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(REVIEW ARTICLE)

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Medicinal plants to control oral pathogens and oral biofilms: A review

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Abstract

Medicinal plants which showed antimicrobial activity against oral pathogens and inhibited biofilm formation have the capability of eliminating the oral microbes and preventing many oral infections. In the current review, PubMed, Web Science, Science Direct, Researchgate, Academia.edu and Scopus were searched to determine the medicinal plants with antibacterial effects against the common oral pathogens.

Keywords: Oral; Pathogens; Biofilm; Periodontal Diseases; Gingivitis; Mouth Wash

1. Introduction

The destructive periodontal diseases are bacterial infections that colonize the tooth surface, gingival margin and subgingival environment [1-2].

Although 300 bacterial species were contributed to the biofilm of the periodontal pocket, but a much smaller number of species were closely related to incidence and persistence of periodontitis, included *Aggregatibacter actinomycetemcomitans, Porphyromonas gingivalis, Prevotella intermedia, Prevotella nigrescens, Treponema denticola, Treponema forsythia, Fusobacterium nucleatum, Eikenella corrodens, Eubacterium nodatum, Peptostreptococcus Sp., Streptococcus intermedius, Campylobacter rectus* and *Capnocytophaga sp*[3].

In the last decades the use of drugs derived from medicinal plants has markedly increased. Herbal medicine showed an efficacy in almost every aspect of oro-dental treatments with wide range of antimicrobial effects [4-5].

The current review was designed to highlight the therapeutic effects of medicinal plant in oral pathogens and oral biofilms.

2. Medicinal plants with antibacterial activity against oral pathogens

2.1. *Arctium lappa*

The antimicrobial activity of rough extracts from leaves of *Arctium lappa* and their phases was tested *in vitro* against microorganisms commonly found in the oral cavity, specifically in endodontic infections, *Enterococcus faecalis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Bacillus subtilis* and *Candida albicans*. The *Arctium lappa* constituents exhibited a great microbial inhibition potential against the tested endodontic pathogens [6-9].

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2.2. *Althaea officinalis*

A methanolic extract prepared by exhaustive extraction from marshmallow root has been shown to possess an inhibiting activity able to diminish significantly the periodontal pathogens resident in the oral cavity (*Porphyromonas gingivalis, Prevotella spp., Actinomyces odontolyticus, Veilonella parvula, Eikenella corrodens, Fusobacterium nucleatum, Peptostreptococcus spp.*)[10-11].

2.3. *Anthemis nobilis*

The extract and essential oil of Roman chamomile flower head showed antibacterial activity against *P. gingivalis*. The antimicrobial effects were evaluated by disk diffusion method. The results indicated that the means of inhibition zone for chamomile extract and essential oil were 13.33±3.4 and 20.5±0.5 respectively [12-13].

2.4. *Calendula officinalis*

The methanol extract and 10% decoction of the plant's flowers showed antimicrobial activity against facultative aerobic periodontal bacteria (*Porphyromonos gingivalis*, *Prevotella* spp., *Furobacterium nucleatum, Caphocytophaga gingivalis, Veilonella parvula, Eikenella corrodens, Peptostreptococcus micros* and *Actinomyces odontolyticus)* with MIC 2048 mg/l [14].

Mouthwashes containing Calendula officinalis reduced the number of microorganisms adhered to the sutures after extraction of unerupted third molars compared to the control group [15].

In studying the efficacy of Calendula officinalis in reducing dental plaque and gingival inflammation, plaque index (PI), gingival index (GI), sulcus bleeding index (SBI), and oral hygiene index-simplified (OHI-S). It appeared that *C.* officinalis induced statistically significant reduction in the scores of PI, GI, SBI (except OHI-S) ($P<0.05$) [16-17].

