difference between Oral-B® Pro-Expert® and Elmex Anti-Cavity showed no statistically significant difference in glycolytic inhibition (p=0.5092).

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Delta pH after 2hrs incubation #</th>
<th>(SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elmex Anti-Cavity</td>
<td>-0.037 (0.002) a</td>
<td></td>
</tr>
<tr>
<td>Oral-B® Pro-Expert®</td>
<td>0.052 (0.004) a</td>
<td></td>
</tr>
<tr>
<td>Zendium Classic</td>
<td>1.263 (0.164) b</td>
<td></td>
</tr>
<tr>
<td>Crest® Decay Prevention</td>
<td>1.148 (0.052) b</td>
<td></td>
</tr>
<tr>
<td>No Bacteria Control</td>
<td>-0.044 (-0.002)</td>
<td></td>
</tr>
<tr>
<td>No Treatment Control</td>
<td>1.752 (0.090)</td>
<td></td>
</tr>
</tbody>
</table>

# Average (n=6) values with different letter designation are statistically significantly different (p < 0.05), SD = Standard deviation

Delta pH: A lower delta change indicates greater acid inhibition efficacy.
ANTICARIES AND HARD TISSUE ABRASION EFFECTS OF A “DUAL-ACTION” WHITENING, SODIUM HEXAMETAPHOSPHATE TARTR Control Dentifrice

**CONCLUSION**
- Laboratory results confirm the anticaries properties and demonstrate hard tissue safety of sodium fluoride/sodium hexametaphosphate dentifrice.

**OBJECTIVE**
To examine the anticaries efficacy and hard tissue abrasivity of sodium hexametaphosphate compared to positive control, clinically tested dentifrices, 
in vitro.

**MATERIALS AND METHODS**
- **pH cycling fluoride uptake:** 3 mm diameter enamel cores were prepared from extracted human teeth. Artificial caries-like lesions were made on each core. Treatment with dentifrice slurry occurred 4 times per day, 1 minute each time, with one-hour soaking in saliva in between. Cores were exposed to 3 hours of demineralization between 2nd and 3rd treatments each day. After 6 treatment days, specimens were analyzed for fluoride uptake.
  - Dentifrices tested were: Crest® Dual Action Whitening, sodium hexametaphosphate with 1100 ppm fluoride (F) as sodium fluoride (NaF); Crest® Cavity Protection, a clinically proven positive control dentifrice with 1100 ppm F; a dose response control dentifrice with 250 ppm F as NaF; a placebo negative control dentifrice with <1 ppm F.
- **Remineralization/inhibition of demineralization:** Prepared human premolars and molars were coated with acid resistant varnish, leaving a 3 x 2 mm window on one surface which served as an entry site for subsurface demineralization. A demineralization/ remineralization model was used to model a daily demineralization of 6 hours, 16 hours remineralization by saliva, and twice a day treatment to enhance remineralization or inhibit demineralization. Overall relative mineral loss from lesions was calculated.
  - 4 dentifrices were tested in each of 2 studies. First study: Crest® Dual Action Whitening, sodium hexametaphosphate with 1100 ppm F as NaF; a clinically proven positive control dentifrice with 1100 ppm F, conventional silica; a dose response control dentifrice with 250 ppm F as NaF; placebo negative control dentifrice with <1 ppm F. Second study: the dose response control dentifrice was replaced with a second positive control (a tartar control dentifrice with 1100 ppm F, 3.3% pyrophosphate); three other dentifrices were identical to the first cycle products.

**RESULTS**
- **Fluoride uptake study:** There was no statistical difference in fluoride uptake (an indicator of anticaries activity) between the sodium hexametaphosphate dentifrice and the clinically proven dentifrice with the same fluoride source.
- **Remineralization/inhibition of demineralization studies:** In study 1, the sodium hexametaphosphate dentifrice was equivalent to the dentifrice with the same fluoride source. In study 2, there was no significant difference between the sodium hexametaphosphate dentifrice and either a pyrophosphate tartar control clinically proven dentifrice or a silica-containing clinically proven positive control dentifrice.
- **Abrasion studies:** Relative Dentin Abrasion (ROA) and Relative Enamel Abrasion (REA) were similar between the sodium hexametaphosphate dentifrice and the clinically proven dentifrice with silica abrasive. Silica-containing dentifrices showed markedly lower REA values versus the alumina-containing dentifrice. Results confirmed the chemical whitening action of the sodium hexametaphosphate on tooth surfaces.
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 (e.g., silica) and those that work by chemical stain control (e.g., sodium hexametaphosphate).

SODIUM HEXAMETAPHOSPHATE AND STAIN REMOVAL

- 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 (e.g., dentifrice, chewing gum).

CONCLUSION

- Use of 0.454% stannous fluoride sodium hexametaphosphate dentifrice yielded significant reductions in tooth stain in clinical studies, without increased extrinsic stain accumulation in longer term randomized controlled trials, or appreciable evidence from spontaneous consumer reports.

OBJECTIVE

This meta-analysis was conducted to evaluate tooth staining with a 0.454% stannous fluoride sodium hexametaphosphate dentifrice.

MATERIALS AND METHODS

- Evidence of extrinsic tooth stain formation or removal for a single phase 0.454% stannous fluoride sodium hexametaphosphate dentifrice (Crest® Pro-Health™) was assessed from clinical trials outcomes and spontaneous consumer reports.
- The inclusive meta-analysis involved 14 randomized controlled trials to assess stain removal or deposition under controlled usage conditions, and spontaneous reports of all types from uncontrolled usage, over periods of up to 6 months.
- Extrinsic stain was assessed by measurement (Lobene Index), clinical examination and/or solicited or unsolicited report.

RESULTS

- The meta-analysis included 175 subjects in controlled trials of stain removal, 1041 subjects in other randomized controlled trials with 2-6 month usage, and 2246 spontaneous consumer reports of all types. The clinical trials population exhibited considerable diversity with respect to demographics and baseline stain.
- In the composite stain removal trials, 0.454% stannous fluoride sodium hexametaphosphate dentifrice yielded significant (p<0.05) reductions in tooth stain, ranging from 76% at Week 2 to 89% at Week 6. In prospective 2-6 months trials, there was 1 report of tooth stain with the 0.454% stannous fluoride dentifrice, not significantly different in occurrence versus dentifrice controls.
- Tooth stain accounted for less than 0.1% of spontaneous dentifrice reports, well below unsolicited testimonials.
Extrinsic Stain Removal Efficacy of a Stannous Fluoride Dentifrice with Sodium Hexametaphosphate

CONCLUSION

- In two studies, Crest® Pro-Health™ demonstrated significant extrinsic stain removal versus 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 two independent, double-blind, randomized six-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 eight central and lateral incisors at baseline.
- Oral soft and hard tissue examinations were also conducted.
- Subjects were randomized to either the stannous fluoride + sodium hexametaphosphate toothpaste or positive control toothpaste.
- Subjects used their assigned dentifrice twice a day for six 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 two 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).


RESULTS (continued)

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

CONCLUSION

- In two independent clinical trials, a novel 0.454% stannous fluoride/sodium hexametaphosphate dentifrice (Crest® Pro-Health™) showed comparable extrinsic stain removal compared to a positive control whitening dentifrice (Colgate® Total® + 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 pre-existing natural extrinsic stain.

MATERIALS AND METHODS

- Crest® Pro-Health™ (0.454% stannous fluoride/sodium hexametaphosphate; SnF₂/SHMP) was compared to a positive control whitening dentifrice (Colgate® Total® + Whitening), in two 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 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 re-examined.

RESULTS

- 29 subjects (15 in the SnF₂/SHMP 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 SnF₂/SHMP group and the control group, respectively, in Study 1; and 96.6% and 94.4% for the SnF₂/SHMP 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

<table>
<thead>
<tr>
<th>Dentifrice</th>
<th>Baseline Mean (SD)</th>
<th>2-week adjusted change mean (SE)</th>
<th>Comparison to baseline P-values</th>
<th>2-week between treatment P-values</th>
<th>Median % stain removal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive Control</td>
<td>1.65 (0.538)</td>
<td>0.94 (0.080)</td>
<td>&lt;0.0001</td>
<td>0.929</td>
<td>61.9</td>
</tr>
<tr>
<td>SnF₂/SHMP</td>
<td>1.56 (0.406)</td>
<td>0.95 (0.087)</td>
<td>&lt;0.0001</td>
<td>61.8</td>
<td></td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Dentifrice</th>
<th>Baseline Mean (SD)</th>
<th>2-week adjusted change mean (SE)</th>
<th>Comparison to baseline P-values</th>
<th>2-week between treatment P-values</th>
<th>Median % stain removal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive Control</td>
<td>2.64 (1.000)</td>
<td>2.60 (1.044)</td>
<td>&lt;0.0001</td>
<td>0.761</td>
<td>94.4</td>
</tr>
<tr>
<td>SnF₂/SHMP</td>
<td>2.95 (1.166)</td>
<td>2.61 (1.044)</td>
<td>&lt;0.0001</td>
<td>96.6</td>
<td></td>
</tr>
</tbody>
</table>

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Extrinsic Whitening Effects of Sodium Hexametaphosphate – A Review Including a Dentifrice with Stabilized Stannous Fluoride

CONCLUSION
• This is a review of clinical and laboratory data demonstrating the whitening benefits of sodium hexametaphosphate in three formulations: 1) sodium hexametaphosphate and sodium fluoride dentifrice; 2) sodium hexametaphosphate chewing gum; and 3) sodium hexametaphosphate and stabilized stannous fluoride dentifrice (Crest® Pro-Health™).

OBJECTIVE
To review data from clinical and laboratory studies that demonstrate the extrinsic whitening benefits of sodium hexametaphosphate in three formulations.

MATERIALS AND METHODS
• Background: Ingredients commonly used in oral care products to control stain are peroxide, abrasives and chemical agents. An advanced chemical agent is sodium hexametaphosphate, a long-chain condensed phosphate, which chemically removes existing surface discoloration and gives long-lasting inhibition of adsorption of new-stain chromogens.

• Sodium hexametaphosphate and sodium fluoride dentifrice: Laboratory studies have shown the chemical actions of the dentifrice in prevention and removal of tea stains, and the inhibition of stain induced by chlorhexidine and tea. Six-month clinical studies have shown the benefits using the Crest® Pro-Health™.

• Sodium hexametaphosphate and stabilized stannous fluoride dentifrice: In vitro studies demonstrated the stain control benefits of Crest® Pro-Health™ using a hydroxyapatite-powder stain model and prevention of tea-stain deposition onto hydroxyapatite. In two 6-month clinical studies using Crest® Pro-Health™ and a practice-based evaluation, no extrinsic tooth staining has been associated with extended use of this dentifrice.

Full text available in the Research Database at www.dentalcare.com


Extrinsic Stain Removal Efficacy of a 0.454% Stannous Fluoride Dentifrice

CONCLUSION
• The research demonstrated a comparable extrinsic stain removal efficacy of the stannous fluoride dentifrice with sodium hexametaphosphate (Crest® Pro-Health™) relative to the positive control dentifrice.

OBJECTIVE
To evaluate the extrinsic stain removal benefit of a 0.454% stannous fluoride (SnF₆)₂/sodium hexametaphosphate containing dentifrice (Crest® Pro-Health™).

MATERIALS AND METHODS
• This was a 6-week, parallel groups, double-blind, randomized and controlled clinical trial in which the SnF₆ dentifrice was compared with a positive control (Colgate® Total® Plus Whitening).

