Journal of Dentistry 160 (2025) 105886

Contents lists available at ScienceDirect

Journal of Dentistry

journal homepage: www.elsevier.com/locate/jdent

A randomised, controlled, trial investigating the effect of tooth brushing with a sodium bicarbonate toothpaste for 12 weeks compared to a conventional fluoride toothpaste on gingivitis

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ARTICLE INFO

Keywords:
Oral hygiene
Plaque biofilm removal
Sodium bicarbonate
Toothbrushing
RCT

ABSTRACT

Objectives: To determine the effect on gingival inflammation of toothbrushing with sodium bicarbonate toothpaste for 12 weeks compared to brushing with a conventional fluoride toothpaste.
Methods: An ethically-approved, single-centre, controlled, examiner-blind, randomized, two-treatment arm, parallel study in consenting healthy ≥18yr participants with ≥20 teeth diagnosed with localised gingivitis. Approximately 200 eligible participants brushed for 2weeks with a fluoride acclimatization toothpaste before randomization to brushing 2/daily with a sodium bicarbonate (test) or fluoride (control) toothpaste. No pre-prophylaxis was conducted prior to study start. Modified gingival index (MGI), bleeding index (BI) and Turesky plaque index (TPI), were measured at baseline, 3, 6 and 12weeks. Participants completed a diary for compliance monitoring.
Results: 190 participants were randomised, 188 completed the study. The test group demonstrated a statistically significant reduction in number of bleeding sites from baseline to 12-weeks ($p = 0.0032$), 6-weeks ($p = 0.0031$) and 3-weeks ($p = 0.0091$), and compared to control group from baseline to 12-weeks ($p = 0.0013$). The test group showed significantly (all $p < 0.0001$) decreased mean MGI score from baseline to 3-weeks, 6-weeks, and 12-weeks compared to control group; significantly decreased mean overall TPI score from baseline to 3-weeks ($p = 0.0012$), 6-weeks ($p = 0.0058$), and 12-weeks ($p < 0.0001$) compared to control; and significantly reduced mean interproximal TPI scores compared to control group from baseline to 3-weeks ($p = 0.0022$), 6-weeks ($p = 0.0099$) and 12-weeks ($p < 0.0001$).
Conclusions: Twice daily toothbrushing with a sodium bicarbonate toothpaste significantly improved oral health reducing localised gingivitis compared to brushing with a conventional fluoride toothpaste, measured by BI, MGI and TPI over 12 weeks.
Clinical Significance: Localised, gingivitis can be resolved or prevented with excellent home-use oral hygiene measures, but this is rarely achieved with mechanical brushing alone. Twice daily toothbrushing with sodium bicarbonate toothpaste demonstrated added value in reducing localised gingivitis and improving oral health compared to brushing with a conventional fluoride toothpaste.

1. Introduction

The vast majority of periodontal diseases are initiated by the accumulation of microbial biofilms on the teeth [1]. If the biofilms are not regularly dispersed or disrupted by self-performed oral hygiene measures, they become dysbiotic as local conditions favour the emergence of pathogenic species that lead to chronicity of soft-tissue inflammation or gingivitis [2].

Gingivitis, a reversible condition, is a necessary pre-requisite for those susceptible to periodontitis, the primary prevention of

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https://doi.org/10.1016/j.jdent.2025.105886
Received 14 April 2025; Received in revised form 2 June 2025; Accepted 5 June 2025
Available online 6 June 2025

periodontitis involving the treatment of gingivitis and reducing sites that bleed on probing (BOP) [3]. Periodontitis is a deeper and more damaging inflammation that destroys the alveolar bone, and if undiagnosed/managed, progresses over years to cause tooth loss. Periodontitis is the 6th most common human disease [4] and not only negatively influences speech, nutrition, social confidence, wellbeing and overall quality of life, but also associates with premature mortality and several systemic diseases and their complications [5]. Given the prevalence and preventable nature of periodontitis, new ways of thinking about gingival health are needed to increase awareness and tangible actions. The Economist Intelligence Unit (EIU) report [6] emphasized the economic and societal benefits of action and inaction in the early treatment of periodontitis. The main conclusion of the EIU investigation of this oral health condition, gingivitis, is that prevention, diagnosis and management of periodontitis is cost-effective, and could save even more costs associated with other health conditions that share risk factors with periodontitis such as diabetes and heart conditions.

For adult gingivitis, 70-100 % worldwide prevalence figures have been reported [7], with 93.9 % in an adult United States of America (USA) population [8] and 97.9 % in an adult Chinese population [9], although lower figures have been observed in European populations (40-50 %) [3]. West et al [10] found BOP was common in a >3500 adult population in seven European countries, with BOP detected at a minimum of one site in 86.7 % of participants; 34.2 % BOP in <10 % sites with probing depths ≤3 mm (gingival health) of participants; 28.7 % BOP for localised gingivitis (10 %>30 % BOP sites) and 37 % of sites BOP for generalised gingivitis (>30 % BOP sites) in this cohort.

According to the 2018 classification of periodontal and peri-implant diseases and conditions [11,12], bleeding on probing is the primary parameter to set thresholds for gingivitis and for periodontal health [13], with <10 % bleeding sites representing health. In comparison to MGI measurement, which primarily assesses the appearance of the gingivae, bleeding measurement is more objective. This classification also considers the concept of localized gingivitis (10 %-30 % bleeding sites) versus generalized gingivitis (>30 % bleeding sites), thereby offering a more precise depiction of a participant's bleeding or inflammatory status. Historically, most periodontal studies relied on the absolute number of bleeding sites, potentially leading to inaccurate information due to variations in the number of measurable sites among participants.

Further, the presence of long-term gingivitis is the best indicator for tooth loss [14]. More recently gingivitis per se has been associated with systemic conditions like cardiovascular diseases and Alzheimer's Disease, with bacteria entering the blood circulation and impacting upon the processes that cause for heart disease [15] or Alzheimer's Disease [16] respectively; and inducing inflammation throughout the body, negatively affecting the control and complications of type 2 diabetes [17,18]).

Gingivitis can be prevented and resolved through effective plaque control; however this is rarely achieved [19]. With the addition of professional prophylaxis significant reductions in inflammation can however be achieved resulting in lowered plaque scores [3]. At home gingival improvements are primarily achieved via mechanical plaque removal i.e., toothbrushing [3,20–24], evidence clearly demonstrates individuals struggle to achieve this goal on a daily basis. As a result, adjunctive therapies have been developed to enhance plaque removal and reduce marginal gingival inflammation, including mouthrinses and /or toothpastes [25].

Baking soda or sodium bicarbonate has been documented as beneficial for cleaning teeth and aiding plaque removal for many years, also being considered to have low abrasivity [26–28]. It is hypothesized that sodium bicarbonate toothpaste properties are attributable to: (1) its physical properties as its large crystals aid in displacing plaque from the tooth surface; (2) interactions with plaque matrix by dissolved sodium bicarbonate, which may, for example, reduce plaque viscosity of the polysaccharide matrix which bind the bacteria together and make it more readily removable by the toothbrush; (3) its ability to favour the disruption of plaque biofilm by improving the penetration of biofilm by toothbrush bristles [28,29].

