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Alternative therapies in controlling oral malodour: a systematic review

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ALTERNATIVE THERAPIES IN CONTROLLING ORAL MALODOUR: A SYSTEMATIC REVIEW

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ABSTRACT

Focused question: Is there a role for alternative therapies in controlling intra-oral halitosis? Treatments other than tongue cleaning and anti-halitosis products containing zinc, chlorhexidine and cetylpyridinium chloride were considered as alternative therapies.

Materials and Methods: Four databases were searched (PubMed, EMBASE, Web of Science and The Cochrane Library). Inclusion criteria were: examination of alternative halitosis therapies, study population with oral malodour, a (negative or positive) control group and evaluation of the breath odour via organoleptic and/or instrumental assessment. Data were extracted for descriptive analysis.

Results: The screening of 7656 titles led to the inclusion of 26 articles. Analysis showed heterogeneity concerning the population of interest (from cysteine-induced to genuine halitosis), the examined treatment and the reported outcomes. This made a meta-analysis impossible.

Essential oils, fluoride containing products and herbal substances were the most studied. Results varied enormously and none of the active ingredients had an unambiguous positive effect on the malodour. The risk of bias was assessed as high in all articles.

Conclusion: Given the fact that little evidence was found for each of the investigated treatments, it could be concluded that there is currently insufficient evidence that alternative therapies are of added value in the treatment of halitosis.

CLINICAL RELEVANCE

Scientific rationale: Halitosis is a common problem causing social isolation. Out of embarrassment, patients search the internet, leading to many questions about alternative solutions (e.g. oil pulling, herbs). This is the first systematic review on these alternative therapies.

Principal findings: Results varied among studies. Some promising results were found for fluoride containing toothpastes and probiotics. For other products (such as herbal and antibacterial products and essential oils) results were inconsistent. Long-term follow-up studies on these products are scarce. Moreover, the quality of the studies was poor.

Practical implications: No clear evidence was found to support a certain alternative anti-halitosis therapy.

INTRODUCTION

Halitosis is a term used to describe a bad smelling breath. With a prevalence of 32% worldwide, it is a widespread condition which can have far-reaching consequences (Silva et al., 2018). Out of embarrassment, this can lead to the avoidance of social contacts.

In most cases, the cause can be found in the oral cavity, this is known as intra-oral halitosis or 'oral malodour' (Delanghe et al., 1997, Dadamio et al., 2013a, Dadamio et al., 2013b). Intra-oral halitosis is caused by volatile sulphur components (VSC's), such as methyl mercaptan, hydrogen sulphide and dimethyl sulphide (Tangerman and Winkel, 2007). Anaerobic bacteria are the most important producers of VSC's (Persson et al., 1990). This occurs by the degradation of sulphur-containing amino acids found in the saliva, exfoliated epithelial cells and on the dorsum of the tongue (Tonzetich and Kestenbaum, 1969, Yaegaki and Sanada, 1992, Rosenberg, 1996). Hence, intra-oral halitosis is frequently associated with the presence of tongue coating, inflammation (periodontitis, gingivitis and candidosis), carious lesions, overhanging restorations and xerostomia (Delanghe et al., 1997, Quirynen et al., 2009, Scully and Greenman, 2012). For the minority of the cases, the source is a pathologic condition outside the mouth, which is called extra-oral halitosis (Quirynen et al., 2009). Pseudo-halitosis is a condition where the patient complains of malodour but this is not perceived by others. Counselling and oral hygiene measures suffice in this case. On the other hand, when the patient still believes to suffer from malodour despite this therapy, the case is referred to as halitophobia (Seemann et al., 2014, Yaegaki and Coil, 2000).
For research purposes, cysteine challenge testing can be a powerful tool to induce oral malodour. Patients are instructed to rinse with an aqueous solution of cysteine. This is broken down by the oral bacteria and hydrogen sulphide is produced. Also, it creates an environment favouring growth of the oral bacteria that generate malodour (Kleinberg and Codipilly, 2002).

Halitosis can be diagnosed with an organoleptic and/ or an instrumental examination. The former is preferably done by a panel of trained and calibrated odour judges (Rosenberg, 1996, Nachnani et al., 2005). For instrumental measurement, instruments such as Halimeter® or OralChroma™ can be used. Gas chromatography can be applied to obtain a more complete profile of the breath odour, although it is expensive and labour-intensive.

Improvement of the oral hygiene regimen is thus crucial in the treatment of intra-oral halitosis. This encompasses the correct use of a toothbrush, interdental aids, but most importantly the use of a tongue scraper (Outhouse et al., 2006, Van der Sleen et al., 2010, Slot et al., 2015). Different systematic reviews showed that tongue cleaning alone can significantly reduce oral malodour (Outhouse et al., 2006, Van der Sleen et al., 2010, Dadamio et al., 2013a, Dadamio et al., 2013b, Slot et al., 2015). If tongue cleaning is not sufficient, a mouthwash can be recommended (Dadamio et al., 2013b, Seemann et al., 2014). Three previously published systematic reviews investigated the effect of mouth rinses on oral malodour, irrespective of the active ingredients. All three found evidence to support a beneficial effect of CHX, CPC and Zn, but only limited research on other over the counter products. (Blom et al., 2012, Fedorowicz et al., 2008, Slot et al., 2015).

There is an increasing interest in alternative therapies by patients and in scientific literature (Goldstein and Epstein, 2000). This resulted in several publications regarding the therapy of bad breath, for example oil pulling. Although a plethora of articles are available in the field of halitosis, until this date, no systematic review has ever been performed in this area to give an overview of the evidence.

The aim of this systematic review was therefore to systematically review the literature concerning the effect of alternative oral malodour therapies.

MATERIALS AND METHODS

The focused question of this systematic review was: “Is there a role for alternative therapies in controlling malodour?”. The population of interest were patients with bad breath. The intervention of interest were alternative treatments (defined as all treatments outside the "classic" treatment strategies supported by previous systematic reviews, namely tongue cleaning and specific anti-halitosis formulations containing a combination of zinc and an antibacterial component). These had to be compared with at least one (positive or negative) control treatment. The outcome of these studies was assessed using instrumental or organoleptic measurements. To ensure an optimal comparison between the treatments due to the lack of long-term studies, a subdivision was made regarding follow-up, namely immediate effect (0-12 hours), short-term (<2 weeks), medium-term (≥2 weeks) and long-term (≥3 months) effects.

SEARCH STRATEGY

The US National Library of Medicine National Institutes of Health (PubMed), Excerpta Medical Database by Elsevier (EMBASE), Web of Science and The Cochrane Library were searched up to January 2019, without restriction on publication date. Terms referring to halitosis or oral malodour and alternative therapies were used. To further define the search terms concerning "alternative" treatments, we used our knowledge about the current literature, gained information by talking to our patients and searched the internet and social media. The complete search with the respective search terms was added as supporting information in the online version of this article.

The eligibility criteria were:

- Studies conducted in humans:
    - ≥ 18 years
    - In good general health
- Studies written in English
- Intervention: “alternative” treatments for halitosis: products without CHX, CPC or zinc or interventions different than tongue cleaning

- Comparison: there should be at least one control group, regardless of its nature: positive or negative control
- Outcome: breath evaluation via one or more of the following methods:
    - Organoleptic scoring (OLS)
    - VSC levels assessed using instrumental measurements (Halimeter, OralChroma, Breathron, gas chromatography)

SCREENING AND SELECTION

All titles and subsequently the abstracts were screened according to the eligibility criteria. This was done independently by two reviewers (AW and FV). Moreover, all of the the qualifying full-text papers were read by the two reviewers. If any disagreement occurred, the two reviewers tried to resolve this by an additional discussion. When this was not sufficient, the judgement of a third reviewer (IL) was decisive.

QUALITY ASSESSMENT

The assessment of risk of bias was performed using the Cochrane Collaboration's 'Risk of Bias' tool. In short, six evidence-based domains were scored, i.e. selection bias, performance bias, detection bias, attrition bias, reporting bias and other bias. Within each domain, the risk of bias was judged as high, low or unclear. Each score was complemented with quotes from the paper and additional comments. The quality assessment was independently done by the two reviewers (AW and FV) and then a comparison was made. When a disagreement occurred, a third reviewer (IL) was decisive.

META-ANALYSIS

Due to the heterogeneity of the studies a quantitative analysis (meta-analysis) could not be performed. The data is therefore presented descriptively.

RESULTS

Search results and study characteristics

The search resulted in 11370 articles in total. After removal of duplicates, 7429 articles were excluded based on title and 181 based on abstract. 46 full text manuscripts were screened for eligibility and finally, 26 were included. More details can be found in Figure 1.

