

## REVIEW ARTICLE

# A review of the current literature on management of halitosis

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**Halitosis is an unpleasant or offensive odour, emanating from the oral cavity. In approximately 80% of all cases, halitosis is caused by microbial degradation of oral organic substrates. Major degradation products are volatile sulphur-containing compounds. In this review, the available management methods of halitosis and their effectiveness and significance are presented and discussed. Undoubtedly, the basic management is mechanically reducing the amount of micro-organisms and substrates in the oral cavity. Masking products are not, and anti-microbial ingredients in oral healthcare products are only temporary effective in reducing micro-organisms or their substrates. Good short-term results were reported with chlorhexidine. Triclosan seems less effective, essential oils and cetylpyridinium chloride are only effective up to 2 or 3 h. Metal ions and oxidizing agents, such as hydrogen peroxide, chlorine dioxide and iminium are active in neutralizing volatile sulphur-containing compounds. Zinc seems to be an effective safe metal at concentrations of at least 1%. The effectiveness of active ingredients in oral healthcare products is dependent on their concentration and above a certain concentration the ingredients can have unpleasant side effects. Tonsillectomy might be indicated if (i) all other causes of halitosis are managed properly; (ii) halitosis still persists and (iii) crypts in tonsils are found to contain malodorous substrates.**

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## Introduction

Halitosis is an unpleasant or offensive odour emanating from the oral cavity, leading to discomfort and psycho-

social embarrassment. In approximately 80% of all cases, halitosis is caused by oral conditions, defined as oral malodour (Miyazaki *et al*, 1995; Delanghe *et al*, 1997). There seems consensus that oral malodour results from tongue coating, periodontal disease, periimplant disease, deep carious lesions, exposed necrotic tooth pulps, pericoronitis, mucosal ulcerations, healing wounds, impacted food or debris, imperfect dental restorations, unclean dentures and factors causing decreased salivary flow rate (Yaegaki and Sanada, 1992a,b; Morita and Wang, 2001a,b; Morita *et al*, 2001; Kleinberg *et al*, 2002; Hinode *et al*, 2003; van Steenberghe, 2004; Verran, 2005; Liu *et al*, 2006). Undoubtedly, the tongue is a major site of oral malodour production, whereas periodontal disease and other factors seem only a fraction of the overall problem (Bosy *et al*, 1994; Stamou *et al*, 2005; Rosenberg, 2006). The oral malodour arises from microbial degradation of organic substrates present in saliva, crevicular fluid, oral soft tissues and retained debris. Major microbial degradation products are volatile sulphur-containing compounds (Tonzetich, 1977). Non-oral aetiologies of halitosis include disturbances of the upper and lower respiratory tract, some systemic diseases, metabolic disorders, medications and carcinomas (Tangerman, 2002). The three primary methods for measuring halitosis are organoleptic measurement, gas chromatography and sulphide monitoring.

Before halitosis may be managed effectively, an accurate diagnosis must be achieved. An accurate diagnosis depends on analysis of data collected from patient history and physical examination. The patient history should contain main complaint, medical, dental and halitosis history, information about diet and habits, and third part confirmation confirming an objective basis to the complaint. Parts of the physical examination are extraoral examination, intraoral examination with special attention paid to the tongue and the periodontal tissues, and upper respiratory tract examination. After taking history and proper physical examination, halitosis can be classified into categories of genuine (oral or extraoral) halitosis, pseudo-halitosis and halitophobia

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(Murata *et al*, 2002). Pseudo-halitosis is obviously not perceived by others, although the patient stubbornly complains of its existence. Halitophobia is diagnosed if no physical or social evidence exists suggesting that halitosis is present, whereas the patient persists in believing that he or she has halitosis. Pseudo-halitosis and halitophobia are further left out of consideration.

In this review, the available management methods of genuine halitosis, their effectiveness and significance for both clinicians and patients are presented and discussed. The available methods leading to lowering of oral malodour level can be divided into: usage of masking products, mechanical reduction of micro-organisms and their substrates, chemical reduction of micro-organisms, and chemical neutralization of odorous compounds, including volatile sulphur-containing compounds. Patients diagnosed as suffering from non-oral halitosis should be referred to a clinic for otorhinolaryngology or internal medicine for appropriate treatment.

### Masking products

Usage of masking products only is never a real management of halitosis. Nevertheless, some commercially available products, such as mints, toothpastes, mouthrinses, sprays and chewing gums, attempt to control halitosis with pleasant flavours and fragrances. Mints and chewing gum without active ingredients had no significant effect on tongue dorsum malodour 3 h after use (Greenstein *et al*, 1997; Yaegaki *et al*, 2002). After 3 h, similar organoleptic and sulphide monitor scores were observed for subjects who chewed either a menthol-containing gum or a neutral unsweetened gum or no gum. A short masking effect appeared only with the menthol-containing gum and may be the result of the menthol (Reingewirtz *et al*, 1999).