• A total of 60 healthy adults with visible natural stain of the facial surfaces on 4 of the 6 maxillary anterior teeth were enrolled into the study.

• Following baseline examination, subjects were randomly assigned to one of the two treatment groups based on baseline Lobene composite scores and gender. Subjects brushed at least twice daily as they normally would for 6 weeks.

• Clinical examinations including extrinsic stain evaluation and oral soft/hard tissue examination were conducted at baseline, week 3 and week 6. An experienced dental examiner using Lobene stain index evaluated extrinsic stain.

• The Baseline to post-treatment average 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.

RESULTS
• Of the 60 subjects who were randomized to treatment, 58 completed the study.

• Both of the treatment groups provided statistically significant extrinsic stain removal at both Week 3 and Week 6 relative to Baseline (p < 0.0001).

• The percent of Lobene composite scores with a greater than 0.5 unit reduction from Baseline was 81% at Week 3 and 97% at Week 6 for the SnF₆ dentifrice group.

• There was no statistically significant difference between the two treatment groups (p > 0.5). All test products were well tolerated.

Full text available in the Research Database at www.dentalcare.com

Extrinsic Whitening Effects of Sodium Hexametaphosphate – A Review Including a Dentifrice with Stabilized Stannous Fluoride

RESULTS

- The review presented laboratory and clinical data that demonstrated the benefits of sodium hexametaphosphate in controlling extrinsic stain in dentifrice with sodium fluoride, dentifrice with stabilized stannous fluoride and in chewing gum formulations.

CONCLUSION

- Under laboratory conditions, a sodium hexametaphosphate dentifrice produced superior stain prevention to commercially available dentifrices.

OBJECTIVE

To develop laboratory studies to evaluate the actions of the chemical components of dentifrices in non-abrasive prevention and removal of tea stains.

MATERIALS AND METHODS

- 12 commercially available dentifrices were tested including one hexametaphosphate toothpaste (Crest® Dual Action Whitening).
- Hydroxyapatite (HAP) powders were used as model surfaces to study the adsorption and desorption activities of chromogen attachment, retention and curing during stain formation.
- Powder models were developed for the evaluation of the whitening actions of dentifrices: Powder Stain Prevention Model (PSPM) and Powder Stain Removal Model (PSRM).
- PSPM: HAP powder was pre-treated with toothpaste supernates before testing resistance to post-treatment adsorption of tea extracts. Quantitative color testing was measured by colorimeter and qualitative results photographically.
- PSRM: Pre-stained and dried HAP powder was exposed to the supernatants of dentifrice slurry. Changes in the color of powders were compared as before.
- An in vitro cycling model was developed, using synthetic enamel chips, to test the chemical effects of toothpastes on stain in the presence of salivary pellicle. Chips were rotated in pooled human saliva for four hours to promote pellicle formation. After drying overnight, chips were exposed to cycles of treatment with saliva, toothpaste slurry, 0.12% chlorhexidine and tea, in specified strengths and order/time sequences over 4 days. Color readings were taken by chromameter.


Laboratory Studies on the Chemical Whitening Effects of a Sodium Hexametaphosphate Dentifrice
**Laboratory Studies on the Chemical Whitening Effects of a Sodium Hexametaphosphate Dentifrice**

**RESULTS**
- **Stain removal and prevention** – apatite powder studies: HAP powdertreated with sodium hexametaphosphate-containing dentifrice prevented tea stain deposition almost completely. Similarly, the sodium hexametaphosphate dentifrice almost completely removed the tea stains from the HAP powder.
- **In vitro cycle model** – synthetic enamel chip studies: sodium hexametaphosphate was shown to be a strongly chemically active agent for stain prevention.

**Stain Prevention Results from Laboratory Studies**

![Graph showing Stain Prevention Results from Laboratory Studies]

Treatments are statistically different p<0.05. Additional data reported in paper (Table IV).

**Hexametaphosphate Dentifrice Effects Pellicle Conditioning Films**

**CONCLUSION**
- Hexametaphosphate dentifrice produced pellicles with decreased thickness lasting 8 h following topical intervention. Surface phosphate was increased in hexametaphosphate treatment as was surface calcium. Hexametaphosphate dentifrice modulation of conditioning films lasts for periods up to 8 hours.

**OBJECTIVE**
Hexametaphosphate (HMP) is added to dentifrices as a calcium phosphate surface active builder to provide conditioning, tartar control and whitening benefits. In these studies duration of HMP dentifrice effects on pellicle coated surfaces was assessed using surface energy and X-ray photoelectron spectroscopy (XPS) methodologies.

**MATERIALS AND METHODS**
- Bovine enamel blocks were sectioned and mounted in methacrylate. Surfaces were serially polished to 0.3 mm to a mirror finish prior to testing.
- For all experiments, pellicle conditioning films were prepared by 16 h immersion of specimens in reconstituted saliva. To simulate effects of treatments on conditioning film thickness, an overnight pellicle coated enamel was examined in a cycling protocol.
- Pellicle coated surfaces were dipped – soaked 25% w/w dentifrice slurries for periods of 2 or 5 min (film thickness studies) in dentifrice: Crest® Cavity Protection – non HMP; Crest® Vivid White™ Night – HMP (non treated were not soaked) and then re immersed in reconstituted saliva 8 full hours.
- Specimens were then removed for film thickness and composition analysis. The effects of treatments on conditioning film thicknesses and chemical composition were examined by XPS.

Hexametaphosphate Dentifrice Effects Pellicle Conditioning Films

RESULTS

• Pellicle conditioning film thicknesses were significantly reduced by HMP dentifrice as compared with Crest® Cavity Protection and non-treated controls (nm ± SD)= 3.23(0.65)a:3.90(0.43)b:3.95(0.52)b and surface calcium and phosphate increased (%± SD) calcium = 1.88(0.67)a: 1.12(0.33)b: 0.72(0.63)b and phosphorus = 1.90(0.75)a: 1.04(0.71)b: 0.80(0.70)b (a=b p < 0.05 Students t).

Hexametaphosphate Effects on Tooth Surface Conditioning Film Chemistry – In Vitro and In Vivo Studies

CONCLUSION

• Sodium hexametaphosphate dentifrice produced stronger and more durable effects on surface film chemistry than pyrophosphate or polymeric-based dentifrices.

OBJECTIVE

To examine the effects of a sodium hexametaphosphate dentifrice, compared to other commercially available toothpastes, on the surface chemistry of conditioning film-coated dental enamel in vitro and in vivo.

MATERIALS AND METHODS

• Tested products: a sodium hexametaphosphate dentifrice (Crest® Dual Action Whitening), and 6 commercially available fluoride dentifrices, three with and three without an anticariogenic agent.

• In vitro studies on tooth surface conditioning films: to examine dentifrice effects on film thickness, surface energy, and zeta potential, and recovery of pellicle conditioning films following treatment. Pellicle films were prepared by immersing enamel blocks in reconstituted, pooled saliva for 16 hours. Blocks were then treated with dentifrices by brushing or dipping; dipping simulates exposure of inaccessible, interproximal areas to the chemical-only actions of dentifrice slurry. Enamel surfaces were assessed for rates and differences in reacquisition of salivary conditioning film and for surface energy. Zeta potential, effects on surface charge of enamel, was analysed on powdered enamel – from human teeth – that had been exposed to reconstituted saliva for 16 hours to prepare dental pellicles, and then treated for one minute with dentifrice water supernates.

• In vivo studies on surface wetting: to determine whether dentifrice use alters the ability to wet intraoral surfaces after repeated use. At the beginning of each 3-4 day test period, participants followed a prescribed cleaning regimen to achieve common levels of oral cleanliness. Participants then brushed twice a day with their assigned dentifrice. Surface conditioning film was measured on 3 separate days: pre-morning hygiene, post-morning brushing, pre-lunch a.m., and post-lunch mid-afternoon.

Comparative Clinical Effectiveness of Two Dual-Phase Whitening Dentifrices


CONCLUSION
• In this meta-analysis of two dual phase whitening dentifrices, only the whitening dentifrice without peroxide showed a significant reduction in yellowness after 14 days use.

OBJECTIVE
Clinical research was conducted to compare the effectiveness of two dual-phase whitening dentifrices.

MATERIALS AND METHODS
• Two clinical trials were conducted at different centers under the direction of different investigators, in order to compare the clinical response seen with dual phase whitening dentifrices.
• Subjects were randomized to Colgate® Simply White® Advanced Whitening Toothpaste, a dual phase dentifrice with 1% hydrogen peroxide and manganese gluconate as an activator, or Crest® Vivid White™, a dual phase dentifrice without peroxide or manganese gluconate. Subjects were provided the manufacturers’ instructions for use.
• In each trial, whitening was measured objectively on the maxillary teeth via digital image analysis using well-established and standard methods for \( L^* a^* b^* \) color change. A meta-analysis was conducted using the pooled raw data from the two clinical trials.


Hexametaphosphate Effects on Tooth Surface Conditioning Film Chemistry – In Vitro and In Vivo Studies

RESULTS
• Conditioning films were sensitive to mechanical and chemical actions. Toothbrushing with dentifrice (abrasive/chemical action) produced similar results amongst the products, removing on average 70-80% of film.
• Dipping (chemical action only) produced more varied results with dentifrices containing pyrophosphate and hexametaphosphate producing the greatest effects of 60-75%.
• Conditioning film-coated enamel produced a negative zeta potential. Generally, dentifrice treatment slightly decreased zeta potential. Enamel surfaces treated with polymers produced the greater decreases, whilst hexametaphosphate dentifrice produced a further decrease.
• Compared to control dentifrices, the hexametaphosphate dentifrice was found to have lower water contact angles (i.e. produced surfaces that were more hydrophilic) in vivo during toothpaste use.
• Collectively, results show hexametaphosphate acts to desorb conditioning films, influencing processes such as calculus development and stain development.
Comparative Clinical Effectiveness of Two Dual-Phase Whitening Dentifrices

RESULTS

- A total of 54 healthy adults were randomized to peroxide or no-peroxide dentifrices.
- After 2 weeks, the adjusted mean (SE) for $\Delta b^*$ (yellowness) was -0.13 (0.078) for the peroxide group, and -0.20 (0.075) for the no-peroxide group. Only the no-peroxide group differed significantly ($p = 0.011$) from baseline.
- Results were generally similar for $\Delta L^*$, with adjusted means (SE) of 0.04 (0.094) and 0.14 (0.090) in the peroxide and no-peroxide groups, respectively. While the no-peroxide group showed directionally better whitening, groups did not differ significantly.
- Both dentifrices were well tolerated over the 14-day treatment period.

Removal of Extrinsic Stain Using a 7.0% Sodium Hexametaphosphate Dentifrice: A Randomized Clinical Trial

CONCLUSION

- Sodium hexametaphosphate dentifrice produced significant reductions in composite stain in both the gingival and body tooth areas compared to a sodium fluoride control dentifrice at 3 and 6 weeks.

OBJECTIVE

To assess the whitening effects of a sodium hexametaphosphate dentifrice on existing extrinsic stain using a stain-induction model.

