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Review article

State of the art of mouthwashes: a review

Estado da arte dos enxaguatórios bucais: uma revisão

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Abstract

Objective: to establish the state of the art of mouthwashes regarding the chemical control of oral biofilm and unwanted effects in the oral cavity. **Materials and Methods:** an electronic search was carried out in the following databases: PubMed, Clinical key, Dentistry & Oral Science Source, Science direct, and Scopus, using the keywords: "dental plaque, chemical control, dental plaque and chemical control". Articles that had mouthwashes as their focus in the present and those that may be highlighted in the future were included in the review. **Results:** 260 documents were obtained. After filtering according to the inclusion criteria, seven full-text documents were used for analysis. **Conclusion:** the development and clinical application of oral antiseptics require applied research to solve the daily problems of patients. Mouthwashes that include a natural component as an active principle have shown, according to the studies included, a good percentage of inactivation of the pathogenesis of the oral biofilm, so future studies should focus on these, paving the way for natural products that reduce the percentage of adverse effects in the oral cavity.

Keywords: Biofilm. Essential Oils. Chlorhexidine.

Resumo

Objetivo: estabelecer o estado da arte dos enxaguatórios bucais, em relação ao controle químico do biofilme bucal e dos efeitos indesejados na cavidade oral. **Materiais e Métodos:** foi realizada uma busca eletrônica nas bases de dados: Pubmed, Clinical key, Dentistry & Oral Science Source, Science direct e Scopus, utilizando as palavras-chave: “dental plate,chemical control, dental placa andchemical control”. Foram incluídos na revisão artigos que tenham os enxaguatórios bucais como foco principal hoje e aqueles que possam estar em destaque no futuro. **Resultados:** obteve-se um total de 260 documentos. Após triagem para o uso dos critérios de inclusão, um total de 7 documentos de texto completo foram usados para análise. **Conclusão:** o desenvolvimento e a aplicação clínica de antissépticos orais requerem pesquisas aplicadas para solucionar os problemas cotidianos dos pacientes. Enxaguantes envolvendo um componente natural como princípio ativo têm apresentado, de acordo com os estudos incluídos, um bom percentual de inativação da patogênese do biofilme bucal, portanto estudos futuros devem ser redirecionados nestes, abrindo caminho para produtos naturais que reduzam o percentual de efeitos adversos na cavidade oral.

Palavras-chave: Biofilme. Óleos essenciais. Clorexidina.

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Introduction

Bacterial colonies can accumulate on the surface of the teeth, developing biofilms and causing periodontal disease[1]. Maintaining oral hygiene by regularly removing biofilm and food deposits plays a major role in preventing dental caries and periodontal disease[2]. Taking into account that human dysbiosis has an important microbiological component in the appearance and development of these, it is essential to know that bacteria play a crucial role as initiators of dysbiosis in the oral cavity, whether chronic or acute[3].

Although brushing and flossing are the most reliable sources for mechanical control of biofilm, some factors such as lack of manual ability and lack of interest hinder its positive impact. The effectiveness of mechanical removal of biofilm is very limited, as well as its results in the medium and long term[4].

To help control the deleterious action of biofilm in the oral cavity of patients, numerous anti-biofilm chemical agents in different formulations are recommended by dentists to improve oral health by controlling oral biofilm[1]. Antimicrobial mouthwashes can disrupt biofilm formation by inhibiting the growth, metabolism, and colonization of oral bacteria[5].

The first recorded evidence of the use of mouthwashes was in alternative medicine and pseudo-medicine (Ayurveda) in the Indian subcontinent for the treatment of gingivitis. Hippocrates II (460 BC to 370 BC) proposed a formula of salt, alum, and vinegar. However, the first record of mouthwashes containing antimicrobial agents was made by the American dentist and oral microbiologist, Willoughby D. Miller in the late 19th century, who suggested that phenolic compounds could decrease gingivitis by using the compound diluted for a certain period[6].

Although the chemical control of biofilm helps maintain oral health, these chemical agents have side effects. Therefore, there is an ongoing search within the basic sciences and dentistry for mouthwashes with comparable efficacy and fewer unwanted side effects. Recently, much emphasis has been placed on natural products that aid oral hygiene with little to no side effects[1].

Among some of the natural products used is Aloe vera, which is a medicinal plant with mucilaginous tissue in the center of the leaf. Aloe vera mouthwash has been used recently because, in addition to its safety, it is also cheap and easy to obtain, has no side effects, and is effective in reducing biofilm-causing bacteria[2].

