The Effects of Oral Rinses on Halitosis

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Abstract

Oral rinses are increasingly becoming an important treatment option for halitosis. There are few products on the market that have been thoroughly evaluated in clinical trials designed to test for the long-term efficacy of mouthrinses in the management of this disorder. This review looks at some of the potential causes and detection methods of oral malodor along with the bacterial, microbiological and biochemical processes involved. The article presents the available literature on clinical trials evaluating the efficacy and mechanisms of action of the different types of oral rinses used in the reduction of plaque and gingivitis, in addition to rinse studies geared more specifically to the treatment of halitosis.

Oral rinses are one of the therapeutic approaches to the treatment of halitosis. However, knowledge and understanding of this condition are in their infancies, and there are only a few products on the market geared specifically to the eradication of oral malodor. In addition, there is a paucity of clinical trials to substantiate the efficacy of these products for halitosis.

Halitosis can be symptomatic of many localized and systemic disorders of a normal physiological, pathological or psychiatric nature. Malodor caused by normal physiological processes and behaviors is usually of a transitory nature, such as "morning breath" and foul breath resulting from ingesting pungent foods, such as onion and garlic. Halitosis can be symptomatic of a more serious pathological disorder; but most breath malodor, in otherwise healthy people, stems from the oral cavity. The way to differentiate between an oral and nonoral etiology of patient complaints is to compare the odor emanating from the mouth with that from the nostrils. For those with no systemic disease and presenting with healthy dentition and gingiva, the malodor generally originates on the tongue dorsum. Significantly more bacterial cells attach as compared to other oral mucosal areas. The quantity of tongue coating has been reported to be many times greater in periodontal patients as compared to normal subjects. But even in persons with healthy periodontal tissue, oral malodor is more likely to originate from the tongue dorsum.[1-5]

Recent scientific evidence reports that in addition to tooth brushing and oral rinsing, tongue cleaning should be an essential part of oral health care. This practice has not played much of a role in Western culture but is more practice in Africa, Asia and South America. An early 20th century researcher recommended daily tongue cleaning when it was found that the tongue dorsum was a breeding ground for *Staphylococci* and *Streptococci*.[6] A clean tongue should be a healthy pink color; a whitish haze on the tongue is indicative of bacterial buildup. The more recent interest of including the tongue as an integral part of mouth care has precipitated an increase of tongue scraping devices on the market.

Volatile Sulfur Compounds

The tongue geography provides an excellent putrefactive habitat for gram-negative anaerobes that metabolize proteins as an energy source via breakdown of proteinaceous substrates from impacted food particles and sloughed off oral cellular debris. In a healthy mouth, dead epithelial cells are shed into the saliva, swallowed and digested fast enough so that they do not putrefy and cause halitosis. Inflammation causes these cells to be shed at a faster rate than the saliva can cleanse. Bacterial action then hydrolyzes the proteins

to amino acids; and three of the amino acids that contain sulfur functional groups — methionine, cysteine and cystine — are the precursors to volatile sulfur compounds (VSCs). These gaseous substances, responsible for malodor, consist primarily of hydrogen sulfide (H_2S), dimethyl sulfide [$(CH_3)_2S$], methyl mercaptan (CH_3SH) and sulfur dioxide (SO_2). Methionine is reduced to methyl mercaptan, and cysteine and cystine are reduced to hydrogen sulfide in the presence of sulfhydrase-positive microbes This microbial activity is favored at a pH of 7.2 and inhibited at a pH 6.5 (also inhibited in 0.02M glucose).[1,3,4,7]

Proteolytic activity has been associated mainly with gram-negative bacteria that reside in the oral cavity, including the following: *Treponema denticola, Porphyromonas endodontalis, Prevotella intermedia, Prevotella melaninogenica, Rothia dentocariosa, Haemophilus, Veillonella alcalescens, Porphyromonas gingivalis, Capnocytophaga, Fusobacterium nucleatum, Bacteroides forsythus* and *Stomatococcus mucilaginus*, a gram-positive microbe.[1] Methyl mercaptan has been found to be the main component of tongue dorsal surface malodor in patients with periodontal disease, whereas hydrogen sulfide predominates in orally healthy subjects. The levels of 2-ketobutyrate, a byproduct of methionine metabolism, are increased in the oral cavity of patients with periodontal disease.[3,4,8]

