Scholars Journal of Dental Sciences
Abbreviated Key Title: Sch J Dent Sci
ISSN 2394-4951 (Print) | ISSN 2394-496X (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Efficacy & Safety of a Triple Combination Chlohexidine Mouthwash Compared to Plain Chlorhexidine Mouthwash in the Management of Gingivitis: A Randomized, Controlled, Open Label Multicentre Study

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DOI: https://doi.org/10.36347/sjds.2026.v13i08.002 | **Received:** 02.06.2026 | **Accepted:** 14.07.2026 | **Published:** 11.08.2026

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Abstract **Original Research Article**

This study aimed to evaluate the clinical efficacy and safety of test mouthwash, a triple combination formulation containing chlorhexidine gluconate (0.20% w/v), sodium fluoride (0.05% w/v), and zinc chloride (0.09% w/v), in improving gingival health, plaque control, and halitosis among healthy individuals. A 28-day randomized interventional study was conducted comparing Triple Combination Chlohexidine mouthwash with plain chlorhexidine mouthwash. Clinical parameters, including Gingival Index (GI), Plaque Index (PI), Sulcus Bleeding Index, halitosis (organoleptic) scores, periodontal pocket depth, and oral hygiene status, were assessed at baseline, Day 15, and Day 28. Safety evaluation was performed through monitoring of adverse events and tolerability. Both treatments demonstrated statistically significant improvements across all evaluated parameters ($p < 0.0001$). However, test mouthwash showed consistently superior clinical efficacy. The Gingival Index was reduced by 70.41% in the test group compared to 51.59% in the comparator group. Similarly, plaque scores decreased by 68.90% in the test group compared to 51.38% in the comparator group. The Sulcus Bleeding Index demonstrated a reduction of 71.96% in the test group compared to 50.48% with the comparator. Notably, halitosis reduction was more pronounced in the test group, achieving a 98.8% decrease, indicating near-complete resolution. Improvements in periodontal pocket depth and oral hygiene index scores further supported the superior performance of the test formulation. In addition, patient-reported outcomes indicated faster symptom relief and greater overall acceptability. No treatment-emergent adverse events were reported, and both formulations were well tolerated. Overall, Triple Combination Chlohexidine mouthwash provides superior oral health benefits through a synergistic combination of antimicrobial, remineralizing, anti-inflammatory, and astringent actions. It significantly enhances gingival health, plaque control, bleeding reduction, and halitosis management, with excellent safety and tolerability. The formulation represents a comprehensive, multi-targeted approach for effective periodontal maintenance and serves as a valuable adjunct to routine oral hygiene practices.

Keywords: Periodontal disease; Gingivitis; Chlorhexidine; Triple combination mouthwash; Zinc chloride; Plaque control; Halitosis; Oral hygiene.

1. INTRODUCTION

Periodontal diseases constitute a diverse group of chronic inflammatory conditions that affect the supporting tissues of the teeth and remain a significant global oral health challenge. These diseases can develop at various stages of life; however, their prevalence, severity, and associated clinical consequences—including clinical attachment loss, alveolar bone resorption, and eventual tooth loss—tend to increase with advancing age [Rajhans *et al*., 2011]. The two principal clinical forms, gingivitis and periodontitis, represent different stages within the disease continuum. Gingivitis is characterized by a reversible inflammatory response limited to gingival tissues, whereas periodontitis is an irreversible, multifactorial condition involving progressive destruction of the periodontal

ligament and alveolar bone, often culminating in pocket formation and gingival recession [Ramamurthy *et al*., 2018; Kinane *et al*., 2017]. The transition from gingivitis to periodontitis is governed by a complex interplay between microbial challenge and host immune-inflammatory responses.

The oral cavity harbors a highly complex and dynamic microbiological ecosystem composed of diverse microbial species inhabiting distinct anatomical niches. Under physiological conditions, these microorganisms coexist in a balanced symbiotic relationship with the host. However, perturbations in the local microenvironment—such as inadequate oral hygiene can disrupt this balance, leading to microbial dysbiosis and disease initiation. The formation of dental plaque biofilm is a highly orchestrated process that begins with the adsorption of salivary proteins onto oral surfaces, resulting in the formation of an acquired pellicle. This pellicle facilitates the selective adhesion of pioneer bacterial species, followed by microbial proliferation, co-aggregation, and maturation into structurally organized biofilms. These biofilms are embedded within an extracellular polymeric matrix composed of polysaccharides, proteins, lipids, and extracellular DNA, which enhances microbial persistence and confers increased resistance to antimicrobials and host defense mechanisms [Marsh, 2006; Flemming *et al*., 2010]. Consequently, biofilms play a central role in the pathogenesis of major oral diseases, including dental caries and periodontal diseases, both of which impose a substantial burden on healthcare systems worldwide [Bertolini *et al*., 2022].

The initiation and progression of periodontal diseases are strongly linked to the accumulation and maturation of dental plaque biofilm along the gingival margin and within the subgingival environment. When undisturbed, these biofilms undergo compositional and structural changes, favoring the proliferation of pathogenic microorganisms and the establishment of a dysbiotic microbial community. This dysbiosis triggers a sustained inflammatory response, leading to gingival inflammation in its early stages and, if left unmanaged, to the destruction of periodontal supporting structures in periodontitis. Importantly, gingivitis remains a reversible condition with appropriate plaque control, whereas periodontitis is characterized by irreversible tissue breakdown and long-term functional impairment [Kaur *et al*., 2021].

Effective plaque control remains the cornerstone of both prevention and management of periodontal diseases. Mechanical methods, including tooth brushing and interdental cleaning, are considered essential for disrupting dental biofilm. However, these approaches may not always achieve optimal plaque removal, particularly in anatomically challenging areas or among individuals with limited manual dexterity. As a result, adjunctive chemical plaque control agents have been widely advocated to enhance oral hygiene measures. Among these, mouthwashes play a significant role due to their ability to access areas that are otherwise difficult to reach through mechanical means. These agents function by reducing microbial load, inhibiting bacterial adhesion, and interfering with biofilm maturation and metabolic activity [Daly *et al*., 2019; Addy, 1986].

Chlorhexidine gluconate is widely regarded as the gold standard antiplaque and antigingivitis agent owing to its broad-spectrum antimicrobial activity and high substantivity. Its ability to bind to oral tissues and be gradually released over time allows for prolonged antimicrobial effects [Jones, 1997]. Despite its proven efficacy, the long-term use of chlorhexidine is often associated with undesirable adverse effects, including extrinsic tooth staining, altered taste perception, and mucosal irritation, which may affect patient compliance and limit its extended use in routine oral care [Alyami *et al*., 2020].

To overcome these limitations and enhance therapeutic effectiveness, there has been growing interest in combination mouthwash formulations that incorporate multiple active agents with complementary mechanisms of action. Triple combination mouthwashes typically integrate chlorhexidine gluconate, sodium fluoride, and zinc salts, thereby targeting multiple aspects of oral disease pathogenesis.

Chlorhexidine exerts its antimicrobial action primarily through disruption of bacterial cell membranes and precipitation of intracellular components, leading to cell death. It also inhibits pellicle formation, reduces bacterial adhesion, and interferes with biofilm development, thereby limiting microbial colonization and plaque accumulation [Jones, 1997]. Sodium fluoride plays a crucial role in maintaining enamel integrity by promoting remineralization, inhibiting demineralization, and exerting antibacterial effects through inhibition of key metabolic enzymes involved in acid production [Featherstone, 2000; Buzalaf *et al*., 2011]. Zinc chloride enhances oral health through its antimicrobial effects, modulation of bacterial metabolism, and neutralization of volatile sulfur compounds responsible for oral malodor. Additionally, its astringent properties may contribute to reduction in gingival inflammation and bleeding [Young *et al*., 2003].

The integration of these agents in a single formulation offers a comprehensive and potentially synergistic approach to oral health management by simultaneously targeting microbial biofilms, enamel demineralization, and inflammatory processes. Test product is one such triple combination formulation designed to provide enhanced therapeutic benefits beyond those achieved by chlorhexidine alone.

In light of the growing interest in multi-targeted oral care strategies, the present study is undertaken to evaluate the efficacy and safety of a triple combination mouthwash compared with plain chlorhexidine mouthwash in improving gingival health among healthy individuals.

2. MATERIAL & METHODS

2.1. Study Design and Participants

This study was designed as an open-label, interventional, prospective, multicenter, randomized, controlled, two-arm, parallel-group clinical study to evaluate the efficacy and safety of a triple-combination mouthwash compared with plain chlorhexidine mouthwash in participants with gingivitis. The total study duration was 28 days and included four scheduled visits (Figure 1): Visit 1 (Day 1) for screening and enrollment, followed by Visit 2 (Day 7), Visit 3 (Day 15), and Visit 4 (Day 28) for subsequent assessments.

Eligible participants were screened according to predefined inclusion and exclusion criteria after obtaining written informed consent. Baseline evaluations included demographic characteristics, medical and dental history, general health status, findings from physical and oral examinations, and documentation of concomitant medications. Comprehensive clinical dental assessments and subjective assessments were conducted at each visit. Safety was monitored throughout the study period through the recording and assessment of adverse events.

Participants were randomized into two groups: the test group receiving the triple-combination mouthwash and the comparator group receiving plain chlorhexidine mouthwash (Figure 2). This allocation facilitated a comparative evaluation of the effectiveness of the two study products in the management of gingivitis.

For product administration, approximately 10 mL of the assigned mouthwash was dispensed and used undiluted. Participants were instructed to rinse thoroughly for 30–60 seconds, ensuring adequate contact with all oral surfaces, including the teeth and gingival tissues, and to expectorate without swallowing. The assigned mouthwash was used twice daily (in the morning after breakfast and at night before bedtime) throughout the 28-day treatment period.

All participants were instructed to adhere strictly to the study procedures, including compliance with the prescribed regimen and all study-related guidelines and restrictions, throughout the duration of the study.

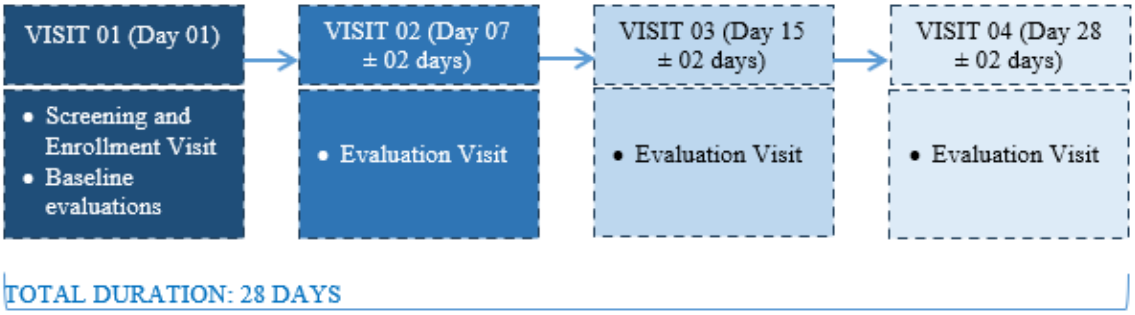

Figure 1: Schematic diagram of study visits

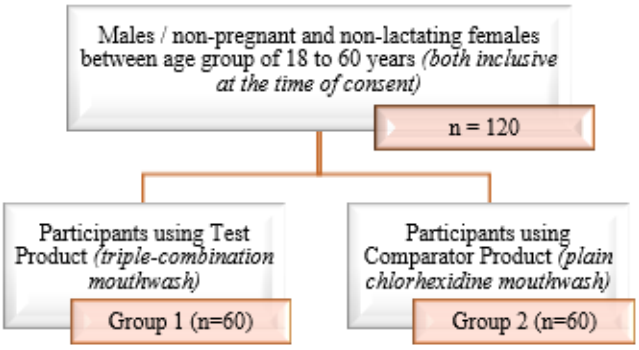

Figure 2: Schematic diagram of study population

Considering an anticipated attrition rate of 20%, a total of 120 participants (60 per group) were planned for enrollment to ensure that at least 100 evaluable participants (50 per group) would complete the study. All 120 screened participants were enrolled (60 in the test group and 60 in the comparator group), and all participants completed the study as per the protocol (Table 1)

Table 1: Study participants

Disposition	Test (N = 60) n (%)	Comparator (N = 60) n (%)	Overall (N = 120) n (%)
Screened participants	-	-	120 (100)
Screen fail participants	-	-	0 (0)
Enrolled participants	60 (100)	60 (100)	120 (100)
Study completed participants	60 (100)	60 (100)	120 (100)
Discontinued/withdrawn participants	0 (0)	0 (0)	0 (0)
Abbreviation(s): N = number of participants in the specified group; n = number of participants in the specified category.			

