REVIEW ARTICLE

The Effectiveness of Mouthwashes With Various Ingredients in Plaque Control: A Systematic Review and Meta-Analysis

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ABSTRACT

Objective • Our study sought to present a solid comprehensive overview of the efficiency of active ingredients in mouthwash to control dental plaque.

Source • Cochrane Library, the Library of Medicine, (MEDLINE-PubMed), Web of Science database core collection, the database of the American Dental Association (ADA) Center for Evidence-based Dentistry and Scopus database were used for our review and meta-analysis.

Methodology • This was a systematic review that included papers with and without a meta-analysis on the efficacy of mouthwashes with various active ingredients in the control of dental plaque. *In vitro* and animal experiments were excluded from the study. Methodologic quality assessment was carried out with AMSTAR. The estimated plausible risk of unfairness was calculated according to the recording, reporting and methodologic quality of the selected systematic reviews per the PRISMA recommendations for systematic reviews.

Results • 580 initial hits were reported and 22 papers were chosen for the overview (kappa = 0.89; good agreement). Of these, 12 studies presented moderate methodologic consistency. In these studies, chlorhexidine (CHX) was the most beneficial in monitoring dental plaque data, and 4 meta-analyses showed that essential oils (EO) also had substantial antiplaque activity.

Conclusion • Descriptive and experimental studies have shown that CHX and EO have antiplaque activity that is useful in maintaining good oral hygiene. (*Altern Ther Health Med.* 2021;27(5):52-57).

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INTRODUCTION

It is universally accepted that disease prevention and treatment are absolutely necessary, and researchers are committed to decreasing the likelihood of their occurrence. As the mouth is the main conduit for feeding, oral and dental health is of the utmost importance. Bacteria are constantly forming in the mouth; they utilize micronutrients from saliva and food to grow exponentially if their numbers are not kept in check by practicing proper oral hygiene[1] or due to a disease process, the bacteria along with leftover food particles will develop into a thin biofilm of plaque; a sticky colorless substance that forms on the surface of teeth. The prevalence of periodontal disease is on the rise worldwide; subgingival plaque[2,3] is being correlated with stenotic coronary artery plaques,[4] which implies the importance of practicing oral hygiene. Despite advances in medicine and technology, modern mechanical oral hygiene methods are insufficient.[5-7] Throughout the world research has proved that the prevalence of periodontal disease is on the rise and dental plaque is the overarching etiologic factor,[2,3] suggesting that despite the medical and technologic advancements and innovations in the field, currently applied mechanical oral hygiene practices are inadequate.[5-7] This has been attributed to a multitude of factors, most notably that individuals fail to consistently perform adequate plaque control and oral hygiene.[6] In order to combat this limitation other modalities of plaque control started gaining traction as adjunctive methods along with the mechanical measures.[8]

The history of oral hygiene practice in humans dates back approximately 6000 years; the first recorded evidence of mouthwash use was in alternative and pseudomedicine (Ayurveda)[9] in the Indian subcontinent for the treatment of gingivitis.[10] Hippocrates II (460 BC to 370 BC) proposed a formulation of salt, alum and vinegar.[11] However, the first proposal to use mouthwashes containing antimicrobial agents was made by the American dentist and first oral microbiologist Willoughby D. Miller in the late 19th century. He suggested that phenolic compounds could improve gingivitis when the inflamed gingiva is subjected to the diluted compound for a certain period.[12] As a delivery system, mouthwashes have proven to be ideal for carrying active ingredients capable of altering the permeability of the bacterial membrane, interfering with its metabolism and hindering its ability to adhere to the surface of the teeth.[13,14] The use of mouthwash is widely understood and a common practice in the majority of people, whether it is used to combat gingivitis or bad breath. For a long time, mouthwashes have been available over-the-counter (OTC), and this has slowly but surely allowed mouthwash to become a household item that is part of routine hygiene for many people.[15-17]