VSCs are toxic substances that have been found to damage the collagen and proteoglycan components in connective tissue by cleaving disulfide bonds. This deaggregation of the extracellular matrix allows microbes to permeate the oral mucosa.[1] Studies have found methyl mercaptan, more specifically, to reduce collagen content in fibroblast cultures, suggesting that a similar process may occur in severely inflamed periodontal tissue, with methyl mercaptan playing a modulation role in fibroblast cell metabolism.[1,9] The Halimeter is an instrument used for the detection and measurement of VSCs. The Periotemp is an instrument used to measure the temperature of subgingival areas. "Hot" pockets can be indicative of a disease process involving microbial activity.

Mouthrinse Formulations

A difficulty in formulating a mouthrinse for the treatment of halitosis involves the delicate balance of eliminating the offending microbes, while maintaining the dynamic balance of normal flora, as well as preventing an overgrowth of opportunistic pathogens. In addition, the specific bacterial species and their cooperative interactions responsible for breath malodor have yet to be fully elucidated. The quality of saliva is an active player in this intricate balance. Saliva lubricates and oxygenates the oral cavity as well as aids in digestion, acts as a buffering agent and provides antimicrobial properties to supplement the individual's vast arsenal of immune functions.[7] Any treatment that increases saliva flow and tongue action, including the chewing of fibrous vegetables and sugarless gum, will help decrease malodor. At this stage of oral malodor treatment, for otherwise healthy individuals, the clinical emphasis is on an attempt to freshen the breath by sufficiently decreasing the odoriferous VSCs generated by a variety of microbial populations. This is accomplished in part by mouthrinses containing active ingredients with antiseptic properties.

The oral rinse is a supplement to thorough mechanical cleaning of teeth, gums, other oral tissues and, especially, the tongue dorsum. Most commercial mouthrinses mask odors, which has a short-lived effect, as well as provide antiseptic properties. Prevention of malodor that lasts beyond 30 minutes after rinsing is a result of the antiseptic compounds, but often even these substances do not provide long-lasting effects.[10,11] Mouthrinses are best used before going to bed as their effects are likely to be longer-lasting at this time. Rinsing with water is only minimally helpful, since water has no antiseptic properties and often merely washes away saliva, which does have such properties. "Mouthrinses cannot kill all the offending microbes, most of which survive antiseptic attacks protected under thick layers of plaque and mucus."[2]

Most mouthrinses include alcohol, propylene glycol, methyl salicylates, glycerin, sodium bicarbonate, cresols, bromides, boric acid, surfactants such as sodium lauryl sulfate, sweeteners, flavorings and food colorings. The common active antimicrobial agents areessential oils; phenolic derivatives; hydrogen peroxide; quaternary ammonium compounds; benzalkonium chloride; chlorhexidine; chlorine dioxide; sodium benzoate; sodium perborate; monofluorophosphate; sanguinarine, an alkaloid herbal extract; cetylpyridium chloride; triclosan; delmopinol hydrochloride; fluorides; and zinc salts.

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Adverse Effects

Some generalized irritations to the oral cavity caused by mouthrinse ingredients are desquamation, ulceration, inflammation, gingivitis and petechiae. In addition, any of these substances can be a potential allergen, especially for the atopic patient.[12]

With long-term use, it has been reported that the alcohol in commercial rinses may bring about some adverse effects. It has been reported that ethanol in oral rinses induces painful oral sensations.[13] The most prevalent problem with ethanol is that it can dry the oral tissues. This condition in itself can induce oral malodor, since a critical quantity of saliva, in addition to the saliva quality with its antiseptic components, is necessary to maintain a clean healthy oral condition. A dry mouth is the condition leading to morning breath. While a person is sleeping, the saliva flow is decreased, thereby drying the mouth. Proteinaceous components in the oral cavity, including those in the stagnant saliva (the protein concentration of saliva is 20 times greater than that of carbohydrate), provide a ready supply of substrates for microbial action. Under these conditions, the gram-negative anaerobic population dominates.[3]

