Extrinsic Whitening Effects of Sodium Hexametaphosphate—A Review Including a Dentifrice With Stabilized Stannous Fluoride

Abstract: The number of tooth whitening products available to patients has grown dramatically during recent years. While peroxide is the primary agent found in products that bleach and remove intrinsic sources of discoloration, various ingredients are incorporated in formulations to remove and inhibit extrinsic sources of tooth discoloration, ie, tooth stain. Recently, an advanced antitartar ingredient with extrinsic-stain–inhibiting benefits was introduced: sodium hexametaphosphate. This long-chain condensed phosphate, also known as polyphosphate, chemically removes existing stains and provides long-lasting inhibition of new-stain chromogen adsorption. Sodium hexametaphosphate was originally introduced in a sodium fluoride dentifrice formulation and was later marketed in a chewing gum delivery system. Recently, sodium hexametaphosphate was launched in another dentifrice formulation containing stabilized stannous fluoride (Crest® Pro-Health). This article reviews published clinical and laboratory data demonstrating sodium hexametaphosphate’s extrinsic whitening benefits in all three formulations.

Patient demand for whiter teeth has shown unprecedented growth in recent years. To effectively counsel patients on tooth whitening options, it is important to understand the nature of the discoloration. Tooth color is affected by both internal and external properties. Intrinsic tooth discoloration refers to chromogen found below the enamel and is often associated with natural aging of the dentition, fluorosis, tetracycline damage, or years of tobacco use. This stain is most effectively treated with peroxide-based systems, such as bleaching gels used in trays or whitening strips.1

Extrinsic discoloration occurs when stain forms on the tooth surface. Chromogens contributing to surface stain often originate from dietary sources (eg, coffee, tea, red wine), tobacco, or certain oral therapeutics like chlorhexidine. Three classes of ingredients are commonly incorporated in oral care products to control extrinsic stain: peroxide, abrasives, and chemical agents. While the tooth-whitening efficacy of hydrogen peroxide has been well-established in certain delivery systems,1 the application of peroxide in dentifrices is challenging because of formulation factors and shortened treatment times. Abrasives are insoluble components added to dentifrice formulations and prophylaxis pastes to physically remove tooth stain.2,3 Substances routinely added to modern dentifrices include metal oxides (eg, aluminum oxide), mineral salts (eg, calcium pyrophosphate, calcium carbonate, and sodium carbonate), precipitated silica, and pumice (Table 1).

Agents in the third class of ingredients for extrinsic stain control derive their whitening benefit from a chemical mechanism. Calcium phosphate refusal.

Learning Objectives

After reading this article, the reader should be able to:

- describe the stain inhibition mechanism of sodium hexametaphosphate.
- discuss technical and clinical data showing esthetic benefits of a sodium fluoride/sodium hexametaphosphate dentifrice.
- explain the stain-control effect of a stabilized stannous fluoride/sodium hexametaphosphate dentifrice.
surface active builders (CPSABs), such as pyrophosphate, are among the most common ingredients in this class. These agents have a strong binding affinity for tooth minerals, such as calcium phosphate in dental enamel or dentin.4,7 During adsorption to mineral sites, CPSABs have been shown to desorb portions of adsorbed proteins, including pellicle proteins containing stain chromogen.8,9 The ability of these agents to provide whitening benefits increases with the length of the molecule. Longer molecules with a higher molecular weight have more binding sites, giving them a greater chance of adsorption and retention on the tooth surface.

One of the most advanced CPSABs is sodium hexametaphosphate.10,11 Sodium hexametaphosphate contains 10 to 12 repeating pyrophosphate subunits, which gives it a stronger attraction to calcium hydroxyapatite relative to other agents in its class (Figure 1). Sodium hexametaphosphate’s multiple binding sites translate to greater coverage of the tooth surface, increasing its potential retention and substantivity. Sodium hexametaphosphate alters salivary conditioning films, contributing to its ability to remove existing surface discolouration and inhibit new chromogens from being adsorbed to proteins in the pellicle.12 Numerous published clinical and technical studies demonstrate sodium hexametaphosphate’s stain-control benefits in dentifrice and chewing gum delivery systems.13-19

A Sodium Hexametaphosphate and Sodium Fluoride Dentifrice

In 2000 and 2001, sodium hexametaphosphate was introduced in dentifrice formulations containing 0.243% sodium fluoride (Crest® MultiCare® Advanced Cleaning, Crest® Dual Action Whitening®). The whitening efficacy of the sodium fluoride/sodium hexametaphosphate dentifrice was evaluated in numerous in vitro and in vivo studies.