As is the case with highly sought after products, companies and manufacturers are very competitive, and hope to secure and dominate the largest chunk of the consumer market. To push the boundaries, they release more and more products in order to achieve a greater variety, along with making grand and audacious—and mostly unsubstantiated—claims about the potency of their products. Dental professionals are faced with the responsibility of analyzing available products and reading the related literature in order to make informed and updated recommendations to their patients, and be able to answer their patients' questions confidently.[17] A large number of studies are published every year, often but not always with conflicting findings. These variations could be attributed to chance, study flaws or inter-study differences, such as variations in the sampling process. The immense volume of the literature, combined with inexplicably ambiguous results, makes it difficult for practitioners to sift through it all and stay up to date on every topic. Systematic reviews address these limitations by identifying, critically evaluating and integrating the findings of the individual studies,[18,19] as well as identifying relationships, contradictions, and inconsistencies in the literature to provide theories about the reasons behind such inconsistencies. Finally, they provide valid guidelines for practices and policies, allowing professionals to make evidence-based decisions and recommendations.[20-22]

The objective of this systematic review is to represent a solid wide-ranging overview with respect to the efficacy of active ingredients in mouthwashes to control dental plaque.

MATERIALS AND METHODS

Protocol Development

The protocol used to assess the methodologic quality of this systematic review was AMSTAR-2,[23] which can be accessed through at *https://amstar.ca/Amstar-2.php.* AMSTAR (a tool to evaluate systematic reviews), was further developed in 2017—AMSTAR 2—to enable judgement of systematic reviews of both randomized and non-randomized control trials. AMSTAR 2 is a revised instrument that has simpler response categories with a total of 16 items and is not intended for score generation.

Focused Question

The question this systematic review is attempting to answer is: How effective are mouthwashes with different active ingredients in controlling and combating dental plaque in adults ≥18 years of age based on the body of evidence gathered from existing literature of both systematic and meta-reviews?

Search Strategy

The International Prospective Register of Systematic Reviews (PROSPERO) was searched to ensure that no systematic review that tackles the same topic was being undertaken as of April 8, 2019, then a record of this study was submitted on the same day to PROSPERO, indicating that a systematic review was in progress. This systematic review was conducted from April 28, 2019 to February 14, 2020. Articles dated before April 16, 2019 that conformed to the inclusion criteria were included in the analysis.

To ensure that all good quality articles were accounted for, all-inclusive search criteria were developed, and a total of 4 prominent and reputable databases were selected and queried. They include the Cochrane Library, that contains the DARE database for systematic reviews; the National Library of Medicine, (MEDLINE-PubMed); Web of Science database core collection (a Clarivate Analytics company), the database of the American Dental Association (ADA) Center for Evidence-Based Dentistry; and Elsevier's Scopus database. These sources were searched for eligible articles that were aligned with the purpose of this study. The structure of the search design was to include all systematic reviews and meta reviews.

Search scientific terms in PubMed, Cochrane Oral Health Group, Web of Science (Clarivate Analytics), Center for Evidence-based Dentistry (ADA) and Scopus (Elsevier). Mouthwash (capital M or small m) OR Mouthwashes (capital M or small m) OR Mouthrinse OR mouthrinse OR Mouthrinses OR mouthrinses. Once as [MeSH] and once as [free text word]. Filter used: systematic review OR meta review OR meta-analysis. The research protocol was appropriately adapted for the 4 queried electronic databases. Inter-database variations in sentence building and vocabulary rules were taken into account.

Selection Criteria

The study selection was carried out in 2 phases. In the first stage, titles and abstracts were autonomously screened for selection by 2 reviewers (A.I.E. and G.K.K.), based on predetermined inclusion and exclusion criteria and disagreements were resolved by dissuasion and consensus.

If the title met the eligibility criteria, the article was selected; if it did not, the abstract was read carefully for compatibility. Only the latest version of an updated study was chosen. The study references that met the eligibility criteria were manually screened for further published articles meeting the criteria. There were no attempts to hide the names of the authors or the journals. The inclusion criteria were:

- Systematic reviews alone and with a meta-analysis
- Publications printed in the English language
- Research performed in humans
- Patients ≥18 years of age
- In appropriate general health conditions such as chemical plaque control measures employed in control of gingival and periodontal diseases
- Intervention: mouthwashes with different ingredients
- Outcome: plaque control

The exclusion criteria were:

- *In vitro* studies
- Animal studies
- Publications represented as abstracts only, editorials and correspondence sectors
- Plaque on dental implants
- Orthodontic patients