Baicalein and Miswak's mouthwashes have also been studied. Baicalin prevents the formation of biofilms by inhibiting the bacterial density detection system (Quorum Sensing). On the other hand,

Miswak was evaluated as a chemical agent for its antibacterial, antifungal, and anti-cariogenic properties[8].

Cetylpyridinium chloride (CPC) mouthwashes also have an important role in recent research. The addition of zinc lactate has been proposed to increase the ability of CPC mouthwashes for both biofilm and gingivitis reduction. A randomized controlled trial found that this combination substantially increased the anti-biofilm and anti-gingivitis effects of CPC compared to a CPC-only mouthwash[9].

The main objective of this review was to establish a current and future vision of mouthwashes, understanding their importance and effectiveness individually and in comparison with other mouthwashes of natural or chemical composition, as indicated by the studies in the selected articles.

Materials and Methods

A literature review study was developed through an electronic search using databases such as PubMed, clinical key, Dentistry & Oral Science Source, ScienceDirect, and Scopus using validated keywords such as dental plaque, chemical control, and the combination dental plaque and chemical control.

Selection criteria

The search for documents in English and Spanish was limited from 2020 to 2022, using the criteria established by the PRISMA methodology. For the review of the articles, the analysis of the titles was carried out, which allowed filtering of the noisy data. Then, the abstracts were read and studied, analyzing that the inclusion criteria were clearly expressed in the selected documents, such as the methodology used. A classification of the articles was carried out, selecting those that met the inclusion criteria, then, they were analyzed and discussed as complete articles. The inclusion criteria established were: review articles, systematic reviews, clinical trials, and exploratory articles. Exclusion criteria were: cross-sectional articles, retrospective cohort studies, pilots, clinical cases, case reports, letters to the editor, and book chapters.

Data processing

The collected information was organized in a data table in Word to condense relevant data for readers. Authors, titles, and main results are shown. A small statistical analysis was made with measures of central tendency expressed in percentages.

Results

A total of 260 references were obtained by searching the keywords Dental plaque, Chemical control, and the combination: Dental plaque and Chemical control. Of the results obtained, only seven (7) complete articles were considered, excluding 252 references due to noisy data, differences with the topic evaluated, cross-sectional articles, clinical cases, and book chapters (Figure 1).

Figure 1. Selection flowchart.

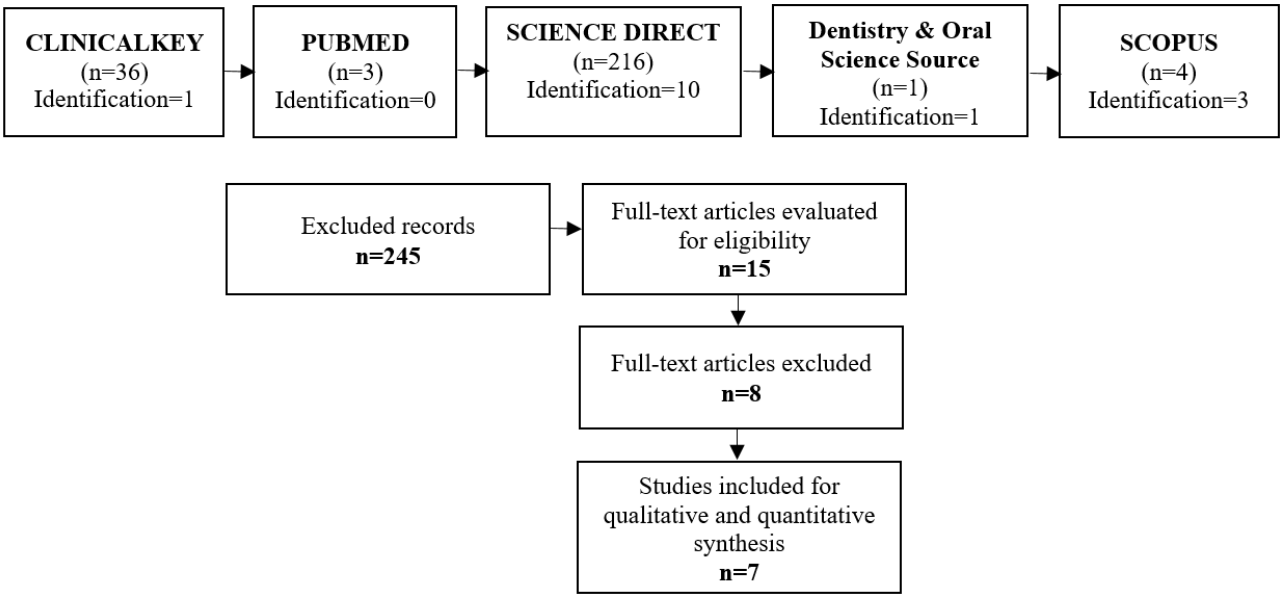

Table 1. Characteristics of the included studies.

