

The Effect of Four Mouthrinses on Oral Malodor

CE 2

Abstract: The purpose of the study was to compare the efficacy of four mouthrinses in clinical outcomes of changes in oral malodor measurements in a 4-week, randomized, double-blind, longitudinal clinical trial in adults. The four rinses were coded as Products 1, 2, 3, and 4 so that neither the examiners nor subjects had the knowledge of treatment. Of the four mouthrinses, two were commercially available mouthrinses with essential oils (EO) or chlorine dioxide plus zinc (CD/Zn) as active ingredients (Products 1 and 4), one mouthrinse was a formulation containing cetylpyridinium chloride (Product 2), and one was a placebo (Product 3). A total of 99 subjects who met the study criteria were assigned randomly to one of the four groups. At three separate visits (0, 2, and 4 weeks), subjects received an examination of the oral soft tissues and were assessed for baseline oral malodor by two organoleptic judges and a laboratory instrument that measures oral malodor. Subjects were instructed to use the assigned rinse, and the measurements were performed again after 2 and 4 hours. Throughout the 4-week study period, each subject was asked to use the assigned rinse twice daily per the manufacturer's recommended directions. The results showed that the four mouthrinses reduced oral malodor within 4 hours after a single usage, with Product 2 being the most effective and the placebo being the least effective. Daily use of EO, CD/Zn, and placebo rinses for up to 4 weeks did not reduce oral malodor from week 0 baseline values, and the effects on oral malodor were comparable among these three mouthrinses. Product 2 was the only mouthrinse that reduced oral malodor from baseline values after 2 and 4 weeks of daily use.

Loretta C. Borden, MS

Eros S. Chaves, DDS

James P. Bowman

Barbara M. Fath

Consumer Products Testing Division
Hill Top Research, Inc.
Cincinnati, Ohio

Garry L. Hollar

Director of Regulatory Affairs
Discus Dental, Inc.
Culver City, California

Learning Objectives:

After reading this article, the reader should be able to:

- recognize the impact of oral malodor on an individual's oral hygiene and social life.
- discuss the causes of oral malodor.
- recognize the difference between four mouthrinses and their effect on oral malodor.
- identify the need for mouthrinses with both short-term and long-term efficacy in reducing oral malodor.

Oral malodor, or bad breath, is a generic descriptive term for foul smells emanating from the mouth. It includes ozostomia, stomatodysodia, halitosis, and fetor oris or fetor ex ore, which denotes different sources of oral malodor.¹ It has been estimated that 20% to 60% of the population suffers from chronic oral malodor, and in approximately half of these individuals, the problem becomes serious enough to create personal discomfort and social embarrassment.²⁻⁴ Oral malodor has also been reported in children 2 to 7 years old⁵ and 5 to 14 years old.⁶ Because of the potential impact of oral malodor on personal life, sufferers often make desperate attempts to mask their oral malodor with mints and chewing gum, compulsive brushing, and repeated use of mouthrinses.

In most cases, the problem of oral malodor has been shown to originate in the oral cavity, where conditions that favor the retention of anaerobic, mainly gram-negative bacteria, lead to the development of bad breath. In addition to periodontal pockets, the most important retention site is the dorsum of the tongue with its numerous papillae.^{7,8} Volatile sulfur compounds (VSCs), primarily hydrogen sulfide and methyl mercaptan, appear to be responsible for much of the malodor. A number of systemic diseases, such as diabetes mellitus, uremia, and hepatic diseases, may also induce

Table 1—Organoleptic Evaluation at Week 0

	Mouthrinse	N	Mean	(SD)	Change	(SEM) [*]	% Reduction	P Value [†]
Product 1/ EO	Baseline	25	4.14	(0.70)	—	—	—	—
	15 mins	25	0.96	(0.79)	-3.18	(0.18)	76.81	.0001 [‡]
	2 hrs	25	2.90	(0.98)	-1.24	(0.18)	29.95	.0001 [‡]
	4 hrs	25	3.72	(0.89)	-0.42	(0.14)	10.14	.0117 [‡]
Product 2/ CPC	Baseline	25	4.22	(0.56)	—	—	—	—
	15 mins	25	0.18	(0.32)	-4.04	(0.12)	95.73	.0001 [‡]
	2 hrs	25	2.16	(1.06)	-2.06	(0.19)	48.82	.0001 [‡]
	4 hrs	25	3.28	(0.82)	-0.94	(0.14)	22.27	.0001 [‡]
Product 3/ Placebo	Baseline	23	3.93	(0.68)	—	—	—	—
	15 mins	23	0.24	(0.33)	-3.70	(0.16)	93.92	.0001 [‡]
	2 hrs	23	2.41	(0.65)	-1.52	(0.20)	38.67	.0001 [‡]
	4 hrs	23	3.72	(0.54)	-0.22	(0.12)	5.52	.1169
Product 4/ CD/Zn	Baseline	22	4.02	(0.52)	—	—	—	—
	15 mins	22	0.25	(0.37)	-3.77	(0.11)	93.79	.0001 [‡]
	2 hrs	22	2.52	(0.87)	-1.50	(0.14)	37.29	.0001 [‡]
	4 hrs	22	3.50	(0.82)	-0.52	(0.12)	12.99	.0007 [‡]