2.3 Ethics

The study was conducted in accordance with the approved protocol and adhered to the ethical principles outlined in the Indian Council of Medical Research (ICMR) guidelines, the International Council for Harmonisation Good Clinical Practice (ICH-GCP, Step 5), and the Declaration of Helsinki. The study protocol (Version 01) was reviewed and approved by an Institutional Ethics Committee registered with the Central Drugs Standard Control Organization (CDSCO) on 08 August 2025. The trial was prospectively registered with the Clinical Trials Registry of India (CTRI) on 13 August 2025, prior to the enrollment of participants. Written informed consent was obtained from all participants before their inclusion in the study. Participant confidentiality was maintained throughout the study, and all data were handled in compliance with applicable data protection and regulatory requirements, including the General Data Protection Regulation (GDPR).

2.4 Test Product(s)

The CloHex ADS mouthwash was an antiseptic mouthwash manufactured by Dr. Reddy's Laboratories Ltd., India, containing chlorhexidine gluconate, sodium fluoride, and zinc chloride as the primary active ingredients. This combination is designed to provide broad-spectrum oral care, offering antimicrobial and anti-plaque effects, prevention of dental caries, and reduction of oral malodor. Additionally, it aids in controlling plaque and tartar formation and can be used as an adjunct in the management of conditions such as gingivitis and oral mucositis.

2.5 Inclusion Criteria

Males and non-pregnant, non-lactating females aged 18 to 60 years (inclusive) at the time of providing informed consent were included in the study. Participants were required to be in general good health, as determined by the investigator based on medical history and vital signs. Key inclusion criteria included the presence of mild to severe gingivitis (score 1–3), periodontal pocket depth ≤3 mm, and a minimum of 20 natural permanent teeth with scorable buccal and lingual surfaces. In addition, participants were required to have detectable oral malodor, ranging from slight to strong (Organoleptic Scoring Scale score 2–4).

2.6 Exclusion Criteria

Participants were excluded from the study if they were pregnant, lactating, or planning pregnancy and unwilling to use acceptable contraception; had known hypersensitivity to chlorhexidine or any study product components; or had fixed/removable prostheses or orthodontic appliances. Individuals with oral tumors or severe periodontal disease (e.g., purulent exudate, tooth mobility, or significant attachment/bone loss requiring treatment) were also excluded. Participants with significant systemic illnesses, including HIV, hepatitis, uncontrolled hypertension, hyperthyroidism, acute cardiac or circulatory disorders, diabetes mellitus, or immunological diseases, were excluded. Additional exclusions included chronic use of corticosteroids, immunosuppressants, or antibiotics; use of chlorhexidine, antibiotics, or topical oral medications within the past 3 months; dialysis; increased bleeding risk; need for urgent dental care; heavy alcohol consumption; tobacco use; participation in another clinical study within 30 days; or any condition deemed unsuitable by the investigator.

2.7 Efficacy Endpoint(s)

2.7.1 Primary Endpoint(s)

The primary efficacy endpoints were to evaluate and compare the effect of the test and comparator products on gingivitis, as assessed by the Gingival Index (GI) at baseline (Day 01), Day 07 (±2 days), Day 15 (±2 days), and Day 28 (±2 days). All assessments were performed by a qualified dental surgeon using a standardized 4-point scoring scale (Table 2).

Table 2: Scoring criteria for Gingival Index (GI)

Score	Criteria
0	Normal gingiva (natural coral pink gingival with no e/o inflammation)
1	Mild inflammation (slight change in color, slight edema. no bleeding on probing)
2	Moderate inflammation (redness, edema and glazing. bleeding upon probing)
3	Severe inflammation (marked redness and edema/ulceration/tendency to bleed spontaneously)

Additionally, the proportion of participants achieving a Gingival Index score of 0 was evaluated at Day 07 (±2 days), Day 15 (±2 days), and Day 28 (±2 days).

Safety was assessed as a primary endpoint by determining the proportion of participants experiencing treatment-emergent adverse events (TEAEs) throughout the study duration.

2.7.2 Secondary Endpoint(s)

The secondary efficacy endpoints included the evaluation of the effect of the study products on plaque formation, gingival bleeding, halitosis, periodontal pocket depth, and oral hygiene status.

Plaque formation was assessed using the Silness–Löe Plaque Index (0–3 scale), gingival bleeding using the Sulcus Bleeding Index (0–3 scale), halitosis using the Organoleptic Scoring Scale (0–5 scale), and Oral hygiene status was evaluated using the Simplified Oral Hygiene Index (OHI-S), based on oral debris (0–3 scale) and calculus (0–3 scale). These parameters were evaluated at baseline (Day 01), Day 07 (±2 days), Day 15 (±2 days), and Day 28 (±2 days). Periodontal pocket depth was measured using a periodontal probe and graded as follows: 0–3 mm (no/mild periodontitis), ≥4 mm to <6 mm (moderate), and ≥6 mm (severe). These assessments were performed at baseline (Day 01) and Day 28 (±2 days).

Additionally, the proportion of participants achieving a score of 0 for plaque index, bleeding index, and organoleptic score was evaluated at Day 7 (±2 days), Day 15 (±2 days), and Day 28 (±2 days).

Subjective evaluations were conducted using structured questionnaires assessing gum bleeding, oral malodor, and teeth staining at Day 1, Day 7, Day 15, and Day 28. Assessments of oral hygiene, gum health, gum tightening effect, and product tolerability were performed at Day 7, Day 15, and Day 28. Participants' perception of product attributes, including taste, freshness, cooling sensation, and mouthfeel, was evaluated at Day 28. Safety was monitored throughout the study by recording adverse events (AEs) and serious adverse events (SAEs) during scheduled visits and via participant self-reporting.

2.8 Statistical analysis

The statistical analysis was performed using SAS® statistical software (Version: 9.4 or higher; SAS Institute Inc., USA). Demographic and study data were summarized with descriptive statistics (N, mean, standard deviation, median, minimum, and maximum) for continuous variables and frequencies and percentages for categorical variables. The primary endpoints, including gingival index scores were analyzed using paired *t*-tests for within-group comparisons and two-sample *t*-tests for between-group comparisons. The proportions of participants achieving a Gingival Index score of 0 and experiencing treatment-emergent adverse events (TEAEs) were summarized as counts and percentages. Secondary endpoints (plaque index, bleeding index, halitosis, and pocket depth) were analyzed using Wilcoxon signed-rank and rank-sum tests. Oral hygiene index (OHI-S) was analyzed using paired *t*-tests and two-sample *t*-tests. Proportion of participants achieving a score of 0 for plaque index, bleeding index, and organoleptic score were summarized using counts and percentages. Subjective evaluations were summarized as counts and percentages. Safety endpoints were listed only. All statistical tests used a significance level of $\alpha \leq 0.05$, and two-tailed tests were applied for all analyses involving statistical testing.

3. RESULTS

3.1. Participant Demography

Table 3: Demography

Category/Statistics	Test (N = 60)	Comparator (N = 60)	Overall (N = 120)
Age (Completed Years)			
n	60	60	120
Mean ± SD	39.7 ± 10.97	38.5 ± 11.06	39.1 ± 10.98
Median	40.5	37.0	39.0
Min, Max	20, 60	20, 60	20, 60
Gender [n (%)]			
Male	25 (41.67)	27 (45.00)	52 (43.33)
Female	35 (58.33)	33 (55.00)	68 (56.67)

Abbreviation(s): Max = maximum; Min = minimum; N = number of participants in the specified group; n = number of participants in the specified category; SD = standard deviation.
Note: Percentages are based on the number of participants in the specified treatment.

A total of 120 Asian participants were enrolled in the study, including 52 males and 68 females, with ages ranging from 20 to 60 years and a mean age of 39.1 years (Table 3).

Participants were randomized equally into two groups: the test group (n = 60) and the comparator group (n = 60). The test group comprised 25 males and 35 females, with a mean age of 39.7 years (range: 20–60 years). The comparator group included 27 males and 33 females, with a mean age of 38.5 years (range: 20–60 years).

3.2 Efficacy Assessments

3.2.1 Assessment of Gingivitis using Gingival Index

In the Test Group, the mean Gingival Index (GI) score decreased from 1.75 at baseline to 1.37 on Day 7, 1.01 on Day 15, and 0.53 on Day 28, indicating a progression from moderate to mild gingivitis. This corresponded to reductions of 22.18%, 42.73%, and 70.41% at Days 7, 15, and 28, respectively (all $p < 0.0001$), reflecting 1.27-, 1.72-, and 3.29-fold improvements (Table 4, Figure 3).

In the Comparator Group, the mean GI score decreased from 1.77 at baseline to 1.52 on Day 7, 1.25 on Day 15, and 0.86 on Day 28, also indicating a shift from moderate to mild gingivitis. The corresponding reductions were 14.32%, 29.63%, and 51.59% (all $p < 0.0001$), with 1.17-, 1.42-, and 2.06-fold improvements at the respective timepoints (Table 4, Figure 3).

Between-group comparisons demonstrated that test mouthwash was significantly more effective than comparator mouthwash at all assessment timepoints. The test product achieved 1.48-fold greater reduction in GI score at Day 7, 1.40-fold at Day 15, and 1.33-fold at Day 28 (all $p < 0.0001$).

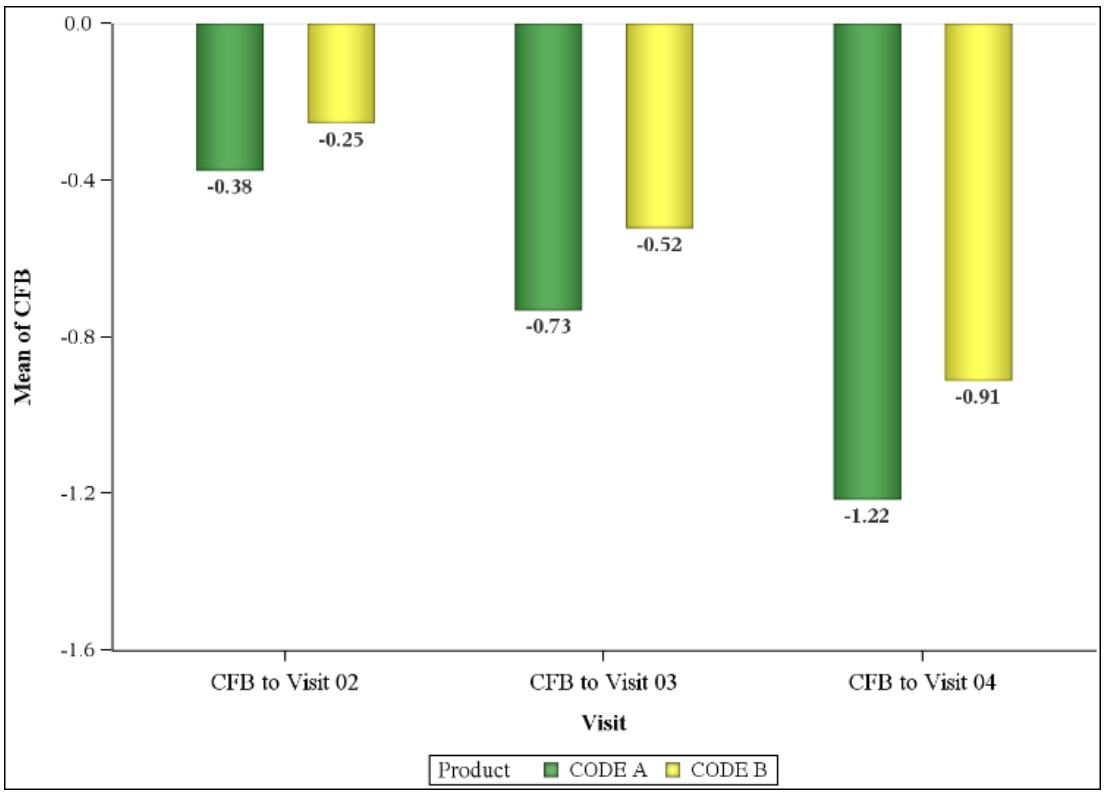

Figure 3: Assessment of Gingivitis using Gingival Index

Table 4: Assessment of Gingivitis using Gingival Index

Visit	Statistics	Test (n=60)	Comparator (n=60)
Visit 01	Mean ± SD	1.75 ± 0.415	1.77 ± 0.373
	Median	1.60	1.70
Visit 02	Mean ± SD	1.37 ± 0.377	1.52 ± 0.324
	Median	1.30	1.50
CFB to Visit 02	Mean ± SD	-0.38 ± 0.075	-0.25 ± 0.077
	Median	-0.40	-0.20
	X times improvement*	1.27	1.17
	p-value*	<.0001	<.0001
	X times improvement	1.48	
	p-value	<.0001	

