

Plants for oral biofilms eradication: literature review

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ABSTRACT Oral Biofilm is a collection of microbial cell colonies related to periodontal diseases and caries. Biofilm bacteria were more resistant to antimicrobial agents than in the planktonic phase. The rapid progression of bacterial resistance to antimicrobial agents such as chlorhexidine has encouraged researchers to find alternative antimicrobial agents from natural plant products with low side effects. The purpose of this review was to summarize plants that contain bioactive compounds for biofilm eradication in terms of preventing caries and periodontal diseases. The method was used Systematic Review without Meta Analysis. Articles to be reviewed were searched from Pubmed, Cochrane, Science Direct, and Google Scholar databases using the PRISMA method and hand searching. The last selected articles were analyzed using narrative analysis. There are 1,610 articles specified in the first stage and only 18 articles left in the final extraction stage. Plants that contain bioactive compounds for oral biofilm eradication include *Piper betle* (betel), *Psidium sp.*, *Mangifera sp.*, *Mentha sp.*, *Caesalpinia sappan* (secang), *Baccharis dracunculifolia*, *Laurus nobilis* L. (dafnah), *Croton nepetaefolius*, *Salvadora persica* (miswak), *Dryopteris crassirhizoma*, *Diospyros kaki* Thunb. (persimmon), *Ginkgo biloba*, *Azadirachta indica* (neem), *Camellia sinensis*, *Lippia alba*, *Cymbopogon citratus* (lemongrass), *Citrus aurantifolius*, *Tamarindus indica* (sour), *Syzygium cumini* (jamblang), *Embllica officinalis* (malacca), *Acacia Arabica* (prickly acacia), *Terminalia chebula* (myrobalan), *Terminalia bellerica* (bahera), *Carica papaya*, *Ocimum basilicum* L. (basil), and *Myrmercodia pendans*. These plant bioactive compounds are belong to the group of alkaloids, terpenoids, and polyphenols which were tested in the form of single compounds or mixtures, especially against *Streptococcus mutans*. In conclusion, 26 plant species have reported containing bioactive compounds tested in the form of single or mixed extracts to eradicate oral bacterial biofilm.

KEYWORDS: Plants, eradication, natural products, oral biofilm

INTRODUCTION

The collection of microorganisms colonies attached to biotic and abiotic surfaces and embedded in the extracellular polysaccharide (EPS) matrix will form a biofilm. The biofilm will support these microorganisms to survive in an unfavorable environment.¹⁻⁴ In addition to oral cavities, it can cause several diseases to host.^{3,5} Oral biofilms found on the tongue, buccal mucosa, supragingival or subgingival. Oral biofilm formation begins with a pellicle which facilitates the initial attachment of microbes. There is an interaction between pellicles and adhesins on the surface of microbial cells. Then, it will strengthen the attachment of microbial cells to oral cavity surfaces and give a supporting facility to newcomer microbes. The increasing of microbes in the biofilm results in EPS matrix formation. Biofilms will grow more mature and more complex, which

will eventually reach the dispersion stage to form new biofilms on other surfaces.²⁻⁶

The EPS matrix produced by biofilm bacteria plays a role in determining the virulence of the biofilm. Bacteria can communicate with each other within the biofilm structure using quorum sensing.⁶ Quorum sensing plays a significant role in regulating the formation of biofilms and EPS matrix and enabling regulation of antimicrobial resistance gene expression.⁷ The metabolism of microorganisms that live in the oral cavity biofilm can change the surrounding environment to form an atmosphere that supports the growth of pathogenic bacteria. The dominance of pathogenic bacteria allows the emergence of oral diseases such as caries and periodontal disease.⁸

Microorganisms in the biofilm, especially bacteria, are 10-1000 times more resistant to