Characteristics about study design are presented in Table 1. Two articles, namely Hu et al. 2003 and Hu et al. 2005, presented data from the same experiment.
The examined population varied greatly between all studies, from the number of included subjects (ranging from 12 to 284) to the type of halitosis patients that were included. Subjects with either genuine halitosis (14 studies), morning bad breath (8 studies) or cysteine-induced malodour (3 studies) were examined. The included studies used different criteria for selecting the population of interest and 6 studies did not define these criteria. Moreover, there was no uniformity in the threshold values that were used for defining halitosis, neither organoleptically, nor instrumentally (table 1).

The duration of the experiments was heterogenous. Studies were allocated according to their duration for an easier comparison (table 2 & 3).
The most popular method to evaluate the breath odour was instrumentally, which was done in 13 studies. Six studies used organoleptic evaluation and 7 studies combined both methods. For both organoleptic and instrumental testing, there was a variation in the manner of performing the examination and reporting the results (table 2 & 3).

Study outcomes

To provide a better overview of the results, studies investigating similar products were grouped together. All but one studies investigated a product with a chemical effect, only the breezy candy examined in the study by Barak and Katz (2012) was also assumed to have a mechanical scraping effect.

Fluoride containing toothpastes

Seven studies investigated products with fluoride as main ingredient, of which 4 found positive results. Three experiments tested the effect of Crest® toothpaste on halitosis (Gerlach et al., 1998, Lodhia et al., 2008, Chen et al., 2010). The immediate effect of this

toothpaste was rather limited. At short term, the results were contradictory (Gerlach et al., 1998, Chen et al., 2010). Four studies that investigated Colgate Total® toothpaste found a significant improvement of bad breath up to three weeks (Niles et al., 1999, Sharma et al., 1999, Hu et al., 2003, Hu et al., 2005, Sharma et al., 2007). This positive effect was not assessed in the study of Gerlach et al. (1998).

Essential oils

Of all essential oil containing products Listerine® was investigated most frequently, namely in four studies. In three studies, the immediate and short-term effects were significantly better than the control group (Borden et al., 2002, Carvalho et al., 2004, Erovic Ademovski et al., 2016). However, when compared to baseline only one study found a significant improvement (Borden et al., 2002). No beneficial effect could be found for an essential oil containing toothpaste (Olshan et al., 2000).

Herbal substances

Seven studies investigated products containing herbal substances. The immediate effect of green tea was tested in three studies (Lodhia et al., 2008, Porciani and Grandini, 2016, Farina et al., 2012). Only tablets with green tea extract were shown to have a significant immediate effect (Porciani and Grandini, 2016). The herbal mucoadhesive tablet examined by Sterer and co-workers (2013) reduced VSC's and the organoleptic score significantly better than placebo. Other studies investigating herbal products showed less remarkable results (Rosing et al., 2002, Sakagami et al., 2016, Farina et al., 2012, Watanabe et al., 2018).

Probiotics

The effect of probiotics on halitosis was investigated in three medium-term studies. One tested a chewing gum containing *Lactobacillus reuteri* DSM 17938 and ATCC PTA 5289. The other two examined tablets with a combination of *L. salivarius* and *L. reuteri,* or *L. salivarius* WB21. While the effects on the VSC's were inconclusive, the decrease of the organoleptic score was superior to placebo in all three studies (Keller et al., 2012, Suzuki et al., 2014, Penala et al., 2016).

Antibacterial substances

Another group composed of products with an antibacterial effect targeting the intra-oral sulphur producing bacteria. Two mouth rinses, Retardex® and Plax®, respectively containing

chlorine dioxide and triclosan, were able to treat bad breath significantly better than placebo. Despite the good results, these scores were not statistically significantly different compared to baseline (Carvalho et al., 2004, Erovic Ademovski et al., 2016). In the study by Barak and Katz (2012), the immediate effect of breezy candy was significantly better than placebo.

Enzymes

Two authors studied the effects of enzymes that act upon the formation of volatile sulphur gasses by bacteria, however the products did not perform better than placebo (Nohno et al., 2012, Tian et al., 2013).

Chewing gums and mints

The effect of chewing gums or mints on bad breath was poor (Lodhia et al., 2008, Rosing et al., 2009).

Quality assessment

The summary of the Cochrane quality assessment of the included studies is presented in Figure 2. Many of the studies showed a high risk of bias in several of the assessed domains.

DISCUSSION

There is an increase in interest among patients, clinicians and researchers in alternative therapies for controlling oral malodour. Up to now, studies about this topic were never reviewed systematically. This study, according to our knowledge, is the first systematic review on this subject. In general, contradictory results were encountered for all products under investigation, which makes it difficult to formulate an unambiguous conclusion. The most promising products were fluoride containing products and probiotics. More research is needed to be able to recommend specific formulations for these products.

Limitations

A first limitation of our systematic review was that many of the included studies seemed company driven. Nine out of 25 studies explicitly mentioned they were funded by the industry (Barak and Katz, 2012, Borden et al., 2002, Chen et al., 2010, Erovic Ademovski et al., 2016, Gerlach et al., 1998, Keller et al., 2012, Porciani and Grandini, 2016, Sakagami et al., 2016, Tian et al., 2013) and in 4 studies employees of the company providing the product contributed to the research and are co-authors of the article (Niles et al., 1999, Olshan et al., 2000, Sharma et al., 2007, Sharma et al., 1999). Funding bias may be present since all but one of these studies concluded that the examined product had a positive effect on oral malodour.

A second drawback of this review was the heterogeneity among the included studies. This made it difficult to compare across the studies and made a meta-analysis of the results impossible. This heterogeneity included variations in the studied population, i.e. type of oral malodour (genuine halitosis, morning bad breath or cysteine induced halitosis), sample size, smoking habits, gender, age and periodontal health. Moreover, some studies included, next to the study intervention, interventions that may impact the breath odour, such as oral hygiene instructions and a professional prophylaxis (table 1). At last, the studies reported different evaluation methods and units/scales (table 2).

A third drawback was the low quality of the studies as assessed by the Cochrane tool. Moreover, some contradictions in the articles made them difficult to interpret. Inconsistencies were noticed in regard to the study population in a number of articles. In three studies, the number of subjects mentioned in the text did not correspond to the

graphs or tables (Borden et al., 2002, Sakagami et al., 2016, Suzuki et al., 2014). In three other studies, contradictions were encountered in the results mentioned in the text and in the graphs or tables (Rosing et al., 2002, Sterer et al., 2013, Penala et al., 2016). In the study by Penala et al. (2016), it was not mentioned which strains of the probiotics were evaluated. Knowing different strains have different efficacies, it is important that it is properly reported in the study (Fuller, 1989). If correspondence details were found, the respective authors were contacted regarding these inconsistencies. We received an answer of two authors and these corrected values were used in this review (Sakagami et al., 2016, Suzuki et al., 2014). For the other studies, the values in the graphs or tables were regarded to be correct.

Clinical implications

Within the limitations of this study, there is some evidence that fluoride-based toothpastes and probiotics may be beneficial in treating oral malodour. For the toothpastes, Colgate Total® was one of the most backed-up products found in this review. However, it is difficult to translate the positive findings about this product into clinical guidelines as the composition of this product has changed. In the new formula triclosan is replaced by zinc and arginine (Gerlach et al., 1998, Niles et al., 1999, Sharma et al., 1999, Hu et al., 2003, Hu et al., 2005, Sharma et al., 2007). Little evidence is available on other ingredients, such as herbs and essential oils. However, these products are often promoted fiercely via different sources.

Future research

For future research it is important that the studied population reflects the target population likely to be using the product. Therefore, the study design should always mention the applied inclusion criteria for selecting subjects and the results of the breath examination at baseline. Preferably, the diagnosis of halitosis and the evaluation of the effects of an anti-halitosis product should combine organoleptic and instrumental examination. Both have a complementary function and are necessary to make a firm conclusion. Studies applying only one form of examination might falsely diagnose subjects as non-halitosis patients, for example participants diagnosed with higher organoleptic scores but without the detection of VSC's. Nonetheless, these patients should also be considered a halitosis patient. Gas chromatography and Selected Ion Flow Tube Mass Spectometry (SIFT-MS) can be of added

value in these cases. More research has emerged on the latter as an instrument in breath analysis. The main advantage of this instrument is the analysis of gasses other than VSC's, more specifically volatile organic compounds (Ross et al., 2009, Spaněl and Smith, 2011, Saad et al., 2018).

Moreover the participants should also be instructed about precautionary measures that are important to obtain an unbiased result when assessing the breath odour. Smoking and consumption of alcohol, garlic and spicy foods should be prohibited during the pre-measurement period. It is also important to include this information in the article so that the reader can interpret the results in that light. If it is impossible to mention this in the main article, for example due to the word limit, the protocol should at least be available online.