### Mechanical reduction of micro-organisms and their substrates

Mechanical reduction of micro-organisms and their substrates can be achieved by taking a solid breakfast, improving hyposalivation, using chewing gum, brushing the teeth, flossing, using toothpicks, tongue cleaning and professional oral health care.

#### *Breakfast, improving hyposalivation and chewing gum*

Fasting, during longer periods or during the night, was suggested as being a physiological cause of temporary halitosis, so-called bad morning breath, resulting from stagnation of epithelial and food debris on the soft oral tissues. Passage of solid food over the surface of the tongue could remove the tongue coating (Kleinberg and Westbay, 1992). Subjects who exhibited early morning halitosis, showed significant reductions of hydrogen sulphide by 60% and methyl mercaptan concentrations by 83% 1 h after breakfast, without any oral cleaning procedures (Tonzetich and Ng, 1976). Subjects who were free of caries, periodontal disease and visible tongue coating, demonstrated chromatographically substantially reduced concentrations of volatile

sulphur-containing compounds in morning breath after consumption of a hard, dry bread roll, without any oral cleaning procedures (Suarez *et al*, 2000).

Extreme hyposalivation increased the production of volatile sulphur-containing compounds (Kleinberg *et al*, 2002; Koshimune *et al*, 2003). However, between a group of healthy patients with, and a control group without halitosis, no differences in salivary flow rate were found (Oho *et al*, 2001). In an earlier study, variations in the level of unstimulated saliva could not explain the variance in volatile sulphur-containing compounds in a group of subjects with bad breath (Rosenberg *et al*, 1991). A lower level of saliva during the night is physiological. The level of saliva may be lowered as well by mouth breathing or snoring. The effect, bad morning breath, may be quite easily treated by salivary stimulation. Salivary stimulation by eating breakfast, chewing or consuming acid food and saliva substitutes diminished the effect of hyposalivation (Norris *et al*, 1984; Mackie and Pangborn, 1990; Kleinberg and Westbay, 1992; Edgar *et al*, 1994; Bots *et al*, 2004).

Chewing gum may have a mechanical role in stimulating the salivary flow and thus cleaning surfaces of teeth (Edgar *et al*, 1994; Reingewirtz *et al*, 1999; Bots *et al*, 2004). However, by cysteine challenge testing was demonstrated that chewing of a gum without any active ingredient reduced halitosis only modestly (Wåler, 1997a). The basis of cysteine challenge testing is rooted in two fundamental aspects of the halitosis process. When broken down by oral bacteria, cysteine produces hydrogen sulphide. This volatile product, when ionized, contributes to the lowering of the oxidation–reduction potential, which is the primary physico-chemical factor favouring growth of Gram-negative oral anaerobes (Kleinberg and Codipilly, 2002). Sugarless chewing gum had no effect on volatile sulphur-containing compounds concentrations (Yaegaki *et al*, 2002).

#### *Brushing the teeth, flossing, using toothpicks*

Mechanical cleaning of teeth, such as brushing the teeth, flossing and using toothpicks reduced the amount of oral bacteria and substrates, thereby presumably reducing oral malodour (Coil *et al*, 2002; Tanaka *et al*, 2003). However, clinical studies revealed that brushing the teeth exclusively was not very effective in reducing oral malodour scores (Yaegaki and Sanada, 1992c; Kleinberg and Codipilly, 2002). Furthermore, in subjects free of caries, periodontal disease and tongue coating, exclusively brushing the teeth had no appreciable influence on the concentration of volatile sulphur-containing compounds in morning breath, when compared with no brushing and rinsing the mouth with water (Suarez *et al*, 2000).

#### *Tongue cleaning*

Various instruments can be applied to the tongue and by gentle pressure the majority of the tongue coating can be scraped off (Yaegaki *et al*, 2002). Brushing the dorsum of the tongue with a toothpaste was more effective than brushing the teeth. Levels of volatile sulphur-containing

compounds could be reduced for at least 1 h by brushing the teeth and the tongue, and then rinsing the mouth with water (Tonzetich, 1971, 1978; Tonzetich and Ng, 1976). Other studies found a relationship between tongue cleaning and the reduction of both organoleptic scores and levels of volatile sulphur-containing compounds (Bosy *et al*, 1994; Suarez *et al*, 2000; Seemann *et al*, 2001). In patients with high levels of oral malodour, a regular toothbrush was statistically significantly less effective in tongue cleaning than a device that brushed and scraped, or a scraper. Because of the limited duration of the effect, the efficacy remained questionable (Seemann *et al*, 2001). Scraping the tongue after cysteine challenge testing reduced halitosis only modestly, but brushing the tongue dorsum was remarkably effective (Kleinberg and Codipilly, 2002). Two weeks of tongue brushing or scraping by a group of patients free of periodontitis resulted in negligible reductions in bacteria on the tongue, whereas the amount of tongue coating decreased significantly. Therefore, tongue cleaning seems to reduce the substrates for putrefaction, rather than the bacterial load (Quirynen *et al*, 2004).

