ROLE OF MEDICINAL HERBS IN PREVENTION AND TREATMENT OF DENTAL DISEASES

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Abstract
Oral diseases are major health problems with dental caries and periodontal diseases among the most important preventable global infectious diseases. Oral health influences the general quality of life and poor oral health is linked to chronic conditions and systemic diseases. The association between oral diseases and the oral microbiota is well established. Of the more than 750 species of bacteria that inhabit the oral cavity, a number are implicated in oral diseases. The development of dental caries involves acidogenic and aciduric Gram-positive bacteria (Mutans streptococci, Lactobacilli and Actinomycetes). Periodontal diseases have been linked to anaerobic Gram-negative bacteria (Porphyromonas gingivalis, Actinobacillus, Prevotella and Fusobacterium). Given the incidence of oral disease, increased resistance by bacteria to antibiotics, adverse affects of some antibacterial agents currently used in dentistry and financial considerations in developing countries, there is a need for alternative prevention and treatment options that are safe, effective and economical. While several chemical agents are available commercially, these chemicals can alter oral microbiota and have undesirable side-effects such as vomiting, diarrhea and tooth staining. Hence, the search for alternative yet safe products continues and natural phytochemicals isolated from plants used as traditional medicines come as good alternatives. In this review, plant extracts or phytochemicals that inhibit the growth of oral pathogens, reduce the development of biofilms and dental plaque and reduce the symptoms of oral diseases will be discussed further.

Key words- Dental diseases, Herbs, Medicinal plants

Introduction
Oral diseases continue to be a major health problem worldwide.¹ Dental caries and periodontal diseases are among the most important global oral health problems, although other conditions like oral and pharyngeal cancers and oral tissue lesions are also of significant concern.² Oral health is integral to general well-being and relates to the quality of life that extends beyond the functions of the craniofacial complex. The link between oral diseases and the activities of microbial species that form part of the microbiota of the oral cavity is well established.³ Over 750 species of bacteria inhabit the oral cavity (50% of which are yet to be identified) and a number of these are implicated in oral diseases.³ The global need for alternative prevention and treatment options and products for oral diseases that are safe, effective and economical comes from the rise in disease incidence (particularly in developing countries), increased resistance by pathogenic bacteria to currently used antibiotics and chemotherapeutics, opportunistic infections in immune-compromised individuals and financial considerations in developing countries.⁴, ⁵ Despite several chemical agents being commercially available, these can alter oral microbiota and have undesirable side-effects such as vomiting, diarrhea and tooth staining.⁶, ⁷ Hence, the search for alternative products continues and natural phytochemicals isolated from plants used in traditional medicine are considered as good alternatives to synthetic chemicals.⁸ The natural products derived from medicinal plants such as neem, tulsi, amla, dhatura, nimbu etc. have proven to be an abundant source of biologically active compounds, many of which have become the basis for the development of new lead chemicals for pharmaceuticals. With respect to diseases caused by microorganisms, the increasing resistance in many common pathogens to currently used therapeutic agents, such as antibiotics and antiviral agents, has led to renewed interest in the discovery of novel anti-infective compounds. As there are approximately 500 000 plant species occurring worldwide, of which only 1% has been phytochemically investigated, there is great potential for discovering novel bioactive compounds from these sources. Therefore, the purpose of this review is to present some recent examples of traditional medicinal plant extracts or phytochemicals that have been shown to inhibit the growth of oral pathogens, reduce the development of dental plaque, and reduce the symptoms of oral diseases.

Antibacterial Activity of Crude or Total Plant Extracts
Many studies investigating the activity of traditional medicinal plants against oral pathogens have been limited to examination of crude aqueous or organic solvent extracts. In most cases, the investigators have simply sought to validate the traditional medicinal use of the plant. For example, the use of Drosera peltata...
antimicrobial activity against S. mutans, S. sanguis and S. sobrinus, with MIC values of 31.25–62.5 μg/mL-1.\(^{(14)}\)

Two recent studies have examined a number of plants traditionally used in Brazil\(^{(15)}\) or South Africa\(^{(16)}\), respectively, for activity against oral pathogens. All four Brazilian plant extracts, Cocos nucifera (Palmae), Ziziphus joazeiro (Rhamnaceae), Caesalpinia pyramidalis (Fabaceae) and Aristolochia cymbifera (Aristolochiaceae), were active against the test bacteria, with the ethanol extract of A. cymbifera being themost effective (MIC = 0.1–4.0mg/mL-1).