^{*}Change from the baseline value of each mouthrinse
[†]Wilcoxon signed rank test
[‡]Significant reduction in oral malodor

metabolic products that are detectable as oral odors.^{1,7}

The recommended initial treatment strategy is to identify the exact cause of the oral malodor, which can be difficult.^{4,9} Oral hygiene, particularly the daily use of a tongue cleaner, can be effective in reducing the risk of oral malodor. In addition to etiologic therapy, oral care products, including mouthrinses, toothpastes, and chewing gums, may be used to mask the malodor.^{9,10} It has been suggested that products containing metal ions, especially zinc, are effective in inhibiting odor formation because of their neutralizing effect on sulfur compounds.⁴ Because of the implication of bacteria in producing malodor, there has been an increasing interest in using antibacterial mouthrinses to control oral malodor. Mouthrinses containing essential oils (EOs), chloride dioxide plus zinc (CD/Zn), or an oil-water-cetylpyridinium chloride (CPC) combination have been shown to reduce the organoleptic scores of individuals with moderate levels of oral malodor. These results were found in the absence of tongue cleaning, although in several studies the findings are controversial and sometimes contradictory.^{2,9}

The purpose of this study was to compare the effect of BreathRx™ Mouthrinse^a to two

commercially available rinses on oral malodor in adults in a 4-week, randomized, double-blind, longitudinal clinical trial. A placebo rinse was also included in the study to serve as the negative control.

Materials and Methods

The study was conducted according to applicable Good Clinical Practices and Standard Operating Procedures of Hill Top Research, Inc. Before conducting the study, protocols and pertinent documents were submitted and approved by an Institutional Review Board (IRB) in accordance with Title 21 of the Code of Federal Regulations, Parts 50 and 56. An informed consent letter was provided to and signed by each of the study participants before the initiation of the project. There was one amendment to the consent form, which was submitted and approved by the IRB before the recruitment of subjects. The amendment informed the subjects that they would be required to stay at the study site for approximately 6 hours instead of 5 hours.

The four test mouthrinses were provided by the study sponsor in coded, identical packages as Product 1, 2, 3, and 4 so that neither the examiners nor the subjects had the

^aDiscus Dental, Inc., Culver City, CA 90232; (800) 422-9448

Table 2—Organoleptic Evaluation at Week 2

	Mouthrinse	N	Mean	(SD)	Change	(SEM) [*]	% Reduction	P Value [†]
Product 1/ EO	Baseline	23	4.11	(0.67)	—	—	—	—
	15 mins	23	0.59	(0.63)	-3.52	(0.19)	85.71	.0001 [‡]
	2 hrs	23	2.43	(1.13)	-1.67	(0.19)	40.74	.0001 [‡]
	4 hrs	23	3.50	(0.89)	-0.61	(0.17)	14.81	.0025 [‡]
Product 2/ CPC	Baseline	25	3.70	(0.52)	—	—	—	—
	15 mins	25	0.08	(0.24)	-3.62	(0.13)	97.84	.0001 [‡]
	2 hrs	25	2.08	(0.92)	-1.62	(0.19)	43.78	.0001 [‡]
	4 hrs	24	3.23	(0.77)	-0.46	(0.19)	12.39	.0340 [‡]
Product 3/ Placebo	Baseline	22	4.20	(0.63)	—	—	—	—
	15 mins	22	0.16	(0.24)	-4.05	(0.13)	96.22	.0001 [‡]
	2 hrs	22	2.77	(0.95)	-1.43	(0.20)	34.05	.0001 [‡]
	4 hrs	22	3.66	(0.66)	-0.55	(0.16)	12.97	.0019 [‡]
Product 4/ CD/Zn	Baseline	19	4.03	(0.74)	—	—	—	—
	15 mins	19	0.13	(0.28)	-3.89	(0.16)	96.73	.0001 [‡]
	2 hrs	19	2.32	(1.20)	-1.71	(0.25)	42.48	.0001 [‡]
	4 hrs	19	3.34	(0.93)	-0.68	(0.17)	16.99	.0013 [‡]

^{*}Change from the baseline value of each mouthrinse

[†]Wilcoxon signed rank test

[‡]Significant reduction in oral malodor

knowledge of treatment. They were:

1. Listerine[®] Antiseptic Rinse^b, a commercially available, EO-based rinse (Product 1).
2. BreathRx[™] Mouthrinse, a formulation containing CPC (Batch # BTM-008A) (Product 2).
3. A placebo rinse (Batch # BTM-007P) (Product 3).
4. Oxygene[®] Mouthwash with Zinc^c, a commercially available, CD/Zn-based rinse (Product 4).

The repackaging of the EO-based rinse was performed using good manufacturing practice procedures. The CD/Zn rinse was left in the original manufacturer's sealed bottle with the label covered over.

To obtain a study population that represented typical users of the test mouthrinses, study subjects were recruited from local communities. Potential subjects were interviewed by phone and screened for their eligibility to participate in the study according to the following inclusion criteria:

1. In good general health based on medical history and oral soft tissue examination.
2. A man or woman between 18 and 65 years of age.

3. Willing to sign the informed consent form and comply with the protocol procedures.
4. Two-judge average intensity score of ≥ 4 on a scale of 5 and no single score of < 3 .
5. Minimum of 16 natural teeth, including at least 4 molars.
6. Availability of the subject to complete the 4-week study.