In vitro Data

Laboratory studies were conducted to demonstrate the chemical actions of the sodium fluoride/sodium hexametaphosphate dentifrice in the nonabrasive prevention and removal of tea stains.13 Powdered hydroxyapatites were used as substrates, representing enamel and dentin, for adsorption of tea chromogens. Color change was evaluated qualitatively. In one set of experiments, powders were treated with various dentifrice supernates before exposure to tea to simulate stain prevention. The sodium fluoride/sodium hexametaphosphate dentifrice resulted in almost complete prevention of tea-stain deposition. Powdered hydroxyapatites also were treated with this dentifrice after exposure to tea to indicate stain removal. The sodium fluoride/sodium hexametaphosphate treatment showed almost complete removal of tea components (Figure 2). These results exemplify the chemical actions of sodium hexametaphosphate toward dental stain removal and prevention. The extrinsic-stain–inhibition benefits of sodium hexametaphosphate also have been shown quantitatively in an in vitro cycling stain model with synthetic enamel chips that involved salivary pellicle formation and stain induced by chlorhexidine and tea over 5 days.

Table 1—Sources of Tooth Stain and Common Treatments

<table>
<thead>
<tr>
<th>Sources of Stain</th>
<th>Agents to Remove/Prevent Stain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intrinsic tooth stain</td>
<td>Natural aging of dentition</td>
</tr>
<tr>
<td></td>
<td>Peroxide (hydrogen, carbamide)</td>
</tr>
<tr>
<td></td>
<td>Tetracycline</td>
</tr>
<tr>
<td></td>
<td>Fluorosis</td>
</tr>
<tr>
<td></td>
<td>Prolonged tobacco use</td>
</tr>
<tr>
<td>Extrinsic tooth stain</td>
<td>Diet (cola, tea, red wine)</td>
</tr>
<tr>
<td></td>
<td>Peroxide</td>
</tr>
<tr>
<td></td>
<td>Tobacco</td>
</tr>
<tr>
<td></td>
<td>Abrasives</td>
</tr>
<tr>
<td></td>
<td>Oral therapeutics</td>
</tr>
<tr>
<td></td>
<td>– Aluminum oxide</td>
</tr>
<tr>
<td></td>
<td>Poor oral hygiene</td>
</tr>
<tr>
<td></td>
<td>– Calcium carbonate</td>
</tr>
<tr>
<td></td>
<td>– Silica</td>
</tr>
<tr>
<td></td>
<td>Chemical agents</td>
</tr>
<tr>
<td></td>
<td>– Sodium pyrophosphate</td>
</tr>
<tr>
<td></td>
<td>– Sodium tripolyphosphate</td>
</tr>
<tr>
<td></td>
<td>– Sodium hexametaphosphate</td>
</tr>
</tbody>
</table>

5The Procter & Gamble Company, Cincinnati, OH 45202; 800-492-7378
6Zimmer Dental, Carlsbad, CA 92008; 800-854-7019
Stain formation was assessed using digital image analysis. The sodium fluoride/sodium hexametaphosphate dentifrice provided stain inhibition superior to a variety of commercial dentifrices, supporting the qualitative findings.