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antimicrobial agents than bacteria in the planktonic phase.^{9,10} This may be because the biofilm acts as a barrier both physically and chemically, which prevents the penetration of antimicrobial agents and increases the ability of microbes to survive under conditions of unbalanced nutrition.¹⁰ These problems encourage researchers to find new agents as alternatives to antibacterial and antibiofilm, especially natural plant products. Plants have a way of defending themselves from an unfavorable environment by carrying out secondary metabolism. Bioactive compounds are a product of secondary metabolic processes, and some of these bioactive compounds have been reported to contain antimicrobial properties.^{11,12,13}

Controlling oral biofilm is one way to prevent these diseases. Reducing biofilm can be used mechanically by brushing teeth or chemically by mouthwash containing an antimicrobial compound.^{2,8,10,14} Chlorhexidine 0.2% is the most effective mouthwash and has been widely used for a long time and has become standard gold

mouthwash. Chlorhexidine has strong power and broad-spectrum antibacterial activity. However, it has disadvantages: long-term use can cause staining of the teeth,^{8,10} erosion of the mucosa, and an unpleasant taste in the mouth.^{2,15,16} Extensive use over a long period also causes a problem of bacterial resistance to chlorhexidine.¹⁷

The ability of plant bioactive compounds to eradicate oral biofilm and as an antimicrobe has been recorded in several databases. Only a few a summary has reported or a few selected plants that have been studied until the clinical stage to be used widely or for therapeutic purposes as ingredients for making drugs. In this study, we will summarize and review several plants that have oral cavity biofilm eradication activity. And they were published by Pubmed, Science Direct, Cochrane, and Google scholar through the Preferred Reporting Items for Systematic Reviews without Meta-Analyses (PRISMA) method.

MATERIALS AND METHODS

Tools

This study used Mendeley as a reference manager, Critical Appraisal Skills Program (CASP)¹⁸ to assess the quality of selected studies in the Randomized Control Trial (RCT) article and the Modified CONSORT checklist¹⁹ for In Vitro studies. The sample was searched using a laptop.

Materials

The material for this study is articles that have been published in Pubmed, Google Scholar, Cochrane, and Science Direct databases.

Procedures

This descriptive study used a systematic review method by Preferred Reporting Items for Systematic Reviews without Meta-Analyses (PRISMA)²⁰ and manual hand searching. Articles were searched from PubMed, Science Direct, Cochrane, and Google Scholar databases using Boolean operators and keywords ((plant OR medicinal plant OR herb OR natural product OR natural source OR plant extract) AND (anti-plaque OR anti-biofilm OR antibacterial activity)) AND (oral biofilm OR dental plaques). Inclusion criteria were articles published in 2011-2021, available in full text, published in Indonesian and English, were not reviews studies, RCTs, and experimental reports that studied plant bioactive compounds for biofilm eradication and were related to caries bacteria or periodontal disease. Articles that did not report plants' antibiofilm compounds and a

high risk of bias were excluded from this study. Several articles in the articles reference have been searched for and did not appear in searches using the database but are closely related to the topic, including Indonesian articles, manually hand searched.

The first step PRISMA method is identification. There were 1,610 articles identified from the four databases. Then, ten duplicated articles were removed. The second step will do to screening according to title and abstract. It was 1546 articles excluded, and 55 articles proceeded to the next step. The third step is assessing the eligibility of article content. The Modified CONSORT checklist¹⁹ was used to determine in vitro studies on dental materials and the Critical Appraisal Skills Program (CASP)¹⁸ for Randomized Control Trial (RCT) studies. There are 40 articles removed in the eligibility step. The reason for eliminating in was 16 articles did not report the plant bioactive compounds, eight articles did not report the eradication activity of oral biofilm, 1 article was not indexed in Scopus, two articles were not available in full text, and 13 articles were inaccessible and not related to oral pathogens. Finally, only 18 articles entered the final step for qualitative analysis that are 15 articles were obtained of PRISMA method selection and three articles manual hand searched. Then, the 18 selected articles, 17 of them reported on in vitro studies, and only 1 reported on clinical studies in humans using RCT. Lastly, the narrative

approach was used as a qualitative analysis. The research procedure is shown in **Figure 1**.