Any subject with one or more of the following conditions were excluded:

1. Gross oral pathoses that the investigators thought may compromise the protocol.
2. Orthodontic devices.
3. Partial or complete dentures.
4. Any systemic disease that the investigators thought may interfere with the study.
5. History of irritation or sensitivity to oral products.
6. Pregnant or lactating women as determined by medical history.
7. Periodontal disease (pocket depth > 4 mm and/or bleeding on probing on > 6 sites but nonadjacent) or gross neglect of oral hygiene.
8. Smokers.
9. Prophylactic antibiotic coverage for routine dental therapy.
10. Use of systemic antibiotics or prescription mouthwash 21 days before the study.

^bPfizer, Inc., Morris Plains, NJ 07950; (973) 385-6120

^cOxyfresh Worldwide, Inc., Spokane, WA 99216; (800) 540-7656

Table 3—Organoleptic Evaluation at Week 4

	Mouthrinse	N	Mean	(SD)	Change	(SEM)*	% Change	P Value†
Product 1/ EO	Baseline	21	4.12	(0.59)	—	—	—	—
	15 mins	21	0.48	(0.62)	-3.64	(0.13)	88.44	.0001‡
	2 hrs	21	2.64	(1.09)	-1.48	(0.20)	35.84	.0001‡
	4 hrs	21	3.67	(0.71)	-0.45	(0.14)	10.98	.0069‡
Product 2/ CPC	Baseline	23	3.80	(0.67)	—	—	—	—
	15 mins	23	0.11	(0.26)	-3.70	(0.16)	97.14	.0001‡
	2 hrs	23	1.96	(0.74)	-1.85	(0.16)	48.57	.0001‡
	4 hrs	23	3.24	(0.80)	-0.57	(0.16)	14.86	.0015‡
Product 3/ Placebo	Baseline	22	4.14	(0.64)	—	—	—	—
	15 mins	22	0.25	(0.34)	-3.89	(0.15)	93.96	.0001‡
	2 hrs	22	2.36	(0.79)	-1.77	(0.17)	42.86	.0001‡
	4 hrs	22	3.98	(0.65)	-0.16	(0.16)	3.85	.3896
Product 4/ CD/Zn	Baseline	18	4.08	(0.65)	—	—	—	—
	15 mins	18	0.47	(0.61)	-3.61	(0.18)	88.44	.0001‡
	2 hrs	18	2.50	(1.04)	-1.58	(0.18)	38.78	.0001‡
	4 hrs	18	3.58	(0.90)	-0.50	(0.19)	12.24	.0114‡

*Change from the baseline value of each mouthrinse

†Wilcoxon signed rank test

‡Significant reduction in oral malodor

11. Current participation in other dental or investigational trials.
12. Patients on concomitant drug therapy were not included in the study based on the discretion of the investigator/examiner.
13. History of alcohol abuse.
14. Evidence of a recent history of bronchitis, tonsillitis, or sinusitis.

In addition, subjects were excluded from the study if they received emergency dental treatment or if loss of teeth placed them below the minimum teeth requirements. Any subject treated with antibiotics or antibacterial agents during the course of the study were also dropped. Subjects were instructed to refrain from routine dental treatments, except for emergencies, for the duration of the study.

Qualified subjects were randomly assigned to one of the four groups, each with a minimum of 20 subjects. The subjects were asked to use the assigned mouthrinse twice daily following the supplied instructions for use. They were provided with standard fluoride toothpaste and standard soft toothbrushes, and were required to not use any other dental devices or products during the study period. It was recognized that subject compliance was essential and imperative to the reliability and accuracy of the clinical data. To maximize the compli-

ance, the investigators reviewed and emphasized the instructions with each subject. Compliance was also monitored by reviewing daily logs of each subject's mouthrinse use along with quantification of the remaining mouthrinse returned at each visit.

A medical history was collected from each accepted subject. At each of the three visits (0, 2, and 4 weeks), subjects received an oral soft tissue examination and were assessed for baseline oral malodor by two organoleptic judges and a laboratory instrument that measures oral malodor (Halimeter[®],^d). The oral soft tissue examination included observations of the lips, buccal mucosa, floor of the mouth, tongue, hard and soft palate, and gingiva. All findings were recorded as normal or abnormal. All abnormal findings, such as signs of sloughing, erythema, ulceration, or edema, were recorded and described on the evaluation form. Each parameter was scored as normal, mild, moderate, or marked. The subject was then instructed to use the assigned rinse, and the organoleptic measurements were performed after 15 minutes, 2 hours, and 4 hours, respectively. Halimeter[®] measurements were performed after 2 and 4 hours. The organoleptic measurements were performed independently by two

^dInterscan Corporation, Chatsworth, CA 91313-2231; (800) 458-6153

Table 4—Change of Baseline* Organoleptic Values From Week 0 After Twice Daily Use of Four Mouthrinses for 2 and 4 Weeks

	Mouthrinse	N	Mean	(SD)	Change	(SEM)*	% Change	P Value†
Product 1/ EO	Week 0	25	4.14	(0.70)	—	—	—	—
	Week 2	23	4.11	(0.67)	0.02	(0.15)	0.53	>.5
	Week 4	21	4.12	(0.59)	0	(0.14)	0	>.5
Product 2/ CPC	Week 0	25	4.22	(0.56)	—	—	—	—
	Week 2	25	3.70	(0.52)	-0.52	(0.13)	-12.32	.0016§
	Week 4	25	3.80	(0.67)	-0.41	(0.17)	-9.79	.0355§
Product 3/ Placebo	Week 0	23	3.93	(0.68)	—	—	—	—
	Week 2	22	4.20	(0.63)	0.23	(0.17)	5.78	.154
	Week 4	22	4.14	(0.64)	0.16	(0.18)	4.04	.4455
Product 4/ CD/Zn	Week 0	22	4.02	(0.52)	—	—	—	—
	Week 2	19	4.03	(0.74)	0	(0.16)	0	>.5
	Week 4	18	4.08	(0.65)	0.06	(0.18)	1.38	>.5

