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ORIGINAL ARTICLE

A randomized double-blind clinical trial evaluating comparative plaque and gingival health associated with commercially available stannous fluoride-containing dentifrices as compared to a sodium fluoride control dentifrice

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Abstract

Background: Gingivitis is a non-specific inflammatory lesion in response to the accumulation of oral biofilm and is a necessary precursor to periodontitis. Enhanced oral hygiene practices, including utilization of a dentifrice that could significantly improve plaque accumulation and gingival inflammation, is desirable to prevent and treat gingivitis and potentially prevent progression to periodontitis. This clinical study aimed to investigate the effect of a new stannous fluoride-containing dentifrice with 2.6% ethylenediamine tetra acetic acid (EDTA) as an anti-tartar agent to reduce plaque index and gingival index over a 3-month study period compared to other commercially-available fluoride-containing dentifrices.

Methods: This double-blind, randomized controlled clinical study evaluated plaque, gingival inflammation, and sulcular bleeding in patients using one of five commercially available fluoride-containing dentifrices The dentifrices tested contained: 0.454% stannous fluoride and 2.6% EDTA (D1), 0.24% sodium fluoride (C), and 0.454% stannous fluoride (D2-D4). One hundred fifty subjects participated over a 3-month period. Co-primary endpoints were improvements

JOURNAL OF Periodontology

in plaque index (PI) and modified gingival index (mGI) from baseline values. No professional cleaning was performed during the study period.

Results: All subjects in the study demonstrated statistically significant improvements in all measures of oral hygiene over the 3-month study period. Subjects using dentifrice 1 (D1) showed statistically significantly greater reductions in PI, mGI, and modified sulcular bleeding index (mSBI) compared with all other commercially-available dentifrices tested ($p < 0.00001$).

Conclusions: A new dentifrice with 0.454% stannous fluoride and 2.6% EDTA demonstrated significant improvements in clinical parameters associated with gingivitis compared to other sodium and stannous fluoride containing dentifrices.

KEYWORDS
bleeding, gingivitis, inflammation, oral hygiene, plaque control, prevention

1 | INTRODUCTION

Oral microbial dysbiosis is associated with the development of dental caries, gingivitis, periodontitis, peri-implant mucositis, and peri-implantitis.[1–5] These diseases are pervasive and have significant health, financial, and psychological impacts on individuals and societies.[6–9] Dental biofilm begins to form immediately after cessation of oral hygiene measures with the adhesion of initial colonizing microorganisms to the dental pellicle.[10] Over 800 species of microbes have been found in dental biofilm; and as dental biofilm accumulates, the environment becomes more conducive for more pathogenic microbiota.[11,12]

Given the impact of biofilm-mediated oral diseases on individual patients and society in general,[6–9] the regular and effective removal of biofilm from tooth surfaces is an integral part of the prevention and treatment of both caries and periodontal diseases. Despite the importance of patient-delivered oral hygiene measures, often insufficient to fully prevent and/or control disease, in part due to suboptimal delivery of home care.[13] In fact, despite recommendations that patients use a manual or powered toothbrush for at least 2 min twice daily,[14] patients perform an overage 45–70 s of toothbrushing per day.[15] Further, most patients do not adequately perform interproximal cleaning with daily flossing frequency estimated to be as low as 26%.[16] Based upon these findings, the importance of regular biofilm removal and disruption for the promotion of optimal oral health cannot be overstated,[17] and the employment of enhanced oral hygiene practices to reduce microbial dysbiosis may be critically important to establish and maintain oral health.[18]

In order to augment the effectiveness of patient-delivered oral hygiene regimens and enhance dental biofilm disruption, the use of chemotherapeutic agents, including those in dentifrices, have been employed. Some anti-plaque components present in commercially available dentifrices are associated with adverse symptoms such as taste alteration, tooth structure staining, dental abrasion, dentinal sensitivity, and reactive gingival lesions.[19]

