Original Article

Resurgence of Phytomedicine Use in Dentistry

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ABSTRACT

Plaque-related diseases, dental caries and periodontal diseases are among the most important preventable global infectious diseases. In addition to mechanical plaque removal nowadays the phytomedicine use is gaining attention throughout the world. Plants are rich in a wide variety of secondary metabolites, such as tannins, terpenoids, alkaloids, and flavonoids, which have been found to have antimicrobial properties. The phytomedicine, today, symbolize safety, in contrast to the synthetics that are regarded as unsafe to humans and the environment. Plant extracts have been used in dentistry for reducing inflammation, as antiplaque agents, for preventing release of histamine and as antiseptics, antioxidants, antimicrobials, antifungals, antibacterials, antivirals and analgesics. The aim of this paper is to consider the resurgence of phytomedicine use in Dentistry.

Keywords: Phytomedicine, Dentistry, Antimicrobial, Caries, Periodontal diseases.

INTRODUCTION

The mouth provides an ecosystem conducive to the colonization and growth of a diverse range of microorganisms, of which bacteria are the most common and abundant. The largest accumulations of bacteria are found as dental plaque on the tooth surface[1].

Plaque-related diseases, dental caries (dental decay) and periodontal diseases, are probably the most common bacterial diseases occurring in man. Control of dental plaque-related diseases has traditionally relied on non-specific removal of plaque by mechanical means. However, the individual response of the host and other confounding factors can influence disease initiation and progression. Antimicrobial approaches, including the use of antimicrobial agents, represent a valuable complement to mechanical plaque control. However, increasing problems of resistance to synthetic antimicrobials have encouraged the search for alternative natural products[2]. According to the World Health Organization

(WHO), as many as 80% of the world's people depend on traditional medicine (herbal) for their primary healthcare needs. The development of indigenous medicines and the use of medicinal plants carry considerable economic benefits in the treatment of various diseases[3]. In the developed countries, Plants are the source of more than 25% of prescription and over-the-counter preparations[4]. Therefore, the aim of this paper is to consider the emerging trends of plant base therapy in dentistry.

PLANT-BASED THERAPY

Finding healing powers in plants is an ancient idea. People on all continents have long applied poultices and imbibed infusions of hundreds, if not thousands, of indigenous plants, dating back to prehistory[5]. Plant based therapy are staging a comeback and phytomedicine 'resurgence' is happening all over the world.

Plants synthesize a wide range of aromatic substances, the majority being phenols or their oxygen-substituted derivatives. To date thousands of photochemical have been shown to have antimicrobial activity.

Classification of phytochemicals

Useful antimicrobial phytochemicals can be divided into several classes[5]:

Simple phenols and phenolic acids

These consist of a single substituted phenolic ring. Examples include caffeic acid, catechol and pyrogallol. Those phenolic compounds possessing a C3 side chain at a lower level of oxidation and containing no oxygen are classified as essential oils.

Quinones

Aromatic rings with two ketone substitutions. These are responsible for plant pigments. Anthraquinones in particular are recognised for their antimicrobial activity.

Flavones, flavonoids and flavonols

Flavones are phenolic structures containing one carbonyl group. The addition of a 3-hydroxyl group yields a flavonol. Flavonoids are also hydroxylated phenolic substances where the C6-C3 unit is linked to an aromatic ring. This group demonstrates a broad range of antimicrobial activity. For example, catechins as found in green tea.

Tannins and coumarins

Phenolic substances that are polymeric or consisting of fused benzene and pyrone rings respectively.

Terpenoids/essential oils

The essential oil fraction gives fragrance to plants. Such oils are highly enriched in compounds based on an isoprene structure. These are classified as terpenes, and when terpenes contain additional elements, usually oxygen, these are termed terpenoids. Examples of common terpenoids are menthol and camphor (monoterpenoids) and farnesol and artemisin (sesquiterpenoids). Terpenes and terpenoids have a wide spectrum of activity against bacteria, fungi, viruses and protozoa.

Alkaloids

Heterocyclic nitrogen compounds. The diterpenoid nalkaloids have commonly been found to possess antimicrobial properties.

Lectins/antimicrobial peptides

Often positively charged and contain disulphide bridges.