A number of recent clinical studies across a number of clinical research sites have now been conducted evaluating the efficacy of 67 % sodium bicarbonate toothpastes to reduce plaque biofilm and provide improvements in gingival health [30–37], with the standard ADA methodology including a prophylaxis prior to use of study products [27]. A recent systematic review and meta-analysis [38] showed a significant improvement of gingival index, bleeding index, and plaque index in patients using 67 % sodium bicarbonate toothpaste as compared with control subjects, for modified gingival index and bleeding scores. Valkenburg et al [37] in a meta-analysis investigating the efficacy of sodium bicarbonate toothpastes in controlling plaque and gingivitis, highlighted bicarbonate toothpastes showed 'promising results with respect to plaque in single use studies', however only a small improvement in gingival health (as measured by bleeding scores) relative to a control, however this may reflect variability and uncertainly in the composition of the sodium bicarbonate toothpastes, ranging from 35 % to 67 % w/w. Parkinson et al [39] conducted a pooled analysis on participant level-data from six clinical studies demonstrating twice daily use of a 67 % sodium bicarbonate toothpaste effectively removed plaque from all tooth sites, and resulted in clinically significant improvements in gingival health indices, both overall and for all the tooth regions investigated, compared with a control non-sodium bicarbonate following 24 weeks twice daily use.

The aim of this study was to evaluate and compare the efficacy of a marketed toothpaste containing 67 % w/w sodium bicarbonate and 0.31 % w/w sodium fluoride (Corsodyl Original Toothpaste® GSK consumer health, Weybridge, UK) to a conventional sodium monofluoride toothpaste negative control toothpaste (Colgate Cavity Protection®Colgate-Palmolive, Guildford UK), to reduce gingival inflammation as well as plaque biofilm accumulation in a population with localised gingivitis (10 %-30 % number of bleeding sites) after 12 weeks home use. The null hypothesis being that there would be no difference in gingival inflammation and plaque accumulation, recorded by modified gingival index (MGI), bleeding index (BI) and Turesky plaque index (TPI) after 12 weeks toothbrushing, with either test (sodium bicarbonate) toothpaste or control (conventional fluoride) toothpaste. Pre-prophylaxis was not carried out for either group to better reflect a world scenario.

2. Methods

This was a single-centre, controlled, single clinical examiner blinded, randomised, two-arm, parallel, clinical study in healthy participants with clinically measurable gingivitis. The study was planned to investigate the efficacy of twice daily toothbrushing with a dentifrice containing 67 % w/w sodium bicarbonate and 0.31 % w/w sodium fluoride, without pre-prophylaxis compared to a marketed regular fluoride toothpaste after 12-week, with regard to gingival inflammation. The study was conducted in accordance with Good Clinical Practice Guidelines and the Declaration of Helsinki at a UK Dental School, with ethical approval given by an NHS Research Ethics committee (in accordance with the Internation Organization for the Standardisation (ISO) requirements (ref: 22/YH/0285). The study was registered a priori with www.clinicaltrials.gov (ref: NCT05654662). Consort flow chart, Fig. 1.

Primary outcome measure:

Change in number of bleeding sites (NBS) [40] for the test product, sodium bicarbonate / sodium fluoride toothpaste at 12-weeks compared to baseline

Secondary outcome measures comparing test product, sodium bicarbonate / sodium fluoride toothpaste, to negative control toothpaste conventional fluoride toothpaste for:

- Change from baseline in number of bleeding sites at 3, 6, and 12 weeks

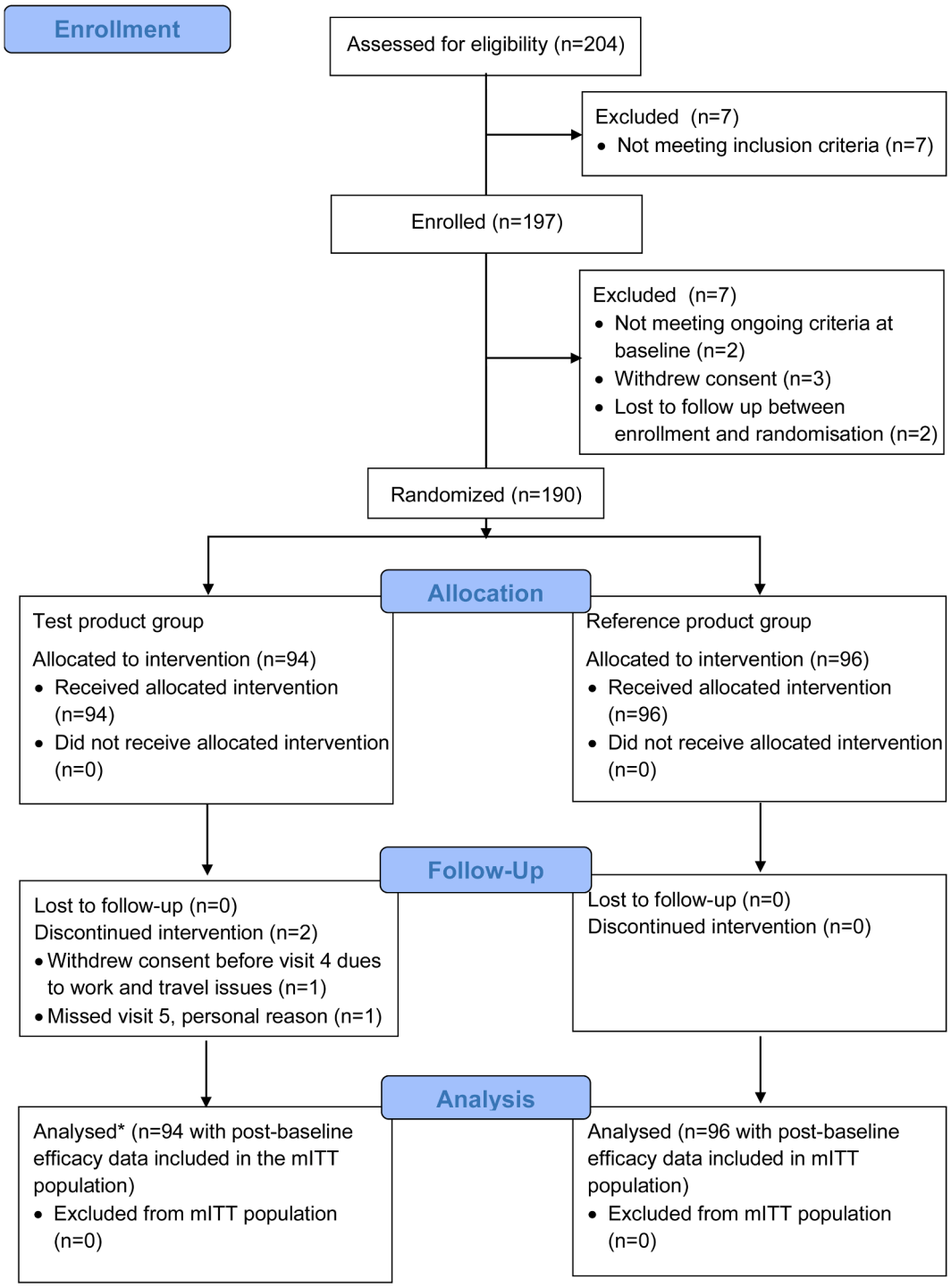

Fig. 1. Consort diagram showing participant flow through the study. *missing data handling strategies were employed as part of the MMRM analyses.

