clinical data

Clinical Studies - Oral Hygiene

BreathRx Clinical Pak
General Information

What is bad breath?

Halitosis or oral malodor is a condition which involves offensive odor emanating from the mouth and other hollow cavities such as the nose and sinuses. This is differentiated from bad breath which emanates from the lungs when certain foods are digested. Small odor molecules from these foods (usually onions, garlic and peppers) enter the bloodstream with some making their way into the lungs. These are then exhaled causing bad breath. Oral malodor is generally caused by volatile sulfur compounds (VSC's) which are gases with unpleasant odors even at very low concentrations. These VSC's consist primarily of hydrogen sulfide, methyl mercaptan, dimethyl sulfide and dimethyl disulfide. VSC's caused by Gram-negative bacteria are usually associated with oral conditions contributing to a shift from Gram-positive bacteria to Gram-negative bacteria. When this happens, sulfur containing amino acids are hydrolyzed by Gram-negative anaerobic bacteria in an alkaline environment. Production and release of these VSC's and subsequent detection of these oral malodorous substances appears to depend on multiple local factors which include:

Salivary pH
Reduced ambient oxygen concentration
Substrate available for bacterial metabolism
Bacterial production

Food particles and sloughed off oral cellular debris (substrate materials) are the main sources of protein in the oral cavity. In a healthy mouth, dead epithelial cells are shed into the saliva, swallowed and digested fast enough so that the epithelial cells do not putrefy and cause halitosis. Decreased saliva levels lead to excess food and cellular debris build up creating substrate and an increase in Gram-negative bacteria on the tongue and in gingival crevices. Decreases in saliva can also cause the pH of the mouth to increase over 7.2. An increase in the oral pH leads to higher levels of colonization of Gram-negative bacteria.

Types of Oral Malodor1

Physiological	Pathological
Transitory	Chronic
Morning Breath	Mouth
Hunger Breath	Nose / Sinuses
Menstrual Breath	Tonsils / Pharynx
Food / Drugs	Digestive System
No systemic illness	Systemic illness
Less intense	More intense
Distinct in quality	Nondescript
Generaly responds to oral hygiene	Requires treatment of underlying cause

There are two types of oral malodor physiological (transitory) and pathological (chronic). Physiological malodor tends to be less persistent and generally responds to good oral hygiene practices. Pathological malodor is more intense and persistent.

The underlying cause of the halitosis must be treated for the patient to get a significant reduction in odor levels. In physiological halitosis, this decrease in saliva and increase in oral pH can be associated with age, hunger, morning breath, menstrual cycle or drug use (See Table 1).

The underlying causes in pathological halitosis can be in the oral cavity, the nose or sinus, the tonsils, the digestive organs or can also originate from the regional or systemic pathosis such as diabetic ketosis, gastritis, gastric ulcer, oesophagitis, pyloric stenosis or hepatitis.4,5 If the patient has frequent and excessive postnasal drip, this may be a contribute to a persistent daytime oral malodor (See Table 2).

The most likely source of bad breath in individuals with good oral hygiene and healthy periodontal tissues is the back of the tongue. The oral cavity is the main contributor to bad breath in 85 percent of patients with halitosis. Approximately 10 - 15 percent of chronic halitosis is linked to more serious diseases with sinusitis and diabetes being the two most common ones. Halitosis caused by these types of diseases has distinct smells that can help lead to a specific diagnosis (See Table 3).

Table 1 / 6

Drugs that cause dryness of the mouth contribute to bad breath	
CNS agents	**Others**
Antiparkinsonians	Antihistamines / decongestants
Antipsychotics	Anticholinergics
Narcotics	Antihypertensives
Antidepressants	

Table 2 / 6

Oral Conditions Causing Oral Malodor	
Periodontitis	Gingivitis
Apthous ulcers	Traumatic ulcers
Dental abscesses	Herpetic infections
Candidiasis	Oral cancer
Xerostomia	Poor oral hygiene

Non Oral Sources Causing Oral Malodor	
Nose / Sinuses Tonsils / Pharynx Digestive Organs	Pulmonary Systemic Illness
Systemic Illness	**Psychiatric**
Diabetic Ketoacidosis Liver Failure Renal Failure	Schizophrenia Olfactory reference syndrome