Future studies should concentrate on the long-term effect of anti-halitosis products, since this is the most relevant for genuine halitosis patients and these long-term studies are scarce. Nevertheless, the definition of long-term follow up is not clear in literature. It was suggested that a product targeting intra-oral halitosis must significantly reduce malodour in two independent 3-week, controlled, clinical studies (Wozniak, 2005). On the other hand, for examining the immediate effect of a product, morning bad breath and the cysteine challenge method are still very relevant models.

Conclusion

The current systematic review was performed to answer the numerous questions from patients about alternative therapies for halitosis. Since halitosis is still a subject that is socially avoided, patients often search the internet before they consult a clinician, where several products are promoted as being the ultimate treatment for bad breath. However, this review clearly demonstrated a lack of high-quality, long-term studies on these products. It can be concluded that there is insufficient scientific evidence to recommend any alternative anti-halitosis product to the patients.

CONFLICT OF INTEREST AND SOURCE OF FUNDING

None of the authors have a conflict of interest to report. This study was not funded.

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Fig 1. Process of search, selection and analysis

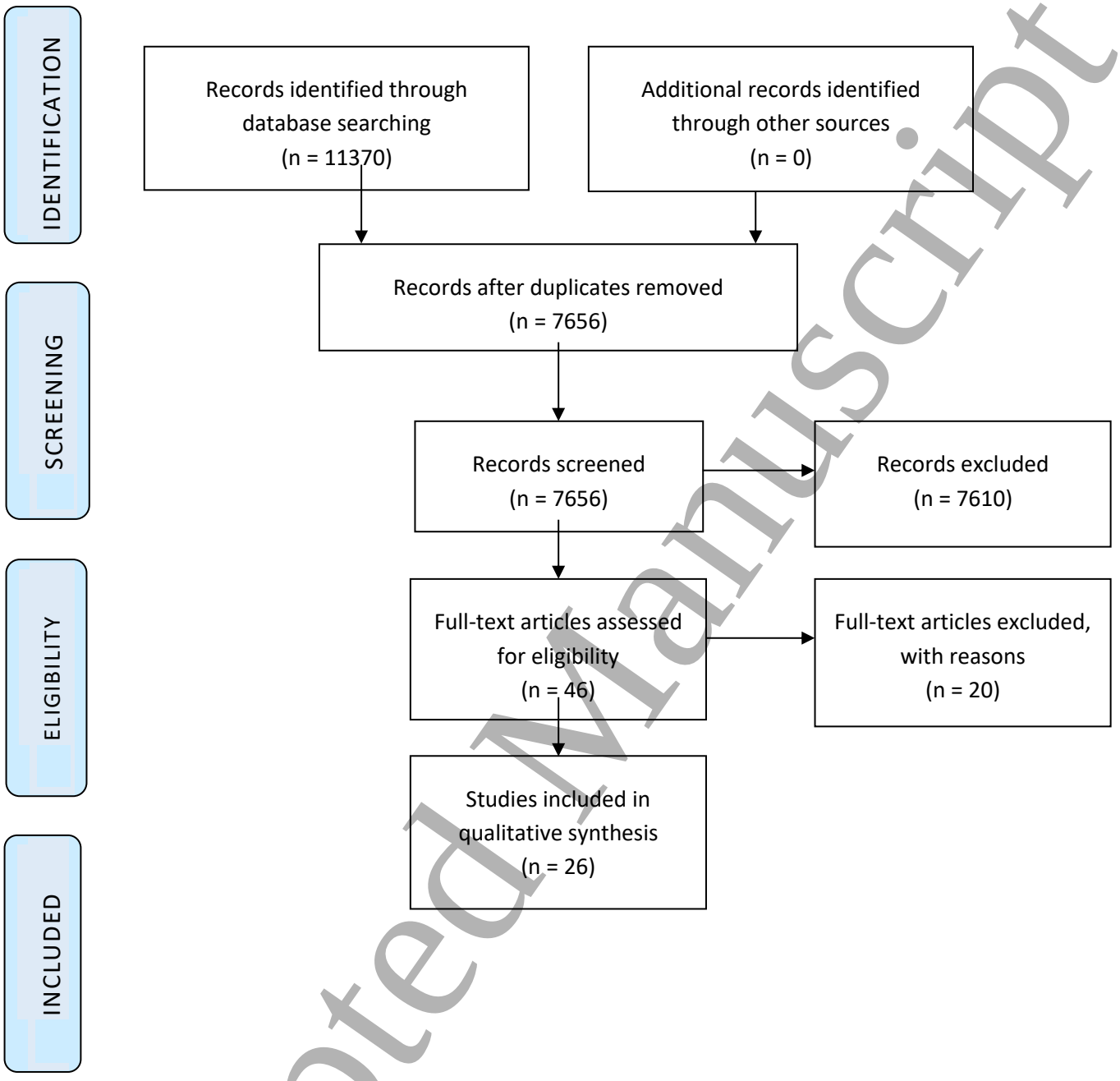
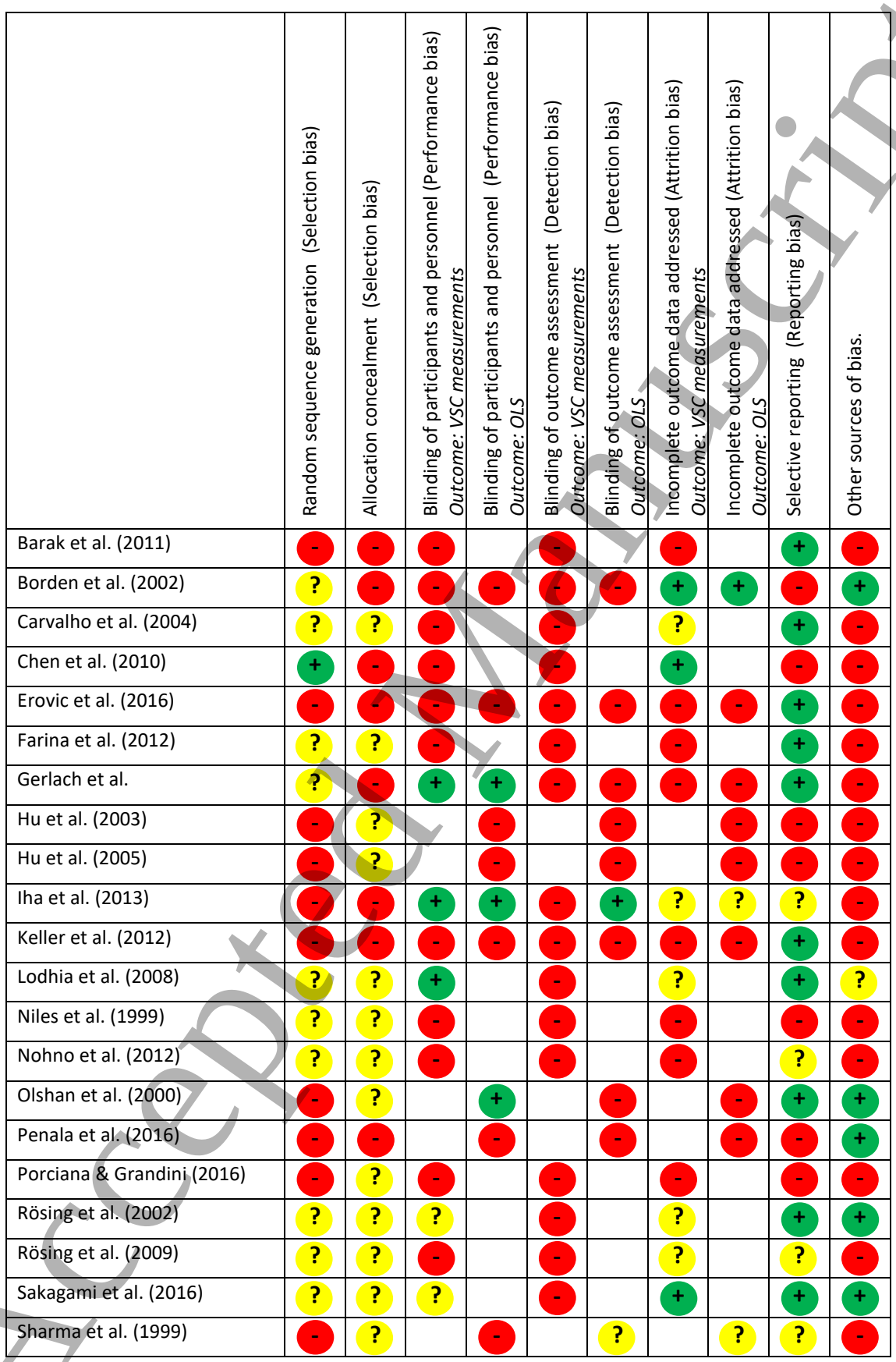