Authors	Type of Study	Types of mouthwashes	Conclusions
Ozma *et al.*, 2021[7]	Review article	Baicalin	Baicalin prevents bacterial damage to host cells and increases its effectiveness when in synergy with antibiotics.
Spuldaro *et al.*, 2020[10]	Review article	Listerine with alcohol/without alcohol	Mouthwashes with alcohol and without alcohol showed efficacy in controlling the formation of supra and subgingival biofilm. Those that did not contain alcohol showed greater efficacy.
Nordin *et al.*, 2020[8]	Review article	Miswak.	Miswak's clinical effects include antiplaque, antigingivitis, anti-cariogenic, promoting gingival wound healing, whitening properties, preservation of orthodontic chains, and biocompatibility with oral cells.
Pattnaik *et al.*, 2021[1]	Randomized controlled clinical trial	Aloe vera, hydrogen peroxide, and Cetylpyridinium chloride	The antiplaque and antibacterial efficacy of the aloe vera mouthwash was similar to that of the cetylpyridinium chloride mouthwash and significantly better than that of the hydrogen peroxide mouthwash.

Gerson *et al.*, 2021[9]	Randomized clinical trial	Cetylpyridinium chloride with zinc lactate and essential oils	The group that used a mouthwash containing cetylpyridinium chloride plus zinc lactate and fluoride had significantly greater antibiofilm and antigingivitis effects than the one that used essential oils and the control group both in the whole mouth and on the interproximal surfaces of the teeth.
Saurabh *et al.*, 2021[11]	Prospective, triple-blind, randomized clinical trial	Chlorhexidine 0.2%, Hiora, and Achyrantes Aspera	Hiora mouthwash and mouthwash containing Achyranthes aspera are potent antiplaque agents and can be used as natural alternatives to 0.2% chlorhexidine mouthwash. No adverse reactions, harmful effects, or stainings were observed in the participants during the study.
Alnouri *et al.*, 2020[2]	Randomized clinical trial	Aloe vera, Chlorhexidine, Distilled water	The use of Aloe vera mouthwash is effective in reducing the biofilm index in children.

Essential oils

They are a group of anti-biofilm agents that, from the studies by De Paola, where it was established, among other aspects, that the use of thymol, menthol, and methyl salicylate can reduce the biofilm of the oral cavity by 34% after six months of continuous use, they can be used daily as a chemical control of dental biofilm, with a variety of clinical and microbiological effects[12].

As a modern vision of this group of anti-biofilm agents, recent studies such as that of Kowalczyk et al.[13] mention that thymol and thyme essential oil are part of the current search for new directions of biological or therapeutic activities of natural plant substances with structures known as these essential oils, which have demonstrated antibiofilm, antifungal, anti-leishmaniasis, antiviral, and anticancer properties. In addition, new therapeutic presentations, such as nanocapsules containing these constituents [14], may be favorable in medical practice and create opportunities for their broader use. It is important to highlight that the extensive application of thymol and thyme essential oil in medical practice is very promising, then further research and analysis are required.

It is now known that in vitro physicochemical assays characterize most essential agents as antioxidants[15]. It is also observed that, in eukaryotic cells, these chemical agents can act as pro-oxidants affecting internal cell membranes and organelles such as mitochondria. Depending on the type of essential oil and its concentration, they exhibit cytotoxic effects on living cells but are generally not genotoxic. In some cases, changes in intracellular redox potential and mitochondrial dysfunction induced by essential oils may be associated with their ability to exert anti-genotoxic effects. These findings suggest that, at least in part, the beneficial effects of essential oils are due to their pro-oxidant effects at the cellular level.

