## ORIGINAL ARTICLE

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# **Oral malodor reduction by a combination of chemotherapeutical and mechanical treatments**

Received: 8 November 2005 / Accepted: 22 March 2006 / Published online: 19 April 2006 © Springer-Verlag 2006

Abstract Bacterial proliferation and plaque accumulation on the surface of the tongue are major factors contributing to oral malodor. In this research, we used subjective and objective methods to evaluate the breath benefit of a triclosan-containing dentifrice (Blend-a-Med Complete Night) with and without tongue brushing in a randomized, examiner-blinded, three-period crossover clinical trial. Twenty-nine adults (mean age 40.2 years) with morning malodor were randomly assigned to a treatment sequence: triclosan dentifrice, triclosan dentifrice plus tongue brushing, and a control dentifrice (Crest Cavity Protection). The subjects used each product four times in 27 h with a 2-day wash-out period between treatments. Halimeter measurements were taken at baseline and at 3, 24 and 27 h. Subject questionnaire data assessing the breath quality were collected at 24 and 27 h. Both triclosan regimens showed significant improvement in oral malodor (p < 0.03) relative to the control. Significant (p=0.035) malodor benefit was observed when tooth brushing with triclosan dentifrice was supplemented with tongue brushing. The triclosan dentifrice was associated with significant improvement (p < 0.05) in morning mouth feel and feeling of clean and fresh breath during the day relative to the control. There were no adverse events reported. The triclosan dentifrice was effective against overnight and daytime oral malodor. Supplementing routine brushing with tongue brushing resulted in additional breath improvement and breath benefits of the triclosan dentifrice were first-person noticeable.

**Keywords** Clinical trials · Oral malodor · Triclosan · Halimetry

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## Introduction

Oral malodor is a common condition that affects most of the population at some point in their lives [25]. Although the majority of cases are associated with physiological or transient conditions, it is estimated that 10 to 30% of the individuals may suffer from chronic malodor [20]—a condition that can contribute to emotional stress, low selfesteem, lack of confidence, and social isolation. Increased public awareness and demand for breath malodor remedies resulted in a substantial growth of the breath industry and saturation of the market with breath-improving products such as mints, chewing gum, breath sprays, pills, etc. Although some of these products provide modest breath improvement [14], the majority only have a short-term "masking" effect on bad breath and are, essentially, ineffective [30].

Breath malodor is caused by volatile odorous substances (mainly volatile sulfur compounds-VSC) present in the air exhaled from the oral cavity or the nasal passages [35, 42]. It is widely accepted that 85 to 90% of all cases of bad breath have an intra-oral origin (oral malodor), while the remaining 10-15% are of an extra-oral origin caused by certain respiratory and gastro-intestinal infections, systemic diseases, metabolic disorders or medications [5, 30, 42]. Production and release of VSC in the oral cavity depends on multiple factors, among which are bacterial population of the mouth, availability of substrates for bacterial metabolism, and salivary flow [12, 32]. McNamara et al. identified gram-negative anaerobic bacteria as the primary source of VSC generation [19]. Low salivary flow, particularly at nighttime, creates a favorable environment for bacterial proliferation and putrefaction and results in a physiological "morning breath"-a most common breath complaint [39, 44]. Although VSC are not the only constituents of oral malodor (some volatile amines have been associated with bad breath as well), numerous publications, including the fundamental work of Tonzetich, showed that the VSC are the main components of oral malodor [35, 42, 44]. Tonzetich et al. have demonstrated that the concentration of CH<sub>3</sub>SH and H<sub>2</sub>S in morning mouth air

can alone account for the oral malodor [43]. The role of volatile substances other than VSC as main components of oral malodor has been disputed by many authors and was not experimentally substantiated [13, 18, 34, 44]. Therefore, VSC are commonly considered to be appropriate markers of oral malodor. The concentration of VSC in the exhaled air measured with a portable sulfide monitor, Halimeter, showed to be highly correlated with the organoleptic breath assessment, which still remains to be a standard of oral malodor estimation [12, 22, 27]. Moreover, a linear relationship between the organoleptic scores and log sulfide concentration and high sensitivity of organoleptic judges to changes in VSC concentration and to  $H_2S$  in particular has been demonstrated [6, 28].