Fig 2. Cochrane quality assessment



Sharma et al. (2007)	-	?		-		?		?	?	-
Sterer et al. (2013)	?	?	+	+	-	-	?	?	+	+
Suzuki et al. (2014)	-	-	-	-	-	-	-	-	-	-
Tian et al. (2013)	?	?		-		-		-	?	-
Watanabe et al. (2018)	+	?	?		-		?		?	-

+ = low risk of bias

? = unclear risk of bias

- = high risk of bias

(1) Random sequence generation (Selection bias):

low risk: 8% / unclear: 46% / high: 46%

(2) Allocation concealment (Selection bias):

low risk: 0% / unclear: 65% / high: 35%

(3) Blinding of participants and personnel (Performance bias) Outcome: VSC measurements:

N/A: 27% / low: 15% / unclear: 12% / high: 46%

(4) Blinding of participants and personnel (Performance bias) Outcome: OLS:

N/A: 46% / low: 15% / unclear: 0% / high: 39%

(5) Blinding of outcome assessment (Detection bias) Outcome: VSC measurements

N/A: 27% / low: 0% / unclear: 0% / high: 73%

(6) Blinding of outcome assessment (Detection bias) Outcome: OLS

N/A: 46% / low: 4% / unclear: 8% / high: 42%

(7) Incomplete outcome data addressed (Attrition bias) Outcome: VSC measurements

N/A: 27% / low: 12% / unclear: 27% / high: 34%

(8) Incomplete outcome data addressed (Attrition bias) Outcome: OLS

N/A: 46% / low: 4% / unclear: 16% /high: 34%

(9) Selective reporting (Reporting bias)

N/A: 0% / low: 42% / unclear: 27% / high: 31%

(10) Other sources of bias

N/A: 0% / low: 23% / unclear: 4% / high: 73%

Table 1. Overview of the included studies and their main features

Authors (year), country	Study design & duration	Definition of halitosis	♂/♀ Mean age Age range	Patients under investigation BL	Patients under investigation End	R/ under investigation (versus control treatment)	Regimen, WP, additional treatments	Evaluation points	Conclusion of the authors of the original paper
Barak et al. (2012), Israel	RCT 150 min	NR	♂: 48 ♀: 27 38 ± 14 (18-64)	15	15	Commercial lollipops without abrasive capabilities or antibacterial substances	WP: - Single consumption No MR	BL 10min 60min 150min	The combined effect of abrasion by microcapsules with zinc supplement represents a novel and successful approach for the treatment of halitosis.
				15	15	Breezy abrasive candy with 0.5% zinc gluconate			
				15	15	Breezy abrasive candy with 1% propolis and 0.25% zinc			
				15	15	Breezy abrasive candy			
Borden et al. (2002), USA	RCT 4w	Two-judge average OLS of ≥ 4 on a scale of 5 and no single score of < 3	♂: 29 ♀: 66 NR (19-65)	15	15	BreathRx MR, a formulation containing CPC	WP: - 2x/d No other dental devices or products	0w, 2w & 4w: BL, 15min (only OLS), 2h, 4h	The results showed that the four mouthrinses reduced oral malodor within 4 hours after single usage, with product 2 being the most effective and the placebo being the least effective. Daily use of essential oil, CD/Zn, and placebo rinses for up to 4 weeks did not reduce
				23	22	Placebo rinse			
				22	18	Oxygene MR with zinc, a commercially available, CD/Zn-based rinse			
				25	21	Listerine Antiseptic Rinse, a commercially available, essential oil-based rinse			

									oral malodor from week 0 baseline values and the effects on oral malodor were comparable among these three mouthrinses. Product 2 was the only mouthrinse that reduced oral malodor from baseline values after 2 and 4 weeks of daily use.
Carvalho et al. (2004), Brazil	CO 4d	NR (Morning breath)	♂: 7 ♀: 5 NR (19-23)	12	NR	Negative control: hydro-alcoholic Periogard®: 0.12% CHX gluconate (Colgate Palmolive, Division of Kolynos do Brasil Ltda, Osasco, SP, Brazil) Positive control: 0.2% CHX Cepacol®: 0.05% cetylpyridinium (Gessy Lever Co., Unilever Division, Vinhedo, SP, Brazil) Plax®: 0.03% triclosan + 0.2% copolymer (Colgate Palmolive, Division of Kolynos do Brasil Ltda, Osasco, SP, Brazil) Listerine®: 0.064% thymol, 0.09% eucalyptol and 0.042% menthol (Procter & Gamble Laboratories, Surrey, UK)	WP: 15d 2x/d 1min 15ml New standard TB and TP without antimicrobial agents during 15d WP. At BL professional profylaxis including tongue cleaning. No OH during study.	BL: 8h00 on day 1 5d: 12h post	These findings suggest that mouthrinses can reduce morning bad breath, and that such a reduction is not attributable only to the reduction of supragingival plaque formation.

Chen et al. (2010), USA	CO 28h	VSC ≥ 120ppb	♂: 14 ♀: 19 20 ± NR (NR)	33	33	0.454% stabilized SnF TP + tongue brushing	WP: 5d 4x/28h 2min 10ml rinse water 5d pre-experimental phase & WP: brush 2x/d with Crest Cavity Protection TP	BL 24h 28h	The present study demonstrated the safety and effectiveness of the 0.454% stannous fluoride dentifrice in the malodor control relative to a negative control.
						0.243% NaF TP + tongue brushing			
						0.454% stabilized SnF TP (Crest Gum Care) (Procter & Gamble, Cincinnati, OH, USA)			
						0.243% NaF TP (Crest Cavity Protection) (Procter & Gamble, Cincinnati, OH, USA)			
Erovic et al. (2016), Sweden	CO 12h	OLS ≥ 2 + VSC > 160ppb (Halimeter) + at least 2 gases examined by OralChroma above cutoff value	♂: 7 ♀: 17 49 ± 11 (31-68)	24	24	Water (placebo)	WP: 1w Single rinse (12h prior to examination) No other MR	12h	All treatments resulted in reduction in halitosis 12h after rinsing compared to placebo. Hydrogen sulphide and methyl mercaptan were most effectively reduced by zinc acetate and chlorhexidine diacetate.
							1min 10ml		
						Zinc acetate (0.3%)- and CHX diacetate (0.025%)-containing MR (SB12®, Meda OTC, Stockholm, Sweden)	1min 10ml		

						Zinc lactate-(0.14%), CHX (0.5%), CPC (0.05%) containing MR (Halita®, DentAid, Barcelona, Spain)	1min 15ml		
						Zinc acetate (0.3%), CHX diacetate (0.025%) containing MR with a less amount of mint and menthol than SB12 (SB12 mild®, Meda OTC, Stockholm, Sweden)	1min 10ml		
						Zinc chloride- (0.9%) and essential oil (thymol, eukalyptol, methyl salicylate)-containing MR (Listerine® Total Care, Johnson & Johnson, NJ, USA)	30s 20ml		
						Chlorine dioxide, trisodium phosphate-, citric acid-, sodium bicarbonate and sodium chlorite-containing MR (RetarDEX®, Periproducts, London, UK)	30s 10ml		
Farina et al. (2012), Brazil	CO 3h	VSC > 110ppb after rinsing with acetylcysteine	♂: NR ♀: NR NR (19-43)	30	30	12% CHX gluconate	WP: 1w 10 ml acetylcysteine, 30s Mouth closed for 60s Repeat step 1&2 90min: 10 ml acetylcysteine, 30s	BL: 1min after acetylcysteine IA: 1min post 90min 180min	We concluded that *Curcuma Zedoaria* and *Camellia Sinensis*, prepared as infusions and used as mouthwashes, did not have a residual neutralizing effect on VSC.
						Water (placebo)			
						Camellia sinensis (green tea) (1 sachet with 1.5g of ground green tea leaves in 200ml water for 3min, 1h cooling) (Herbarium, Colombo, Brazil)			

