Herbal extracts in oral health care - A review of the current scenario and its future needs

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Submitted: 14-04-2014 Revised: 17-05-2014 Published: 04-08-2015

ABSTRACT

Background: Oral diseases are among the major public health problems and the commonest of chronic diseases that affect mankind. The application of natural products for the control of oral diseases is considered as an interesting alternative to synthetic antimicrobials due to their lower negative impact, and for the effort to overcome primary or secondary resistance to the drug during therapy. **Objective:** To review the current evidence on the antimicrobial efficacy of 10 plant extracts on dental caries and plaque microorganisms. **Materials and Methods:** A comprehensive literature search was made by one of the authors for 2 months in PubMed, PubMed Central, MEDLINE, LILACS/BBO, Cochrane database of systematic reviews, SCIENCE DIRECT, and Google scholar databases. The results from the relevant published literatures are discussed. **Summary and Conclusion:** The extracts of *Azadirachta Indica, Ocimum sanctum, Murraya koenigii* L., *Acacia nilotica*, *Eucalyptus camaldulensis, Hibiscus sabdariffa, Mangifera indica,* Psidium guajava, Rosa indica, and *Aloe barbadensis* Miller have all been found to inhibit certain dental caries and periodontal pathogens. The current evidence is on individual plant extracts against bacteria involved in either caries or periodontitis. "Herbal shotgun" or "synergistic multitarget effects" are the terms used for the strategy of combining different extracts. The research assessing the antimicrobial efficacy of a combination of these plant extracts against dental caries and periodontal pathogens is the need of the hour, and such research will aid in the development of a novel, innovative method that can simultaneously inhibit two of the most common dental diseases of mankind, besides slowing the development of drug resistance.

Key words: Antimicrobial efficacy, dental caries, herbal extracts, *Lactobacillus acidophilus*, periodontitis, *Streptococcus mutans*

INTRODUCTION

Oral health/dental health is an inseparable part of general health. Oral health has an effect on general health as it causes considerable pain and suffering. It has an impact on a person's speech, selection of food, quality of life, and well-being. In view of the prevalence of oral diseases, their impact on individuals and society, and the expense of their treatment, oral diseases may be considered a major public health problem and they are listed among the most common of the chronic diseases that affect mankind. Oral diseases are the fourth most expensive diseases to treat in certain countries.[1]

According to the World Health Organization (WHO) report, dental caries, though exhibiting a declining trend in many parts of the industrialized world, is still an important public health concern in many developing countries. The statistics suggest that dental caries affect 60-90% of schoolgoing children in developing countries.[2] Loss of teeth because of periodontitis often causes discomfort, and compromises the esthetics and function. Moreover, recent studies suggest an association between chronic low-grade infections such as periodontitis and systemic health problems (preterm low birth weight, cardiovascular diseases, diabetes mellitus, and chronic obstructive pulmonary disease).[3] The treatment of established dental diseases is very expensive and may not be considered a realistic strategy, especially for the economically deprived sections of the society. Treating dental caries alone, which is estimated at US$ 3513 per 1,000 children is more than the total health budget for children in many low-income countries.[1] There is an immediate need for

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Access this article online

Quick Response Code:

Website: www.phcogrev.com

DOI: 10.4103/0973-7847.162101

promoting preventive strategies that are socially acceptable, easily available, and at the same time be cost-effective. This calls for the evolution of innovative strategies that are robust, efficient, and feasible.