#### *Professional oral health care*

Professional oral health care was delivered by dental hygienists once a week to a group of elderly patients, needing daily nursing care. The dental hygienists cleaned the teeth, the dentures, the buccal mucosa and the tongue. They used hand scalers, an electric toothbrush, an interdental brush and a sponge brush. A control group received only denture cleaning and swabbing the oral cavity with a sponge brush. The professional care reduced the levels of methyl mercaptan significantly (Adachi *et al*, 2002). Patients with periodontitis underwent a one-stage full-mouth disinfection, combining scaling and root planing of teeth with the application of chlorhexidine, or consecutive root planings per quadrant at a 1- to 2-week interval. The full-mouth disinfection resulted in a faster and additional reduction in organoleptic scores, even after 2 months. However, the levels of volatile sulphur-containing compounds remained unchanged in both groups (Quirynen *et al*, 1998).

### **Chemical reduction of micro-organisms**

Toothpastes and mouthrinses with antimicrobial properties can reduce oral malodour by reducing the number of micro-organisms chemically (Brading and Marsh, 2003). Often used active ingredients in these products are chlorhexidine, triclosan, essential oils and cetylpyridinium chloride. Other effective chemical agents are allylpyrocatechol, L-trifluoromethionine and dehydroascorbic acid.

#### *Chlorhexidine*

Chlorhexidine has a bactericidal and bacteriostatic antiplaque effect as a result of the dicationic nature of the chlorhexidine molecule (Addy and Moran, 1997; Jones, 1997). In several studies, a 0.2% chlorhexidine

mouthrinse produced significant reductions in volatile sulphur-containing compounds levels and in organoleptic scores (Rosenberg *et al*, 1991; van Steenberghe *et al*, 2001; Carvalho *et al*, 2004). Similar results with 0.12% chlorhexidine-(di)gluconate were reported in combination with teeth and tongue brushing (Bosy *et al*, 1994; De Boever and Loesche, 1995). A mouthrinse containing 0.025% chlorhexidine was only moderate effective, whereas a concentration of 0.2% was much more effective and even showed a tendency to improved effect during 3 h (Young *et al*, 2003a). In adolescents with halitosis, organoleptic scores were significantly reduced after tongue cleaning with a hard toothbrush, wetted with 0.12% chlorhexidine gluconate. It was not possible to discriminate between the influence of the mechanical cleaning and the chlorhexidine (Cicek *et al*, 2003). Therefore, it is uncertain if the results were due to chlorhexidine, to cleaning of the teeth and the tongue, or to both. Chlorhexidine has the side effects of tooth staining and an unpleasant taste at concentrations from at least 0.2% (Jones, 1997; Young *et al*, 2003a). Tooth staining seems to be the result of a local precipitation reaction between tooth-bound chlorhexidine and chromogens found within foodstuffs and drinks. Furthermore, the activity of chlorhexidine is reduced in the presence of anionic agents, found in certain types of toothpaste (Jones, 1997). Chlorhexidine concentrations in mouthrinses till 0.12% and mucosa exposure not exceeding 1 min twice a day, seem the best procedure to protect tastes in clinical practice (Marinone and Savoldi, 2000).

#### *Triclosan*

Lipid-soluble triclosan, 2,4,4'-trichloro-2'-hydroxydiphenylether, is the most widely used antibacterial and antiplaque agent in oral care products. It is insoluble in water and has to be solubilized in organic solvents or detergents. Triclosan has a broad spectrum of antimicrobial activity against bacteria, especially the Gram-negative anaerobic species (Brading *et al*, 2004). The antimalodour effect was not maintained when oils, oily substances and uncharged detergents were used as solubilizers (Young *et al*, 2002). A toothpaste containing 0.3% triclosan, 2.0% of a copolymer of polyvinyl methyl ether maleic acid and 0.243% sodium fluoride has been shown in double-blind clinical trials to be significantly better than a placebo toothpaste in reducing organoleptic scores up to 12 h. However, the benefit of triclosan was relatively small, when compared with the placebo toothpaste. The copolymer is claimed to improve the retention of the triclosan within the oral cavity (Niles *et al*, 1999; Sharma *et al*, 1999). Addition of a special grade of silica did not further improve the efficacy of the toothpaste in reducing organoleptic scores (Sharma *et al*, 2002). The same toothpaste was associated with a significant decrease of hydrogen sulphide-producing bacteria (Sreenivasan, 2003; Vazquez *et al*, 2003). An increase of volatile sulphur-containing compounds, occurring during the development of experimental gingivitis, was reduced by toothpastes containing 0.3% triclosan (Nogueira-Filho *et al*, 2002). Raising the

level of triclosan from 0.2% to 0.3% in a calcium carbonate-based system, was suggested enhancing its activity (Brading *et al*, 2004).