While all tartar control toothpastes contain chelators (e.g., sodium hexametaphosphate, sodium pyrophosphate *aka* tetrasodium pyrophosphate, sodium tripolyphosphate *aka* pentasodium triphosphate, malic acid copolymer, citric acid, EDTA *aka* edathamil, and others); previous studies have demonstrated the efficacy of a new dental gel with EDTA, in reducing oral plaque deposits, gingival inflammation, and probing depths with minimal patient-reported side effects or impact upon tooth surface microarchitecture and microhardness.[20–26]

While only one of these reports evaluates a formulation that includes stannous fluoride,[26] the comparative efficacy of a similar dentifrice formulation without stannous fluoride in plaque and gingival inflammatory reduction is consistent across studies.[20–26] A critique of previous investigations included a lack of comparison between multiple commercially-available dentifrices, including a direct comparison with other stannous fluoride formulations.[20–26]

This study sought to investigate the effects of a new dental gel toothpaste containing 0.454% stannous fluoride (Livionex, Los Gatos, CA) on clinical plaque deposits and gingival inflammation in patients without provider-delivered care over a 3-month period. The new dentifrice was compared to four other commercially available dentifrices.

2 | MATERIALS AND METHODS

2.1 | Study design and participants

This single-center, double-blind, randomized, controlled clinical study evaluated plaque accumulation, gingival inflammation, and sulcular bleeding in individuals using five commercially-available dentifrices over a 3-month period. This project was performed at the University of California Irvine and approved by the University Institutional Review Board (IRB) (UCI IRB 2013-9778 and 2002-2805) and registered at ClinicalTrials.gov (#NCT02271815). All procedures were conducted in accordance with the Helsinki Declaration of 1975, as updated in 2013.[27] All study activities followed good clinical practice for the conduct of research and no substantial changes were made to the protocol and/or study design after the commencement of the study.

Qualifying individuals from university staff, students, faculty, local community, local dental offices, and low-cost dental clinics were invited to participate in this research. Inclusion criteria were as follows: (1) males or females ≥ 18 years of age with a minimum of 25 teeth; (2) baseline mean whole-mouth plaque index ≥ 2.0,[28] (3) baseline mean whole-mouth modified gingival index ≥ 2.0,[29] (4) baseline mean whole-mouth modified sulcular index ≥ 1.0,[30] (5) ability to provide written informed consent and comply with study visits as described in the protocol, and (6) availability for follow up via telephone. Exclusion criteria included: (1) pregnant females; (2) participation in another clinical trial within 30 days of baseline; (3) a history of periodontitis and/or clinical probing depths ≥4 mm; (4) urgent dental needs; (5) history of adverse effects after use of oral care products, including dentifrices and mouth rinses, and/or allergy to personal care/consumer products or their ingredients; (6) unable or unwilling to sign the informed consent form; (7) diagnosis of immune deficiency diseases (e.g., HIV/AIDS, poorly controlled diabetes mellitus); (8) use of anti-tumor necrosis factor alpha (anti-TNF-α) medication, anti-inflammatory drugs, or immune suppressants; (9) use of systemic antibiotics within 3 months prior to baseline; (10) other systemic conditions or medication use at baseline that the principal investigator adjudicated may affect the patient's ability to participate with study requirements (including the use of local antibiotics for oral diseases/conditions); and (11) cigarette smoking. Informed consent was obtained from eligible participants. These participants were then randomly assigned by a computer-generated block randomization in a 1:1:1:1:1 ratio to receive one of five commercially available dentifrices containing 0.24% sodium fluoride (one dentifrice), 0.454% stannous fluoride (four dentifrices). Recruitment occurred on a rolling basis beginning in January 2022 and all study visits were completed by a single examiner by April 2022.

2.2 | Study products and interventions

In this double-blind study design, study participants and study examiner were blinded to randomization throughout the study duration. Participants did not receive a professional dental cleaning during the study duration. Subjects were provided with a new manual toothbrush (Oral-B, Pro-Flex, Procter & Gamble Company, Cincinnati, OH) and were given standardized instructions in the sulcular brushing method using the tell-show-do method by a study dentist with over 25 years of experience. All study products were packaged in uniform, unlabeled white numbered tubes.

