Clinical efficacy of a stannous fluoride toothpaste stabilized with zinc phosphate in reducing supragingival calculus formation compared to a sodium monofluorophosphate toothpaste: A randomized controlled trial

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Abstract: Purpose: To evaluate the comparative clinical efficacy of a test toothpaste containing 0.454% stannous fluoride stabilized with zinc phosphate as compared to a regular fluoride toothpaste containing 0.76% sodium monofluorophosphate in controlling supragingival calculus formation over a 12-week period. **Methods:** A randomized, single-center, double-blind, parallel-group study was conducted in Bangkok, Thailand. Healthy adults (n= 100) with a baseline Volpe-Manhold Calculus Index score ≥7.0 were randomized to either the stannous fluoride (Test) or sodium monofluorophosphate (Control) group. After a dental prophylaxis, subjects brushed twice daily for 12 weeks. Supragingival calculus was assessed using the Volpe-Manhold Calculus Index. The primary efficacy endpoint was the comparison of baseline-adjusted mean calculus scores at 12 weeks, analyzed using ANCOVA. **Results:** 97 subjects completed the study. At 12 weeks, the Test Group had baseline adjusted mean Volpe-Manhold score of 11.47, while the Control Group had a score of 17.48. The Test Group demonstrated a statistically significant 34.4% (P< 0.001) less supragingival calculus formation compared to the Control Group. (*Am J Dent* 2026;39:73-76).

Clinical significance: A toothpaste containing 0.454% stannous fluoride provided a statistically significant and clinically relevant reduction in supragingival calculus formation compared to a standard sodium monofluorophosphate fluoride toothpaste after 12 weeks of use.

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Introduction

Supragingival dental calculus is a mineralized deposit found in adult populations worldwide and fundamentally defined as calcified dental plaque. The formation of calculus begins with the adherence of a pellicle, an acellular protein film, on the tooth surface, which lays the foundation for bacterial colonization and, ultimately, the formation of biofilm, known as dental plaque.[1] The transformation from soft plaque to hard calculus takes place when biofilm mineralizes with calcium phosphate salts.[2] Calcifying plaques can become mineralized up to 50% in just 2 days.[3]

The clinical significance of dental calculus lies in its physical structure. The porous and rough exterior created by mineralization provides an ideal surface for accumulation of a plaque biofilm that is more difficult to remove through mechanical means.[2] This protective reservoir for potentially pathogenic bacteria can lead to further dysbiosis and inflammatory gingival disease.[4] Therefore, chemical interventions have been designed to interrupt the mineralization of plaque and halt calculus formation. Many chemical anti-calculus actives added to toothpastes operate by inhibiting crystal growth. Pyrophosphates and zinc ions (Zn^{2+}) are well-known crystal growth inhibitors that operate through different mechanisms.[5] Pyrophosphates, which are endogenous to human saliva, act through chelation of the positively charged calcium ions, whereas Zn^{2+} acts by substituting calcium within the crystal lattice and disrupting regular crystal formation.[5]

This clinical trial evaluated the efficacy of a stannous fluoride (SnF_2) toothpaste[a] stabilized with zinc phosphate [$Zn_3(PO_4)_2$] in the inhibition of calculus formation compared to a commercially available sodium monofluorophosphate (Na_2PO_3F) toothpaste.[a] SnF_2 is a well-known antibacterial agent, reducing the metabolic activity of bacterial biofilms; however, its clinical efficacy is dependent on stannous (Sn) maintaining a 2+ oxidation state.[6,7] Stabilization with $Zn_3(PO_4)_2$ allows for a toothpaste formula with increased bioavailability of Sn^{2+} and F^- ions without sacrificing the flavor and esthetics of the toothpaste, which are important factors to consider in dental hygiene compliance.[6] In addition to the stabilization benefits, the inclusion of $Zn_3(PO_4)_2$, a common dental material, leverages the inclusion of positively charged Zn^{2+} ions that directly interfere with the formation of calcium phosphate crystal lattice of dental calculus.[8]

The dual action of the SnF_2 toothpaste stabilized with $Zn_3(PO_4)_2$, where SnF_2 targets the plaque matrix while Zn2+ targets the mineralization process, led to the hypothesis that this test toothpaste will provide a greater inhibition of calculus formation in the high-calculus adult population analyzed here compared to commercially available Na_2PO_3F toothpaste.