The established practices to prevent dental caries and periodontal diseases are the use of fluorides in different forms and mechanical plaque control in combination with professional care, respectively. However, in reality, a major bulk of the population will not have adequate dexterity and motivation that are necessary to maintain optimum oral hygiene. This is especially true in rural areas. Antimicrobial mouth rinses have also been suggested as adjuncts for mechanical plaque control methods. The most commonly used antiplaque agent is chlorhexidine gluconate. The use of chlorhexidine has some potential drawbacks like altered taste sensation, staining of teeth, and development of resistant bacteria that incapacitate its application on long-term basis. There exists a need to develop some innovative strategies that act against both dental caries and periodontal diseases simultaneously. One such strategy would be to explore the abundantly available medicinal plants in nature. The "naturally occurring" active ingredients in plant medicines restore health, with minimal harmful effects and maximum efficiency. The use of natural products is a comprehensive remedy that includes promotive and preventive strategies in the maintenance of health. Natural herbs used either exclusively or in combination are proven to be safe and effective in the management of various oral health problems such as halitosis, bleeding gums, mouth ulcers, and dental caries. Herbal products have the dual advantage of minimal side effects and being alcohol and/or sugar-free, which are the two most common ingredients found in other over-the-counter products. Some bacteria utilize these ingredients and release byproducts that cause halitosis. Systematic reviews play an important role in aiding clinical decision-making. This review is an attempt to assess the antimicrobial efficacy of 10 plant extracts on dental caries and plaque microorganisms.

MATERIALS AND METHODS

Research question

To summarize the current evidence on the antimicrobial efficacy of 10 plant extracts on dental caries and plaque microorganisms.

Research protocol

A written research protocol was prepared before retrieving the literature. The protocol emphasized the methods for literature search, screening, and data extraction to minimize bias before starting the literature search.

Literature search

A comprehensive literature search was done by one of the authors for 2 months from 07-20-2013 to 09-19-2013 from PubMed, PubMed Central, MEDLINE, LILACS/BBO, Cochrane database of systematic reviews, SCIENCE DIRECT, and Google scholar databases. The following search terms were employed in a sequential order for electronic retrieval of the required literature from the databases.

- Antimicrobial efficacy
- Herbal extracts
- Oral microflora
- *Streptococcus mutans* and/or *Lactobacillus acidophilus*
- Plaque colonizers
- Zone of inhibition
- Minimum inhibitory concentration (MIC).

First stage screening

The journal articles with any of the above cited search terms either in the title, abstract, or keywords were considered for the initial screening. The titles and abstracts of these articles were checked for relevance in the present review. This initial screening was performed by two investigators. The type of study, herbal extracts, comparative groups, the microorganisms investigated, methods employed for antimicrobial efficacy testing, and outcome measures were noted in a standardized electronic data extraction sheet.

A preliminary list of studies on the antimicrobial efficacy of herbal extracts on dental caries (*S. mutans* and *L. acidophilus*) and plaque microorganisms (primary, secondary, and tertiary plaque colonizers) was prepared following the initial screening. Then, a list of 10 herbal extracts commonly available in central India was prepared and the articles investigating the antimicrobial efficacy of these 10 herbal extracts on dental caries and plaque microorganisms were considered in the next phase.

Second stage screening and selection of articles

The abstracts of these articles were scrutinized by the investigators. The studies which were *in vitro* in nature, where the language of publication was comprehensible to the investigators and the outcome parameters were either zone of inhibition and/or MIC were listed out. Review articles and letters to editors (not containing primary data) were not considered for final review.

Quality appraisal

The full text of these selected articles was thoroughly scrutinized for the methodology, outcome measures, and relevance for the present review. The final list of articles on the antimicrobial efficacy of freshly prepared extracts of neem (*Azadirachta indica*), tulsi (*Ocimum sanctum*), curry leaves (*Murraya koenigii L.*), babul (*Acacia nilotica*), eucalyptus (*Eucalyptus camaldulensis*), sorrel (*Hibiscus sabdariffa*), mango (*Mangifera indica*), guava (*Psidium guajava*), rose (*Rosa indica*), and Aloe vera (*Aloe barbadensis Miller*) was prepared.

Data extraction

The list of articles finally considered for data extraction and the key facts in these selected articles are summarized in Table 1.