- Change from baseline in BI at 3, 6, and 12 weeks
- Change from baseline in mean Modified Gingival Index (MGI) [41] at 3, 6 and 12-weeks
- Change from baseline in mean Turesky Modification of the Quigley Hein Plaque Index (TPI) [42] for overall and interproximal plaque at 3, 6 and 12-weeks

2.1. Participants

Participants were recruited by the study site database of volunteers. The eligible study population comprised healthy adults aged ≥18 years, with clinically determined plaque induced localised gingivitis (bleeding sites 10-30 %) at baseline [12] and whole mouth mean Turesky Plaque Score >=1.5, with at least 20 teeth comprising 40 evaluable surfaces. Exclusion criteria included subjects with signs of periodontitis (periodontal probing depth>3mm)pregnancy; breastfeeding;; current or recurrent systemic disease, dental pathology or medication that could have affected study outcomes; current or recent (<6 months) smoker; use of smokeless forms of tobacco; bleeding tendency due to medication, medical condition or disorder; orthodontic appliances, recent (<12 months) alcohol or substance abuse; tongue or lip piercing; antibiotics

within 14-days of screening or during study; restorations that could have interfered with study assessments; dentures (partial or full); dental prophylaxis or bleaching within 12 weeks of screening; carious lesions or active periodontal disease; non-plaque induced gingivitis, any condition or medication that was causing xerostomia, or a site or sponsor employee. Participants were randomised into the study provided they satisfied all the participation selection criteria.

2.2. Study products

Two study products were evaluated in separate treatment arms: Test toothpaste containing 67 % w/w sodium bicarbonate and 0.310 % w/w sodium fluoride (Corsodyl Original Toothpaste®, GSK consumer health, Weybridge, UK; Control fluoride toothpaste containing 0.76 % w/w sodium monofluorophosphate (total fluoride 1450 ppm, (Colgate® Cavity Protection; UK Marketed product, Colgate-Palmolive.). The study toothpastes were supplied in tubes over-wrapped in opaque vinyl with any branding obscured to maintain the study blind.

2.3. Study visits

The study comprised of five visit assessments conducted by a gold standard calibrated clinical examiner who performed all the clinical examinations. At visit-1 (screening) participants provided written informed consent and a medical history was taken. Participants underwent full oral soft tissue (OST) and hard tissue (OHT) examination. Eligible participants (fulfilling the inclusion criteria, exclusion criteria, medical history, demographics, prior/current medications) were provided with washout toothpaste, a standard fluoride toothpaste (US Colgate® Cavity Protection; Colgate-Palmolive Company, New York, NY, USA), (the same toothpaste as the control product) and manual toothbrush, and were instructed to brush twice daily at home in their usual manner for two-weeks. Participants recorded each brushing in the provided diary. Participants were not permitted to use any other oral-care products during the study.

At the start of the treatment period (11 to 17 days after the screening visit), participants were asked to return to the site with overnight plaque (abstained from oral hygiene for 12-hours +6/-2 hours). At this baseline visit (visit-2) participants underwent full OST and OHT examinations, assessments of gingival inflammation (MGI), gingival bleeding (BI), periodontal pocket depth (ppd) and supragingival plaque (TPI). Ongoing eligibly included a participant with 10 %< BOp < 30 %, and mean whole mouth TPI score ≥1.5, ppd ≤3mm. Participants outside of the these required criteria were discontinued. Participants were randomised to receive either the test or control product by research dental nurses in the order that they were deemed eligible to continue to the study treatment phase. Participant randomisation was provided by a central system (using an interactive response technology), with appropriate training provided to relevant study staff before the study was initiated. Participants were not stratified. The investigator, clinical examiner and monitor were blinded to product participants received, with separate study site staff involved in the dispensing and supervision in a separate clinical area to the examining clinician. Participants could withdraw at any time.

At visits 2, 3, 4, and 5, repeatability data was generated for MGI and TPI assessments from replicate examinations on the same participant if possible, separated by a minimum of 10 minutes.

All participants undertook supervised toothbrushing with oral hygiene instruction to facilitate understanding the dose of toothpaste to be used and instructions to brush for at least 1-minute with their assigned product, twice daily. Participants were asked to return to site after 3, 6, and 12 weeks (visits 3, 4 and 5 respectively) with overnight plaque. Study toothpaste and diaries were reviewed at each visit and full OST, BI, MGI and TPI were assessed. At visit-5 participants also had OHT examination and prophylaxis if required. Supervised brushing was performed again at visits 2 and 5 to facilitate compliance with dosing and brushing instructions.

2.4. Assessments

The BI assessment where 0 = No bleeding after 30 seconds, 1 = Bleeding observed within 30 seconds of probing and 2 = Bleeding observed immediately on probing [40] was assessed at 6 sites per tooth (mesiobuccal, buccal, distobuccal, mesiolingual/palatal, lingual/palatal, and distolingual/palatal). All scorable teeth in one quadrant were probed approximately 30 seconds prior to recording the gingival units with bleeding present.

The number of bleeding sites for each participant at each visit was calculated as the number of evaluable tooth sites with a BI score of either 1 or 2.

The MGI [41] (Table 1) assessment focused on visual symptoms of gingivitis (redness, texture and oedema), on four sites per tooth (buccal/ lingual/palatal papilla & marginal gingiva). The MGI score for each participant at each visit was calculated as the sum of index values over all evaluable tooth sites, divided by the number of evaluable tooth sites.

Plaque was assessed using the Turesky modification of the Quigley Hein Plaque Index (TPI) [42], where 0 = no plaque, 1 = separate flecks of plaque at the cervical margin, 2 = thin continuous band of plaque (up to 1 mm) at the cervical margin, 3 = band of plaque wider than 1 mm but covering <1/3 of the tooth surface, 4 = plaque covering ≥1/3 but <2/3 of the tooth surface, 5 = plaque covering ≥2/3 of the tooth surface). Third molars and non-natural teeth were excluded from this assessment. The TPI was assessed at six sites per tooth (buccal/ lingual/palatal for distal body and mesial sites). The overall TPI score for each participant was calculated as the sum of index values over all evaluable tooth sites, divided by the number of evaluable tooth sites. The interproximal TPI for each participant at each visit was calculated as the sum of index values over all evaluable distal + mesial tooth sites, divided by the number of evaluable distal + mesial tooth sites.

2.5. Statistical analysis

A sample size of 100 participants per treatment group (before presumed 6 % drop out rate) was required to provide at least 90 % power to achieve two-tailed statistical significance ($p \leq 0.05$) for the primary outcome measure (change from baseline to 12-weeks in the number of bleeding sites in the test product group). Previous data indicated that with this sample size power would exceed 80 % for the secondary outcome measure to determine the change from baseline to 12-weeks in the number of bleeding sites in the test group compared to control group.