It is believed that the dorso-posterior region of the tongue is the primary source of malodor production in the oral cavity [16, 44]. The papillary structure and large surface area of the tongue provide a favorable environment for bacterial proliferation and plaque accumulation. The ability of the tongue to harbor microorganisms was first discovered in 1920 when Sarrazin provided scientific evidence supporting bacterial presence on the tongue surface [33]. Hartley et al. [8] showed that people with high oral malodor levels have higher total bacterial counts and higher fraction of gram-negative anaerobes on the tongue surface compared to those with low malodor levels. Strong positive correlations were found between tongue coating scores and production of VSC in the oral cavity [21, 41].

Considering the primary role of oral bacteria and plaque in VSC formation, adequate oral hygiene (tongue cleaning, in particular) and use of antimicrobial agents are the two most advocated malodor treatments. Tongue cleansing dates back to antiquity when the procedure was a part of a religious ritual. Tongue brushing was a common practice among early Hindus, Buddhists, and Muslims; tongue scrapers were frequently used in Europe in 1700s and early 1800s [3]. The practice was largely neglected in the late 19th-20th century until recently when the importance of tongue hygiene in overall oral and dental health has finally gained attention [43]. It was demonstrated that supplementing routine tooth brushing with tongue brushing reduced the rate of plaque formation and total plaque accumulation [7] and decreased the production of VSC [39] and oral malodor [4]. Tonzetich et al. demonstrated that proper oral hygiene that included tongue brushing significantly reduced early morning malodor [43]. In addition to a malodor reduction benefit, removing plaque from the tongue improves taste and smell perception [10, 24]. In a 2-week study of the effect of tongue brushing and tongue scraping on tongue microflora, Quirynen et al. [24] discovered that neither procedure reduced the microbial load on the tongue; however, the tongue coating was decreased significantly with both devices. On the contrary, use of antimicrobial agents, such as chlorhexidine, hydrogen peroxide, and triclosan causes significant shifts in the tongue microflora [26] and, in addition to mechanical plaque removal, is an effective method of malodor reduction.

Triclosan is a broad-range anti-bacterial agent that has been widely used in skin care products, disinfectants, soaps, and oral hygiene products. It is effective against many types of both gram-positive and gram-negative bacteria and some fungi [31]. At low concentrations triclosan is bacteriostatic, and at high concentrations it is bactericidal. At bacteriostatic levels, triclosan disrupts bacterial fatty acid synthesis by inhibition of enoyl-acyl carrier protein reductase—an enzyme involved in the pathway [9, 38]. The bactericidal effect of triclosan results from triclosan-induced K<sup>+</sup> leakage from the microbial cells, followed by membrane damage and destruction [40]. Triclosan has been successfully used in dentifrices and mouthwashes and shown to be effective in the reduction of gingivitis, plaque, and oral malodor [2, 15, 23, 45]. In multiple studies addressing long-term use of oral hygiene products containing triclosan, no alteration of oral microflora and no evidence of bacterial resistance were found [11, 36, 37].

This new research was conducted to evaluate the effects of a combination regimen that included the use of triclosan dentifrice and tongue brushing on VSC production and subjective assessment of breath.

#### **Materials and methods**

This study was a randomized, examiner-blinded, threeperiod crossover clinical trial that compared the oral malodor reduction benefit of a triclosan-containing dentifrice with two brushing regimens to that of a control dentifrice. The study took place in a dental clinic in Cincinnati, OH, USA. Volunteers were pre-qualified for the study based on the VSC concentration in their morning breath over a 3-day period as determined with a Halimeter (Interscan, Chatsworth, CA, USA). Twenty-nine healthy adults who had shown evidence of reproducible morning oral malodor and had at least 20 natural teeth were selected for the study. Subjects who had used chlorhexidine mouth rinses or antibiotics 2 weeks before the study initiation, required antibiotic pre-medication for dental procedures, presented with upper respiratory infections, or were of poor oral/general health were excluded from the study. Subjects who developed a condition during the study that required the use of antibiotics were disgualified.

