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Review

Antimicrobial Effect of Medicinal Plants Against *Streptococcus mutans*: A Literature Review

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Abstract: The present study aims to evaluate, through a literature review, the antimicrobial potential of medicinal plants against Streptococcus mutans. Method: A bibliographic search was conducted in the PubMed database using the descriptors "phytotherapy," "medicinal plants," and "*Streptococcus mutans*," either combined or not, covering the period from 2011 to 2021. The search resulted in 99 articles. In the initial screening, 79 articles were excluded for not being related to the topic. Twenty articles were selected, but only 12 met the eligibility criteria, which included studies evaluating the antimicrobial effect of a single medicinal plant on S. mutans only. Among the results, several plant species with antimicrobial potential against S. mutans were identified, including *Annona senegalensis*, *Melia azedarach*, *Copaifera langsdorffii*, *Copaifera officinalis*, *Zingiber zerumbet*, *Terminalia chebula*, *Trachyspermum ammi*, *Ocimum sanctum*, *Teucrium polium*, *Vitis vinifera L.*, and *Cinnamomum zeylanicum Blume*. In summary, all studies showed antimicrobial effects against *S. mutans*, with particular emphasis on the studies with copaiba oil, *M. azedarach* crude extract, and *T. polium*, which demonstrated superior and comparable results to the effects of chlorhexidine, respectively.

Keywords: Phytotherapy; Medicinal plants; *Streptococcus mutans*.

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1. Introduction

A doença cárie é considerada uma das patologias mais prevalentes em todo o mundo. O desenvolvimento das lesões cariosas está relacionado à aderência de microrganismos na superfície dentária, associado à ingestão frequente de carboidratos fermentáveis. Assim, pode-se dizer que os principais mecanismos para prevenção da cárie são a remoção do biofilme por meios mecânicos, como a escovação e o uso do fio dental, além do controle dietético e, para pacientes com alto risco de cárie, o uso de métodos químicos. Os biofilmes são comunidades complexas de microrganismos envolvidos por uma matriz autoproduzida de substâncias poliméricas extracelulares (EPS) que aderem uns aos outros e a uma superfície. A matriz de EPS fornece aos microrganismos uma maior tolerância aos agentes antimicrobianos, em comparação à sua forma planctônica.

Os *Streptococcus mutans* desempenham um papel importante na formação do biofilme dental cariogênico. Isso se deve à sua capacidade de sobreviver em ambientes de baixo pH, produzindo ácido através do metabolismo de carboidratos da dieta. Além disso, na presença de sacarose, essas bactérias produzem glicosiltransferases (Gtf-B, -C, e -D), que desempenham papéis importantes na formação de um biofilme mais cariogênico, através da produção de polímeros extracelulares que favorecem a adesão bacteriana, alteram a estrutura do biofilme e, consequentemente, sua porosidade e permeabilidade, facilitando a difusão de nutrientes.

Atualmente, a clorexidina (CHX) é considerada o padrão ouro dos antissépticos orais; no entanto, seu uso prolongado pode causar efeitos colaterais indesejáveis, como alterações na coloração do esmalte e da língua, mudanças no paladar, queimaduras em tecidos moles, dor e um gosto residual desagradável na boca. Por conta disso, há um interesse crescente no desenvolvimento de substâncias capazes de substituir a clorexidina.

Outro ponto relevante é o surgimento de microrganismos resistentes aos antibióticos, o que representa um desafio para o tratamento de infecções e demanda novas abordagens terapêuticas. Como resultado, o efeito de produtos derivados de plantas tem sido amplamente estudado, com o objetivo de identificar ações biológicas efetivas, desde atividades antimicrobianas até antitumorais. Esses produtos podem ser extraídos de diferentes partes das plantas, como cascas de troncos, frutos, raízes, folhas e sementes, e são econômicos, eficazes e geralmente apresentam alta tolerância ou poucos efeitos adversos, dependendo da concentração utilizada. Assim, eles se tornam uma alternativa promissora aos antibióticos, especialmente no tratamento de lesões cariosas em pacientes de alto risco.

Diante disso, o presente estudo tem como objetivo realizar uma revisão de literatura sobre o potencial antimicrobiano das plantas medicinais contra *Streptococcus mutans*.

2. Methodology

For this study, a bibliographic search was conducted in the PubMed database using the descriptors "phytotherapy," "medicinal plants," and "*Streptococcus mutans*," either combined or not, covering a 10-year period. Data collection concluded on June 4, 2021, and a total of 99 articles were identified.

The selection of articles began with a rigorous analysis of the titles and abstracts of the retrieved articles. Initially, articles that did not address the proposed theme were excluded, such as studies on bacteria involved in periodontal diseases and other oral manifestations, as well as review articles, resulting in the exclusion of 79 articles. Subsequently, the full texts of 20 articles were evaluated, and only those that focused on the antimicrobial effect of a single medicinal plant specifically against S. mutans were included, leaving a total of 12 articles. The search flowchart is presented in Figure 1.