The Modified Intent-to-Treat population was used for all analyses. All p-values presented are two-sided and assessed at the 5 % significance level. The primary outcome measure was assessed using a mixed model with repeated measures (MMRM) to assess the adjusted least square mean (LSM) change from baseline in the number of bleeding sites (NBS) for the test product at Week 12. The change from baseline was the dependent variable; fixed effects were time point, treatment group and

Table 1
Modified gingival index scoring system [41].

Score	Description
0	Absence of inflammation
1	Mild inflammation; slight change in colour, little change in colour; little change in texture of any portion of the marginal or papillary gingival unit
2	Mild inflammation; criteria as above but involving the entire marginal or papillary gingival unit
3	Moderate inflammation; glazing, redness, oedema, and/or hypertrophy of the marginal or papillary gingival unit
4	Severe inflammation; marked redness, oedema and/or hypertrophy of the marginal or papillary gingival unit, spontaneous bleeding, congestion, or ulceration.

time point by treatment group interaction; the covariate was the baseline number of bleeding sites. The secondary NBS outcomes (change from baseline at Weeks 3 and 6 and comparison between treatment groups at Weeks 3, 6 and 12) were estimated from the same MMRM used for the primary outcome. A sequential testing strategy was used to adjust for multiplicity for the comparison between test and control groups in the NBS at week 12. This was only assessed for confirmatory evidence if the primary outcome (change from baseline within the test product at week 12) achieved a statistically significant reduction.

For other secondary outcome measures, the same MMRM was applied except with the respective baseline value as the covariate. Participant was included as a repeated measure with unstructured covariance matrix. The Kenward-Roger degrees of freedom approach was applied. Using these models, the adjusted LSM changes from baseline for each treatment group (testing for a non-zero change from baseline) and the difference between treatment groups (testing for a non-zero difference between groups) are presented along with 95 % confidence intervals (95 % CI) and p-values.

A post-hoc analysis of the percentage of subjects achieving <10 % of bleeding sites across all their assessable sites at Week 12 was conducted, with comparison between treatment groups using a chi-square test.

The repeated MGI and TPI assessments were analysed with a Fleiss-Cohen weighted kappa coefficient (k), along with 95 % CI, to assess intra-rater reliability. Reliability was deemed excellent if $k > 0.75$, fair to good if k 0.4-0.75, and poor if $k < 0.4$.

3. Results

Participant flow through the study is shown in Fig. 1. Of the 204 participants screened, 197 were enrolled and 190 participants were randomized, 94 to the test and 96 to the control group, with 188 participants completing the study. Six participants (two from the test and four from the control group) reported a total of six Treatment Emergent Adverse Events (TEAEs) during the study, four of which were oral (two in test product group, both were gingival injury; two were in reference group, one was gingival bleeding, and one was toothache). The two non-oral TEAE were both in reference group. Five of the six TEAEs were mild in intensity, and one was moderate (control group, toothache); all were resolved at the end of the study. All study products were generally well tolerated.

Overall, 71.6 % of the randomized participants were female (73.4 % in the test and 69.8 % in the control group). The mean age of the randomized participants was 39.5 years (standard deviation (SD) 12.6), the mean age in the test group being 39.2 years (SD 12.1) and in the control group 39.8 years (SD 13.2). The majority (75.8 %) of participants were white (77.7 % in the test and 74.0 % in the control group); 10 % were Asian (7.5 % in the test and 12.5 % in the control group); 6.3 % were black (4.3 % in the test and 8.3 % in the control group); and 7.9 % were mixed race (10.6 % in the test and 5.2 % in the control group).

Participant compliance with the study toothbrushing regimen was excellent in both groups. The mean brushing compliance over 12 weeks was 99.9 % in the control and 100 % in the test group.

There was excellent intra-examiner repeatability for both the Modified Gingival Index (MGI) assessments (κ = 0.9060; 95 % CI 0.8976, 0.9143) and the Turesky Plaque Index (TPI) assessments (κ = 0.9454; 95 % CI 0.9414, 0.9494).

Clinical scores at baseline are shown in Table 2 and were similar for both groups.

The efficacy of the test toothpaste to reduce gingival bleeding after 3, 6 and 12-weeks brushing is shown in Table 3. Within the control group the mean number of bleeding sites slightly increased post baseline, while the mean BI remained the same or slightly decreased, but the reductions were not significant. By contrast, within the test product group the number of bleeding sites reduced at all three time points, and there were statistically significant reductions in the number of bleeding sites from baseline to week 3 and from baseline to week 12 (primary objective of the study). Similarly, within the test, but not the control group there was a reduction in BI score from baseline, the reduction being significant at 3, 6 and 12-weeks.

A comparison of the change from baseline in the mean number of bleeding sites and the mean bleeding index between the test and control groups is shown in Table 4. The test group showed a significantly greater decrease from baseline in mean bleeding sites and mean bleeding index as compared to the control group at 3, 6 and 12 weeks.

Table 2
Baseline scores for gingival bleeding, gingival inflammation and plaque accumulation.

	Control (N = 96) Mean (SD)	Test (N = 94) Mean (SD)
Number of Bleeding sites	29.6 (7.56)	29.9 (8.46)
Bleeding Index (BI) score	0.23 (0.077)	0.23 (0.082)
MGI score	0.82 (0.276)	0.85 (0.287)
Overall TPI score	2.13 (0.447)	2.16 (0.444)
Interproximal TPI score	2.42 (0.500)	2.43 (0.495)

Table 3
Change from baseline in gingival bleeding.

Visit	Treatment Group	Analysed n	Adjusted Mean (SE)	95 % CI	p-Value
Mean number of bleeding sites					
Week 3	Test (N = 94)	90	−2.4 (1.02)	−4.5, −0.4	0.0181
	Control (N = 96)	91	1.4 (1.02)	−0.6, 3.4	0.1817
Week 6	Test (N =94)	92	−2.4 (1.26)	−4.9, 0.0	0.0541
	Control (N = 96)	92	2.9 (1.25)	0.4, 5.3	0.0227
Week 12	Test (N = 94)	92	−4.3 (1.44)	−7.2, −1.5	0.0032
	Control (N = 96)	96	2.3 (1.42)	−0.5, 5.1	0.1045
Mean BI score					
Week 3	Test (N = 94)	90	−0.04 (0.008)	−0.05, −0.02	<0.0001
	Control (N = 96)	91	−0.01 (0.008)	−0.02, 0.01	0.4999
Week 6	Test (N = 94)	92	−0.04 (0.009)	−0.06, −0.02	<0.0001
	Control (N = 96)	92	−0.00 (0.009)	−0.02, 0.02	0.9569
Week 12	Test (N =94)	92	−0.06 (0.011)	−0.08, −0.03	<0.0001
	Control (N = 96)	96	−0.01 (0.011)	−0.03, 0.01	0.4729

SE = standard Error

Table 4
Change from baseline in gingival bleeding, comparison of test and control with negative values favouring test product.