General Information
Table 3/2

Disease	Psychiatric
Diabetes Liver failure	Acetone, fruity Sweetish, musty, “amine” odor resembling a fresh cadaver
Acute rheumatic fever	Acid, sweet
Lung abscess	Foul, putrefactive
Blood dyscrasias	Resembling decomposed blood
Liver cirrhosis	Resembling decaying blood
Uremia, kidney failure	Ammonia or urine
Toxemia, gastrointestinal disorder, neuropsychiatric	Varies, poor oral hygiene intensifies the odor
Fever, dehydration, macroglobulinemia	Odor due to xerostomia with poor oral hygiene and toxic waste products accumulated
Sjorgen’s syndrome, Syphilis	Fetid
Eosinophilic granuloma, Letter-Siwe disease, Hand-Schuller-Christian disease	Fetid breath and unpleasant taste
Scurvy	Foul breath of fudodpirochetal stomatitis
Wegner’s granulomatosis	Necrotic, putrefactive
Diphtheria, dysentery, measles	Extremely foul odor resembling acute necrotising
Pneumonia, scarlet fever, tuberculosis, syphilis	Gingivostomatitis, but much more intense and fetid

Information

Zytex™

Zytex™, the special ingredient complex in BreathRx products, contains three

active ingredients: zinc chloride, thymol and eucalyptus oil. This combination neutralizes extra volatile sulfur compounds (VSC's) and kills the Gram-negative bacteria responsible for their formation. Zinc chloride has been shown to be one of the most effective deodorants for malodor in orally healthy populations. It causes a significant reduction in VSC's7. Aqueous solutions of zinc salts in mouth rinses reduce and inhibit VSC formation in the oral cavity1,8. Zinc has an affinity to sulfur and odorizes sulfhydryl groups with zinc ions forming stable mercaptides with the substrate, the precursors, and/or the VSC's directly 9. Thymol and eucalyptus are phenolic oils which are known to have antibacterial effects10. Specifically, studies have shown that thymol has an antagonistic effect against Staphylococcus aureus, Salmonella typhimerium, Streptococcus mutans, S. sanguis, S. mitis, and S. milleri as well as Prevotella buccae, P. oris and P. intermedia11.

References

1. Lu, Dominic, July 1982, Halitosis: An Ideologic Classification, a Treatment Approach, and Prevention, Mosby's Volume 54, No. 1

2. Durham T.M., T. Malloy and E.D. Hodges, 1993, Halitosis: Knowing When "Bad Breath" Signals Systemic Disease, Geriatrics 48: 55-59

3. Kleinberg I. and G. Westbay 1990, Oral Malodor, Ontario Review Oral Biology Medicine 1 (4): 247-259

4. Tonzetich, J. 1977, Production and Origin of Oral Malodor: A Review of Mechanisms and Methods of Analysis, J. Periodontal 48 (1): 13-20

5. Rosenberg M. 1990, Bad Breath: Diagnosis and Treatment, University of Toronto Dental Journal 3 (2): 7-11

6. Johnson B.F., 1992, Halitosis or the Meaning of Bad Breath, Journal of General Internal Medicine 7: 649-656

7. Rosenberg, M., ed. 1995, Bad Breath: Research Perspectives 66-67, 90-91

8. Yaegaki K. and T. Suetaka 1989, The Effect of Zinc Chloride Mouthwash on Production of Oral Malodor, The Degradation of Salivary Cellular Elements and Proteins, J. Dental Health; 39:377-86.

9. Ng W. and J. Tonzetich, 1984, Effect of Hydrogen Sulfide and Methyl Mercaptan on the Permeability of Oral Mucosa. Journal Dent Res, 63: 994-7.

