Herboceutics: a new direction in periodontics: A review

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Abstract
Herbal medicine is both promotive and preventive in its approach and is a common form of alternative therapy throughout the world. Consequently, Herbal medicines are finding their more and more usefulness in the arena of dentistry and their armamentarium. Natural herbs like triphala, tulsipatra, jyestiamadh, neem, clove oil, pudina, ajwain and many more are used either as whole single herb or in combination and havebeen scientifically proven to be safe and effective medicine against various oral health problems like bleeding gums, halitosis, mouth ulcers and preventing tooth decay. The major strength of these natural herbs is that their use has not been reported with any side effects till date. This paper is aimed at reviewing, various herbal extracts and their effects on periodontal diseases.

Keywords: Herbal medication, Herbal dentistry, Mouthwashes, Periodontal, Dentistry

Introduction
Herbal medications in both prophylaxis and treatment of various diseases turned to be a popular form of therapy throughout the world. Many side effects associated with traditional medicines have been averted by using herbal medicines and thus they are safer to use.

By definition, **'traditional'** use of herbal medicines implies substantial historical use. In many developing countries, a large proportion of the population relies on traditional practitioners and their armamentarium of medicinal plants in order to meet health care needs.(1)

Among Europeans living in the New World, the use of botanicals was a reaction against invasive or toxic mainstream medicinal practices of the day. During the Dark Ages, the Arab world continued to excavate their own older works and to build upon them. Of course, Asian cultures were also busy compiling their own pharmacopoeia. In the West, the Renaissance years saw a revival of ancient medicine, which was built largely on plant medicinals.(2)

Mouth rinses have been used for centuries for medicinal and cosmetic purposes, but it is only in recent years that the rationale behind the use of chemical ingredients has been subject to scientific research and clinical trials. Apart from this, all herbal mouth rinses do not contain alcohol and/or sugar, two of the most common ingredients found in most other over-the-counter products. The problem of these ingredients is that the microorganisms that cause bad breath and halitosis feed on these ingredients, and release by products that cause halitosis. Thus, by use of a herbal mouth rinse, we can avoid these ingredients, which itself is one step forward towards better oral hygiene and better health.(3)

Although many popular herbal products have helped to control dental plaque and gingivitis, they have been used for a short time and only as an adjunct to other oral hygiene measures such as brushing and flossing. Various herbal products and their extracts such as Guava, Pomegranate, Neem, Propolis, Tulsi, Green Tea, Cranberry, Grapefruit etc., have shown significant advantages over the chemical ones. Natural mouth washes may offer significant advantages over the chemical ones. If such mouthwashes can be formulated which can be easily prepared and used safely by people at home using natural products, it may lead to improvement in the general dental health of the population.(4)

Major Groups of Antimicrobial Compounds from Plants
Plants have an almost limitless ability to synthesize aromatic substances, most of which are phenols or their oxygen-substituted derivatives. Some, such as terpenoids, give plants their odors; others (quinones and tannins) are responsible for plant pigment.5

I. Phenolics and polyphenols
i. Simple phenols and Phenolic acids
Some of the simplest bioactive phytochemicals consist of a single substituted **phenolic ring. Cinnamic and caffeic acids** are common representatives of a wide group of **phenylpropane**-derived compounds which are in the highest oxidation state **(Fig. 1)Catechol and pyrogallol both are hydroxylated phenols**, shown to be toxic to microorganisms. **Catechol has two−H groups, and pyrogallol**has three.(5) In addition, some authors have found that more highly oxidized phenols are more inhibitory.(6) The mechanisms thought to be responsible for phenolic toxicity to microorganisms include enzyme inhibition by the oxidized compounds.(7)