Materials and Methods

Interventions - Test product: A toothpaste containing 0.454% SnF_2 stabilized with $Zn_3(PO_4)_2$.[a] Control product: A toothpaste containing 0.76% Na_2PO_3F.[a]

Study design - This randomized controlled trial consisted of a double-blind, two-cell, parallel group design, involving female and male participants between the ages of 18 and 70 from the Bangkok, Thailand area. The study was conducted between May 17, 2017 and October 6, 2017 at the Faculty of Dentistry, Mahidol University, Bangkok, Thailand.

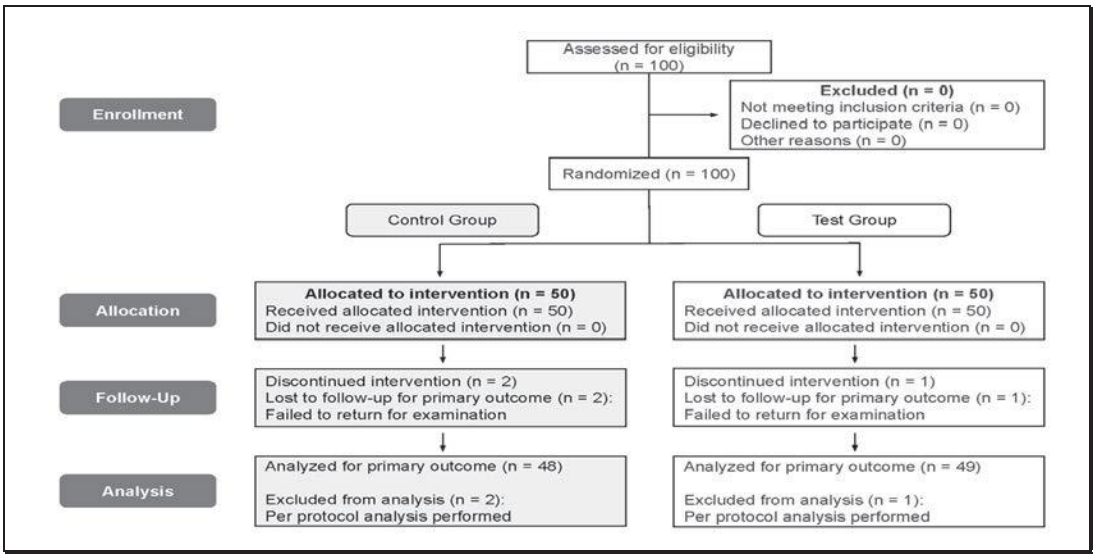

Figure. Randomized Clinical Trial Flow Diagram. CONSORT flow diagram of participant inclusion and exclusion from study and analysis.

Study population - One-hundred subjects were recruited to participate based on inclusion criteria and randomized into one of two treatment groups. Ninety-seven participants completed the 20-week trial period. The resulting data was analyzed in a per protocol manner.

Inclusion & exclusion criteria - To be included in the study, subjects were required to (1) sign an Informed Consent form, (2) be considered in general good health by the practitioner, (3) be between the ages of 18 and 70, (4) have at least six scoreable mandibular anterior teeth without large restorations or prosthetic crowns, (5) exhibit a Volpe-Manhold Calculus Index (VMI) score $\geq$ 7.0, and (6) be capable of participating for the full 20 weeks of study. Exclusion characteristics applied to this study were standard for calculus formation clinical trials during this time and reflect the same criteria seen in Kraivaphan et al.[9]

Study protocol - Pre-Test Phase - Prior to the beginning of the 12-week test phase, qualifying adult male and female subjects experienced an 8-week pre-test phase of the study, during which they received an oral soft and hard tissue evaluation and a complete oral prophylaxis and were provided with the control toothpaste and a soft bristle adult toothbrush with instructions to brush teeth twice a day for 1 minute.

Baseline visit - After 8 weeks of brushing with the control toothpaste, subjects were examined for baseline supragingival calculus formation via VMI. Qualifying subjects were then randomized into one of two treatment groups with balanced gender and baseline calculus scores. Subjects that entered the 12-week test phase were given oral prophylaxis to bring VMI scores to zero for all participants. Participants were then given an assigned toothpaste, depending on treatment group, and a soft bristle adult toothbrush for home use. All participants were instructed to brush once in the morning and once at night for 1 minute with approximately 1.5 grams of their assigned toothpaste for a period of 12 weeks. Prior to each study visit, subjects were instructed to refrain from brushing their teeth and eating and drinking for 4 hours.