2.5. *Cichorium intybus*

The low molecular mass (LMM) extract of Cichorium intybus var. Silvestre (red chicory) has been shown to inhibit virulence-linked properties of oral pathogens including *Streptococcus mutans, Actinomyces naeslundii* and *Prevotella intermedia*. HPLC-DAD-ESI/MS (2) was used to investigate the compounds contained in this extract for their anti-virulence activity. The extract contained a number of components, including oxalic, succinic, shikimic and quinic acids, which interfere with the growth and virulence traits (i.e., biofilm formation, adherence to epithelial cells and hydroxyapatite) of oral pathogens involved in gingivitis and tooth decay. Succinic and quinic acid seem to be the most potent, mainly by interfering with the ability of oral pathogens to form biofilms (either through inhibition of their development or promotion of their disruption). The author's poastulated that one or more of these compounds may modulate plaque formation *in vivo*, which is a prerequisite for the development of both caries and gingivitis [18-19].

2.6. *Citrus species*

The antimicrobial potential and the minimum inhibitory concentration (MIC) of aqueous and ethanol (cold and hot) extracts of Citrus sinensis peel extracts was investigated against *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis* and *Prevotella intermedia*, using agar well diffusion method. The results showed that *Prevotella intermedia* and *Porphyromonas gingivalis* were resistant to aqueous extracts while *Aggregatibacter actinomycetemcomitans* was inhibited at very high concentrations. Hot ethanolic extracts showed significantly higher zone of inhibition than cold ethanolic extract. Minimum inhibitory concentration of hot and cold ethanolic extracts of Citrus sinensis peel ranged between 12-15 mg/ml against all three periodontal pathogens [20-21].

2.7. *Coriandrum sativum*

Coriandrum sativum essential oil possessed antifungal activity against *Candida* species isolates from the oral cavity of patients with periodontal disease. 2-hexen-1-ol, 3-hexen-1-ol and cyclodecane were determined as the active constituents in the oil [22-23].

2.8. *Cuminum cyminum*

Antimicrobial activities and biofilm-formation preventive properties of *Cuminum cyminum* essential oils and chlorhexidine were assessed against *Streptococcus mutans* and *Streptococcus pyogenes*. The minimal bactericidal concentrations (MBC) of the oils and chlorhexidine and microbial decimal reduction time (D value) were determined. *Cuminum cyminum* induced mild antibacterial and *in vivo* biofilm preventive effects (less than chlorhexidine). *In vivo* experiments conducted on male and female volunteers who brushed with essential oil blended toothpastes indicated

that lower concentrations of the oils were significantly higher ($p<0.001$) and effective during the course of the study as compared to chlorhexidine[24-25].

2.9. *Cyperus rotundus*

The growth and acid production of *Streptococcus mutans* were reduced by the tuber extract of *Cyperus rotundus*. *S. mutans* is known as the causative bacteria in the formation of dental plaque and dental caries. Moreover, the same tuber extract inhibited the adherence of *S. mutans* to saliva coated hydroxyapatite beads. Glucosyl transferase enzyme, which synthesized water-insoluble glucan from sucrose, was also inhibited by the tuber extract. Accordingly *Cyperus rotundus* inhibited cariogenic properties of S. *mutans*[26-27].

2.10. *Eucalyptus species*

The antimicrobial properties of aqueous and alcoholic extracts of Eucalyptus leaves was investigated against the most cariogenic bacteria in mouth (Mutans streptococci and Lactobacilli) and against *Candida albicans*. There was statistically highly significant difference ($P< 0.001$) between different concentrations of the aqueous and alcoholic extracts on the sensitivity of the isolates, whilst the alcoholic extract was more effective than aqueous extract just at low concentrations. At 100 and 150 mg/ml the alcoholic and the aqueous extracts showed more potent effect than 2mg/ml chlorhexidine against Mutans streptococci and *Candida albicans*. Minimum bactericidal concentration for the aqueous extract was 5-8mg/ml, 6-10mg/ml and 3-7mg/ml against Mutans streptococci, Lactobacilli and *Candida albicans* respectively while that of alcoholic extract was 4-8mg/ml, 6-10mg/ml and 2-6mg/ml against the same microorganisms respectively [28-29].

2.11. *Ficus carica*

Bark of *Ficus religiosa* was dissolved in 67% ethanol. Extract was then subjected to antimicrobial efficacy tests against primary plaque colonizers and periodontal pathogens. *Ficus religiosa* showed antibacterial activity against primary plaque colonizers at 48 h with mean zone of inhibition of 2.6 ± 0.54 mm [30].

