Digital plaque imaging evaluation of a stabilized stannous fluoride dentifrice compared with a triclosan/copolymer dentifrice

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Abstract: Purpose: To compare the relative plaque control efficacy of a marketed 0.454% stabilized stannous fluoride (SnF_2) dentifrice relative to a triclosan/copolymer dentifrice using digital plaque imaging analysis (DPIA). **Methods:** This was a randomized, two-treatment, double-blind, parallel group design study that compared SnF_2 and triclosan/copolymer dentifrices over a period of 3 weeks. DPIA was used to capture a digital image of the maxillary and mandibular anterior facial surfaces of 12 teeth and to calculate plaque area coverage. Overnight DPIA images were taken at a baseline visit after which subjects were randomly assigned to one of the two treatment groups and were required to brush with their assigned dentifrice according to each manufacturer's instructions. Subjects had DPIA assessments on two separate days at the end of Week 3. **Results:** 96 subjects were randomized to treatment. Plaque area data for 47 subjects per treatment group were compared at Week 3 using ANCOVA. The SnF_2 group demonstrated a statistically significant reduction in overnight plaque at Week 3 compared to baseline (P= 0.002). The reduction for the triclosan group at Week 3 compared to baseline was not statistically significant (P= 0.24). At Week 3, the SnF_2 group demonstrated a 17% lower adjusted mean for overnight plaque relative to the triclosan group with a mean difference that was statistically significant (P< 0.05). The Week 3 adjusted mean change from baseline in overnight plaque for the SnF_2 group was 3 times greater versus that of the triclosan group (P< 0.05). (*Am J Dent* 2013;26:303-306).

Clinical significance: This comparison between marketed dentifrices indicates that a stabilized stannous fluoride dentifrice provided significantly greater overnight plaque inhibition versus a triclosan/copolymer dentifrice.

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Introduction

It is well understood that supra-gingival plaque can be effectively reduced through a good daily oral hygiene regimen, however mechanical hygiene alone is insufficient for optimal oral hygiene. Inhibition of plaque re-growth is also an important consideration when identifying ways to optimize plaque control. Dentifrices that offer good plaque re-growth inhibition have the potential to provide enhanced oral health benefits for the user. Differentiating between dentifrices in terms of their anti-plaque properties therefore requires assessment of plaque re-growth inhibition, commonly measured as overnight plaque accumulation.

Digital plaque imaging analysis (DPIA) is an established method for measuring dental plaque.[1-6] DPIA provides an objective, reliable, reproducible and standardized means of quantifying plaque coverage. This method is linear with respect to plaque area coverage and also produces a source image, so data can be analyzed in various ways following study completion. The DPIA method plays an important role in differentiating between dental products in terms of their plaque control effectiveness in comparative randomized clinical studies.

To ensure patients can make informed choices between available dentifrices, it is important to know the relative anti-plaque benefits not only of innovative dentifrice technologies as they are introduced, but also to know the relative effectiveness of those dentifrices in common use. Agents with reported anti-plaque properties found in marketed dentifrices vary by region and include stabilized stannous fluoride,[1-7] triclosan/copolymer,[8,9] zinc citrate[10] and chlorhexidine.[11] Using DPIA methodology, the anti-plaque advantages of a novel 0.454% stabilized stannous fluoride formulation versus either a marketed chlorhexidine digluconate dentifrice or a zinc citrate dentifrice have been demonstrated.[4,6] The present study compared the relative overnight anti-plaque benefits of a stannous fluoride dentifrice relative to a marketed triclosan/copolymer dentifrice using the DPIA methodology.

Materials and Methods

Treatment products - The test dentifrice in this study was Crest Pro-Health Clean Mint Paste[a] with 0.454% stabilized stannous fluoride, referred to here as SnF_2. The comparator dentifrice was Colgate Total Clean Mint Paste[b] with 0.30% triclosan, 0.24% sodium fluoride and 2% polyvinyl-methyl ether maleic acid (copolymer), referred to here as triclosan.