Visit	Analysed		Comparison of test with control toothpaste		
	Test n	Control n	Adjusted Mean Difference (SE)	95 % CI	p-Value
Number of bleeding sites					
Week 3	90	91	−3.8 (1.44)	−6.7, −1.0	0.0091
Week 6	92	92	−5.3 (1.78)	−8.8, −1.8	0.0031
Week 12	92	96	−6.6 (2.03)	−10.6, −2.6	0.0013
Mean BI score					
Week 3	90	91	−0.03 (0.011)	−0.05, −0.01	0.0051
Week 6	92	92	−0.04 (0.013)	−0.07, −0.01	0.0034
Week 12	92	96	−0.05 (0.015)	−0.08, −0.02	0.0022

Additionally, a post-hoc analysis showed a statistically significant higher proportion of participants in the test group (25.0 %) reached health with <10 % bleeding sites at week 12 compared to 13.5 % of the participants in control group ($p = 0.0459$).

The efficacy of the test toothpaste to reduce gingival inflammation after 3, 6 and 12-weeks brushing is shown in Table 5. Gingival inflammation as measured by MGI was significantly improved from baseline in both groups at all time points.

A comparison of the change from baseline in the mean MGI between the test and control groups is shown in Table 6. The reductions in MGI from baseline were significantly greater in the test as compared to the control group at all time points.

The efficacy of the test toothpaste to reduce plaque accumulation after 3, 6 and 12-weeks brushing is shown in Table 7. There were statistically significant reductions in the mean overall TPI score and the mean interproximal TPI score from Baseline to weeks 3, 6, and 12 in both control and test groups, with the test group significant to $p < 0.0001$ for all three time points for both mean overall and mean interproximal TPI scores.

The test group demonstrated statistically significant greater reductions in both the mean overall TPI score and the mean interproximal TPI score from baseline to weeks 3, 6 and 12 compared to the control group (Table 8).

4. Discussion

Toothbrushing twice daily with a 67 % sodium bicarbonate and fluoride toothpaste demonstrated that there was a significant intragroup reduction in the number of bleeding sites from baseline to 12 weeks in participants with localised gingivitis, 10 %-30 % bleeding sites [11,12], without a prior dental prophylaxis. Further, and more importantly, there was a significant intergroup difference in the reduction in number of bleeding sites from baseline to 12 weeks between the test group, using sodium bicarbonate and fluoride toothpaste, and the control group brushing with a marketed fluoride control toothpaste. The null hypothesis was rejected.

The pattern of overall improvement in gingival health in the present study, according to the definitions of gingival health and localised gingivitis in the 2018 periodontal classification of gingivitis [12], was clinically and statistically significant across all gingival and plaque indices at all time points throughout the three month study. These results confirmed the premise of this study, that toothbrushing twice daily with sodium bicarbonate toothpaste, is an effective mechanical adjunct in toothbrushing for a home use oral care regimen for managing localised gingival inflammation and improving oral health. Interestingly, the treatment effect of the sodium bicarbonate toothpaste could be seen as early as 3 weeks use.

This result is supported by the systematic review and meta-analysis by [38], authors showing a significant improvement of modified gingival index, bleeding index, and plaque index with participants using 67 % sodium bicarbonate toothpaste as compared with control products – generally in studies commencing with a dental prophylaxis. Further, a

Table 5
Change from baseline in Gingival inflammation.

Visit	Treatment Group	Analysed n	Adjusted Mean (SE)	95 % CI	p-Value
Mean MGI					
Week 3	Test (N =94)	90	−0.12 (0.014)	−0.15, −0.09	<0.0001
	Control (*N* = 96)	91	−0.04 (0.014)	−0.07, −0.01	0.0097
Week 6	Test (N =94)	92	−0.19 (0.019)	−0.22, −0.15	<0.0001
	Control (*N* = 96)	92	−0.06 (0.019)	−0.10, −0.03	0.0010
Week 12	Test (N =94)	92	−0.24 (0.021)	−0.28, −0.19	<0.0001
	Control (*N* = 96)	96	−0.10 (0.021)	−0.14, −0.06	<0.0001

Table 6
Change from baseline in gingival inflammation, comparison of test and control.

Visit	Analysed		Comparison of test with control toothpaste		
	Test n	Control n	Adjusted Mean Difference (SE)	95 % CI	p-Value
Mean MGI					
Week 3	90	91	−0.08 (0.20)	−0.12, −0.04	<0.0001
Week 6	92	92	−0.12 (0.027)	−0.18, −0.07	<0.0001
Week 12	92	96	−0.14 (0.030)	−0.20, −0.08	<0.0001

Table 7
Change from baseline in dental plaque accumulation.

Visit	Treatment Group	Analysed n	Adjusted Mean (SE)	95 % CI	p-Value
Mean overall TPI score					
Week 3	Test (N =94)	90	−0.32 (0.033)	−0.39, −0.26	<0.0001
	Control (*N* = 96)	91	−0.17 (0.033)	−0.23, −0.10	<0.0001
Week 6	Test (N =94)	92	−0.31 (0.043)	−0.40, −0.23	<0.0001
	Control (*N* = 96)	92	−0.14 (0.043)	−0.23, −0.06	0.0011
Week 12	Test (N =94)	92	−0.41 (0.047)	−0.50, −0.32	<0.0001
	Control (*N* = 96)	96	−0.12 (0.046)	−0.21, −0.03	0.0103
Mean interproximal TPI score					
Week 3	Test (N =94)	90	−0.35 (0.036)	−0.42, −0.28	<0.0001
	Control (*N* = 96)	91	−0.19 (0.036)	−0.26, −0.12	<0.0001
Week 6	Test (N =94)	92	−0.34 (0.047)	−0.43, −0.25	<0.0001
	Control (*N* = 96)	92	−0.17 (0.047)	−0.26, −0.08	0.0004
Week 12	Test (N =94)	92	−0.42 (0.052)	−0.53, −0.32	<0.0001
	Control (*N* = 96)	96	−0.12 (0.052)	−0.22, −0.02	0.0183

Table 8
Change from baseline in overall and interproximal dental plaque accumulation, comparison of test and control.

Visit	Analysed		Comparison of test with control toothpaste		
	Test n	Control n	Adjusted Mean Difference (SE)	95 % CI	p-Value
Overall mean TPI score					
Week 3	90	91	−0.15 (0.047)	−0.25, −0.06	0.0012
Week 6	92	92	−0.17 (0.061)	−0.29, −0.05	0.0058
Week 12	92	96	−0.29 (0.066)	−0.42, −0.16	<0.0001
Interproximal mean TPI score					
Week 3	90	91	−0.16 (0.051)	−0.26, −0.06	0.0022
Week 6	92	92	−0.17 (0.066)	−0.30, −0.04	0.0099
Week 12	92	96	−0.30 (0.073)	−0.45, −0.16	<0.0001

pooled analysis of participant level-data from long-term gingivitis clinical studies, demonstrate that twice daily use of a 67 % sodium bicarbonate toothpaste effectively removed plaque from all tooth sites, resulting in clinically significant improvements in measures of gingival health, overall and for all the tooth regions investigated, compared with a non-sodium bicarbonate (regular) toothpaste following 24 weeks twice daily use [39].