Table 1: Summary of the articles considered for discussion in the present review

Author details	Plant extract	Research question	Microorganisms	Outcome assessed	Major conclusion
Prashanth *et al*.[4]	Neem and mango twigs	Antimicrobial efficacy testing	*S.mutans,S. sanguis* and *S. salivarius*	Mean diameter of inhibition zone	Mango and neem extracts exhibited inhibitory effect against all the bacteria with maximum efficacy at 50% concentration
Agarwal *et al*.[5]	Tulsi leaves *(Ocimum sanctum)*	Antimicrobial efficacy testing	*S. mutans*	Mean diameter of inhibition zone	Tulsi at 4% concentration offered the maximum efficacy against *S. mutans* and could be considered in the prevention of dental caries
Sunitha *et al*.[6]	Curry leaf *(Murraya koenigii L.)* and *Aloe vera* using distilled water and ethyl alcohol as solvents	Antimicrobial efficacy testing	*Streptococcus mutans, Streptococcus mitis, Lactobacillus casei, Lactobacillus brevis, Lactobacillus acidophilus, Actinomyces viscosus*	Mean diameter of inhibition zone	Aqueous aloe vera extracts inhibited the maximum of six microorganisms, followed by thealcoholic curry leaves extracts. Using of these plant extracts as home remedies creates an oral environment which is unfavorable for microbes
Dabur *et al*.[7]	Babul *(Acacia nilotica)* using n-hexane, chloroform, acetone, methanol and water as solvents for extraction	Antimicrobial and antifungal efficacy testing	*E. Coli* *Candida albicans*	Minimum Inhibitory concentration	Aqueous extracts were the most effective compared to extracts derived from other solvents
Deshpande *et al*.[8]	Babul *(Acacia nilotica)*	Antimicrobial efficacy testing	*Streptococcus mutans*	Mean diameter of inhibition zone Minimum Inhibitory concentration	The ethanol extract showed more significant activity against *Streptococcus mutans* compared to petroleum ether extract
Pai *et al*.[9]	Babul *(Acacia nilotica)*	Antifungal efficacy testing	*Candida albicans*	Mean diameter of inhibition zone	A.nilotica exhibited antifungal effect and it has the potential to be used as a cheap and convenient adjuvant to pharmaceutical antifungal agents
Nagata *et al*.[10]	Eucalyptus using ethanol and petroleum ether as solvents for extraction	Antimicrobial efficacy testing	*P. gingivalis, Prevotella intermedia, Fusobacterium nucleatum, Actinobacillus actinomycetemcomitans, Treponema denticola*		
Takarada *et al*.[11]	Eucalyptus oil	Antimicrobial efficacy testing	*Porphyromonas gingivalis, Actinobacillus actinomycetemcomitans, Fusobacterium nucleatum, Streptococcus mutans,* and *Streptococcus sobrinus*	Minimum Inhibitory concentration	Macrocarpals A, B and C were effective against periodontopathic bacteria. Among tested bacteria, P. gingivalis displayed the greatest sensitivity to macrocarpals and hence, eucalyptus extracts may be useful in preventing periodontal disease
Nagarajappa *et al*.[12]	*Hibiscus rosa-sinensis*	Antimicrobial efficacy testing	*S. mutans* *L. acidophilus*	Mean diameter of inhibition zone and Minimum Inhibitory concentration	The extract was found to be effective against the bacteria and contained compounds with therapeutic potential
Tsai *et al*.[13]	*Rosa damascene* *Rosmarinus officinalis*	Antimicrobial efficacy testing	*S. mutans* *S. sanguinis* *S. sorbinus*	Minimum Inhibitory concentration	The crude methanolic extract of rosemary suppressed the growth of cariogenic streptococci and could be considered as anticaries agents
George *et al*.[14]	*Aloevera* (*Aloebarbadensis* Miller)	Antimicrobial efficacy testing	*S. mutans, S. mitis Lactobacillus acidophilus, Enterococcusfaecalis, Prevotella intermedia, Peptostreptococcus anaerobius, Candida albicans*,	Mean diameter of inhibition zone	Aloe vera tooth gel was as effective as two commercially popular toothpastes in controlling all of the organisms used in the study

MIC=Minimum inhibitory concentration

The entire procedure employed in the review is diagrammatically represented in Figure 1.

DISCUSSION

The use of natural products and herbal medicines has been documented in the past. They have been reported to be effective in the management of many infections in general. Some of these have been assessed in the recent past for their antimicrobial potential against oral bacteria.[15] The present review was an attempt to summarize the existing published literature pertaining to the usefulness of 10 plants with ethnopharmacological background in promoting oral health. These plants have been selected in view of their easy availability in India.