At the study initiation visit, all subjects reviewed and signed the informed consent. Demographic information and medical and dental history were collected and inclusion/exclusion criteria were verified. To standardize brushing and to eliminate interference from use of antimicrobial dentifrices and antiseptic mouth rinses with the study results, all subjects underwent a 1-week acclimation period before study initiation. During the acclimation period, each subject was instructed to brush twice a day with the 0.243%-sodium-fluoride-containing dentifrice (Crest Cavity Protection, Procter & Gamble, Cincinnati, OH, USA) in his/her customary manner. The subjects were randomly assigned to one of six treatment sequences consisting of all orderings of the following three regimens:

- brushing teeth with a dentifrice containing 0.321% sodium fluoride and 0.280% triclosan (Blend-a-Med Complete Night, Procter & Gamble, Cincinnati, OH, USA)
- brushing teeth and tongue with a dentifrice containing 0.321% sodium fluoride and 0.280% triclosan (Blenda-Med Complete Night, Procter & Gamble, Cincinnati, OH, USA)
- brushing teeth with a control dentifrice containing 0.243% sodium fluoride (Crest Cavity Protection, Procter & Gamble, Cincinnati, OH, USA)

All test products were over-labeled to ensure blinding. Each treatment period was 27 h in duration with VSC Halimeter measurements taken by a trained professional at baseline and at 3, 24, and 27 h. Product distribution and product use instructions were conducted in a protected area away from the Halimeter and the examiner to maintain blinding. Calibration of the Halimeter was performed according to the manufacturer's recommendations. Before each measurement, the subjects were instructed to keep their mouth closed for 2 min and not to swallow, which allowed sufficient build-up of VSC in the oral cavity. A disposable tube was placed into an opening located on the screen that separated the subjects from the instrument. The subjects placed their lips around the tube and held their breath as the instrument drew air from the mouth to the sensing chamber. The operator recorded the peak concentration of VSC displayed in parts per billion. The subjects were instructed to abstain from any oral hygiene, eating, drinking, smoking, using breath mints, and chewing gum after 11:00 p.m. the night before the baseline and 24 h visits. In addition, all subjects agreed not to consume highly seasoned foods during the study and to abstain from wearing scented products on days when breath evaluations were performed. All baseline and 24 h visits were scheduled between 7:00 a.m. and 9:00 a. m. to facilitate compliance. After the baseline breath measurements were taken, each subject received the assigned product and both oral and written product use instructions. The first product use was performed under supervision. The subjects assigned to the control treatment and to the triclosancontaining dentifrice with "brushing teeth only" regimen brushed for 2 min with a full brush head of the product swishing the product around their mouth for an additional 30 s, expectorating and rinsing with 15 ml of water for 10 s. The subjects assigned to the triclosan-containing dentifrice with the "brushing teeth and tongue" regimen brushed their teeth for 2 min with a full brush head of the product swishing the product around the mouth for an additional 30 s and then spitting. After that, the tongue was arbitrarily divided into six sections: upper left, middle and right (toward the dorsum) and lower left, middle and right sections (toward the tip). The subjects brushed each segment of the tongue with three vertical strokes beginning with the upper half of the tongue without additional dentifrice and then rinsed with 15 ml of water for 10 s. The subjects refrained from eating, drinking, or smoking until the 3 h visit.

Approximately 3 h after the baseline visit, all subjects reported to the clinic for the breath measurement. After a provided standardized lunch, all subjects brushed their teeth with the assigned product under supervision. The subjects were instructed to brush at home in the evening before 11 p.m. and to refrain from eating, drinking, or smoking after the evening brushing. Approximately 24 h after the baseline measurement, the subjects returned to the clinic for breath assessment and supervised brushing. Each treatment period was completed at a 27 h visit when the subjects returned the test products and a VSC measurement was taken. To minimize any possible carry-over effect, each treatment period was followed by a 2-day wash-out period when participants brushed their teeth with Crest Cavity Protection dentifrice twice a day. To avoid possible cross-contamination, toothbrushes were replaced after each treatment and wash-out period.