*The prerinse baseline at each appointment (weeks 0, 2, and 4)

†Change from the week 0 baseline value of each mouthrinse

‡Wilcoxon signed rank test

§Significant reduction in oral malodor

experienced, calibrated judges. The subjects were instructed to close their mouths for 2 minutes and to not swallow during that period. The subjects were then asked to breathe out gently, at a distance of 10 cm from the nose of the organoleptic judge, and the organoleptic odors were assessed according to a 5-point scale¹¹:

- 0 = No odor present.
- 1 = Barely noticeable odor.
- 2 = Slight but clearly noticeable odor.
- 3 = Moderate odor.
- 4 = Strong offensive odor.
- 5 = Extremely foul odor.

The Halimeter® (Model RH-17K) was balanced with a zero reading and, to ensure the accuracy of each reading, the measurements followed the manufacturer's instructions. For the mouth reading, the short end of a flexible drinking straw was inserted approximately 1/2 inch into the subject's slightly parted lips, which were gently touching the straw. The subjects were instructed to hold their breath for 5 to 10 seconds until a peak in VSCs was reached. Readings for the VSCs were then recorded. For the throat and posterior tongue, the drinking straw was inserted approximately 3 inches into the subject's mouth near the throat. The subjects were instructed to hold their breath for 5 to 10 seconds, and the VSC reading was recorded. For the nasal passage/sinus, the straw was inserted 1/4 inch to 1/2 inch

into each nostril. Subjects were instructed to hold their breath 5 to 10 seconds, after which time the VSC value was recorded.

For data analyses, mean organoleptic and Halimeter® scores as well as the mean and percent changes from week 0 baseline to weeks 2 and 4 baselines were calculated. The within-treatment data were analyzed using the Wilcoxon signed rank test. For the between-treatment analyses, Kruskal-Wallis contingency table technique was used. When statistically significant differences were detected, multiple comparison tests were performed to determine differences among products.

Results

A total of 138 subjects were recruited and signed the consent form. After screening examinations, 99 subjects who met the study criteria were enrolled and completed the first visit (week 0). Three subjects were disqualified as result of a low organoleptic score of 2 and one subject withdrew consent after completing the first visit. Therefore, data collected from 95 subjects, including 29 men and 66 women who ranged in age from 19 to 65 years, were included in the analysis.

A total of 209 bottles of mouthrinses were distributed to the subjects, and four bottles (two for Product 1/EO and one each for Products 3/Placebo and 4/CD/Zn) were not

Table 5—Efficacy of Four Mouthrinses in Reducing Baseline Organoleptic Scores after a Single Rinse at Week 0

Rinse	Reduction of Organoleptic Scores from Baseline Values		
	15 Minutes	2 Hours	4 Hours
Product 2/CPC	-4.04	-2.06	-0.94
Product 4/CD/Zn	-3.77	-1.50	-0.52
Product 3/Placebo	-3.70	-1.52	-0.22
Product 1/EO	-3.18	-1.24	-0.42

Mean changes in organoleptic scores from baseline values. Values with brackets are not significantly different as determined using Kruskal-Wallis contingency table test and multiple comparison method.

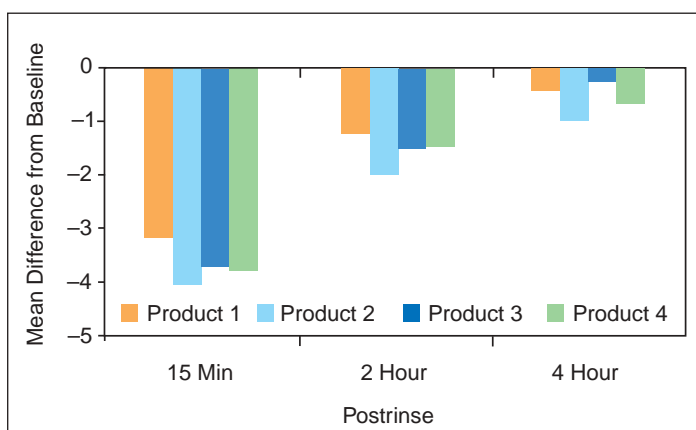


Figure 1—Reduction of organoleptic scores from baseline values after a single rinse of four mouthrinses at week 0.

returned. Two subjects inadvertently discarded three bottles. No specific reason was given for the other missing bottle. As indicated by subjects' diaries, all 95 subjects used the assigned mouthrinse according to instructions on the label and met the compliance criteria. The product usage was relatively even among subjects in the four product groups. Eleven subjects missed between one and five at-home rinses; however, it is the authors' opinion that these deviations did not affect the outcome of the study.

There were 13 adverse events, including lip blisters, localized gingival edema, and canker sores, reported by 13 subjects during the course of the study. One subject was hospitalized with cellulitis, which was determined to be nonrelevant to the mouthrinse used. The subject was treated for her condition and was discontinued from the study. After careful evaluation, it was determined that these

adverse events were unlikely to be related to the product usage.