MATERIALS AND METHODS

- Healthy subjects with 16 natural teeth, with 7 of 8 gradable incisors, were eligible for this 9-week study with a pre-treatment phase followed by a treatment phase.
- Pre-treatment: This comprised a 3-week stain induction regimen with chlorhexidine and tea to promote extrinsic stain on the incisors. Subjects were provided with a low abrasive 0.243% sodium fluoride dentifrice and instructed on oral hygiene and rinsing for this time period: 30 seconds brushing on the lingual and facial surfaces of the anterior teeth with water; remaining teeth then brushed with the supplied dentifrice for 30 seconds; after a.m. brushing and at midday, subjects rinsed with 15 ml of a double-strength brewed tea and tap water solution for 60 seconds, and after p.m. brushing with 15 ml 0.12% chlorhexidine gluconate for 30 seconds, and then again, after expectorating, with the tea solution for a further 60 seconds.
- Baseline extrinsic stain was measured on both the facial and lingual surfaces, further divided into gingival and body regions, of each tooth. Stain was measured for intensity (0-3) and area (0-3) using the Lobene index. Composite scores were calculated (intensity x area).
- Treatment: Subjects with measurable extrinsic stain were randomized to a 0.243% sodium fluoride experimental dentifrice containing 7% sodium hexametaphosphate or a 0.243% sodium fluoride negative control dentifrice for a 6-week treatment period. Subjects brushed twice daily for one minute, including 30 seconds on the facial and lingual surfaces of the anterior teeth. Extrinsic stain was re-assessed at 3 and 6 weeks to evaluate short- and long-term whitening.
- Oral soft tissue examinations took place at each visit.

Removal of Extrinsic Stain Using a 7.0% Sodium Hexametaphosphate Dentifrice: A Randomized Clinical Trial

RESULTS

- 94 subjects were randomized to the experimental sodium hexametaphosphate group and 88 subjects were randomized to the control group.
- The group using sodium hexametaphosphate whitening dentifrice showed statistically significantly lower stain scores on the Lobene index for all measures (composite, area and intensity) than the control group at both 3 and 6 weeks (P <0.04); at 6 weeks, composite, area and intensity stain scores were reduced by 29%, 25% and 24%, respectively.
- Significant stain reduction was seen at 3 and 6 weeks for the sodium hexametaphosphate dentifrice relative to the control dentifrice for all gingival margin stain measures (P <0.04); for composite tooth body stain (P <0.04) at 3 and 6 weeks; and for tooth body stain area at 6 weeks (P = 0.04).

Week 6 Stain Reduction: sodium hexametaphosphate dentifrice benefit over control

Extrinsic Stain Prevention with a Combination Dentifrice Containing Calcium Phosphate Surface Active Builders Compared to Two Marketed Controls

CONCLUSION

- The sodium hexametaphosphate dentifrice significantly (p<0.05) reduced stain area (30%) and composite stain (33%) compared to control following 3 weeks treatment.

OBJECTIVE

To compare the stain reduction efficacy of an experimental whitening dentifrice relative to a marketed high-abrasive dentifrice and a marketed control dentifrice.

MATERIALS AND METHODS

- Treatments: 1) an experimental dual-phase whitening dentifrice containing 0.243% sodium fluoride, 3.5% hexametaphosphate and 1.25% soluble pyrophosphate; 2) a marketed high abrasive dentifrice containing 0.76% sodium monofluorophosphate; 3) a marketed control dentifrice containing 0.243% sodium fluoride.
- Generally healthy subjects with at least 7 natural incisors were enrolled in the 6-week study.
- Baseline stain levels were measured, prophylaxis given and subjects randomized to either the experimental dentifrice or one of the two marketed controls.
- At baseline, subjects started daily rinsing with 0.12% chlorhexidine gluconate and a double-strength tea solution to produce rapid staining. After morning brushing and at midday, subjects rinsed with 15 ml of tea solution for 60 seconds. After their evening oral hygiene, subjects rinsed with 15 ml 0.12% chlorhexidine gluconate for 30 seconds and, after expectorating, with the tea solution for a further 60 seconds.
- Subjects brushed twice daily for at least 60 seconds, including at least 30 seconds on the facial and lingual aspects of the anterior teeth. All toothbrushing with the assigned dentifrice was unsupervised.
- Extrinsic stain was measured at Weeks 3 and 6 on the facial and lingual surfaces of incisor teeth using the Lobene method to assess intensity (0-3) and area/extent (0-3). A composite stain score was calculated for each subject (an average of intensity x extent).
Extrinsic Whitening

Extrinsic Stain Removal with a Sodium Hexametaphosphate-Containing Dentifrice: Comparisons to Marketed Controls


CONCLUSION
- Sodium hexametaphosphate-containing dentifrice effectively removed extrinsic stain following 6 weeks of treatment, and was comparable to a more abrasive dentifrice.

OBJECTIVE
To compare chemical and mechanical stain removal of extrinsic tooth stain using a modified, rapid, clinical trial model.

MATERIALS AND METHODS
- Treatments were: 1) an experimental whitening dentifrice containing 0.243% sodium fluoride, 3.5% hexametaphosphate and 1.25% soluble pyrophosphate, and with a radioactive dentin abrasion (RDA) of 109; 2) a marketed higher abrasive (RDA of 145) dentifrice with aluminum oxide and 0.76% sodium monofluorophosphate; 3) a marketed lower abrasive (RDA of 95) control dentifrice with 0.243% sodium fluoride.
- 105 generally healthy subjects with at least 7 natural incisors were enrolled in a 9-week study.
- Subjects were given a prophylaxis before beginning an unsupervised 3-week stain induction regimen of limited brushing and rinsing with chlorhexidine and tea. Subjects were provided with a low abrasive 0.243% sodium fluoride dentifrice and instructed to brush twice daily. Instructions on rinsing and brushing were given throughout the induction phase.
- After induction, baseline extrinsic stain was measured for intensity (0-3) and extent (0-3) using the Lobene index.
- Subjects were randomly assigned to one of 3 dentifrice groups and instructed to brush all teeth for 60 seconds, including 30 seconds on anterior teeth, twice daily, using their assigned dentifrice.
- Stain removal efficacy – on the gingival and body areas of both the facial and lingual surfaces of each tooth – was measured at Weeks 3 and 6 using the Lobene method. Safety was also assessed at this time. A composite stain score was calculated for each subject (an average of intensity x extent).

RESULTS
- 96 subjects completed the study.
- Adjusted stain scores were highest in the control group and generally lowest in the sodium hexametaphosphate group at Weeks 3 and 6.
- At Week 3, the sodium hexametaphosphate group showed a 30% reduction in stain area, a 20% reduction in stain intensity, and a 33% composite stain reduction compared to the control group.
- At Week 6 findings were similar.
- The high-abrasive dentifrice appeared directionally superior to the control dentifrice at both Weeks 3 and 6, but the differences were not statistically significant.
- All three products were well tolerated.
Extrinsic Whitening effects of hexametaphosphate dentifrice on stain Removal and Calculus


**Conclusion**
- Hexametaphosphate is a strongly retained ingredient, showing stain loosening actions (with overnight wash out) and highly efficient inhibition of calculus mineralization in vitro. This supports clinical actions of Crest® Vivid White and Crest® Vivid White™ Night hexametaphosphate-containing dentifrices.

**Objective**
- In these studies the retentive actions of HMP on extrinsic stain removal and on prevention or calculus deposition were evaluated in specialized protocols in vitro.

**Materials and Methods**
- Bovine enamel blocks stained via the Stookey PCR method were pre-measured for CIELAB L* color and then cycled through a treatment sequence where they were chemically treated with water dentifrice supernates (treatments including Crest® Cavity Protection, CCP, control dentifrice or Crest® Vivid White Night – HMP containing dentifrice), immersed in saliva overnight, and then brushed in the morning with CCP (300 gm/50 strokes) in a V8 brushing machine after which color was re-measured.
- In a separate experiment the mPGM plaque mineralization biofilm model was used to assess HMP dentifrice efficacy as compared to CCP dentifrice with application frequencies of 1x/d and alternate days respectively.

**Results**
- Stained pellicle L* CIELAB significantly changed by 1.36(0.36)-CCP and 2.46(0.62)-CVWN showing that HMP dentifrice treatment loosened stains for removal (183 % increase) 8 hours after treatments.
- mPGM calculus % inhibition showed: CCP control (0); Crest® Tartar Control – pyrophosphate 29.8; Crest® Vivid White Night 1/2 treat – 54.0; Crest® Vivid White™ (standard vivid white) treatment – 69.5 (all mPGM different significantly @ p < 0.05).

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**Extrinsic Stain Removal with a Sodium Hexametaphosphate-Containing Dentifrice: Comparisons to Marketed Controls**

**Results**
- 94 subjects completed the study: 35 in the sodium hexametaphosphate group, 27 in the high abrasive group, 32 in the control group.
- At Weeks 3 and 6, subjects showed significant (P < 0.01) stain area reduction from baseline of 25.8% and 39.2%, respectively, using sodium hexametaphosphate dentifrice, and 33.7% and 32.7%, respectively, using the high abrasive dentifrice.
- At Week 6, significant reductions in stain intensity from baseline were seen for the sodium hexametaphosphate dentifrice (35.3%, P <0.01) and the high abrasive dentifrice (23.7%, P <0.05).

**Percent Stain Reduction Relative to Baseline**

- Significant reductions from baseline were also seen for composite stain at 6 weeks (P <0.01) with the sodium hexametaphosphate group showing 40.8% less stain and the high abrasive group 35.3% less.
- The low abrasive control dentifrice showed no significant reductions in stain at either timepoint.
- At 3 weeks, subjects using the sodium hexametaphosphate or high abrasive dentifrices showed statistically significant reductions in extrinsic stain area compared to control (p < 0.05), a 25% and 27% stain reduction, respectively.
- At 6 weeks only the sodium hexametaphosphate group showed a significant reduction in stain area (P = 0.023), or 29% benefit, compared to the control.
- There were no statistically significant differences between the three groups for stain intensity or composite stain at either timepoint.

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**Effects of Hexametaphosphate Dentifrice On Stain Removal and Calculus**

**Results**
- 94 subjects completed the study: 35 in the sodium hexametaphosphate group, 27 in the high abrasive group, 32 in the control group.
- At Weeks 3 and 6, subjects showed significant (P < 0.01) stain area reduction from baseline of 25.8% and 39.2%, respectively, using sodium hexametaphosphate dentifrice, and 33.7% and 32.7%, respectively, using the high abrasive dentifrice.
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**Significant reductions from baseline were also seen for composite stain at 6 weeks (P <0.01) with the sodium hexametaphosphate group showing 40.8% less stain and the high abrasive group 35.3% less.

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**At 6 weeks only the sodium hexametaphosphate group showed a significant reduction in stain area (P = 0.023), or 29% benefit, compared to the control.

**There were no statistically significant differences between the three groups for stain intensity or composite stain at either timepoint.**
Extrinsic Stain Removal Efficacy of a Dual-phase Dentifrice

CONCLUSION
• The research demonstrated the superior extrinsic stain removal efficacy of the dual-phase dentifrice with sodium hexametaphosphate relative to a negative control dentifrice.

OBJECTIVE
To evaluate the extrinsic stain removal benefit of a sodium hexametaphosphate containing dual-phase dentifrice.

MATERIALS AND METHODS
• This was a parallel groups, examiner-blind, randomized and controlled clinical trial in which the dual-phase dentifrice (Crest® Vivid White™) was compared with a negative control (Colgate® Cavity Protection).
• A total of 203 healthy adults with natural stain on their anterior teeth were enrolled into the study. Following baseline examination, subjects were randomly assigned to one of the two treatment groups based on baseline Lobene composite scores, smoking status (yes/no), tea/coffee consumption (yes/no), and gender.
• Subjects brushed twice daily, at least one minute every time (including 30 seconds on the facial and lingual surfaces of the anterior teeth) over 6 weeks. Clinical examinations including extrinsic stain evaluation and oral soft tissue examination were conducted at BL, week 3 and 6. Extrinsic stain removal was evaluated on the anterior teeth by dental examiners using Lobene stain index.