A 2019 meta-analyses, which included a previous network meta-analysis, found only a modest effect for 67 % sodium bicarbonate as compared to other active agents [43,44]. However, both meta-analyses, excluded studies with less than 6 month follow up. ADA guidance for conduct of gingivitis studies [45] states that a 6 months treatment period is needed to demonstrate efficacy of treatment effect, however a recent study [46]) suggests a clear relationship can be demonstrated between 1-, 3-, and 6-month gingival bleeding outcomes in gingivitis clinical studies. This suggests that meta-analyses should consider studies of shorter duration and has possible positive implications for patient care, clinical practice guidelines, protocols, and policies.

A consideration in proving efficacy of an anti-plaque agent in trial design is whether the therapy is intended to prevent or to manage gingivitis. Many studies begin with participants receiving a professional oral prophylaxis [39], and those in the systematic review and meta-analysis [38] in accordance with antiplaque and anti-gingivitis study design recommendation [47]. However, when participants have a prophylaxis prior to study start, this alone may restore some level of gingival health, which is not representative of the real-world situations, and does not account for health inequalities. In the current dental climate some patients no longer attend dental practices as regularly for recommended dental prophylaxis and indeed a high percentage of the public only attend for dental emergencies.

Therefore due to the substantial volume of literature supporting 67 % sodium bicarbonate therapeutic effect under standardized conditions, this study generated clinical records reflecting real world data (without a prophylaxis at screening or baseline), and the magnitude of plaque reduction with a diagnosis of localised gingivitis [3], aiding understanding and knowledge as to who could benefit most from home-use oral hygiene regimes. The conclusions from this study offers a realistic evaluation of sodium bicarbonate toothpaste and clearly demonstrate the strong treatment effect of tooth brushing twice daily with 67 % sodium bicarbonate toothpaste.

This present study utilised a number of indices to attempt to understand the effect on sodium bicarbonate containing toothpastes on the plaque scores and gingival tissues. Gingival health is best reflected in reduced BI to <10 % BI sites and 0 MGI scores, whilst plaque scores may not always follow due to the susceptibility of the individual to plaque and the host response. Plaque scores nevertheless are helpful in interpreting the results in the development and evaluation of ingredients for gingivitis prevention or treatment. While most of the earlier studies on brushing with sodium bicarbonate included participants with MGI score 1.75 to 2.3 and 20 or more bleeding sites [38], this present study followed the updated classification of periodontal and peri-implant diseases and condition [12], to target participants who are at the early stage of gingivitis, localised gingivitis with 10 to 30 % bleeding sites and without periodontal probing pocket depth of >3 mm.

A number of single use clinical studies conducted evaluating 67 % sodium bicarbonate toothpastes have reported that the greatest plaque removal advantage for sodium bicarbonate toothpastes compared with control was the lingual interproximal areas [31,33,35,36,48] however, in the pooled analysis [39] did not demonstrate this hypothesis. The present study did not focus on plaque removal at specific sites however, there were statistically significant reductions in the mean overall TPI score and the mean interproximal TPI score from baseline to weeks 3, 6, and 12 in both control and test groups. The test group was significantly more effective for all three time points for both mean overall and mean interproximal TPI scores. This indicates that toothbrushing with sodium bicarbonate toothpaste was effective at plaque disruption in the interdental areas, which are usually the hardest to clean effectively with the toothbrush, demonstrating the superior ability of this active ingredient as an effective plaque removal agent. This supports the theory that sodium bicarbonate toothpaste displaces and interacts with plaque from the tooth surface, making it more readily removable by the toothbrush [28,29].

The clinically significant results of oral health improvement are strengthened and supported by the good repeatability of the clinician, excellent participant compliance and a low participant dropout rate. To acquire reliable and real-time participant data on compliance in this study, an e-diary was trialled, which was a new innovative process. The study design also benefitted from the use of multiple indices to measure gingival inflammation and it's effect on gingival tissues, and crucially did not include a pre-prophylaxis at baseline so that the efficacy of the toothpastes could be determined in a real life situation.

Critically, the majority of periodontal diseases are totally preventable and treatable with excellent mechanical oral hygiene measures, however, this is rarely achieved. Many oral healthcare professionals (OHPs), let alone patients, fail to recognise the significance of bleeding gums or gingivitis. Sufficient patient behaviour change, oral hygiene education, with regular reiteration and patient compliance is sadly lacking for individuals to convert from gingivitis to oral health. Oral health prevention is often given lip service and this is perpetuated in many countries due to the remuneration system [49] with gingivitis going untreated. The role of home care led by patients is of paramount importance to prevent gingivitis and periodontitis, with an economic analysis showing [6] that both eliminating gingivitis (the precursor to periodontitis) using home care prevention techniques such as tooth brushing, and increasing the rate of diagnosis and management of periodontitis, has a positive return on investment, [6]. Making efforts to eliminate gingivitis, thus preventing progression to periodontitis, would save considerable costs over a 10-year time period compared with 'business as usual'. Neglecting to manage gingivitis can significantly increase costs and reduce Healthy Life Years (HLYs); therefore an emphasis on self-care and prevention is critical from both an individual and a societal perspective. Important work to reskill professionals with understanding of the systemic and long-term impact of inflammation, and to promote prevention of gingival inflammation is needed. In this present study, although not an explicit study outcome, analysis showed at week 12 a quarter of the participants in the test group reached oral health with <10 % bleeding sites which is a which is a strong marker of success and the ultimate goal of care.

In conclusion, the results of this study demonstrate that toothbrushing with the test product containing 67 % w/w sodium bicarbonate was able to show effective reduction in gingival bleeding, inflammation, and plaque accumulation, compared to toothbrushing with a regular fluoride toothpaste, as early as 3 weeks of product use. Use of these efficacious agents with a mechanical mode of action as adjuncts to toothbrushing needs to be encouraged for gingivitis sufferers in home use oral hygiene regimes to improve oral and overall systemic health.

CRediT authorship contribution statement

Nicola X. West: Writing – review & editing, Writing – original draft, Supervision, Project administration, Conceptualization. **Jianhong Qiu:** Writing – review & editing, Methodology, Conceptualization. **Alexander J. Pollard:** Writing – review & editing, Writing – original draft. **Maria Davies:** Writing – review & editing, Writing – original draft. **Gary Smith:** Writing – review & editing, Formal analysis. **Paola Gomez-Pereira:** Writing – review & editing, Project administration, Methodology, Conceptualization. **Joon Seong:** Writing – review & editing, Supervision, Project administration.

Declaration of competing interest

The authors declare the following financial interests/personal

relationships which may be considered as potential competing interests:

Nicola West reports financial support and equipment, drugs, or supplies were provided by Haleon plc. Jianhong Qiu reports a relationship with Haleon plc that includes: employment. Paola Gomez-Pereira reports a relationship with Haleon plc that includes: employment. Gary Smith reports a relationship with Haleon plc that includes: employment. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

Staff from the Clinical Trials Unit at Bristol Dental School contributed to the work presented in this manuscript. We would like to acknowledge Sky Franklin for reviewing and preparing the manuscript for submission. The authors would like to thank all participants, Mizpah Lamptey (study manager), Anousheh Alavi and everyone involved in conducting the studies. clinicaltrials.org: NCT05654662.