Cetylpyridinium Chloride

The use of this agent as an anti-biofilm has been tested for a long time in different experimental models[16]. The results regarding its ability to control biofilm are low, even in different presentations or in combination with other agents. Some studies where CPC is evaluated as an anti-biofilm agent report that its ability to inhibit biofilm is around 30%, which is still low but is similar to that of essential oils. On the contrary, other studies mention that the capacity of CPC to control bacteria in the mouth in the long term does not exceed 20%, which makes it a biofilm control chemical agent with low effectiveness[17]. Its mechanism of action is the increase in the permeability of the bacterial wall, which increases bacterial lysis with low substantivity. As reported with most of these chemicals, the main unwanted effect of this agent is the appearance of staining in the oral cavity, especially stains on the teeth.

Chlorhexidine

It is mentioned in most scientific publications as the reference chemical agent in the control of oral biofilm due to the percentage of reduction of bacterial plaque that it shows, which in some cases is between 40 and 60%[18]. It is also known that chlorhexidine has a high substantivity, whose main biological and therapeutic effect is the decrease of the formation of the acquired biofilm and the increase in the lysis of the bacterial wall. Due to its ability to adhere to oral surfaces, it has a much longer effect, which is reflected both in its ability to control bacteria and in the ability to produce unwanted effects in the oral cavity, such as stains, loss of taste, and the presence of ulcers in mucous membranes[19].

D Limonene

It is a natural substance that has been used for some years as a flavoring in different industries. D limonene is extracted from the peels of citrus fruits by various extraction processes and it shows a high potential for current and future utility due to its wide range of therapeutic effects[20].

Within the therapeutic effects of D Limonene, we can mention: antioxidant[21], anticancer[22], antibacterial[23], antifungal [24], and especially, its ability to inactivate the Sars-Cov-2 virus in the oral cavity[25], which makes this type of mouthwash highly desirable due to the global public health situation.

Discussion

Biofilm formation is a physiological process that occurs around and on the surfaces of the teeth, which is associated with the presence of dental caries and periodontal disease in its various clinical forms. Currently, there are mechanisms to eliminate or inhibit biofilm, mechanically or chemically, brushing and flossing being the main ones to delay its growth. However, anti-biofilm chemical agents are a great adjunct to mechanical instruments but not a replacement for them. [26].

Numerous chemical agents inhibit biofilm growth, as mentioned by Raubert et al. in their study, where they made a comparison of essential oils (EO) with and without alcohol, finding better results for the test group, which showed a 23.9% reduction in the biofilm index and a 10.4% reduction in the gingivitis index in two weeks in patients who used EO without alcohol; however, the difference was not significant. In the same study, a comparison was made between EO without alcohol and cetylpyridinium for six (6) months, obtaining better results with EO without alcohol with a reduction of 26.5% in the biofilm index and 20.5% in that of gingivitis. On the other hand, EO without alcohol and 0.2% chlorhexidine with zinc fluoride were also compared, but good results were not obtained in biofilm reduction[10].

Today, many plant-based kinds of toothpaste help inhibit biofilm without using chemical agents. Chakravarthy *et all*[27] stated that vegetal products are a safe long-term alternative for preserving optimal oral health. It is crucial when selecting an anti-biofilm agent not only the amount of inhibition it achieves but also the least amount of side effects or undesired effects derived from its clinical application, as mentioned by Cavalca-Cortelli. et al. in 2014[28], these authors reported that numerous factors are decisive when selecting the biofilm chemical control agent of patients who use dental prostheses and that the mechanical control of this bacterial mass consists of a combination of a manual or electric brush and toothpaste, as well as the devices for interdental cleaning. Although many chemical agents exhibit antimicrobial benefits when used for denture disinfection, only a few can be used safely.

Conclusion

The last word has not yet been said in the clinical application and development of oral antiseptics, implying that research is lacking, especially the one applied to the solution of daily problems in dental patients, specifically concerning the control of dental biofilm. The limited capacity of most patients to keep adequate and effective oral hygiene should be emphasized, which is reflected in the high prevalence of caries and periodontal disease detected in dental offices.

The use of new technologies in the field of dental biofilm chemical control agents is aimed at the development of nanocapsules, which facilitates the reduction of concentrations and the possibility of getting to inaccessible places for current presentations, which are not capable of reaching all the reservoirs of the oral cavity, such as deep periodontal pockets.

Pharmaceutical companies developing and commercializing these chemical agents imply that plant-derived options that show good biofilm control capabilities and few unwanted effects on patients are being explored.

Contribution of the authors

All authors approved the final manuscript and declared themselves responsible for all aspects of the work, including its accuracy and integrity.

Conflict of interests

The manuscript was prepared and reviewed by all the authors, who declare that no conflict of interest compromises the validity of the results.

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