% CFB to Visit 02	Mean ± SD	-22.18 ± 5.532	-14.32 ± 3.071
	Median	-21.24	-14.29
Visit 03	Mean ± SD	1.01 ± 0.306	1.25 ± 0.281
	Median	0.95	1.20
CFB to Visit 03	Mean ± SD	-0.73 ± 0.128	-0.52 ± 0.119
	Median	-0.70	-0.50
	X times improvement*	1.72	1.42
	p-value*	<.0001	<.0001
	X times improvement	1.40	
	p-value	<.0001	
% CFB to Visit 03	Mean ± SD	-42.73 ± 4.709	-29.63 ± 3.814
	Median	-42.86	-29.92
Visit 04	Mean ± SD	0.53 ± 0.194	0.86 ± 0.203
	Median	0.50	0.80
CFB to Visit 04	Mean ± SD	-1.22 ± 0.243	-0.91 ± 0.207
	Median	-1.20	-0.90
	X times improvement*	3.29	2.06
	p-value*	<.0001	<.0001
	X times improvement	1.33	
	p-value	<.0001	
% CFB to Visit 04	Mean ± SD	-70.41 ± 5.394	-51.59 ± 4.571
	Median	-68.75	-52.79

Treatment Specification: Test = Triple Combination Chlohexidine mouthwash; Comparator = Plain chlorhexidine mouthwash.
Abbreviation(s): CFB = change from baseline; Max = maximum; Min = minimum; N = number of participants in specified group; n = number of participants in specified category; SD = standard deviation.
Note 1: CFB = Post Baseline –Baseline.
Note 2: The p-value are calculated using the Two sample t-test for between group analysis.
Note 3: The p-values are calculated using the Paired t-test for within group analysis.*
*Note 4: The * indicates within group analysis.*
Note 5: X times improvement= Baseline/Post Baseline; X times improvement=A/B*
*Note 6: % CFB = ((Post Baseline –Baseline)/Baseline) *100; % Difference =((A-B)/abs(B))*100*
Note 7: Visit 01: Screening and Enrollment Visit (Day 01) and Baseline evaluations; Visit 02: Evaluation Visit (Day 07 ± 02 days); Visit 03: Evaluation Visit (Day 15 ± 02 days); Visit 04: Evaluation Visit (Day 28 ± 02 days) and End of Study.

3.2.2 Proportion of participants achieving gingival index score of 0

Both test mouthwash and comparator mouthwash were evaluated for their ability to achieve complete resolution of gingivitis (Gingival Index score = 0). No participants in either group achieved a Gingival Index score of 0 at any of the assessed timepoints (Table 5).

3.2.3 Proportion of participants with treatment-emergent adverse events (TEAEs) throughout study duration.

No treatment-emergent adverse events (TEAEs) were reported in either group during the study period, indicating that both study interventions were well tolerated.

3.2.4 Assessment of plaque formation using plaque index and disclosing agent

In the **Test Group**, the mean Plaque Index score decreased from 1.77 at baseline to 1.40 on Day 7, 1.01 on Day 15, and 0.56 on Day 28, indicating a marked reduction in plaque accumulation. This corresponded to reductions of 21.35%, 43.69%, and 68.90% at Days 7, 15, and 28, respectively (all $p < 0.0001$), reflecting 1.27-, 1.76-, and 3.17-fold improvements (Table 6, Figure 4).

In the **Comparator Group**, the mean Plaque Index score decreased from 1.75 at baseline to 1.47 on Day 7, 1.18 on Day 15, and 0.85 on Day 28. These changes corresponded to reductions of 16.20%, 32.35%, and 51.38% (all $p < 0.0001$), with 1.19-, 1.48-, and 2.06-fold improvements across the respective timepoints (Table 6, Figure 4).

Between-group comparisons demonstrated that test mouthwash was significantly more effective than comparator mouthwash at all assessed timepoints. The test product achieved 1.33-fold greater reduction at Day 7, 1.36-fold at Day 15, and 1.35-fold at Day 28 (all $p < 0.0001$).

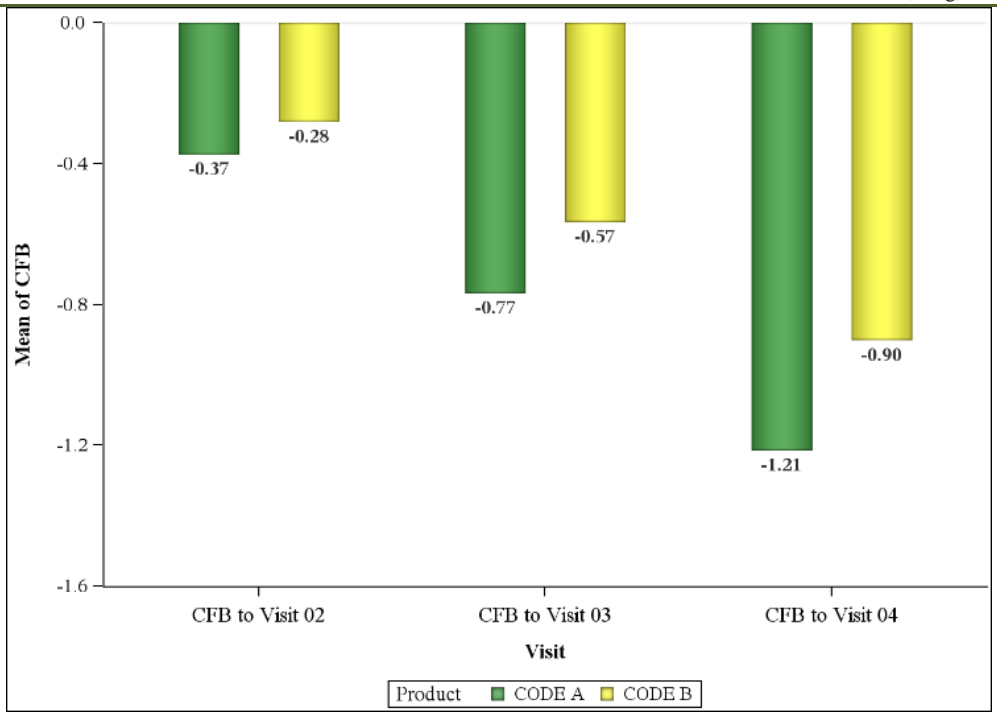

Figure 4: Assessment of plaque formation using plaque index and disclosing agent

Table 5: Proportion of participants achieving gingival index score of 0

Visit	Gingival Index Score Achieved	Test (n=60) n (%)	Comparator (n=60) n (%)
Visit 02	Yes	0 (0)	0 (0)
	No	60 (100)	60 (100)
Visit 03	Yes	0 (0)	0 (0)
	No	60 (100)	60 (100)
Visit 04	Yes	0 (0)	0 (0)
	No	60 (100)	60 (100)

Treatment Specification: Test = Triple Combination Chlohexidine mouthwash; Comparator = Plain chlorhexidine mouthwash.
Abbreviation(s): N = number of participants in specified group; n = number of participants in specified category.
Note 1: Percentages are based on the number of participants in the specified treatment.
Note 2: Visit 02: Evaluation Visit (Day 07 ± 02 days); Visit 03: Evaluation Visit (Day 15 ± 02 days); Visit 04: Evaluation Visit (Day 28 ± 02 days) and End of Study.

Table 6: Assessment of plaque formation using plaque index and disclosing agent

Visit	Statistics	Test (n=60)	Comparator (n=60)
Visit 01	Mean ± SD	1.77 ± 0.368	1.75 ± 0.369
	Median	1.75	1.65
Visit 02	Mean ± SD	1.40 ± 0.325	1.47 ± 0.330
	Median	1.40	1.40
CFB to Visit 02	Mean ± SD	-0.37 ± 0.106	-0.28 ± 0.063
	Median	-0.40	-0.30
	X times improvement*	1.27	1.19
	p-value*	<.0001	<.0001
	X times improvement	1.33	
	p-value	<.0001	
% CFB to Visit 02	Mean ± SD	-21.35 ± 5.376	-16.20 ± 2.817
	Median	-21.24	-16.67
Visit 03	Mean ± SD	1.01 ± 0.255	1.18 ± 0.262
	Median	1.00	1.10
CFB to Visit 03	Mean ± SD	-0.77 ± 0.148	-0.57 ± 0.133
	Median	-0.80	-0.50
	X times improvement*	1.76	1.48
	p-value*	<.0001	<.0001

	X times improvement	1.36	
	p-value	<.0001	
% CFB to Visit 03	Mean ± SD	-43.69 ± 5.118	-32.35 ± 3.798
	Median	-43.48	-33.33
Visit 04	Mean ± SD	0.56 ± 0.174	0.85 ± 0.188
	Median	0.60	0.80
CFB to Visit 04	Mean ± SD	-1.21 ± 0.237	-0.90 ± 0.209
	Median	-1.20	-0.90
	X times improvement*	3.17	2.06
	p-value*	<.0001	<.0001
	X times improvement	1.35	
	p-value	<.0001	
% CFB to Visit 04	Mean ± SD	-68.90 ± 5.570	-51.38 ± 4.373
	Median	-68.99	-50.00

Treatment Specification: Test = Triple Combination Chlohexidine mouthwash; Comparator = Plain chlorhexidine mouthwash.
Abbreviation(s): CFB = change from baseline; Max = maximum; Min = minimum; N = number of participants in specified group; n = number of participants in specified category; SD = standard deviation.
Note 1: CFB = Post Baseline –Baseline.
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Note 5: X times improvement= Baseline/Post Baseline; X times improvement=A/B*
*Note 6: % CFB = ((Post Baseline –Baseline)/Baseline) *100; % Difference =((A-B)/abs(B))*100*
Note 7: Visit 01: Screening and Enrollment Visit (Day 01) and Baseline evaluations; Visit 02: Evaluation Visit (Day 07 ± 02 days); Visit 03: Evaluation Visit (Day 15 ± 02 days); Visit 04: Evaluation Visit (Day 28 ± 02 days) and End of Study.

3.2.5 Proportion of participants achieving plaque index score of 0

Both test mouthwash and comparator mouthwash were evaluated for their ability to achieve complete resolution of plaque (Plaque Index score = 0). No participants in either group achieved a Plaque Index score of 0 at any of the assessed timepoints (Table 7).

3.2.6 Assessment of bleeding gums using Sulcus Bleeding Index

In the **Test Group**, the mean Sulcus Bleeding Index score decreased from 1.68 at baseline to 1.33 on Day 7, 0.94 on Day 15, and 0.49 on Day 28, indicating a progressive reduction in gingival bleeding and a substantial improvement over time. This corresponded to reductions of 21.30%, 45.02%, and 71.96% at Days 7, 15, and 28, respectively (all $p < 0.0001$), reflecting 1.26-, 1.79-, and 3.45-fold improvements (Table 8, Figure 5).

In the **Comparator Group**, the mean Sulcus Bleeding Index score decreased from 1.70 at baseline to 1.48 on Day 7, 1.20 on Day 15, and 0.85 on Day 28, indicating improvement, although to a lesser extent than that observed in the test group. These changes corresponded to reductions of 13.42%, 29.67%, and 50.48% (all $p < 0.0001$), with 1.15-, 1.42-, and 2.01-fold improvements across the respective timepoints (Table 8, Figure 5).

Between-group comparisons demonstrated that test mouthwash was significantly more effective than comparator mouthwash at all assessed timepoints. The test product achieved 1.54-fold greater reduction at Day 7, 1.48-fold at Day 15, and 1.39-fold at Day 28 (all $p < 0.0001$).