#### *Essential oils*

In the history of mankind, the Egyptians made extensive use of essential oils for cosmetics as well as medicinal purposes. Among others the products were used in the embalming process. During the following periods, the medicinal properties of essential oils were applied for several health problems. Essential oils are odorous, volatile products of plant secondary metabolism, many of them possessing strong antimicrobial properties (Kalemba and Kunicka, 2003). The short-term effect of a mouthrinse containing essential oils and menthol was evaluated in comparison with a placebo. Based on its masking effect, the experimental mouthrinse was more effective against oral malodour than the placebo during 0.5 h. At 1 h and up to 3 h, the greater effectiveness was maintained by a sustained reduction in the levels of odorigenic bacteria (Pitts *et al*, 1981, 1983). In clinical trials, an essential oil-containing toothpaste as well as an essential oil-containing toothpaste with addition of 1% zinc citrate, were significantly and equally more effective than a control toothpaste in reducing oral malodour from 1.5 to 2 h (Olshan *et al*, 2000).

#### *Cetylpyridinium chloride*

Quaternary ammonium compounds, such as benzalkonium chloride and cetylpyridinium chloride, inhibit bacterial growth (Xiong *et al*, 1998). A chromatographically determined significant reduction in both the hydrogen sulphide and methyl mercaptan levels of subjects with good oral health was reached with a mouthrinse, containing a quaternary ammonium compound and alcohol (Solis-Gaffar *et al*, 1975). Daily usage of a two-phase oil–water mouthrinse containing cetylpyridinium chloride reduced oral malodour over a 6-week period, when compared with a similar mouthrinse without cetylpyridinium chloride (Kozlovsky *et al*, 1996). A similar cetylpyridinium containing mouthrinse was effective with an 80% reduction of volatile sulphur-containing compounds during 3.5 h (Yaegaki and Sanada, 1992c). Using cysteine challenge testing, a mouthrinse containing cetylpyridinium plus domiphen bromide was minimally effective in reducing halitosis (Kleinberg and Codipilly, 2002). Also using cysteine challenge testing, a mouthrinse containing 0.025% cetylpyridinium was not more effective than water, whereas a concentration of 0.2% was only moderately effective (Young *et al*, 2003a).

#### *Allylpyrocatechol*

Betel quid, composed of *Piper betel* leaves or inflorescences, fresh areca fruit and slaked lime paste, is a natural masticator in many countries. Tobacco can be added to the mixture, but betel leaves are also chewed exclusively. Among others, it is used to remove halitosis (Wang *et al*, 2001; Ramji *et al*, 2002). However, epidemiological studies showed that betel quid chewing is

closely related to some oral mucosal lesions, such as oral submucous fibrosis, oral leukoplakia and oral cancer (Jeng *et al*, 2001; Avon, 2004). Arecoline and safrole are thought to be the major toxic ingredients in betel quid (Shieh *et al*, 2003). Study results exhibited marked depression of the volatility of methyl mercaptan by betel quid and by a mixture of areca fruit and slaked lime paste. The depression was more marked when increasing amounts of slaked lime paste were added or when the slaked lime paste was replaced with alkaline salts (Wang *et al*, 2001). A bioassay-guided fractionation yielded allylpyrocatechol as the major active principle. This non-toxic product showed promising antimicrobial activity against obligate anaerobes (Ramji *et al*, 2002).

#### *L-Trifluoromethionine*

Methyl mercaptan arises from the bacterial metabolism of methionine. It was shown with an *in vitro* study that the growth of *Porphyromonas gingivalis*, a periodontal micro-organism that produces large amounts of mercaptan, was strongly inhibited by L-trifluoromethionine, a fluorinated derivative of methionine (Yoshimura *et al*, 2002).

#### *Dehydroascorbic acid*

Full-strength oxidizing lozenges were effective in reducing tongue malodour over a period of 3 h (Greenstein *et al*, 1997). The effect may be due to the activity of dehydroascorbic acid, generated by peroxide-mediated oxidation of ascorbate present in the lozenges.