Prashanth *et al*.[4] in their *in vitro* study have found the aqueous extract of *Azadirachta Indica* to be effective against *S. mutans, S. sanguis, S. salivarius*, and S. *mitis*. The mean diameters of inhibition zone against these bacteria at 5%, 10%, and 50% concentrations were 2.4 mm, 3.4 mm, and 3.8 mm (*S. mutans*); 2 mm, 3 mm, and 3.4 mm (*S. sanguis*); 1.5 mm, 2.5 mm, and 2.9 mm (*S. salivarius*); and 1.5 mm, 2 mm, and 2.7 mm (*S. mitis*). The mean inhibition zone against these bacteria increased as the concentration increased. The maximum efficacy of the extract was found against *S. mutans* at 50% concentration. The extracts of

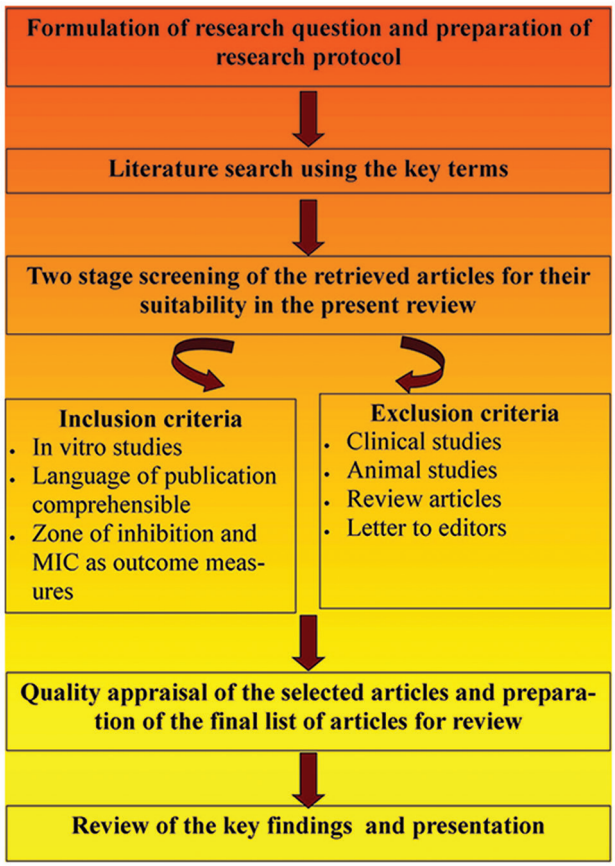

Figure 1: Diagrammatic representation of the research protocol

Azadiratchta indica have been claimed to contain active ingredients like alkaloids, saponins, flavanoids, sterols, resins, tannins, oils, gum, chloride, fluoride, silica, sulfur, and calcium. The authors concluded that the presence of fluoride offers anticariogenic benefits; silica acts as an abrasive agent to prevent accumulation of plaque; alkaloids exert analgesic action; oils exert analgesic, antiseptic, and carminative effects; and tannins act as astringent and form a protective coating on the tooth enamel that aids in caries prevention.

Agarwal *et al*.[5] evaluated the antimicrobial efficacy of ethanolic extract of *Ocimum sanctum* against *S. mutans,* the principal bacteria in the causation of dental caries. Fifteen different concentrations of the extract ranging from 0.5% to 10% have been evaluated. Five different volumes (10 μL, 20 μL, 30 μL, 50 μL, and 75 μL) of these extracts in different concentrations were assessed. Although the herbal extract inhibited the bacteria at all concentrations with higher volumes, the maximum inhibition was found at 4% concentration while using 75 μL (22 mm). The antimicrobial efficacy of *Ocimum sanctum* was mainly attributed to the presence of eugenol (1-hydroxy-2-methoxy-4-allylbenzene). Apart from this, the other important constituents claimed to be responsible antimicrobial efficacy were ursolic acid and carvacrol. The authors concluded that the extracts of *Ocimum sanctum* may be recommended for use on a long-term basis in view of its easy availability and cost-effectiveness. Moreover, the easy accessibility and minimal side effects of the herb make it culturally acceptable even in rural areas.