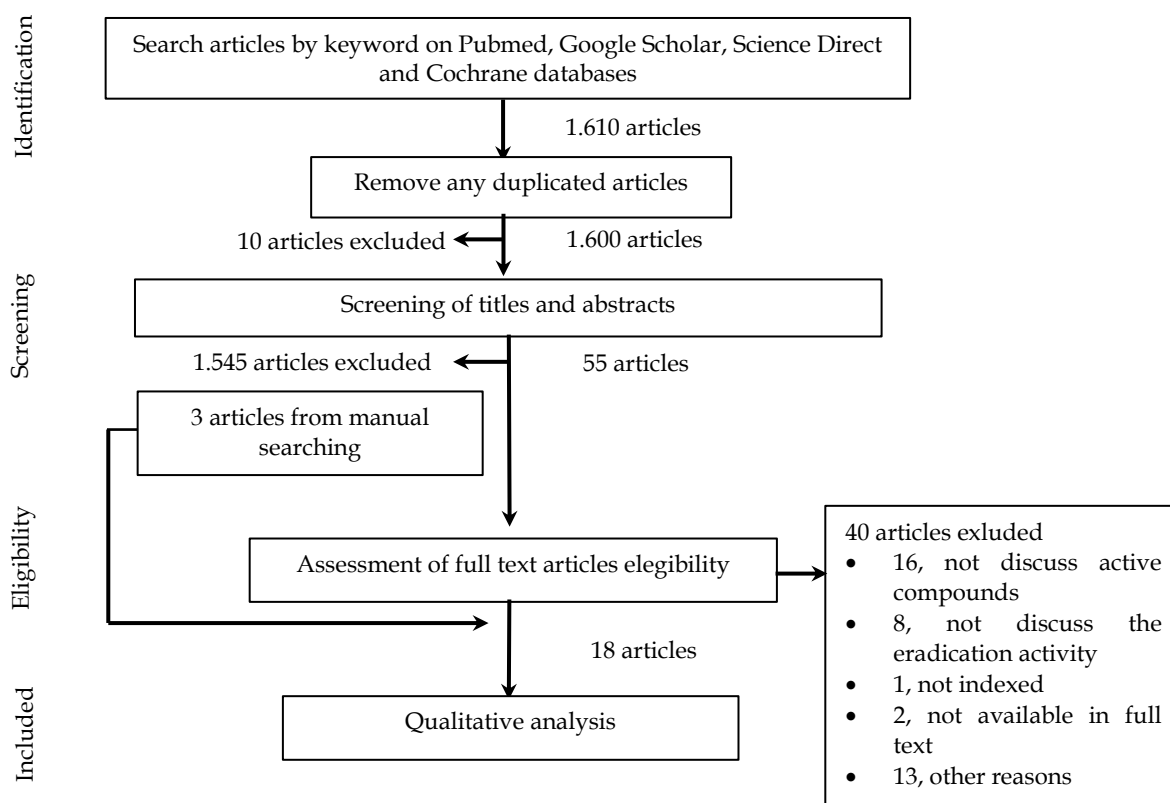


Figure 1 Flowchart of article search based on the PRISMA method

RESULTS

A plant containing an anti oral biofilm identified from 18 selected articles in this study are *Piper betle* (betel)²¹, *Psidium sp.*²², *Mangifera sp.*²², *Mentha sp.*²², *Caesalpinia sappan* (secang)⁸, *Baccharis dracunculifolia*¹⁰, *Laurus nobilis L.* (dafnah)¹¹, *Croton nepetaefolius*²³, *Salvadora persica* (siwak)²⁴, *Dryopteris crassirhizoma*²⁵, *Diospyros kaki* Thunb. (persimmon)²⁶, *Ginkgo biloba*²⁷, *Azadirachta indica* (neem)²⁸, *Camellia sinensis*²⁸, *Lippia alba*²⁹, *Cymbopogon citratus* (citronella)²⁹, *Citrus aurantifolia*¹³, *Tamarindus indica* (tamarind)⁹, *Syzygium cumini* (jamblang)⁹, *E. officinalis* (malacca)⁹, *Acacia Arabica* (thorny acacia)³⁰, *Terminalia chebula* (myrobalan)³⁰, *T bellerica* (bahera)³⁰, *Carica papaya*³¹, and *Ocimum basilicum L.* (basil)³², and *Myrmercodia pendans* (ant nest)³³ (Table 1). It can be seen that limiting keywords and database sources determine the number of articles that report in plants antibiofilm compounds. In addition, several similar studies in Indonesia language were not identified, while searching in English language keywords. The whole article only reported the activity of plant bioactive compounds against caries and periodontal-causing bacteria.