RESULTS
• Of the 200 subjects who were randomized to treatment, 195 were available for the 3-week examination and 193 subjects completed the study.
• The dual-phase dentifrice exhibited statistically significant (P<0.01) reduction in Lobene stain composite scores when compared to the negative control dentifrice at week 6. Adjusted mean Lobene composite reduction for the dual-phase dentifrice group (0.32) was twice as big as the negative control group (0.16).
• Change in Lobene stain extent (area) contributed primarily to the overall composite score reduction. Both examiners observed similar stain removal benefit for the dual-phase dentifrice. All test products were well tolerated over the 6-week treatment period.

Colgate® is a registered trademark of Colgate-Palmolive.

Stain Removal of Experimental Nighttime Dentifrice and Power Brush/Dentifrice Control

CONCLUSION
• Use of the daytime/nighttime dentifrice combination removed appreciable extrinsic stain, similar in magnitude to a sonic toothbrush plus regular dentifrice.

OBJECTIVE
This research was conducted to evaluate the clinical effectiveness of an experimental nighttime whitening dentifrice versus a marketed power brush with stain removal evidence as the study control.

MATERIALS AND METHODS
• A total of 30 generally healthy adults with visible extrinsic facial stain on 6 anterior teeth were randomly assigned to one of two regimens. The experimental group received a manual soft brush, a regular anticavity toothpaste (Crest® Cavity Protection) for the AM, and an experimental whitening dentifrice (Crest® Vivid White™ Night with sodium hexametaphosphate) for the PM. The control group received a power sonic toothbrush (Sonicare® Advance 4100) and the regular dentifrice for AM and PM. Subjects were instructed to brush twice daily for two minutes using the assigned regimen over a 14-day period. Stain area and intensity were measured using a standard index (Modified Lobene) at baseline, and after 7 & 14 days treatment.

RESULTS
• Mean (SD) age was 47.9 (13.12) years, and all subjects completed the 14-day study.
• The population presented with appreciable stain at baseline, with composite stain mean (SD) of 2.71 (0.554) and 2.76 (0.924) in the experimental and control groups, respectively. Both groups exhibited significant (p < 0.0001) stain reduction at Week 1. There was incremental stain removal from Week 1 to Week 2.
• At the end-of-treatment, median composite stain was 85% removed in the experimental group and 89% in the control. Groups did not differ significantly (p = 0.37) on Week 2 composite stain.
• Both regimens were well-tolerated.

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Extrinsic Whitening

KEY messages (continued)

• Consumers prefer less “yellow” and uniformity of color. They fall into 4
general groups based on “smile satisfaction/dissatisfaction”: following
dental prophylaxis, between prophylaxes, without prophylaxis, or after
bleaching treatment.

• There are 3 established agents for tooth whitening: bleaches, abrasives,
and chemicals.

  – Bleaches: most effective in producing maximum change. The consumer
and dental professionals commonly use hydrogen peroxide and
 carbamide peroxide (adduct of hydrogen peroxide and urea), available
as gels and strips, to remove extrinsic and intrinsic stain. But bleaching
has limitations, most particularly lack of stain prevention.

  – Abrasives: insoluble components of dentifrices that include metal oxides,
mineral salts, silica and pumice. They remove stain physically, but are
not as effective as bleaches, and are limited by affecting only extrinsic
stain, safety, and lack of applicability to some stain areas.

  – Chemicals: calcium phosphate surface active builders (CPSAB), a
phosphate group of molecules first incorporated into dentifrices in the
1980s as sodium pyrophosphate. They reduce dental calculus, which
acquires stain easily, and thus reduce stain. They also have inherent anti-
stain properties, but are limited in effectiveness due to desorption and
hydrolytic breakdown in the mouth.

• The limitations of pyrophosphate salts have been overcome by advanced
technology enabling the use of polymeric or condensed phosphates, such
as sodium hexametaphosphate, in dental formulations.

• A dual phase, sodium fluoride whitening dentifrice has been developed,
which incorporates sodium hexametaphosphate and has improved
and long-lasting anti-tartar, stain prevention and stain removal properties.
This special issue of The Journal of Clinical Dentistry® summarizes laboratory
and clinical evidence supporting these benefits.

CONCLUSION

• An advanced dual-phase whitening dentifrice with sodium
hexametaphosphate and sodium fluoride has been introduced to provide
significant benefits for whitening and calculus control.

OBJECTIVE

To introduce papers of clinical and laboratory studies showing the chemical
advantages of sodium hexametaphosphate.

KEY MESSAGES (continued)

• Since the 1950s, and the introduction of clinically proven fluoride in dental
formulations, dentifrices have become the preferred vehicle for delivering
agents to treat therapeutic and cosmetic oral conditions, such as caries,
gingivitis, dental plaque and calculus, and hypersensitivity.

• Therapeutic advances have been the major thrust of research in previous
decades, but cosmetic benefits have become a growing sector of research
and of increasing interest to the consumer.

• Tooth appearance is influenced by occlusion and color, and it is the latter
to which current research has been devoted.

• Tooth color is affected by internal and external properties. Internally,
dentin is generally a uniform shade, seen through the outer enamel.
It ranges through white, gray, yellow
or tan, but is affected by local
concentrations of chromogens that
produce yellow staining from food
stuffs such as tea or wine, or by
changes in translucence/reflectance.
Externally, discoloration is caused by
chromogen components adsorbed or
incorporated onto the tooth surface.


CONCLUSION

An advanced dual-phase whitening dentifrice with sodium
hexametaphosphate and sodium fluoride has been introduced to provide
significant benefits for whitening and calculus control.

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incorporated onto the tooth surface.
Calculus

Calc·u·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 sodium fluoride and formulations with stannous fluoride.

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

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 Crest® Pro-Health™ versus a positive control dentifrice.

MATERIALS AND METHODS
- Crest® Pro-Health™ (0.454% stabilized stannous fluoride/13% sodium hexametaphosphate) was compared to a marketed, tartar control 0.30% triclosan/0.243% sodium fluoride/2% Gantrez copolymer control dentifrice (Colgate® Total®).
- Study subjects were 81 adult participants with ability to form at least 1.5 mm of calculus on anterior mandibular teeth (lingual surfaces) in 8-week pre-test 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 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 stannous fluoride/sodium hexametaphosphate group than the triclosan/copolymer group at both Months 3 and 6 (p<0.0001).
- Compared to the triclosan/copolymer group, the stannous fluoride/sodium hexametaphosphate group showed a 54% reduction (adjusted means) in calculus accumulation at Month 3 and a 56% reduction at Month 6.
CONCLUSION

• The experimental dentifrice revealed significant anticalculus efficacy versus the control regardless of levels of baseline calculus formation.

OBJECTIVE

To compare the anticalculus efficacy of an experimental dentifrice (0.454% stabilized stannous fluoride/sodium hexametaphosphate) with a negative control (Crest® Cavity Protection, 0.243% sodium fluoride).

MATERIALS AND METHODS

• This was a randomized, examiner-blind, parallel group study.
• After a 3-month run-in, qualifying subjects were randomized to the experimental or control dentifrice to use twice a day for six months.
• Volpe-Manhold Index and oral soft tissue examinations were conducted at baseline, 3 and 6 months.
• Additional analyses were performed separately at 3 and 6 months on three subgroups categorized into high, medium, and low calculus-forming subjects.

RESULTS

• Compared to the control group, the experimental dentifrice group had a mean calculus score statistically significantly lower at both 3 months (50%) and 6 months (55%) post-treatment (p<0.001).
• Compared to control scores, mean experimental dentifrice calculus scores at 3 and 6 months were statistically significantly lower at both timepoints for the high, medium and low calculus forming sub-groups (p<0.001).
• Both products were generally well tolerated.
RESULTS (continued)

ResuLTs

Calculus anticalculus efficacy and safety of a novel Whitening dentifrice containing sodium hexametaphosphate: a Controlled six-month Clinical Trial


ConCLusI on

• The sodium hexametaphosphate dentifrice showed superior anticalculus efficacy and comparable safety results compared to a sodium fluoride/triclosan positive control dentifrice and a standard sodium fluoride negative control dentifrice.

OBJe CTIVe

To establish the anti-calculus efficacy and long-term safety of a new sodium hexametaphosphate dentifrice.

MAterials and methods

• A 7% sodium hexametaphosphate/0.243% sodium fluoride dentifrice was compared to two controls:
  - a 0.243% sodium fluoride dentifrice without an anticalculus agent
  - an anticalculus dentifrice with a 0.243% sodium fluoride/triclosan/copolymer

• Subjects were generally healthy and had at least 16 teeth, including at least 5 out of 6 lower anterior teeth.

• The study began with a 2-month pretest period to assess calculus formation after prophylaxis.

• Subjects who presented with sufficient calculus – Volpe-Manhold Calculus Index of 7 mm – were given another pretreatment prophylaxis and then randomly assigned to one of the 3 treatment groups.

• Subjects brushed their teeth unsupervised for at least one minute twice a day for 6 months.

• At 3 and 6 months of treatment, oral soft tissue was examined and calculus accumulation assessed.

• Calculus was measured on the lingual surfaces of the six anterior teeth using the Volpe-Manhold Index.

Adjusted mean Volpe-Manhold Index calculus scores: experimental (stannous fluoride/sodium hexametaphosphate) dentifrice versus negative control dentifrice. Figure courtesy of the Journal of Contemporary Dental Practice (www.thejcdp.com).
Anticalculus Efficacy and Safety of a Novel Whitening Dentifrice Containing Sodium Hexametaphosphate: A Controlled Six-Month Clinical Trial

RESULTS
- 551 subjects were assigned to one of the three treatment groups, and 532 and 523 were evaluated at 3 and 6 months, respectively.
- The calculus score for the sodium hexametaphosphate dentifrice was statistically significantly lower than both the control dentifrices at both timepoints, showing tartar reductions at Months 3 and 6 of 10% and 16%, respectively, compared to the triclosan/copolymer group, and 16% and 19%, respectively, compared to the sodium fluoride group.
- All products were well tolerated.

Conclusions
- Laboratory results showed that sodium hexametaphosphate dentifrice has excellent potential clinical activity in the prevention of supragingival calculus formation.

OBJECTIVE
To assess the anticalculus potential of a dual-action, whitening dentifrice containing sodium hexametaphosphate in the laboratory.

MATERIAL REVIEWED
- Products tested: a sodium hexametaphosphate anticalculus dentifrice (Crest® Dual Action Whitening), 3 marketed anticalculus products with proven clinical efficacy, and a conventional sodium fluoride negative control dentifrice (no anticalculus agent).
- Two calculus profile-testing methods were used:
  - pH stat mineralization inhibition assays: this technique showed the surface affinity for and adsorption properties of sodium hexametaphosphate to enamel surfaces, as well as its crystallization inhibition properties, by determining its effects on the mineralization reactions of hydroxyapatite (HAP). The technique also acts as an initial screen for the potential tartar control activity of an agent. Mineralization was conducted under 2 conditions: 1) hexametaphosphate was added directly to the mineralization solution; 2) to mimic toothbrushing exposure, minerals were pre-treated with hexametaphosphate dentifrice.
  - Plaque biofilm calcification model: dentifrices were tested on plaque grown from human saliva under conditions to promote mineralization, thus mimicking the known steps of dental calculus mineralization.

