

Phytotherapeutic Agents - A Refreshing Approach To Periodontal Therapy

Abstract

There is a long and venerable history of the use of herbs to improve dental health and promote oral hygiene. Plants contain phytochemicals such as alkaloids, tannins, essential oils and flavonoids which have pronounced antimicrobial activity and has been used as anti-inflammatory, antibiotic, analgesic and sedative agents. Plants have also been incorporated into dentifrices and have been used to provide natural chewing gums for oral hygiene, to treat toothache, gingivitis and periodontal disease. Phytotherapy has a potentially valuable role as an adjunct for the management of gingival and periodontal disease. Therefore, purpose of this review is to present some recent examples from the literature of studies that have served to validate the traditional use of medicinal plants with specific biological activity. In particular, 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 will be discussed subsequently. Clinical studies that have investigated the safety and efficacy of such plant-derived medicines will also be described.

Key Words

phytonutrients, periodontal therapy, phytochemicals, herbs

Introduction

As the scientific community is seeking alternatives to conventional treatment, periodontal researchers have found that phytotherapeutic agents are advantageous for suppressing bacteria that lead to periodontal diseases. So, there is a pronounced interest in the development of phytotherapeutic agents for the periodontal needs and therapy.

The word "phytotherapy" is a Latin term. The latin prefix phyto stands for plant and is called phuton in Greek (previously, phuto). Therapy comes from the Latin word therapia, originally from Greek therapeia, from therapeuein which means to treat medically. In other words "phytotherapy", means treatment with herbal medicine. Phytotherapy mainly refers to use of medicinal plants or herbs to prevent or cure diseases or to improve health conditions.

Historical Background

Plants (herbs) and naturally derived products from plants (herbal supplements) have been used to treat health ailments and have been relied upon since the beginning of recorded human history. One of the oldest surviving medical document, the Egyptian Ebers Papyrus, dated around 1550 BC, contains herbal remedies for over 876 illnesses. Hippocrates, the "Father of Medicine", in his writings

contains references to over 250 medicinal plants and herbs. The scientific evidence-based literature also supports the efficacy and safety of numerous herbs today (Cohan and Jacobsen, 2000).^[1]

Phytotherapy relies more on phytonutrients with the discovery that many plant food components can not only modify physiological function but also aid in medical practices such as drug delivery. Also, several plants and plant parts have anti-inflammatory, antioxidant, antibacterial, astringent and other useful properties.^[2]

Hence, this article is aimed at highlighting the properties of plants and plant derived products that can be used in the periodontal therapy.

Aloevera

The Aloe vera that belongs to a Liliaceae family has been used for centuries for its medicinal and skin care properties. "Alloeh" meaning shining bitter substance, while "vera" in Latin means true. The Greek scientists regarded Aloe vera as the universal panacea.^[3] The aloevera leaf consists of two different parts: central mucilaginous and peripheral bundle sheath cells. The parenchymal makes up the inner portion of the aloe leaves and produces a clear, thin tasteless jelly like material called Aloe vera gel.^[4] Aloe vera contains 75 potentially active constituents: vitamins,

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enzymes, minerals, sugars, lignins, saponins, salicylic acids and amino acids.^[5] Aloe vera is a potent anti-inflammatory agent and inhibits the cyclooxygenase pathway and reduces prostaglandin E2 production from arachidonic acid.^[1] Aloe vera molecule synergizes with plant growth factors to repair and produce growth causing inhibition of pain and inflammation, stimulation of fibroblasts to functionally produce collagen & proteoglycans which increases wound tensile strength. It has proven its efficacy as anti-inflammatory, antiviral, antibacterial and antioxidative and enhancing defence mechanisms increasing its use as a herbal remedy in periodontal disease and other oral conditions.