This study revealed that plant bioactive compounds as anti oral biofilm deposited most in different parts (leaves, cambium, bark, pulp, rind, seeds, or bulbs) in every plant. Plants produce a bioactive compound as secondary metabolites for surviving in hazardous conditions such as thorns, extreme weather.¹² Various plant secondary metabolites chemically grouped into terpenes, steroids, alkaloids, polysaccharides, peptides, and aromatics, most of which have antimicrobial, antiviral, anticancer, anti-parasitic, and anti-allergic properties.^{12,34,35} Secondary metabolites as anti-biofilm work to inhibit bacterial growth by inhibiting bacterial cells attached to the surface, inhibit the activity of glycolytic enzymes, inhibit biofilm formation, and degrading the existed biofilms.^{13,31,33}

Alkaloids as anti biofilms have been reported capable of binding to the amyloid matrix protein of the EPS biofilm *Staphylococcus epidermidis* and inhibiting biofilms' formation of *Staphylococcus aureus*.¹² Terpenoids from *M. pendans* can also eradicate the biofilm formed as much as 40% within 1 minute. Another ability of terpenoids is to inhibit glucosyltransferase activity in *S. mutans* and

Streptococcus sobrinus.³³ Low molecular weight terpenoids can affect the integrity of the cell membrane and the release of planktonic cells from the biofilm.^{13,33} Polyphenols from natural ingredients have antibiofilm activity by inhibiting quorum sensing (QS).¹² Inhibition of QS by the active compound will interfere with signal delivery activity for biofilm formation, thereby reducing biofilm virulence.¹

Aromatic compounds and phenols can disrupt the cytoplasmic membrane, which refers to the death of microbial cells and can inactivate bacterial enzymes.⁸ Leaf extract of *Psidium* sp., *Mangifera* sp., *Mentha* sp. and their mixtures are reported to contain phenolic compounds, namely gallic acid, apigenin, quercetin, quercetin-3-O-glucoside, succinic acid, and quinic acid. All types of extracts have been proven effective in reducing the number of bacteria *S. mutans* and *S. sanguinis* both in monospecies and multispecies form, biofilm and two types of culture medium, sucrose culture and without sucrose.²² *B. dracunculifolia* is reported to contain artemisin, baccharin, flavonoids, diterpenes, and triterpenes which have antibacterial, antifungal, and antiulcer effects. As an antibiofilm essential oil of *B. dracunculifolia* was reported to reduce the amount of Colony Forming Unit (CFU) biofilm *S. mutans* and reached $(53.3 \pm 21.4)\%$ - $(91.1 \pm 4.9\%)$.¹⁰ The active compound 4-chromanol from leaves is *P. betle* more sensitive in reducing Gram-negative bacteria because it can penetrate bacterial membranes and can overcome resistance related to changes in membrane proteins and lipopolysaccharides.²¹ Casbane diterpene, the active compound from *Croton nepetaefolius*, has a hydrophobic group that causes these compounds to optimally pass through cell membranes and inhibit cell growth, mainly Gram-negative bacteria.²³