Organoleptic Measurements

The average baseline organoleptic scores at the initiation of the study were 4.14 for Product 1/EO, 4.22 for Product 2/CPC, 3.93 for Product 3/placebo, and 4.02 for Product 4/CD/Zn. The values are not statistically different, indicating that the initial average level of oral malodor was balanced among the four groups.

The organoleptic scores from baseline, 15-minute, 2-hour, and 4-hour evaluations after a single rinse with four test mouthrinses at weeks 0, 2, and 4 are summarized in Tables 1 through 3, respectively. The within-treatment analyses using Wilcoxon signed rank test evaluated the changes from baseline at each visit. Mean changes and percent changes from baseline at each visit were also calculated. The data showed significant decreases ($P < .05$) in oral malodor for all of the rinses at all post-treatment evaluations except the placebo at the 4-hour evaluation in weeks 0 and 4 (Tables 1 and 3). The baseline organoleptic data from weeks 0, 2, and 4, which were collected before the use of the rinses, were further analyzed and the results showed that Product 2/CPC was the only mouthrinse that significantly reduced oral malodor ($P < .05$) after twice daily use for 2 and 4 weeks (Table 4). The other three mouthrinses did not have a significant effect on the baseline organoleptic data obtained from weeks 2 and 4 compared to week 0.

The results of comparison among the four test mouthrinses in reducing organoleptic scores after a single use at week 0 are presented in Table 5 and illustrated in Figure 1. Product 2/CPC was comparable to Product 4/CD/Zn in reducing the organoleptic score at the 15-minute and 2-hour evaluations; however, Product 2/CPC was significantly more effective than the placebo and Product 1/EO ($P < .05$). At the 4-hour evaluation, the reduction of organoleptic scores observed in the subjects using Product 2/CPC was significantly higher ($P < .05$) than the subjects using the other three rinses (Table 5).

Further analysis of the baseline organoleptic data from weeks 0, 2, and 4, which were collected before the use of the rinses, showed that Product 2/CPC was the only mouthrinse that reduced oral malodor after twice daily use

Table 6—Efficacy of Four Mouthrinses in Reducing Baseline Organoleptic Scores After Twice Daily Use for 2 and 4 Weeks

Rinse	Reduction from Week 0 Baseline Values	
	2 Week	4 Week
Product 2/CPC	-0.52	-0.41
Product 4/CD/Zn	0	0.06
Product 1/EO	0.02	0
Product 3/Placebo	0.23	0.16

Mean changes in baseline organoleptic scores from Week 0. Values with brackets are not significantly different as determined using Kruskal-Wallis Contingency Table Test and Multiple Comparison Method.

for Product 1/EO, 98.8 for Product 2/CPC, 88.1 for Product 3/placebo, and 73.3 for Product 4/CD/Zn. For throat readings, the initial average baseline readings were 98.2 for Product 1/EO, 136 for Product 2/CPC, 106 for Product 3/placebo, and 99.7 for Product 4/CD/Zn. No attempts were made to balance the initial Halimeter® baseline values, as the organoleptic score was the primary parameter for group balancing. While the Halimeter® values, particularly those from throat, appeared to vary among the groups, they were not statistically different.

Because of possible interference to the performance of the Halimeter® immediately after the use of mouthrinses, these measurements were performed at 2- and 4-hour evaluation after the rinse. The within-treatment analysis of the Halimeter® data from the front of the mouth found significant decreases in scores ($P < .05$) with all of the products at the 2- and 4-hour evaluations in week 0. In addition, Product 2/CPC showed significant decreases in Halimeter® readings ($P < .05$) at the 4-hour evaluation in weeks 2 and 4, while Product 1/EO showed significant decreases ($P < .05$) at the 4-hour evaluation in week 2 and the 2-hour evaluation in week 4. The within-treatment analysis of the Halimeter® data obtained from the throat indicated significant decreases with Product 1/EO at both evaluations in week 0 and at the 2-hour evaluation in week 4 ($P < .05$). Significant reduction ($P < .05$) was also observed in Product 2/CPC at both the 2- and 4-hour evaluations in weeks 0 and 2 and at the 4-hour evaluation in week 4. Product 4/CD/Zn rinse was found to significantly reduce ($P < .05$) the Halimeter® readings at the 2- and 4-hour evaluations in week 0.

Table 7 presents the changes of baseline Halimeter® readings of the mouth from week 0 after twice daily use of four mouthrinses for 2 and 4 weeks. Significant reductions ($P < .05$) from week 0 baseline were detected in the groups using Product 1/EO, Product 2/CPC, and Product 4/CD/Zn at weeks 2 and 4. Product 3/placebo also produced a significant reduction at week 4 ($P < .05$). Analysis of the data collected from the throat found significant reductions from week 0 baseline with Products 1/EO, 2/CPC, and 4/CD/Zn mouthrinses at both weeks 2 and 4 (Table 8). No significant differences were found for the placebo rinse.