The study products were:

1. Dentifrice containing 0.454% stannous fluoride (LivFresh Dental Gel SF, Livionex Inc., Los Gatos, CA). (Referred to as D1)
2. Dentifrice with 0.24% sodium fluoride (AIM multi-benefit cavity protection gel toothpaste, Church & Dwight, Ewing, NJ). (Referred to as Control)
3. Dentifrice with 0.454% stannous fluoride (Parodontax Daily Fluoride Anticavity and Antigingivitis Toothpaste, GlaxoSmithKline, Brentford, UK). (Referred to as D2)
4. Dentifrice with 0.454% stannous fluoride (Colgate Total SF; Colgate-Palmolive, New York, NY). (Referred to as D3)
5. Dentifrice with 0.454% stannous fluoride (Crest Pro-Health; The Procter and Gamble Company, Cincinnati, OH). (Referred to as D4).

Participants were instructed to brush with the study material twice daily for 2 min using a pea-sized amount of the provided dentifrice. Subjects were instructed to use only study oral hygiene products and to refrain from use of other oral hygiene products, including interproximal cleaning devices for the study duration. Compliance was confirmed with once-weekly telephone contact. Dentifrice tubes were collected by study personnel at monthly visits and tubes were weighed to measure compliance. Masked dentifrice tubes were replenished at monthly visits with the same dentifrice originally assigned at baseline. Each subject received an incentive of $25 per visit in accordance with the IRB-approved protocol.

2.3 | Data collection

Age, sex, and race/ethnicity were recorded for all enrolled subjects. Study participants were seen at baseline (day 0) and monthly thereafter. Subjects initiated brushing protocols with their assigned dentifrice at the baseline (day 0) study visit, which corresponded with study

JOURNAL OF Periodontology

enrollment. The study duration was 3 months (90 ± 5 days) and clinical outcomes were assessed at baseline (day 0) and final visit (90 ± 5 days). Clinical variables were recorded at both study visits by one blinded and calibrated dentist (P.W.S.) with 25 years of experience. All examinations were performed by one examiner and calibration exercises were performed every 3 months with an acceptable minimum of 90% intra-examiner agreement. Clinical measurements assessed included:

1. Plaque Index (PI): Quigley Hein with Turesky modification[28]
2. Modified Gingival Index (mGI): Silness and Löe gingival index without the bleeding on probing component[29]
3. Modified Sulcus Bleeding Index (mSBI).[30]

Additionally, patient-reported oral hygiene compliance and patient-perceived dentifrice efficacy and tolerance were assessed through weekly telephone calls with study personnel. All patients were asked about their brushing duration and frequency as well as any reported adverse events.

The co-primary efficacy endpoints were improvement in mean PI and mGI at 3 months as compared to baseline. The secondary efficacy endpoint included improvements in mSBI. The prospective study objective was to compare the relative efficacy of five commercially available fluoride-containing dentifrices. Safety was monitored throughout the study by assessing the incidence, timing, and severity of adverse events as well as by the overall assessment of oral health by the examiner at the final study visit. Subjects were also provided with a direct telephone number to contact in the case of any adverse events (AEs) or serious adverse events (SAEs).

2.4 | Sample size and statistical analysis

This investigation was a comparative study using multiple commercially available stannous fluoride and sodium fluoride containing toothpastes.

Sample size calculations were based on prior studies using D1 and a single commercially-available stannous fluoride toothpaste as control. A standard deviation of 0.257 for gingival index and a limit of 0.22 (10% of the final GI value of 2.2) was used. Using a significance level (alpha) of 0.05 (5%) and a Power (1-beta) of 0.8 (80%), the necessary sample size required was 15 subjects per treatment group or a total size of 75 subjects. For an abundance of caution, and in order to meet ADA Seal of Acceptance requirements, the principal investigator increased the treatment group size to 30 subjects per group. There were five groups of stannous fluoride and sodium fluoride containing toothpaste. A total of 150 study subjects were randomized across each group in a 1:1:1:1:1 ratio.

Statistical significance was measured using a two-tailed Student's T-test. Because multiple comparisons between the five groups were made, this resulted in 10 comparisons for each measurement (i.e., plaque index, mGI, mSBI). Therefore, a Bonferroni correction was used to modify the alpha (p-values) required for statistical significance. This correction implies that the test at $p = 0.05$ significance should be correctly tested at a statistical significance of $p = 0.005$ (0.05/10). Additionally, analysis of covariance (ANCOVA) was also performed to account for the variation in the baseline values in the indices across various groups.