**Antibacterial Activity of Propolis**

Propolis (a resinous mixture that honey bees collect from tree buds, sap flows, or other botanical sources) has been shown to exhibit good antimicrobial activity against a range of oral bacteria and inhibit the adherence of S. mutans and S. sobrinus to glass. It was also shown to be a potent inhibitor of water-soluble glucan synthesis. Uzel et al.\(^{(17)}\) also investigated the activity of propolis against a number of microorganisms, including S. mutans and S. sobrinus. Propolis showed antimicrobial activity similar to chlorhexidine and greater than clove extract in a study investigating the ability of these chemicals to inhibit the growth of microbes obtained from the saliva of periodontally healthy subjects and those with chronic periodontitis.\(^{(15)}\)

While Nidus vespae (honey bee hive extract) is similar to propolis, it contains additional material including waxes and aromatic oils. Like propolis, extracts and fractions of Nidus vespae have been shown to exert antimicrobial activity toward a number of oral microorganisms, in particular S. mutans.\(^{(19)}\)

**Antibacterial Activity of Purified Phytochemicals**

The following section describes the studies of phytochemicals that have been shown to be active against oral pathogens. The studies are grouped according to the general class of phytochemicals investigated.

**Flavonoids and Other Polyphenols**- In a study of a number of methanolic plant extracts, two active isoprenylflavones, artocarpin and artocarpesin, were isolated from Artocarpus heterophyllus (Moraceae). These inhibited the growth of numerous cariogenic and oral bacteria, including mutans and other oral streptococci, actinomyces and lactobacilli, at MIC values of 3.13–12.5 μg/mL-1.\(^{(20)}\) Flavonone phytoalexins from Sophora exigua (Leguminosae)
have been shown to inhibit the growth of numerous cariogenic bacteria, with 5,7,2,4-tetrahydroxy-8-lavandulylflavanone being the most active. [21] *Erythrina variegata* (Leguminosae) is used in folk medicine in tropical and subtropical regions and displays a number of biological properties, including antibacterial activity. [22]

The root bark of *Morus alba* (Moraceae) has been used as a traditional medicine in Asian countries and exhibits antibacterial activity against food poisoning microorganisms. The compound displayed an MIC of 8 μg/mL-1 against *S. mutans*, which was comparable to chlorhexidine and vancomycin (1 μg/mL-1).

A similar mode of antibacterial action has been reported for the compound isopanduratin A isolated from *Kaempferia pandurate* (Zingiberaceae). [23]

Many components of tea (*Camellia sinensis*, Theaceae), exhibit anticariogenic effect through various modes of action, including bactericidal effects on oral bacteria, prevention of adherence of bacteria to tooth surfaces, inhibition of glucan production and inhibition of amylases. [24] Monomeric polyphenols, particularly simple catechins such as epicatechin, epicatechin gallate, and epigallocatechin gallate are believed to be responsible for these biological effects. [24, 25] The paste of tender leaves of *Psidium guajava* (Myrtaceae) has been used traditionally to maintain oral hygiene, while other parts of the plant have various bioactive properties. The anti-adherent properties of this plant were supported by the reduction of cell-surface hydrophobicity observed in “early settler” plaque bacteria (*S. mitis, S. sanguinis* and *Actinomyces*) exposed to 1mg/mL-1 *P. guajava* extract [26].

Recently, a proteomics approach was used to show that treatment of *S. mutans* with a low concentration (1.6%, v/v) of a *Psidium cattleianum* water extract resulted in the down regulation of genes involved in lactic acid production, general metabolism and glycolysis. [27] At higher concentrations (25–100%, v/v), the extract was able to inhibit *S. mutans* biofilms.