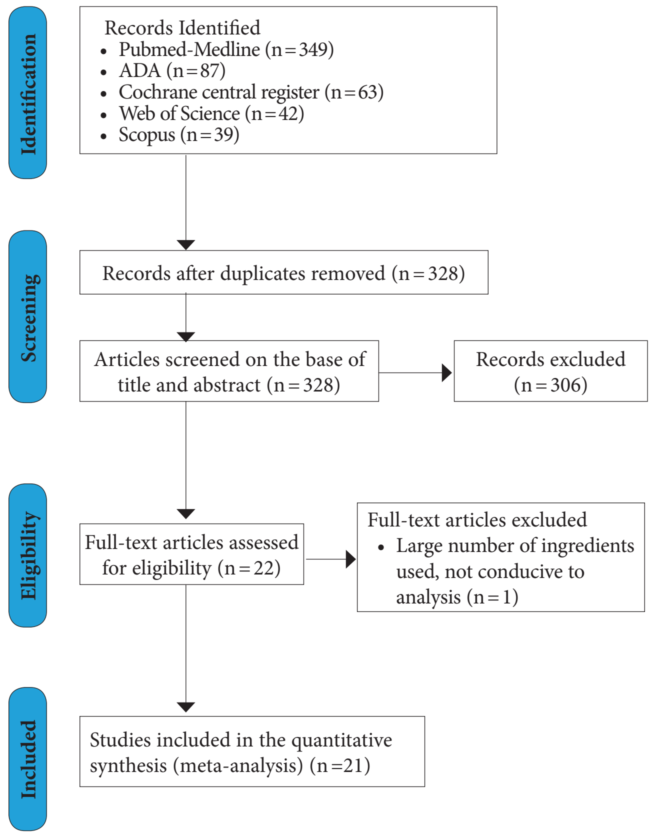

Figure 1. The flow chart of screening and selection of related publications.

Quality of Reporting, Hazard of Bias and Heterogeneity Assessment

The quality, risk of bias and heterogeneity assessment of the selected studies were autonomously carried out and any dissimilarity between the investigators was resolved by discussion and consensus. The assessment for reporting quality of reviews of randomized trials was done via Consolidated Standards of Reporting Trials (CONSORT) specification for reporting random controlled trials.[24,25] It contains a 22-item checklist; each item was determined to be yes/inadequate/unclear/no/inapplicable, for all trials.

The estimated plausible risk of bias was performed by recording, reporting and the methodologic value of the selected systematic reviews according to PRISMA[26,27] recommendations for the writing of systematic reviews. A total of 27 items was assessed. A perfect score of 100% was only achieved if each item was given a positive rating; studies with a score of 100% were included in the review. The total risk of bias of the selected studies, clarity of evidence, result consistency and publication bias, among other factors, were taken into account. The interpretation of the assessed risk of bias was: 0% to 40% = high risk, 40% to 60% = substantial risk, 60% to 80% = moderate risk, 80% to 100% = low risk.

The heterogeneity between articles involved in the meta-analysis was examined via the chi-square test and the I^2 statistic. The result of the chi-square for $P < .1$ was indicative of substantial statistical heterogeneity. Along with the Grades of Recommendation, Assessment, Development and Evaluation (GRADE)[28] guidelines for rating the quality of evidence, arbitrary parameters for interpreting I^2 value can be used as a rough estimate of consistency. An $I^2 \geq 50\%$ indicated moderate heterogeneity, an $I^2 > 75\%$ indicated substantial heterogeneity, while an $I^2 < 50\%$ indicated inconsequential heterogeneity and was considered acceptable.

Data Extraction and Evidence Grading

Data concerning the study quality, focus question, search results and outcomes were processed for extraction from articles fulfilling the selection criteria. The data was extracted, categorized, summarized and graded independently. Questions and dissimilarities between the investigators were finalized via fruitful discussion followed by consensus. Categorization was carried out based on the active ingredients in the mouthwashes.

RESULTS

The main outcomes of this review are shown in Figure 1 and Table 1.

Table 1. Main Characteristics of Investigated Studies.