3 | RESULTS

Full compliance with study protocols was reported by all enrolled subjects throughout the study period. No AEs or SAEs were reported throughout the study period. A summary of participant demographics is included in Table 1. Study participants ranged from 19 years to 29 years old with a mean average age of 23.2 years. The study population was 48% female and 52% male. No statistically significant differences in age, gender, and/or race/ethnicity were seen between groups at baseline. There were statistically significant differences at baseline for PI, mGI, and mSBI between groups (Table 2). Due to these baseline differences, this study used change (and percentage change) in clinical parameters from the baseline for the most accurate comparisons. Study findings are summarized in Tables 3 and Figures 1 and 2. In addition, an ANCOVA was also performed on the net changes in the indices, and the results are summarized in Table 4.

3.1 | Plaque index

PI was reported as whole-mouth mean values. The findings related to PI at baseline and 3 months are reported in Table 2. All groups demonstrated statistically significant improvement in whole mouth plaque scores throughout the study. The D1 group demonstrated a statistically significantly larger reduction in whole mouth PI compared to other groups ($p < 0.00001$). The results are summarized in Tables 3 and 4.

3.2 | Modified gingival index

Full mouth mean mGI was reported for all five dentifrice groups at baseline and 3 months.[29] The findings related to mGI at baseline and 3 months are reported in Table 2.

TABLE 1 Study population demographics.

	Control	D1	D2	D3	D4
AA-African-American	0	1	0	1	0
AS-Asian	10	10	10	9	11
C-Caucasian non-Hispanic	1	3	5	5	3
C/H-Caucasian/Hispanic	17	12	13	15	14
M- More than 1 race	2	3	1	0	2
PI- Pacific Islander	0	1	1	0	0
Total	30	30	30	30	30
Mean age	24	22	25	22	23
Age range	21–28	18–28	18–29	18–26	19–27
Male	16	16	14	17	15
Female	14	14	16	13	15

Note: Control = AIM; D1 = LivFresh SF; D2 = Parodontax; D3 = Colgate Total SF; D4 = Crest Pro Health.

TABLE 2 Net changes and percentage changes from baseline to 3 months, by group.

	Control	D2	D3	D4	D1
Plaque index					
Baseline	2.16	2.28	2.49	2.27	2.63
3 Month	1.95	2.02	1.97	1.74	1.22
Change	−0.21	−0.26	−0.51	−0.54	−1.41
Standard deviation	0.09	0.19	0.29	0.23	0.28
% Change	−9.91%	−11.04%	−19.89%	−23.17%	−53.29%
% Standard deviation	3.95%	6.39%	8.75%	8.73%	7.64%
Gingival index					
Baseline	2.43	2.32	2.63	2.41	2.52
3 Month	2.23	1.90	2.10	1.70	1.30
Change	−0.20	−0.42	−0.54	−0.71	−1.21
Standard deviation	0.08	0.13	0.19	0.21	0.23
% Change	−8.40%	−17.96%	−20.28%	−29.23%	−47.99%
% Standard deviation	3.40%	5.52%	6.64%	7.04%	7.28%
Bleeding on probing index					
Baseline	2.42	2.28	2.63	2.38	2.51
3 Month	2.22	1.88	2.09	1.71	1.32
Change	−0.20	−0.41	−0.53	−0.68	−1.20
Standard deviation	0.07	0.04	0.07	0.21	0.20
% Change	−8.29%	−17.90%	−20.18%	−28.01%	−47.41%
% Standard deviation	3.03%	4.27%	6.53%	7.22%	6.62%

Note: Control = AIM; D1 = LivFresh SF; D2 = Parodontax; D3 = Colgate Total SF; D4 = Crest Pro Health.

All study participants, regardless of group, demonstrated statistically significant improvement in whole mouth mGI over the study period and the D1 group demonstrated a significantly larger improvement in mGI compared to other groups ($p < 0.00001$). The results are summarized in Tables 3 and 4.