II. Quinone
Quinones are aromatic rings with **two ketone** substitutions.**(Fig. 1)**They are ubiquitous in nature and are characteristically highly reactive. These compounds, being colored, are responsible for the browning reaction

in cut or injured and melanin synthesis pathway in human skin.[8] The switch between **diphenol (or hydroquinone)** and **diketone (or quinone)** occurs easily through oxidation and reduction reactions. Hydroxylated amino acids may be made into quinones in the presence of suitable enzymes, such as a polyphenoloxidase.[9] The reaction for the conversion of tyrosine to quinone is shown in **Fig. 2.**

In addition to 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.[10]

III. Flavones, Flavonoids, and Flavonols

Flavones are phenolic structures containing one carbonyl group (as opposed to the two carbonyls in quinones). The addition of a **3-hydroxyl group** yields a flavonol. **Flavonoids**[11] are also hydroxylated phenolic substances but occur as a **C_6-C_3**unit linked to an aromatic ring. Since they are known to be synthesized by plants in response to microbial infection[12] and havebeen found in vitro to be effective antimicrobial substances against a wide array of microorganisms. More lipophilic flavonoids may also disrupt microbial membranes.

Flavonoid compounds exhibit inhibitory effects against multiple viruses. Numerous studies have documented the effectiveness of flavonoids such as **swertifrancheside,**[13] **glycyrrhizin** and **chrysin** against HIV. More than one study has found that flavone derivatives are inhibitory to **respiratory syncytial virus (RSV).**

IV. Tannins

"Tannin" is a general descriptive name for a group of polymeric phenolic substances capable of tanning leather or precipitating **gelatin** from solution, a property known as **astringency**. Their molecular weights range from 500 to 3,000[14] and they are found in almost every plant part. They are divided into two groups, **hydrolysable** and condensed **tannins.** Hydrolyzable tannins are based on gallic acid, usually as multiple esters with d-glucose, while the more numerous condensed tannins (often called **proanthocyanidins)** are derived from flavonoid monomers **(Fig. 1).** Tannins may be formed by condensations of flavan derivatives which have been transported to woody tissues of plants. Alternatively, tannins may be formed by polymerization of quinone units.[9]

V. Coumarins

Coumarins are phenolic substances made of fused **benzene and α-pyrone rings**. They are responsible for the characteristic odor of hay. Their fame has come mainly from their antithrombotic, anti-inflammatory, and vasodilatory activities. **Warfarin** is a particularly well-known coumarin which is used both as an oral anticoagulant and, interestingly, as a rodenticide.[15]It may also have antiviral effects. **Coumarins** have been found to stimulate macrophages, which could have an indirect negative effect on infections. More specifically, coumarin has been used to prevent recurrences of cold sores caused by HSV-1 in humans.

VI. Terpenoids

The fragrance of plants is carried in the so called **quintaessentia**, or essential oil fraction. These oils are secondary metabolites that are highly enriched in compounds based on an isoprene structure **(Fig. 2)** They are called **terpenes**, their general chemical structure is $C_{10}H_{16}$, and they occur as **diterpenes, triterpenes, and tetraterpenes (C_{20}, C_{30}, and C_{40}),** as well as **hemiterpenes (C_5) and sesquiterpenes (C_{15}).** When the compounds contain additional elements, usually oxygen, they are termed **terpenoids.**

Terpenenes or terpenoids are active against bacteria, fungi, viruses, and protozoa. In 1977, it was reported that 60% of essential oil derivatives examined to date were inhibitory to fungi while 30% inhibited bacteria.[16] The triterpenoidbetulinic acid is just one of several terpenoids which have been shown to inhibit HIV. The mechanism of action of terpenes is not fully understood but is speculated to involve membrane disruption by the lipophilic compounds.

VII. Alkaloids

Heterocyclic nitrogen compounds are called **alkaloids**. The first medically useful example of an alkaloid was **morphine**, isolated in 1805 from the Greek word Morpheus the **God of Dreams**. Codeine and heroin are both derivatives of morphine. **Solamargine**, a glycoalkaloid from the berries of **Solanumkhasianum**, and other alkaloids may be useful against HIV infection as well as intestinal infections associated with AIDS.[17] While alkaloids have been found to have microbiocidal effects. **Berberine** is an important representative of the alkaloid group.