Malvidin-3,5-diglucoside (malvin) was identified as the active constituent of an ethanol extract of *Alcea longipedicellata* (Malvaceae) responsible for activity against oral streptococci, with MIC values of 160–200 μg/mL-1. [28]

Macelignan (20 μg/mL-1) displayed rapid antibacterial activity and completely eliminated viable *S. mutans* within 1 min. It also showed preferential activity against other cariogenic bacteria. Macelignan also displayed antibiofilm activity against *S. mutans, S. sanguis* and *A. viscosus* [29].

The antibacterial activities of an ethanol extract of the seeds of *Piper cubeba* were described above. Naringin, a polymethoxylated flavonoid commonly found in citrus fruit and an FDA-approved health supplement, was shown to inhibit the growth of periodontal pathogens and other common oral microorganisms (9.8–125mg mL-1). [30] Using time-kill assays, naringin was shown to be particularly effective against *Actinobacillus actinomycetemcomitans* and *P. gingivalis* with significant growth inhibition within 3 h and greater inhibition with increasing incubation time and naringin concentration.

**Terpenes**- Bakuchiol isolated from Ayurvedic medicinal plant, *Psoralea corylifolia* (Fabaceae), has shown activity against numerous Gram-positive and Gram-negative oral pathogens (MIC = 1–4 μg/mL-1). It was able to inhibit the growth of *S. mutans* under a range of sucrose concentrations, pH values and in the presence of organic acids in a temperature-dependent manner and also inhibited the growth of cells adhered to a glass surface. [31]

**Alkaloids**- The alkaloid berberine isolated from *C. rhizoma* (Ranunculaceae) showed bactericidal activity against oral bacteria, with greatest activity against *A. actinomycetemcomitans* (MIC = 13 μg/mL-1) and *P. gingivalis* (MIC = 20 μg/mL-1), although much less activity was observed against *Lactobacillus* and *Streptococcus* species. Berberine also inhibited the collagenase activity of *A. actinomycetemcomitans* and *P. gingivalis*.

**Sugar Alcohols**- Xylitol is a sugar alcohol naturally found in plants that is used as an artificial sweetener in many foods. [32] Its anticariogenic properties were investigated by adding 0.78–50% xylitol to broth cultures of *S. mutans, S. salivarius* and *S. sanguis*, incubating at 37° C for 18 hrs and determining the optical density of the cultures. *Streptococcus mutans* was the only bacterium significantly inhibited by xylitol at 1.56%, while all bacteria showed statistically significant inhibition at levels above 1.56%. The study concluded that xylitol exhibited anticariogenic effects by inhibiting the growth of *S. mutans* while not affecting other streptococci as part of the normal oral flora. [32]
**Other Phytochemicals** - Several constituents found in hops (female flower clusters of a hop species *Humulus lupulus* from Cannabaceae), have been found to display antibacterial activity against *S. mutans*, *S. salivarius* and *S. sanguis* in disc diffusion assays. These antibacterial activities were enhanced in the presence of ascorbic acid or when pH was lowered, suggesting that this effect was the result of the acidic nature of ascorbic acid. Furthermore, the antibacterial activity of 20% ethanol was found to increase in the presence of beta acid or thymol. The antimicrobial properties of a number of commercially available dentifrices (agents used along with toothbrush to clean and polish natural teeth) containing herbal products have been evaluated against oral pathogens. Thirty-nine natural products were tested for their antibacterial properties against four strains of *S. mutans* and their ability to prevent adherence of the bacteria. The information about the traditional uses of the medicinal plants has been compiled in Table 1.