### **Chemical neutralization of odorous compounds**

Toothpastes, mouthrinses, lozenges and other products can reduce halitosis by chemically neutralizing odorous compounds, including volatile sulphur-containing compounds. Often used active ingredients of these products are metal ions and oxidizing agents. Metals, such as zinc, sodium, stannous and magnesium are thought to interact with sulphur. The interaction forms insoluble sulphides. The mechanism proposed is that metal ions oxidize the thiol groups in the precursors of volatile sulphur-containing compounds (Tonzetich, 1978; Ng and Tonzetich, 1984). However, no positive correlation was found between metal ions affinity for sulphur and their inhibiting effect on volatile sulphur-containing compounds (Wåler, 1997b). Oxidizing agents might reduce halitosis by reducing conditions necessary for metabolizing sulphur-containing amino acids to volatile sulphur-containing compounds.

#### *Zinc*

Mouthrinses containing zinc were effective in reducing oral malodour, as registered by the usual measurement methods (Schmidt and Tarbet, 1978; Tonzetich, 1978). Zinc has to be present in a specific quantity. The addition of 0.5 mg zinc acetate to a mouthrinse and a chewing gum showed no significant effect, but the addition of 2 mg resulted in significant reductions of

45% of volatile sulphur-containing compounds levels (Wåler, 1997a). Using cysteine challenge testing, a mouthrinse containing zinc chloride was effective in reducing halitosis, depending on the concentration. At a concentration of 12 mM zinc, the effectiveness was more pronounced and prolonged than at a concentration of 3 mM (Kleinberg and Codipilly, 2002). A mouthrinse containing 1% zinc was most effective 1 h after use, but was still very effective after 3 h. The mouthrinse had a somewhat unpleasant taste, whereas a 0.1% concentration was found acceptable, but had only a minor effect. The unpleasant taste may be overcome in commercial products by masking with other ingredients (Young *et al*, 2003a).

#### *Sodium bicarbonate*

There is a long tradition of using sodium bicarbonate in oral cleaning in Japan. Also in North America, many people like to use sodium bicarbonate to clean their teeth. The popular name of this product is baking soda. The effectiveness of toothpastes containing sodium bicarbonate in reducing oral malodour was indicated subjectively and also organoleptically and chromatographically in reducing the amounts of volatile sulphur-containing compounds (Brunette, 1996). Toothpastes containing 20% or more sodium bicarbonate had a significant malodour-reducing effect for time periods up to 3 h (Brunette *et al*, 1998). Additional studies are needed to determine how sodium bicarbonate might be applied most effectively, for instance in toothpaste or mouthrinse. Furthermore, studies are needed to find out the working mechanism of sodium bicarbonate. As yet, it is not clarified if the effect is real bactericidal or a transformation of volatile sulphur-containing components to a non-malodorous form.

#### *Stannous*

A toothpaste-containing stannous fluoride was more effective than water, 8 h after tooth brushing, but the patients still suffered from halitosis (Gerlach *et al*, 1998). Toothpaste containing stannous fluoride and amine fluoride showed only minor changes in volatile sulphur-containing compounds in morning breath of students who refrained from oral hygiene procedures (Quirynen *et al*, 2002).

#### *Magnesium*

Epsom Salt<sup>®</sup>, an agent originally developed in 1695 and derived from a well in Epsom, England, is used as a cathartic in patients with impaired renal function or treating eclampsia of pregnancy (Morris *et al*, 1987; Nordt *et al*, 1996). It contains almost 100% magnesium sulphate. Toxicity is uncommon in healthy subjects at doses of around 10 g day<sup>-1</sup>. Minor elevation of serum magnesium, is characterized by nausea, headache, flushing, warmth and lightheadedness. At higher doses the cardiovascular, respiratory and neuromuscular systems are affected. Magnesium in serum has the risk of hypermagnesaemia. In large doses, magnesium acts like curare (Ferdinandus *et al*, 1981). In rare cases, people are using Epsom Salt<sup>®</sup> as a gargle for halitosis. A case

was reported of severe hypermagnesaemia, following chronic gargling with Epsom Salt<sup>®</sup>, which resulted in coma, cardiopulmonary arrest, and finally the death of the patient (Birrer *et al*, 2002).

#### *Hydrogen peroxide*

The potential of hydrogen peroxide for reducing the levels of salivary thiol precursors of oral malodour was investigated in 10 volunteers. The mean reduction by 1-min tooth brushing with a toothpaste containing 0.67% hydrogen peroxide and 5.48% sodium bicarbonate was 59% 0.5 h after application. However, it was not possible to discriminate between the influence of hydrogen peroxide and of sodium bicarbonate. Other studies revealed that sodium bicarbonate is not or only minimally active at concentrations below 20% (Grigor and Roberts, 1992; Brunette *et al*, 1998). In subjects free of caries, periodontal disease and visible tongue coating, mouth rinsing with 3% hydrogen peroxide produced reductions of up to 90% of oral volatile sulphur-containing compounds in morning breath for 8 h, measured chromatographically (Suarez *et al*, 2000).