A breath questionnaire was completed by all subjects at the 24 and 27 h visits to assess the participants' subjective opinion regarding the quality of their breath. At 24 h, the subjects were asked to rate the following statement: "My breath feels cleaner and fresher now than it typically does when I wake up in the morning." At the 27 h visit, statements "My breath is fresh", "My breath is clean", and "My tongue feels clean" were evaluated. Each statement was rated on a scale of -4 ("disagree the most possible") to 4 ("agree the most possible").

Analysis of covariance for a crossover design with repeated measures was applied to model the mean level of VSC on the natural logarithm scale. The model included the baseline VSC measurement as a continuous covariate and class variables for treatment, period, and hour. Subject was included as a random class variable. The treatment by hour interaction was also modeled and evaluated. The baseline and adjusted VSC means were transformed back to the original scale. The questionnaire response data were analyzed using analysis of variance to assess treatment differences in the mean response to each question at either 24 or 27 h. All comparisons were tested at a one-sided 0.05 level of significance. The relationship between the subjective and the objective breath measurements was investigated by calculating Pearson correlation coefficient.

#### Results

A total of twenty-nine adult volunteers were enrolled into the study and randomly assigned to a treatment sequence. Ages ranged from 21 to 59 years with the mean age of 40.2 years. Females accounted for 79% of the sample size. Demographic information is summarized in Table 1. Twenty-six subjects completed all three treatment periods. One subject was excluded from analysis because of antibiotic use for an unrelated medical condition during part of the study. Two other subjects missed a total of three sampling visits. All other subjects/visits were evaluable and were included in the analysis.

VSC concentration in the oral cavity, measured by a Halimeter, was the primary efficacy outcome of the study.

 Table 1
 Baseline demographic characteristics

All subjects randomized (N=29) <sup>a</sup>		
Age (years)		
Mean (SD)	40.2 (10.9)	
Minimum-maximum	21-59	
Sex <sup>b</sup>		
Female	23 (79%)	
Male	6 (21%)	
Race <sup>b</sup>		
Asian Oriental	2 (7%)	
African American	4 (14%)	
Caucasian	21 (72%)	
Asian Indian	2 (7%)	

<sup>a</sup>Number of subjects randomized to treatment

<sup>b</sup>Number and percent of subjects in each category

There were no statistically significant differences between the treatments with respect to the baseline mean VSC score (p>0.25). Treatment by hour interaction was found not to be statistically significant (p=0.723), indicating that treatment differences were consistent over time.

Relative to the control treatment, both triclosan regimens demonstrated significant oral malodor reduction (p<0.001 and p=0.026, respectively). Adjusted mean VSC values for the 3, 24, and 27 h endpoints were 168.8, 181.5, and 143.1 ppb for a triclosan dentifrice with tooth brushing regimen and 151.4, 163.1, and 126.2 ppb for triclosan dentifrice with tooth and tongue brushing, respectively. For the control dentifrice, the corresponding VSC concentrations were 205.6, 194.9, and 159.2 ppb, respectively. A comparison of two triclosan regimens showed that supplementing tooth brushing with tongue brushing resulted in an additional breath benefit over tooth brushing alone (p=0.035). Figure 1 summarizes the adjusted mean VSC scores converted back to the original scale for the three post-baseline visits.

A subjective questionnaire was used to estimate the quality of morning and daytime breath and mouth feel as perceived by the subjects. Questionnaire results are presented in Table 2. For morning breath evaluated at 24 h post-baseline ("Breath feels cleaner and fresher now than





it typically does when I wake up in the morning"), the two triclosan regimens showed at least one unit higher breath satisfaction (p < 0.05) when compared to that of the control. There was no significant difference between the two triclosan regimens (p > 0.05). There were no adverse events reported in the clinical trial and there were no subjects who discontinued treatment because of product-related reasons.