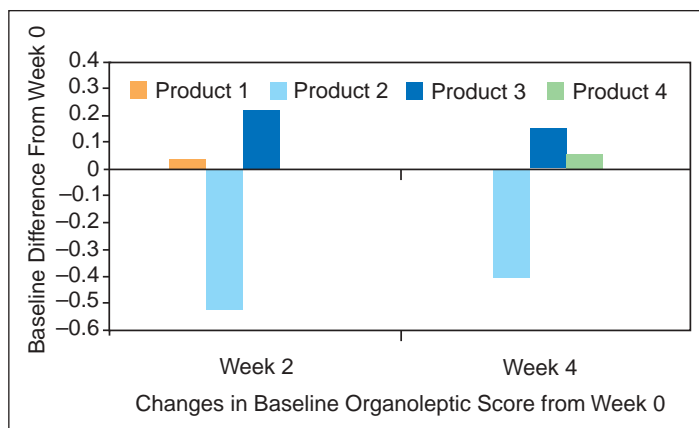


Figure 2—Changes in baseline organoleptic scores from baseline values after twice daily use of four mouthrinses at weeks 2 and 4.

for 2 and 4 weeks (Table 6 and Figure 2). The reduction of the average organoleptic score induced by twice daily use of Product 2/CPC for 2 weeks was significantly higher ($P < .05$) than the other three mouthrinses, and it was also significantly better ($P < .05$) than the placebo at the week 4 evaluation. Products 1/EO and 4/CD/Zn were comparable to Product 3/placebo after twice daily use for 2 and 4 weeks (Table 7).

Halimeter® Measurements

Tests for normality were conducted on the Halimeter® data, and the results indicated that the data were not normally distributed. Therefore, nonparametric methods were used for data analyses.

The average baseline Halimeter® mouth readings at the initiation of the study were 89

Table 7—Change of Baseline* Organoleptic Values From Week 0 After Twice Daily Use of Four Mouthrinses for 2 and 4 Weeks

	Mouthrinse	N	Mean	(SD)	Change	(SEM)*	% Reduction	P Value†
Product 1/ EO	Week 0	25	89.04	(74.09)	—	—	—	—
	Week 2	23	46.87	(54.58)	-43.22	(12.39)	48.54	.0002‡
	Week 4	21	23.43	(13.64)	-68.90	(16.06)	77.39	.0001‡
Product 2/ CPC	Week 0	25	98.80	(92.06)	—	—	—	—
	Week 2	25	31.96	(15.40)	-66.84	(18.97)	67.65	.0001‡
	Week 4	23	24.30	(9.66)	-77.87	(19.71)	78.82	.0001‡
Product 3/ Placebo	Week 0	23	88.09	(93.74)	—	—	—	—
	Week 2	22	52	(39.75)	-39.86	(20.15)	45.25	.0575
	Week 4	22	55.09	(62.31)	-36.77	(23.42)	41.75	.0317‡
Product 4/ CD/Zn	Week 0	22	73.32	(73.05)	—	—	—	—
	Week 2	19	31.47	(15.36)	-47.63	(17.48)	64.97	.0025‡
	Week 4	18	25.89	(19.24)	-53.28	(15.45)	72.67	.0001‡

*Change from the week 0 baseline value of each mouthrinse

†Wilcoxon signed rank test

‡Significant reduction in oral malodor

There were no significant differences in Halimeter® readings obtained from the mouth among the four rinses, regardless of the measurements taken at the 2- and 4-hour evaluations after a single rinse at each visit or the baseline values after 2 and 4 weeks of twice daily use. Significant differences were detected from the Halimeter® data that was obtained from the throat at the 2-hour evaluation. Products 1/EO, 2/CPC, and 4/CD/Zn resulted in significantly greater reductions from baseline Halimeter® readings than the placebo rinse ($P < .05$) (Table 9). Numerically, Product 2/CPC induced the greatest reductions among the four rinses, although the differences were not significant with Products 1/EO and 4/CD/Zn at the 2-hour evaluation and with the other three rinses at the 4-hour evaluation (Table 9 and Figure 3).

Significant differences among products were also detected in the reduction of Halimeter® measurements obtained from the throat at the week 2 evaluation. Product 4/CD/Zn showed significantly larger baseline differences from week 0 baseline than Product 3/placebo (Table 10). However, the greatest numerical reductions were again observed with Product 2/CPC at both the 2- and 4-week evaluations (Table 10 and Figure 4).

Discussion

Oral malodor is a multi-etiological condition. While certain systemic diseases can cause

oral malodor, the majority of sufferers may have a local cause in the oral cavity. An increasing volume of research has shown that certain oral flora, particularly gram-negative anaerobes from the tongue or periodontal areas, are the main microorganisms capable of releasing VSCs from their proteolytic activity of debris and other material. VSCs are a family of gases that are considered primarily responsible for oral malodor.^{7,8}

Mouthrinses have increasingly become an important option in the treatment of oral malodor. The use of mouthrinses was initially considered for cosmetic purposes, and their effects on oral hygiene were believed to be transitory.^{12,13} However, in 1986, the Council on Dental Therapeutics of the American Dental Association established guidelines for the acceptance of chemotherapeutic products for the control of dental plaque and gingivitis.¹⁴ Antimicrobial mouthrinses are now considered an integrated part of daily dental hygiene practice.^{13,15} EOs and CD/Zn are the active ingredients commonly used in mouthrinses for the treatment of oral malodor.^{2,9,16,17} BreathRx™ mouthrinse (Product 2/CPC in the present study) is a formulation containing CPC, EOs, and CD/Zn. The two commercial mouthrinses, which were included in the study for the purpose of comparison, contain either EOs or chloride dioxide and CD/Zn as active ingredients.