A medical condition of dry mouth called xerostomia can be treated with an alcohol-free enzyme mouthwash, specially formulated with three antibacterial enzymes, lysozyme, glucose oxidase and lactoperoxidase; the latter two combine with their substrates to produce the hypothiocyanite ion that inhibits the growth of bacteria. Although clinical evidence for efficacy is limited, the idea of using natural saliva components to treat oral conditions is promising for the future of dental care.[14]

There is some controversy as to whether the use of alcohol rinses are associated with oral cancer.[12,15] The alcohol content of commercial oral rinses varies from 5 percent to 26.9 percent, but most have 5 percent to 7 percent. The recent decision by the FDA states that there is no evidence to support the removal of alcohol from over-the-counter products. However, since there have been reported cases of mouthrinse-induced hypoglycemia and fatal poisoning, especially in children,[16] the ADA Council on Dental Therapeutics has recently voted to require manufacturers of mouth washes that contain greater than 5 percent alcohol and carr the ADA seal of acceptance to place child-safety caps and warning labels on the bottles.[12]

Quaternary Ammonium and Decapinol Rinses

Commercial mouthrinses containing antibacterial quaternary ammonium compounds have been found to be associated with a significant decrease in hydrogen sulfide and methyl mercaptan as compared to a deionized water placebo mouthrinse.[17] This would suggest some degree of benefit as a malodor rinse. Delmopinol HCl (3-(4 propylheptyl)-4-morpholinoethanol hydrochloride) rinse has demonstrated efficacy as a prevention measure against gingivitis in the absence of mechanical plaque control,[18] however there are few if any trials on its effectiveness in controlling halitosis.

Zinc Rinses

Clinical trials conclude that zinc mouthrinses are very effective for reducing oral malodor in some people with good oral health. The zinc rinses (in chloride or citrate form) have been found to significantly reduce oral VSC concentrations for a duration greater than three hours. A zinc mouthrinse performed significantly better than a water rinse in reducing and maintaining VSC levels below the objectionable malodor threshold, when used overnight (10 hours).[1] Other investigations have suggested that zinc mouthwashes counteract the toxicity of volatile sulfur compounds. Zinc ion (Zn^{+2}) is known to play a role in wound healing, by functioning as a prosthetic group in DNA polymerase. After treatment of damaged oral mucosa with a 0.22 percent zinc chloride rinse, tissue permeability was restored to a state similar to that observed in a control group.[1] The zinc ion also functions as an odor inhibitor by preventing disulfide group reduction to thiols and by reaction with the thiol groups in VSCs, thus converting them to non-odorous substances.

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Chlorhexidine Rinses

Chlorhexidine digluconate, useful in decreasing gingivitis and plaque buildup, is an active ingredient in certain ADA-approved commercial mouthrinses. It is one of two mouthrinses shown to reduce gingivitis in long-term clinical trials and appears to be the most effective antiplaque and antigingivitis agent known today.[2,19] It has been found to enhance the gingival healing process following scaling and root planing.[19] Chlorhexidine in tablet form with xylitol and fluoride has been found to work as well as a conventional chlorhexidine rinse in reducing oral plaque.[20] Both tablet and rinse forms used by Military Academy cadets, refraining from mechanical tooth cleaning, worked equally as well to decrease plaque and periodontal index scores, and both were significantly more effective than a sodium fluoride rinse.[21] In a clinical trial[22] comparing six commercial mouthrinses with a dentifrice slurry on oral plaque regrowth found the regrowth (after prophylaxis) to be significantly reduced by a chlorhexidine rinse compared to an oxidizing rinse of peroxyborate, while the latter rinse significantly outperformed all the other rinses with active ingredients of sodium monofluorophosphate, sodium benzoate, cetylpyridium chloride and saline (0.7 percent NaCl). However, chlorhexidine efficacy as a mouthrinse to control halitosis has not been stud-

The antimicrobial action of triclosan involves interference with bacterial synthesis of ribonucleic acid and protein.[30]

ied extensively. More recently, a phenolic compound mouthwash was awarded the ADA Council on Dental Therapeutics' Seal of Acceptance as an aid in controlling plaque and gingivitis, but it has little efficacy as a mouthrinse for controlling chronic halitosis.[10,11,23,24]