3.3 | Modified sulcular bleeding index

Full mouth mean mSBI was reported for both test and control groups at baseline and 3 month evaluations.[30] The findings related to mSBI at baseline and 3 months are reported in Table 2. All enrolled study subjects

JOURNAL OF Periodontology

TABLE 3 Pairwise statistical analysis of percentage changes by index, each dentifrice has been compared to other dentifrices.

	Plaque index			Gingival index			Modified sulcus bleeding index		
	% Change			% Change			% Change		
	p-Value[a]	T-Stat	df	*p*-Value[a]	T-Stat	df	*p*-Value[a]	T-Stat	df
D1 vs. Control	<0.00001	27.63	33	<0.00001	26.99	31	<0.00001	29.43	31
D4 vs. Control	<0.00001	7.58	31	<0.00001	14.59	32	<0.00001	13.79	30
D3 vs. Control	<0.00001	5.69	31	<0.00001	8.72	33	<0.00001	9.05	31
D2 vs Control	0.41	0.82	37	<0.00001	8.08	37	<0.00001	10.05	42
D1 vs. D2	<0.00001	23.23	52	<0.00001	18.00	46	<0.00001	20.24	40
D4 vs. D2	<0.00001	6.13	44	<0.00001	6.90	48	<0.00001	6.60	36
D3 vs. D2	<0.0001	4.47	44	0.15	1.47	51	0.11	1.60	39
D1 vs. D3	<0.00001	15.66	54	<0.00001	15.40	56	<0.00001	16.04	58
D4 vs. D3	0.15	1.45	58	<0.00001	5.07	57	<0.00001	4.41	55
D1 vs. D4	<0.00001	14.22	54	<0.00001	10.15	57	<0.00001	10.85	56

Note: Control = AIM; D1 = LivFresh SF; D2 = Parodontax; D3 = Colgate Total SF; D4 = Crest Pro Health.

[a]Because 10 comparisons are being made on the same data set, Bonferroni correction is used. This means that the test at $p = 0.05$ significance should be correctly tested at a statistical significance of $p = 0.005$ (0.05/10).

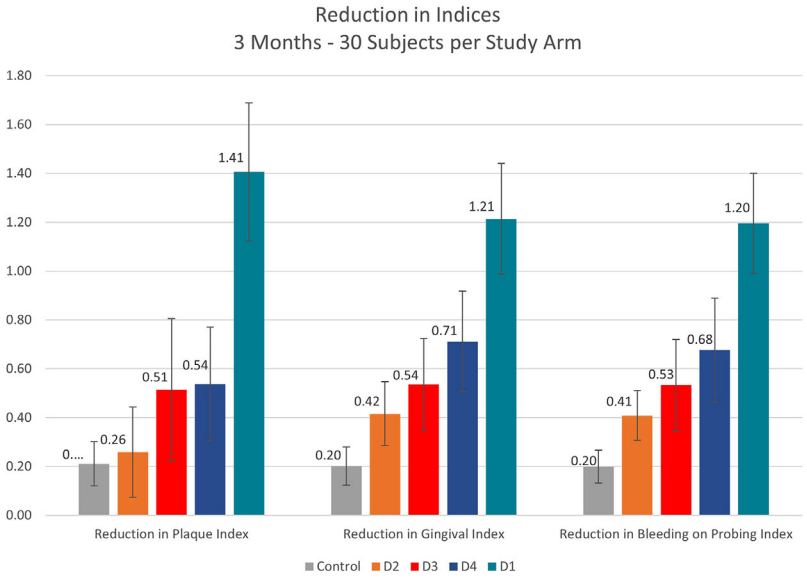

FIGURE 1 Reduction in clinical indices after 3 months after use of five commercially available fluoride-containing dentifrices.