						Curcuma Zedoaria (2.2g of powdered root in 200ml water for 5min , 1h cooling) (Panizza, Taboão da Serra, Brazil)	180min: 10 ml acetylcysteine, 30s No other MR		
Gerlach et al. (1998), USA	RCT 5d	OLS ≥ 4	♂: 82 ♀: 302 45 ± NR (18-77)	96	375	Bottled distilled water (Life Technologies, Grand Island, NY)	WP: - 2x/day 1min Regular soft-bristled TB Dose cups for bottled water	BL 1d & 5d: 3, 6, 8 h post	This research establishes the comparative breath efficacy of three commercial dentifrices in a study model that may prove relevant for other dentifrice clinical trials.
				96		0.45% SnF TP (Crest® Gum Care) (The Procter & Gamble Co., Cincinnati, OH)			
				96		0.243% NaF and 5% pyrophosphate TP (Crest® Tartar Protection) (The Procter & Gamble Co., Cincinnati, OH)			
				96		0.24% NaF and 0.30% triclosan/polymer TP (Colgate® Total) (Colgate-Palmolive Co., New York, NY)			
Hu et al. (2003), China & Hu et al. (2005), China	RCT 3w	Mean OLS > 7 & < 8.6 (no individual score <4) *(Hu et al. 2003)*	♂: 43 ♀: 38 45* ± NR (22-70)	40	40	0.243% NaF in a silica base (Colgate® Cavity Protection Winterfresh Gel)	WP: - 2x/d 1 min Rinse with 20ml bottled water for 10s *(Hu et al. 2003)*	BL 1,5h 4h 12h 1w: 12h post 2w: 12h post 3w: 12h post	*(Hu et al. 2003)* Thus, the overall results of the double-blind clinical study support the conclusions that Colgate® Total® Advanced Fresh toothpaste is efficacious for the control of oral malodor for up to 12 hours in the daytime and up to 12 hours overnight.
				41	41	0.30% triclosan, 2% polyvinylmethylether/maleic acid (PVM/MA) copolymer and 0.243% NaF in a 10% high-cleaning silica base (Colgate® Total® Advanced Fresh)			

									(Hu et al. 2005) In conclusion, the results of this double-blind clinical study clearly indicate that a dentrifice containing triclosan/copolymer/NaF provides effective control of oral malodor for up to 12h.
Iha et al. (2013), Japan	RCT 4w	Mean OLS ≥ 1.5	♂: 4 ♀: 14 55 ± 10 (33-71)	9	9	CPC-containing control gel (0.01%)	WP: - 3x/d after meal 1cm gel TB, gingival massage & tongue scraping No eating, drinking or rinsing 30min after	BL 28d	Mouth cleaning with hinokitiol-containing gel may be effective for reduction of oral malodor.
				9	9	Hinokitiol (0.01%-0.2%) containing oral gel (REFRE-CARE H; EN Otsuka Pharmaceutical Co. Ltd, Iwate, Japan)			
Keller et al. (2011), Denmark	CO 2w	OLS ≥ 1	♂: 10 ♀: 20 22 ± NR (19-25)	12	25	CG without any added bacteria (BioGaia AB (Lund, Sweden))	WP: 3w 2x/d 10min 1h after food intake	BL 14d	The results demonstrated that probiotic chewing gums may have some beneficial effect on oral malodour assessed by organoleptic scores. The results indicate that the probiotic gum may affect bacteria that produce malodourous compounds other than VSCs.
				16		CG with *Lactobacillus Reuteri* DSM 17938 and with *Lactobacillus reuteri* ATCC PTA 5289 ($1x10^8$ CFU/CG) (BioGaia AB (Lund, Sweden))			

Lodhia et al. (2008), Canada	CO 3h	H_2S > 1.5ng/10ml and/or CH_3SH > 0.5ng/10ml	♂: 15 ♀: 0 NR (NR)	15	NR	Crest™ TP (Procter & Gamble, Cincinnati, OH, USA)	WP: 1w 3min Oral B® 40 TB	BL IA 1h 2h 3h	We concluded that green tea was very effective in reducing oral malodor temporarily because of its disinfectant and deodorant activities, whereas other foods were not effective.
						CG containing xylitol, maltose and flavors	2min		
						Mints	2 tablets 2min		
						Parsley seed oil product	2 capsules No water		
						Green-tea powder (670mg)	Powder dissolved on back portion of the tongue		
Niles et al. (1999), USA	CO 7d	VSC ≥ 10 ng/ml	♂: NR ♀: NR NR (NR)	20	19	0.243% NaF in a silica base TP	WP: 1w 2x/d 60s	BL 7d, overnight 7d, 7h post	In summary, it can be concluded that Colgate Total Toothpaste provides effective control of malodor both for seven hours and overnight after toothbrushing, thereby allowing for long-lasting fresh breath protection.
						0.3% triclosan and 2.0% of a PVM/MA polyvinylmethyl ether/maleic acid copolymer in a 0.243% NaF/silica base (Colgate® Total TP)	1w pre-experimental phase: commercially available fluoride TP		
Nohno et al. (2012), Japan	CO 7d	NR	♂: 14 ♀: 0 35 ± NR (23-54)	14	14	Placebo tablets: – 64.8% palatinose – 33.0% maltitol – 2.0% sucrose fatty acid ester – 0.1% aspartame	WP: 14d 3x/d 6d	BL IA 7d	The results of the study suggest that the tablets containing acitidine had an accumulative effect in reducing VSC in

						– 0.1% particle silicon dioxide Test tablet = placebo tablet, but with 3.0% actinidine & 61.8% palatinose	Regular OH		mouth air with long-term use.
Olshan et al. (2000), USA (Trial 1)	CT 240 min	OLS ≥ 6.0 and ≤ 8.4 and no individual rating ≤ 4.0	♂: 24 ♀: 56 43* ± NR (NR)	86	40	Negative control TP (The Warner-Lambert Consumer Healthcare Division of the Warner-Lambert Consumer Group of Pfizer, Morris Plains, NJ, USA)	WP: - 60s brushing 10s rinsing with 20ml of bottled water 2d before BL: Colgate MFP Regular No other MR, mints, mouth sprays or other deodorant products	BL 30, 60, 90, 120, 180 and 240 min post	The essential oil dentifrices were significantly more effective (p≤ 0.033) than the control in reducing intrinsic oral malodor from 90 to 120 min.
					40	Essential oil TP (The Warner-Lambert Consumer Healthcare Division of the Warner-Lambert Consumer Group of Pfizer, Morris Plains, NJ, USA)			
Penala et al. (2016), India	RCT 3m	OLS > 2	♂: NR ♀: NR 45 ± NR (25-59) Patients with periodontitis	16	14	SRP + Placebo MR + placebo solution for subgingival application	WP: - BL: full-mouth SRP in 2 sessions within 48h One capsule in 10ml distilled water Rinse 1min, 2x/day, 15days Subgingival delivery at BL, 1w, 2w, 4w	BL 1m 3m	Within the limitations of the study, the present investigation showed that the adjunctive use of probiotics offers clinical benefit in terms of pocket depth reduction in moderate pockets and reduced oral malodor parameters.
				16	15	SRP + PB MR + PB solution for subgingival application PB capsule: *Lactobacillus salivarius* (2 x 10^9 CFU) + *Lactobacillus reuteri* (2 x 10^9 CFU) (Unique Biotech laboratories, Hyderabad)			

							OHI		
Porciana & Grandini (2016), Italy	CO 30 min	VSC ≥ 75ppb	♂: 23 ♀: 31 37 ± 12 (18-58)	57	54	Tablet without active ingredients (Mentos Pure Fresh) (Perfetti Van Melle S.p.A., Lainate, MI, Italy) Test tablet: 0.05% green tea extract (3 tablets: 1mg polyphenol) (Perfetti Van Melle S.p.A., Lainate, MI, Italy)	WP: 48h 3 tablets, one after another 3d before start of the study: TP with only sodium monofluorophosphate	BL IA 30min	Tablets containing green tea extract can statistically significantly reduce the oral VSC levels immediately, and after 30 minutes. Moreover, the test tablets reduced oral VSC significantly more than the control tablets.
Rösing et al. (2002), Norway (Trial 2)	CO 120 min	NR	♂: NR ♀: NR NR (29-46)	7	NR	Aqueous solution of zinc acetate 0.1% (Sigma Chemicals) Sorriso Herbal = herbal containing MR (Kolynos do Brasil) Kolynos Fluor = fluoride- and triclosan-containing MR (Kolynos do Brasil) Kolynos Bicarbonato = a triclosan- and sodium bicarbonate-containing MR (Kolynos do Brasil)	WP: ≥ 5d 5ml of a 6-mM solution of L-cysteine 90s mouth closed 10ml MR, 1min	30min 60min 120min	It may be concluded that some commercial mouthrinses are markedly less effective than a simple and cheap solution of zinc acetate.