Resurgence of phytomedicine use in dentistry

Mainstream medicine is now being increasingly receptive to the use of antimicrobial and other drugs derived from

plants, as traditional antibiotics become ineffective and as new, particularly viral, diseases are emerging which are intractable to these drugs. Another reason for the renewed interest in plant antimicrobials in the past 20 years has been the rapid rate of (plant) species extinction[6]. This is a common thinking among natural-products chemists and microbiologists that the multitude of potentially useful phytochemical structures which could be synthesized chemically is at risk of being lost irretrievably[7]. Lastly, the human immunodeficiency virus (HIV) has lead to intensive investigation into the plant derivatives which may be effective, especially for use in underdeveloped and developing nations with little access to expensive western medicines.

Use of plant-derived substances in oral care products

Natural antibacterial substances are now attracting attention as useful antimicrobials to be incorporated into various oral health care products. For example, extracts of miswak, tea tree oil, peppermint, green tea and manuka honey have all recently been incorporated into such products to enhance their antimicrobial properties.

Honey (figure 1)

Honey is a viscid and sweet secretion stored in the honey comb by various species of bees, such as: Apis dorsata, Apis florea, Apis indica, Apis mellifica, belonging the natural order Hymenotera (Family: Apideae) using nectar from flowers. Honey has been used to treat infected wounds since as long as 2000 years before bacteria were discovered to be the cause of infection. The antibacterial property of honey was first recognized in 1892 by Van Ketel. Manuka honey from New Zealand is associated with an unidentified phytochemical component. Manuka honey is a monofloral honey obtained from the species *Leptospermum scoparium* and has a long-standing reputation in New Zealand folklore for its antiseptic properties[8]. This contains glucose oxidase which generates hydrogen peroxide in the presence of water. It inhibits the growth of various cariogenic and periodontopathic bacteria.

Green tea (figure 2)

Green tea (Camellia sinensis) regarded for a long time as a health product. Green tea is important source of polyphenol antioxidants. Polyphenols including epigallocatechin 3 gallate (EGCG) constitute the most interesting components in green tea leaves. Green tea has the potential to protect against various malignant, cardiovascular and metabolic diseases. There is a growing body of evidence pointing a beneficial role of green tea and its polyphenols in oral health[9]. It Controls the plaque-related diseases and dental caries. Its extracts have been shown to kill *Str. Mutans* and *Str. sobrinus*. It acts by Inhibiting bacterial adherence, acid production, and glucosyl transferase activity[4].

Essential oils (lavandula, eucalyptus oils, peppermint oil and sage oil) (figure 3)

Lavender oil is extracted from Lavandula angustifolia (also known as Lavandula. officinalis, spica and vera), of the Lamiaceae (Labiatae) family. Eucalyptus essential oil is extracted from Eucalyptus globulus of the Myrtaceae family. Peppermint oil is extracted from Mentha piperita of the Labiatae family. Sage oil is extracted from Salvia officinalis of the Labiatae family. All the oils are bactericidal with the exception of lavandula, inhibit adhesion of *P. gingivalis* and *Str. Mutans*[4]. The clinical efficacy of EO and chlorhexidine rinses in the reduction of plaque and gingivitis has been extensively assessed. Essential oils are less efficient in reducing gingivitis and periodontitis in comparison to chlorhexidine. However, EO does not cause staining, alter taste perception or promote calculus formation, and is not

impaired in terms of efficacy in the presence of toothpaste[10].

Tea tree oil (figure 4)

Tea tree oil (TTO) is derived from the paper bark tea tree (Melaleuca alternifolia of the Myrtaceae family)[11]. TTO has a broad-spectrum antimicrobial, antifungal, antiviral, antioxidant and anti-inflammatory effect[12]. Through various studies it has been concluded that the local delivery of TTO gel in case of chronic periodontitis may have some beneficial effects to augment the results of the conventional periodontal therapy. The TTO group had significant reduction in Gingival Index (GI), Papillary Bleeding Index (PBI). Moreover, it places a focus on the value of monitoring GCF levels of PTX3 as a marker of periodontal tissue healing[12,13].