VIII. Polypeptides

Peptides which are inhibitory to microorganisms were first reported in 1942. They are often positively charged and contain disulfide bonds. Their mechanism of action may be the formation of ion channels in the microbial membrane or competitive inhibition of adhesion of microbial proteins to host polysaccharide receptors.[18]

Mixtures

The chewing stick is widely used in African countries as an oral hygiene aid (in place of a toothbrush).[19] Chewing sticks come from different species of plants, and within one stick the chemically active component may be heterogeneous. Crude extracts of one species used for this purpose, **Serindeiawerneckei,** inhibited the periodontal pathogens **Porphyromonas gingivalis and Bacteroides melaninogenicus** in-vitro.[20]

Experimental Approaches

Extraction Methods

Water is almost universally the solvent used to extract activity of the desired herbal products. Dried plant parts can be added to oils or petroleum jelly and applied externally.[21] Initial screenings of plants for possible antimicrobial activities typically begin by using crude aqueous or alcohol extractions and can be followed by various organic extraction methods. Since nearly all of the identified components from plants active against microorganisms are **aromatic** or **saturated** organic compounds, they are most often obtained through initial ethanol or methanol extraction.[22] (**Table 1)** lists examples of extraction solvents and the resultant active fractions reported in recent studies.

Table 1: Solvents used for active component extraction

Water	Ethanol	Methanol	Chloroform	Dichloromethanol	Ether	Acetone
Anthocyanins	Tannins	Anthocyanins	Terpenoids	Terpenoids	Alkaloids	Flavonols
Starches	Polyphenols	Terpenoids	Flavonoids		Terpenoids	
Tannins	**Polyacetylenes**	Saponins			**Coumarins**	
Saponins	Flavonol	Tannins			**Fatty acids**	
Terpenoids	Terpenoids	**Xanthoxyllines**				
Polypeptides	**Sterols**	**Totarol**				
Lectins	Alkaloids, **Propolis**	**Quassinoids, Lactones,** Flavones, **Phenones** Polyphenols				