Rösing et al. (2009), Brazil (experiment 2)	C0 30 min	NR	♂: 7 ♀: 7 NR (20-35)	14	NR	CG containing xylitol, sorbitol, mannitol and zinc citrate CG containing sucrose	WP: 1d 5ml of cysteine 6 mM VSC assessment after 1, 5, 15 and 30min = baseline curve CG VSC assessment after 1, 5, 15 and 30min = test curve	1min 5min 15min 30min	It can be concluded that VSC production is diminished after chewing gum and that the use of chewing gums reduces temporarily the VSC production enhanced by cysteine rinses.
Sakagami et al. (2016), Japan	CO 5w	NR	♂: 11 ♀: 1 NR (NR)	12	NR	Placebo TP: hydroxyapatite, calcium carbonate, water, silica, glycerine, polyethylene glycol, xylitol, menthol, saccharin sodium, sucrose palmitate, sodium copper chlorophyllin, cellulose gum, sodium laurate, isopropylmethyphenol (IPMP) (0.1%) (Sampo Pharmaceutical Co., Ltd., Tokyo, Japan) Ingredients of placebo TP + alkaline extract of the leaves of Sasa senanensis Rehder (26.2%) (Daiwa Biological Research Institute Co., Ltd., Kawasaki, Kanagawa, Japan)	WP: NR 3x/d after meals 1w ordinary TP for baseline values	4-5 x /w at 11h00 1w,2w, 3w, 4w, 5w	The present study provides for the first time the basis for anti-halitosis activity of Sasa senanensis Rehder (SE).
Sharma et al. (1999), Canada	CT 12h	OLS ≥ 5 on a 9-point hedonic scale	♂: 26 ♀: 37 37* ± NR (18-60)	32	NR	TP with 0.243% NaF in a silica base	WP: - Brushing with soft-bristled TB in regular and customary manner	BL 12h	Thus, the results of this double-blind clinical study support the conclusion that Colgate Total Toothpaste provides effective control of breath odor at
				31	NR	0.3% triclosan and 2.0% PVM/MA copolymer (a copolymer of methoxyethylene and maleic acid) in a 0.243% NaF/silica base (Colgate® Total TP, Colgate-Palmolive Co., New York, NY)			

							No MR or breath mints		twelve hours after brushing the teeth.
Sharma et al. (2007), Canada	CT 12h	OLS ≥ 5 on a 9-point hedonic scale	♂: 28 ♀: 48 38 ± NR (18-60)	37	37	TP with 0.243% NaF in a silica base	WP: - Brushing with soft-bristled TB in regular and customary manner No MR or breath mints	BL 12h	Thus, the results of this double-blind study, conducted according to Guidelines by the Council on Scientific Affairs of the American Dental Association, support the conclusion that Colgate Total dentifrice provides effective control of breath odor at 12 hours after brushing the teeth.
				39	39	0.3% triclosan and 2.0% PVM/MA copolymer (a copolymer of methoxyethylene and maleic acid) in a 0.243% NaF/silica base (Colgate® Total TP, Colgate-Palmolive Co., New York, NY)			
Sterer et al. (2013), Israel	CT 24h	OLS ≥ 2 on a 5-point scale	♂: 21 ♀: 19 26 ± 2 (NR)	14	NR	Placebo mucoadhesive tablet (no active ingredients)	WP: - Apply to palate 1d: after dinner 2d: after breakfast	BL: day 1 16h00-17h00 Day 2 16h00-17h00	These results demonstrate the efficacy of the herbal formulation delivered using a mucoadhesive tablet for day-long prevention of oral malodor.
				12	NR	Commercial MR (Listerine®, Cool Mint®, Pfizer)	Gargle for 30s 1d: before bedtime 2d: morning		

				14	NR	Herbal mucoadhesive tablet (HMT): – hydroxypropyl cellulose (Hercules Co., Wilmington, DE) + carbopole (Goodrish Co., Cleveland, OH) in 4:1 ratio – active ingredients: equal amounts of Echinacea (Echinacea augustifolia), Mastic gum (Pistacia lentiscus), Lavender (lavandula augustifolia) and Sage (salvia officinals) (SupHerb. Nazeret Ilit IL)	Apply to palate 1d: after dinner 2d: after breakfast No other breath products		
Suzuki et al. (2014), Japan	CO 14d	OLS > 1.5 on a 5-point scale	♂: 4 ♀: 19 44 ± 12 (22-67) Patients with periodontitis	26	23	Placebo tablet: 280mg xylitol Tablet with 6.7 x 10^8 CFU *Lactobacillus salivarius* WB21 + 280mg xylitol	WP: 14d 3x/d Dissolve on the tongue No other PB products	BL 14d	These results indicated that daily oral consumption of tables containing probiotic lactobacilli could help to control oral malodor and malodor-related factors.
Tian et al. (2013), USA	CO 180 min	H_2S > 1.5ng/10ml or CH_3SH > 0.5ng/10ml in morning mouth air prior to brushing	♂: 9 ♀: 6 NR (25-50)	15	NR	Control gum (Wrigley Extra sugar-free stick gum, banana flavor) CG with 0.01% of allyl isothiocyanate and 0.1% zinc lactate (Wrigley Extra sugar-free stick gum, banana flavor)	WP: ≥ 3d 1 CG for 12min Expectorate	BL 12min 60min 120min 180min	Chewing gum containing low levels of allyl isothiocyanate can effectively reduce oral malodor. The effect is strengthened when allyl isotiocyanate is

						CG with 0.01% of AITC (Wrigley Extra sugar-free stick gum, banana flavor)			combined with a low level of zinc lactate.
Watanabe et al. (2018), Japan	CT 4w	H_2S ≥ 112 ppb + CH_3SH ≥ 26 ppb + $(CH_3)_2S$ ≥ 8ppb	♂: 10 ♀: 11 40 ± 12 (18-59)	10	NR	Placebo gum: – 38.22% gum base (Gum Base Co. S.p.A., Milano Italy) – 37.50% isomaltose – 10.85% mannitol – 2.63% sorbitol – 0.30% aspartame – 0.15% acesufame K – 6.16% flavors – 2.90% Talc – 1.00% silicon dioxide – 0.30% E473 (sucrose ester of fatty acids)	WP: - 6x/d 2 CG for 15min No other CG	BL 2w 4w	The results suggest that PYC chewing gum is effective in reducing oral malodor by decreasing the accumulation of tongue coating and the number of hydrogen sulfide-producing bacteria in saliva.
				11	NR	PYC gum: – 0.42 % Pycnogenol (PYC) (Horpag Research Ltd.) (2.52mg/tablet) – 38.22% gum base (Gum Base Co. S.p.A., Milano Italy) – 37.50% isomaltose – 10.23% mannitol – 2.63% sorbitol – 0.30% aspartame – 0.15% acesufame K – 6.16% flavors – 2.90% talc – 1.00% silicon dioxide – 0.50% E473 (sucrose ester of fatty acids)			

NR = not reported
RCT = Randomized Controlled Trial; CT = Clinical Trial; CO = Crossover
Yrs = years; m = months; w = weeks; d = days; h = hours; min = minutes
VSC = volatile sulfur compounds; OLS = organoleptic score; ppb =parts per billion
BL = baseline; IA = Immediately after investigated treatment; POST = … s/min/h after investigated treatment
WP = washout period; OH = Oral Hygiene; OHI = Oral Hygiene Instruction; PB = Probiotic; SRP = scaling and rootplaning; TP = toothpaste; TB = toothbrush;
MR = mouthrinse; CFU = colony-forming units; CHX = chlorhexidine; CPC = cetylpyridinium chloride; CG = chewing gum; CD/Zn = chloride dioxide plus zinc;
SnF = stannous fluoride; NaF = sodium fluoride

Table 2. Overview of the organoleptic results of the included studies

					Immediate effect (0-12h)								Short term (<2w)				Medium term (≥2w)			
					T1				T2				T3				T4			
Author	**Groups**	**Method**	**Score**	**BL**		**T1**	**Δ_{T1} (%)**	***p***		**T2**	**Δ_{T2} (%)**	***p***		**T3**	**Δ_{T3} (%)**	***p***		**T4**	**Δ_{T4} (%)**	***p***
Borden et al., 2002	Placebo	2 judges 0-5 scale	NR	3.93± 0.68	15 min	0.24± 0.33°	-3.70 (-94%)	-	4h	3.72±0.54	-0.22 (-6%)	-	NR				4w	4.14±0.64	+0.21* (+19%*)	-
	BreathRx MR			4.22± 0.56		0.18± 0.32°	-4.04 (-96%)	**S**		3.28±0.82°	-0.94 (-22%)	**S**						3.80±0.67°	-0.42* (-10%*)	**S**
	Oxygene MR			4.02± 0.52		0.25± 0.37°	-3.77 (-94%)	NS		3.50±0.82°	-0.52 (-13%)	NS						4.08±0.65	+0.06* (+1%*)	NS
	Listerine Antiseptic			4.14± 0.70		0.96± 0.79°	-3.18 (-77%)	**S**		3.72±0.89°	-0.42 (-10%)	NS						4.12±0.59	-0.02* (-0%*)	NS
Erovic et al., 2016	Water	Judges NR 0-5 scale	NR	≥2	12h	2.3±0.9	ND	-	NR				NR				NR			
	SB12			≥2		1.2±0.8	ND	**S**												
	Halita			≥2		1.4±0.9	ND	**S**												
	SB12 mild			≥2		1.5±1.0	ND	**S**												
	Listerine			≥2		1.6±1.1	ND	**S**												
	RetarDEX			≥2		1.3±1.0	ND	**S**												
Gerlach et al., 1998	Water	2 judges 6 point scale	NR	4.55	3h	3.23	-1.32* (-29%*)	-	8h	4.01	-0.54* (-12%*)	-	104 h	4.13	-0.42* (-9%*)	-	NR			
	Crest Gum Care			4.60		2.85	-1.75* (-38%*)	**S**		3.99	-0.61* (-13%*)	NS		3.73	-0.87*(-18.91%*)	**S**				