**Clinical Research**

The extrinsic whitening benefits of sodium hexametaphosphate also have been demonstrated in clinical research. Two 6-week clinical trials illustrate the stain-removal benefits of sodium fluoride dentifrices containing sodium hexametaphosphate using the Lobene stain index.\(^ {14,15} \) In one study, a dentifrice containing 0.243% sodium fluoride and 7% sodium hexametaphosphate was compared to a 0.243% sodium fluoride control dentifrice for extrinsic stain removal.\(^ {14} \) After receiving a prophylaxis, subjects rinsed with chlorhexidine/tea for 3 weeks to induce stain. Subjects presenting with stain were then randomized to the sodium hexametaphosphate dentifrice or control and were instructed to brush twice daily for 6 weeks. Stain was assessed at baseline and at 3 and 6 weeks. The sodium fluoride/sodium hexametaphosphate dentifrice was statistically significantly superior to the control dentifrice for stain removal at both time points, demonstrating a 29% improvement over control at 6 weeks. Stain-removal benefits also were observed in a second 6-week clinical study evaluating a 0.243% sodium fluoride dentifrice containing sodium hexametaphosphate.\(^ {15} \) The study involved a stain induction period, similar to that previously described. Subjects randomized to the sodium fluoride/sodium hexametaphosphate dentifrice demonstrated statistically significant reductions in induced extrinsic stain after 3 and 6 weeks of twice-a-day brushing.

The stain-prevention benefits of sodium hexametaphosphate also have been shown in published clinical research.\(^ {16} \) A 6-week, randomized, controlled clinical trial evaluated the efficacy of a 0.243% sodium fluoride dentifrice containing sodium hexametaphosphate vs a 0.243% sodium fluoride control dentifrice for prevention of induced stain. After 3 weeks of brushing, subjects in the sodium hexametaphosphate dentifrice group exhibited 33% less stain (\( P < .05 \)) relative to the control. Similar trends were observed after 6 weeks of use, with the sodium hexametaphosphate group showing reductions of 26% (\( P = .055 \)). The sodium hexametaphosphate dentifrices were well-tolerated in all clinical trials.

**Sodium Hexametaphosphate Chewing Gum**

While dentifrice formulations continue to be a primary delivery system for cosmetic and therapeutic oral health agents, interest in other vehicles has grown in recent years. Chewing gum is an attractive alternative because of its portability and widespread consumption in certain countries.\(^ {20} \) Based on the whitening results seen with sodium fluoride dentifrice formul-
tions, sodium hexametaphosphate was added to a chewing gum formulation (Orbit® White®) as another treatment option for patients seeking control of extrinsic stain. Several laboratory and clinical studies were conducted to validate sodium hexametaphosphate’s positive impact on tooth color when used in a chewing gum formulation.

**In vitro Data**

Preliminary in vitro research has demonstrated that a chewing gum containing sodium hexametaphosphate inhibits extrinsic tea-stain formation on hydroxyapatite powder (representing enamel and dentin) relative to water and placebo gum. In these studies, saliva was collected from subjects after chewing with two pellets of placebo gum or sodium hexametaphosphate chewing gum. Hydroxyapatite powders were then exposed to pooled saliva or water control. After sample preparation, the powder treatments were exposed to a filtered tea solution and dried. Results showed that chewing with sodium hexametaphosphate gum produced significant resistance in susceptibility of hydroxyapatite powder surfaces to stain-chromogen acquisition relative to chewing with placebo gum or no gum.

**Clinical Research**

Findings from two published clinical trials validate the outcomes of the technical research. A 2-period, randomized, double-blind, placebo-controlled, crossover study was conducted to compare the stain-prevention/removal benefit of a chewing gum containing 7.5% sodium hexametaphosphate relative to a placebo chewing gum. Each treatment period lasted 2 days separated by a minimum washout time of 72 hours in between. On enrollment, subjects received a dental prophylaxis limited to the anterior 12 teeth. Tooth color was assessed using digital image analysis at the baseline visit and at the end of the day 1 and day 2 visits. The treatment protocol consisted of first rinsing for 60 seconds with 10 mL of 0.12% chlorhexidine solution, then chewing 2 pellets of the assigned chewing gum (either placebo or 7.5% sodium hexametaphosphate gum) for 5 minutes, and finally rinsing with 10 mL of cold tea solution for 60 seconds. No oral hygiene was permitted other than the use of the test products. Each subject followed the same regi-

Wm Wrigley Jr Company, Chicago, IL 60611; 312-644-2121

men eight times, once per hour, throughout the day during both treatment periods. At the end of day 1 (8 cycles), subjects chewing the sodium hexametaphosphate gum had significantly whiter teeth, representing a 23% improvement in tooth whiteness (based on mean \(\Delta L^*\)) vs subjects chewing the placebo gum. A statistically significant improvement also was seen at the end of day 2 (16 total cycles) for the sodium hexametaphosphate chewing gum.