Plant bioactive compounds were given to bacteria in the form of a single crude extract (*Psidium* sp., *Mangifera* sp., *Mentha* sp.) or a mixture of plant crude extract, ethanol or hexane extract (*S. persica*), or a single isolate (ginkgolic acid, the active compound of Ginkgo biloba leaves and seed skins, the active compound of n-hexane fraction *D. crassi* (*B. dracunculifolia*). Parts of plants that contain active compounds to be used as anti biofilms also vary, ranging from leaves (*P. betle*, *L. nobilis* L., *C. sinensis*, *C. citratus*, *G. biloba*, *C. papaya*,), fruit (*Psidium* sp., *Mangifera* sp., *Mentha* sp., *T. chebula*, *T. bellerica*, *E. officinalis*, *C. aurantifolia*), wood core or cambium (*C. sappan*), plant stems or stalks (*C. nepetaefolius*, *S. persica*), seeds (*G. biloba*), and tubers (*M. pendans*). Various extracts concentration and plant parts determine the strength of plant antibiofilm potency. For example, the Minimum

Biofilm Eradication Concentration (MBEC) value of ethanol extract *P. betle* to eradicate 50% biofilm *S. mutans* is 0.78 ± 0.74 mg/ml. In comparison, the eradication of 90% biofilm is required 6.25 ± 0.58 mg/ml. MBEC of ethanol extract *P. betle* for eradication of 50% and 90% biofilm *A. actinomycetemcomitans* was 0.78 ± 0.11 mg/ml and 3.13 ± 0.28 mg/ml.²¹

Several plant's bioactive compounds have been shown antibacterial activity in the planktonic phase, including *T. indica* (tamarind), *S. cumini* (jamblang), and *E. officinalis* (malacca).⁹ On the other hand, single isolates linoleic acid from the n-hexane fraction of *D. crassirhizoma* as much as 200 g/ml was reported to reduce 50% of biofilms. The study concluded that linoleic acid could reduce the weight of the biofilm without reducing the number of cells by interfering with the formation of the biofilm matrix but without killing bacteria. So, Linoleic acid is more effective on the biofilm than on planktonic bacteria.²⁵

Most of the selected articles in this study conducted antibiofilm experiments using *S. mutans* as an object treatment. Several plant bioactive compounds inhibit glucosyltransferase activity resulting in decreasing sucrose synthesis and suppressing the initiation and elongation of glycan chains (biofilm component). *S. mutans* are pioneers that initiate bacterial attachment in the tooth surfaces. Glucosyltransferases (Gtfs) secreted by *S. mutans* will bind to the bacterial cell and saliva-coated teeth. They also attract other bacteria or microorganisms that will make thickened biofilm. Tooth demineralization or the initial occurrence of caries caused by acid as a by-product of glucosyltransferase activity. Inhibiting Gtfs activity, in addition to controlling biofilm formation, control biofilm virulence as well.³⁶

Plant antibiofilm that have been reported are still in the experimental stage. Only a few plants have been applied directly as mouthwash (*S. persica* or siwak, 0.5% tea, 2% Neem, 0.2% v/v *O. basilicum* L.). Tea (0.5%) and 2% Neem also reported reducing dental plaque in respondents and producing other positive effects such as increasing salivary pH and improving oral health, with the highest levels of effectiveness being 0.5% Tea, 2% Neem, respectively.²⁸ However, Developing plant bioactive compounds as oral antibiofilm in preventing dental caries and periodontal disease still needs more study. The most important study is clinical to overcome the resistance of oral bacteria to the antibacterial agent.

Table 1 Summary of literature review on the plant for **oral biofilm** eradication