10. Rosenberg, M., ed. 1995, Bad Breath: Research Perspectives, 64-65

11. Didry N., L. Dubruil, and M. Pinkas 1994, Activity of Thymol, Carvacrol, Cinnamaldehyde and Eugenol on Oral Bacteria, Pharmaceutica Acta Helvetiae 69:25-28

Efficacy tests Summary

Minimum Inhibitory Concentration

Minimum Inhibitory Concentration (MIC) is the lowest concentration of antimicrobial agent showing no visible growth of an organism in broth dilution tests. Although the MIC is not an absolute value, it does give the physician an indication of the concentration of antimicrobial agent required to inhibit growth of the infecting organism. The BreathRx Anti-Bacterial Mouth Rinse,

Purifying Toothpaste and Anti-Bacterial Tongue Gel were tested on the following anaerobic/facultative bacterial strains that may be associated with halitosis: Eubacterium lentum, Fusobacterium nucleatum, Porphyromonas endodontalis, Porphyromonas gingivalis, Prevotella intermedia in serial dilutions. The bacteria were then incubated under anaerobic conditions at 35ÞC for 16-20 hours and examined for growth. ATCC (American Type Culture Collection) - this is a control organism used as a standard in comparison of MIC results to establish that the test is being done correctly. PPM (Parts Per Million) indicates the dilution of the product expressed in parts per million required to kill the organism.

BreathRx Anti-Bacterial Mouth Rinse
Table4

Results			
Microorganisms	ATCC#	MIC	PPM
Eubacterium lentum	43055	1 : 8	125000
Fusobacterium nucleatum	25586	1 : 16	62500
Porphyromonas endodontalis	35406	1 : 4	250000
Porphyromonas gingivalis	33277	1 : 16	62500
Prevotella intermedia	25611	1 : 8	125000

Summary
Serial two-fold dilutions of the mouthrinse were tested against the bacteria indicated in Table 4. Minimum inhibitory concentration was read as the lowest concentration of drug showing no visible growth . The MIC for all the organisms ranged from 1:4 - 1:16 (i.e. all the P. endodontalis bacteria are killed when the mouthrinse is diluted 1:4 times.)

BreathRx Purifying Toothpaste
Table 5

Results			
Microorganisms	ATCC#	MIC	PPM
Eubacterium lentum	43055	1 : 8	125000
Fusobacterium nucleatum	25586	1 : 16	62500
Porphyromonas endodontalis	35406	1 : 8	1250000
Porphyromonas gingivalis	33277	1 : 16	62500
Prevotella intermedia	25611	1 : 16	62500

Summary
The Purifying Toothpaste was tested against the same five bacteria as shown in Table 5. Minimum Inhibitory Concentration for all the bacteria ranged from 1:8 - 1:16.

BreathRx Anti-Bacterial Tongue Gel
Table 6

Results			
Microorganisms	ATCC#	MIC	PPM
Eubacterium lentum	43055	1 : 8	125000
Fusobacterium nucleatum	25586	1 : 16	62500
Porphyromonas endodontalis	35406	1 : 4	250000

Porphyromonas gingivalis	33277	1 : 16	62500
Prevotella intermedia	25611	1 : 16	12500

Summary
Against the five bacteria listed in Table 6, the Anti-Bacterial Tongue Gel exhibited MIC ratios of 1:4 - 1:16 in serial two-fold dilution tests.

Efficacy tests Summary

Log reduction
This test is used to determine a product's effectiveness in reducing bacterial populations over a specified period of time. The BreathRx Anti-Bacterial Mouth Rinse, Purifying Toothpaste and Anti-Bacterial Tongue Gel were tested on the following anaerobic/facultative bacterial strains that may be associated with bad breath: Eubacterium lentum, Fusobacterium nucleatum, Porphyromonas endodontalis, Porphyromonas gingivalis, Prevotella intermedia at 0 time, 1 minute and 5 minute exposures. The bacteria were then plated and counted for the reduction in the number of colony forming units. The control was a phosphate buffered saline solution. Log Reduction is defined as follows and is addressed in whole numbers: 1 Log Reduction - 90.0% Reduction, 2 Log Reduction - 99.0% Reduction, 3 Log Reduction - 99.9% Reduction in colony forming units. For example, at the end of five minutes, there was a log reduction of 2.0 for the Purifying Toothpaste against the bacteria E. lentum. This is equivalent to a 99.0% reduction in colony forming units. Concentration of organisms is a count of colony forming units expressed in whole number to the tenth power.