The antimicrobial activity of methanol extract of figs was studied against oral bacteria [*Streptococcus mutans*(ATCC 25175), *Streptococcus sanguinis* (ATCC 10556), *Streptococcus sobrinus* (ATCC 27607), *Streptococcus ratti* (KCTC 3294), *Streptococcus criceti* (KCTC 3292), *Streptococcus anginosus* (ATCC 31412) and *Streptococcus gordonii* (ATCC 10558), *Aggregatibacter actinomycetem comitans* (ATCC 43717), *Fusobacterium nucleatum* (ATCC 51190), *Prevotella intermedia* (ATCC 49046) and *Porphyromonas gingivalis* (ATCC 33277)]. The methanolic extract showed (MICs: 0.156 to 5 mg/ml and MBCs: 0.313 to 5 mg/ml) against the tested oral bacteria. The combination of methanolic extract and ampicillin or gentamicin showed synergistic effect against oral bacteria [31-32].

2.12. *Glaucium corniculatum*

The antimicrobial activity of the water, ethanolic and methanolic extracts (1.25-10 mg) of powdered whole *Glaucium corniculatum* was evaluated against mouth microflora (streptococci, bacillus, actinomycetes, diphteroids, lactobacillus and candida). The results showed that *Glaucium corniculatum* extracts possessed antimicrobial effect and the least effective concentration was 2.5%. The ethanol extract was the most effective followed by methanol then aqueous extract. The antimicrobial effect was differ among different microflora, Streptococci were the most sensitive microorganisms while bacillus was the least sensitive to the extract [33].

2.13. *Hibiscus rosa-sinensis*

The antibacterial activity of the methanolic and ethanolic extract of *Hibiscus rosa-sinensis* petals was evaluated against dental pathogen, *Streptococcus mutans* in different concentration. The high concentration of 300 µl methanol extract of *Hibiscus rosa-sinensis* showed strong activity (27.33±1.632) against this pathogen [76].

The antimicrobial activity of *Hibiscus rosa sinensis* extracts was examined against Gram positive and Gram-negative bacteria and fungal strains by measuring zone of inhibition. The leaf extract showed high activity against *Staphylococcus aureus* at very low concentration (2.5µg/ml) compared to *E.coli*, *Bacillus subtilis,* leaf extract also showed high activity against *Candida parapsilosis* at a very low concentration (2.5µg/ml) compared to *Aspergillus niger.* The *Hibiscus Rosa-sinensis* root extract showed high activity against all the bacteria at very low concentration (2.5µg/ml). Root extract showed high activity against *Candida parapsilosis* and *Aspergillus niger* at a very low concentration (2.5µg/ml) compared to *Trichophyton rubrum.* The flowers extract showed activity against *E.coli* and *Staphylococcus aureus* (12 mm) at very low concentration (2.5µg/ml). Flower extract also showed high activity against *Candida parapsilosis* and *Aspergillus niger* at a very low concentration (2.5µg/ml)[34]. The antibacterial activity of the methanolic and ethanolic extract of *Hibiscus rosa-sinensis* petals was evaluated against dental pathogen, *Streptococcus mutans* in different

concentration. The high concentration of 300 µl methanol extract of *Hibiscus rosa-sinensis* showed strong activity (27.33±1.632) against this pathogen [35-36].

2.14. *Jasminum sambac*

The antimicrobial efficacy of Jasminum sambac leaf extracts was evaluated against six bacteria (Staphylococcus aureus, Streptococcus mutans, S. pyogenes, S. sobrinus, S. sanguinis and Lactobacillus acidophilus) and one fungi (Candida albicans) causing dental infections. The methanol extract was more efficient in comparison to other extracts. The zone of inhibition ranged between 12.3±0.57-17.3±0.57 mm at 200 mg/ml, respectively. Minimum inhibitory concentration for methanol extract was 3.12-25 mg/ ml [37-38].

2.15. *Juglans regia*

The effect of acetone and aqueous extracts of *J. regia* was studied by testing on salivary samples of patients suffering from dental carries. Antimicrobial assay was carried out using disc diffusion method. Acetone extract was found to be effective as anti-cariogenic medicine [39].