Subjects, study design and procedures - The study protocol was approved by the U.S. Investigational Review Board, Inc. (US IRB 2011UPRC/05). Ninety-nine subjects gave their signed informed consent to participate in the study. This study had a double-blind, two-treatment, parallel group, randomized design consisting of a standard acclimation period, baseline plaque assessments, test product randomization and distribution, and finally, 3-week plaque assessments on two separate days. Initial visits consisted of a screening and acclimation usage period for subjects to a common regular anti-cavity dentifrice (Crest Cavity Protection,[a] 0.243% sodium fluoride) and an ADA manual toothbrush[c] including baseline plaque measurements for overnight accumulation and immediate post-brushing. Balancing the mean baseline plaque assessments for each group,

Table 1. Demographic characteristics.

Characteristic statistics	SnF_2 group (N=48)	Triclosan group (N=48)	Overall (N=96)	P-value
Age: Years				
Mean (SD)	36.9 (12.79)	36.3 (14.93)	36.6 (13.83)	0.832[a]
Min. - Max.	19 - 72	19 - 71	19 - 72	
Gender: # (%)				
Female	35 (73%)	33 (69%)	68 (71%)	0.653[b]
Male	13 (27%)	15 (31%)	28 (29%)	

[a] Two-sided P-value comparing treatment groups using ANOVA.
[b] Two-sided P-value comparing treatment groups using a chi-squared test.

subjects were randomized to one of two test dentifrice groups and used the assigned product with a regular manual toothbrush according to the manufacturer's instructions for a 3-week period. At the end of the third week of test dentifrice use, plaque assessments were performed on two separate days as a repeated measurement to reduce variation.

Following their consent to participate, subjects were screened for overnight plaque and their ability to remove it.

At the acclimation visit, subjects were assessed according to entry criteria for their eligibility to participate in the study. The study exclusion criteria were: severe periodontal disease; rampant caries; active treatment for periodontitis; fixed orthodontic appliances; or other diseases or conditions that could be expected to interfere with subjects safely completing the study. Eligible subjects were assigned a kit box containing their acclimation products, and subjects were instructed to brush twice daily. Subjects returned their acclimation products at the baseline visit, which was scheduled for approximately 2 weeks after the acclimation visit.

At the baseline visit, an oral soft tissue examination was performed and any adverse effects were recorded. Digital plaque images were taken for the subjects and they brushed their teeth using their acclimation toothbrush and dentifrice. Subjects were then scheduled for the product distribution visit and were instructed to continue acclimation product use.

At the product distribution visit, subjects were randomly assigned to one of the two treatment groups, stratified according to their plaque area coverage, gender, and age. Subjects were given a treatment kit box with their assigned treatment dentifrice and a soft manual toothbrush (Oral-B Indicator[a]), and were instructed to use their respective product according to the manufacturer's instructions during the 3-week treatment phase. For purposes of double blinding, test dentifrice tubes were overwrapped and packaged in identical treatment kit boxes, which were dispensed in a protected area separate from the examination area and out of the view of the clinical examiner. Subjects assigned to the SnF_2 dentifrice were instructed to apply at least a 1-inch strip of dentifrice onto their toothbrush and brush twice a day (morning and evening) for at least 1 minute. Subjects assigned to the triclosan dentifrice were instructed to brush their teeth thoroughly, preferably after each meal or at least twice a day.

At the end of Week 3 of test product use, subjects returned on each of two separate days after having refrained from eating, drinking, and performing any oral hygiene that morning. At each of the two visit days during Week 3, study continuance was re-assessed and any adverse effects were recorded, after which subjects disclosed plaque followed by digital plaque imaging. Subjects used their test products until the final visit of Week 3.

Table 2. Summary statistics of overnight plaque area (%).

Treatment group	N	Mean (SD)	Min. - Max.	P-value
Baseline				
SnF_2	48	15.38 (10.92)	3.24 to 51.03	0.8207[a]
Triclosan	48	14.90 (9.69)	1.27 to 43.59	
Week 3				
SnF_2	47	11.64 (8.19)	1.50 to 35.14	
Triclosan	47	13.79 (8.53)	0.86 to 37.53	
Week 3 change from Baseline				
SnF_2	47	-3.64 (7.49)	-36.23 to 7.60	0.0017[b]
Triclosan	47	-1.13 (6.43)	-22.27 to 15.14	0.2360[b]

SD = Standard deviation.
[a] Two-sided P-value comparing treatment groups at baseline using ANOVA.
[b] Two-sided P-value comparing Week 3 to baseline using a paired difference t-test.