Quality of daytime breath and mouth feel was evaluated at 27 h post-baseline. For the statement "Breath is fresh", both triclosan regimens scored significantly higher than the control (p < 0.05). Relative to the control treatment, both triclosan regimens resulted in a 1.0 unit higher satisfaction in breath freshness. There were no statistically significant differences between the two triclosan regimens (p>0.05). The triclosan treatments were also associated with higher satisfaction in regards to clean breath (p < 0.05, "Breath is clean" statement) compared to that of the control. There was a 0.7 unit higher satisfaction for the standard tooth brushing regimen and 0.9 unit higher satisfaction for the teeth and tongue brushing regimen relative to the control. The triclosan regimens did not differ significantly from each other again (p>0.05). For the triclosan dentifrice with a tongue brushing regimen, the feeling of clean tongue ("Tongue feels clean" statement) was rated significantly higher compared to the two other treatments (p < 0.05) with a 1.3 unit difference from the control and a 0.9 unit difference from the triclosan with tooth brushing only treatment. There was no statistically significant difference between the triclosan dentifrice and the control dentifrice when only teeth were brushed (p>0.05).

#### Discussion

This clinical study demonstrated that a combination of chemical and mechanical approaches can be successfully used in treating oral malodor. The novelty of this research was in combining an objective mean of oral malodor measurement—halimetry—with self-perception of breath

Table 2 Treatment comparison, questionnaire data

Time/question	Improvement vs the control, questionnaire units	
	Triclosan + teeth brushing	Triclosan + teeth and tongue brushing
Hour 24		
Breath feels cleaner/fresher now than it typically does when I wake up in the morning.	1.08 s	1.03 s
Hour 27		
Breath is fresh	1.04 s	1.00 s
Breath is clean	0.71 s	0.91 s
Tongue feels clean	0.41	1.28 s

*s* Statistically significantly greater than control

quality and in demonstrating that treatment effects of the triclosan dentifrice can be both objectively measured and subjectively perceived. Chemical treatment of malodor involved the use of an antimicrobial agent-triclosan-that has been shown to be effective against odorogenic oral bacteria [1, 17]. Previous studies demonstrated that triclosan-containing products were effective against oral malodor [2, 23]. The chemotherapeutical effect of triclosan on oral malodor was confirmed in the present study. The malodor benefit of Blend-a-Med Complete Night dentifrice (0.280% triclosan) was apparent regardless of the treatment regimen and was consistent over the three post-baseline visits. Because the dorsal surface of the tongue provides a favorable environment for bacterial proliferation and plaque accumulation, a dual action of an antimicrobial agent and mechanical tongue debridement was thought to provide an additional breath benefit. The combination treatment was achieved by swishing the triclosan dentifrice around the mouth immediately after tooth brushing to allow contact of an antimicrobial agent with the surface of the tongue, followed by mechanical tongue brushing. Because the antimicrobial action of triclosan and the effect of tongue brushing on oral malodor have been previously established in separate studies, the objective of this research was not to prove one or the other method of oral malodor reduction but, rather, to evaluate the magnitude of benefit of routine tooth brushing with the particular triclosan-containing dentifrice (regimen adapted by the majority of the population) and of a combination regimen of tooth brushing with a triclosan dentifrice and tongue brushing (regimen used by a smaller fraction of the population). For this reason, the effectiveness of both treatments was evaluated relative to routine brushing with a regular dentifrice, and including a second control group of tooth and tongue brushing with a regular dentifrice was thought to be unnecessary. Supplementing routine brushing with tongue brushing resulted in a significantly lower level of VSC production. These findings are consistent with the dorsum of the tongue being a primary source of oral malodor and suggest that incorporating tongue brushing into everyday tooth brushing routine is important in managing oral malodor. In the study, the subjects were specifically instructed to brush the posterior segment of the tongue, the area primarily associated with oral malodor. In reality, it is most likely that, during brushing, many subjects did not reach far enough to contact the posterior third of the dorsum. In addition, treatment was unsupervised at home and brushing proficiency was not monitored. We observed a moderate improvement from supplementing the tooth brushing with the tongue brushing. We speculate that a more thorough cleaning of the posterior third of the dorsum would have yielded an even greater response. The effectiveness of triclosan dentifrice with and without tongue brushing with respect to VSC generation by oral bacteria supports the microbial etiology of oral malodor.

