



## ROLE OF HERBS IN DENTAL CARIES: A REVIVING AGE OLD CONCEPT

Mukut Seal<sup>1</sup>, Pratim Talukdar<sup>2</sup>, Radhika Maniyar<sup>3</sup>, Shivakumar G C<sup>4</sup>,  
Sahana S<sup>5</sup> and Sankalp Verma<sup>6</sup>

<sup>1</sup>Department of Dentistry, FAA Medical College & Hospital, Barpeta, Assam

<sup>2</sup>Daswani Dental College & Research Centre, Kota

<sup>3</sup>M.R Ambedkar Dental College & Hospital, Bangalore

<sup>4,5</sup>BBD College of Dental Sciences, Lucknow

<sup>6</sup>Oral physician Sri sai Hospital, Moradabad

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### ABSTRACT

Dental caries is a widely prevalent infectious disease afflicting the humans worldwide, second only to the common cold despite knowledge of most advanced sciences and technologies in dental practice. Medicinal plants have been documented for prevention and cure of many systemic diseases since ancient times. The application of natural products for the control of oral diseases is considered as an interesting alternative to synthetic antimicrobials due to their fewer side effects. Hence the search for alternative products continues and natural phyto-chemicals isolated from plants used in traditional medicine are considered as good alternatives to synthetic chemicals. This article brings an insight of known medicinal plants helpful in treatment of dental caries.

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### INTRODUCTION

Despite great improvements in the oral health, oral diseases continue to be a major problem worldwide. These include dental caries, periodontal problems, edentulousness, oromucosal lesions and oropharyngeal cancers. Among these dental caries is steadily rising affecting all age groups in the developing countries as well as developed countries. Dental caries is defined as an irreversible microbial disease of the calcified tissues of the teeth, characterized by demineralization of the inorganic portion and destruction of the organic substance of the tooth, which often leads to cavitation.<sup>1</sup> Formation of dental caries is caused by the colonization and accumulation of oral microorganisms, and adherence is the first step in the colonization process.<sup>2</sup>The primary initial colonizers include Streptococcus species, among which *S. mutans* is predominantly involved followed by Lactobacilli spp and Actinomyces spp. *S. mutans* can synthesize firmly-bound glucan from sucrose by the cooperative actions of glucosyltransferase (GTF) In addition, glucan-binding lectin (GBL), produced by the bacteria, plays an important role in glucan-dependent cell aggregation. A promising approach for the prophylaxis of dental caries is then based on the inhibition

of the *S. mutans* adherence to hydroxyapatite and subsequent colonization of the tooth surface.<sup>3</sup>

Plants and plant products have been successfully used since ages for medical and dental purposes. Sustainable ethnomedicine, for the global community, is perceived as one approach to protect the planetary biodiversity, and subsequently, the global health of the animal and human populations.<sup>4</sup>Epidemiological research reveals that as much as 70–80% or more of the global population uses traditional medicine(TM), with the majority reliant on herbs and plants.<sup>5</sup>

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 immunocompromised individuals and financial considerations in developing countries. Despite several agents being commercially available, these chemicals can alter oral microbiota and have undesirable side-effects such as vomiting, diarrhea and tooth staining.<sup>6</sup>Also bacterial resistance to most of the antibiotics such as cephalosporins, penicillins,

metronidazole, tetracyclines and other derivatives used to cure oral diseases have been well documented.<sup>7</sup>Hence, use of phytotherapy can prove to be an alternative solution to this.

In dentistry, phytomedicine has been used as anti-inflammatory, antibiotic, analgesic, sedative agents and also as endodontic irrigants.<sup>8</sup>The aim of this paper is to review the known medicinal plants helpful in treatment of dental caries. Numerous studies have evaluated the effectiveness of plants and plant products against oral pathogens, while many have emphasized on the ability of plant products to inhibit the formation of dental biofilms by reducing the adhesion of oral pathogens to the tooth surface which is the initial step in the formation of dental plaque leading to progression of dental caries.

### **Antimicrobial Activity of Herbs and Herbal Constituents against Oral Pathogens**

Plants produce the diverse range of bioactive molecules from its different parts such as leaves, stem, latex, bark, root, flower, and seeds, known as secondary metabolites that are involved in defense mechanism against microorganisms. Bioactive molecules found in plants are tannins, alkaloids, saponins, cardiac glycosides, steroids, terpenoids, flavonoids, phenolic compounds, and many more.<sup>9</sup>

**Polyphenols:** Some of the simplest bioactive phytochemicals consist of a single substituted phenolic ring. The mechanisms thought to be responsible for phenolic toxicity to microorganisms include enzyme inhibition by the oxidized compounds, possibly through reaction with sulfhydryl groups or through more nonspecific interactions with the proteins.

