



3.A.2.2. ***Evaluation of 0.454% Stannous Fluoride Dentifrice Formulation for Reducing Plaque and Gingivitis Using the Toothshield Clinical Model (Appendix 6)***

Subsequent to the Plaque Subcommittee's review, Procter & Gamble conducted a 21-day experimental gingivitis (EG) clinical study, supervised by Dr. Mark Putt, MSD, PhD at University Park Research Center, Fort Wayne, Indiana. The main objective of the study was to evaluate the effects of commercial and experimental dentifrices containing different antimicrobial systems on dental plaque accumulation and prevention of gingivitis under accelerated conditions of plaque formation and gingivitis. The study design was a modification⁵⁰ of the EG model described by Loe *et. al*⁵¹. Because the EG model is most suited for testing mouthrinses and presents challenges recruiting and retaining subjects for the 21-day study period due to the absence of toothbrushing of the whole mouth, the current study utilized a modified design to address these challenges which have been thoroughly described in the literature. The modification involved promoting gingivitis in a specific region of the mouth (i.e. mandibular quadrant) by covering the area during brushing with a tooth shield while allowing subjects to still brush the remaining three quadrants of their mouth. For treatment purposes, undiluted dentifrice is applied directly to the tooth shield and held in place while brushing. Consequently, treatment effects can be assessed by the agent alone (under the tooth shield), and by the agent in combination with brushing.

The study was conducted in two phases: (1) a pre-trial hygiene period to reduce existing plaque and gingivitis. Gingivitis scores at the beginning of the first phase were used to randomly assign subjects to equivalent groups for the trial period, and (2) a trial period of 21 days during which toothbrushing was suspended in either the

⁵⁰ Putt MS, Van der Weijden GA, Kleber CJ, Saxton CA: Validation of a 21-day, Partial-Mouth Gingivitis Model for Evaluating Chemotherapeutic Dentifrices. *J Periodont Res* 28:301-307, 1993.

⁵¹ Loe, H, Theilade E, Jensen SE: Experimental Gingivitis in Man. *J Periodontol* 36:177-187, 1965.

left or right mandibular quadrant which was fitted with the tooth shield. Subjects brushed all non-shielded teeth with 1.5 g of their assigned dentifrice for 1 minute twice daily while wearing the tooth shield. The tooth shield was filled with approximately 1.5 g of the same dentifrice. Following brushing and expectoration of the dentifrice slurry, subjects removed the tooth shield from the covered teeth and rinsed once with 15 ml of water for 10 seconds to remove any remaining toothpaste.

The study compared a 0.454% SnF₂ dentifrice vs. a dentifrice placebo which had no antigingivitis/anti-plaque agent. Clinical assessments were made at baseline and final (after 21 days of using the toothshields) using the following parameters: (a) gingivitis (for brushed teeth and those protected by the toothshield) using the Modified Gingival Index for inflammation and the Gingival Bleeding Index. In addition gingival status was assessed at the final visit using the Löe-Silness Gingival Index, (b) plaque index on brushed teeth and those protected by the toothshield using the modified Quigley-Hein Plaque Index, and (c) overall soft tissue health. Additionally, dentifrice effects on bacterial accumulation along the buccal maxillary gumline were also determined.

Results in the table below show the treatment effects observed for the shielded sites. When compared against the negative control, 0.454% stannous fluoride dentifrice provided significant ($p < 0.001$) reductions, ranging from 22 to 43% across the various gingival indices. The 0.454% stannous fluoride dentifrice also significantly ($p < 0.0001$) reduced plaque coverage by 19%. These data are presented below.

Effect of Stannous Fluoride Dentifrice on Gingivitis and Plaque Indices in Experimental Gingivitis Model at Day 21 (Shielded Sites)

| Index | Negative Control Dentifrice (n=39) | 0.454% SnF₂ Dentifrice (n=38) | Final % Benefit | Comparison p-values (Treatment vs. Negative Control)^a |
|---|---|---|------------------------|---|
| Gingival Bleeding Index | 0.51 (0.050) | 0.29 (0.054) | 43 | 0.0025 |
| Modified Gingival Index | 1.72 (0.058) | 1.34 (0.059) | 22 | <0.0001 |
| Löe-Silness Gingival Index | 1.11 (0.053) (n=38) | 0.73 (0.061) (n=34) | 34 | <0.0001 |
| Modified Quigley-Hein Plaque Index | 3.75 (0.067) | 3.03 (0.068) | 19 | <0.0001 |

^a p-values for comparisons are one-sided in the direction of greater efficacy for the 0.454% SnF₂ dentifrice treatment

In addition to the statistically significant effect observed in general plaque mass reduction, the study also examined the effects on total facultative anaerobes and gram-negative anaerobes along the gingival margin. Recall that the Plaque Subcommittee indicated that pathogenic bacteria along the gingival margin were a precipitating factor of gingivitis. Consistent with overall plaque mass reductions, significant reductions ($p \leq 0.0001$) were measured in several broad classes of bacteria along the gingival margin. As bacteria are a major component of plaque-associated gingivitis, this independent objective measure supports the proposition that 0.454% stannous fluoride dentifrice provides meaningful and consumer relevant antiplaque benefits.

**Effect of Stannous Fluoride Dentifrice on Bacterial Accumulation Along Buccal
Maxillary Gumline at Day 21**

(Log 10/CFU/mL)

| | Negative Control Dentifrice (n=26) | 0.454% SnF₂ Dentifrice (n=25) | Comparison p-values (Treatment vs. Negative Control)^a |
|--|---|---|---|
| Total Facultative Anaerobes | 6.79 (0.073) | 6.34 (0.075) | <0.0001 |
| Gram-negative Anaerobes | 5.82 (0.107) | 5.24 (0.109) | 0.0001 |

^a p-values are one-sided in the direction of greater efficacy for the 0.454% SnF₂ dentifrice treatment