Results
- 551 subjects were assigned to one of the three treatment groups, and 532 and 523 were evaluated at 3 and 6 months, respectively.
- The calculus score for the sodium hexametaphosphate dentifrice was statistically significantly lower than both the control dentifrices at both timepoints, showing tartar reductions at Months 3 and 6 of 10% and 16%, respectively, compared to the triclosan/copolymer group, and 16% and 19%, respectively, compared to the sodium fluoride group.
- All products were well tolerated.
In Vitro Studies of the Anticalculus Efficacy of a Sodium Hexametaphosphate Whitening Dentifrice

RESULTS

- pH stat mineralization inhibition assays: hexametaphosphate in solution showed a strong affinity for HAP surfaces as well as good inhibitory activity of HAP crystal growth. HAP surfaces pretreated with a sodium hexametaphosphate dentifrice showed decreased mineralization. When hexametaphosphate was applied topically, the reduction was 69%.

- Plaque biofilm calcification model: plaque biofilm calcification was significantly inhibited when exposed to hexametaphosphate supernate treatment. Treatment with sodium hexametaphosphate dentifrice produced superior and statistically significant reductions in plaque mineralization compared to the other tested products.

Anticalculus Effects of a Novel, Dual-Phase Polypyrophosphate Dentifrice: Chemical Basis, Mechanism, and Clinical Response

CONCLUSION

- This is a description of the structure of sodium hexametaphosphate (also referred to as polypyrophosphate), its chemistry, the mechanism of calculus formation and inhibition, and the calculus control activity of sodium hexametaphosphate dentifrice.

OBJECTIVE

To review the anticalculus effects of a novel, dual-phase sodium hexametaphosphate/sodium fluoride dentifrice, including its chemistry and tartar control activity.

MATERIAL REVIEWED

- The prevalence of significant calculus formation approaches 90% in the population. Calculus is formed by the mineralization and coalescence of mineral within plaque, and removal can only readily be accomplished through professional scaling, often in areas difficult to visualize and/or access.

Photo courtesy of White and Gerlach, from the Journal of Contemporary Dental Practice.
Anticalculus Effects of a Novel, Dual-Phase Polypyrophosphate Dentifrice: Chemical Basis, Mechanism, and Clinical Response

Material Reviewed (continued)

- Calculus deposition may be readily prevented by topical application of various mineralization inhibitors such as those found in so-called “tartar control” toothpastes. Pyrophosphate is the first widely-marketed anticalculus ingredient. It binds to the mineral surface and disrupts the mineral building process. Sodium hexametaphosphate (polypyrophosphate) is an advanced form of pyrophosphate, having greater surface affinity than pyrophosphate and offering improved chemical stain control and anticalculus effects.

- In a preliminary 6-week clinical study two experimental sodium fluoride/sodium hexametaphosphate (7% and 9% sodium hexametaphosphate) dentifrices and a marketed sodium fluoride tartar control dentifrice containing 5% pyrophosphate were compared. Calculus scores (Volpe-Manhold Index) were reduced (11-19%) for the experimental groups compared to the control group.

Results of Review

- This review described the formation of calculus, the chemical structure and mechanism of action of pyrophosphate, and the advanced surface chemistry of sodium hexametaphosphate in the control of calculus.
- A preliminary clinical study demonstrating the superior calculus control efficacy of experimental sodium hexametaphosphate dentifrices compared with a marketed sodium fluoride tartar control dentifrice (containing 5% pyrophosphate) is described.

Breath Malodor

- Breath malodor is a common social concern. Most breath odor results from gram-negative anaerobic bacteria in the oral cavity, 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 Breath

- 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.


**Hydrogen Sulphide Production Inhibition**

*P&G data on file*

**CONCLUSION**

- Oral-B® Pro-Expert® was found to be more effective than the other treatments at inhibiting hydrogen sulphide production, which is linked with breath malodour, in this in-vitro test.

**OBJECTIVE**

Breath malodour can be a result of accumulation of gram negative anaerobe bacteria in the oral cavity, primarily on the tongue. When gram negative bacteria metabolise amino acids, volatile sulphur compounds, like hydrogen sulphide, are produced.1) The inhibition of these bacteria, minimises the amount of volatile sulphur compounds produced and therefore may result in a fresher breath.

**MATERIALS AND METHODS**

- Treatments tested: Oral-B® Pro-Expert® (SnF$_2$), Parodontax Fluoride (NaF), Meridol (AmF/SnF$_2$), Crest® Decay Prevention (NaF), Zendium Classic (NaF) and water.
- Dentifrice supernatants and lead acetate impregnated filter strips were added to concentrated saliva in sealed vials.
- Vials were incubated overnight at 37°C and visual assessment of presence of black precipitate (lead sulphide) was made for each treatment.

**RESULTS**

- Oral-B® Pro-Expert® showed superior prevention of hydrogen sulphide production compared to all other treatments assessed.

![Representative sample of 3 replica's](image)

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Black precipitate qualitative score for each replica (formation of Lead sulphide through reaction of hydrogen sulphide with lead acetate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zendium Classic (n=3)</td>
<td>++ / ++ / +++</td>
</tr>
<tr>
<td>Parodontax Fluoride (n=3)</td>
<td>++ / ++ / +++</td>
</tr>
<tr>
<td>Meridol (n=2)</td>
<td>++ / +++</td>
</tr>
<tr>
<td>Oral-B® Pro-Expert® (n=3)</td>
<td>0 / 0 / 0</td>
</tr>
<tr>
<td>Crest® Decay Prevention (n=3)</td>
<td>+++ / ++ / +++</td>
</tr>
<tr>
<td>Water – control (n=3)</td>
<td>*** / ++ / +++</td>
</tr>
</tbody>
</table>


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**Comparison of Breath Efficacy of Stannous Fluoride and Triclosan/Copolymer Dentifrice**


**CONCLUSION**

- This research demonstrates the ability of the 0.454% stabilized stannous fluoride dentifrice with sodium hexametaphosphate to deliver superior breath benefits relative to a triclosan/copolymer marketed control over 24 hours.

**OBJECTIVE**

This randomized and controlled, crossover clinical trial compared the breath protection effectiveness of 0.454% stabilized stannous fluoride (SnF$_2$) dentifrice with sodium hexametaphosphate to triclosan/copolymer marketed control dentifrice (Colgate® Total®) over 24 hours.

**MATERIALS AND METHODS**

- One hundred four healthy adult subjects were randomized to unique treatment sequences ordering use of the test dentifrices.
- Subjects brushed once in the morning and once at bedtime, with breath quality evaluated at 3 and 24 hours after initial dosing by monitoring of volatile sulfur compounds using a halimeter. A washout of 2-3 days followed.
- To better satisfy the assumptions of analysis of variance (ANOVA) and to reduce the influence of any extreme observations, the natural logarithm of total VSCs measured by a halimeter was analyzed.

**RESULTS**

- There were no statistically significant differences between the two dentifrices at 3 hours (p=0.34).
- The SnF$_2$ dentifrice provided significantly superior reductions in volatile sulfur compounds relative to the triclosan/copolymer marketed control over 24 hours (p<0.01).

Colgate® and Colgate® Total® are registered trademarks of the Colgate-Palmolive Company.
Effects of 0.454% SnF<sub>2</sub> Dentifrice on Daytime and Overnight Malodor

CONCLUSION

- The use of the 0.454% SnF<sub>2</sub> 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 day time and overnight oral malodor reduction benefit of a 0.454% SnF<sub>2</sub> therapeutic dentifrice with short-term and long-term use.

MATERIALS AND METHODS

- The study was a randomized, double-blinded, two-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 0.454% SnF<sub>2</sub> Crest® Pro-Health™ dentifrice (SnF<sub>2</sub> 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 wash-out 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 SnF<sub>2</sub> 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 SnF<sub>2</sub> and the control dentifrice, respectively. The mean daytime hedonic scores were 2.4 and 4.1 at Day 8 for the SnF<sub>2</sub> and the control dentifrice, respectively.
Oral Malodor Reduction with 3-week Use of 0.454% SnF₂ Dentifrice


CONCLUSION

• Three-week use of the 0.454% SnF₂ 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% SnF₂ therapeutic dentifrice on oral malodor.

MATERIALS AND METHODS

• The study was a randomized, double-blinded, two-treatment, parallel design clinical trial.
• After completing an acclimation period, 71 subjects with existing oral malodor were randomized to one of the two treatments: 0.454% SnF₂ Crest® Pro-Health™ dentifrice (SnF₂ 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 SnF₂ 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 SnF₂ dentifrice and the control dentifrice, respectively.
• Relative to the control, the use of the SnF₂ dentifrice resulted in significantly (p < 0.0001) greater reduction in oral malodor at both visits. Both treatments were well-tolerated.
**The Oral Malodor Efficacy of a 0.454% Stannous Fluoride Dentifrice**

**CONCLUSION**
- The present study demonstrated the safety and effectiveness of the 0.454% stannous fluoride dentifrice in the malodor control relative to a negative control.

**OBJECTIVE**
To compare the oral malodor protection efficacy of a 0.454% stannous fluoride dentifrice versus a negative control (0.243% sodium fluoride) using Halimeter as the measurement.

**MATERIALS AND METHODS**
- This was a 4 treatment, 5 periods, examiner-blinded, cross-over and randomized study design.
- Healthy subjects who met the entrance criteria were enrolled into the study. After baseline halimeter measurement, subjects were randomly assigned to one of the four treatments (SnF$_2$ dentifrice groups, with or without tongue brushing; negative control dentifrice groups, with or without tongue brushing) based on baseline halimeter scores, age, and gender. Test products were used three times a day.
- Breath measurement was taken 24 hours after baseline the next day morning, followed by a product treatment. Final breath measurement was taken four hours post-treatment that was 28 hours after baseline.

**RESULTS**
- Thirty-three subjects were enrolled and completed the study.
- The adjusted mean volatile sulfur compound (VSC) levels were significantly lower in the SnF$_2$ groups than the NaF groups, at both 24 (p<0.01) and 28 (p<0.001) hours post baseline time points.
- Tongue brushing did not provide additional statistically significant breath benefits when compared to toothbrushing alone.
- Both dentifrices were well tolerated.


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**Short-Term Breath Efficacy of Stannous Fluoride Dentifrice**

**CONCLUSION**
- Results from this trial demonstrate the ability of the experimental 0.454% stabilized stannous fluoride dentifrice with sodium hexametaphosphate to deliver superior breath benefits relative to a sodium fluoride negative control, both throughout the day and overnight using both halimeter and organoleptic breath measurements.

**OBJECTIVE**
This randomized and controlled, crossover clinical trial compared the breath protection effectiveness of an experimental 0.454% stabilized stannous fluoride (SnF$_2$) dentifrice with sodium hexa-metaphosphate to that of 0.243% sodium fluoride (NaF) negative control dentifrice over 24 hours.

**MATERIALS AND METHODS**
- Twenty-nine healthy adult subjects were randomized to unique treatment sequences ordering use of the test dentifrices and three toothbrushing regimens (toothbrushing, toothbrushing plus controlled rinsing, toothbrushing plus tongue brushing).
- Subjects brushed once in the morning and once at bedtime, with breath quality evaluated at 1.5, 3, 8 and 24 hours after initial dosing by monitoring of volatile sulfur compounds (VSCs) using a halimeter and second-person organoleptic grading. A washout of 2-3 days followed.
- The natural logarithm of total VSCs measured by a halimeter and the organoleptic assessments by a panel of four judges was analyzed. For both endpoints, analysis of covariance was used to assess both product and regimen effects.