Chewing sticks (figure 5)

In Asia, Africa, South America, and throughout the Islamic countries, selected plants are used as chewing sticks to maintain good oral health[14]. The World Health Organization has even supported their use as an effective 'tool' for oral hygiene. Chewing sticks are derived from a wide range of plant species, and within an individual stick the active antimicrobial components may be heterogeneous. For example, the active components of the Nigerian chewing stick (*Fagara zanthoxyloides*) have been found to consist of various alkaloids[15]. *Salvadora persica* contains salvadorine and trimethylamine, which are shown to exhibit anti-bacterial effects on cariogenic bacteria such as *Streptococcus mutans*. It has been shown that these active principles support periodontal health[16], reduces the accumulation of biofilm-like dental plaque formation and exhibits fungistatic activity against *Candida albicans*[17].

The plant *Randia uliginosa* belongs to the family Rubiacea. The plant grows in dry deciduous forests, native to Bangladesh, India, Sri Lanka, and Thailand. Bark extracts of "Randia Uliginosa" has also been found effective against oral pathogens including S. aureus Escherichia coli, Lacto bacillus, and Enterococcus fecalis[18]. Goldenseal (Hydrastis Canadensi) has been found to have antimicrobial properties against oral pathogens such as *S. mutans* and *Fusobacterium nucleatum*[19].

Curcuma longa (figure 6)

Turmeric (haldi), a rhizome of Curcuma longa, is a flavourful yellow-orange spice. The active constituents of turmeric are the flavonoid curcumin (diferuloylmethane) and various volatile oils including tumerone, atlantone, and zingiberone. It has several effects like Antioxidant, Anti-inflammatory, Hepatoprotective, Anti-microbial, Anti-mutagenic, and protective effects on the cardiovascular system. It is being used in various consistencies for dental application in the form of *Mouth wash,* Local drug delivery system, Subgingival irrigant, pit and fissure sealant etc. Its role in the treatment of cancers is very promising[20]. Curcumin suppresses the production of interleukin-6 in provetella intermedia lipopolysaccharide-activated raw 264.7 cells and inhibits the growth and acid production of S. mutans at concentrations from 0.5 to 4 mg/ml[21,22].

Aloe vera (figure 7)

Aloe vera is a medicinal plant with anti-inflammatory, antimicrobial, antidiabetic and immune-boosting properties. The gel consists of 98-99% water and the remaining 1-2% contains the active compounds, including aloesin, aloin, aloe-emodin, aloemannan, acemannan, aloeride, naftoquinones, methylchromones, flavonoids, saponin, sterols, amino acids and vitamins. Fani M *et al*[23] investigated the Inhibitory activity of Aloe vera gel on some clinically isolated cariogenic and periodontopathic bacteria. They found that S. mutans was the

species most sensitive to Aloe vera gel with a MIC of 12.5µg/ml, while A. actinomycetemcomitans, P. gingivalis, and B. fragilis were less sensitive, with a MIC of 25-50 µg/ml ($P < 0.01$). It was concluded that Aloe vera gel at optimum concentration could be used as an antiseptic for prevention of dental caries and periodontal diseases. In another study it was found that toothpaste containing aloe vera showed significant improvement in gingival and plaque index scores as well as microbiologic counts compared which was comparable to those achieved with toothpaste containing triclosan[24].

Triphala (figure 8)

Triphala has been used in Ayurveda from time immemorial and has many potential systemic benefits. It is the combination of ripe, healthy and dried fruits in equal quantities of Amalaki (Emblica officinalis), Haritaki (Terminalia Chebula), Vibhitaki (Terminalia Belerica). Much revered in Ayurveda, triphala has been proven to have antibacterial, antiviral, antifungal actions[25]. Bajaj N *et al* concluded that 0.6% *Triphala* have an inhibitory effect on plaque, gingivitis, and growth of *Streptococcus mutans* and Lactobacillus[26]. Studies done by Maurya *et al* and Jagtap AG *et al* supported the use of *Triphala* for the cure of periodontal diseases and dental caries[27,28].