Randomization - Qualifying subjects that met the inclusion/exclusion criteria were randomly assigned to one of two treatment groups. Neither the examiner nor the participants were aware of the identity of the product allocation. Study subjects were assigned a subject identification number in chronological order from 001 to 100 and were randomized to a study group following a computer-generated randomization list.

Blinding - Qualifying subjects, clinical study site personnel, and the statistician were blinded to product assignment. All toothpastes had a white over-wrapping paper for product identity concealment. Each tube had a label with study group code, instructions for at-home use, safety information, and emergency contact information.

Outcome assessment - Volpe-Manhold Calculus Index - A single examiner performed all the clinical examinations in this study. Supragingival calculus was scored using VMI.[10-14] Supragingival calculus formation was measured in the mesio-, mid-, and disto-planes on the lingual surfaces of the six mandibular anterior teeth with a millimeter-graduated periodontal probe. The resulting 18 sites were added to produce an overall VMI score for each subject.

Oral soft and hard tissue examination - Soft and hard tissue examinations involved the assessment of the soft and hard palate, gingival and buccal mucosa, mucogingival fold, sublingual, and submandibular areas, tongue, salivary glands, and the tonsillar and pharyngeal areas.

Adverse events - Adverse events were determined via interview with the subjects and from a dental examination by the examining dentist.

Statistical analysis - Chi-square analysis was used to determine statistical differences between the treatment groups with respect to gender. Independent t-tests were used to determine statistical differences between the treatment groups with respect to age and with respect to VMI scores at baseline. ANCOVA was used to determine statistical differences with respect to baseline-adjusted VMI scores at the 12-week examination. These were all two-sided hypotheses with a significance level of $\alpha = 0.05$.

Ethics approval - An Informed and Consent form was required to be completed by all eligible participants. The Mahidol Uni-

Table 1. Demographic summary of participants.

Group	Number of participants (females)	Mean age (SD)	Age range
Test group	49 (26)	40.82 (7.93)	23-55
Control group	48 (27)	40.02 (9.28)	20-59
All	97 (53)	40.42 (8.59)	20-59

No statistically significant (P> 0.05) difference between treatment groups respective to age and gender. SD: standard deviation.

versity Institutional Review Board (MU-DT/PY-IRB 2017/023.3003), Bangkok, Thailand, reviewed and approved this study.

Trial registration - The trial was conducted in 2017. To align with current standards of data transparency, the study was retrospectively registered at ClinicalTrials.gov (NCT07223060) on October 29, 2025. The retrospective registration is a consequence of the study's completion prior to the widespread adoption and enforcement of prospective registration policies.

Results

Trial participants and baseline characteristics - Of the 100 subjects included in the study, 97 participants completed the study protocol in full. Three subjects did not complete the 20-week study and were excluded from analysis (Figure). Two subjects from the control group (n= 48) and one subject from the test group (n= 49) failed to return for follow-up examination (Table 1). The two treatment groups did not differ statistically significantly with respect to gender (P= 0.752) and age (P= 0.651).

Mean calculus index scores at the start of the 8-week, pre-test, washout phase was 22.05 for the Test Group and 21.72 for the Control Group (P= 0.758). Following the pre-test phase, baseline mean calculus index scores were 16.94 for the Test Group and 16.92 for the Control Group (P= 0.978) (Table 2). After baseline examination, a prophylaxis was conducted on all participants, in which the VMI scores became zero.

Between treatment group efficacy comparison - After 12 weeks of product use, the Test Group showed a statistically significant 34.4% (P< 0.001) less supragingival calculus formation relative to the Control Group (Table 3). The Test Group presented a baseline-adjusted mean VMI score of 11.47 [95% CI (10.83-12.12)] and the Control Group had a mean VMI score of 17.48 [95% CI (16.83-18.13)].

Safety - Neither examiners nor participants reported any adverse events.