No	Source	Type of research	Research method	Active compound	Test object	Result	Biased
1	21	In Vitro	MBEC assay and MTT assay	4-chromanol (Piper betle)	<i>S. mutans</i> ATCC 25175 and <i>A. actinomyces</i> ATCC 33384	MBEC ₅₀ ethanol extract of <i>P. betle</i> - <i>S. mutans</i> = 0,78 ± 0,74 mg/ml and MBEC ₉₀ ethanol extract of <i>P. betle</i> - <i>S. mutans</i> = 6,25 ± 0,58 mg/ml; and MBEC ₅₀ ethanol extract of <i>P. betle</i> - <i>A. actinomyces</i> = 0,78 ± 0,11 mg/ml and MBEC ₉₀ ethanol extract of <i>P. betle</i> - <i>A. actinomyces</i> = 3,13 ± 0,28 mg/ml	No limits and potential for bias
2	22	In Vitro	Calculation of CFU	Phenol compound: gallic acid, apigenin, quercetin, quercetin-3-O-glucoside, succinic acid, quinic acid (<i>Psidium</i> sp., <i>Mangifera</i> sp., <i>Mentha</i> sp. and their mixed forms)	<i>S. mutans</i> ATCC 25175 and <i>S. sanguinis</i> ATCC BAA-1455	On medium without sucrose: PEM- <i>S. mutant</i> , CFU 1,02 ± 0,14% ; <i>Mangifera</i> sp.- <i>S. mutans</i> , CFU 0,59 ± 0,12%, <i>Psidium</i> sp.- <i>S. mutans</i> , CFU 18,9 ± 5,17% and <i>Mentha</i> sp. - <i>S. mutans</i> , CFU 13,83 ± 3,70%. In medium with sucrose: <i>Psidium</i> sp.- <i>S. mutans</i> + <i>S. sanguinis</i> , CFU 9,85 ± 4,65%; <i>Mentha</i> sp.- <i>S. mutans</i> CFU 2,39 ± 0,98%; <i>Mangifera</i> sp. - <i>S. sanguinis</i> CFU 5,71±1,58% <i>Mangifera</i> sp.- <i>S. mutans</i> CFU and 3,85±1,58%. Mixture: <i>Psidium</i> sp. and <i>Mangifera</i> sp. - <i>S. mutans</i> were able to reduce ±50% of the population. <i>Mentha</i> sp. and PEM leaves ±12-15% of the bacterial population. On SEM observation, only a few bacteria were seen in the biofilm after PEM administration.	No limits and potential for bias
3	8	In Vitro	Cristal violet staining assay	Brazilin (Cambium <i>C. sappan</i>)	<i>S. mutans</i> DMST9567, <i>S. mutans</i> DMST18777, and <i>S. mutans</i> DMST41283	extract <i>C. sappan</i> with MBC value 125 g/mL reduced 95 -98% and <i>brazillan</i> reduced 90-98% of cells <i>S. mutans</i>	It did not reveal limits and potential for bias
4	10	In Vitro	Viable CFU counting	Artepilin C, baccharin, flavonoids, diterpenes, and triterpenes (leaf extract <i>Baccharis dracunculifolia</i>)	<i>S. mutans</i> ATCC® 35688	essential oil <i>B. dracunculifolia</i> 6% reduced 53,3 ± 21,4% to 91,1 ± 4,9% biofilm of clinical isolates of oral mixed bacteria, and 39,3 ± 17,5% of <i>S. mutans</i>	No limits and potential bias