#### *Chlorine dioxide*

Chlorine dioxide (ClO<sub>2</sub>) has the power to oxidize the amino acids methionine and cysteine, both precursors of volatile sulphur-containing compounds (Lynch *et al*, 1997). Using a liquid-air spray device, halitosis patients were treated with professional cleaning and irrigation of all soft tissues in the mouth with aqueous ClO<sub>2</sub>. The clinical results were very good, but it was impossible to discriminate between the effect of professional cleaning and the ClO<sub>2</sub> (Richter, 1996). One double-blind, crossover study demonstrated that a single use of a ClO<sub>2</sub>-containing mouthrinse slightly reduced oral malodour in patients with slightly unpleasant organoleptic scores (Frascella *et al*, 1998). A randomized-controlled, double-blind, parallel group study in similar patients revealed that the same mouthrinse significantly reduced volatile sulphur-containing compounds concentrations in mouth air for at least 8 h post rinsing (Frascella *et al*, 2000). Using cysteine challenge testing, the effectiveness of a mouthrinse containing 1.0% sodium chlorite (NaClO<sub>2</sub>) was more pronounced and prolonged than at a concentration of 0.1% (Kleinberg and Codipilly, 2002).

#### *Iminium*

Sanguinarine has been demonstrated to be effective in chemically neutralizing volatile sulphur-containing compounds, based on its unique chemical iminium structure. Iminium is a non-metal oxidation catalyst, which, at physiological acidity levels, is able to neutralize cysteine as well as hydrogen sulphide and methyl mercaptan (Boulware and Southard, 1984).

#### **Effective combinations of agents**

If different halitosis-reducing agents and ingredients operate by different mechanisms, it is conceivable that combinations may provide an enhanced or synergistic

effect. Some combinations have demonstrated enhanced or synergistic effectiveness in clinical trials.

#### Chlorhexidine and zinc

A chlorhexidine and zinc mouthrinse had a strong effect on volatile sulphur-containing compounds and was effective for at least 9 h. Control rinses with chlorhexidine or zinc alone had a respectively moderate and strong effect for 1 h, but these effects diminished with time, respectively, fast and slightly (Young *et al*, 2003b).

#### Cetylpyridinium chloride and zinc ions

A cetylpyridinium chloride and zinc mouthrinse had a good synergistic effect on volatile sulphur-containing compounds levels after 1 h, but minimal above the effect of zinc alone (Young *et al*, 2003b).

#### Chlorhexidine, cetylpyridinium chloride and zinc

A solution containing chlorhexidine, cetylpyridinium chloride and zinc lactate, was more efficient in reducing organoleptic scores and levels of volatile sulphur-containing compounds than a placebo mouthrinse (van Steenberghe *et al*, 2001; Quirynen *et al*, 2002; Roldán *et al*, 2003). The effectiveness of this solution was confirmed in a double-blind placebo-controlled study (Winkel *et al*, 2003).

#### Sodium and zinc

The addition of 2% zinc to sodium bicarbonate containing toothpastes diminished chromatographic measurements significantly after 3 h (Brunette *et al*, 1998). Using cysteine challenge testing, a mouthrinse freshly combining 0.1% NaClO<sub>2</sub> and 6 nM zinc chloride, was much more effective when compared to separate mouthrinses with 0.1% NaClO<sub>2</sub> or 6 nM zinc chloride. If the agents were combined and left for 4 days, the effectiveness was drastically reduced and further deterioration continued with time (Kleinberg and Codipilly, 2002).

#### Iminium and zinc

Sanguinarine, containing iminium, in combination with zinc was 67% more effective in reducing volatile sulphur-containing compounds from incubated saliva than zinc alone (Boulware and Southard, 1984).

#### Comparison of different (combinations of) agents

The results of studies on the effectiveness of oral healthcare products containing ingredients against halitosis are controversial and sometimes contradictory. Ten relevant studies have been carried out to compare the effect of several products (Rosenberg *et al*, 1992; Kozlovsky *et al*, 1996; Gerlach *et al*, 1998; van Steenberghe *et al*, 2001; Young *et al*, 2001; Borden *et al*, 2002; Quirynen *et al*, 2002; Rösing *et al*, 2002; Carvalho *et al*, 2004; Roldán *et al*, 2004). The results of these studies are summarized in Table 1.

