Targeting oral care with natural products

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INTRODUCTION

Oral care has received greater attention in the past decade, particularly in view of increasing scientific evidence that links poor oral health with the incidence of chronic diseases, such as cardiovascular disease. In general, oral care targets prevention of decay, as well as preservation of tooth and gum health.

Gum disease (periodontal disease) describes bacterial growth and production of metabolic substances that gradually destroy the tissue surrounding and supporting the teeth. The result is inflammation, pain and tooth loss. The causative bacteria reside in plaque, a deposit that forms on the base of the teeth and hardens to form "tartar".

These bacteria grow and attack the tissues causing "gingivitis" characterized by inflamed gums that bleed easily. If left untreated the condition progresses to "periodontal disease" wherein there is severe inflammation, bone damage and tooth loss.

Poor oral hygiene is the major cause of gum disease. Other causes include tobacco use, hormonal changes, stress, certain medications that affect saliva flow or induce abnormal growth of gum tissue, poor nutrition such as high sugar diets and vitamin and mineral deficiencies affecting immune response, illnesses, and physical damage due to clenching and grinding teeth. Poor oral hygiene, improper diet (such as excessive amount of sugary and starchy foods), dry mouth and related factors also trigger microbial attack on the teeth resulting in cavities. Canker sores resulting from poor nutrition and hygiene that affect immune functions are also encountered, and need to be addressed effectively.

Scientific evidence continues to indicate an association between periodontal infections, atherosclerosis and vascular disease. Since dental diseases can be prevented, they represent a modifiable risk factor; and maintaining good oral health should receive high priority in general health maintenance (1).

Current Status of the Oral Care Industry

According to a recent report, oral care is one of the smallest categories in the cosmetics and toiletries industry. However, the striking impact of oral care on general health offers potential for innovative products that cosmetically and nutritionally target healthy teeth and gums. The Center for Disease Control has formed the National Oral Health Surveillance System to improve oral health standards in high risk communities.

NATURAL ORAL CARE MEASURES

Oral care includes antimicrobial, anti-inflammatory and immune support. Traditional cultures have used natural materials for oral care, these are often chewed for healthful and cleansing benefits. Recent research provides scientific validation for the use of these materials as antimicrobial, anti-inflammatory and wound healing agents. Internal "cleansing" with natural materials is also reported to benefit oral health and to help in the management of associated conditions such as halitosis.

Antimicrobials target oral pathogens such as *Streptococcus mutans,* anti-inflammatory and "wound healing" natural extracts offer support to healthy gums and teeth. Examples of natural extracts with scientifically validated efficacy in oral care are presented here.

Coleus Oil
INCI: Coleus Forskohlii Root Oil

Coleus oil is an essential oil extracted from the roots of *Coleus forskohlii,* a plant from the Natural Order Labiatae (Lamiaceae), a family of mints and lavenders. This species

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Coleus forskohlii *roots*

Curcuma longa *roots*

is a perennial herb with fleshy, fibrous roots that grows wild in the warm sub-tropical temperate areas in South Asia. The roots are eaten as a condiment or pickle in India. In recent years *Coleus forskohlii* has gained pharmacological importance as the only known plant source of the biologically active compound, forskolin, and coleus oil is an useful byproduct of forskolin extraction. The newly discovered antimicrobial properties of the oil – of specific composition obtained using a proprietary extraction process (2) – developed by Sabinsa Corporation, render it useful in oral care preparations.

Compounds such as 3-decanone (about 7%), bornyl acetate (about 15%), sesquiterpene hydrocarbons and sesquiterpene alcohols in major concentrations imparts unique pleasing spicy notes to the essential oil. β-sesquiphellandrene (about 13%) and γ-eudesmol (12.5%) were identified in experimental studies on the oil (3).

In laboratory studies, Coleus oil was found to more effectively inhibit the growth of the oral pathogen, *Streptococcus mutans*, which is associated with dental caries (2). The extract is safe to use in oral care formulations, it is non-irritant and its pleasant woody aroma blends well with oral care formulations.

Kaempferia galanga
INCI: Kaempferia Galanga Root Extract

Kaempferia galanga (Lesser galangal, kencur), and *Alpinia galanga* (greater galangal) from the Zingiberaceae family are commonly used as spice ingredients and medicinal herbs in South-east Asia and are valued traditionally for their protective topical effects when applied as pastes. *Kaempferia galanga* rhizome contains about 1.5 to 2% essential oil, whose main components are ethyl cinnamate (25%), ethyl-p-methoxycinnamate (30%) and p-methoxycinnamic acid. *Kaempferia galanga* is a good natural source of a biologically active ester compound ethyl p-methoxycinnamate (4). The antifungal action of ethyl-p-methoxycinnamate is reported in literature (5).