Green Tea

Green tea is one of the most popularly consumed beverage worldwide contains a number of bioactive chemicals and is particularly rich in flavonoids and also contains carotenoids, tocopherols, ascorbic acid (Vitamin C), minerals such as Cr, Mn, Se or Zn, and certain phytochemical compounds.^{[6],[7]} Its healthful properties are largely attributed to polyphenols, chemicals with potent antioxidant properties. The antioxidant

effects of polyphenols appear to be greater than those of vitamin C. Polyphenols contained in teas are classified as catechins. Green tea contains six primary catechin compounds: catechin, gallacatechin, epicatechin, epigallocatechin, epicatechin gallate (EGCg), and epigallocatechin gallate (EGCg). EGCg is the most studied polyphenol component in green tea. The scavenging capacity of catechin and epicatechin molecules depends on their hydrogen donating ability. It is demonstrated that polyphenols have inhibitory effect on the ROS generation as well as on the release of lysosomal enzymes.^[6] Numerous studies in a variety of experimental animal models have demonstrated that catechin possess antioxidant, antimutagenic, antidiabetic, anti-inflammatory, antibacterial and antiviral, and above all, cancer-preventive properties.^{[6],[7],[8]}

Curcumin

Turmeric is a spice that contains the polyphenol curcumin in its rhizome. Turmeric is comprised of a group of three curcuminoids: curcumin (diferuloylmethane), demethoxycurcumin, and bisdemethoxycurcumin as well as volatile oils (tumerone, atlantone, and zingiberone), sugars, proteins, and resins. Curcumin modulates the inflammatory response by down-regulating the activity of cyclooxygenase-2 (COX-2), lipoxygenase, and inducible nitric oxide synthase (iNOS) enzymes; inhibits the production of the inflammatory cytokines tumor necrosis factor-alpha (TNF- α), interleukin (IL) 1, 2, 6, 8, and 12, monocyte chemoattractant protein (MCP), and migration inhibitory protein; and down-regulates mitogen-activated and Janus kinases.^{[9],[10]} In addition to inhibiting lipid peroxidation, curcumin demonstrates free radical-scavenging activity. Curcumin's reported properties include anti-inflammatory,^{[11],[12]} antioxidant,^[13] anti-bacterial,^[14] and wound healing properties^{[15],[16]} are desirable assets, which validate its use in the treatment of periodontitis.

Chamomile

M. chamomilla L. and *M. suaveolens* L.), of the Asteraceae family, is one of the tea ingredients most used worldwide. The whole plant is odoriferous and of value, but the quality is chiefly centred in the

flower-heads or capitula, the part employed medicinally. The essential oil contains a-bisabolol (up to 50%) chamazulene cyclic sesquiterpenes,^{[17],[18]} which directly reduce inflammation and are mild antibacterials. Also, it contains bisabolol oxides, farnesene and spiro-ether, which have anti-inflammatory and antispasmodic actions. It has been used for centuries, particularly because of its anti-inflammatory, antimicrobial, antispasmodic and sedative effects.^[20] The principal chemical components of the flowers include several phenolic compounds, primarily the flavonoids apigenin, quercetin, patuletin, luteolin and their glucosides. The main components of the essential oil extracted from the flowers are the terpenoids alpha-bisabolol and its oxides and azulenes, including chamazulene.^{[21],[22],[23],[24],[25]}

Cranberry

Cranberry (*Vaccinium macrocarpon*) is a shrub that grows in the peat bogs of cold regions of northeastern North America. Cranberry extracts are particularly rich in polyphenols,^[26] including flavanoids, which have biological properties that can be beneficial to human health. Cranberries were also used to "clear the blood", and as treatment for stomach ailments, liver problems, gall bladder disease, vomiting, appetite loss and scurvy.^[27] Eastern Europeans adopted cranberry as a cancer remedy and antipyretic. Cranberry contains discrete flavonoids called condensed tannins, or proanthocyanidins (PACs), that exhibit unique microbial antiadhesion properties. Numerous studies have found that these PACs block uropathogenic bacteria from adhering to the uroepithelium and proliferating^{[28],[29],[30]}. New evidence also suggests this same antiadhesion activity may also be helpful in the prevention of certain ulcers and periodontal disease.^[31]

Punica Granatum

The pomegranate, *Punica granatum* L., an ancient, mystical, and highly distinctive fruit, is the predominant member of two species comprising the Punicaceae family. The pomegranate is native from the Himalayas in northern India to Iran but has been cultivated and naturalized since ancient times over the entire Mediterranean region. Pomegranate is used in several systems of medicine for a variety of ailments. In

Ayurvedic medicine the pomegranate is considered "a pharmacy unto itself" and is used as an antiparasitic agent,^[32] a "blood tonic,"^[33] and to heal aphthae, diarrhea, and ulcers.^[34] Pomegranate also serves as a remedy for diabetes in the Unani system of medicine practiced in the Middle East and India.^[35]