The antimicrobial effects of ethanolic and aqueous extracts of Juglans regia bark were studied against different oral bacteria, *Streptococcus mutans*, *Streptococcus salivarius*, *Streptococcus sanguis*, and *Staphylococcus aureus*. The results showed that *S. sanguis* was the most sensitive and *S. mutans* was the most resistant bacteria for the ethanolic and aqueous extracts. Ethanolic extract possessed significant antibacterial effect against all the tested bacteria. While, aqueous extract did not show antibacterial effect against *S.mutans*, in contrast to ethanolic extract. Aqueous extract had significantly antibacterial effect against *Staphylococcus aureus*, *S. salivarius*, and *S. sanguis* compared to control ($P < 0.0001$), but it did not show effect on *S.mutans* when compared with Erythromycin [40].

The *in vitro* antimicrobial activities of hot and cold bark extracts of two varieties of *Juglans regia*, were tested against four microorganisms related to dental caries (*Streptococcus mutans, Streptococcus sobrinus, Actinomyces viscosus*). Both varieties of *Juglans regia* possessed antibacterial activity, chloroform extracts was the more potent antibacterial. Accordingly, both varieties of *Juglans regia* extracts exerted good anti plaque activity [41].

The antibacterial effects of ethanolic walnut leaf extract were compared with chlorhexidine mouth rinse against *Streptococcus mutans* and *Streptococcus sanguinis* using agar-diffusion and microdilution methods. The results showed that MIC of ethanolic extract of walnut leaf was 125 and 15.6 mg/ml against *Streptococcus mutans* and *Streptococcus sanguinis*, respectively. There was significant different between ethanolic extract and chlorhexidine in the inhibition zone against *Streptococcus mutans* (p=0.000) but no significant difference between them against *Streptococcus sanguinis* (p=0.058)[42].

Juglans regia bark extract showed a broad spectrum antimicrobial activity in a dose dependent manner. It inhibited the growth of several species of pathogenic micro-organisms representing Gram-positive bacteria (*Staphylococcus aureus and Streptococcus mutans*), Gram-negative bacteria (*Esherichia coli* and *Pseudomonas aeruginosa*) and a pathogenic yeast (*Candida albicans*). The extract has either synergistic or additive action when tested with a wide range of antibacterial drugs. It also increased the pH of saliva. Thus, brushing the teeth with this bark may improve oral hygiene, prevent plaque and caries formation, and reduce the incidence of gingival and periodontal infections [43-44].

2.16. *Lawsonia inermis*

The effect of *Lawsonia inermis* leaves infusion in gingivitis healing was studied clincally. Sixty three gingivitis patients were instructed to rinse with 3 concentrations (50000, 10000 and 5000 µg/ml) of *Lawsonia inermis* leaves infusion, 0.1% hexetidine solution, and placebo as control. Bleeding index was decreased in *Lawsonia inermis* leaves infusion at 10000 µg/ml concentratation (80%), more than hexetidine 0.1% (76%) [45-46].

2.17. *Morus Alba*

Kuwanon G isolated from the ethyl acetate fraction of methanol extract of *Morus Alba* was tested for antibacterial activity. MIC of kuwanon G against *Streptococcus mutans* causing dental caries was 8.0 microg/ml. The bactericidal test showed that kuwanon G completely inactivated *S. mutans* at the concentration 20 microg/ml in 1 min. It also significantly inhibited the growth of other cariogenic bacteria such as *Streptococcus sobrinus and Streptococcus sanguis,* and *Porpyromonas gingivalis* causing periodontitis. Electron microscopic examination of the affected microorganisms demonstrated remarkable morphological damage of the cell wall and condensation of the cytoplasm [47].

The effect of crude extract and a purified compound (1-deoxynojirimycin) from *Morus Alba* leaves was evaluated against oral pathogens, *S. mutans*. The purified compound, 1-deoxynojirimycin, showed an 8-fold lower MIC against *S. mutans* than the extract (MICs, 15.6 and 125 mg/l, respectively). The extract strongly inhibited biofilm formation of *S. mutans* at its active accumulation and plateau phases [48].