	Crest Tartar Protection			4.61		3.09	-1.52* (-33%*)	NS		4.04	-0.57* (-12%*)	NS		4.10	-0.51* (-11%*)	NS			
	Colgate Total			4.58		3.30	-1.28* (-28%*)	NS		4.01	-0.57* (-12%*)	NS		4.18	-0.4* (-9%*)	NS			
Hu et al., 2003 & 2005	NaF	4 judges 9 point scale	NR	7.84 ± 0.39	1.5h	5,36 ± 0.65°	-2.48* (-31.6%)	-	12h	7,03 ± 0.70°	-0.81* (-10%)	-	1w	7,14 ± 0.81°	-0.7* (-9%)	-	3w	7,12 ± 0.34°	-0.72* (-9%)	-
	Colgate Total			7.80 ± 0.42		3.06 ± 0.67°	-4.75* (-60.8%)	**S**		3,42 ± 0.72°	-4.38* (-56%)	**S**		3,66 ± 0.50°	-4.14* (-53%)	**S**		3,36 ± 0.50°	-4.44* (-57%)	**S**
Iha et al., 2013	CPC	2 judges 0-5 scale	0.5	1	NR								NR				28d	0.5	-	-
			1	1														1	-	
			1.5	2														1.5	-	
			2	1														2	3	
			2.5	4														2.5	5	
			3	-														3	1	
			3.5	-														3.5	-	
	Hinokitiol		0.5	-														0.5	1	NS
			1	-														1	1	
			1.5	1														1.5	2	
			2	-														2	1	
			2.5	5														2.5	4	
			3	3														3	-	
			3.5	-														3.5	-	
Keller et al., 2011	CG placebo	3 judges 0-5 scale	0-1	-	NR								NR				14d	8%	ND	-
			1-2	40%														28%		
			2-3	28%														28%		
			3-5	32%														36%		
	CG lactobacillus		0-1	-														28%	ND	**S**
			1-2	36%														12%		
			2-3	32%														32%		
			3-5	32%														28%		

Olshan et al., 2000	Negative control TP	4-5 judges 9 point scale	NR	7.33 ± 0.51	30 min	6.63 ± 0.80°	-0.7* (-10%*)	-	240 min	7.48 ± 0.54°	+0.15* (+2%*)	-	NR			NR		
	EO TP			7.34 ± 0.50		4.43 ± 0.96°	-2.91* (-40%*)	**S**		7.36 ± 0.62	+0.02* (+0%*)	NS						
Penala et al., 2016	Placebo	1 judge 0-5 scale	NR	4.43 ± 0.51	NR								NR			3m	1.86 ± 1.03°	-2.57* (-58%*)	-
	PB capsule			4.0 ± 0.93													0.87 ± 0.92°	-3.13* (-78%*)	**S**
Sharma et al., 1999	Placebo	4 judges 9 point scale	NR	6.63±0.59	12h	6.05± 0.80°	-0.58 (-9%*)	-	NR				NR			NR		
	Colgate Total			6.62±0.59		4.78± 0.32°	-1.85 (-28%*)	**S**										
Sharma et al., 2007	Placebo	4 judges 9 point scale	NR	6.49 ± 0.53	12h	6.11 ± 0.74°	-0.38* (-6%*)	-	NR				NR			NR		
	Colgate Total			6.49 ± 0.52		4.65 ± 0.45°	-1.84* (-28%*)	**S**										
Sterer et al., 2013	Placebo tablet	2 judges 5 point scale	NR	2.55 ± 0.55	NR								24h	2.35·	-0.2* (-8%*)	-	NR	
	Control MR			2.45·										2.05·	-0.4* (-16%*)	NS		
	HMT			2.45 ± 0.60										1.7 ± 0.60	-0.75* (-31%*)	**S**		
Suzuki et al., 2014	Placebo tablet	2 judges 5 point scale	NR	2.5*	NR								NR			14d	2.26*°	-0.24* (-48%*)	-
	Test tablet			2.65*													1.83*°	-0.82* (-31%*)	NS

Mean ± standard deviation
°statistically significant lower values compared to baseline
·values obtained from the reported graph
*calculated based on reported averages
S=Statistically significant compared with the control group
NS=Statistically not significant compared with the control group

IA=immediately after
BL=Baseline
NR=non reported
ND=non deductable

Table 3. Overview of the instrumental results of the included studies

					Immediate effect (0-12h)								Short term (<2w)				Medium term (≥2w)			
					T1				T2				T3				T4			
Author	**Groups**	**Method**	**Gasses**	**BL**		**T1**	**Δ_{T1} (%)**	***p***		**T2**	**Δ_{T2} (%)**	***p***		**T3**	**Δ_{T3} (%)**	***p***		**T4**	**Δ_{T4} (%)**	***p***
Barak et al., 2012	Lollipops	HM ppb	All gases	330 ± 260	10 min	NR	ND (-18%·)	-	150 min	NR	ND (-18%·)	-	NR				NR			
	Candy with zinc gluconate			330 ± 260		NR°	ND (-58%·)	**S**		NR°	ND (-58%·)	**S**								
	Candy with propolis and zinc gluconate			330 ± 260		NR°	ND (-42%·)	**S**		NR°	ND (-42%·)	**S**								
	Breezy candy			330 ± 260		NR	ND (-34%·)	**S**		NR	ND (-34%·)	**S**								
	Breezy candy with propolis			330 ± 260		NR	ND (-34%·)	**S**		NR	ND (-34%·)	**S**								
Borden et al., 2002	Placebo	HM ppb	All gases	106.04±80.38	NR								NR				4w	84.45± 81.65	-25.5 (-24%)	-
	BreathRx MR			135.98±132.68														40.13± 27.22°	-86 (-63%)	NS

	Oxygene MR			99.73 ±87.98									31.28± 28.41°	-72.28 (-72%)	NS
	Listerine Antiseptic			98.16 ±60.38									43.95 ± 28.50°	-47.71 (-49%)	NS
Carvalho et al., 2004	Hydro-alcoholic	HM ppb	All gases	173± 145	NR				5d	222 ±140°	+49* (+28%*)	-	NR		
	Periogard			163 ±87						45± 56°	-118* (-72%*)	**S**			
	CHX			154± 144						32 ±13°	-122* (-79%*)	**S**			
	Cepacol			120± 81						98± 61	-40* (-33%*)	NS			
	Plax			169 ± 122						81± 86	-71* (-42%*)	**S**			
	Listerine			150± 118						80±80	-69* (-46%*)	**S**			
Chen et al., 2010	SnF TP + tongue brushing	HM ppb	All gases	184.93	NR				28h	68.72	-116.21*(-63%*)	**S**	NR		
	NaF TP + tongue brushing			183.09						54,60	-128.49*(-70%*)	-			
	SnF TP			188.67						66,69	-121.98*(-65%*)	**S**			
	NaF TP			169.02						52,98	-116.04*(-69%*)	-			
Erovic et al, 2016	Water	OC ppb	H2S	NR	12 h	490.8 ± 432.5	ND	-	NR	NR			NR		
			$(CH_3)SH$	NR		184.3 ± 247.7	ND	-							
			$(CH_3)_2S$	NR		37.4 ± 33.5	ND	-							

	SB12		H2S	NR		67.8 ± 129.3	ND	**S**						
			$(CH_3)SH$	NR		46.0 ± 63.9	ND	**S**						
			$(CH_3)_2S$	NR		23.5 ± 27.8	ND	**S**						
	Halita		H2S	NR		69.6 ± 116.4	ND	**S**						
			$(CH_3)SH$	NR		65.1 ± 83.8	ND	**S**						
			$(CH_3)_2S$	NR		20.9 ± 19.6	ND	**S**						
	SB12 mild		H2S	NR		114.9 ± 264.8	ND	**S**						
			$(CH_3)SH$	NR		94.7 ± 276.1	ND	**S**						
			$(CH_3)_2S$	NR		29.3 ± 69.0	ND	**S**						
	Listerine		H2S	NR		227.0 ± 434.8	ND	**S**						
			$(CH_3)SH$	NR		106.7 ± 209.1	ND	**S**						
			$(CH_3)_2S$	NR		25.6 ± 41.1	ND	NS						
	RetarDEX		H2S	NR		155.3 ± 257.8	ND	**S**						
			$(CH_3)SH$	NR		44.1 ± 78.1	ND	**S**						
			$(CH_3)_2S$	NR		7.4 ± 7.5	ND	**S**						
Farina et al., 2012	Water	HM ppb	All gases	NR	1 min	NR	ND (- 43%)	-	180 min	NR	ND (+22%)	-	NR	NR
	CHX			NR		NR	ND (-59%)	**S**		NR	ND (-69%)	**S**		
	Green tea			NR		NR	ND (-50%)	NS		NR	ND (+31%)	NS		