Authors/ Year Published	Mouthwash Ingredients	Main Type of Analysis	#Studies Included w/PI Index	n	Study Investigators' Conclusion(s)
Jassoma, et al. 2019[29]	Salvadora persica vs CHX	Meta-analysis	19	-	Salvadora persica extract caused noteworthy decrease in plaque score
Almaweri, et al. 2019[30]	Aloe vera vs CHX	Descriptive analysis	6	135 8	Aloe vera is inferior to CHX in plaque reduction
Phimarn, et al. 2019[31]	Triphala	Meta-analysis	11	141 7	Triphala can effectively contribute to plaque control
Mathur, et al. 2018[32]	Camellia sinensis	Descriptive analysis	9	-	Camellia sinensis can be considered an alternative to CHX in sustaining oral hygiene
Dhingra, et al. 2017[33]	Azadirachta indica	Descriptive analysis	3	-	Neem and CHX showed the same curative effects in prime and minor treatment outcomes
Haas, et al. 2016[34]	EO	Meta-analysis	14	-	EO was superior to placebo + MPC and CPC + MPC for reducing plaque and gingival inflammation
Araujo, et al. 2015[35]	EO	Meta-analysis	28	510 6	6 months of clinical trials confirmed the advantage of daily EO rinse use for decreasing plaque and gingivitis.
Serrano, et al. 2015[36]	TCL	Meta-analysis	-	-	Pharmaceuticals with plaque reduction agents are statistically important enhancements for gingival, bleeding and plaque indices.
Van Leeuwen, et al. 2014)[37]	EO	Meta-analysis	5	605	EOs are more beneficial for plaque and gingivitis than vehicle solutions
van Maanen-Schakel, et al. 2014[37]	CHX and H_2O_2	Meta-analysis	4	252	EOs are more beneficial for plaque and gingivitis than vehicle solutions
Van Strydonck, et al. 2012)[39]	CHX	Meta-analysis	30	355 4	CHX solutions with OA vs placebo or control show notable reductions in plaque and gingivitis scores, but an increase in staining scores.
Van Leeuwen, et al. 2011[40]	EO vs CHX	Meta-analysis	19	827	With prolonged use, standard CHX formulations are significantly more effective than EO in plaque reduction.
Hossainian, et al. 2011[41]	H_2O_2	Descriptive analysis	10	384	H_2O_2 solutions do not steadily prevent plaque accumulations when used for short-term monotherapy.
Afennich, et al. 2011[42]	HEX	Descriptive analysis	6	357	HEX showed superior plaque control compared with placebo but still inferior to CHX.
Gunsolley, et al. 2010[43]	More than one	Meta-analysis	-	-	The advantages of anti-plaque, anti-gingivitis mouth solutions are similar to the pros of oral prophylaxis and hygiene instructions at 6 months
Berchier, et al. 2010[44]	0.12% CHX vs 0.2% CHX	Meta-analysis	8	803	0.2% CHX showed small but significant difference in plaque inhibition compared with CHX 0.12%
Haps, et al. 2008[45]	Cetylpyridinium chloride (CPC)	Meta-analysis	8	867	CPC mouthwash when used as adjunct to oral hygiene show an observed but small advantage in preventing plaque accumulation
Addy, et al. 2007[46]	Delmopinol, (DEL)	Weighted point estimate	8	913	Delmopinol 0.2% shows adjunct activity for plaque control, whether used under medical supervision or not
Stoeken, et al. 2007[47]	EO	Meta-analysis	11	281 0	As an adjunct to non- supervised oral hygiene, EO has an advantage regarding plaque and gingivitis reduction compared with placebo or control
Paraskevas, et al. 2006[48]	Stannous fluoride (SnF_2)	Descriptive analysis	3	781	Use of SnF_2 dentifrices results in plaque reduction compared with conventional dentifrices
Gunsolley, et al. 2006[49]	More than one ingredient (CHX, EO, CPC and DEL)	Meta-analysis	-	-	CHX and EO mouthwashes are effective for plaque reduction while CPC showed weak activity. The meta-analysis review for DEL confirms its benefit as an anti-plaque agent.

Abbreviations: CHX, chlorhexidine; CPC, cetylpyridinium chloride; DEL, delmopinol; EO, essential oils; HEX, hexetidine; H_2O_2, hydrogen peroxide; OA, oxygenating agents; SnF_2, stannous fluoride; TCL, triclosan.