Table 1. Medicinal plants and their traditional uses for the treatment of a variety of dental problems

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Binomial</th>
<th>Local/English Name</th>
<th>Family</th>
<th>Part Used</th>
<th>Traditional Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Acorus calamus</td>
<td>Vacha/Sweet flag</td>
<td>Araceae</td>
<td>Rhizome</td>
<td>Paste of the Rhizome is applied to painful teeth and gums.</td>
</tr>
<tr>
<td>2.</td>
<td>Allium Sativum</td>
<td>Lahsun/Garlic</td>
<td>Alliaceae</td>
<td>Bulb</td>
<td>The paste of the bulb is applied to the gums and cavities of infected teeth.</td>
</tr>
<tr>
<td>3.</td>
<td>Bonbax ceiba</td>
<td>Semal/Silk cotton tree</td>
<td>Bombac aceae</td>
<td>Gum</td>
<td>Gum is used to treat toothcare.</td>
</tr>
<tr>
<td>4.</td>
<td>Cinamomum tamala Nees &amp; Ebesm</td>
<td>Tejpatra / Indian Bay-leaf</td>
<td>Lauraceae</td>
<td>Stem Bark</td>
<td>Stem bark juice is applied to the teeth to treat tooth decay and toothache.</td>
</tr>
<tr>
<td>5.</td>
<td>Citrus medica</td>
<td>Nimbu/Lemon</td>
<td>Rutaceae</td>
<td>Fruit</td>
<td>Used to treat bleeding gums in scurvy, due to high content of Vitamin-C.</td>
</tr>
<tr>
<td>6.</td>
<td>Datura stramonium</td>
<td>Dhatura/Mad apple</td>
<td>Solamaceae</td>
<td>Seeds</td>
<td>Seeds mixed with butter are burnt and smoke is inhaled into the mouth.</td>
</tr>
<tr>
<td>7.</td>
<td>Juglens regia</td>
<td>Akhoda/Walnut</td>
<td>Jugulancaceae</td>
<td>Oils &amp; Fruit</td>
<td>Oil &amp; fruits are ised in making traditional tooth powder to cure toothache and Pyorrhoea.</td>
</tr>
<tr>
<td>8.</td>
<td>Justicia adhatoda</td>
<td>Vasing/Malabar nut</td>
<td>Acanthaceae</td>
<td>Twigs</td>
<td>The twigs of the plant are used as tooth picks / brushes to treat Pyorrhoea.</td>
</tr>
<tr>
<td>9.</td>
<td>Myrica esculenta</td>
<td>Kaphal/Box-myrtle</td>
<td>Myricaceae</td>
<td>Bark</td>
<td>The bark is chewed to relieve toothache.</td>
</tr>
<tr>
<td>10.</td>
<td>Ocimum sanctum</td>
<td>Tulsi/Holy basil</td>
<td>Lamiaceae</td>
<td>Leaves</td>
<td>Powder of dry leaves along with salt os applied to painful teeth.</td>
</tr>
</tbody>
</table>
Safety Issues Related to Phytomedicines Used in Dentistry

The clinical studies reviewed above have generally assessed the efficacy of products containing plant-derived products. However, the safety and possible side-effects of such products must also be considered. Indeed, these issues have recently been reviewed by Groppo et al. in relation to natural products used in dentistry. In agreement with other studies of the clinical use of natural products, we propose that there is limited information available about the quality, safety and efficacy of herbal products used in dentistry. Given the possibility of adverse interactions between herbal formulations with conventional drugs, caution should be exercised when using herbal medicines and the need for more clinical studies is recommended. This review also recommends the use of herbal products in other segments of dentistry, as endodontic irrigation and anti-inflammatory agents.

Conclusions

As demonstrated by the examples included in this review, there is considerable evidence that plant extracts, essential oils and purified phytochemicals have the potential to be developed into agents that can be used as preventive or curative agents for oral diseases. While it is encouraging to see a number of clinical trials of such products, further studies on safety and efficacy of these agents will be important to establish their therapeutic benefits, either alone or in combination with conventional therapies. In particular, studies that address research issues such as adequate statistical power, blinding, standardization of extracts or purified compounds, and quality control would be of great value to improve dental care with the help of commonly available natural resources.

References


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