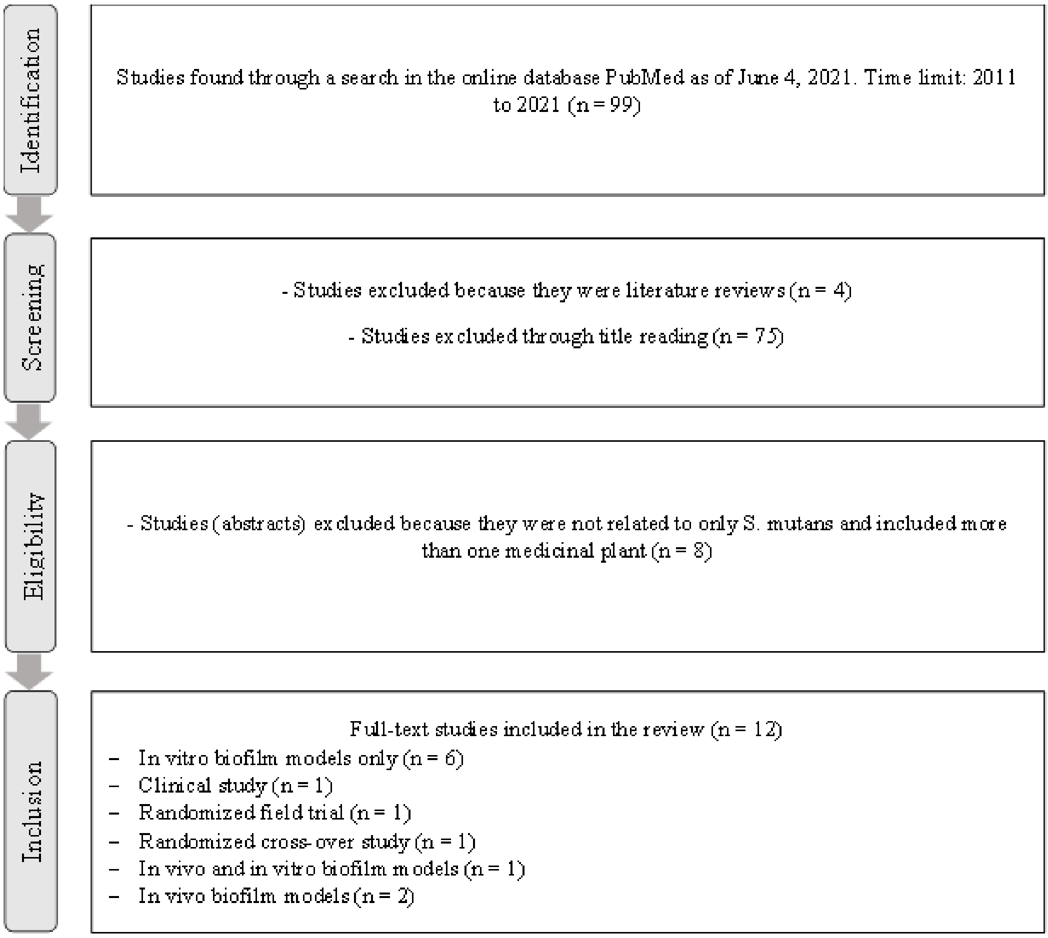
3. Discussion and Conclusion

Among the studies found, the strain ATCC 25175 of S. mutans was the most studied [12, 13, 14, 15], however, ATCC 35668, MTCC 497, ATCC 700610, were also evaluated. These in vitro studies assessed antimicrobial effects through broth microdilution testing and evaluated both antimicrobial and antibiofilm effects [2, 10, 16]. Other approaches included in vivo studies, randomized field trials, clinical studies, and randomized clinical cross-over studies [10, 17, 18, 19]. Evaluating the antimicrobial effect of Annona Senegalensis against S. mutans, four metabolites were isolated from the methanol extract of aerial parts of A. Senegalensis, through bioassay-guided fractionation: catechin, anonaine, asimilobine, and nornantenine. The four compounds studied showed moderate antibacterial activity compared to CHX. Among these, anonaine was the alkaloid that showed the best results, followed by nornantenine. Catechin and asimilobine exhibited low inhibition against S. mutans [12].

Conversely, an evaluation of the in vitro effect of the crude extract (CEx) of Melia azedarach on S. mutans demonstrated results similar to those of CHX 0.12%. The petroleum ether fraction and the CEx exhibited bactericidal effects; however, the ether fraction showed inferior results, likely due to a lower concentration of bioactive compounds in this fraction [13]. The bactericidal effect of copaiba oil (Copaifera officinalis) against S. mutans was assessed, showing better results compared to CHX 0.12%. Regarding the Minimum Bactericidal Concentration, all plates showed bacterial growth after 24 hours, indicating that the compounds did not exhibit bactericidal effects, only bacteriostatic. These findings suggest that copaiba oil has positive effects on inhibiting the growth of S. mutans, presenting concentrations as effective as those of CHX [14].