Current research seems to indicate the most therapeutically beneficial pomegranate constituents are ellagic acid ellagitannins (including punicalagins), punicic acid, flavonoids, anthocyanidins, anthocyanins, and estrogenic flavonols and flavones.^{[36],[37],[38],[39],[40]}

An in vitro assay using four separate testing methods demonstrated pomegranate juice and seed extracts have 2-3 times the antioxidant capacity of either red wine or green tea.^[41]

Pomegranate extracts have been shown to scavenge free radicals and decrease macrophage oxidative stress and lipid peroxidation in animals^[42] and increase plasma antioxidant capacity in elderly humans.^[43] Cold pressed pomegranate seed oil has been shown to inhibit both cyclooxygenase and lipoxygenase enzymes in vitro.^[38]

Numerous in vitro studies^{[44],[45]} and two human trials demonstrate the antimicrobial activity of pomegranate extracts. The growth of *Staphylococcus aureus*, *Streptococcus pyogenes*, *Diplococcus pneumoniae*, *Escherichia coli* O157:H7, and *Candida albicans* was inhibited via direct bacteriocidal or fungicidal activity.

Morinda Citrifolia

Morinda citrifolia is one of the traditional folk medicinal plants in Polynesia, and Southeast Asia, also known as noni. The major components of the whole noni plant have been found such as scopoletin, octoanoic acid, potassium, ascorbic acid (vitamin C), terpenoids, alkaloids, anthraquinones, β -sitosterol, carotene, retinoic acid (vitamin A), flavone glycosides, linoleic acid and amino acids, including calcium and phosphorus.^{[46],[47]}

Noni has been reported for a broad range of usage including antibacterial, antiviral, antifungal, antitumor, antihelmin, analgesic, hypotensive, anti-inflammatory, and immune enhancing effects.^{[46],[48],[49],[50]}

The primary usage of noni is to apply leaves as a traditional topical treatment thought to enhance wound healing. Noni leaf extract was capable of promoting

Plant	Properties And Applications	References
Aloevera	<ul style="list-style-type: none"> Local Drug Delivery System In Periodontal Pockets Inhibit Periodontopathic Bacteria 	<ul style="list-style-type: none"> Bhat G et al (2011)[56] Fani M and Kohanteb J (2012) [57]
Green Tea	<ul style="list-style-type: none"> Local Delivery Along With Srp In Chronic Periodontitis Reduces Aerobic Mouth Bacterial Load, Prevents Plaque Formation On Teeth And Overcomes Halitosis Helpful In Treatment Of Periodontal Disease. 	<ul style="list-style-type: none"> Kudva P et al (2011)[58] Moghbel A et al (2011)[59] Venkateswara B et al (2011) [60]
Curcumin	<ul style="list-style-type: none"> Effect Of Epidermal Growth Factor (Egf) On Urokinase-type Plasminogen Activator (Upa) Expression In Primary Cultures Of Human Gingival Fibroblasts. Subgingival Irrigation Reduces Bleeding On Probing And Redness And Pocket Probing Depth 	<ul style="list-style-type: none"> Smith PC et al (2004)[61] Suhag A et al (2007)[62]
Chamomile	<ul style="list-style-type: none"> Promotes Faster Wound Healing Process Stimulated Re-epithelialization And The Formation Of Collagen Fibers Lowers Both Plaque And Gingival Scores Significantly 	<ul style="list-style-type: none"> Martins MD et al (2009)[63] Duarte CM et al (2011)[64] Pourabbas R et al (2005)[65]
Cranberry	<ul style="list-style-type: none"> Inhibits Lps-induced Il-6, Il-8, And Pge2 Responses Of Gingival Fibroblasts And Fibroblast Intracellular Signaling Proteins Inhibits Synergistic Biofilm Formation By P. Gingivalis And Fusobacterium Nucleatum Significantly 	<ul style="list-style-type: none"> Bodet C et al (2007)[66] Yamanaka A et al (2007)[67]
Punica Granatum	<ul style="list-style-type: none"> Antibacterial And Antifungal Activities Against Oral Pathogens Anti Bacterial Properties Against Periopathogens And Antiplaque Effect Significantly Improves Clinical Signs Of Chronic Periodontitis And Lower Il-1beta And Il-6 Level 	<ul style="list-style-type: none"> Abdollahzadeh et al (2011)[68] Bhadbhade S J et al (2011)[69] Sastravaha Get al (2005)[70]
Morinda Citrifolia	<ul style="list-style-type: none"> Inhibition Of Cytokines, Such As Cox-2, Tnf-α, Il-1α (A), Il-8 And Il-6 [25,28] And Receptor Antagonism Of Bradykinin Promotes Re- Epithelialisation Inhibit Inflammatory Signalling Molecules Such As Pge2, Il-1β And Tnf-α. Inhibits Activity Of Metalloproteinases Enhances In Vitro Osteogenic Differentiation And Matrix Mineralization By Human Periodontal Ligament Cells 	<ul style="list-style-type: none"> Kim et al (2004)[71] Hirazumi H et al (1996)[72] Basar S et al (2009)[73] Xu J et al (2006)[74] Boonantanasarn et al (2012)[75]
Miswak	<ul style="list-style-type: none"> Improves Periodontal Status Reduces Level Of Subgingival Microbiota Antimicrobial Activity As Mouthwash 	<ul style="list-style-type: none"> Darout I A et al (2000)[76] Al-Otaibi M et al (2004)[77] Almas K et al (2005)[78]
Triphala	<ul style="list-style-type: none"> Effective Anti-plaque Agent Inhibitory Effect On Microbial Counts Relieves Signs And Symptoms Of Periodontal Disease 	<ul style="list-style-type: none"> Thomas B et al (2011)[79] Bajaj N et al (2011)[80] Maurya DK et al (1997)[81] Desai A et al (2010)[82]