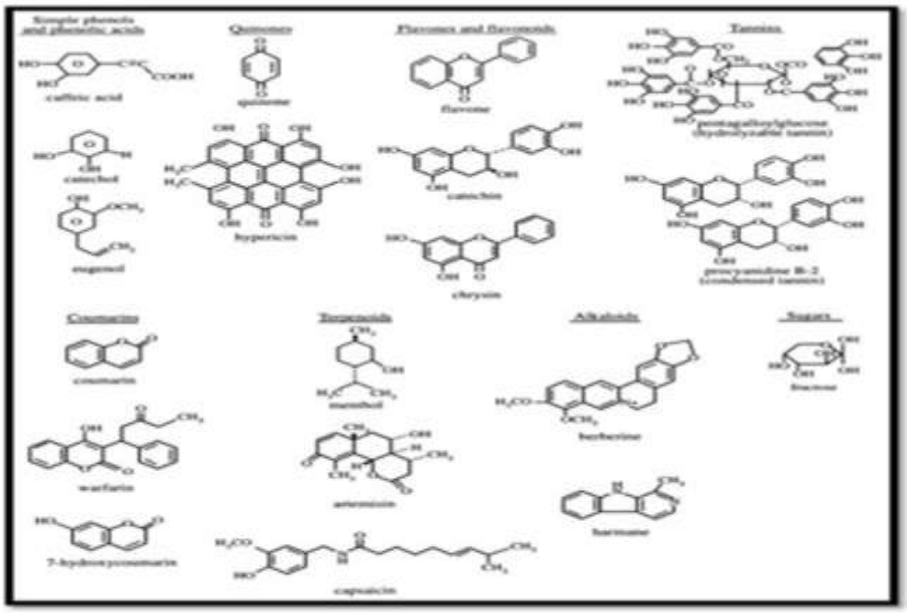

Figure 1 Structures of common antimicrobial plant chemicals

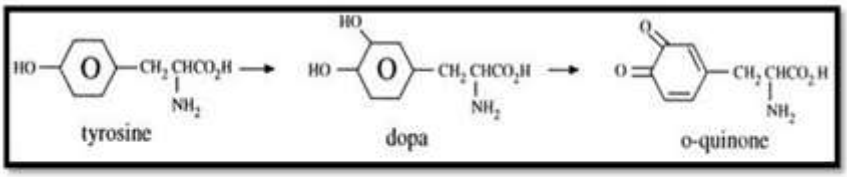

Figure 2
Reaction for the conversion of tyrosine to quinine

Efficacy

In-vitro experiments

i. Bacteria and fungi

Initial screening of potential antibacterial and antifungal compounds from plants may be performed with pure substances or crude extracts.[23] The methods used for the two types of organisms are similar. The two most commonly used screens to determine antimicrobial susceptibility are the broth dilution assay and the disc or agar well diffusion assay. Adaptations such as the agar overlay method may also be used.[24] In some cases, the inoculated plates or tubes are exposed to UV light to screen for the presence of light-sensitizing photochemicals. Other variations of these methods are also used.

ii. Viruses

Several methods are available to detect either virucidal or inhibitory (antiviral) plant activity. Viral replication may be assayed by detection of viral products such as DNA, RNA, or polypeptides. **Vlietinck and Vanden Berghe**[25] have noted that the methods for assaying antiviral substances used in various laboratories are not standardized, and therefore the results are often not comparable their activity is overlooked in screening procedures for antibacterial and antifungal substances.

iii. Protozoa and Helminths

Screening plant extracts for activity against protozoa and helminths can be more complicated than screening for activity against bacteria, fungi, or viruses. **Freiburghaus et al in 1996**[26] used two methods to assay compounds for effectiveness against **Trypanosomabrucei.** These authors also used a fluorescence assay of trypanosome viability in microtiter wells.

In-vivo testing of phytochemicals

Clinical Trials in Humans

Of course, plants have been used for centuries to treat infections and other illnesses in humans, but controlled clinical studies are scarce. A cross-sectional epidemiological study (not a randomized trial) of the effectiveness of chewing sticks versus toothbrushes in promoting oral hygiene was conducted in West Africa. The study's authors found a reduced effectiveness in chewing-stick users compared to toothbrush users and concluded that the antimicrobial chemicals known to be present in the sticks added no oral health benefit.[19] Also, regarding oral health, mouth rinses containing various antimicrobials have been evaluated in humans. Mouth rinses containing phytochemicals were not found to be as effective in decreasing plaque or clinical gingivitis as were Listerine or chlorhexidine.

Various Herbal Agents Used As Mouthwashes

Mouth rinses are widely used as adjuncts to oral hygiene and in the delivery of active agents to the teeth and gums. The ability of these rinses to influence plaque formation and to alter the course of gingival inflammation has been extensively studied. These herbal mouthwashes are gaining popularity as they contain naturally occurring ingredients called as **phytochemicals** that achieve the desired antimicrobial and anti-inflammatory effects. Herbal formulations may be more appealing because they work without alcohol, artificial preservatives, flavors or colors.[27]

Use of guava (Psidiumguajava) as a mouthwash

In Brazil guava is considered as an astringent and diuretic. Chewing sticks when used without toothpaste are very efficient, effective, and reliable in cleaning the teeth of many people in Southern Nigeria. The teeth of the users of chewing sticks are usually strong, clean, fresh, and devoid of dental plaques and caries. In Ghana and in Nigeria the leaves are chewed to relieve toothache. A decoction of the root-bark and leaves is recommended as a mouthwash for swollen gums, ulceration of the mouth. Guava mouthwash is also recommended as a gargle for sore throats, and swelling of the mouth.[28]