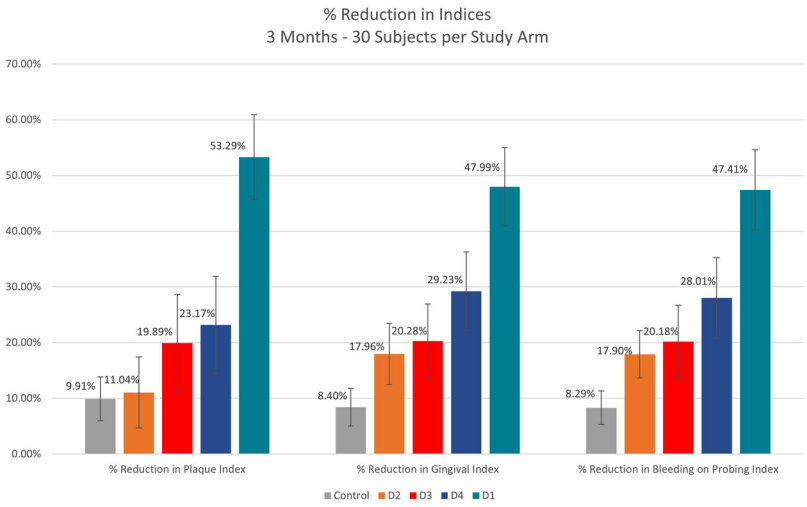

FIGURE 2 Percentage reduction in clinical indices after 3 months after use of five commercially available fluoride-containing dentifrices

TABLE 4 Pairwise statistical analysis of net changes by index using ANCOVA adjusting for baseline variations in the indices.

	Plaque index					Gingival index					Modified sulcus bleeding index				
	Net change					Net change					Net change				
	Adjusted Mean 1	Adjusted Mean 2	*p*-Value*	F-Stat	df	Adjusted Mean 1	Adjusted Mean 2	*p*-Value*	F-Stat	df	Adjusted Mean 1	Adjusted Mean 2	*p*-Value*	F-Stat	df
D1 vs. Control	−1.33	−0.29	<0.00001	307.56	1, 57	−1.20	−0.22	<0.00001	542.41	1, 57	−1.18	−0.21	<0.00001	637.42	1, 57
D4 vs. Control	−0.52	−0.23	<0.00001	51.09	1, 57	−0.71	−0.20	<0.00001	182.88	1, 57	−0.68	−0.19	<0.00001	166.91	1, 57
D3 vs. Control	−0.46	−0.27	0.0005	13.85	1, 57	−0.52	−0.22	<0.00001	54.53	1, 57	−0.52	−0.22	<0.00001	57.81	1, 57
D2 vs. Control	−0.25	−0.22	0.50	0.47	1, 57	−0.42	−0.20	<0.00001	57.31	1, 57	−0.42	−0.19	<0.00001	85.22	1, 57
D1 vs. D2	−1.33	−0.34	<0.00001	316.24	1, 57	−1.17	−0.46	<0.00001	219.99	1, 57	−1.15	−0.30	<0.00001	327.06	1, 57
D4 vs. D2	−0.54	−0.26	<0.00001	39.67	1, 57	−0.69	−0.43	<0.00001	39.64	1, 57	−0.65	−0.43	<0.00001	33.18	1, 57
D3 vs. D2	−0.47	−0.3	0.0015	11.18	1, 57	0.50	−0.45	0.3288	0.97	1, 57	−0.49	−0.45	0.4696	0.53	1, 57
D1 vs. D3	−1.37	−0.56	<0.00001	236.81	1, 57	−1.25	−0.50	<0.00001	232.21	1, 57	−1.23	−0.50	<0.00001	244.30	1, 57
D4 vs. D3	−0.59	−0.46	0.0144	6.37	1, 57	−0.77	−0.48	<0.00001	31.30	1, 57	−0.75	−0.46	<0.00001	30.40	1, 57
D1 vs. D4	−1.31	−0.63	<0.00001	138.89	1, 57	−1.17	−0.75	<0.00001	91.54	1, 57	−1.14	−0.60	<0.00001	117.41	1, 57

Note: Control = AIM; D1 = LivFresh SF; D2 = Parodontax; D3 Colgate Total SF; D4 = Crest Pro Health. Adjusted means are shown comparing the first dentifrice versus the second dentifrice in Column 1. The highlighted *p*-values are not statistically significant.