The antibacterial activity of ethanolic extract of *Morus Alba* leaves was compared with chlorhexidine gluconate against *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, and *Tannerella forsythia*. *P. gingivalis* was the most sensitive organism to the *Morus Alba* extract with MIC value of 1.95 mg/ml; while *T. forsythia* and *P. gingivalis* were more sensitive to chlorhexidine gluconate [49].

The antimicrobial activity of *Morus Alba* crude extract sol–gel with chlorhexidine sol–gel was evaluated against ATCC standard strains of *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, and *Tannerella forsythia*. The minimum inhibitory concentration of *Morus Alba* sol–gel and chlorhexidine sol–gel against *A. actinomycetemcomitans* was 19 and 17 mm, against *T. forsythia* 12 and 21 mm, and against *P. gingivalis* 16 and 18 mm, respectively [50].

2.18. *Morus nigra*

The antibacterial potential of *Morus nigra* leaf hexane, chloroform, methanol, ethyl-acetate and aqueous extracts was studied against *Streptococcus mutans*, *Streptococcus mitis, Staphylococcus aureus, Pseudomonas aeruginosa, Bacillus subtilis* and *Escherichia coli*. The results evidenced that the extracts inhibited the growth of oral bacteria responsible for dental caries [51].

2.19. *Myrtus communis*

The antibacterial effect of aqueous and methanolic extract of Myrtus communis was studied against Actinobacillus actinomycetemcomitans, Porphyromonas gingivalis and Prevotella intermedia. The aqueous extract of Myrtus communis from 20 to 500 mg/ml and methanolic extract from 10-500 mg/ml possessed antibacterial effect against Actinobacillus actinomycetemcomitans, Porphyromonas gingivalis and Prevotella intermedia. The MIC was achieved at 10 mg/ml for aqueous and methanolic extracts of Myrtus communis against the tested microorganisms [52].

The antimicrobial activities of Myrtus communis oil (3.9-1000 µg/ml) was studied against some oral pathogens (thirty strains of *Streptococcus mutans, Aggregatibacter actinomycetemcomitans, Porphyromonas gingivalis* and 20 strains of Streptococcus pyogenes and *Candida albicans*) isolated from patients with dental caries, periodontal diseases, pharyngitis and oral lesions associated with artificial dentures. All isolates were sensitive to the oil at 125-1000 µg/ml producing inhibition zones of 8.1-41.25 mm. All of *S. pyogenes*, *S. mutans* and *C. albicans* strains were sensitive to 62.5 µg/ml while 70% (21/30) of *A. actinomycetemcomitans* and 66.6% (20/30) of *P. gingivalis* were resistant to these concentrations. All *S. pyogenes* and *S. mutans* strains were sensitive to 31.25 µg/ml. All *S. pyogenes* strains were sensitive to 15.6 and 7.8 µg/ml of the oil. The minimum inhibitory concentrations of the oil against *S. pyogenes, S. mutans, C. albicans, A. actinomycetemcomitans* and *P. gingivalis* were 29.68 ± 4.8, 31.25 ± 0, 46.9 ± 16, 62.5 ± 0 and 62.5 ± 0 µg/ml, respectively[53].

2.20. *Polygonum aviculare*

The effectiveness of a natural Mexican Sanguinaria extract (*Polygonum aviculare*) was investigated against gingivitis in 60 male dentistry students between the ages of 18 and 25 years. The participants used Sanguinaria extract (1 mg/ml) in oral rinse twice daily for 2 weeks (no tooth-brushing was allowed). The O'Leary Plaque Index and the Löe and Silness Gingivitis Index were recorded. The results showed that the Mexican Sanguinaria extract in oral rinse significantly decreased gingivitis from day 0 -14. The plaques were mechanical flushed easily [54].