BreathRx Purifying Toothpaste

Eubacterium lentum

Exposure Time				Concentration of Organisms	% Reduction	Log Reduction
Time	Control	Product	Con.	Prod.	Con.	Prod.
0 min	$2.5x10^6$	$1.2x10^5$	47.9	97.7	0.3	1.6
1 min	$2.3x10^6$	$9.0x10^4$	56.3	98.1	0.4	1.7
5 min	$1.9x10^6$	$5.0x10^4$	60.4	99.0	0.4	2.0

BreathRx Anti-Bacterial Tongue Gel Fusobacterium nucleatum

Exposure Time				Concentration of Organisms	% Reduction	Log Reduction
Time	Control	Product	Con.	Prod.	Con.	Prod.
0 min	$1.4x10^6$	$1.6x10^5$	12.5	90.0	0.1	1.0
1 min	$2.1x10^6$	$2.4x10^4$	12.5	98.5	0.1	1.8
5 min	$1.2x10^6$	$3.0x10^4$	25.0	99.8	0.1	2.7

Porphyromonas endodontalis

Exposure Time				Concentration of Organisms	% Reduction	Log Reduction
Time	Control	Product	Con.	Prod.	Con.	Prod.
0 min	$1.9x10^6$	$1.4x10^5$	20.8	94.2	0.1	1.2
1 min	$1.5x10^6$	$6.0x10^4$	37.5	97.5	0.2	1.6
5 min	$1.2x10^6$	$2.2x10^4$	50.0	99.8	0.3	3.0

Porphyromonas gingivalis

Exposure Time				Concentration of Organisms	% Reduction	Log Reduction
Time	Control	Product	Con.	Prod.	Con.	Prod.
0 min	6.7x105	$1.1x10^5$	26.4	87.9	0.1	0.9
1 min	3.5x105	$2.1x10^4$	61.5	97.7	0.4	1.6
5 min	3.1x105	$4.0x10^4$	65.9	99.7	0.5	2.5

Prevotella intermedia

Exposure Time				Concentration of Organisms	% Reduction	Log Reduction
Time	Control	Product	Con.	Prod.	Con.	Prod.
0 min	1.9x106	1.0x104	26.4	98.0	0.0	1.7
1 min	1.4x106	5.0x103	30.0	99.8	0.2	2.6
5 min	1.1x106	2.4x103	45.0	99.9	0.3	2.9

Summary

BreathRx Purifying Toothpaste As indicated in the table, E. lentum had a 97.7-99.0% reduction rate with BreathRx Purifying Toothpaste. When tested against F. nucleatum it showed a 90.0 to 99.8% reduction in colony forming units. P. endodontalis came in at 94.2 to 99.8% reduction. A reduction of 87.9-99.7% in colony forming units was shown against P. gingivalis. And lastly, P. intermedia had one of the greatest kill rates with a reduction in colony forming units of 98.0-99.0%

BreathRx Anti-Bacterial Mouth Rinse

Eubacterium lentum

Exposure Time				Concentration of Organisms	% Reduction	Log Reduction
Time	Control	Product	Con.	Prod.	Con.	Prod.
0 min	$2.5x10^6$	$1.1x10^5$	47.9	97.7	0.3	1.6

1 min	$2.1x10^6$	$7.0x10^4$	56.3	98.5	0.4	1.8
5 min	$1.9x10^6$	$2.0x10^4$	60.4	99.6	0.4	2.4

Porphyromonas endodontalis

Exposure Time				Concentration of Organisms	% Reduction	Log Reduction
Time	Control	Product	Con.	Prod.	Con.	Prod.
0 min	$1.9x10^6$	$1.0x10^5$	20.8	95.8	0.1	1.4
1 min	$1.5x10^6$	$8.0x10^4$	37.5	96.7	0.2	1.5
5 min	$1.2x10^6$	2.3x103	50.0	99.9	0.3	3.0