[a]Because 10 comparisons are being made on the same data set, Bonferroni correction is used. This means that the test at $p = 0.05$ significance should be correctly tested at a statistical significance of $p = 0.005$ (0.05/10).

demonstrated significant improvement in whole mouth mSBI over the study period and the D1 group demonstrated a significantly larger improvement in mSBI compared to the other groups ($p < 0.00001$). The results are summarized in Tables 3 and 4.

4 | DISCUSSION

Previous studies have reported on the impact of the D1 dentifrice formulated without fluoride in patients with gingivitis and periodontitis.[20–26,31] These studies have demonstrated enhanced plaque reduction and improved gingival health in patients with gingivitis.[20,31] Additionally, when the D1 formulation without fluoride was utilized in Stage I/II periodontitis patients[32–34] investigators demonstrated increased reductions in periodontal probing depths, plaque, and gingival inflammation and bleeding when compared to control dentifrice.[23] These findings are particularly encouraging as periodontitis patients demonstrate and increased risk of periodontitis disease progression.[35,36] Despite adequate treatment and ongoing periodontal maintenance, individuals with a history of periodontitis demonstrate an increased risk of periodontal attachment loss and tooth loss over time.[35,36] Further, in treated individuals with more rapid diseases progression (i.e., Grade C periodontitis), dental biofilm dysbiosis persists even in the absence of clinically detectable signs and symptoms of disease, which may account for the elevated risk of periodontal disease progression.[37] It should be noted that this investigation focused on individuals with gingivitis without a history of periodontitis. Control of supragingival oral biofilm in patients with gingivitis has been shown to be effective in reducing the risk of development of periodontitis,[38] but in individuals with established periodontitis, deep probing depths may serve as a reservoir for dysbiotic microorganisms that could fuel continued periodontal disease activity and progression.

It should be noted that decreased biofilm accumulation is not associated with any chemical anti-microbial properties (which are limited to Stannous Fluoride), but instead is associated with electrostatic repulsion of bacteria from the tooth surface. Macroscopic fragmentation of the dental biofilm layer has been associated with improved clinical gingival and plaque indices in patients utilizing D1 without stannous fluoride based upon in vivo multiphoton microscopy and optical coherence tomography (OCT) digital imaging.[21] EDTA usage in the commercially available D1 gel dentifrice without stannous fluoride has been shown to be safe for oral hard and soft tissues.[39,40]

One previous investigation evaluated the D1 formulation used in this study,[26] but the positive control dentifrice utilized in that investigation was a commercially available

JOURNAL OF Periodontology

sodium fluoride toothpaste and did not allow for direct comparison with other commercially available stannous fluoride containing dentifrices.

All dentifrices tested in this investigation demonstrated statistically significant reductions in plaque index, modified gingival index, and modified sulcular bleeding index. Notably, the new D1 gel dentifrice demonstrated superiority to all other tested dentifrices for all clinical parameters tested (Figures 1 and 2). The overall improvement in oral hygiene for all groups may be, in part, associated with the Hawthorne effect (the alteration of behavior by the subjects of a study due to their awareness of being observed) which could cause the subjects to become more rigorous in their oral hygiene, over the study period, compared to before the study.[41] It should be noted, however, the relative efficacy analysis could still indicate superiority in the case of the Hawethorn effect improving all subjects' oral hygiene delivery. This investigation and the significant reduction in plaque and gingival inflammation seen with the D1 gel dentifrice, could suggest that the unique mechanism of action of charge repulsion on biofilm accumulation may allow for a significant enhancement in oral home care outcomes for patients.

All patients are susceptible to gingivitis with dental biofilm accumulation and initiation of meticulous oral hygiene measures in such patients can re-establish gingival health.[42,43] Gingivitis is a necessary precursor to destructive periodontitis, but not all individuals who develop gingivitis progress to periodontitis, indicating the role of the host immune-inflammatory response in the development and disease progression of periodontitis.[44–46] While periodontal health on a reduced periodontium in a periodontitis patient can be reestablished,[46] patients who have a history of periodontitis continue to demonstrate an elevated risk of disease progression and an oral biofilm profile associated with periodontitis.[35–37,47,48] These findings highlight the importance of oral hygiene measures aimed at the removal and delayed re-formation of dysbiotic dental biofilm associated with gingivitis, and later, periodontitis to prevent the destructive attachment loss that is characteristic of periodontal disease.[46]