2.21. *Prunus cerasus*

The effects of a phenolic extract of *Prunus cerasus* juice on the growth, adherence, and protease activity of *P. gingivalis* were studied in addition to investigation of the protective effect of *Prunus cerasus* extract on the disruption of the oral epithelial barrier induced by *P. gingivalis*. The extract which contained procyanidins and quercetin and its derivatives, attenuated *P. gingivalis* growth, reduced adherence to an experimental basement membrane matrix model, and decreased the protease activities of *P. gingivalis*. The extract also exerted a protective effect on the integrity of the oral epithelial barrier in an *in vitro* model infected with *P. gingivalis*. Furthermore, it prevented a decrease in trans-epithelial electrical resistance as well as the destruction of tight junction proteins (zonula occludens-1 and occludin)[55].

The effects of two *Prunus cerasus* fractions on oral pathogens (*Candida albicans*, *Streptococcus mutans*, and *Fusobacterium nucleatum*), as well as on the barrier function of oral epithelial cells were studied. Although the fractions

showed poor antimicrobial activity, but they inhibited biofilm formation by the three oral pathogens in a dose dependent manner. The fractions also attenuated the adherence of *C. albicans* and *S. mutans* to a hydroxylapatite surface as well as the adherence of *F. nucleatum* to oral epithelial cells. Treating oral epithelial cells with fractions also significantly enhanced the barrier function as determined by the transepithelial electrical resistance [56].

The effect of sour cherry extract on salivary α-amylase activity and on the level of *Streptococcus mutans* in human saliva were investigated on 70 patients. Saliva samples were collected for the measurement of α-amylase activity and the salivary *S. mutans* level before and after chewing a gum with or without cherry extract. Salivary α-amylase activity and *S. mutans* levels were decreased earlier in the presence of sour cherry extract than those of control cases. Chewing gum with sour cherry extract may be useful for the prevention of dental caries [57].

2.22. *Punica granatum*

The extract of *Punica granatum* inhibited the adherence of many microorganisms in the oral cavity. While, the hydroalcoholic extract was effective against dental plaque associated microorganisms [58-59].

2.23. *Quercus infectoria*

The methanolic extract of *Quercus infectoria* gall also possessed concentration dependent antibacterial effects against dental pathogens included multidrug resistant *Staphylococcus aureus, Pseudomonus aeruginosa* and *Escherichia coli*. The extract was more active against *Escherichia coli* than against other tested bacteria[60].

The antibacterial activity of methanol and acetone extracts of the galls of *Quercus infectoria* was investigated against oral bacteria which are known to cause dental caries and periodontitis (two Gram-positive bacteria: *Streptococcus mutans* ATCC 25175 and *Streptococcus salivarius* ATCC 13419, and two Gram-negative bacteria: *Porphyromonas gingivalis* ATCC 33277 and *Fusobacterium nucleatum* ATCC 25586). Both extracts showed inhibition zones which did not differ significantly against each tested bacteria. Among all tested bacteria, *S. salivarius* was the most susceptible. The MIC ranges for methanol and acetone extracts were the same, (between 0.16 and 0.63mg/ml) and the MBC value, for methanol and acetone extracts, was in the range of 0.31–1.25 mg/ml and 0.31–2.50 mg/ml, respectively[61].

2.24. *Quercus brantii*

A mucoadhesive gel was formulated from the seed hull of *Quercus brantii* and fruits of *Coriandrum sativum* for the treatment of periodontitis. The antibacterial activity of formulation was studied against *Porphyromonas gingivalis*. The gel produced significant growth inhibition zones against *P. gingivalis*. It was suitable formulation for the treatment of periodontitis, exhibited high value of mucoadhesion, showed controlled release of drug and easily delivered into the periodontal pocket [62].

3. Conclusion

Herbal medicine showed an efficacy in almost every aspect of oro-dental treatments. Herbal agents have been employed in dentistry to decrease inflammation, as antioxidants, analgesic, anesthetic, as antimicrobials, antiseptics, analgesics and wound healers. In the current review, we tried to discuss the medicinal plants which possessed antimicrobial activity against oral pathogens. However, determination of the active ingredients in addition to clinical trials, are required to investigated the efficacy, safety, cost-effectiveness, and characterization of these natural therapies.

Compliance with ethical standards

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Disclosure of conflict of interest

The author confirmed that there is no conflict of interest.

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