**RESULTS**
- The SnF$_2$ dentifrice provided significantly superior reductions in volatile sulfur compounds relative to the NaF negative control when measured via a halimeter at every assessment (p < 0.02) over 24 hours, regardless of brushing regimen used.
- The SnF$_2$ dentifrice also demonstrated statistically significant reductions in organoleptic scores when compared to the NaF negative control over 8 hours (p<0.02), regardless of brushing regimen. However, at 24 hours, the difference between products measured by the odor judges was dependent upon the regimen.

Short-Term Breath Efficacy of Stannous Fluoride Dentifrice

RESULTS (continued)
- Subjects using the tongue brushing regimen showed a statistically significant benefit for the SnF₂ dentifrice versus the NaF negative control (p<0.05).

Long-Term Breath Efficacy of Stannous Fluoride Dentifrice

CONCLUSION
- This research demonstrates the ability of the experimental 0.454% stabilized stannous fluoride dentifrice with sodium hexametaphosphate to deliver superior breath benefits relative to the sodium fluoride negative control by monitoring of volatile sulfur compounds and microbial populations over a 4 week usage period.

OBJECTIVE
This randomized and controlled, blinded, 2-period crossover clinical trial was conducted to assess cumulative breath benefits with twice daily use of an experimental 0.454% stabilized stannous fluoride (SnF₂) dentifrice with sodium hexametaphosphate relative to 0.243% sodium fluoride (NaF) negative control dentifrice over a 4-week period.

MATERIALS AND METHODS
- Twenty healthy adult subjects were randomly assigned to one of two sequences specifying the order of use of the test dentifrices for each of the 4-week treatment periods.
- Oral malodor was measured using a halimeter to monitor volatile sulfur compounds (VSCs) at Hour 0, and again at 3 and 8 hours post-brushing on Visit Days 0, 7, 14, 21 and 28 of each treatment period.
- Gingival microbial sampling to quantitate total facultative anaerobes and Gram-negative anaerobes was conducted at Hour 0, 3 and 8 hours on Day 0, 7, 14 and 28. A 1-week washout period was scheduled between periods.
- All VSC data and mean log10 cfus for the microbial populations generated at individual time points were evaluated via analysis of covariance (ANCOVA). Trends over time were assessed using a mixed model Analysis of Variance. All comparisons were tested using a two-sided 0.10 level of significance.

RESULTS
- The SnF₂ dentifrice provided significantly superior reductions in VSCs relative to the NaF negative control with a statistically significant trend for the 8 hour time points to decrease over 4 weeks for the SnF₂ dentifrice (p<0.01).
- The mean number of total facultative anaerobes and Gram-negative anaerobes for the SnF₂ dentifrice were statistically significantly lower than the NaF negative control by 4 weeks (p<0.01).
Breath: A Comparison of Breath Efficacy and Antimicrobial Efficacies of Various Antimicrobial Systems Present in Commercial Dental Products


CONCLUSION

- Based on their overall efficacy profile, this study suggests that the rank order in potency of the various antimicrobial systems present in commercial dental products is: chlorhexidine > SnF₂ > triclosan ≥ essential oils.

OBJECTIVE

The purpose of this study was to profile and compare the breath, germ kill, and anti-inflammatory properties of several different anti-microbial systems used in commercial dental products in an acute use human trial.

MATERIALS AND METHODS

- 18 volunteers participated in a single blind, randomized, Latin square crossover, negative-controlled, clinical trial. There were 9 treatment legs in total; 5 legs had commercial products while 4 were experimental products (results not reported here).
- The commercial products tested and their respective antimicrobial systems were:
  - Crest® Cavity Protection (negative control)
  - Colgate® Total® (triclosan)
  - Listerine Essential Care® (essential oils)
  - Crest® Gum Care (SnF₂)
  - Peridex® (chlorhexidine).
- Subjects treated themselves three times over a single day – morning, afternoon, and bedtime – brushing with their assigned dentifrice for 1 minute or rinsing with their assigned mouth rinse for 30 seconds. Prior to treatments, baseline measures were taken followed the next day by final measures.
- Subjects were measured primarily for breath status (morning breath and cysteine challenge) and total facultative and gram-negative anaerobes present on tongue, along gum line, and within a gingival pocket, and, secondarily, for sub-gingival IL1-ß levels.
Breath Effects of Three Marketed Dentifrices: A Comparative Study Evaluating Single and Cumulative Use

RESULTS

- Products containing either chlorhexidine or SnF2 provided significant (one-sided p<0.05) mean reductions versus the negative control across nearly all primary measures.
- Overall, reductions observed with chlorhexidine were generally greater than those seen with the SnF2 system.
- The triclosan-containing product generated a significant mean reduction in one primary measure—sub-gingival, total facultative anaerobes.
- The essential oils antimicrobial system produced no significant reductions in any measure.
- Only chlorhexidine and SnF2 systems produced directional (sig. at p<0.15) reductions in IL1-ß levels.

CONCLUSION

- This study demonstrates the comparative breath efficacy of three dentifrices using a clinical model that may prove relevant for other dentifrice clinical trials.

OBJECTIVE

To evaluate the effects of three dentifrices on breath malodor using organoleptic grading and halimeter measurements.

MATERIALS AND METHODS

This was a randomized, examiner blind, parallel group study. 384 healthy adults with oral malodor were randomized to 1 of 4 brushing groups:

- antimicrobial dentifrice with 0.45% stannous fluoride;
- antitartar dentifrice with 0.243% sodium fluoride and 5% pyrophosphate;
- antimicrobial dentifrice with 0.24% sodium fluoride and 0.30% triclosan/copolymer.
- negative control, bottled distilled water.

Breath odor was measured over a five-day period using second-person organoleptic grading and measurement of volatile sulfur levels.

RESULTS

- Following treatment, adjusted mean organoleptic scores and volatile sulfur levels were lowest for the stannous fluoride dentifrice group, with this group exhibiting superior breath quality compared to the negative control at three hours after a single brushing, and again at all cumulative use time points.
- While all test dentifrices showed some activity, only stannous fluoride had a second-person (organoleptic) breath benefit.
- Breath effects for the other two dentifrices were limited to reductions in volatile sulfur levels at hours 99 and 104 for the antitartar sodium fluoride pyrophosphate dentifrice, and at hour 99 only for the antimicrobial sodium fluoride triclosan/copolymer dentifrice.

A Novel Dentifrice Technology for Advanced Oral Health Protection: A Review of Technical and Clinical Data on Stabilized Stannous Fluoride and Sodium Hexametaphosphate Dentifrice

Full text available in the Research Database at www.dentalcare.com


CONCLUSION

• This is a review of clinical and laboratory data for Crest® Pro-Health™ to support claims of multiple benefits: antibacterial, antiplaque, antgingivitis, antihyponsensitivity, anticaries, anticalculus, and whitening.

REVIEW

• Globally, dentifrice plays an important role in good oral hygiene. Toothpastes aid in general cleaning and also serve as an excellent vehicle for delivery of agents that deliver therapeutic and cosmetic benefits.

• Key examples of using dentifrice to provide added benefits include the introduction of the first fluoridated toothpaste clinically proven to fight caries in 1955 (Crest® Cavity Protection) and the launch of the first tartar control dentifrice (Crest® Tartar Control) in the mid-1980’s.

• Numerous agents have been evaluated during the last three decades. The multi-benefit segment has been a focus area, which is very popular among U.S. consumers.
Other Topics

Practice-Based Evaluation of a Stannous Fluoride-Sodium Hexametaphosphate Dentifrice

KEY RESULTS/CONCLUSIONS

- Crest® Pro-Health™ showed excellent patient and professional acceptance as well as noticeable oral health improvements. These factors are important in driving compliance.

- In this practice-based study, nearly 7 of 10 dental professionals observed improvements in their patients’ oral health and two-thirds of patients intended to continue using Crest® Pro-Health™ following the extended use evaluation.

OBJECTIVE

To evaluate the professional observations of dentists/hygienists and the personal experience of patients based on their use of Crest® Pro-Health™ toothpaste over an extended period.

MATERIALS AND METHODS

- Dentists/hygienists across the US were invited to participate in the study. Enough Crest® Pro-Health™ samples were provided to supply a small group of patients for 3-4 months.

- Dental professionals assessed their patients’ oral health status at the beginning of the evaluation and at their return visit. Conditions included gingival bleeding, inflammation, calculus, extrinsic stain and sensitivity.

- Patients completed a questionnaire at their return visit.

RESULTS

- 1267 surveys were collected from dentists/hygienists and 1078 from patients.

- Approximately 75% of evaluations were based on 3-4 months of use. The remaining patients used the product up to 6 months.

- Specific responses analyzed were those where,
  (i) dentists/hygienists provided pre- and post-oral health assessments and gave answers to questions, and
  (ii) patients rated the product overall and gave answers to questions.

Professional Responses

- Two-thirds of all professionals observed improvement in their patients’ oral condition after the trial period. Specific improvements include:
  - gingival bleeding
  - gingival inflammation
  - calculus formation

- Improvement was also noted by 61% of professionals for sensitivity and 57% of professionals for staining.

- 91% of professionals who observed improvement would recommend Crest® Pro-Health™.

- Overall, 8 in 10 professionals said they would recommend Crest® Pro-Health™.
RESULTS (continued)

Patient Opinion
- 88% of patients rated Crest® Pro-Health™ positively (Excellent/Very Good/Good).
- 77% of trial participants who had noticeable improvements in their oral health intended to continue using Crest® Pro-Health™. Two-thirds of all patients in the evaluation intended to continue using Crest® Pro-Health™.
- Roughly 9 of 10 patients rated Crest® Pro-Health™ positively for “keeping mouth healthy”, “cleaning teeth thoroughly”, being a “comprehensive toothpaste”, making “gums healthier” and “freshening breath”.
- 8 of 10 subjects rated Crest® Pro-Health™ positively for reducing surface stains and gingival bleeding.

CLINICAL COMMENT
Crest® Pro-Health™ is a unique dentifrice formulation combining stannous fluoride and sodium hexa-metaphosphate. Stannous fluoride is an antibacterial fluoride that helps protect against plaque, gingivitis, caries and dentinal hypersensitivity. Sodium hexametaphosphate is an advanced whitening and anticalculus agent. In rigorous clinical trials, the stannous fluoride-sodium hexametaphosphate dentifrice technology has demonstrated statistically significant improvements for a broad range of conditions, such as gingival bleeding, gingival inflammation, tooth sensitivity, extrinsic stain formation, and supragingival calculus. Findings from this large, practice-based assessment complement the clinical results. In combination, the clinical data and practice-based evaluations provide sound evidence for incorporating Crest® Pro-Health™ in patients’ daily oral hygiene regimen.

Percentages of professionals indicating they would recommend Crest® Pro-Health™ and percentage of patients who rated Crest® Pro-Health™ positively (good/very good/excellent)

CONCLUSION
- Methods have been developed to stabilize stannous fluoride (SnF₂) in dentifrice formulations. Clinical trials have shown that stabilized SnF₂ markedly reduces gingivitis and has antibacterial effects that are additional to those of fluoride.