Despite the reversible nature of gingivitis and its role as the pathological precursor to periodontal disease, gingivitis prevalence remains high and reported oral home care is suboptimal.[15,16,49–51] Since gingivitis is reversible and the treatment of gingivitis and promotion of periodontal health can help to prevent the development of destructive periodontitis, adjuvant oral hygiene aids, including this new D1 gel dentifrice, could allow for delay of dysbiotic biofilm formation without behavioral changes that may be difficult to establish and maintain.[52,53] Such a dentifrice formulation that could potentially reduce biofilm and gingival inflammation below threshold levels with brushing alone might be particularly impactful for individuals with suboptimal oral hygiene practices or elevated risk for periodontitis development.

This study has several strengths, including the documented improvements for all tested dentifrices, which are similar in scope to those seen in previous investigations of oral care products.[19] This may indicate that subjects' application of oral hygiene practices improved simply due to study participation. The individuals included in this study had high baseline levels of plaque and gingival inflammation, indicating that they had suboptimal baseline levels of oral hygiene and were at high risk for the development of dental plaque-related dental diseases, including caries and periodontal diseases. Since individuals with worse oral hygiene are at increased risk, improvement in this population would be the most impactful. This investigation utilized standardized protocols for multiple commercially-available dentifrices allows for assessment of the improved efficacy of the D1 dentifrice as compared to other commonly used dentifrices. Further, this study also employed both sodium and stannous fluoride dentifrice formulations, which then allowed for a more direct comparison of the D1 formulation compared to other stannous fluoride containing dentifrices. This study also disallowed interproximal cleaning and no alterations were made in other oral hygiene practices, which may better reflect the oral home care practices of patients. Last, the improvements seen in this study were accomplished without psychological interventions or intensive behavior modification strategies. This may allow for immediate integration into oral hygiene recommendations and education practices that are ongoing by dental healthcare professionals.

There are also several limitations to the current investigation. This study population included individuals who were generally young and healthy nonsmokers, which may have reduced the generalizability of the results for dentifrices tested when they are used in the general population. There were no baseline periodontal examinations, which then did not allow assessment of changes in periodontal parameters, such as probing depth and clinical attachment level. Given that previous research with a similar dentifrice that did not contain fluoride demonstrated improved probing depth reduction in treated periodontitis patients undergoing periodontal maintenance,[23] future investigations should include such a baseline examination to fully capture any potential additional benefits of dentifrices in common clinical usage. This investigation focused on plaque accumulation and gingival inflammation. While plaque accumulation has been associated with increased caries rates, long-term in vivo investigations may be necessary to determine the efficacy of the D1 dental gel in reducing caries development and/or caries progression.

5 | CONCLUSION

The results of this clinical study demonstrate that use of the innovative D1 gel dentifrice with 0.454% stannous fluoride resulted in clinically and statistically significant improvements in whole-mouth plaque levels and signs of gingival inflammation and bleeding when compared to other commercially available sodium and stannous fluoride containing dentifrices. This may indicate a benefit for individuals with gingival inflammation and/or suboptimal oral hygiene practices to improve overall oral health.

AUTHOR CONTRIBUTIONS

Petra Wilder-Smith contributed to the conception, study design and management, clinical observation, data collection, and evaluation. Thair Takesh contributed to study management and design. Petra Wilder-Smith and Thair Takesh also contributed to, statistical design, data analysis, and data interpretation; Maria L. Geisinger contributed to data interpretation, drafted and critically revised the manuscript; Charles M.Cobb, Joan Otomo Corgel, Nicolaas C. Geurs, Peter L. Jacobsen, and Brian Novy contributed to data interpretation, and critical manuscript revision. All authors gave final approval and agreed to be accountable for all aspects of the work to ensure that questions related to the accuracy or integrity of any part of the work were appropriately investigated and resolved.

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CONFLICT OF INTEREST STATEMENT

The authors report no conflicts of interest related to this study.

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