Image analysis - The DPIA method used to capture and analyze plaque coverage has been previously described.[1-6] The DPIA system with UV illumination was standardized prior to use and once daily a color standard was centered and imaged, then removed prior to imaging subjects. To obtain digital images, subjects disclosed their plaque with fluorescein as follows: first they rinsed for 10 seconds with 25 ml of phosphate buffer, they then rinsed for 1 minute with 5 ml of 1,240 ppm fluorescein in phosphate buffer, and finally they rinsed three times for 10 seconds each with 25 ml of phosphate buffer.

The images captured for each subject were of the anterior facial surfaces of six maxillary and six mandibular teeth, and plaque pixels were classified to calculate the percentage of the tooth covered with plaque divided by the total tooth area (both tooth areas with and without plaque) as follows:

$$\% \text{ plaque area coverage} = [\text{plaque pixels} / (\text{tooth pixels} + \text{plaque pixels})] \times 100$$

The computer analysis results were checked for consistency and accuracy by an expert in image analysis who was blinded to the assigned treatment.

Statistical methods - Approximately 100 subjects (50 per treatment group) were planned to be enrolled in the study. Forty-eight subjects per group completing this trial provides at least 80% power to detect a mean difference between the test groups for overnight plaque area using two-sided testing with a 5% significance level. This estimate assumed an effect size (mean test group difference divided by the standard deviation) of approximately 0.578 or higher.

Group demographic characteristics were compared using ANOVA or chi-square tests. For Week 3, the overnight plaque area was averaged among the 2 days for each subject. For each test dentifrice, the comparison to baseline for mean plaque area was investigated using a paired-difference t-test. For baseline, ANOVA was used for comparing groups for mean plaque area. For Week 3, ANCOVA was used to compare treatment groups for mean plaque area and change from baseline with the baseline measurement as a covariate. Statistical tests were two-sided using the 5% significance level.

Results

Study population - A total of 99 subjects gave their informed consent to participate in the study and of these, 96 qualified subjects were randomized equally to the two treatment groups.

Table 3. Week 3 treatment comparison of overnight plaque area (%) treatment.

Group	Week 3 Adjusted Mean (SE)	Week 3 change from baseline Adjusted Mean (SE)	P-value
SnF_2	11.53 (0.82)	-3.57 (0.82)	0.0435[a]
Triclosan	13.90 (0.82)	-1.20 (0.82)	

SE = Standard Error of the Mean.
[a] Two-sided P-value comparing treatment groups using ANCOVA.

In total, 94 subjects completed at least one or both of the Week 3 study days. Table 1 shows the demographic characteristics of the 96 randomized subjects. The randomized subjects ranged in age from 19 to 72 years (mean 36.6 years) and 71% were female. There were no statistically significant treatment group differences in age or gender (P> 0.65).

Overnight plaque - The overall baseline overnight plaque area mean was 15.14 with a standard deviation of 10.27. The baseline overnight plaque mean was 15.38 in the SnF_2 group and 14.90 in the triclosan group, and groups were not statistically different (P= 0.82). Table 2 provides summary statistics of the overnight plaque area data. For Week 3, the SnF_2 group demonstrated a statistically significant (P= 0.002) reduction in mean overnight plaque relative to baseline, however, the mean difference relative to baseline for the triclosan group was not statistically significant (P= 0.24). For Week 3, the SnF_2 group exhibited significantly lower (P< 0.05) mean overnight plaque by 17% relative to the triclosan group with adjusted means (SE) of 11.53 (0.82) and 13.90 (0.82), respectively (Table 3). In addition, the SnF_2 group exhibited significantly greater improvement from baseline by 3.0 times relative to the triclosan group with change from baseline adjusted means of -3.57 and -1.20, respectively (Figure).

Adverse events - Two adverse events were reported in this study, one in the SnF_2 group (subject withdrew at the product distribution visit due to an aphthous stomatitis) and one in the triclosan group (mouth ulceration). The test dentifrices were well tolerated throughout the study.