#### Non-oral management

Reports on management of non-oral aetiologies are very scarce. Tonsillectomy is often cited as an indication for

**Table 1** Results of ten relevant studies comparing the effect of several products

Reference	Result
Gerlach <i>et al</i> (1998)	Sn <sup>2+</sup> > Na <sup>+</sup> /pyrophosphate Sn <sup>2+</sup> > Na <sup>+</sup> /triclosan/copolymer
Young <i>et al</i> (2001)	Cu <sup>2+</sup> > Sn <sup>2+</sup> > Zn <sup>2+</sup>
Borden <i>et al</i> (2002)	CPC > EO CPC > ClO <sub>2</sub> /Zn <sup>2+</sup>
Rösing <i>et al</i> (2002)	Zn <sup>2+</sup> > herbs Zn <sup>2+</sup> > triclosan Zn <sup>2+</sup> > Na <sup>+</sup> /triclosan
Rosenberg <i>et al</i> (1992)	CPC/EO = 0.2%CHX
Kozlovsky <i>et al</i> (1996)	CPC/EO > EO
Carvalho <i>et al</i> (2004)	0.2%CHX > 0.12%CHX > triclosan = EO > CPC
van Steenberghe <i>et al</i> (2001)	CHX/CPC/Zn <sup>2+</sup> > 0.2%CHX/Alc CHX/CPC/Zn <sup>2+</sup> = 0.12%CHX/Na <sup>+</sup>
Quirynen <i>et al</i> (2002)	CHX/CPC/Zn <sup>2+</sup> > 0.2%CHX/Alc = Am <sup>+</sup> /Sn <sup>2+</sup>
Roldán <i>et al</i> (2004)	CHX/CPC/Zn <sup>2+</sup> > 0.12%CHX CHX/CPC/Zn <sup>2+</sup> > 0.12%CHX/Alc CHX/CPC/Zn <sup>2+</sup> > 0.12%CHX/CPC CHX/CPC/Zn <sup>2+</sup> > 0.12%CHX/NA <sup>+</sup>

CHX, chlorhexidine; CPC, cetylpyridinium chloride; EO, essential oils; ClO<sub>2</sub>, chlorine dioxide; Alc, alcohol; Sn<sup>2+</sup>, stannous; Na<sup>+</sup>, sodium; Zn<sup>2+</sup>, zinc; Cu<sup>2+</sup>, cupric; Am<sup>+</sup>, amine; /, in combination with; >, effect significantly better than ...; =, effect not statistically significant different from ....

managing halitosis, though there are no clinical studies supporting this treatment. Only if other causes of halitosis are managed properly and halitosis still persists, and if crypts in tonsils are found to contain malodorous substrates, tonsillectomy may be indicated (Darrow and Siemens, 2002). Clinical studies are exclusively reported on *Helicobacter pylori* infection, the main factor of inflammatory and ulcerative changes in the gastric mucosa (Hoshi *et al*, 2002). One report is presented on management of malodorous intestinal gases by *Escherichia coli* (Henker *et al*, 2001).

#### Eradication of *Helicobacter pylori*

If clinical examination in 260 halitosis patients did not reveal any cause, a C<sub>13</sub>-urea test for detecting *H. pylori* was carried out. Twenty-one tests were performed and seven (33.3%) were positive. This percentage was similar to the percentage of positive tests, found in the 'normal' European population. Three patients started a therapy of amoxicillin, metronidazole and omeprazole. However, none of them noticed a decrease of halitosis (Delanghe *et al*, 1997).

Omeprazole and amoxicillin significantly reduced sulphide monitor and organoleptic scores in about 80% of *H. pylori*-positive dyspeptic patients, whereas mouth rinsing with chlorhexidine failed. The remaining 20% of patients were positively treated by omeprazole, amoxicillin and clarithromycin. Unfortunately, these patients were not examined for intraoral causes of halitosis (Ierardi *et al*, 1998).

In children with *H. pylori* infection, symptoms of halitosis were assessed by a questionnaire. After 6 weeks therapy by lansoprazole, amoxicillin and clarithromycin, the halitosis scores were improved significantly.

Eradication of bacteria was achieved in only 56% of children (Shashidhar *et al*, 2000).

*Helicobacter pylori*-positive patients, who showed no organic lesions on endoscopic examination and no atrophy of the gastric mucosa histopathologically, received omeprazole, amoxicillin and clarithromycin. Endoscopic examination was carried out before and 4–6 weeks after therapy, and halitosis was investigated by a questionnaire. Patients and their relatives were questioned. The patients with confirmed *H. pylori* eradication (74%), reported halitosis reduced from 61% to 3%. Again, patients were not examined for intraoral causes of halitosis (Serin *et al*, 2003).

#### *Escherichia coli*

A girl with increased formation of malodorous intestinal gases was successfully treated with a suspension of living non-pathogenic bacteria *E. coli*. The concept of this treatment is to re-colonize the intestinal tract with normal or other intestinal bacteria and therefore suppress those contributing to the formation of malodorous gases (Henker *et al*, 2001).