5	11	In Vitro	CFU (Crystal Violet staining) and MTT assays	1,8-Cineole, methyl eugenol and -terpinyl Acetate (Leaves of <i>L. nobilis</i> L.)	<i>S. aureus</i> ATCC 6538	The active compound in the essential oil of <i>L. nobilis</i> L reduced biofilms <i>S. aureus</i> $27,2 \pm 8,5\%$ up to $78,4 \pm 1,57\%$. On the MTT assay, the reduction rate was $79,6 \pm 2,27$ to $95,2 \pm 0,56$.	It does not reveal limitations and potential for bias
6	23	In Vitro	Staining with Crystal violet and CFU calculation	Casbane diterpene (Stem of <i>Croton nepetaefolius</i>)	<i>S. mutans</i>	Casbane diterpene 250 ug/ml reduced the bacterial biofilm cells of <i>S. mutans</i> to 94,28%	Reporting bias
7	24	In Vitro	Calculation of CFU and MTS assay	Ethanol Extract and plant stems Hexana <i>S. persica</i>	<i>S. mutans</i> ATCC25175	hexane extract stem <i>S. persica</i> 5 mg/ml was more effective in eradicating <i>S. mutans</i> biofilm than its ethanol extract. chlorhexidine CFU ($0,18 \times 10^2 \pm 0,13 \times 10^2$), hexane extract CFU ($8,7 \times 10^3 \pm 6,1 \times 10^2$) and ethanol extract CFU ($2,9 \times 10^4 \pm 7,5 \times 10^3$), saline +2 % DMSO CFU ($3,6 \times 10^7 \pm 5,5 \times 10^6$)	-
8	25	In Vitro	Calculation of CFU, BCRC and BDRC	n-hexane fraction (HF) and linoleic acid (Root of <i>D. crassirhizoma</i>)	<i>S. mutans</i> UA159	HF and linoleic acid reduced bacterial biofilm depending on the concentration, with values: 50% BCRC HF=100 g/ml and linoleic acid 200 g/ml. 30% BDRC HF= 50 g/ml Linoleic acid= 100 g/ml	-
9	26	In Vitro	Calculation of CFU and SEM	Tannin (<i>Persimmon</i>)	Saliva influenced to form oral cavity biofilms with no clarity on the bacterial biofilm samples used.	extract <i>Persimmon</i> reduced the CFU of biofilms cultured 24 hours, in 6 different concentrations around 65-96% and at 72 hours biofilms achieved 73-97%. Eradication activity depends on the concentration of the extract. PS-M concentration of 4,0 wt% equal to 0,2 wt% chlorhexidine resulted in damage to the biofilm structure.	No biofilm bacteria sample used (selection bias)
10	27	In Vitro	MBRC and SEM	<i>Ginkgoneolic acid</i> (<i>Ginkgo biloba</i> extract)	<i>S. mutans</i> ATCC 25175	Value MBRC ₅₀ <i>Ginkgoneolic acid</i> against <i>S. mutans</i> = 32 mg / mL, the dose of 8 and 16 g/mL resulted in biofilm disintegration in SEM observations. <i>Ginkgoneolic acid</i> 16 g/mL in <i>S. mutans</i> , few and scattered, cells seen with short chains.	-
11	28	RCT	30 subjects were randomly divided into 3 groups	Neem : trimethylamine, chlorides, nimbidin, azadarachtin, lectin,	Oral biofilm	Three effective mouthwash against plaque, gingivitis, maintain oral health and salivary pH, in the order of 0,5% tea, 2% Neem, then 0,2% chlorhexidine.	-

			into chlorhexidine, neem, and tea groups. Before the intervention, the assessment was carried out on DMFT, plaque score, salivary pH, OHIS, and gingival score. Subsequent assessments are carried out every week for three weeks. Side effects were evaluated with a questionnaire.	fluorides in large amounts and silica, sulfur, vitamin C, tannins, saponins, flavonoids, and sterols Tea: polyphenols, green tea catechins, fluoride			
12	29	In Vitro	MBEC	Geraniol and Neral (Citral) (<i>C. citratus</i> essential oil; <i>L. alba</i> essential oil)	<i>S. mutans</i> ATCC 35668	MBEC ₉₅ <i>Lippia alba</i> - <i>S. mutans</i> =0,1 mg/100 mL, MBEC ₉₅ <i>Cymbopogon citratus</i> - <i>S. mutans</i> =0,01 mg/100 mL, MBEC ₉₃ <i>Cymbopogon citratus</i> - <i>S. mutans</i> 0,001 mg/100 mL	-
13	13	In Vitro	MBEC assay	Monoterpenoids (<i>C. aurantifolia</i> shell)	<i>S. mutans</i> UA 159	Monoterpenoids from <i>C.aurantifolia</i> bark can reduce 34,75% <i>S.mutans</i> biofilm with a concentration of 3% within 30 minutes	Does not disclose statistical method used
14	9	In Vitro	MBEC assay	Ethanol, Methanol, acetone (<i>E. officinalis</i> , <i>T. indica</i> , <i>S. cumini</i> , and <i>P. sylvestris</i> , and <i>M.</i>	<i>S. mutans</i>	Ethanol, methanol and acetone of seeds were <i>T. indica</i> and <i>S. cumini</i> extracts able to kill 80% of cells <i>S. mutans</i> in biofilm at a concentration of 500-1000 g/mL and 95% of cells at a concentration of 600-2000 g/mL	-