Sunitha *et al*.[6] in their study found the ethanolic and aqueous extracts of Murraya koenigii L. to be effective against S. mutans. The mean diameter of the inhibition zone of the ethanolic and aqueous extracts was 16 mm and 13.05 mm, respectively. The ethanolic extract was effective in inhibiting Lactobacillus brevis (20.10 mm) and Actinomyces viscosus (17.05 mm). The aqueous extract inhibited Lactobacillus casei (16 mm). The authors attributed the antimicrobial efficacy of curry leaves to its phytochemical constituents such as carotene, beta carotene, calcium, iron, phosphorus, zinc, folic acid, and riboflavin. The chlorophyll of curry leaves was also proposed to be an anticariogenic agent. They claimed that the plant extract creates an oral environment that is unfavorable for microbes. This indirectly reduces the microbial colonization and modifies the oral environment. They concluded that although phytochemicals (plant-derived metabolites) are antimicrobial in nature, they produce other biological activities in oral cavity like induction of immunity, which indirectly reduces the risk of oral diseases.

Dabur *et al*.[7] found the methanolic and aqueous extracts of A. nilotica to exert inhibitory effect on E. coli. The MIC of methanolic and aqueous extracts was 75 μg/mL and 18.75 μg/mL, respectively. Deshpande *et al*.[8] have found the stem bark extracts using ethanol and petroleum ether to be effective in inhibiting S. mutans. The mean diameter of the inhibition zone of ethanol and petroleum ether was 31 mm and 17.05 mm, respectively. The MIC of the ethanolic and petroleum ether

extracts of A. nilotica against S. mutans was 5 mg/mL and 10 mg/mL. Pai *et al*.[9] found the aqueous extracts of A. nilotica to exert antifungal activity against Candida albicans. The mean inhibition zone against C. albicans was 7.6 mm. The antimicrobial and antifungal activities of A.nilotica were attributed to the presence of alkakoids, tannins, saponins, flavonoids, cardiac glycosides, and anthraquinones.

Nagata *et al*.[10] investigated the effect of macrocarpals A, B, and, C on many oral bacteria. The macrocarpals A, B, and C are phloroglucinol derivatives of eucalyptus leaves. Macrocarpals A, B, and C were effective against *P. gingivalis*, which displayed the maximum sensitivity. The MIC of macrocarpals A and B was 1μg/mL while it was 0.5 μg/mL for macrocarpal C. All three compounds successfully inhibited the expression of *P. gingivalis* proteases and the binding of cells to saliva-coated hydroxyapatite by 70-80% at a concentration of 10 μgmL-1. The findings strongly suggest the usefulness of eucalyptus leaf extracts as potent preventive agents against periodontal pathogens. Takarada *et al*.[11] found eucalyptus oil to exert inhibitory effect on various oral bacteria that included S. *mutans, Streptococcus sobrinus, Actinobacillus actinomycetemcomitans, Porphyromonas gingivalis,* and *Fusobacterium nucleatum*.

Nagarajappa *et al*.[12] found the aqueous and ethanol extracts of *Hibiscus rosa-sinensis* derived using both the hot and cold extraction methods to exert inhibitory effect on *L. acidophilus* and *S. mutans*. The extract significantly inhibited the growth of *L. acidophilus* and *S. mutans* ($P \leq 0.05$) with MIC value of 25 μg/mL. The study demonstrated the therapeutic potential of the plant extract against two proven cariogenic bacteria.

Prashanth *et al*.[4] found that the mean diameters of the inhibition zone produced by *Mangifera indica* against *S. mutans* at 10% and 50% concentrations were 1.5 mm and 2.9 mm, respectively. The mean inhibition zones against *S. salivarius, S. mitis,* and *S. sanguis* at 10% and 50% concentrations were 1.1 mm and 1.8 mm, 2.9 mm and 5 mm, and 1 mm and 2.5 mm, respectively. *Mangifera indica* failed to inhibit the growth of these bacteria at 5% concentration even after 48 h of incubation. The antimicrobial efficacy of *Maginfera indica* was attributed to the presence of bitter gums, resins, and tannins. The tannins and resins have an astringent effect on the mucous membrane and are claimed to form a protective layer on the enamel.