The potential effect of copaiba (Copaifera langsdorffii) was also evaluated in an in vivo study where random solutions at different concentrations (1%, 5%, 10%, and 20%) of copaiba oleoresin were used. For the study, two collections were performed. The first was done after patients chewed on plastic film, and the second immediately after the application of copaiba oleoresin on the deciduous molars. Among the concentrations evaluated, 1% was most effective in reducing the bacterial load of S. mutans at a 1:10 dilution. The benefits of the 1% concentration were confirmed when comparing the results of saliva collections at a 1:100 dilution, confirming the antibacterial properties of copaiba at low concentrations [20].

Figure 1: Article selection flowchart.



The antibacterial activity of grape seed extract (Vitis vinifera L.) at different concentrations was assessed and compared with CHX gluconate against S. mutans. Among the evaluated concentrations of grape seed extract (500, 250, and 125 mg/mL), only the higher concentrations (250 and 500 mg/mL) showed significant antibacterial effects. Compared to 2% CHX gluconate, the extract was less effective [15]. The antimicrobial activity of zerumbone (Zingiber zerumbet) against S. mutans was evaluated. Crystals of 98% pure zerumbone were predominantly used in the tests. The results demonstrated a 94.78% reduction in bacterial colonies and a bactericidal effect within 48-72 hours in their logarithmic phase. When cytotoxicity was assessed, results suggested that there is no cytotoxic effect on normal mammalian cells at concentrations up to 100 µg/mL, suggesting a new possibility for prophylactic and therapeutic strategies against S. mutans [16].

Studies assessed the antibacterial effect of Terminalia Chebula extracts on S. mutans (MTCC 497). In the present study, two solvents were compared, water and 70% ethanol. The aqueous extract resulted in a higher MIC than the ethanolic extract, equal to the mouthwashes. At low concentrations, there is a bactericidal effect, while other concentrations may be bacteriostatic. A 2.5% concentration of ethanol extract proved effective in inhibiting S. mutans aggregation, and 1.25% was capable of inhibiting glycolysis, possibly due to the inhibition of glucosyltransferase by tannin. A randomized field trial conducted by the author evaluated the properties of the same plant, observing a more significant reduction (64.14%) after 60 minutes of rinsing, compared to other assessed parameters [21].

The influence of the crude solvent fraction of Trachyspermum ammi, and active compounds on S. mutans (ATCC 700610) was evaluated, and the results showed a higher MIC for the crude extract than for petroleum ether. It was found that the petroleum ether (PE) fraction exhibited a strong effect on adherence at 20 µg/mL (sub-MIC), reducing by 84.25%. In contrast, the crude extract (CR) fraction at this concentration reduced by only 11.57%. Effective reduction by CR was observed at 40 µg/mL. In the presence of thymol at its sub-MIC, a reduction in adherence was observed at 14.59%. Biofilm formation by S. mutans was inhibited by both compounds at 80 µg/mL and 10 µg/mL compared to the control. The decrease in pH was significantly inhibited in the presence of CR fractions (160 µg/mL) and PE (20 µg/mL), starting at pH 7.0 and 7.2, respectively, while after 12 hours of incubation, pH was 6.5 and 6.8, respectively [2].

Clinical studies also evaluated the effectiveness of medicinal plants against S. mutans. The viability of S. mutans in chewing Tulsi (Ocimum sanctum) leaves in children was evaluated through three collections. Collections were extracted over five stages: oral prophylaxis, basal saliva collection (Sample 1), chewing of Tulsi leaves, saliva collection immediately after chewing (Sample 2), and 30 minutes later (Sample 3), respectively. In this study, a significant difference in colony counts was observed, and Sample 3 obtained better results compared to Samples 2 and 1, which had higher counts [18].

In a randomized clinical cross-over study, the effect of a mouthwash containing 2g of Teucrium Polium on the count of S. mutans in saliva was investigated. In summary, two positive effects were observed: a reduction in the number of S. mutans colonies during the use of the mouthwash and an antimicrobial effect lasting at least three weeks after use of the mouthwash, representing a high substantivity of this herb [19].

An in vivo study compared the antimicrobial potential against S. mutans of cinnamon bark oil (Cinnamomum zeylanicum Blume) incorporated into a mucoadhesive in patients with active caries. The results showed that both the cinnamon adhesive and the probiotic-based adhesive had a positive effect. When assessing the antibiofilm effect, the cinnamon adhesive obtained superior results compared to the probiotic group and control. Both adhesives from the studies have the capacity to reduce S. mutans in saliva [17].

4. Conclusion

Among the studies reviewed, only copaiba oil showed superior results compared to CHX. The study using crude extract of M. azedarach demonstrated similar results, and Teucrium Polium emerges as a potential antimicrobial agent due to its high substantivity, suggesting effective and alternative compounds in the prevention of carious lesion formation. However, more comparative studies with CHX are necessary. The other compounds used, although showing significantly lower responses, appear to be a viable alternative and can be instituted as auxiliary chemical methods, acting as adjuncts in caries prevention.

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