Use of pomegranate (Punicagranatum) as mouthwash

Pomegranate is currently finding important applications in the field of dental health. When used regularly in combination with toothpaste that has been reinforced with bioactive botanical extracts, pomegranate containing mouthwash may HT dental plaque and tartar formation by inhibiting the activities of the microorganisms that cause plaque. Additionally, pomegranate compounds possess anti-inflammatory properties.[29]

Research studies shows that pomegranate extract suppresses the ability of these microorganisms to adhere to the surface of the tooth. Plaque may involve four or

more different microorganisms combining forces to colonize the surface of the teeth. Pomegranate fights against the organisms' which adhere by interfering with production of chemicals that bacteria use as "glue".[30] Aspartate aminotransferase enzyme is considered a reliable indicator of cell injury and is elevated among patients with periodontitis.

Use of neem (Azadirachtaindica, A. indica) as a mouthwash

The first known use of neem by the Harrappa culture in ancient India dates back 4500 years. Today, neem extracts are used to treat various skin diseases, as an antiseptic substance, against endo and ectoparasites or simply as a herbal mouthwash.[31] Neem has been shown to have significant effects on both gram-positive and gram-negative organisms and other bacteria that cause a wide array of human and animal diseases. Recent studies have shown Neem to have significant effects on E.coli, Streptococcus and salmonella. Data from **Wolinsky LE et al 1996**[32] studies suggests that neem stick extracts can reduce the ability of some streptococci to colonize tooth surfaces.

In dentistry, aindica demonstrated a good efficacy in the treatment of periodontal disorders. In a small trial from India, it was suggested that a dental gel containing A. indica extract has significantly reduced plaque index and bacterial count as compared to positive controls (chlorhexidine 0.2%). The positive effect on dental health has been reported in epidemiological studies such efficacy of the herbal mouth rinses extract.[33]

Use of propolis as mouthwash

Bee propolis has proved successful against in a range of dental disorders - from plaque and cavities to gum disease and mouth ulcers, as well as having other health benefits. Added to toothpaste, it prevents periodontal disease, and is antiplaque/anti-inflammatory. It can even be used as a dental adhesive and anaesthetic.[34] Anti-inflammatory property of propolis is due to the presence of caffeic acid phenethyl ester **(CAPE)** in propolis.[35] **Amoros et al 1992** found that propolis was active against an acyclovir-resistant mutant of HSV-1, adenovirus Type 2, vesicular stomatitis virus, and poliovirus.[36]

Use of Tulsi (Ocimum sanctum) as a mouthwash

Tulsi is a small plant, sub-shrub which has multiple uses. The leaves are quite effective for the ulcer and infections in the mouth. The herb is useful in teeth disorders. Its leaves, dried in the sun and powdered, can be used for brushing teeth. It can also be mixed with mustered oil to make a paste and used as toothpaste. This is very good for maintaining dental health, counteracting bad breath and for massaging the gums. The anti-inflammatory and anti-infectious properties of tulsi make it a powerful treatment for gingivitis. Ocimum sanctum has been shown to inhibit acute as well as chronic inflammation.[37]

Use of green tea (Camellia sinensis) as a mouthwash

It can be used as a mouthwash or gargle in the treatment of halitosis, laryngitis, sore throat, plaque build-up, tonsillitis and dental caries. It can be used as a new and safe method for the treatment of oral diseases in pregnant women and children as it is free of side effects that chemical mouthwashes cause. Green tea mouthwash has been shown to reduce plaque accumulation, and is free from side effects as of chemical mouthwashes like Chlorhexidine, Listerine.[38]