Table 7: Proportion of participants achieving plaque index score of 0

Visit	Plaque Index Score Achieved	Test (n=60) n (%)	Comparator (n=60) n (%)
Visit 02	Yes	0 (0)	0 (0)
	No	60 (100)	60 (100)
Visit 03	Yes	0 (0)	0 (0)
	No	60 (100)	60 (100)
Visit 04	Yes	0 (0)	0 (0)
	No	60 (100)	60 (100)

Treatment Specification: Test = Triple Combination Chlohexidine mouthwash; Comparator = Plain chlorhexidine mouthwash.
Abbreviation(s): N = number of participants in specified group; n = number of participants in specified category.
Note 1: Percentages are based on the number of participants in the specified treatment.
Note 2: Visit 02: Evaluation Visit (Day 07 ± 02 days); Visit 03: Evaluation Visit (Day 15 ± 02 days); Visit 04: Evaluation Visit (Day 28 ± 02 days) and End of Study.

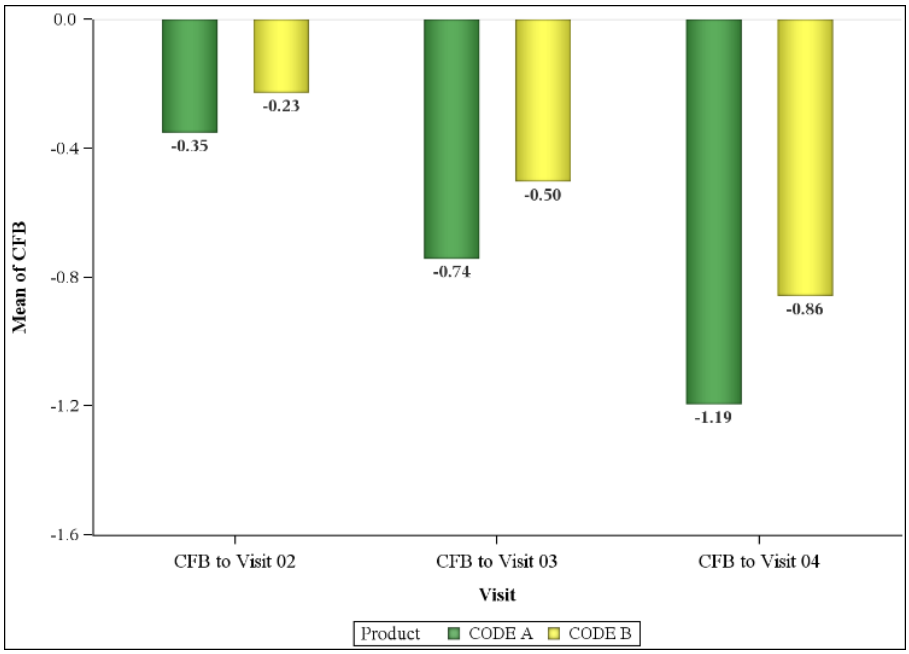

Figure 5: Assessment of bleeding gums using Sulcus Bleeding Index

Table 8: Assessment of bleeding using Sulcus Bleeding Index

Visit	Statistics	Test (n=60)	Comparator (n=60)
Visit 01	Mean ± SD	1.68 ± 0.388	1.70 ± 0.356
	Median	1.65	1.70
Visit 02	Mean ± SD	1.33 ± 0.344	1.48 ± 0.323
	Median	1.30	1.45
CFB to Visit 02	Mean ± SD	-0.35 ± 0.060	-0.23 ± 0.063
	Median	-0.40	-0.20
	X times improvement*	1.26	1.15
	p-value*	<.0001	<.0001
	X times improvement	1.54	
	p-value	<.0001	
% CFB to Visit 02	Mean ± SD	-21.30 ± 3.184	-13.42 ± 3.290
	Median	-21.05	-13.64
Visit 03	Mean ± SD	0.94 ± 0.286	1.20 ± 0.280
	Median	0.90	1.20
CFB to Visit 03	Mean ± SD	-0.74 ± 0.129	-0.50 ± 0.114
	Median	-0.75	-0.50
	X times improvement*	1.79	1.42
	p-value*	<.0001	<.0001
	X times improvement	1.48	
	p-value	<.0001	
% CFB to Visit 03	Mean ± SD	-45.02 ± 5.567	-29.67 ± 4.878
	Median	-45.23	-28.57
Visit 04	Mean ± SD	0.49 ± 0.191	0.85 ± 0.211
	Median	0.50	0.80
CFB to Visit 04	Mean ± SD	-1.19 ± 0.224	-0.86 ± 0.184
	Median	-1.20	-0.90
	X times improvement*	3.45	2.01
	p-value*	<.0001	<.0001
	X times improvement	1.39	
	p-value	<.0001	
% CFB to Visit 04	Mean ± SD	-71.96 ± 6.059	-50.48 ± 5.502
	Median	-71.43	-50.00

Treatment Specification: Test = Triple Combination Chlohexidine mouthwash; Comparator = Plain chlorhexidine mouthwash.

Abbreviation(s): CFB = change from baseline; Max = maximum; Min = minimum; N = number of participants in specified group; n = number of participants in specified category; SD = standard deviation.
Note 1: CFB = Post Baseline –Baseline.
Note 2: The p-value are calculated using the Two sample t-test for between group analysis.
Note 3: The p-values are calculated using the Paired t-test for within group analysis.*
*Note 4: The * indicates within group analysis.*
Note 5: X times improvement= Baseline/Post Baseline; X times improvement=A/B*
*Note 6: % CFB = ((Post Baseline –Baseline)/Baseline) *100; % Difference =((A-B)/abs(B))*100*
Note 7: Visit 01: Screening and Enrollment Visit (Day 01) and Baseline evaluations; Visit 02: Evaluation Visit (Day 07 ± 02 days); Visit 03: Evaluation Visit (Day 15 ± 02 days); Visit 04: Evaluation Visit (Day 28 ± 02 days) and End of Study.

3.2.7 Proportion of participants achieving bleeding index score of 0

Both test mouthwash and comparator mouthwash were evaluated for their ability to achieve complete resolution of gingival bleeding (Sulcus Bleeding Index score = 0). No participants in either group achieved a Sulcus Bleeding Index score of 0 at any of the assessed timepoints (Table 9).

3.2.8 Assessment of halitosis using Organoleptic Scoring Scale

In the **Test Group**, the mean halitosis score at baseline was 3.4, indicating moderate oral malodor. Following treatment, the score decreased to 2.3 on Day 7, 0.9 on Day 15, and 0.1 on Day 28, demonstrating a marked reduction with near-complete resolution of malodor by Day 28. These changes corresponded to reductions of 32.8%, 77.4%, and 98.8% at Days 7, 15, and 28, respectively (all $p < 0.0001$), reflecting 1.46-, 3.87-, and 67-fold improvements (Table 10, Figure 6).

In the **Comparator Group**, the mean halitosis score decreased from 3.4 at baseline to 2.8 on Day 7, 1.8 on Day 15, and 0.7 on Day 28. This corresponded to reductions of 16.4%, 45.7%, and 80.6% (all $p < 0.0001$), with 1.22-, 1.85-, and 4.87-fold improvements (Table 10, Figure 6).

Between-group comparisons demonstrated that test mouthwash was significantly more effective than comparator mouthwash in reducing oral malodor at all assessed timepoints. The test product achieved 1.70-fold greater reduction at Day 7, 1.60-fold at Day 15, and 1.23-fold at Day 28 (all $p < 0.0001$).

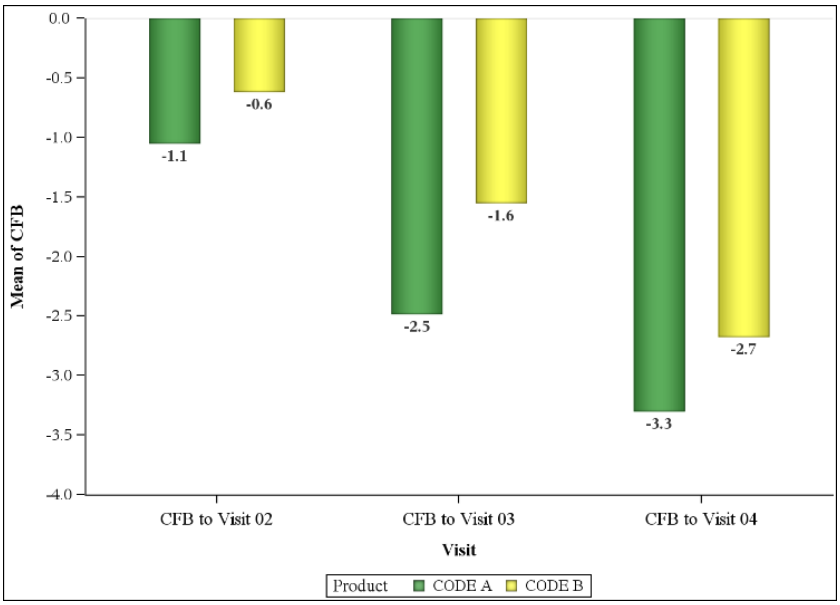

Figure 6: Assessment of halitosis by qualified dental surgeon using Organoleptic Scoring Scale

Table 9: Proportion of participants achieving bleeding index score of 0

Visit	Bleeding Index Score Achieved	Test (n=60) n (%)	Comparator (n=60) n (%)
Visit 02	Yes	0 (0)	0 (0)
	No	60 (100)	60 (100)
Visit 03	Yes	0 (0)	0 (0)
	No	60 (100)	60 (100)
Visit 04	Yes	0 (0)	0 (0)
	No	60 (100)	60 (100)
Treatment Specification: Test = Triple Combination Chlohexidine mouthwash; Comparator = Plain chlorhexidine mouthwash.			

Abbreviation(s): N = number of participants in specified group; n = number of participants in specified category.
Note 1: Percentages are based on the number of participants in the specified treatment.
Note 2: Visit 02: Evaluation Visit (Day 07 ± 02 days); Visit 03: Evaluation Visit (Day 15 ± 02 days); Visit 04: Evaluation Visit (Day 28 ± 02 days) and End of Study.

Table 10: Assessment of halitosis using Organoleptic Scoring Scale

Visit	Statistics	Test (n=60)	Comparator (n=60)
Visit 01	Mean ± SD	3.4 ± 0.71	3.4 ± 0.71
	Median	3.0	3.5
Visit 02	Mean ± SD	2.3 ± 0.70	2.8 ± 0.44
	Median	2.0	3.0
CFB to Visit 02	Mean ± SD	-1.1 ± 0.22	-0.6 ± 0.49
	Median	-1.0	-1.0
	X times improvement*	1.46	1.22
	p-value*	<.0001	<.0001
	X times improvement	1.70	
	p-value	<.0001	
% CFB to Visit 02	Mean ± SD	-32.8 ± 9.06	-16.4 ± 13.28
	Median	-33.3	-25.0
Visit 03	Mean ± SD	0.9 ± 0.81	1.8 ± 0.50
	Median	1.0	2.0
CFB to Visit 03	Mean ± SD	-2.5 ± 0.50	-1.6 ± 0.53
	Median	-2.0	-2.0
	X times improvement*	3.87	1.85
	p-value*	<.0001	<.0001
	X times improvement	1.60	
	p-value	<.0001	
% CFB to Visit 03	Mean ± SD	-77.4 ± 20.65	-45.7 ± 12.60
	Median	-75.0	-50.0
Visit 04	Mean ± SD	0.1 ± 0.22	0.7 ± 0.46
	Median	0.0	1.0
CFB to Visit 04	Mean ± SD	-3.3 ± 0.70	-2.7 ± 0.58
	Median	-3.0	-3.0
	X times improvement*	67.00	4.87
	p-value*	<.0001	<.0001
	X times improvement	1.23	
	p-value	<.0001	
% CFB to Visit 04	Mean ± SD	-98.8 ± 5.49	-80.6 ± 13.26
	Median	-100.0	-75.0

Treatment Specification: Test = Triple Combination Chlohexidine mouthwash; Comparator = Plain chlorhexidine mouthwash.
Abbreviation(s): CFB = change from baseline; Max = maximum; Min = minimum; N = number of participants in specified group; n = number of participants in specified category; SD = standard deviation.
Note 1: CFB = Post Baseline –Baseline.
Note 2: The p-value are calculated using the Two sample t-test for between group analysis.
Note 3: The p-values are calculated using the Paired t-test for within group analysis.*
*Note 4: The * indicates within group analysis.*
Note 5: X times improvement= Baseline/Post Baseline; X times improvement=A/B*
*Note 6: % CFB = ((Post Baseline –Baseline)/Baseline) *100; % Difference =((A-B)/abs(B))*100*
Note 7: Visit 01: Screening and Enrollment Visit (Day 01) and Baseline evaluations; Visit 02: Evaluation Visit (Day 07 ± 02 days); Visit 03: Evaluation Visit (Day 15 ± 02 days); Visit 04: Evaluation Visit (Day 28 ± 02 days) and End of Study.