15	30	In Vitro	Crystal Violet assay, confocal laser scanning system to identify dead and living cells, SEM to see membrane damage in biofilm <i>S. mutans</i>	zapota assay samples) Quercetin, luteolin, saponins, anthraquinones, amino acids, fatty acids, carbohydrates and polyphenols (Bark of tree <i>Acacia arabica</i> , fruit of <i>Terminalia chebula</i> , <i>T. bellerica</i> and <i>E. officinalis</i>)	<i>S. mutans</i> , <i>L. casei</i> , <i>A. viscosus</i>	MBEC MHPE to reduce 91-96% biofilm <i>A. viscosus</i> , <i>L. casei</i> and <i>S. mutans</i> 150 mg/ml SEM results showed disintegration, irregular boundaries, unclear cell margins and damaged biofilm.	Does not state limitations and potential bias
16*	31	In Vitro	Crystal violet (CV) assay and SEM	Alkaloids, steroids/terpenoids, tannins, and flavonoids (Pawpaw leaves (<i>Carica papaya</i> L.))	<i>P. aeruginosa</i>	Papaya leaf extract can degrade 49,02% biofilm <i>P. aeruginosa</i> with a concentration of 25% v/v, temperature 37,5 °C, and contact time 45 minutes. Observation by SEM, the biofilm matrix looks less and is degraded	-
17*	32	In Vitro	Microdilution method with staining Crystal violet	Linalool, nerol, geraniol (Kemangi Leaf)	<i>S. mutans</i>	The best mouthwash formula of the ratio of tween 80 and glycerin 3,75 mL with a concentration of 0,2% v/v degrade biofilm <i>S. mutans</i> by 57,64 ± 6,09%.	-
18*	33	In Vitro	Microdilution method and determination of MBEC	Terpenoid (tuber <i>Myrmecodia pendans</i>)	<i>S. mutans</i> ATCC 25175	Terpenoids from <i>M. pendans</i> can reduce 40% of biofilm <i>S. mutans</i> with an MBEC value of 50 ppm in 1 minute.	-

Notes: MBEC=Minimum Biofilm Eradication Concentration (MBEC50=50% eradication); MTT=3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide ; CFU=Colony Forming Unit; SEM=Scanning Electron Microscope; BCRC=Biofilm Cell Reduction Concentration; BDRC=Biofilm Dry Weight Reduction Concentration; MHPE= Mixed Herbal Powder Extract.

CONCLUSION

From 18 articles selected, it has been reviewing 26 plants only as plants containing bioactive compounds for eradicating oral cavity biofilms, namely *Psidium sp.*, *Mangifera sp.*, *Mentha sp.*, *Caesalpinia sappan* (secang), *Baccharis dracunculifolia*, *Laurus nobilis* L. (dafnah), *Croton nepetaefolius*, *Salvadora persica* (miswak), *Dryopteris crassirhizoma*, *Diospyros kaki* Thunb. (persimmon),

Ginkgo biloba, *Azadirachta indica* (neem, neem), *Camellia sinensis*, *Lippia alba*, *Cymbopogon citratus* (lemongrass), *Citrus aurantifolia*, *Tamarindus indica* (tamarind), *Syzygium cumini* (jamblang), *E. officinalis* (malacca), *Acacia Arabica* (thorny acacia), *Terminalia chebula* (myrobalan), *T. bellerica* (bahera), *Carica papaya*, *Ocimum basilicum* L. (basil), and *Myrmecodia pendans* (ant nest).

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