Porphyromonas endodontalis

Exposure Time				Concentration of Organisms	% Reduction	Log Reduction
Time	Control	Product	Con.	Prod.	Con.	Prod.
0 min	6.7x105	4.2x104	26.4	95.4	0.1	1.3
1 min	3.5x105	7.0x102	61.5	99.9	0.4	3.1
5 min	3.1x105	3.0x102	65.9	100.0	0.5	3.5

Prevotella intermedia

Exposure Time				Concentration of Organisms	% Reduction	Log Reduction
Time	Control	Product	Con.	Prod.	Con.	Prod.
0 min	1.9x106	4.7x104	5.0	97.7	0.0	1.6
1 min	1.4x106	8.0x103	30.0	99.6	0.2	2.4
5 min	1.1x106	1.9x103	45.0	99.9	0.3	3.0

Summary

BreathRx Anti-Bacterial Mouth Rinse When tested, the BreathRx Anti-Bacterial Mouth Rinse had a 97.7-99.6% reduction of E lentum, while F. nucleatum had a reduction of 91.9-99.6% in colony forming units. P. endodontalis performed with a 95.8-99.9% reduction in colony forming units. P. gingivalis showed a 95.4-100% reduction of colony forming units. And finally, P. intermedia had a reduction of colony forming units of 97.7-99.9% . All were very effective at killing the organisms indicated.

BreathRx Anti-Bacterial Tongue Gel

Eubacterium lentum

Exposure Time				Concentration of Organisms	% Reduction	Log Reduction
Time	Control	Product	Con.	Prod.	Con.	Prod.
0 min	$2.5x10^6$	$1.8x10^5$	47.9	96.3	0.3	1.4
1 min	$2.1x10^6$	1.6x105	56.3	96.7	0.4	1.5
5 min	$1.9x10^6$	$4.0x10^4$	60.4	99.2	0.4	2.1

Fusobacterium nucleatum

Exposure Time				Concentration of Organisms	% Reduction	Log Reduction
Time	Control	Product	Con.	Prod.	Con.	Prod.
0 min	$1.4x10^6$	$1.1x10^5$	12.5	93.9	0.1	1.2
1 min	$2.1x10^6$	$5.0x10^4$	12.5	96.9	0.1	1.5
5 min	$1.2x10^6$	2.3x103	25.0	98.6	0.1	1.8

Porphyromonas endodontalis

Exposure Time				Concentration of Organisms	% Reduction	Log Reduction
Time	Control	Product	Con.	Prod.	Con.	Prod.
0 min	1.9x106	1.5x105	20.8	93.8	0.1	1.2
1 min	1.5x106	3.0x104	37.5	98.8	0.2	1.9
5 min	1.2x106	1.8x104	50.0	99.3	0.3	2.1

Porphyromonas gingivalis

Exposure Time				Concentration of Organisms	% Reduction	Log Reduction
Time	Control	Product	Con.	Prod.	Con.	Prod.
0 min	6.7x105	1.2x105	26.4	86.8	0.1	0.9
1 min	3.5x105	2.6x104	61.5	97.1	0.4	1.5
5 min	3.1x105	7.0x103	65.9	99.2	0.5	2.1

Prevotella intermedia

Exposure Time				Concentration of Organisms	% Reduction	Log Reduction
Time	Control	Product	Con.	Prod.	Con.	Prod.
0 min	1.9x106	2.4x104	5.0	98.0	0.0	1.9

1 min	1.4x106	9.0x103	30.0	99.6	0.2	2.3
5 min	1.1x106	3.9x103	45.0	99.8	0.3	2.7

Summary

BreathRx Anti-Bacterial Tongue Gel E lentum, exhibited a reduction of colony forming units of 96.3-99.2% with the BreathRx Anti-Bacterial Tongue Gel. A calculated reduction of colony forming units of 93.9-98.6% with F. nucleatum was shown. Testing at 93.8-99.3% reduction in colony forming units was P. endodontalis. When tested against P. gingivalis, BreathRx Anti-Bacterial Tongue Gel had a reduction of 86.8-99.2%. P. intermedia performed at a reduction in colony forming units of 98.0-99.8%. This was the optimum performer.