3.2.9 Proportion of participants achieving organoleptic score of 0

Both test mouthwash and comparator mouthwash were evaluated for their ability to achieve complete resolution of oral malodor (Organoleptic score = 0). At Day 7, no participants in either group achieved an Organoleptic score of 0, with 0% in both groups demonstrating complete resolution. At Day 15, 40% of participants in the test group achieved an Organoleptic score of 0, whereas no participants (0%) in the comparator group attained this outcome. By Day 28, 95% of participants in the test group achieved an Organoleptic score of 0, compared to 30% in the comparator group (Table 11).

3.2.10 Assessment of pocket depth using a periodontal probe and grading scale

In the **Test Group**, the mean periodontal pocket depth decreased from 2.90 mm at baseline to 2.13 mm at Day 28, indicating a notable improvement in periodontal status. This corresponded to a reduction of 26.57% (p <

0.0001), representing a 1.36-fold improvement (Table 12, Figure 7).

In the **Comparator Group**, the mean pocket depth decreased from 2.90 mm at baseline to 2.53 mm at Day 28, corresponding to a reduction of 13.03% ($p < 0.0001$) and a 1.15-fold improvement (Table 12, Figure 7).

Between-group comparisons demonstrated that test mouthwash was significantly more effective than comparator mouthwash in reducing periodontal pocket depth, achieving a 2.03-fold greater reduction at Day 28 ($p < 0.0001$).

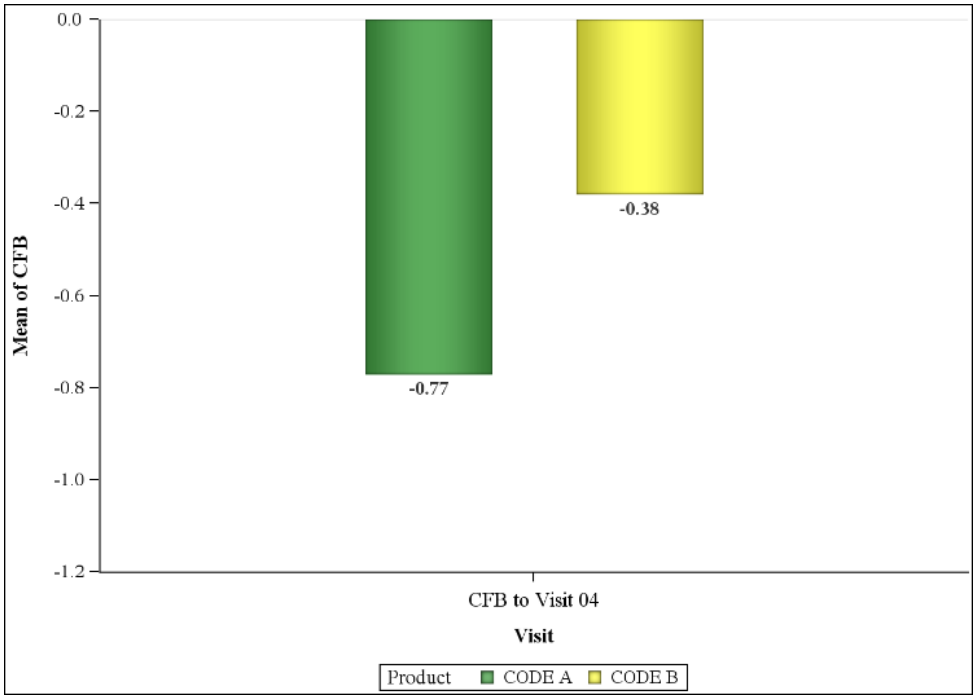

Figure 7: Assessment of pocket depth using a periodontal probe and grading scale

Table 11: Proportion of participants achieving organoleptic score of 0

Visit	Organoleptic Score Achieved	Test (n=60) n (%)	Comparator (n=60) n (%)
Visit 02	Yes	0 (0)	0 (0)
	No	60 (100)	60 (100)
Visit 03	Yes	24 (40.00)	0 (0)
	No	36 (60.00)	60 (100)
Visit 04	Yes	57 (95.00)	18 (30.00)
	No	3 (5.00)	42 (70.00)

Treatment Specification: Test = Triple Combination Chlohexidine mouthwash; Comparator = Plain chlorhexidine mouthwash.
Abbreviation(s): N = number of participants in specified group; n = number of participants in specified category.
Note 1: Percentages are based on the number of participants in the specified treatment.
Note 2: Visit 02: Evaluation Visit (Day 07 ± 02 days); Visit 03: Evaluation Visit (Day 15 ± 02 days); Visit 04: Evaluation Visit (Day 28 ± 02 days) and End of Study.

Table 12: Assessment of pocket depth using a periodontal probe and grading scale

Visit	Statistics	Test (n=60)	Comparator (n=60)
Visit 01	Mean ± SD	2.90 ± 0.167	2.90 ± 0.146
	Median	3.00	3.00
Visit 04	Mean ± SD	2.13 ± 0.169	2.53 ± 0.170
	Median	2.25	2.50
CFB to Visit 04	Mean ± SD	-0.77 ± 0.133	-0.38 ± 0.134
	Median	-0.75	-0.50
	X times improvement*	1.36	1.15
	p-value*	<.0001	<.0001

	X times improvement	2.03	
	p-value	<.0001	
% CFB to Visit 04	Mean ± SD	-26.57 ± 4.271	-13.03 ± 4.500
	Median	-25.00	-16.67

Treatment Specification: Test = Triple Combination Chlohexidine mouthwash; Comparator = Plain chlorhexidine mouthwash.
Abbreviation(s): CFB = change from baseline; Max = maximum; Min = minimum; N = number of participants in specified group; n = number of participants in specified category; SD = standard deviation.
Note 1: CFB= Post Baseline – Baseline.
Note 2: The p-value are calculated using the Two-sample t-test for between group analysis.
Note 3: The p-values are calculated using the Paired t-test for within group analysis.*
*Note 4: The * indicates within group analysis.*
Note 5: X times improvement= Baseline/Post Baseline; X times improvement=A/B*
*Note 6: % CFB = ((Post Baseline –Baseline)/Baseline) *100; % Difference =((A-B)/abs(B))*100*
Note 7: Visit 01: Screening and Enrollment Visit (Day 01) and Baseline evaluations; Visit 04: Evaluation Visit (Day 28 ± 02 days) and End of Study.

3.2.11 Assessment of Oral Hygiene using Simplified Oral Hygiene Index (OHI-S)

In the Test Group, the mean Simplified Oral Hygiene Index (OHI-S) score decreased from 3.52 at baseline to 2.84 on Day 7, 2.04 on Day 15, and 0.99 on Day 28, demonstrating a sustained reduction and substantial improvement in oral hygiene over time. These changes corresponded to reductions of 19.99%, 42.89%, and 72.77% at Days 7, 15, and 28, respectively (all $p < 0.0001$), reflecting 1.24-, 1.72-, and 3.58-fold improvements (Table 13, Figure 8).

In the Comparator Group, the mean OHI-S score decreased from 3.53 at baseline to 3.01 on Day 7, 2.40 on Day 15, and 1.72 on Day 28, indicating a progressive improvement in oral hygiene. These changes corresponded to reductions of 14.98%, 32.35%, and 51.75% (all $p < 0.0001$), with 1.17-, 1.47-, and 2.06-fold improvements across the respective timepoints (Table 13, Figure 8).

Between-group comparisons demonstrated that test mouthwash was significantly more effective than comparator mouthwash in improving oral hygiene at all assessed timepoints. The test product achieved 1.32-fold greater reduction at Day 7, 1.31-fold at Day 15, and 1.40-fold at Day 28 (all $p < 0.0001$).

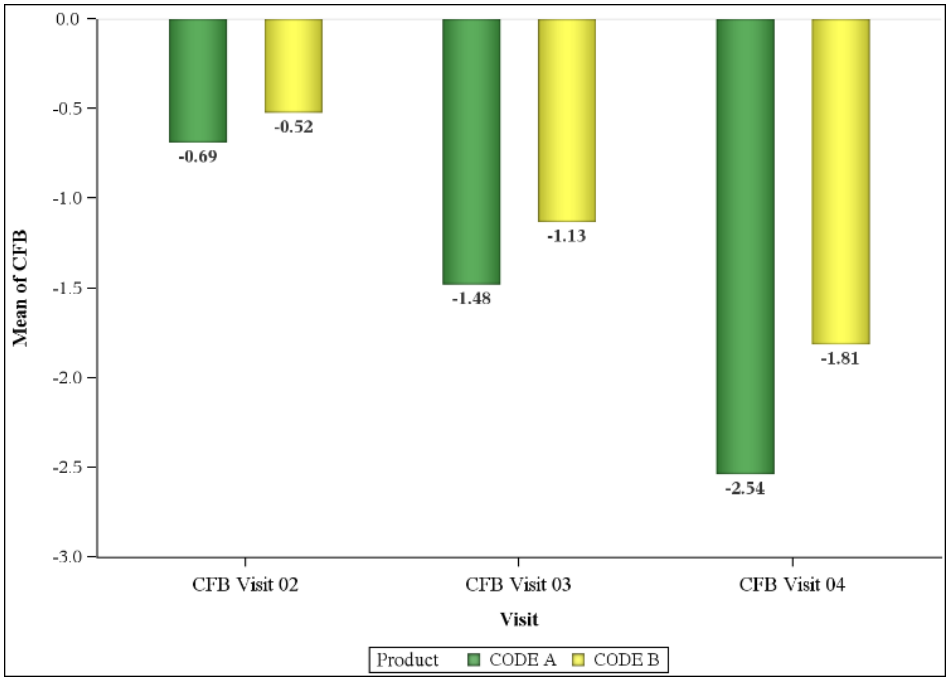

Figure 8: Assessment of Oral Hygiene using Simplified Oral Hygiene Index (OHI-S)

Table 13: Assessment of Oral Hygiene using Simplified Oral Hygiene Index (OHI-S)

Visit	Statistics	Test (n=60)	Comparator (n=60)
Visit 01	Mean ± SD	3.52 ± 0.719	3.53 ± 0.733
	Median	3.55	3.50
Visit 02	Mean ± SD	2.84 ± 0.673	3.01 ± 0.670

	Median	2.85	3.00
CFB to Visit 02	Mean ± SD	-0.69 ± 0.138	-0.52 ± 0.094
	Median	-0.70	-0.50
	X times improvement*	1.24	1.17
	p-value*	<.0001	<.0001
	X times improvement	1.32	
	p-value	<.0001	
% CFB to Visit 02	Mean ± SD	-19.99 ± 4.417	-14.98 ± 2.146
	Median	-19.51	-15.27
Visit 03	Mean ± SD	2.04 ± 0.588	2.40 ± 0.570
	Median	2.00	2.40
CFB to Visit 03	Mean ± SD	-1.48 ± 0.208	-1.13 ± 0.216
	Median	-1.50	-1.10
	X times improvement*	1.72	1.47
	p-value*	<.0001	<.0001
	X times improvement	1.31	
	p-value	<.0001	
% CFB to Visit 03	Mean ± SD	-42.89 ± 6.271	-32.35 ± 3.847
	Median	-42.86	-32.35
Visit 04	Mean ± SD	0.99 ± 0.350	1.72 ± 0.443
	Median	1.00	1.70
CFB to Visit 04	Mean ± SD	-2.54 ± 0.410	-1.81 ± 0.343
	Median	-2.60	-1.80
	X times improvement*	3.58	2.06
	p-value*	<.0001	<.0001
	X times improvement	1.40	
	p-value	<.0001	
% CFB to Visit 04	Mean ± SD	-72.77 ± 5.130	-51.75 ± 4.285
	Median	-72.61	-51.93

Treatment Specification: Test = Triple Combination Chlohexidine mouthwash; Comparator = Plain chlorhexidine mouthwash.
Abbreviation(s): CFB = change from baseline; Max = maximum; Min = minimum; N = number of participants in specified group; n = number of participants in specified category; SD = standard deviation.
Note 1: CFB= Post Baseline – Baseline.
Note 2: The p-value are calculated using the Two-sample t-test for between group analysis.
Note 3: The p-values are calculated using the Paired t-test for within group analysis.*
*Note 4: The * indicates within group analysis.*
Note 5: X times improvement= Baseline/Post Baseline; X times improvement=A/B*
*Note 6: % CFB = ((Post Baseline –Baseline)/Baseline) *100; % Difference =((A-B)/abs(B))*100*
Note 7: Visit 01: Screening and Enrollment Visit (Day 01) and Baseline evaluations; Visit 02: Evaluation Visit (Day 07 ± 02 days); Visit 03: Evaluation Visit (Day 15 ± 02 days); Visit 04: Evaluation Visit (Day 28 ± 02 days) and End of Study.