References

[1] D.F. Kinane, Periodontal disease in children and adolescents: introduction and classification, Periodontol. 2000 26 (2001) 7–15.
[2] M. Kilian, I.L.C. Chapple, M. Hannig, P.D. Marsh, V. Meuric, A.M.L. Pedersen, M. S. Tonetti, W.G. Wade, E. Zaura, The oral microbiome - an update for oral healthcare professionals, Br. Dent. J. 221 (10) (2016) 657–666.
[3] I.L.C. Chapple, F. Van der Weijden, C. Doerfer, D. Herrera, L. Shapira, D. Polak, P. Madianos, A. Louropoulou, E. Machtei, N. Donos, H. Greenwell, A.J. Van Winkelhoff, B.Eren Kuru, N. Arweiler, W. Teughels, M. Aimetti, A. Molina, E. Montero, F. Graziani, Primary prevention of periodontitis: managing gingivitis, J. Clin. Periodontol. 42 (S16) (2015) S71–S76.
[4] M.X. Chen, Y.J. Zhong, Q.Q. Dong, H.M. Wong, Y.F. Wen, Global, regional, and national burden of severe periodontitis, 1990-2019: An analysis of the Global Burden of Disease Study 2019, J. Clin. Periodontol. 48 (9) (2021) 1165–1188.
[5] I.L.C. Chapple, P. Bouchard, M.G. Cagetti, G. Campus, M.-C. Carra, F. Cocco, L. Nibali, P. Hujoel, M.L. Laine, P. Lingström, D.J. Manton, E. Montero, N. Pitts, H. Rangé, N. Schlueter, W. Teughels, S. Twetman, C. Van Loveren, F. Van der Weijden, A.R. Vieira, A.G. Schulte, Interaction of lifestyle, behaviour or systemic diseases with dental caries and periodontal diseases: consensus report of group 2 of the joint EFP/ORCA workshop on the boundaries between caries and periodontal diseases, J. Clin. Periodontol. 44 (S18) (2017) S39–S51.
[6] C. Bishop, Time to take gum disease seriously: the societal and economic impact of periodontitis, Econ. Intell. Unit 2022 (2021) 1–46.
[7] L.J. BROWN, H. LÖE, Prevalence, extent, severity and progression of periodontal disease, Periodontol. 2 (1) (1993) 57–71, 2000.
[8] Y.M. Li, S. Lee, P. Hujoel, M.F. Su, W. Zhang, J. Kim, Y.P. Zhang, W. DeVizio, Prevalence and severity of gingivitis in American adults, Am. J. Dent. 23 (1) (2010) 9–13.
[9] J. Zhang, D. Xuan, W. Fan, X. Zhang, S. Dibart, W. De Vizio, F. Panagakos, Y.-P. Zhang, Severity and prevalence of plaque-induced gingivitis in the Chinese population, Compend. Contin. Educ. Dent. 31 (8) (2010) 624–629.
[10] N.X. West, M. Davies, A. Sculean, S. Jepsen, R. Faria-Almeida, M. Harding, F. Graziani, R.G. Newcombe, J.E. Creeth, D. Herrera, Prevalence of dentine hypersensitivity, erosive tooth wear, gingival recession and periodontal health in seven European countries, J. Dent. 150 (2024) 15.
[11] J.G. Caton, G. Armitage, T. Berglundh, I.L.C. Chapple, S. Jepsen, K.S. Kornman, B. L. Mealey, P.N. Papapanou, M. Sanz, M.S. Tonetti, A new classification scheme for periodontal and peri-implant diseases and conditions - Introduction and key changes from the 1999 classification, J. Periodont. 89 (2018) S1–S8.
[12] I.L.C. Chapple, B.L. Mealey, T.E. Van Dyke, P.M. Bartold, H. Dommisch, P. Eickholz, M.L. Geisinger, R.J. Genco, M. Glogauer, M. Goldstein, T.J. Griffin, P. Holmstrup, G.K. Johnson, Y. Kapila, N.P. Lang, J. Meyle, S. Murakami, J. Plemons, G.A. Romito, L. Shapira, D.N. Tatakis, W. Teughels, L. Trombelli, C. Walter, G. Wimmer, P. Xenoudi, H. Yoshie, Periodontal health and gingival diseases and conditions on an intact and a reduced periodontium: Consensus report of workgroup 1 of the 2017 world workshop on the classification of periodontal and peri-implant diseases and conditions, J. Clin. Periodontol. 45 (2018) S68–S77.
[13] L. Trombelli, R. Farina, C.O. Silva, D.N. Tatakis, Plaque-induced gingivitis: Case definition and diagnostic considerations, J. Periodont. 89 (2018) S46–S73.
[14] M. Schätzle, H. Löe, N.P. Lang, W. Bürgin, Å. Ånerud, H. Boysen, The clinical course of chronic periodontitis -: IV.: Gingival inflammation as a risk factor in tooth mortality, J. Clin. Periodontol. 31 (12) (2004) 1122–1127.
[15] M. Sanz, A.M. Del Castillo, S. Jepsen, J.R. Gonzalez-Juanatey, F. D'Aiuto, P. Bouchard, I. Chapple, T. Dietrich, I. Gotsman, F. Graziani, D. Herrera, B. Loos, P. Madianos, J.B. Michel, P. Perel, B. Pieske, L. Shapira, M. Schechter, M. Tonetti, C. Vlachopoulos, G. Wimmer, Periodontitis and cardiovascular diseases, Consensus Report, Glob. Heart 15 (1) (2020) 23.
[16] S.S. Dominy, C. Lynch, F. Ermini, M. Benedyk, A. Marczyk, A. Konradi, M. Nguyen, U. Haditsch, D. Raha, C. Griffin, L.J. Holsinger, S. Arastu-Kapur, S. Kaba, A. Lee, M. I. Ryder, B. Potempa, P. Mydel, A. Hellvard, K. Adamowicz, H. Hasturk, G. D. Walker, E.C. Reynolds, R.L.M. Faull, M.A. Curtis, M. Dragunow, J. Potempa, *Porphyromonas gingivalis* in Alzheimer's disease brains: Evidence for disease causation and treatment with small-molecule inhibitors, Sci. Adv. 5 (1) (2019) eaau3333.
[17] I.L.C. Chapple, R. Genco, Diabetes and periodontal diseases: consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases, J. Periodont. 84 (4S) (2013) S106–S112.
[18] M. Sanz, A. Ceriello, M. Buysschaert, I. Chapple, R.T. Demmer, F. Graziani, D. Herrera, S. Jepsen, L. Lione, P. Madianos, M. Mathur, E. Montanya, L. Shapira, M. Tonetti, D. Vegh, Scientific evidence on the links between periodontal diseases and diabetes: Consensus report and guidelines of the joint workshop on periodontal diseases and diabetes by the International diabetes Federation and the European Federation of Periodontology, Diabetes Res. Clin. Pract. 137 (2018) 231–241.
[19] N.C. Claydon, Current concepts in toothbrushing and interdental cleaning, Periodontol 48 (2008) 10–22, 2000.
[20] P.D. Marsh, Microbiological aspects of the chemical control of plaque and gingivitis, J. Dent. Res. 71 (7) (1992) 1431–1438.
[21] I. Brook, Microbiology and management of periodontal infections, Gen. Dent. 51 (5) (2003) 424–428.