The primary side effect of many antiseptics, including chlorhexidine, is discoloration of teeth and tongue; other side effects can include desquamation and painful lesions, but the latter were not found for chlorhexidine rinse with concentrations of less than 0.2 percent.[25-27] Also, the rinse may promote dental calculus increase, ironically, along with a significant gingivitis decrease.[28] An important consideration for long-term use of chlorhexidine rinse is its potential to disrupt the oral microbial balance, causing some resistant strains to flourish, such as *Streptococcus viridans*.[29] Since chlorhexidine is cationic, it may be inactivated with anionic substances such as phosphates, sulfates and anionic detergents inappropriately used (in conjunction with chlorhexidine) as supplementary mouthrinse ingredients. Also, there may be competitive inhibition in the presence of calcium (Ca^{2+}) ions.[26]

The action of chlorhexidine is thought to be due to its disruption of bacterial cell membrane permeability bringing about cell lysis and death. There is an electrical attraction between this cationic antiseptic rinse and the anionic areas on bacterial cell membranes. Studies have demonstrated a longer persistence of activity in the oral cavity for up to as long as 12 hours as compared to other mouthrinse active ingredients, such as cetylpyridium chloride, a cationic surfactant.

Chlorine Dioxide Rinses

Chlorine dioxide (ClO^2), a strong oxidizing agent, has a high redox capacity with compounds containing sulfur. It functions best in neutral pH at a concentration of two parts per million to destroy sulfur-containing compounds by oxidation of sulfide bonds. The oxidizing agent, also used in water disinfection and in food processing equipment sanitization, oxidatively consumes oral substrates containing cysteine and methionine thus preventing production of VSCs. Since chlorine dioxide readily loses its activity, its stability has been prolonged through a "stabilization" process, which converts chlorine dioxide to molecular chlorine dioxide at a low pH. This stabilized chlorine dioxide is a mixture of the oxychlorine species in addition to sodium chlorite. It has been proposed that chlorite ions in mouthrinse products will be converted to chlorine dioxide in the acidic environment of the oral cavity. Another side in this controversy suggests that "stabilized chlorine dioxide" is a solution of sodium chlorite, containing no free chlorine dioxide and sodium chlorite has no known deodorizing ability. However, adequate clinical investigations are needed to more thoroughly evaluate the behavior of these chemical components under different conditions in the oral cavity. More specifically, long-term clinical trials are required to substantiate the use of chlorine dioxide products in the treatment and control of halitosis.

Triclosan Rinses

Triclosan (2,4,4'-trichloro-2'-hydroxydiphenylether) is a broad spectrum nonionic antimicrobial agent. This lipid-soluble substance, which has been studied for more than two decades, has recently been incorporated into oral care products after many years of use in the cosmetics industry. It has been found to be effective against most types of oral cavity bacteria. The antimicrobial action of triclosan involves interference with bacterial synthesis of ribonucleic acid and protein.[30]

There is some evidence in the literature to support the safe use of triclosan oral rinses in the reduction of plaque and gingivitis.[31,32] However, cetylpyridium chloride and chlorhexidine mouthwashes have been found to be more effective for plaque control than a triclosan rinse[33] or a zinc/triclosan rinse.[34] When compared to an ethanol placebo rinse, both triclosan and chlorhexidine oral rinses significantly outperformed the ethanol rinse on gingival and plaque index scores.[35]

Triclosan's antigingivitis effect may be due to a direct anti-inflammatory action.[31] When formulated with the surfactant sodium lauryl sulfate (SLS), triclosan has been reported to lessen the mucosal irritation effects of SLS[36-38] by its analgesic properties.[39]

The efficacy of triclosan is dependent on its concentration[40] and its supplementation with other components of oral rinses and dentifrices.[32] It has been found to be less effective as a plaque inhibitor in vegetable oil solvents.[41] In long-term clinical trials, triclosan in combination with polyvinylmethyl ether/maleic acid, used as a prebrush mouthrinse, demonstrated significant plaque and gingivitis reduction as compared to a placebo rinse.[42,43] Dentifrice studies of triclosan, formulated with silicone, were effective in the reduction of plaque and gingivitis.[44,45] There is speculation that lipid substances that adhere to teeth, gums and other mucosal surfaces, serve as carriers for the antibacterial hydrophobic triclosan, allowing for its slow, continuous emission into saliva.[46] Long-term studies demonstrate only beneficial ecological changes and no induction of triclosan-resistant opportunistic pathogens.[47,48]

A pilot study paper, "The Efficacy of a Combined Zinc and Triclosan Sys-

tem in the Prevention of Oral Malodour," was presented at the Second International World Workshop on Oral Malodour. The results of the study demonstrated that this system had a cumulative effective, with the reduction of malodor increasing with the duration of product use.