3.2.12 Assessment of Subjective evaluation questionnaires

For reduction in bleeding gums, all participants (100%) in both groups reported bleeding gums while brushing or eating at baseline. In the test group, marked improvement was observed, with 100% reporting reduction by Day 7 and complete resolution (100%) achieved by Day 15, which was sustained through Day 28. In the comparator group, improvement was more gradual, with 33.33% reporting reduction by Day 7, followed by complete resolution (100%) by Day 15 and maintained through Day 28 (Table 14, Figure 9a, 9c).

For reduction in bad breath, 90% of participants in the test group and 93.33% in the comparator group reported oral malodor at baseline. In both groups, the majority had not received professional treatment, while all participants reported self-management and indicated that bad breath interfered with social or workplace interactions. In the test group, improvement was observed in 98.34% by Day 7 and reached complete resolution (100%) by Day 15, sustained through Day 28. In contrast, the comparator group exhibited slower improvement, with 28.33% at Day 7, 91.66% at Day 15, and complete resolution (100%) achieved only by Day 28 (Table 14, Figure 9b, 9d).

For reduction in teeth staining, all participants (100%) in the test group and 98.33% in the comparator group reported staining at baseline. The test group

demonstrated rapid improvement, with 83.34% reporting reduction by Day 7 and complete resolution (100%) by Day 15, sustained through Day 28. In comparison, the comparator group showed limited improvement initially (13.33% at Day 7), which increased to 76.67% by Day 15 and achieved complete resolution (100%) only by Day 28 (Table 14, Figure 9a, 9e).

Regarding gums feeling tight/strong, the test group showed progressive improvement, with 81.67% reporting improvement by Day 7 and 100% by Day 15, sustained through Day 28. The comparator group demonstrated slower improvement, with 18.33% at Day 7, 83.33% at Day 15, and 98.33% by Day 28 (Table 14, Figure 9f).

For visible improvement in the appearance of teeth, the test group reported improvement in 73.34% of participants by Day 7 and 100% by Day 15, sustained through Day 28. In contrast, the comparator group showed gradual improvement, with 15.00% at Day 7, 73.34% at Day 15, and 98.34% by Day 28 (Table 14, Figure 9g).

Regarding baseline oral health status, 21.67% of participants in the test group and 31.67% in the comparator group reported a history of dental caries, while the remaining participants reported no such history (Table 14, Figure 9a).

With respect to tolerability, no participants in the test group reported dryness of mouth at baseline, while 1.67% of participants in the comparator group reported dryness. During the study, absence of dryness of mouth was reported by 91.66% of participants in the test group at Day 7, with no cases at Day 15 and 98.33% at Day 28. In the comparator group, absence of dryness was reported by 33.33% at Day 7, increasing to 98.33% by Day 15 and 100% by Day 28. (Table 14, Figure 9a, 10h). In the test group, No participants in the test group reported burning, stinging, or metallic taste at any timepoint. In the comparator group, mild burning or stinging sensations were reported initially (76.67% reported no symptoms at Day 7), which resolved completely by Day 15 and Day 28. No metallic taste was reported in either group throughout the study period (Table 14, Figure 9i, 9j).

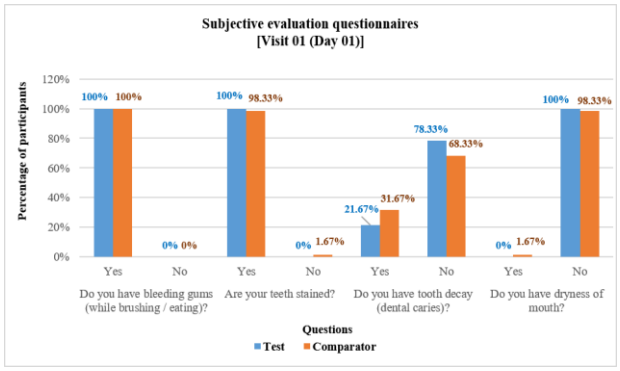

Figure 9a: Subjective evaluation questionnaires (Day 01)

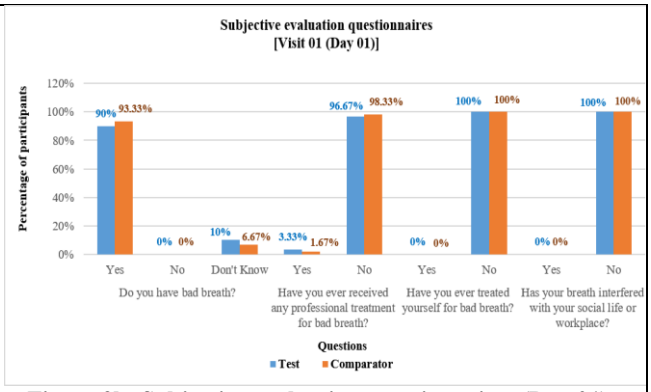

Figure 9b: Subjective evaluation questionnaires (Day 01)

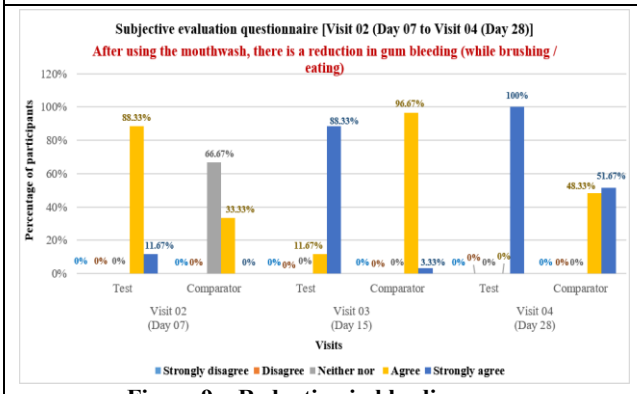

Figure 9c: Reduction in bleeding gums

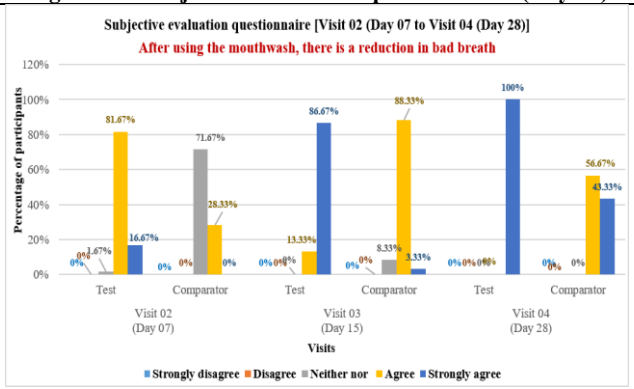

Figure 9d: Reduction in bad breath

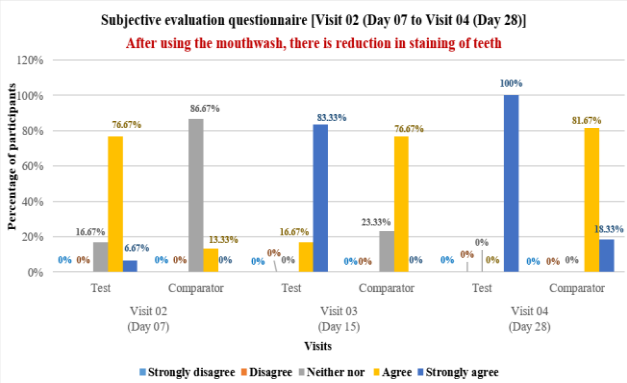

Figure 9e: Reduction in teeth staining

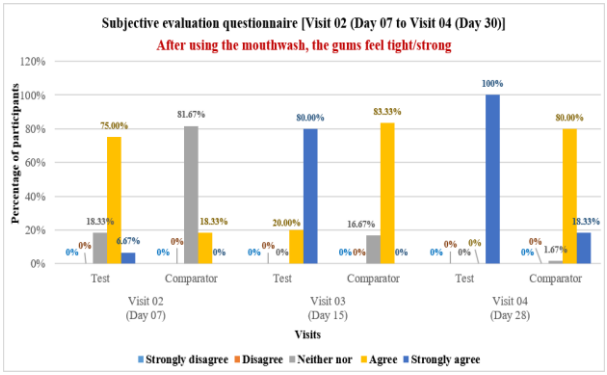

Figure 9f: Gums feeling tight/strong

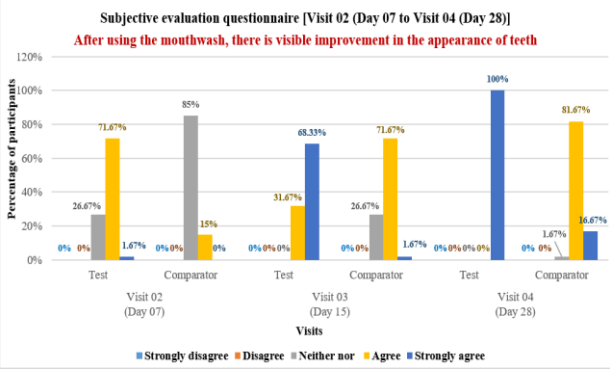

Figure 9g: Visible improvement in the appearance of teeth

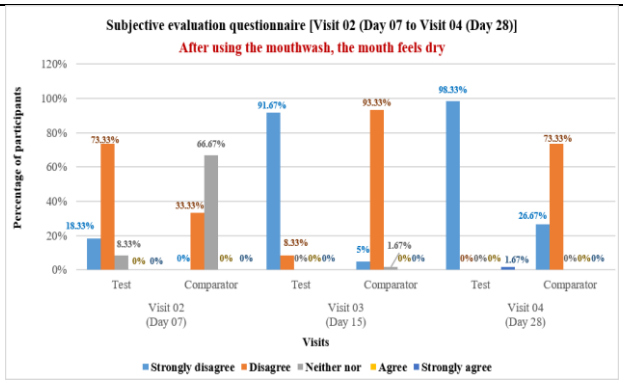

Figure 9h: Dryness of mouth

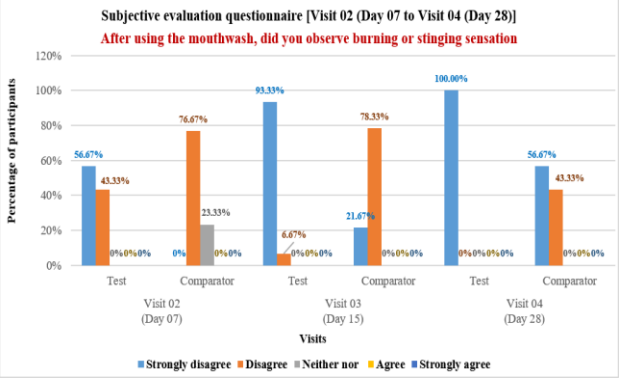

Figure 9i: Burning/Stinging Sensation after using the product

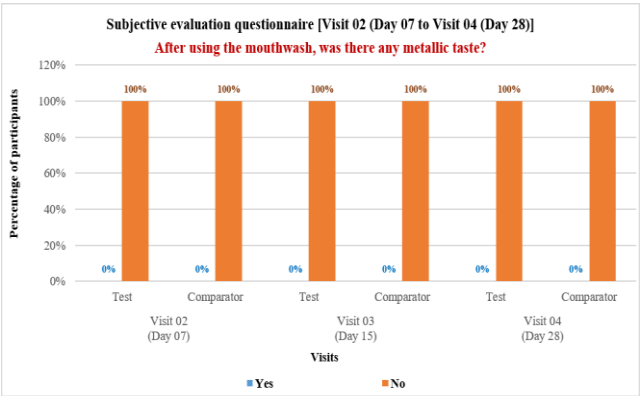

Figure 9j: Metallic after-taste

Figure 9: Assessment of Subjective evaluation questionnaires

Table 14: Subjective evaluation questionnaire

Test (N = 60) n (%)						**Comparator (N = 60) n (%)**					
Question 1		**Do you have bad breath?**									
Response	**Yes**	**No**	**Don't Know**			**Response**	**Yes**	**No**	**Don't Know**		
Visit 01 (Day 01)	54 (90.00%)	0 (0%)	6 (10.00%)			Visit 01 (Day 01)	56 (93.33%)	0 (0%)	4 (6.67%)		
Question 1A		**After using the mouthwash, there is a reduction in bad breath.**									
Response	**Strongly disagree**	**Disagree**	**Neither nor**	**Agree**	**Strongly agree**	**Response**	**Strongly disagree**	**Disagree**	**Neither nor**	**Agree**	**Strongly agree**
Visit 02 (Day 7)	0 (0%)	0 (0%)	1 (1.67%)	49 (81.67%)	10 (16.67%)	Visit 02 (Day 7)	0 (0%)	0 (0%)	43 (71.67%)	17 (28.33%)	0 (0%)
Visit 03 (Day 15)	0 (0%)	0 (0%)	0 (0%)	8 (13.33%)	52 (86.67%)	Visit 03 (Day 15)	0 (0%)	0 (0%)	5 (8.33%)	53 (88.33%)	2 (3.33%)
Visit 04 (Day 28)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	60 (100%)	Visit 04 (Day 28)	0 (0%)	0 (0%)	0 (0%)	34 (56.67%)	26 (43.33%)
Question 2		**Have you ever received any professional treatment for bad breath?**									
Response	**Yes**	**No**				**Response**	**Yes**	**No**			