[22] P. Ower, The role of self-administered plaque control in the management of periodontal diseases: I. A review of the evidence, Dent. Update 30 (2) (2003), 60-4, 66, 68.
[23] G.A. van der Weijden, K.P.K. Hioe, A systematic review of the effectiveness of self-performed mechanical plaque removal in adults with gingivitis using a manual toothbrush, J. Clin. Periodontol. 32 (2005) 214–228.
[24] R.M. Davies, Toothpaste in the control of plaque/gingivitis and periodontitis, Periodontol. 48 (1) (2008) 23–30, 2000.
[25] N. West, I. Chapple, N. Claydon, F. D'Aiuto, N. Donos, M. Ide, I. Needleman, M. Kebschull, BSP implementation of European S3 - level evidence-based treatment guidelines for stage I-III periodontitis in UK clinical practice, J. Dent. 106 (2021) 103562.
[26] A. Winston, R. Lehne, The effect of concentration on the abrasivity of baking soda, Clin. Prev. Dent. 5 (1983) 21–22.
[27] American Dental Association Council on Dental Therapeutics,38th ed., Council on Dental Therapeutics of the American Dental Association1979.
[28] M.S. Putt, K.R. Milleman, A. Ghassemi, L.M. Vorwerk, W.J. Hooper, P.M. Soparkar, A.E. Winston, H.M. Proskin, Enhancement of plaque removal efficacy by tooth brushing with baking soda dentifrices: results of five clinical studies, J. Clin. Dent. 19 (4) (2008) 111–119.
[29] J. Pratten, J. Wiecek, N. Mordan, A. Lomax, N. Patel, D. Spratt, A. Middleton, Physical disruption of oral biofilms by sodium bicarbonate: an in vitro study, Int. J. Dent. Hyg. 14 (3) (2016) 209–214.
[30] A. Ghassemi, L. Vorwerk, W. Hooper, M. Putt, K. Milleman, A four-week clinical study to evaluate and compare the effectiveness of a baking soda dentifrice and an antimicrobial dentifrice in reducing plaque, J. Clin. Dent. 19 (4) (2008) 120–126.
[31] A. Kakar, A. Lomax, M. Siddiqi, N. Wang, S. Ghosh, M. Bosma, Evaluate the efficacy of different concentrations of sodium bicarbonate toothpastes, J. Dent. Res. 93 (2014).
[32] T. Triratana, P. Kraivaphan, C. Amornchat, L. Mateo, B. Morrison, Jr., S. Dibart, Y. Zhang, Comparing three toothpastes in controlling plaque and gingivitis: a 6-month clinical study, Am. J. Dent. 28(April) 68–74.
[33] A. Lomax, S. Patel, N. Wang, K. Kakar, A. Kakar, M.L. Bosma, A randomized controlled trial evaluating the efficacy of a 67% sodium bicarbonate toothpaste on gingivitis, Int. J. Dent. Hyg. 15 (4) (2017) e35–e41.
[34] M.L. Bosma, K.R. Milleman, I. Akwagyiram, D. Targett, J.L. Milleman, A randomised controlled trial to evaluate the plaque removal efficacy of sodium bicarbonate dentifrices in a single brushing clinical model, BDJ Open 4 (1) (2018) 5.
[35] A. Jose, J. Pratten, M.-L. Bosma, K.R. Milleman, J.L. Milleman, N. Wang, Six-month evaluation of a sodium bicarbonate-containing toothpaste for reduction of established gingivitis: a randomized usa-based clinical trial, J. Clin. Dent. 29 (1) (2018) 33–39.
[36] I. Akwagyiram, P. Amini, M.L. Bosma, N. Wang, J. Gallob, Efficacy and tolerability of sodium bicarbonate toothpaste in subjects with gingivitis: A 6-month randomized controlled study, Oral. Health Prev. Dent. 16 (5) (2018) 401–407.
[37] C. Valkenburg, Y. Kashmour, A. Dao, G.A. Van der Weijden, D.E. Slot, The efficacy of baking soda dentifrice in controlling plaque and gingivitis: A systematic review, Int. J. Dent. Hyg. 17 (2) (2019) 99–116.
[38] S. Taschieri, M. Tumedei, L. Francetti, S. Corbella, M. Del Fabbro, Efficacy of 67% sodium bicarbonate toothpaste for plaque and gingivitis control: a systematic review and meta-analysis, J. Evid. Based. Dent. Pract. 22 (2) (2022) 101709.
[39] C.R. Parkinson, A. Butler, M.R. Ling, Antigingivitis efficacy of a sodium bicarbonate toothpaste: Pooled analysis, Int. J. Dent. Hyg. 21 (1) (2023) 106–115.
[40] C.A. Saxton, F.J.G. Vanderouderaa, The effect of a dentifrice containing zinc citrate and triclosan on developing gingivitis, J. Periodont. Res. 24 (1) (1989) 75–80.
[41] R. Lobene R, A modified gingival index for use in clinical trials, Clin. Prevent. Dent. 8 (1986) 3–6.
[42] R.R. Lobene, Use of dental floss effect on plaque and gingivitis, Clin. Prev. Dent. 4 (1982) 5–8.
[43] J. Serrano, M. Escribano, S. Roldán, C. Martín, D. Herrera, Efficacy of adjunctive anti-plaque chemical agents in managing gingivitis: a systematic review and meta-analysis, J. Clin. Periodontol. 42 (S16) (2015) S106–S138.
[44] E. Figuero, D. Herrera, A. Tobías, J. Serrano, S. Roldán, M. Escribano, C. Martín, Efficacy of adjunctive anti-plaque chemical agents in managing gingivitis: a systematic review and network meta-analyses, J. Clin. Periodontol. 46 (7) (2019) 723–739.

[45] A.D. Association, Guidelines for acceptance of chemotherapeutic products for the control of supragingival dental plaque and gingivitis, J. Am. Dental Associat. 112 (4) (1986) 529–532.
[46] T. He, J. Grender, S. Farrell, A.R. Biesbrock, Relationship between 1-, 3-, and 6-Month gingival bleeding outcomes, JDR Clin. Translat. Res. 9 (3) (2024) 286–293.
[47] FDA, Gingivitis: Development and Evaluation of Drugs for Treatment or Prevention, 2005. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/gingivitis-development-and-evaluation-drugs-treatment-or-prevention. (Accessed 09/04/2025.
[48] F.Y. Newby EE, Shaw D, et al Efficacy of sodium bicarbonate toothpastes on gingivitis and plaque, 2014. https://iadr.abstractarchives.com/abstract/14iags-188977/efficacy-of-sodium-bicarbonate-toothpastes-on-gingivitis-and-plaque.
[49] D. G, Time to put your money where your mouth is: addressing inequalities in oral health February 15, 2024, 2024. https://impact.economist.com/perspectives/health/time-put-your-money-where-your-mouth-addressing-inequalities-oral-health. (Accessed 09/04/2025.