A second clinical trial examined the prevention of induced stain deposition through the use of a chewing gum containing 2% sodium hexametaphosphate, a chewing gum containing 3% sodium hexametaphosphate, a placebo gum, or no gum. The randomized, controlled, examiner-blind, 4-period crossover study was carried out over a 4-week period, with each treatment period lasting 2 days separated by 3- to 5-day washouts. The treatment phases were conducted using a design similar to that described for the two studies above. At the end of the 2-day phase (16 total cycles), the difference between no gum and placebo gum was statistically significant, representing a 12.4% reduction in tooth darkness for the placebo gum. Both the 2% and 3% sodium hexametaphosphate gums produced significant whitening benefits relative to the no-gum and placebo-gum treatments. The reduction in tooth darkness for the 2% sodium hexametaphosphate gum was 29.7% vs no gum and 19.8% vs the placebo gum. The 2% and 3% sodium hexametaphosphate gum treatments did not differ significantly.

**A Sodium Hexametaphosphate and Stabilized Stannous Fluoride Dentifrice**

Recently, a novel, patented dentifrice technology has been introduced combining sodium hexametaphosphate with stabilized stannous fluoride. Stannous fluoride has been used for decades as an antimicrobial agent for oral health, but its use has been limited because of poor taste or flavor and the potential for extrinsic tooth stain with extended use. The incorporation of sodium hexametaphosphate with stannous fluoride, however, mitigates these negatives. This new dentifrice, marketed in the United States as Crest® Pro-Health®, offers comprehensive oral health and cosmetic benefits. Stannous fluoride provides protection from caries, pathogenic bacteria, plaque, gingivitis, bad breath, and dentinal sensitivity, while sodi-
um hexametaphosphate provides extrinsic whitening and tartar-control benefits.

In vitro Studies

The stain-inhibition properties of sodium hexametaphosphate have been demonstrated in this new formulation with stannous fluoride. An in vitro evaluation of the extrinsic stain-control benefits of sodium hexametaphosphate used in Crest® Pro-Health was conducted using a hydroxyapatite-powder stain model. A detailed description of the hydroxyapatite-powder stain model has been described previously.11 Crest® Pro-Health was compared with several other treatments, including Crest® Cavity Protection Regular Paste® and Gel-Kam®. Gel-Kam® was used in this study to assess the effects of unprotected stannous fluoride on the stain potential of hydroxyapatite. The assay involved pretreatment of hydroxyapatite powders with the supernatant of the treatment slurries followed by water washing and then exposure to tea solutions. After the final wash, the powders were air-dried and analyzed for changes in color, both visually and colorimetrically.

Figure 3 illustrates the stain-prevention activity of Crest® Pro-Health compared to the other treatments. Pretreatment of hydroxyapatite with Crest® Pro-Health resulted in almost complete prevention of tea-stain deposition onto hydroxyapatite. This is consistent with previous studies where sodium hexametaphosphate has been shown to play a key role in competing with tea-stain chromogens for the same sites on hydroxyapatite mineral surfaces.12 In contrast to the findings with Crest® Pro-Health, the enhanced hydroxyapatite staining seen with the Gel-Kam® treatment indicates the effect of unprotected stannous fluoride in inducing extrinsic stain.

Clinical Studies

The in vitro findings provide a mechanistic explanation for the observed clinical effects of a stabilized 0.454% stannous fluoride/sodium hexametaphosphate dentifrice in two 6-month studies assessing extrinsic stain formation.22,23 In the 6-month calculus study reported separately in this issue, Lobene stain examination was incorporated to evaluate the stain formation potential of the stannous fluoride/sodium hexametaphosphate dentifrice relative to a marketed multibenefit triclosan/copolymer dentifrice (0.30% triclosan, 0.243% sodium fluoride, and 2% Gantrez copolymer).22 At months 3 and 6, extrinsic stain formation was measured on the facial surfaces of the 12 anterior teeth. Results showed virtually no extrinsic tooth stain for either the experimental stannous fluoride/sodium hexametaphosphate dentifrice group or the positive-control group at both time points.