Visit 01 (Day 01)	2 (3.33%)	58 (96.67%)				Visit 01 (Day 01)	1 (1.67%)	59 (98.33%)			
Question 3		**Have you ever treated yourself for bad breath?**									
Response	**Yes**	**No**				**Response**	**Yes**	**No**			
Visit 01 (Day 01)	0 (0%)	60 (100%)				Visit 01 (Day 01)	0 (0%)	60 (100%)			
Question 4		**Has your breath interfered with your social life or workplace?**									
Response	**Yes**	**No**				**Response**	**Yes**	**No**			
Visit 01 (Day 01)	0 (0%)	60 (100%)				Visit 01 (Day 01)	0 (0%)	60 (100%)			
Question 5		**Do you have tooth decay (dental caries)?**									
Response	**Yes**	**No**				**Response**	**Yes**	**No**			
Visit 01 (Day 01)	13 (21.67%)	47 (78.33%)				Visit 01 (Day 01)	19 (31.67%)	41 (68.33%)			
Question 6		**Do you have bleeding gums (while brushing / eating)?**									
Response	**Yes**	**No**				**Response**	**Yes**	**No**			
Visit 01 (Day 01)	60 (100%)	0 (0%)				Visit 01 (Day 01)	60 (100%)	0 (0%)			
Question 6A		**After using the mouthwash, there is a reduction in gum bleeding (while brushing / eating).**									
Response	**Strongly disagree**	**Disagree**	**Neither nor**	**Agree**	**Strongly agree**	**Response**	**Strongly disagree**	**Disagree**	**Neither nor**	**Agree**	**Strongly agree**
Visit 02 (Day 7)	0 (0%)	0 (0%)	0 (0%)	53 (88.33%)	7 (11.67%)	Visit 02 (Day 7)	0 (0%)	0 (0%)	40 (66.67%)	20 (33.33%)	0 (0%)
Visit 03 (Day 15)	0 (0%)	0 (0%)	0 (0%)	7 (11.67%)	53 (88.33%)	Visit 03 (Day 15)	0 (0%)	0 (0%)	0 (0%)	58 (96.67%)	2 (3.33%)
Visit 04 (Day 28)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	60 (100%)	Visit 04 (Day 28)	0 (0%)	0 (0%)	0 (0%)	29 (48.33%)	31 (51.67%)
Question 7		**Do you have dryness of mouth?**									
Response	**Yes**	**No**				**Response**	**Yes**	**No**			
Visit 01 (Day 01)	0 (0%)	60 (100%)				Visit 01 (Day 01)	1 (1.67%)	59 (98.33%)			
Question 7A		**After using the mouthwash, the mouth feels dry.**									
Response	**Strongly disagree**	**Disagree**	**Neither nor**	**Agree**	**Strongly agree**	**Response**	**Strongly disagree**	**Disagree**	**Neither nor**	**Agree**	**Strongly agree**
Visit 02 (Day 7)	11 (18.33%)	44 (73.33%)	5 (8.33%)	0 (0%)	0 (0%)	Visit 02 (Day 7)	0 (0%)	20 (33.33%)	40 (66.67%)	0 (0%)	0 (0%)
Visit 03 (Day 15)	55 (91.67%)	5 (8.33%)	0 (0%)	0 (0%)	0 (0%)	Visit 03 (Day 15)	3 (5.00%)	56 (93.33%)	1 (1.67%)	0 (0%)	0 (0%)
Visit 04 (Day 28)	59 (98.33%)	0 (0%)	0 (0%)	0 (0%)	1 (1.67%)	Visit 04 (Day 28)	16 (26.67%)	44 (73.33%)	0 (0%)	0 (0%)	0 (0%)
Question 8		**Are your teeth stained?**									
Response	**Yes**	**No**				**Response**	**Yes**	**No**			
Visit 01 (Day 01)	60 (100%)	0 (0%)				Visit 01 (Day 01)	59 (98.33%)	1 (1.67%)			
Question 8A		**After using the mouthwash, there is reduction in staining of teeth.**									
Response	**Strongly disagree**	**Disagree**	**Neither nor**	**Agree**	**Strongly agree**	**Response**	**Strongly disagree**	**Disagree**	**Neither nor**	**Agree**	**Strongly agree**
Visit 02 (Day 7)	0 (0%)	0 (0%)	10 (16.67%)	46 (76.67%)	4 (6.67%)	Visit 02 (Day 7)	0 (0%)	0 (0%)	52 (86.67%)	8 (13.33%)	0 (0%)
Visit 03 (Day 15)	0 (0%)	0 (0%)	0 (0%)	10 (16.67%)	50 (83.33%)	Visit 03 (Day 15)	0 (0%)	0 (0%)	14 (23.33%)	46 (76.67%)	0 (0%)
Visit 04 (Day 28)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	60 (100%)	Visit 04 (Day 28)	0 (0%)	0 (0%)	0 (0%)	49 (81.67%)	11 (18.33%)
Question 9		**After using the mouthwash, the gums feel tight/strong**									
Response	**Strongly disagree**	**Disagree**	**Neither nor**	**Agree**	**Strongly agree**	**Response**	**Strongly disagree**	**Disagree**	**Neither nor**	**Agree**	**Strongly agree**
Visit 02 (Day 7)	0 (0%)	0 (0%)	11 (18.33%)	45 (75.00%)	4 (6.67%)	Visit 02 (Day 7)	0 (0%)	0 (0%)	49 (81.67%)	11 (18.33%)	0 (0%)
Visit 03 (Day 15)	0 (0%)	0 (0%)	0 (0%)	12 (20.00%)	48 (80.00%)	Visit 03 (Day 15)	0 (0%)	0 (0%)	10 (16.67%)	50 (83.33%)	0 (0%)
Visit 04 (Day 28)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	60 (100%)	Visit 04 (Day 28)	0 (0%)	0 (0%)	1 (1.67%)	48 (80.00%)	11 (18.33%)
Question 10		**After using the mouthwash, there is visible improvement in the appearance of teeth.**									
Response	**Strongly disagree**	**Disagree**	**Neither nor**	**Agree**	**Strongly agree**	**Response**	**Strongly disagree**	**Disagree**	**Neither nor**	**Agree**	**Strongly agree**
Visit 02 (Day 7)	0 (0%)	0 (0%)	16 (26.67%)	43 (71.67%)	1 (1.67%)	Visit 02 (Day 7)	0 (0%)	0 (0%)	51 (85.00%)	9 (15.00%)	0 (0%)

Visit 03 (Day 15)	0 (0%)	0 (0%)	0 (0%)	19 (31.67%)	41 (68.33%)	Visit 03 (Day 15)	0 (0%)	0 (0%)	16 (26.67%)	43 (71.67%)	1 (1.67%)
Visit 04 (Day 28)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	60 (100%)	Visit 04 (Day 28)	0 (0%)	0 (0%)	1 (1.67%)	49 (81.67%)	10 (16.67%)
Question 11		**After using the mouthwash, did you observe burning or stinging sensation.**									
Response	**Strongly disagree**	**Disagree**	**Neither nor**	**Agree**	**Strongly agree**	**Response**	**Strongly disagree**	**Disagree**	**Neither nor**	**Agree**	**Strongly agree**
Visit 02 (Day 7)	34 (56.67%)	26 (43.33%)	0 (0%)	0 (0%)	0 (0%)	Visit 02 (Day 7)	0 (0%)	46 (76.67%)	14 (23.33%)	0 (0%)	0 (0%)
Visit 03 (Day 15)	56 (93.33%)	4 (6.67%)	0 (0%)	0 (0%)	0 (0%)	Visit 03 (Day 15)	13 (21.67%)	47 (78.33%)	0 (0%)	0 (0%)	0 (0%)
Visit 04 (Day 28)	60 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	Visit 04 (Day 28)	34 (56.67%)	26 (43.33%)	0 (0%)	0 (0%)	0 (0%)
Question 12		**After using the mouthwash, was there any metallic taste?**									
Response	**Yes**	**No**				**Response**	**Yes**	**No**			
Visit 02 (Day 7)	0 (0%)	60 (100%)				Visit 02 (Day 7)	0 (0%)	60 (100%)			
Visit 03 (Day 15)	0 (0%)	60 (100%)				Visit 03 (Day 15)	0 (0%)	60 (100%)			
Visit 04 (Day 28)	0 (0%)	60 (100%)				Visit 04 (Day 28)	0 (0%)	60 (100%)			

Treatment Specification: Test = Triple Combination Chlohexidine mouthwash; Comparator = Plain chlorhexidine mouthwash.
Abbreviation(s): N = number of participants in specified group; n = number of participants in specified category.
Note 1: Percentages are based on the number of participants in analysis Population in the specified product.
*Note 2: Percentage (%) = (number of participants in specified category /number of participants in respective treatment group) *100*
Note 3: Visit 01: Screening and Enrollment Visit (Day 01) and Baseline evaluations; Visit 02: Evaluation Visit (Day 07 ± 02 days); Visit 03: Evaluation Visit (Day 15 ± 02 days); Visit 04: Evaluation Visit (Day 28 ± 02 days) and End of Study.

3.2.9 Assessment of Participants' Perception questionnaires

Participants' perception of the study products was evaluated in terms of taste, freshness, cooling sensation, mouthfeel, and overall acceptability.

In the test group, all participants (100%) reported a favorable sensory experience. The taste was considered appealing, freshness was perceived as long-lasting, and a noticeable cooling sensation after use was reported by all participants. Regarding mouthfeel, 85% of participants perceived the test product to be better than their current mouthwash, while 15% considered it comparable. Overall, all participants (100%) reported liking the test product (Table 15, Figure 10).

In the comparator group, 98.33% of participants reported the taste as appealing, while 1.67% were neutral. Freshness was perceived as long-lasting by 96.67% of participants, with 3.33% reporting neutral responses. Similarly, 96.67% reported a noticeable cooling sensation, while 3.33% were neutral. In terms of mouthfeel, 85% of participants perceived the comparator to be comparable to their current mouthwash, while 15% considered it better. Overall, 98.33% of participants reported liking the comparator product, with 1.67% indicating a neutral response (Table 15, Figure 12).