## Discussion

The American Dental Association has established Acceptance Program Guidelines applying to products designed for managing oral malodour of non-systemic origin (American Dental Association, 2003; Wozniak, 2005). Products considered are active chemical agents as well as mechanical means. Regarding safety and efficacy the guidelines require:

- clinical study of oral soft tissues and teeth;
- monitoring oral flora for the development of opportunistic and pathogenic organisms during a 6-month period obtaining data at baseline, 3 weeks and 6 months, unless the product has already been used for plaque and gingivitis control or whose active ingredient is generally recognized as safe;
- assessment of gingival inflammation with an appropriate index;
- examination of pathological conditions, such as allergic reaction, oral ulceration, candidiasis and secondary infections;
- examination of effect on hard tooth tissues and restorative materials, such as staining, shade alteration and loss of structure;
- assessment of possible toxic or adverse effects;
- patient reports of any changes in taste, saliva flow, burning sensation, xerostomia or other characteristics;
- two independent 3-week clinical studies utilizing an appropriate placebo control;
- crossover or parallel group study design;
- double-blinded assessments;
- study population of individuals from 21 to 65 years of age with intrinsic oral malodour of oral origin;
- exclusion of subjects with advanced periodontitis and subjects who smoke or wear oral appliances;

- oral malodour measurements at a minimum of two appropriate time periods after baseline during a 3-week test period;
- organoleptic examination by two trained and calibrated odour judges or measurement of volatile sulphur-containing compounds using gas chromatography or sulphide monitors;
- evidence of significant reductions in oral malodour of the product *vs* the placebo control;
- evidence that at least 80% of the subjects demonstrate a reduction to questionable or no oral malodour at some time during the management period and
- evidence that microbial resistance does not occur.

None of the studies mentioned in this review meet all ADA-guidelines. Any future study should meet these requirements in order to provide evidence-based results. Nevertheless, within the limitations of the studies reviewed, some careful conclusions can be drawn.

Undoubtedly, the basic management of halitosis is mechanically reducing the amount of micro-organisms and substrates in the oral cavity, with a special attention to the tongue. For subjects with healthy oral conditions and only early morning halitosis, taking a solid breakfast is an effective natural mechanical method.

Masking products are not effective in reducing micro-organisms or their substrates and in neutralizing odorous compounds. With some masking products, such as menthol and mint, only a short-term masking effect of < 2 h of halitosis can be expected.

Chemical reduction of micro-organisms by antimicrobial ingredients in oral healthcare products is only temporary effective. The effectiveness of the ingredients is dependent on their concentration and above a certain concentration the ingredients may have unpleasant side effects. Good short-term results were reported with chlorhexidine. Triclosan seems less effective. Essential oils and cetylpyridinium chloride are only effective for short-time periods of up to 2 or 3 h. Allylpyrocatechol, L-trifluoromethionine and dehydroascorbic acid could be promising antibacterial agents. No clinical trials were found comparing the effect of antimicrobial ingredients in oral healthcare products with the effect of mechanically reducing bacteria and substrates. Chemical ingredients of oral healthcare products seem most effective when applied in addition to instructions in oral hygiene and professional mechanical cleaning (Quirynen *et al*, 2005; Roldán *et al*, 2005).

Metal ions and oxidizing agents are active ingredients of oral healthcare products for chemically neutralizing volatile sulphur-containing compounds. Again, the effectiveness of the active ingredients is dependent on their concentration and above a certain concentration the ingredients can have unpleasant side effects. Zinc seems to be an effective safe metal at concentrations of at least 1%. Oxidizing agents, such as hydrogen peroxide, ClO<sub>2</sub> and iminium are reported to be effective for longer periods of time in patients with slightly unpleasant halitosis. These agents could be used in addition to daily mechanical cleaning in order to reach a day-long effect.

Relevant enhanced or synergistic effects of combinations of chemical agents and ingredients in oral health-care products were demonstrated for:

- chlorhexidine–zinc;
- chlorhexidine–cetylpyridinium chloride–zinc;
- sodium–zinc (exclusively when a fresh mixture is used) and
- iminium–zinc.

Several studies comparing different products showed some products to have superior results to others. Effective products are for instance chlorhexidine and the combination chlorhexidine–cetylpyridinium chloride–zinc. However, randomized, double-blind, placebo-controlled clinical trials are needed to reveal the safest and most effective (combinations of) management and (combinations of) chemical active agents and ingredients and their concentrations.

Although halitosis has often been reported as a symptom related to *H. pylori* infection, it still has to be clarified whether *H. pylori* is inducing halitosis acting alone or together with oral bacteria or even not at all. Reduction or disappearance of halitosis in *H. pylori*-positive patients after bacterial eradication therapy, could be the result of simultaneous eradication of malodour-producing oral bacteria. Future research in *H. pylori*- and halitosis-positive patients should examine the effect of proper management of the oral causes of halitosis.

Managing halitosis, tonsillectomy might be indicated if all other causes of halitosis are managed properly, halitosis still persists and crypts in tonsils are found to contain malodorous substrates.

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