OBJECTIVE
To examine the methods of stabilizing SnF₂, present evidence of its antibacterial properties, review the proposed mechanisms for these effects, and discuss the clinical factors important for maximizing the antimicrobial properties of SnF₂.

KEY MESSAGES
- Stability and biological activity of SnF₂: manufacturers have developed techniques to stabilize SnF₂ for prolonged time periods in aqueous dentifrice formulations. Chelating agents are used that bind stannous fluoride; stannous reservoirs act as a stannous ion supply and as an antioxidant.
- Antiplaque and antigingivitis properties of SnF₂: most studies have found that stabilized SnF₂ has anti-plaque effects; marked effects on gingivitis have been reported. Most often, SnF₂ has been used twice daily at concentrations between 0.1 and 0.45%.
- Anticaries effects: SnF₂ has been reported to reduce the bacterial groups that cause dental caries, but mainly when used twice daily at a concentration of 0.4%.
- Mechanism of action: Fluoride compounds are known to foster remineralization of partially demineralized enamel.
- In addition, SnF₂ has antibacterial and physicochemical effects, such as the covering of exposed dentinal tubules to reduce dentinal hypersensitivity.

Recent Advances in Clinical Research on Toothpastes and Mouthwashes: Clinical Efficacy of Commercial Products for Gingivitis, Tartar Control and Antimicrobial Activity


CONCLUSION

• This special issue summarizes comparative research on therapeutic oral care products – including stabilized stannous fluoride dentifrice – to help guide professionals in making recommendations for home care products.

OBJECTIVE

This paper introduces a special issue of clinical research comparing various oral care products for therapeutic efficacy. It also discusses the complex aspects of developing formulations with biologically active ingredients for controlling dental diseases.

MATERIALS AND METHODS

• Commercial dental products, such as toothpastes and mouthwashes, promote improved dental hygiene.
• Chemotherapeutic additives, such as fluorides, have led to the reduction and control of dental caries, hypersensitivity, supragingival calculus, plaque and gingivitis in Western countries.
• Consumers are faced with a multiplicity of choices and may need professional help in choosing the right product for their oral health needs.
• Professionals in turn may rely on experience of a product, professional endorsements, and/or research data; the latter is the hardest to interpret.

MATERIALS AND METHODS (continued)

• Valid research data should show, at a minimum, efficacy for a product against a placebo, and where possible comparisons to other commercially available products.
• Highlights from the papers included in this issue, which include direct comparisons between commercial dentifrices and/or mouthwashes include:
  • the prevention and treatment of gingivitis and gingival bleeding with a stabilized stannous fluoride dentifrice compared to a triclosan-copolymer dentifrice;
  • the control of gingivitis with a stabilized stannous fluoride dentifrice compared to an essential oils mouthrinse and a baking soda and peroxide dentifrice;
  • the antimicrobial actions of a stabilized stannous fluoride dentifrice compared to a baking soda and peroxide dentifrice and an essential oil mouthrinse.
A “Return” to Stannous Fluoride Dentifrices


CONCLUSION
• In vivo and in vitro data suggest that a stabilized stannous fluoride dentifrice may be of significant benefit for oral health, showing superior efficacy against caries as compared to the original stannous fluoride dentifrice introduced in the 1950s.

OBJECTIVE
To examine the rationale for a “return” to the use of stannous fluoride in toothpastes, and to introduce the research papers showing the safety and efficacy of a stabilized stannous fluoride dentifrice.

KEY MESSAGES
• Stannous fluoride dentifrices were introduced in the 1950s.
• Research underpinned their use at the time and limitations led to other fluoride sources being sought in the 1960s and 70s.
• Original stannous fluoride (SnF₂) dentifrices had limited stability and formulation flexibility, which led to the development and commercialization of sodium monofluorophosphate and sodium fluoride dentifrices for caries control. However, unlike SnF₂, these two fluoride agents do not protect against plaque, gingivitis or dentinal hypersensitivity.
• Changing patterns of oral disease have focused research on agents that provide benefits for dental caries and gingivitis, and the potential benefits of SnF₂ have been reassessed.
• The formulation stability of original SnF₂ toothpastes was improved to give sufficient levels of bioavailability for both anticaries and antigingivitis activity.

• Clinical studies have demonstrated that stabilized SnF₂ dentifrice is effective in reducing gingivitis and gingival bleeding. Antimicrobial activity interfering with plaque metabolic processes associated with plaque virulence appears to be the mechanism for preventing gingivitis.
• A battery of tests predictive of clinical performance show stabilized SnF₂ dentifrice provides improved anticaries reactivity compared to original stannous fluoride dentifrices.
• Together, laboratory and clinical data supports the ‘return’ to SnF₂ dentifrice in stabilized formulations.
CONCLUSION

In this study, the 7.0% sodium hexametaphosphate dentifrice was exceedingly well-tolerated, with significantly fewer symptoms and superior overall tolerance compared to the marketed antitartar dentifrice control.

OBJECTIVE

To assess the relative acute oral tolerance of a dual phase, tartar control dentifrice containing 7.0% sodium hexametaphosphate.

MATERIALS AND METHODS

- A randomized, controlled 4-day clinical trial.
- 159 healthy adult volunteers were randomly assigned to the experimental sodium hexametaphosphate dentifrice or a marketed, single phase, antitartar dentifrice control containing 5.0% ionic pyrophosphate.
- A detailed oral soft tissue examination and interview were conducted each day by blinded evaluators to elicit clinical signs and symptoms associated with ad lib use of the assigned dentifrice.

RESULTS

- A total of 24 subjects (15% of the study population) had new symptoms/signs after baseline.
- By treatment, 9% of subjects in the sodium hexametaphosphate group had new findings, compared to 21% of subjects in the pyrophosphate group, and these groups differed statistically ($p < 0.03$, two-sided) with respect to occurrence.
- In addition, onset, severity, duration and clinical presentation were generally milder in the sodium hexametaphosphate group compared to the pyrophosphate control. Only one subject (in the pyrophosphate group) discontinued treatment early due to oral intolerance.

### RESULTS (continued)

**Comparison of Subject-Related and/or Examiner-Observed Findings by Treatment, All Evaluable Subjects (N=158)**

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<tr>
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<th>Sodium hexametaphosphate</th>
<th>Pyrophosphate</th>
<th>p-value</th>
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<tbody>
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<td>7 (8.7%)</td>
<td>17 (21.8%)</td>
<td>0.027</td>
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<td>Both Signs and Symptoms</td>
<td>1 (1.3%)</td>
<td>1 (9.0%)</td>
<td>0.316</td>
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<tr>
<td>Signs</td>
<td>6 (7.5%)</td>
<td>10 (12.8%)</td>
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<tr>
<td>Symptoms</td>
<td>2 (2.5%)</td>
<td>14 (18.0%)</td>
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</tr>
</tbody>
</table>
Morphology of in Vivo Salivary Pellicles after Exposure to Dentifrices

CONCLUSION
• The roughness and thickness of salivary pellicles is influenced by routine hygiene and oral products including hexametaphosphate containing dentifrices. Mouth perception anecdotally appears also to be influenced by pellicle thickness and structure.

OBJECTIVE
Salivary pellicles are frequently exposed to dentifrices with an impact on their thickness and surface roughness. One can speculate that both properties of salivary pellicles are likely important for oral biological properties as well as intraoral perception of cleanliness.

The aim of this study is to compare the pellicle composition and morphology after exposure to a dentifrice containing fluoride and sodium lauryl sulphate (Crest® Regular, CR) and a dentifrice supplemented with hexametaphosphate (Crest® Dual Action Whitening, CDAW).

MATERIALS AND METHODS
• Enamel blocks were fixed in the flanges of dentures and worn by two denture wearers up to 3 days. Daily oral hygiene on one side of the mouth was established by flushing with a dentifrice slurry, while the other side was brushed. Immediately after the experimental period, samples were removed and analysed by XPS (X-ray photoelectron spectroscopy) for pellicle thickness and AFM (Atomic force microscopy) for surface roughness.
• In separate studies, mouth feel was evaluated on a scale from -2 (bad) to 2 (good) in ten volunteers with a full dentition at various times during the day after one weeks use of dentifrices.

RESULTS
• On average, the use of CDAW yielded smooth pellicle surfaces with a roughness of around 35 nm, which was three times smoother than after use of CR.
• Moreover, in vivo pellicles, after preparation for XPS, had a thickness of 4.0 nm after CR, while after use of CDAW the thickness had decreased to 3.2 nm. These changes were concurrent with a strongly superior mouth feel after the use of CDAW (38.9 % above neutral throughout day) as compared with volunteers using CR (19.9%).

Digital Plaque Imaging Evaluation of the Plaque Inhibition Effects of a Novel Stabilized Stannous Fluoride Dentifrice versus an Amine Fluoride/Stannous Fluoride Dentifrice

KEY CLINICAL RESULTS
• The stannous fluoride (SnF₂) dentifrice was significantly more effective at inhibiting overnight and day time plaque accumulation versus the amine fluoride/stannous fluoride (AmF/SnF₂) dentifrice.

OBJECTIVE
To evaluate the plaque inhibition effects of a novel 0.454% stabilized SnF₂ dentifrice to an amine fluoride/SnF₂ marketed control dentifrice using digital plaque imaging analysis (DPIA).

METHODS
• This was a 10-week, randomised, two-treatment, three-period, double-blind crossover trial comparing a novel SnF₂ dentifrice with stannous chloride to further stabilize the bioavailability of SnF₂ (blend-a-med Clinic Line Gum Protection, Procter & Gamble) and an AmF/SnF₂ control dentifrice (Meridol, Gaba).
• Subjects brushed twice daily with their assigned dentifrice and a standard manual toothbrush during the three treatment periods, each lasting 17 consecutive days and separated by a four-day washout period.
• Visible plaque coverage on the facial surfaces of the 12 anterior teeth (canine to canine) was captured and averaged amongst 3 assessments days at the end of each treatment period (i.e. Days 15, 16, 17) using DPIA.
• Assessments were conducted at the following time points: the morning following lingual only brushing the evening before (A.M. pre-brush); after 40 seconds of full mouth brushing with assigned dentifrice (A.M. post-brush); and during the afternoon (P.M.).
Digital Plaque Imaging Evaluation of the Plaque Inhibition Effects of a Novel Stabilized Stannous Fluoride Dentifrice versus an Amine Fluoride/Stannous Fluoride Dentifrice

RESULTS (continued)
- Twenty-seven subjects were randomised into the study. All subjects completed the trial.
- At each assessment time point, plaque levels for the SnF₂ dentifrice were statistically significantly lower (p<0.0001) compared to those for the AmF/SnF₂ dentifrice.
- A.M. pre-brushing was 21.4% lower, A.M. post-brushing was 22.6% lower, and P.M. plaque was 24.3% lower, respectively.

A Clinical Evaluation of the Anti-Gingivitis Effects of a Regimen Including a Novel Toothbrush with a Flexing Brush Head, 0.454% Stannous Fluoride Dentifrice, CPC Rinse and Floss

KEY CLINICAL RESULTS
- After 6 weeks, the test regimen resulted in 86% less gingival bleeding and 84% less gingivitis than the positive control. Treatment groups differed significantly (p<0.014) for gingival bleeding and gingivitis at Weeks 2, 4 and 6.

OBJECTIVE
To assess clinical gingivitis after using either a test regimen - consisting of a novel manual toothbrush with a flexing brush head, 0.454% stannous fluoride dentifrice, CPC rinse and floss - or receiving a dental prophylaxis.