Similarly, the potential for extrinsic tooth-stain formation after extended use of the stabilized 0.454% stannous fluoride/sodium hexametaphosphate dentifrice was assessed as part of an oral hard/soft tissue examination in a 6-month gingivitis study.23 After a professional prophylaxis, subjects were allocated to either the stannous fluoride/sodium hexametaphosphate dentifrice or a marketed cavity protection dentifrice (Colgate® Cavity Protection4, 0.76% sodium monofluorophosphate) and instructed to brush twice daily for 6 months. All abnormal oral hard/soft tissue findings, including tooth color change, that were noted after baseline or were present at baseline but worsened during investigational product use were recorded as adverse events. No extrinsic tooth staining was observed by the study examiner or reported by the subjects in the study. Collectively, these clinical studies demonstrate that extended use of the stannous fluoride/sodium hexametaphosphate dentifrice is associated with virtually no extrinsic tooth staining when compared to a marketed multibenefit dentifrice or cavity protection dentifrice.

Practice-based Evaluation

After a dental prophylaxis, a natural process of stain accumulation begins on the tooth surface. A study was conducted to assess the rate of stain formation of two experimental stannous
fluoride dentifrices and a marketed multibenefit triclosan/copolymer control dentifrice (Colgate® Total®) in a practice-based, real-world situation. This study was a 3-leg, double-blind, 6-month study conducted in 30 US dental offices, with the 3 products distributed randomly among patients after prophylaxis in each office. Both professionals and patients evaluated the products after 4 and 6 months of use. This article reports results for one of the experimental dentifrices, containing 0.454% stannous fluoride and 13% sodium hexametaphosphate, and the triclosan/copolymer control dentifrice. There were no differences in professional observation of staining between the stannous fluoride/sodium hexametaphosphate experimental dentifrice and the control dentifrice, as evidenced by no difference in tooth discoloration at 4 and 6 months (Table 2). Similarly, patients did not perceive any difference in staining between the two dentifrices. Because triclosan has been reported not to promote tooth-stain formation, these study results confirm the effectiveness of sodium hexametaphosphate in controlling the deposition of surface stains historically associated with stannous fluoride in a practice-based situation.

**Conclusion**

The benefits of sodium hexametaphosphate in controlling stain deposition on the tooth surface have been demonstrated in multiple formulations and delivery systems. In making treatment recommendations to patients seeking to control extrinsic tooth discoloration, it is important to consider their habits and oral health needs. Most patients can easily incorporate a sodium hexametaphosphate dentifrice into their daily oral hygiene regimen. The stabilized stannous fluoride/sodium hexametaphosphate dentifrice is an excellent option for patients seeking comprehensive benefits or who need to control plaque, gingivitis, or sensitivity. Not only does the stannous fluoride/sodium hexametaphosphate formulation provide a broad range of therapeutic benefits (eg, antiplaque, antigingivitis, anticaries, antisensitivity), but it also offers the unique advantage of protection against extrinsic stain and calculus. Other patients may prefer the sodium fluoride/sodium hexametaphosphate dentifrice, which provides anticaries, anticalculus, and extrinsic whitening benefits. Sodium hexametaphosphate chewing gums are an attractive option for patients seeking portable whitening products. While sodium hexametaphosphate chewing gums do not provide the concomitant delivery of topical fluoride, they are a convenient alternative to control extrinsic stain away from home.

**References**


**Table 2—Professional Evaluation of Stannous Fluoride/Sodium Hexametaphosphate Experimental and Triclosan/Copolymer Control Dentifrices**

<table>
<thead>
<tr>
<th></th>
<th>Month 4</th>
<th>Month 6</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Stannous fluoride/SHMP</td>
<td>Triclosan/copolymer</td>
</tr>
<tr>
<td>(n = 70)</td>
<td>(n = 75)</td>
<td>(n = 63)</td>
</tr>
<tr>
<td>Amount of tooth discoloration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>36</td>
<td>31</td>
</tr>
<tr>
<td>A little</td>
<td>51</td>
<td>52</td>
</tr>
<tr>
<td>Moderate to very high</td>
<td>12</td>
<td>18</td>
</tr>
</tbody>
</table>

SHMP = sodium hexametaphosphate.