**Quinones:** Quinones are aromatic rings with two ketone substitutions. They are ubiquitous in nature and are characteristically highly reactive providing a source of stable free radicals, quinones are known to complex irreversibly with nucleophilic amino acids in proteins, often leading to inactivation of the protein and loss of function. For that reason, the potential range of quinone antimicrobial effects is great.

**Flavons and flavonoids:** Their activity is probably due to their ability to complex with extracellular and soluble proteins and to complex with bacterial cell walls, as described above for quinones. More lipophilic flavonoids may also disrupt microbial membranes. Catechins, the most reduced form of the C3 unit in flavonoid compounds, deserve special mention. These flavonoids have been extensively researched due to their occurrence in oolong green teas. It was noticed some time ago that teas exerted antimicrobial activity and that they contain a mixture of catechin compounds. These compounds inhibited in vitro *Streptococcus mutans*.<sup>10</sup>

*Drosera* species contain physiologically active compounds such as flavonoids, ellagic acid and naphthoquinones. These constituents have been reported to possess antimicrobial and anti-inflammatory properties, which are efficacious in the treatment of oral infectious diseases. A study revealed that the aerial parts of the plant *Drosera peltata* showed broad spectrum activity against numerous bacteria of the oral cavity, with greatest activity against *S. mutans* and *S. sobrinus* (MIC = 31.25 and 15.625 µg/mL, resp.). Plumbagin was identified as the active component of this extract.<sup>11,12</sup>

A study was conducted to screen the antibacterial potential of *Ficus benghalensis* against seven strains of oral bacteria which contained phenols, saponins, alkaloids and flavonoids. The

results revealed that *Ficus benghalensis* showed maximum inhibition for species of *L. rhamnosus*, *S. mutans*, *B. subtilis*, followed by *E. coli*, *S. aureus*, *S. epidermidis*. The minimum inhibitory antibacterial concentration of petroleum ether extracts of *F. benghalensis* was found to be 12.5mg/ml for *E. coli*, 25mg/ml for *S. mutans*, 50mg/ml for *L. rhamnosus* and *S. epidermidis* while for *B. subtilis* and *S. aureus* it is found to be 100mg/ml.<sup>13</sup>

Polyphenols occurring in cocoa, coffee and tea can have a role in the prevention of cariogenic processes, due to their antibacterial action. Cocoa polyphenol pentamers significantly reduce biofilm formation and acid production by *Streptococcus mutans* and *S. sanguinis*. In the same way, trigonelline, caffeine and chlorogenic acid occurring in green and roasted coffee interfere with *S. mutans* adsorption to saliva-coated hydroxyapatite beads. Studies carried out on green, oolong and black tea indicate that tea polyphenols exert an anti-caries effect via an antimicrobial mode-of-action, and galloyl esters of ( )-epicatechin, ( )-epigallocatechin and ( )-gallocatechin show increasing antibacterial activities.<sup>14</sup> Crude ethanol extracts of *Piper cubeba* (*Piperaceae*) exhibited good antimicrobial properties against a range of cariogenic pathogens (MIC = 90–200 µg/mL).<sup>15</sup>

A study was conducted to screen the selected Indian plants for their antibacterial efficacy against four cariogenic bacteria *Lactobacillus acidophilus*, *Lactobacillus casei* (MTCC-1423), *Streptococcus mutans* (MTCC 890) and *Staphylococcus aureus* (MTCC-96). It was seen that Ethyl acetate and hexane extract of *Eucalyptus globules* was found most effective against *L. acidophilus* with MIC value 31 µg/ml and 62 µg/ml, respectively. Ethyl acetate extracts of *Acacia nilotica* and methanolic extract of *E. globules* also exhibited antibacterial activity against *S. mutans* and *L. casei* with MIC value of 50 µg/ml. Qualitative analysis of *E. globules* revealed the presence of alkaloids, terpenoids, phenolic compounds, and cardiac glycosides. Other herbs which showed good anticariogenic properties against *S. mutans*, *L. acidophilus* and *casei* include *Anacardium occidentale*, *Lantanacamera*, *Azadirachta indica*, *Manilkara zapota*, *Punica granatum*, *Carica papaya*, and *Tagetes patula*.<sup>9</sup>

Studies show that mulberry extracts are rich in phytochemicals and have antimicrobial potential against harmful pathogens. In a study kuwanon G was separated from methanolic extract of *M. alba* it showed antimicrobial activity with minimum inhibitory concentration (MICs) of 8.0 µg/mL against *S. mutans*. The study also revealed that at the concentration of 20 µg/mL it totally inactivate *S. mutans* in 1 min and similarly kuwanon G also inhibits the proliferation of *S. sanguis*, and *S. sobrinus*.<sup>16</sup> 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. A methanolic extract of *P. guajava* leaves was shown to exhibit inhibitory activity against two strains of *S. mutans* attributed to the active compound, quercetin-3-O- $\alpha$ -l-arabinopyranoside or guaijaverin, which had MIC values of 2–4 mg/mL. At sub-MIC values, guaijaverin was also able to inhibit acid production of the test bacteria.<sup>6,17</sup>