wound healing in an animal model.^[51] In addition, the crude extract of noni leaf has been traditionally used in patients with bone fractures or dislocation to promote tissue repair and decrease inflammation.^[46] It is well established that bone and periodontal tissue repair or regeneration requires growth factors to induce progenitor/precursor cells to differentiate and produce matrix mineralization.^[52]

Miswak

Pencil-sized sticks of various plants are fashioned from certain plant - parts and are chewed on one end until they become frayed into a brush. The brush-end is used to clean the teeth in a manner similar to the use of a toothbrush. When used in this manner, they are commonly referred to as chewing sticks or Miswak. The conventional meaning of Miswak is 'stick used on teeth and gums to clean them.' Farooqi et al(1968)^[53] isolated benzyloisothiocyanate from *Salvadora persica* root, they claimed to have found saponins along with tannins, silica, a small amount of resin, trimethylamine, a fairly large amount of alkaloidal constituents, B-sitosterol, m-anisic acid, salvadoura

[1,3-Bis-(3-methoxy-benzyl)-urea] and a high content of minerals in the root: 27.06%.

Triphala

Triphala is a tridoshic formula of fruits of *Terminalia belerica* (Family: Combretaceae), *Terminalia chebula* (Family: Combretaceae) and *Embllica officinalis* (Family: Euphorbiaceae). It is considered a nourishing, balancing and rejuvenating formula that helps the body to detoxify and supports the digestive action. Its phytochemical constituents are tannin, gallic acid, chebulagic acid, ellagic acid, phenols, glycosides and flavonoids. Conditions for which Triphala is employed include headache, dyspepsia, constipation, liver conditions, ascites and leucorrhoea. It is also used as a blood purifier that can improve the mental faculties and it possesses anti-inflammatory, analgesic, anti-arthritis, hypoglycemic and anti-aging properties.^{[54],[55]}

Summary & Conclusion

Phytotherapy, the most ancient medication, is still useful today. Some

unstudied plants may still have hidden secrets for the medical world. However, concerns from scientists, professionals and customers continuously arise, due to increases in the use of phytochemicals. Quality, safety, long-term adverse effects and toxicity are the primary concerns. The scientific evidence supporting their use requires closer scrutiny and expansion before it can be fully accepted as part of everyday practice. Even though not every traditional custom has been scientifically validated, they need not be summarily dismissed as quackery. Proponents of both modern and traditional medicine need to shed long-held beliefs and accept existing evidence before such practices can be truly integrated into present-day periodontal therapy.

As demonstrated by the examples included in this Literature 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 treatment therapies for oral diseases. While it is encouraging to see a number of clinical trials of such products,

further studies of the safety and efficacy of these agents will be important to establish whether they offer therapeutic benefits, either alone or in combination with conventional therapies, that can help to reduce the overall burden of oral diseases worldwide.

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