Table 8—Change of Baseline Halimeter® Throat Readings From Week 0 After Twice Daily Use of Four Mouthrinses for 2 and 4 Weeks

	Mouthrinse	N	Mean	(SD)	Change	(SEM)*	% Reduction	P Value†
Product 1/ EO	Week 0	25	98.16	(60.38)	—	—	—	—
	Week 2	23	71.57	(60.99)	-23	(11.77)	23.43	.0065‡
	Week 4	21	43.95	(28.50)	-47.71	(10.54)	48.61	.0001‡
Product 2/ CPC	Week 0	25	135.96	(132.68)	—	—	—	—
	Week 2	25	52.80	(38.56)	-83.16	(27.75)	61.17	.0004‡
	Week 4	23	40.13	(27.22)	-86	(26.02)	63.25	.0001‡
Product 3/ Placebo	Week 0	23	106.04	(80.38)	—	—	—	—
	Week 2	22	106.77	(99.90)	-3.18	(21.29)	3	>.5
	Week 4	22	84.45	(81.65)	-25.5	(19.02)	24.05	.1527
Product 4/ CD/Zn	Week 0	22	99.73	(87.98)	—	—	—	—
	Week 2	19	35.58	(17.92)	-70.16	(18.82)	70.35	.0001‡
	Week 4	18	31.28	(28.41)	-72.28	(16.65)	72.48	.0001‡

*Change from the week 0 baseline value of each mouthrinse
 †Wilcoxon signed rank test
 ‡Significant reduction in oral malodor

Table 9—Comparison of Efficacy of Four Mouthrinses in Reducing Baseline Halimeter® Throat Scores After a Single Rinse at Week 0

Rinse	Reduction of Halimeter® Scores from Baseline Values	
	2 Hour	4 Hour
Product 2/CPC	-83	-73.04
Product 4/CD/Zn	-47.64	-52.95
Product 1/EO	-44.04	-39.28
Product 3/Placebo	-13.30	-20.78

Mean changes in Halimeter® throat score from baseline values. Values with brackets are not significantly different as determined using Kruskal-Wallis contingency table technique and multiple comparison method.

Although oral malodor is a common problem, there is still a lack of reliable means for its objective measurement. The Halimeter® is a specialized device available to measure VSCs in the mouth; however, its accuracy and reliability have been questioned. In addition, the components of oral malodor may not be limited to VSCs, and thus, the measurements may not be completely reflective of clinical situations. Therefore, a number of investigators have suggested that in practice the objective

assessment of malodor is still best judged by the human sense of smell (ie, the organoleptic method).^{4,7} In the present study, both the organoleptic method and Halimeter® measurements were used for the evaluation of oral malodor. The organoleptic evaluation was performed by two experienced, calibrated examiners and served as the primary parameter for the evaluation of oral malodor. With the secondary data obtained from the Halimeter® measurement, the methods for evaluating oral malodor used in this particular study were appropriate and adequate.

The data obtained at each of the three visits indicated that a single use of the mouthrinses was effective in significantly reducing oral malodor for up to 4 hours. This finding is in agreement with that reported by a previous study¹⁵ in which a single use of a CD/Zn mouthrinse significantly reduced mouth odor intensity for at least 4 hours. While possible therapeutic efficacy may not be completely ruled out, the reduction of oral malodor up to 4 hours after a single rinse may largely be a masking effect, as the placebo rinse was also effective (Tables 1 through 3). In addition, the mechanical cleansing of the oral cavity during the rinse may also help temporarily reduce the odor.

However, the significant reductions of oral malodor over the course of 4 weeks in subjects using BreathRx™ mouthrinse may not be attributed to the masking effect. The

Table 10—Comparison of Efficacy of Four Mouthrinses in Reducing Week 0 Baseline Halimeter® Throat Scores After Twice Daily Use for 2 and 4 Weeks

Rinse	Reduction from Week 0 Baseline Values	
	2 Week	4 Week
Product 4/CD/Zn	-70.16	-72.28
Product 2/CPC	-83.16	-86
Product 1/EO	-23	-47.71
Product 3/Placebo	-3.18	-25.50

Mean changes in baseline Halimeter® throat score from week 0. Values with brackets are not significantly different as determined using Kruskal-Willis contingency table technique and multiple comparison method.

measurements of oral odor were taken before the use of the rinse at each visit (weeks 0, 2, and 4 baseline). Because the subjects were asked to not brush their teeth, rinse their mouths, and eat after 11:00 PM the evening before each visit, the oral odor evaluated had been stable for at least 9 hours when the baseline organoleptic and Halimeter® measurements were taken. Among the four mouthrinses, BreathRx™ was the only one that reduced the baseline organoleptic score at both the 2- and 4-week visits (Table 6 and Figure 2). Although the two commercial mouthrinses were effective in reducing oral odor for up to 4 hours after a single use (Table 5), the baseline organoleptic scores of oral malodor remained the same after twice-daily use for 2 and 4 weeks (Table 6).