The effect of triclosan dentifrice with two brushing routines on morning and daytime VSC concentration was explored in the study. Unpleasant morning malodor is the most common breath complaint. The origin of this physiological condition is also microbial as low salivary flow at night favors bacterial stagnation and proliferation in the oral cavity. To standardize morning breath assessment, the subjects were asked to allow at least 8 h between the nighttime brushing and morning assessment and to refrain from eating, drinking, or performing any oral hygiene during that time period. Both triclosan regimens were effective and resulted in lower levels of morning VSC concentrations, providing 7% (tooth brushing) and 16% (tooth and tongue brushing) greater reduction in VSC concentration compared to the control dentifrice.

The effects of triclosan and tongue brushing on daytime VSC concentration were measured 3 h after the morning brushing over a 2-day period. Tooth brushing with the triclosan dentifrice resulted in 18 and 10% lower level of VSC concentration when compared to the control dentifrice at the 3 and 27 h post-baseline visits, respectively. The corresponding percentages for teeth and tongue brushing with triclosan were 26 and 21%, respectively. Given that subjects were instructed to refrain from eating, drinking, and oral hygiene for 3 h between the morning brushing and daytime breath assessment, the higher rate of VSC reduction during the day than overnight can be attributed to reduced plaque formation rate and lower bacterial counts as the result of increased salivation compared to nighttime.

It is well known that oral malodor is a condition with both patho-physiological and psychological components. A product should ideally address both the objective and subjective components by effectively treating the underlying cause of malodor and providing consumer-noticeable improvement in the quality of breath. Previous research has demonstrated that consumers are generally unable to rate the intensity of their oral malodor [29]. For this reason, quantitative breath assessment was not considered for subjective questionnaire. Rather, in the present study, we asked the study participants to evaluate the quality of their overnight and daytime breath. The effect of the triclosan dentifrice on the quality of breath compared to the control, as judged by the subjects, was apparent and statistically significant at both visits. In the morning, the triclosan dentifrice was rated significantly higher than the control dentifrice on the question "Breath feels cleaner and fresher now than it typically does when I wake up in the morning." However, no additional benefit of tongue brushing on morning breath rating was observed when compared to the teeth brushing regimen. At the 27 h evaluation (daytime breath), the triclosan dentifrice regimens gave a noticeably cleaner and fresher breath when compared to brushing with the control dentifrice. Similarly to the morning evaluation, there was no significant difference between the tooth and tooth and tongue brushing regimens. However, with longterm use, the perception of the effect of tongue brushing on the overall mouth feel may become more pronounced.

The effect of tongue brushing became apparent when the subjects were asked to rate the cleanness of their tongue. It is logical to assume that those mechanically removing plaque from the tongue surface would have a cleaner tongue feel than those brushing teeth only. A clean tongue feel question was included in the questionnaire as a control check to assure the quality of the data. As expected, tongue brushing with the triclosan dentifrice resulted in significant increase in clean tongue perception when compared to just teeth brushing either with the control or the triclosan dentifrice. There was no difference observed in clean tongue feel between the two teeth only brushing regimens. All questionnaire data for triclosan treatments were positively correlated with the reduction of VSC concentration measured by a Halimeter.

The study demonstrated that triclosan-containing Blenda-Med Complete Night dentifrice was more efficacious than the control dentifrice in daytime and overnight oral malodor control. The clinical relevance of the magnitudes of breath reduction seen for both regimens is, at this point, unclear. Most of the research published on the breath benefit of triclosan-containing dentifrices evaluated a longterm cumulative benefit of triclosan rather than looking at the short-term immediate and overnight effects. However, a consistency between the objective Halimeter data and the subjective consumer perception of breath suggests that the benefit may be, in fact, actual. Additional research to examine improvements in organoleptic rating and longterm cumulative benefit of Blend-a-Med Complete Night is indicated. Further clinical research may be necessary to determine whether the short-term results seen with this dentifrice can be generalized to other combinations of toothpaste and brushing regimens.

Acknowledgements The authors acknowledge Lynn Downey, Susan Fiedler, Pelin Gunenc, Rob Hinkle, Stephen McClanahan, Victoria Milyanenkova, and Lisa Saletta for their contributions to study preparation and execution.

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