Discussion

This 12-week study effectively demonstrated the significant inhibition of calculus formation by the test SnF_2 toothpaste compared to a commercially available Na_2PO_3F control toothpaste. The study population exhibited a clear inclination toward calculus formation during the pre-test phase in which they brushed regularly with a fluoride toothpaste and had average VMI scores well-within the range considered to be "rapid-forming".[15] The administration of prophylaxis prior to the test phase ensured that the study could properly determine if chemical intervention would reduce calculus formation in a population of calculus-prone adults. Since plaque becomes fully

Table 2. Unadjusted mean Volpe-Manhold Calculus Index Scores at the Pre-Test Phase, Baseline, and Week 12.

Treatment group	Pre-test Mean (SD)	Baseline Mean (SD)	12-week Mean (SD)
Test group	22.05 (5.59)	16.94 (3.85)	11.48 (4.12)
Control group	21.72 (4.96)	16.92 (4.09)	17.47 (4.24)

Baseline measurements were taken after an 8-week, pre-test, washout phase. After baseline examination, a prophylaxis was conducted on all subjects, in which the Volpe-Manhold Calculus Index scores became zero. There were no statistically significant differences between the two treatment groups at the pre-test phase (P= 0.758) and baseline (P= 0.978) with respect to calculus index scores. SD: standard deviation.

Table 3. Baseline-adjusted Mean Volpe-Manhold Calculus Index Scores after 12 Weeks of product use.

Treatment group	Adjusted Mean (SE)	Adjusted 95% CI	% difference (significance)
Test group	11.47 (0.32)	10.83-12.12	34.4%
Control group	17.48 (0.32)	16.83-18.13	(P< 0.001)

A positive value for between treatment percentage difference indicates less tartar formation in the Test Group relative to the Control Group. Significance between baseline-adjusted means was determined by ANCOVA. SE: standard error.

mineralized within 12 days of biofilm establishment for rapid calculus formers and 20 days for slow formers, the 12-week timeline for intervention fully encompassed potential for calculus establishment.[3]

The resulting 34.4% less calculus formation after 12 weeks of brushing with the SnF_2 toothpaste compared to the control toothpaste was significant and reflected in the literature. This same toothpaste formulation was tested for anti-calculus efficacy in a similar population from Bangkok, Thailand against an herbal toothpaste and a negative control.[9] Compared to the negative control, the SnF_2 toothpaste test group had 38.5% less calculus formation after 12 weeks of use. Another study[8] showed that a group tested with SnF_2 toothpaste with zinc citrate, as opposed to $Zn_3(PO_4)_2$, exhibited 21.7% less calculus formation than the negative control group after 12 weeks. These similar studies indicate that the resulting percentage of calculus reduction in this study is within an expected range. However, it is important to note that results of independent clinical trials cannot be directly compared.

In addition to stabilizing SnF_2 and providing positively charged Zn^{2+} ions that directly interfere with the mineralization of dental plaque, there is reason to believe that the inclusion of $Zn_3(PO_4)_2$ may contribute to preserved levels of salivary pyrophosphate, providing an added benefit to this toothpaste formulation.[5] Supraphysiological concentrations of Zn^{2+} ions, as are delivered topically in toothpaste, are inhibitory to alkaline phosphatase's pyrophosphatase function.[16] This competitive inhibition as demonstrated in vitro competes with the enzyme's substrate for its active site. While this original research was performed on human intestinal alkaline phosphatase and a 2024 review[17] identified that the direct evidence for the inhibition of human salivary enzymes by zinc is scarce, it is possible that this enzymatic inhibition potentially provides secondary anti-calculus benefits. Further research on human salivary enzymes is warranted.

While benefiting from a randomized, double-blind design, the use of a standardized and validated scoring index, and the inclusion of an 8-week pre-test phase to ensure a population

of rapid-forming calculus. This study has some limitations. First, the homogeneity of a single-center study conducted in Bangkok, Thailand could present a population that is limited in its generalizability to other populations with different oral hygiene habits, diets, and genetic predispositions. Additionally, while single-examiner bias was partially managed given the examiner was blinded to the product allocation, having multiple examiners who are calibrated and standardized can further reduce this specific risk.

Within the parameters of this 12-week, double-blind, clinical study, the test toothpaste containing SnF_2 stabilized with $Zn_3(PO_4)_2$ resulted in statistically significant inhibition of supragingival calculus formation compared to a standard Na_2PO_3F toothpaste. These findings support the hypothesis that this SnF_2 toothpaste is an effective option for individuals seeking calculus control.

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