Data obtained from the Halimeter® measurements support the organoleptic findings that Product 2/CPC (BreathRx™) induced the highest reduction of the readings at both the 2- and 4-week visits (Tables 9 and 10 and Figures 3 and 4). However, the placebo rinse (Product 3/placebo) also showed reductions of oral odor. As a negative control, the placebo rinse was expected to produce minimal effects, as was the case of organoleptic evaluation obtained in the study. Therefore, it is possible that the data indirectly support the statement that while the Halimeter® measurements may be useful, the assessment of malodor is still best judged by the organoleptic method.^{4,7}

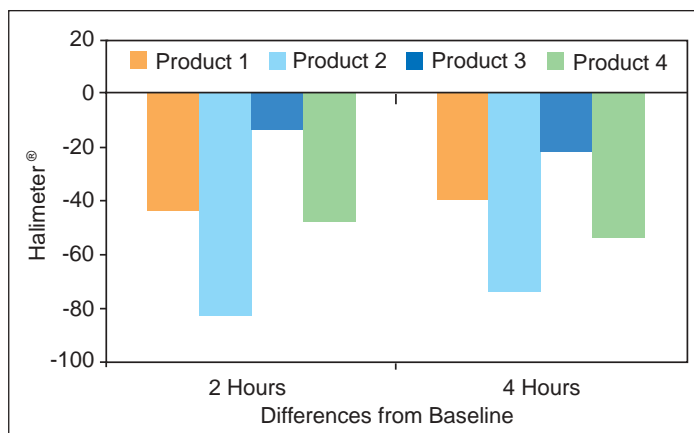


Figure 3—Reduction of throat scores from baseline values after a single rinse of four mouthrinses at week 0.

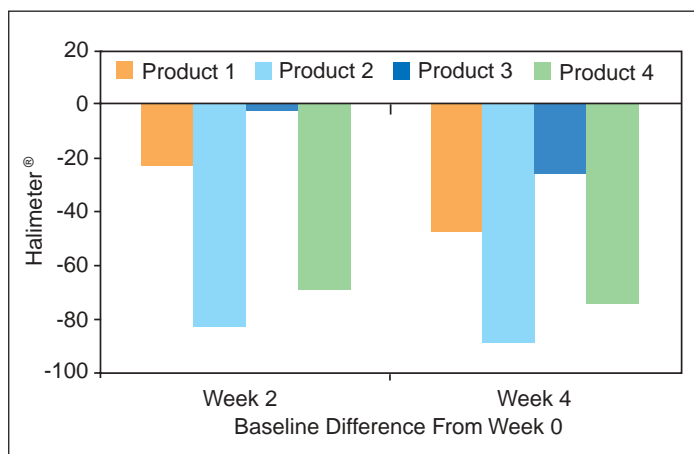


Figure 4—Changes in throat scores from baseline values after twice daily use of four mouthrinses at weeks 2 and 4.

There are few mouthrinses on the market that have been thoroughly evaluated in clinical trials for their long-term efficacy in the management of oral malodor. The overall results from this 4-week, randomized, double blind, longitudinal clinical trial have demonstrated that the mouthrinse with CPC (BreathRx™) has short-term (up to 4 hours) as well as long-term (up to 4 weeks) efficacy in reducing oral malodor. An additional advantage of this mouthrinse is that it contains no alcohol, which has been a concern to certain subjects, making it a promising formula for the problem of oral malodor.

Conclusion

Under conditions of the present study, it is concluded that:

- The four mouthrinses tested are all capable of reducing oral malodor within 4 hours after a single product usage, with the mouthrinse containing CPC being the

most effective and the placebo rinse the least effective.

The daily use of the two commercial mouthrinses (EO or CD/Zn as active ingredient) and the placebo rinse for up to 4 weeks did not reduce oral malodor from week 0 baseline scores.

Product 2/CPC (BreathRx[®]) was the only mouthrinse that reduced oral malodor from week 0 baseline scores after 2 and 4 weeks of daily use.

Product 2/CPC (BreathRx[®]) was more effective than the other three mouthrinses in reducing oral malodor.

Disclosure

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Quiz 2

- Ozostomia, stomatodysodia, halitosis, fetor oris or fetor ex ore all denote different sources of:**
 - bacterial infections.
 - viral infections.
 - oral malodor.
 - salivary inconsistencies.
- Conditions that favor the retention of which bacteria lead to the development of bad breath?**
 - Aerobic, mainly gram-negative
 - Anaerobic, mainly gram-negative
 - Aerobic, mainly gram-positive
 - Anaerobic, mainly gram-positive
- Diabetes mellitus, uremia, and hepatic diseases may also induce what that are detectable as oral odors?**
 - Increased salivary pH
 - Decreased salivary pH
 - Metabolic products
 - Bacterial overgrowths
- Products containing metal ions, especially what, are effective in inhibiting odor formation because of their neutralizing effect on sulfur compounds?**
 - Silicon
 - Aluminum
 - Magnesium
 - Zinc
- A placebo rinse was also included in the study to serve as the:**
 - negative control.
 - positive control.
 - negative variable.
 - positive variable.
- What methods were used for data analysis of the within-treatment data?**
 - Chi-squared
 - Logarithmic
 - T-squared
 - Wilcoxin signed rank test
- In what year did the Council on Dental Therapeutics of the American Dental Association establish guidelines for acceptance of chemotherapeutic products for the control of dental plaque and gingivitis?**
 - 1966
 - 1976
 - 1986
 - 1996
- The objective assessment of malodor that is judged by the human sense of smell is the:**
 - olfactory method.
 - optic method.
 - volatility method.
 - organoleptic method.
- Reduction of oral malodor of up to 4 hours after a single rinse may largely be a:**
 - salivary response.
 - masking effect.
 - data collection anomaly.
 - statistically evaluation anomaly.

Please see tester form between pages 572 and 573.

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