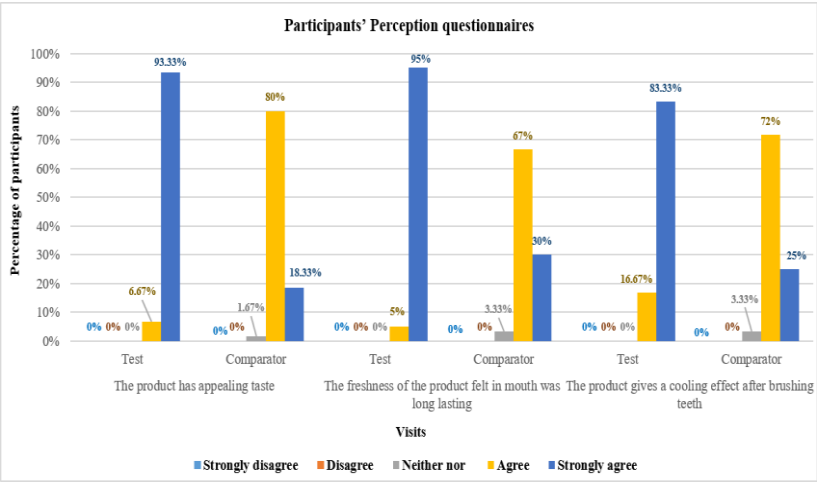

Figure 10a: Appealing Taste, Freshness, Cooling Effect

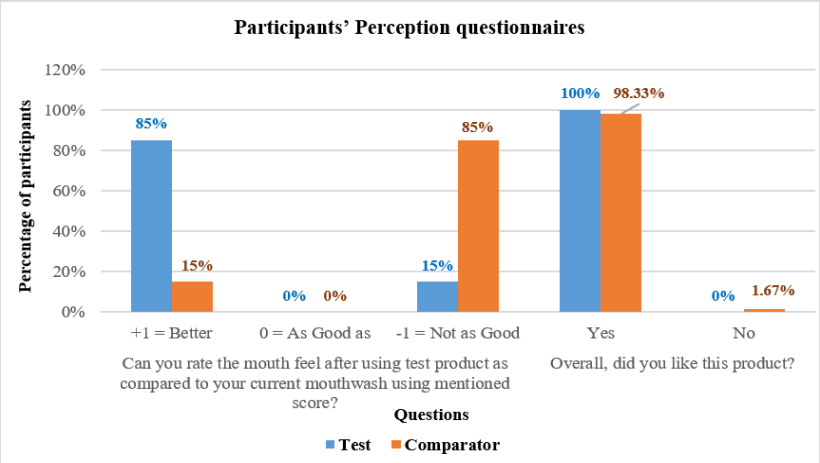

Figure 10b: Mouth Feel and Overall Likeability

Figure 10: Assessment of Participants' Perception questionnaires

Table 15: Participants' Perception questionnaires

Response	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
Question 1	**The product has an appealing taste.**				
Test (N = 60) n (%)	0 (0%)	0 (0%)	0 (0%)	4 (6.67%)	56 (93.33%)
Comparator (N = 60) n (%)	0 (0%)	0 (0%)	1 (1.67%)	48 (80.00%)	11 (18.33%)
Question 2	**The freshness of the product felt in mouth was long lasting.**				
Test (N = 60) n (%)	0 (0%)	0 (0%)	0 (0%)	3 (5.00%)	57 (95.00%)
Comparator (N = 60) n (%)	0 (0%)	0 (0%)	2 (3.33%)	40 (66.67%)	18 (30.00%)
Question 3	**The product gives a cooling effect after brushing teeth.**				
Test (N = 60) n (%)	0 (0%)	0 (0%)	0 (0%)	10 (16.67%)	50 (83.33%)
Comparator (N = 60) n (%)	0 (0%)	0 (0%)	2 (3.33%)	43 (71.67%)	15 (25.00%)
Response	**+1 = Better**	**0 = As Good as**	**-1 = Not as Good**		
Question 4	**Can you rate the mouth feel after using test product as compared to your current mouthwash using mentioned score?**				
Test (N = 60) n (%)	51 (85.00%)	0 (0%)	9 (15.00%)		
Comparator (N = 60) n (%)	9 (15.00%)	0 (0%)	51 (85.00%)		
Response	**Yes**	**No**			
Question 5	**Overall, did you like this product?**				
Test (N = 60) n (%)	60 (100%)	59 (98.33%)			
Comparator (N = 60) n (%)	0 (0%)	1 (1.67%)			

Treatment Specification: Test = Triple Combination Chlohexidine mouthwash; Comparator = Plain chlorhexidine mouthwash.
Abbreviation(s):N = number of participants in specified group; n = number of participants in specified category.
Note 1: Percentages are based on the number of participants in analysis Population in the specified product
*Note 2: Percentage (%) = (number of participants in specified category /number of participants in respective treatment group)*100*
Note 3: Visit 04: Evaluation Visit (Day 28 ± 02 days) and End of Study.

3.3 Safety Assessments

No instances of local intolerance were reported in any participant during the study, indicating a favorable safety profile of the test product. Furthermore, no adverse events (AEs) or serious adverse events (SAEs) were observed during the 28-day treatment period or up to the end of the study.

4. DISCUSSION

Periodontal diseases constitute a significant global health burden and are characterized by chronic inflammation of the tooth-supporting structures, driven by complex interactions between polymicrobial biofilms

and dysregulated host immune responses [Kinane *et al*., 2017; Sanz *et al*., 2020]. Contemporary understanding of periodontal pathogenesis emphasizes the concept of microbial dysbiosis, wherein a shift from a symbiotic microbial community to a pathogenic consortium—dominated by keystone pathogens such as *Porphyromonas gingivalis*—initiates and perpetuates disease progression. These pathogens manipulate host defense mechanisms, resulting in persistent inflammation through the upregulation of pro-inflammatory mediators, including interleukins (IL-1β, IL-6), tumor necrosis factor-α (TNF-α), and matrix metalloproteinases (MMPs), ultimately leading to connective tissue degradation and alveolar bone resorption [Marsh, 2006; Kinane *et al*., 2017].

Given this multifactorial etiology, therapeutic strategies that simultaneously target microbial biofilms and host inflammatory pathways are essential for effective periodontal management. In the present study, the triple combination mouthwash demonstrated significantly greater improvements across all clinical parameters compared to plain chlorhexidine, supporting the concept that multi-mechanistic formulations provide enhanced therapeutic benefits.

The superior reduction in gingival inflammation observed in the test group may be attributed to its combined antimicrobial and host-modulating effects. Chlorhexidine reduces bacterial load by disrupting cell membranes and inducing cytoplasmic leakage, thereby minimizing the antigenic stimulus responsible for inflammatory responses [Jones, 1997]. The addition of zinc further augments this effect by inhibiting bacterial proteases and virulence factors, while also modulating inflammatory signaling pathways and stabilizing cellular membranes. These combined actions contribute to reduced tissue destruction and enhanced gingival healing, explaining the greater reduction in Gingival Index scores [Lynch, 2011].

Biofilm disruption plays a central role in periodontal therapy; however, mature biofilms exhibit increased resistance due to the presence of an extracellular polymeric substance (EPS) matrix, which limits antimicrobial penetration and promotes microbial persistence [Flemming *et al*., 2010]. While chlorhexidine is effective against planktonic bacteria and early biofilm formation, its efficacy may be reduced in mature biofilms. The addition of zinc enhances antibiofilm activity by interfering with bacterial adhesion, co-aggregation, and enzymatic metabolism, thereby disrupting biofilm maturation at multiple stages [Marsh, 2006; Young *et al*., 2003]. This synergistic interaction likely accounts for the significantly greater plaque reduction observed with the triple combination formulation.

Consistent with these findings, the test group demonstrated a greater reduction in gingival bleeding. Bleeding on probing is a sensitive marker of underlying inflammation and vascular changes within gingival tissues. Zinc chloride contributes to improved outcomes through its astringent properties, promoting protein precipitation and reducing capillary permeability, thereby decreasing bleeding. In addition, its antimicrobial action further reduces inflammatory stimuli, resulting in improved gingival health [Lynch, 2011].

The substantial improvement in halitosis observed with the triple combination mouthwash highlights an important therapeutic advantage. Oral malodor is primarily caused by volatile sulfur compounds (VSCs), such as hydrogen sulfide and methyl mercaptan, produced by anaerobic bacteria. While chlorhexidine reduces the bacterial load, zinc exerts a direct chemical effect by binding to sulfur-containing compounds and converting them into non-volatile, insoluble forms. This dual mechanism—comprising microbial suppression and chemical neutralization—provides superior control of halitosis and explains the near-complete resolution observed in the test group [Young *et al*., 2003].

Although the observed reduction in periodontal pocket depth was modest, it remains clinically relevant given the non-invasive nature of the intervention. This improvement likely reflects a reduction in inflammatory edema and microbial burden within the gingival sulcus, contributing to stabilization of periodontal tissues and prevention of disease progression [Sanz *et al*., 2020].

A key strength of the triple combination mouthwash lies in its pharmacodynamic synergy, wherein each component targets complementary aspects of disease pathogenesis. Chlorhexidine gluconate provides potent and sustained antimicrobial activity through membrane disruption, high substantivity, and inhibition of pellicle formation and bacterial colonization [Jones, 1997]. Zinc chloride exerts multiple effects, including inhibition of bacterial metabolism and virulence, disruption of biofilm maturation, neutralization of volatile sulfur compounds, and reduction of gingival inflammation through its astringent properties [Young *et al*., 2003; Lynch, 2011]. Sodium fluoride contributes by promoting enamel remineralization through fluorapatite formation, reducing enamel solubility, and inhibiting bacterial metabolic activity via enzyme inhibition [Featherstone, 2000; Buzalaf *et al*., 2011].

The integration of these agents enables a comprehensive, multi-level therapeutic approach that targets biofilm structure, microbial metabolism, pathogenic virulence, and host inflammatory responses, while simultaneously enhancing enamel resistance and controlling oral malodor. This coordinated mechanism of action provides a clear explanation for the superior clinical outcomes observed with the triple combination

mouthwash compared to chlorhexidine monotherapy [Flemming *et al*., 2010; Marsh, 2006].

Patient-reported outcomes further corroborated these findings, with participants in the test group experiencing faster and more pronounced improvements in gingival bleeding, oral malodor, and overall comfort. Importantly, the formulation demonstrated excellent tolerability, with minimal reports of adverse sensory effects such as burning or taste alteration, which are commonly associated with chlorhexidine use [Alyami *et al*., 2020].

Finally, the absence of treatment-emergent adverse events (TEAEs) and serious adverse events (SAEs) throughout the study underscores the favorable safety profile of the formulation. Taken together, these findings suggest that the triple combination mouthwash offers a superior benefit–risk profile and represents an effective adjunctive strategy for comprehensive periodontal care.

5. CONCLUSION

The triple combination mouthwash demonstrated significantly greater efficacy than plain chlorhexidine in improving key clinical outcomes, including gingival inflammation, plaque accumulation, gingival bleeding, and oral malodor. The superior clinical performance observed can be attributed to the synergistic interaction of chlorhexidine, sodium fluoride, and zinc chloride, which collectively target multiple pathogenic mechanisms underlying periodontal disease. These include disruption of microbial biofilms, modulation of host inflammatory responses, inhibition of bacterial metabolic activity, and enhancement of enamel resistance. Importantly, the formulation exhibited excellent safety and tolerability, with no reported adverse events, supporting its suitability for routine and potentially long-term use as an adjunct to mechanical plaque control measures. Overall, the findings reinforce the concept that multi-targeted therapeutic strategies provide a more comprehensive and effective approach than monotherapy in the management of plaque-induced gingival diseases.

Limitations: The authors acknowledge few limitations of the study, including short duration study and absence of microbiological analysis warranting larger, long-term trials for validation.

Data Availability statement

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request, subject to applicable approvals and permissions.

Ethics statement

This study was conducted in accordance with applicable ethical guidelines and regulatory requirements. Ethical approval was obtained from the OM Institutional Ethics Committee (CDSCO-registered) prior to initiation of the study. Written informed consent was obtained from all participants before enrollment. The study was prospectively registered with the Clinical Trials Registry of India (CTRI) under registration number CTRI/2025/08/111509.

Conflict of Interest

This study was funded by Dr. Reddy's Laboratories Ltd. Navita Budhiraja, Seema Bhagat, Arti Sanghavi and Dr Syed Mujtaba Hussain Naqvi are employees of the sponsoring organization. All other authors declare no competing interests. Each author has reviewed and approved the content as well as the conclusions presented in this manuscript.

Acknowledgments

The authors thank the study participants for their valuable contribution to this research. We also acknowledge the support and contributions of the Cliantha Research team in the successful conduct of this study.

Funding: This study was funded by Dr. Reddy's Laboratories Ltd.

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