STUDY DESIGN
- This was a randomised, controlled, examiner-blind, 2-treatment parallel-group study composed of healthy adult volunteers with mild-to-moderate gingivitis.
- 50 qualified subjects were enrolled; each treatment group contained 25 subjects. Twenty-three subjects in each treatment group completed the study and all data that was collected was considered evaluable.
- Subjects ranged in age from 18 to 50 years and 74% of the subjects were female. Treatment groups were well balanced on demographic characteristics (p>0.35) and baseline gingivitis scores and number of bleeding sites (p>0.47).
A Clinical Evaluation of the Anti-Gingivitis Effects of a Regimen Including a Novel Toothbrush with a Flexing Brush Head, 0.454% Stannous Fluoride Dentifrice, CPC Rinse and Floss

**STUDY DESIGN**

- Subjects were randomised to one of the following two groups:
  - Test: No dental prophylaxis and Oral-B Clinic Line Pro-Flex Manual Toothbrush (OM044), blend-a-med Clinic Line Gum Protection toothpaste (0.454% stannous fluoride), Oral-B Clinic Line Rinse (0.07% CPC) and Oral-B Clinic Line Floss. Subjects were instructed to: brush and rinse (20mL for 30 sec each time) twice daily; floss the whole mouth once daily; and use the products in place of normal oral hygiene for the duration of the study.
  - Positive Control: Dental prophylaxis followed by 6 weeks use of Colgate Cavity Protection toothpaste (0.76% sodium monofluorophosphate) and the Oral-B Indicator soft manual toothbrush. Subjects were instructed to: brush thoroughly with the products provided twice daily; use the products in place of normal oral hygiene for the duration of the study; and refrain from flossing for the duration of the study.
  - Gingival inflammation and bleeding were assessed clinically at Baseline (prior to prophylaxis for control group), and at Weeks 2, 4 and 6 using the Löe-Silness Gingival Index.

A Study to Assess the Anti-plaque Effects of a Regimen including a Novel Stannous Fluoride Dentifrice, Power Toothbrush and Floss

**KEY CLINICAL RESULTS**

- After 4 weeks of use, the test regimen (stannous fluoride dentifrice, power brush and floss) demonstrated a 59.7% reduction in prehygiene (overnight) plaque and a 50.9% reduction in post-hygiene plaque versus the control regimen group ($p \leq 0.004$). Results were similar at Week 2. See Figures 1–3.
  - The beneficial effects of a dental prophylaxis were maintained by the test regimen, as demonstrated by post-hygiene plaque levels that were similar to post-prophylaxis scores at Weeks 2 and 4 ($p \geq 0.33$). The control regimen did not maintain the effects of the prophylaxis, having significantly higher post-hygiene plaque scores compared to post-prophylaxis at both time points ($p \leq 0.007$).
  - Only the test regimen showed significant reductions in pre-hygiene and post-hygiene plaque relative to baseline.

**FIGURE 1.**

**FIGURE 2.**

- $^*$ Difference between groups was significantly different ($p \leq 0.007$)
- $^{**}$ Baseline and Prophy scores are means
- $^{**}$ Difference between groups was significantly different ($p \leq 0.007$)
- $^{**}$ Baseline and Prophy scores are means

**OBJECTIVE**

To assess the anti-plaque effect of a regimen including a novel stannous fluoride dentifrice, an oscillating-rotating power toothbrush and dental floss versus a negative control regimen.

**STUDY DESIGN**

This was a randomized, controlled, single-blind, 2-treatment parallel group study involving 47 healthy adult volunteers with plaque. Following an acclimation period and a dental prophylaxis, subjects were randomized to 1 of 2 regimens:
A Study to Assess the Anti-plaque Effects of a Regimen including a Novel Stannous Fluoride Dentifrice, Power Toothbrush and Floss

**TEST REGIMEN (continued)**
- AZ® PRO-HEALTH Clinical Gum Protection toothpaste (0.454% stannous fluoride)
- Oral-B® Professional Care SmartSeries 5000 with SmartGuide power toothbrush with Oral-B FlossAction® brush head
- Oral-B® Glide® PRO-HEALTH Clinical Protection for Professionals floss

**CONTROL REGIMEN**
- AZ® Cavity Protection toothpaste (0.243% sodium fluoride)

Subjects in the test regimen were instructed to brush for 2 minutes, using “Daily Clean” mode, twice daily. They were also instructed to floss the whole mouth once daily.

Subjects in the control regimen were instructed to brush thoroughly twice daily. They were asked to refrain from flossing for the duration of the study.

Post-dental prophylaxis, overnight (pre-hygiene) and post-hygiene plaque were measured by digital image analysis of fluoresceindisclosed plaque.

**FIGURE 3.**
DPIA images of subjects representative of percent reduction for each group

<table>
<thead>
<tr>
<th></th>
<th>Control Regimen Subject 5002</th>
<th>Test Regimen Subject 5009</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(NaF dentifrice, manual brush)</td>
<td>(SnF₂ dentifrice, power brush, floss)</td>
</tr>
</tbody>
</table>

**BASELINE**
- Pre-hygience
- Post-hygience

**WEEK 2**
- Pre-hygience
- Post-hygience

**OBJECTIVE**
To assess gingivitis after using either a test regimen, consisting of a novel stannous fluoride dentifrice, an oscillating-rotating power toothbrush and floss, or receiving a dental prophylaxis at Baseline followed by use of a regular anti-cavity toothpaste and soft, manual toothbrush.

A Clinical Trial to Assess the Effect of a Regimen including a Novel Stannous Fluoride Dentifrice, Power Toothbrush and Floss on Gingivitis

**KEY CLINICAL RESULTS**
- The test regimen group (stannous fluoride dentifrice, power toothbrush and floss) had 71% fewer bleeding sites at Week 4 and 95% fewer bleeding sites at Week 6 compared to the control group (dental prophylaxis at baseline, regular anti-cavity toothpaste and soft manual toothbrush) \( p< 0.001 \). See Figures 1 & 2.
- At Week 6, 83% of subjects in the test regimen group exhibited no bleeding at any measured site.
- The test regimen group also showed a 68% reduction in gingivitis (GI) at Week 4 and a 95% reduction in GI at Week 6 compared to the control group (\( p< 0.001 \)). See Figure 3.
- Both groups showed a significant reduction in bleeding and gingivitis at Weeks 2, 4 and 6 relative to baseline (\( p \leq 0.008 \)).

**FIGURE 2.**
Number of Bleeding Sites

<table>
<thead>
<tr>
<th></th>
<th>Treatment</th>
<th>Test Regimen</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjusted Mean</td>
<td>( 0.15 )</td>
<td>( 0.10 )</td>
<td>( 0.05 )</td>
</tr>
<tr>
<td><strong>Löe-Silness Gingivitis Index</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>Test Regimen</td>
<td>Control</td>
</tr>
<tr>
<td>Adjusted Mean</td>
<td>( 0.15 )</td>
<td>( 0.10 )</td>
<td>( 0.05 )</td>
</tr>
</tbody>
</table>

* Difference between groups was significantly different (\( p<0.001 \))
** Baseline scores are means


**FIGURE 3.**
Löe-Silness Gingivitis Index

<table>
<thead>
<tr>
<th></th>
<th>Treatment</th>
<th>Test Regimen</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjusted Mean</td>
<td>( 0.15 )</td>
<td>( 0.10 )</td>
<td>( 0.05 )</td>
</tr>
</tbody>
</table>

* Difference between groups was significantly different (\( p<0.001 \))
** Baseline scores are means

**OBJECTIVE**
To assess gingivitis after using either a test regimen, consisting of a novel stannous fluoride dentifrice, an oscillating-rotating power toothbrush and floss, or receiving a dental prophylaxis at Baseline followed by use of a regular anti-cavity toothpaste and soft, manual toothbrush.

* Nova Southeastern University; \( 1 \) The Procter & Gamble Company.
A Clinical Trial to assess the effect of a Regimen including a Novel Stannous Fluoride Dentifrice, Power Toothbrush and Floss on Gingivitis

STUDY DESIGN (continued)

This was a randomized, controlled, examiner-blind, 2-treatment parallel group study that involved 46 healthy adult subjects with mild to moderate gingivitis. Subjects were assigned to 1 of 2 groups:

- Test regimen: no dental prophylaxis and AZ® Pro-Health Clinical Gum Protection toothpaste (0.454% stannous fluoride), Oral-B® Professional Care SmartSeries 5000 with SmartGuide powered toothbrush with the Oral-B FlossAction® brush head and Oral-B® Glide® Pro-Health Clinical Protection for Professionals floss.

- Control group: dental prophylaxis at Baseline followed by use of AZ® Cavity Protection toothpaste and an Oral-B® Indicator regular, soft manual toothbrush.

Subjects in the test regimen were instructed to brush for 2 minutes, using “Daily Clean” mode, twice per day. They were also instructed to floss the whole mouth once daily.

Subjects in the control regimen were instructed to brush thoroughly twice daily. They were asked to refrain from flossing for the duration of the study. Gingival inflammation and bleeding were assessed clinically after 2, 4 and 6 weeks using the Löe-Silness Gingivitis Index.

Treatment groups were compared using the analysis of covariance method with baseline as a covariate. Statistical tests were two-sided using a 5% significance level.

FIGURE 1.
Depiction of average number of gingival bleeding sites

<table>
<thead>
<tr>
<th></th>
<th>Dental prophylaxis and standard manual brushing</th>
<th>AZ Pro-Health Test Regimen (no prophylaxis, SnF2 dentifrice, power brush and floss)</th>
<th>Dental prophylaxis and standard manual brushing</th>
<th>AZ Pro-Health Test Regimen (no prophylaxis, SnF2 dentifrice, power brush and floss)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>12.9</td>
<td>12.9</td>
<td>6.1</td>
<td>6.3</td>
</tr>
<tr>
<td>Week 2</td>
<td>7.5</td>
<td>2.1</td>
<td>10.0</td>
<td>0.5</td>
</tr>
<tr>
<td>Week 4</td>
<td></td>
<td>71% less bleeding</td>
<td></td>
<td>95% less bleeding</td>
</tr>
</tbody>
</table>

1 Nova Southeastern University; 2 The Procter & Gamble Company.
A Randomized Clinical Trial to Evaluate the Effects of a Novel 0.454% Stannous Fluoride Dentifrice on Gingivitis

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.

<table>
<thead>
<tr>
<th></th>
<th>Novel stannous dentifrice</th>
<th>Control dentifrice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>14.9</td>
<td>16.1</td>
</tr>
<tr>
<td>Month 1</td>
<td>12.7</td>
<td>15.9</td>
</tr>
<tr>
<td>Month 2</td>
<td>10.6</td>
<td>14.4</td>
</tr>
<tr>
<td>Month 3</td>
<td>9.4</td>
<td>13.3</td>
</tr>
</tbody>
</table>

FIGURE 2.

Percent improvement in bleeding relative to baseline:

<table>
<thead>
<tr>
<th></th>
<th>Novel stannous dentifrice</th>
<th>Control dentifrice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Month 1</td>
<td>35%</td>
<td>12%</td>
</tr>
<tr>
<td>Month 2</td>
<td>41%</td>
<td>17%</td>
</tr>
<tr>
<td>Month 3</td>
<td>46%</td>
<td>13%</td>
</tr>
</tbody>
</table>

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® Clinical Gum Protection, Procter & Gamble) or a control toothpaste with 0.76% sodium monofluorophosphate (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.

Reference:
RW Gerlach, P Amini