Two-Phase Rinses

Two-phase oil-water mouthrinses are being tested to control halitosis. A recent clinical trial[49] reported significant long-term (six-week) reductions in malodor, from the whole mouth and the tongue dorsum posterior, for the two-phase oil-water rinse group as compared to the control group using a commercial rinse. The efficacy is thought to be related to reduction of odor-producing microbes on the tongue dorsum posterior because of a polar attraction between oil droplets and bacterial and oral epithelial cells. The oil-water rinse also contained cetylpyridium chloride, which promotes the adhesion of microbes to oil droplets. However, there was no significant difference between the two groups for volatile sulfur compound levels, bleeding index, gingival index, saliva diamine (putracine and cadaverine) levels and oral microbial levels measured by the rate of oxygen depletion in expectorated sterile milk/saliva samples. In addition, the control mouthrinse decreased plaque more significantly than the two-phase rinse.

Alternative dental health services also suggest the use of chlorophyll oral rinses in addition to spirulina and algae products reported to contain antimicrobial properties.

A clinical trial[27] investigated the effects of a two-phase rinse on the production of volatile sulfide in vivo and in vitro, as well as the efficacy of mouthrinses over a duration greater than three hours. Sixty dental students were divided randomly into three rinse groups: 1) two-phase containing olive oil, essential oils, cetylpyridium chloride 2) chlorhexidine rinse and 3) placebo with the same concentration of food color and sweetener as the other two rinses. Malodor measurements, using the halimeter, the oxygen-depletion and organoleptic tests, taken eight to 10 hours after use the oral rinse use, demonstrated that both the two-phase rinse group and the chlorhexidine rinse group significantly decreased the level of volatile sulfur compounds as compared to the placebo. Both performed significantly better with respect to the placebo group, with the chlorhexidine group performing significantly better than the two-phase group measured by oxygen depletion. In addition, the chlorhexidine group performed significantly better compared to the placebo (but not the two-phase) group on the organoleptic tests. The mechanism of action for the oil-water system has been discovered to be oil adsorption to the hydrophobic sites on bacterial cell membranes. The chlorhexidine worked more effectively in the three assessments.

A short-term two-phase mouthrinse investigation involving 20 healthy male volunteers used a mouthrinse containing an oil phase with olive oil and essential oils and an aqueous phase with cetylpyridium chloride. In comparison to a water rinse control group, an 80 percent reduction of sulfides was observed. In addition, "volatile sulfide and 2-ketobutyrate productions from methionine in a saliva putrefaction system were completely inhibited by the two-phase mouthwash."[8]

Alternative Remedies

The Second International World Workshop on Oral Malodor, held in Belgium, offered an abstract presentation on natural controls for bad breath that concluded that chewing a gum containing tea extracts was useful to control bad breath. Also recommended were natural deodorants such as copper chlorophyll and sodium copper chlorophyllin. Alternative dental health services also suggest the use of chlorophyll oral rinses in addition to spirulina and algae products reported to contain antimicrobial properties.

One antiplaque breath product is a tablet composed of an effervescent active ingredient, a specially treated polymer of silicon dioxide and sodium bicarbonate, the latter of which acts as a buffering agent and mild bacteriocide. A mechanism of action for this complex is reported to involve the adsorption of microbes and other oral organic debris to the silicon dioxide polymer. There is a pilot study in progress to determine the efficacy of the product for the treatment of malodor.

Conclusion

Many of the oral rinses available today are being used for the prevention and/or treatment of oral malodor, but for the chronic bad breath condition, many rinses offer little to no help, and others have been formulated for other purposes.[5] Much more research is required to develop an efficacious mouthrinse for the alleviation of halitosis. The treatment of halitosis is a relatively new field in dentistry and many of the treatments thus far have involved a trial-and-error approach. The knowledge and experience gained so far will facilitate further clinical investigations on this topic and eventually lead to improved diagnostic techniques and treatment [illegible]

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