	Curcuma Zedoaria			NR		NR	ND (-51%)	**S**		NR	ND (+30%)	NS							
Gerlach et al., 1998	Water	HM ppb	All gases	4.74	3h	4.56	-0.09* (-2%*)	-	8h	4.20	-0.27* (-6%*)	-	104 h	4.29	-0.18* (-4%*)	-	NR		
	Crest Gum Care			4.76		4.39	-0.37* (-8%*)	**S**		4.09	-0.67* (-14%*)	**S**		4.00	-0.76* (-16%*)	**S**			
	Crest Tartar Protection			4.74		4.51	-0.23* (-5%*)	NS		4.19	-0.28* (-6%*)	NS		4.16	-0.58* (-12%*)	**S**			
	Colgate Total			4.80		4.50	-0.3* (-6%*)	NS		4.18	-0.62* (-13%*)	NS		4.29	-0.51* (-11%*)	NS			
Jha et al., 2013	CPC	GC ng/10ml	H_2S	2.2± NR	NR								NR				28d	3.6±NR	+1.4* (+64%*)	-
			$(CH_3)SH$	2.2± NR														3.0±NR	+0.8* (+36%*)	-
	Hinokitiol		H_2S	3.6± NR														2.0±NR °	-1.6* (-44%*)	**S**
			$(CH_3)SH$	2.5± NR														0.9±NR °	-1.6* (-64%*)	NR
Keller et al., 2011	CG placebo	HM ppb	All gases	954 ± 600	NR								NR				14d	962 ± 583	+8* (+0%*)	-
	CG lactobacillus			1233 ± 572														1011 ± 630	-222*(-18%*)	NS
Lodhia et al., 2008	Crest TP	GC ng/10ml	H_2S	3.9±0.4	IA	3.4±0.6	-0.5* (-13%*)	-	3h	3.4± 0.5	-0.5* (-13%*)	-	NR				NR		
			$(CH_3)SH$	2.0± 0.2		1.7±0.3	-0.3* (-15%*)	-		1.6± 0.3	-0.4* (-20%*)	-							
	CG		H_2S	3.9± 0.5		4.2±0.5	+0.3* (+8%*)	NR		4.4± 0.5	+0.5* (+13%*)	NR							
			$(CH_3)SH$	1.9± 0.2		2.0±0.2	+0.1* (+5%*)	NR		2.3± 0.3	+0.4* (+21%*)	NR							
	Mints		H_2S	3.9± 0.5		4.0±0.5	+0.1* (+3%*)	NR		3.9± 0.4	0*(0%*)	NR							

			$(CH_3)SH$	2.1±0.3		2.2±0.3	+0.1* (+5%*)	NR		2.4±0.4	+0.3* (+14%*)	NR				
	Parsley oil		H_2S	4.1±0.5		4.2±0.5	+0.1* (+2%*)	NR		4.6±0.6	+0.5* (+12%*)	NR				
			$(CH_3)SH$	2.0±0.2		1.9±0.2	-0.1* (-5%*)	NR		2.2±0.3	+0.2* (+10%)	NR				
	Green tea		H_2S	3.6±0.4		3.2±0.3	-0.4* (-11%*)	NR		3.8±0.4	+0.2* (+6%*)	NR				
			$(CH_3)SH$	1.8±0.1		0.8±0.2°	-1* (-56%*)	NR		1.8±0.2	0 (0%)	NR				
Niles et al., 1999	NaF TP	GC ng/ml	NR	15.16 ± 3.13	NR								7d post	7.10 ± 2.32°	-8.06* (-54%)	-	NR
	Colgate Total TP			16,19 ± 3.71										5.62 ± 1.75°	-10.57* (-65%)	**S**	
Nohno et al., 2012	Placebo tablets	OC ppb	H2S $(CH_3)SH$ $(CH_3)_2S$	308.8 ± 67.1	IA	96.8 ± 25.4°	-212* (-69%*)	-	NR				7d	343.4 ± 112.9	+34.6* (+11%*)	-	NR
	Test tablets			589.9 ± 159.3		193.7 ± 47.9°	-396.2* (-67%*)	NR						297.6 ± 103.4°	-292.3* (-50%*)	NR	
Porciani et al., 2016	Control Tablet	OC ppb	H2S $(CH_3)SH$ $(CH_3)_2S$	165 ± 76	IA	108 ± 61°	-57 ± 40 (-35%*)	-	30 min	153 ± 75	-12 ± 23 (-7%*)	-	NR				NR
	Test tablet			166 ± 90		71 ± 40°	-94 ± 6 (-53%*)	**S**		117 ± 63°	-48 ± 54 (-29%*)	**S**					
Rösing et al., 2002	Zinc acetate	GC NR	H2S $(CH_3)SH$	NR	30 min	NR	ND (-96%)	-	120 min	NR	ND (-69%)	-	NR				NR
	Sorriso Herbal			NR		NR	ND (-29%*)	**S**		NR	ND (-13%*)	**S**					
	Kolynos Fluor			NR		NR	ND (-51%*)	**S**		NR	ND (-31%*)	**S**					

	Kolynos Bicarbonato			NR		NR	ND (-25%*)	**S**		NR	ND (-13.86%*)	**S**								
Rösing et al., 2009	Control CG	HM ppb	All gases	NR	1 min	NR	ND (-3 ± 6%)	-	30 min	NR	ND (-15 ± 19%)	-	NR				NR			
	Sucrose CG			NR		NR°	ND (-24 ± 20%)	**S**		NR	ND (-14 ± 18%)	NS								
Sakagami et al., 2016	Placebo TP	Breathron ppb	NR	388 ± 118	NR								1w	375 ± 65	-13* (-3%*)	NR	4w	NR	ND	NR
	TP with alkaline extracts			388 ± 118										371 ± 77	-17* (-4%*)	NR		182 ± 9	-206* (-53%*)	NR
Sterer et al., 2013	Placebo	HM ppb	All gases	139·	NR								24h	141·	+2* (+1%*)	-	NR			
	MW			139·										133·	-6* (-4%*)	NS				
	HMT			137·										113	-24* (-17%*)	**S**				
Suzuki et al., 2014	Placebo tablet	GC ng/10ml	H2S $(CH_3)SH$ CH_3SCH_3	8.0 ± NR	NR								NR				2w	5.8 ± NR	2.2* (-28%*)	-
	Test tablet			7.7 ± NR														3.1 ± NR°	4.6* (-60%*)	**S**
Tian et al., 2013	Control CG	GC ng/10ml	H2S $(CH_3)SH$	NR	12 min	NR°	ND (-47%)	-	180 min	NR	ND(+27%)	-	NR				NR			
	CG with AITC and zinc lactate			NR		NR°	ND (-89%)	**S**		NR°	ND(-24%)	**S**								
	CG with AITC			NR		NR°	ND (-68%)	NS		NR	ND(-9%)	NS								
Watanabe et al., 2018	Placebo gum	OC ppb	H2S	263.0 ± 166.5	NR								NR				4w	147.1 ± 144.4	-115.9 (-44%*)	-

			$(CH_3)SH$	71.1 ± 72.1				18.5 ± 22.9	-52.6 (-74%*)	-
			$(CH_3)_2S$	15.5 ± 11.6				16.2 ± 28.9	+0.7 (+5%*)	-
	PYC gum		H2S	226.1 ± 132.9				32.2 ± 33.7°	-193.9 (-86%*)	**S**
			$(CH_3)SH$	81.1 ± 49.5				10.1 ± 14.4°	-71 (-88%*)	NS
			$(CH_3)_2S$	30.6 ± 29.2				11.5 ± 22.5°	-19.1 (-62%*)	NS

Mean ± standard deviation
NR=non reported
ND=non deductable
*calculated based on reported averages
S=Statistically significant compared with the control group
NS =Statistically not significant compared with the control group
°statistically significant lower values compared to baseline

HM=Halimeter
OH=OralChroma
IA=immediately after
BL=Baseline
GC = gas chromatography