Azadirachta indica (meliaceae) (figure 9)

Azadirachta indica (neem), a Meliaceae family tree, has been used in India for several decades for the treatment of several diseases in dentistry. Neem leaves have been used in the treatment of gingivitis and periodontitis. The possible mechanism of anti inflammatory action of neem is by inhibiting prostaglandin E and 5 HT and thus reducing the inflammation. The antibacterial action can be explained by "Azadiachtin" that is known to destroy bacterial cell wall and thus inevitably inhibit the growth of bacteria[29], also the breakdown of cell wall disturb osmotic pressure and leads to cell death. The studies done by Botelho *et al*[30] and Chatterjee A *et al*[31] reported that *A. indica* based mouth rinse is highly efficacious and the results demonstrated a significant reduction of gingival, bleeding, and plaque indices. Patel and Ventakrishna (1988) reported a significant reduction in probing depth and gain in clinical attachment level by its use. Therefore it may be used as an alternative therapy in the treatment of dental disease[32].

Newbouldia laevis (figure 10)

An extract which was made from the leaves of the tree, Newbouldia laevis (a medium sized angiosperm of the Bignoniaceae family) was tested as a bactericide for the bacteria which were implicated in dental caries and it was found that Newbouldia laevis had a bactericidal action against Streptococci mutans and Lactobacilli[33].

Hydroalcoholic extract (HAE) of pomegranate, Punica granatum (Punicaceae) (figure 11)

The pomegranate mouthrinse has an antiplaque effect. Pomegranate extract has been found to be efficacious against Aggregatibacter actinomycetemcomitans (A.a.), Porphyromonas gingivalis (P.g.), and Prevotella intermedia (P. i.). Strains *in vitro*[34]. In another study Punica granatum (pomegranate) extract was found to be very effective against dental plaque micro organisms, decreasing the CFU/ml by 84% (CFU x 10(5)), before mouth-rinse: 154.0 +/- 41.18; after mouthrinse: 25.4 +/- 7.76)[35].

Side effects and safety issues related to phytomedicines used in dentistry

The 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 evaluated. Some adverse effects like dematitis, hyper sensitivity, cardiovascular toxicities and pulmonary toxicities[36] have been reported in some studies (Table 1). Given the possibility of adverse interactions between phytomedicine formulations with conventional drugs, caution should be implemented when using phytomedicines and the need for more clinical studies is recommended.

CONCLUSION

The use of plant based therapy continues to increase hastily across the world. Many people take phytomedicines now for their health care in different national health care settings. 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 used as preventative or treatment therapies for oral diseases in various consistencies. While it is encouraging to see a number of clinical trials of such products, further studies of the side effects and efficacy of these agents will be important to establish their therapeutic benefits, either alone or in combination with conventional therapies, that can help to reduce the total burden of oral diseases universally. Therefore these can be considered as wonder plants to heal the suffering humanity.

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Table 1. Side effects and toxicities of some phytomedicines

Phytomedicine	Side effects
Green tea[37]	Restlessness, irritability, sleeping problems, tremor, heart palpitations, loss of appetite, upset stomach, nausea, frequent urination, and skin rash.
Curcuma longa[38]	Nausea and diarrhoea. When applied to the skin, turmeric can cause irritation and allergic contact dermatitis reactions.
Azadirachta indica[39]	Dermatitis
Aloe vera[40,41]	Allergic contact dermatitis, oral mucositis
Phytomedicine	**Toxicities**
Jin bu huan poisoning[42]	Bradycardia
Ginkgo Bilbo[43]	Epileptic seizures
Melaleuca alternifolia (Myrtaceae)[44-46]	Ataxia, unresponsiveness, drowsiness, hypersensitivity reactions and allergic contact dermatitis

Figure 1. Honey

Figure 2. Green tea

(a)

(b)

(c)

(d)

Figure 3. Essential oils (a) lavandula (b) eucalyptus oils (c) peppermint oil and (d) sage oil

Figure 4. Honey

(a)

(b)

(c)

(d)

Figure 5. Chewing sticks (a) Nigerian chewing stick (b) *Salvadora persica* (c) *Randia uliginosa* (d) Goldenseal

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Figure 6. Curcuma longa

Figure 7. Aloe vera

Figure 8. Triphala

Figure 9. *Azadirachta indica* (Meliaceae)

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Figure 10. Newbouldia laevis

Figure 11. Pomegranate, *Punica granatum* (Punicaceae)