Although the published literature demonstrates the antimicrobial efficacy of *Psidium guajava,*[16,17] we could not find any studies demonstrating the antimicrobial potential of these extracts on oral bacteria. *P. guajava* contained guajaverin, psidiolic acid, and other essential oil constituents such as 1.8-cineol, monoterpenes, ρ-cimen, and acetate of α-terpenil, which may offer antimicrobial benefits.[16]

Tsai *et al*.[13] assessed the antimicrobial potential of *Rosa damascene* and *Rosmarinus officinalis* against *S. mutans, S. sanguinis, and S. sorbinus*. The MIC of *Rosa damascene* (flower extract) against these bacteria was > 8 mg/mL. The MIC of *Rosmarinus officinalis* leaf extracts against S. mutans, S. sanguinis, and *S. sorbinus* was *4 mg/mL, 2 mg/Ml, and 4 mg/mL*. Although the results revealed that the crude methanolic extract of rosemary inhibited the growth of cariogenic streptococci, its activity against periodontal pathogens such as *Porphyromonas gingivalis* and *Prevotella intermedia* needs to be evaluated. In view of limited knowledge on the efficacy of rosemary extracts and its constituents against periodontal pathogens, the authors recommended further studies to explore antiplaque or antigingivitis potential of the extract.

Sunitha *et al*.[6] found the aqueous extracts of *Aloe vera* to inhibit *S. mutans* (13.05mm), *S. mitis* (15.15mm), *L. brevis* (15.7 mm), *L. acidophilus* (17.95 mm), and *A. viscosus* (17 mm). The ethanolic extract was also found to be effective against *L. brevis* (13.25 mm) and *A. viscosus* (13.05 mm). George *et al*.[14] found the *Aloe vera* tooth gel to inhibit the growth of *Streptococcus mutans, L. acidophilus, Prevotella intermedia, Candida albicans, Enterococcus faecalis, and Peptostreptococcus anaerobius*. The *Aloe vera* gel was found to contain many active constituents (more than 75), such as enzymes, sugars, lignin, vitamins, minerals, salicylic acids, amino acids, and saponins. *Aloe vera* contains a latex compound that has been found to be bacteriostatic in nature. Thus, the antimicrobial activity of *Aloe vera* against these microorganisms was attributed to these constituents.

"Herbal shotgun" or "synergistic multitarget effects" are the terms used for the strategy of combining different extracts. Here, the herbal extracts and drugs are combined to offer a multitargeted approach through their synergistic action. This mechanism may offer maximum benefits with an added benefit of slowing down the rate of development of bacterial resistance to synergistic drug combinations.[18]

CONCLUSION

The use of herbal extracts for the control of oral/dental diseases is considered an interesting alternative to synthetic antimicrobials due to their lower negative impact and to overcome intrinsic (primary) resistance or secondary resistance to the drug during therapy. The current evidence suggests all the 10 plant extracts have antimicrobial efficacy against dental caries and periodontal pathogens. Most of these studies have been conducted using individual plant extracts on certain bacteria that are involved in either dental caries or periodontitis. The authors of all these studies have recommended further research before considering them for clinical use. Some authors have recommended the use of these plant extracts in combination. The research assessing the antimicrobial efficacy of a combination of these plant extracts against dental caries and periodontal pathogens is the need of the hour, and such research will aid the development of a novel, innovative method that can simultaneously inhibit the two most common dental diseases of mankind, besides lowering the development of drug resistance.

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How to cite this Article: Chandra Shekar BR, Nagarajappa R, Suma S, Thakur R. Herbal extracts in oral health care - A review of the current scenario and its future needs. Phcog Rev 2015;9:87-92.

Source of Support: Nil, **Conflict of Interest:** None declared