Discussion

The antimicrobial and plaque prevention properties of stannous fluoride are well known[12-16] and stabilized 0.454% stannous fluoride dentifrice provides broad oral health benefits that include plaque reduction.[7] The present study compared the anti-plaque efficacy of the stabilized 0.454% stannous fluoride (SnF_2) formulation with another commercially available dentifrice formulated as triclosan/copolymer. Triclosan is an agent known to have antimicrobial properties, and the triclosan/copolymer dentifrice formulation has been shown to have benefits for plaque reduction and for improving gingival health.[17,18]

The present study had a parallel group design with a 3-week treatment period, and subjects were instructed to brush their teeth with the assigned treatment dentifrice according to the manufacturer's instructions and in place of their normal hygiene regimen. This exposure was sufficient to reveal a statistically significant lower mean overnight plaque for the SnF_2 group relative to both baseline (P= 0.002) and compared to the triclosan group (P< 0.05). With 3 weeks of regular everyday use, three times greater mean overnight plaque improvement from baseline was observed for the SnF_2 dentifrice versus the triclosan dentifrice.

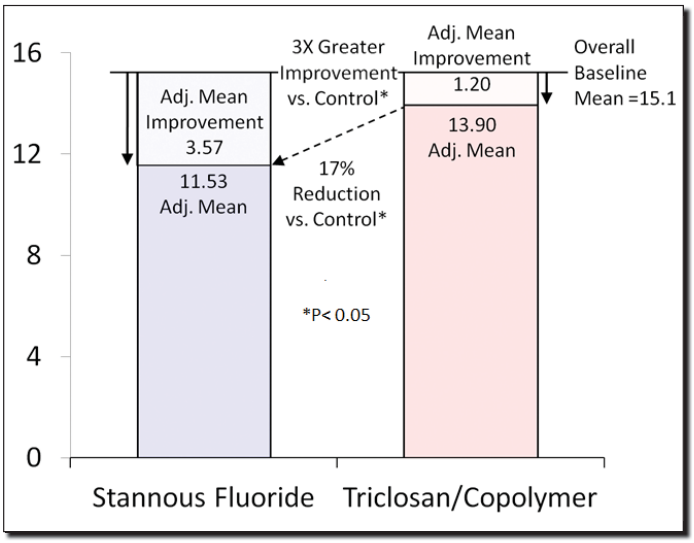

Figure. Week 3 - overnight plaque area adjusted mean and mean improvement by group.

The relative performance of these two dentifrices is consistent with findings from a recently published study which compared the same stannous fluoride and triclosan/copolymer dentifrices over a 6-week use period.[19] The randomized, double-blind, parallel-group trial used the Rustogi et al Modified Navy Plaque Index to compare plaque reduction from baseline after 3 and 6 weeks of treatment. While both treatment groups showed a statistically significant reduction from baseline in mean overnight plaque values at Weeks 3 and 6, there was a statistically significant lower mean overnight plaque level for the SnF_2 group compared to the triclosan group at both Weeks 3 and 6. Thus, research from the examiner-based evaluation and the objective DPIA method reported here show consistent results.

Collectively, the plaque control advantage for stabilized stannous fluoride dentifrice relative to marketed products demonstrated in these and earlier studies,[2-6] confirmed that plaque re-growth inhibition can be achieved by chemical means through agents incorporated into dentifrice formulations and showed that the choice of chemical agent is a crucial factor. The present study showed that dentifrices formulated with stabilized 0.454% stannous fluoride have the potential for providing users with clinically important overnight plaque re-growth inhibition benefits.

Effective plaque control is known to be crucial for the prevention of periodontal disease, which remains a global oral healthcare concern.[20-23] By identifying and confirming the relative oral health care benefits of different dentifrices through randomized controlled comparative clinical studies that adopt advanced methodologies to assess plaque levels, consumers and dental professionals can be confident of reliable data on which to base their choice of oral healthcare products. A stabilized 0.454% stannous fluoride dentifrice has the potential to contribute to improving the everyday oral healthcare of individuals by offering plaque re-growth inhibition benefits.

In conclusion, the results of the present study demonstrated anti-plaque advantages for the stabilized stannous fluoride dentifrice relative to triclosan/copolymer dentifrice.

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b. Colgate-Palmolive Company, New York, NY, USA.
c. American Dental Association, Chicago, IL, USA.

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