Camellia sinensis, or Green tea, has a wide variety of pharmacological activities. Green tea contains polyphenols especially the major four catechins, that is, **(-)-epigallocate chingallate(EGCG), (-)-epicatechingallate (ECG), (-)-epicatechin (EC), and (-)-epigallocatechin (EGC)].** Catechins showed an in vitro-bactericidal activity against odor-producing, periodontal bacteria, P. gingivalis, and Prevotella species. Catechins and its derivatives could reduce periodontal breakdown by inhibiting collagenase and cysteine proteinase activity of P. gingivalis.[39]

Use of cranberry (Vaccinium macrocarpon) juice as mouthwash

The name cranberry is derived from craneberry, first named by early European settlers in America because of their resemblance to head, neck and bill of crane. It contains **polyphenols, vitamins, proteins, flavonoids and other rare phytochemicals.** It has antimicrobial, anti-inflammatory and anti-tumour activities.

Cranberry constituent inhibits the adhesion of cariogenic bacteria on the tooth surface. This was due to the anti-adhesion activity of cranberry constituent. It does not destroy the bacteria but prevents it from adhering to the tooth structure resulting in a controlled oral flora.[40]

Use of Sodium bicarbonate as a mouthwash

A mouthwash can be prepared by dissolving one teaspoon of sodium bicarbonate in a glass of water. Sodiumbicarbonate can improve taste and it neutralises acids and thus prevents erosion. It is bland and will not irritate the oral mucosa in patients with xerostomia or oral ulcerative disease.[41] Sodium bicarbonate mouthwash is sometimes used to remove viscous saliva and to aid visualization of the oral tissues during examination of the mouth

Use of Alum as a mouthwash

Alum containing mouthwashes have also been used over a period of time and have been shown to be effective in plaque reduction. In periodontology, Using of alum as mouth wash has been practiced, but only a few studies

was carried out regarding this mouthwash. **MourughanK et al in 2004**[42] showed a positive effect of alum on gingival health was observed and an inhibitory effect on oral microbiota was recorded. **Liu et al study in 2004**[43] studied the cytocompatibility and cytotoxic effect of three different extracts of gingival retraction cords on human gingival fibroblasts.

Use of oil pulling as a mouthwash therapy

Oil pulling or oil swishing, is a traditional Indian folk remedy that involves swishing oil in the mouth for claimed oral and systemic health benefits. Using this method, surgery or medication could be prevented for a number of chronic illnesses. The oil therapy is preventive as well as curative. The exciting aspect of this healing method is its simplicity. Ayurveda advises oil gargling to purify the entire system; as it holds that each section of the tongue is connected to different organ such as to the kidneys, lungs, liver, heart, small intestines, stomach, colon, and spine, similarly to reflexology.[44]

Commercial Availability and Safety of Compounds

A wide variety of plant extracts, mixtures, and single plant compounds are available worldwide without a prescription through health food stores and vitamin retailers. For example, preparations of flavones **(brand names Flavons 500 and Citrus Bioflavonoids)** are sold by supplement suppliers.

In 1994, passed the Dietary Supplement Health Education Act, which required the Food and Drug Administration to develop labeling designed for products containing ingredients such as **vitamins, minerals, and herbs** intended to supplement the diet. The new rules, issued in late **1997**, required products to be labeled as a dietary supplement and carry a **"Supplement Facts"** panel with information similar to the **"Nutrition Facts"** panels appearing on processed foods. The first investigational new drug application for herbal pharmaceuticals, available by prescription, was submitted in 1997.[45]

Conclusion

An attempt has been made to outline some of the commonly available herbs and plants, and certain fruits, which are readily available, and can be used as effective mouthwashes. In 1989, a patent had been filed at the European Patent Office stating that the combination of herbal extracts leads to the synergistic reduction of both dental plaque and gingival bleeding. Of late, the commercial use of these products in toothpaste and for oral irrigation delivery has increased manifold. A number of clinical studies have shown the effects of using mouth washes extracted from herbs such as Sanguinarina, Myrtuscommunis, Qureucusinfectoria, Capparisspinosa and Cinnamon in the prevention of dental plaque accumulation and subsequent gingival inflammation.

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