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<sup>18</sup>

Sugar alcohols: Xylitol is a sugar alcohol naturally found in plants that is used as an artificial sweetener in many foods. 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 18h and determining the optical density of the cultures. *S. 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 that are part of the normal oral flora.<sup>6,19</sup>

### Herbal Extracts Inhibiting the Bacterial Adhesion

Dental biofilm is associated with the initiation and progression of tooth decay and periodontal diseases. It is believed that reducing the mass of mutans streptococci in dental biofilm could lower the incidence of dental caries. The use of anti-adhesion agents that disengage mutans streptococci from the dental biofilm or interfere with their adhesion, without affecting their viability, may prove clinically advantageous, as selective pressure and overgrowth of resistant bacteria would be avoided. Cranberry juice is known to affect urinary tract infections. This effect is mediated by its action as an anti-adhesion agent. The constituent of the juice exhibits anti-coaggregation activity against a variety of oral bacteria. This fraction is highly soluble in water, devoid of proteins, carbohydrates and fatty acids. It strongly affects biofilm formation via a sucrose-dependent mechanism. The effect is mediated by inhibiting the synthesis of the polysaccharides glucan and fructan by immobilized and soluble glucosyltransferase and fructosyltransferase.<sup>20</sup>

Two methods, adherence to glass and adherence to saliva-coated hydroxyapatite (S-HA), were used to assess the effect of ethanol extracts of six plants on the adherence of *S. mutans*. Extracts of *Andrographis paniculata* (Acanthaceae), *Cassia alata* (Leguminosae), *Camellia sinensis*, *Psidium guajava* and *Harrisonia perforata* (Simaroubaceae) were able to inhibit one or both strains of *S. mutans* tested using both methods, although relatively high concentrations were required (MIC<sub>50</sub> values of 3–5 mg/mL). Overall, the active extracts were less effective in inhibiting adherence to S-HA than to glass, suggesting that salivary glycoproteins are important in bacteria-surface interactions, leading to stronger adherence to S-HA. *Camellia sinensis* extract exhibited the greatest inhibition of glucosyltransferase activity while *Andrographis paniculata* extract showed greatest inhibition of glucan-binding lectin activity of both strains.<sup>3,6</sup>

Crude aqueous extracts of Piper betle, a plant which has been used traditionally for the control of oral diseases in South East Asia, have been shown to inhibit the growth, adherence and glucan production of *S. mutans*.<sup>21</sup>

Aqueous and methanol extracts of cloves from *Syzygium aromaticum* (Myrtaceae) were shown to affect the cariogenic properties of *S. mutans*, as exhibited by the ability of the extracts to inhibit adhesion of the bacteria to glass, reduce cell surface hydrophobicity and inhibit the production of glucosyltransferase.<sup>6,22</sup>

**Essential oils (EO):** The antibacterial properties of essential oils are well-known and activity against bacteria found in the oral cavity, including pathogens, has been documented. Indeed, there is evidence that commercial mouthwashes containing essential oils are useful in the long-term control of plaque and mild to moderate gingivitis and are preferred to those containing chlorhexidine for long-term daily use.<sup>6</sup>

A study aimed to evaluate the activity of EO and their fractions against planktonic cells of *S. mutans*, showed that highest activities were observed for *Aloysiagratisissima* (Verbenaceae) and *Alysiatraphylla* (Verbenaceae) (125–250 µg/mL), *Baccharis dracunculifolia* (Asteraceae), *Lippia sidoides* (Verbenaceae), *Mikania glomerata* (Asteraceae), *Siparunaguianensis* (Monimiaceae), *Syzygium aromaticum* (Myrtaceae) (62.5–125 µg/mL), and *Coriandrum sativum* (Apiaceae) (31.2–62.5 µg/mL).<sup>23</sup>

The activity of Tea tree oil (TTO) against an extensive collection of oral bacterial isolates was investigated by Hammer *et al.* who determined MIC and MBC values in the range 0.003–2.0% (v/v). Further, time-kill assays showed that exposure of *S. mutans* and *Lactobacillus rhamnosus* to 0.5% (v/v) TTO resulted in >3 log reduction of viable cells within 30 s. The activity of TTO against oral pathogens was supported in a study involving this and other essential oils, including manuka oil, eucalyptus oil, lavender oil and rosemary oil. In addition to their inhibitory and bactericidal activities, most of the oils were able to inhibit the adhesion of *S. mutans*.<sup>6,24,25</sup>

### CONCLUSION

It is a very common belief worldwide that 'herbal products' are safe. Therefore, people increasingly rely on their medicinal properties for different purposes. 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 preventative or treatment therapies for oral diseases. The literature is scarce with regard to information on the quality, safety and efficacy of herbal plants for use in dentistry. Further studies are needed to investigate the side effects, toxicity and drug interactions of these plants for dental applications.

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