DISCUSSION

This study reviewed the existing data provided in the context of methodical analyses of the effectiveness of active ingredients in mouthwash to control dental plaque. Since there are several such reviews available, we only included systematic review; this form of study typically offers more data than individual observational studies alone. Solid, reliable evidence emerged from 36 studies evaluating chlorhexidine (CHX) and essential oils (EO) to demonstrate that these components actively reduce plaque.[37,39] In the meta-analysis, however, the evidence also indicates mild to substantial heterogeneity. Therefore, it is not easy to compare these 2 different-based chemical agents or to conclude that 1 component will be more effective than the other.

Mouthwash is essentially a way of supplying active components to the mouth cavity in which all the outer surfaces of the dentition come into contact with the mouth solution after rinsing for 20 to 30 seconds.[50] Most of them are made of a foundation of H_2O or H_2O-alcohol, with additional color, surfactant and humectant for their pharmaceutical characteristics. Mouthwash and its active components are introduced to the mouth for a comparatively brief amount of time before they are expelled from the oral cavity. Furthermore, the activity of certain compounds may be decreased by the proteins found in saliva.[51] The property of substantivity means that potential antibacterial effects are maintained over even longer periods, at least for certain chemicals (such as CHX).[52] Substantivity relates to the capacity of an agent to be stored in the oral cavity and extracted with long-term conservation of potency. The strength and rate of interaction of the antiplaque agent influences its average oral retention. Comparing CHX with the non-ionized form of delmopinol accounts for the majority of absorbed delmopinol, which can be explained by the pKa-value for delmopinol, the significant difference in water solubility between its cationic and non-ionized forms.[53]

There are 2 types of bacteria in the mouth: free-floating (planktonic) saliva bacteria and "biofilm" dental plaque, a 3-dimensional population adhering to all oral surfaces of up to 700 different bacterial organisms. Dental plaque, which can be manually detached by active brushing and flossing, is the chief reason for oral diseases. Most individuals have a huge amount of plaque left behind on the teeth that is relatively unchanged by mechanical means of plaque management. This plaque, which could be removed initially by brushing or scraping with a finger, hardens and then poses a threat to gingivitis growth and ultimately to mobility and loss of teeth.

Salvadora persica miswak tooth-cleaning sticks, used for centuries as a natural toothbrush, detached plaque more quickly than brushing the teeth.[29,54] The study concerning schoolchildren needed guidance and supervision to be given since most kids were unfamiliar with the correct miswak usage technique. Analysis of *S persica* miswak has been found to contain β-sitosterol and m-anisic acid; chlorides, salvadourea, and gypsum; organic compounds such as derivatives of pyrrolidine, pyrrole, and piperidine; glycosides such as salvadoside and salvadoraside; and flavonoids such as kaempferol, quercetin, rutin quercetin, and glucoside quercetin. *S persica* miswak contains approximately 1.0 µg/g of total fluoride, and large amounts of calcium and phosphorus were found to be released into water.

Summary

Antimicrobial mouth rinses are designed to monitor oral biofilm production, growth and maturation, which are highly structured 3-dimensional bacterial populations. Once established, they are hard to penetrate and need mechanical disruption and chemical treatment. By enhancing entrance into the biofilm, CHX has the highest antiplaque efficacy.

CONCLUSION

Descriptive and experimental studies have shown significant evidence that CHX and EO have beneficial antiplaque activity for maintaining good oral hygiene. CHX can be used alone or in combination with conventional toothbrushing to ensure good oral health and hygiene, and numerous research and clinical trials that looked at the efficacy of CHX are promising.

Study Limitations

The study did not include the relationship using mapping analysis between the studies that were included. Test use settings, the intended function of the test, characteristics of the research design and participant demographics were often not presented. The numbers needed to recreate the 2 × 2 results tables used in each analysis often were not addressed. Nanoparticles and natural molecules having significant antiplaque effects in oral healthcare were also not assessed.

Bibliometric analysis would provide more detailed insight to address research questions regarding how beneficial mouthwashes are in the management of periodontal diseases.

CONFLICT OF INTEREST

The authors reported no conflict of interest.

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