This natural extract from a herb from the ginger family is therefore potentially beneficial in preventing yeast infections such as oral thrush, triggered by poor oral hygiene, illness or mechanical stress due to ill-fitting dentures.

Turmeric Oil, Curcuminoids (INCI: Curcuma Longa) and Tetrahydrocurcuminoids

Turmeric oil is obtained by steam distillation or solvent extraction of the powdered rhizome of species of the genus *Curcuma* (Family: Zingiberaceae). Of these species, *Curcuma longa* is the most well known. *Curcuma longa* yields 0.3-7.2% (usually 4-5%) of turmeric oil following steam distillation. The chief constituents of the essential oil are turmerone (60%) and related compounds, and zingiberene (25%) (7).

In India, turmeric is known for its cosmetic and wound healing properties since ancient times. The essential oil has been used as a perfume component and studies have shown that it furnishes antibacterial/antifungal (8-11), and anti-inflammatory action. Curcuminoids are the yellow coloring principles of "curry" the powdered turmeric rhizome. Both these and their colorless derivatives Tetrahydrocurcuminoids offer bioprotectant, antimicrobial, anti-inflammatory, wound healing, and immune support (21).

Oleuropein
INCI: Olea Europaea (Olive) Leaf Extract

Oleuropein is a polyphenolic compound found in plants belonging to the Oleaceae family, of which the olive tree is a member. The olive tree (*Olea europaea*) was known in biblical times as the "Tree of Life". Oleuropein is the major phenolic constituent extracted from olive leaf, (constituting about 19% (w/w)) and from the polar fraction of virgin olive oil. Oleuropein is reported to be hydrolyzed to another biologically active compound, hydroxytyrosol, *in vivo*. A variety of anitimicrobial actions of oleuropein and its associated compounds have been demonstrated *in vitro*. The inhibitory action of oleuropein against the growth and toxin production of *Staphylococcus aureus*, *Bacillis cerus, Pseudomonas syringae* and several other bacterial strains (by oleuropein or its hydrolysis products) *in vitro*, is documented. For example, the presence of low concentrations (0.1% w/v) of oleuropein delayed the growth of *Staphylococcus aureus* in nutrient media, while higher concentrations (0.4-0.6% w/v) inhibited growth completely. Concentrations of oleuropein greater than 0.2% w/v inhibited growth and enterotoxin production in both types of media.

Olive leaves, the source of oleuropein

Oleuropein had bactericidal effects against a broad spectrum of gram-positive and gram-negative bacteria, but no effect was observed against yeast (12). Antiviral properties (13) are also reported *in vitro* and *in vivo.* Although the precise mechanism of antimicrobial action has as yet to be elucidated (12,14) oleuropein and related compounds appear to have surface-active properties that interfere with microbial cell membranes. Oleuropein could also interfere with the synthesis of amino acids that are crucial to viral replication and in the case of retroviruses, neutralize the production of reverse transcriptase and protease. Additionally, oleuropein is also reported to stimulate phagocytosis or the immune response to infection by pathogens (12).

Neem Leaves Extract
INCI: Melia Azadirachta

The Neem tree is traditionally labeled as "The Village Pharmacy" on account of its multifaceted healthful properties. Its properties range from immunomodulatory and anti-inflammatory effects to antimicrobial and pesticidal attributes. The leaves and seeds of Neem yield limonoids with wide biological applications. These have antibacterial, antiviral, insect repellant, anti-protozoal and anti-helmenthic properties (15). The neem twig is traditionally used as a "natural toothbrush".

Neem leaves

A recent study determined the efficacy of a mucoadhesive dental gel containing *Azadirachta indica* leaf extract (25 mg/g) using commercially available chlorhexidine gluconate (0.2% w/v) mouthwash as positive control. The results of the study suggested that the dental gel containing neem extract significantly reduced plaque index and bacterial count as compared to the control group (16).

Green Tea Extract
INCI: Camellia Sinensis Leaf Extract

The catechins in green tea were found to inhibit *Staphylococci* and *Yersinia enterocolitica*. Green tea extracts may make strains of drug-resistant bacteria more

Green tea

sensitive to penicillin. *In vitro* studies on particular antibiotic resistant strains of *Staphylococcus aureus* revealed that addition of green tea extract induced reversal of penicillin resistance. It was found that epicatechin gallate, markedly lowered the minimum inhibitory concentration (MIC) of oxacillin and other beta-lactams (17,18). Extracts of green tea were found to strongly inhibit *Escherichia coli*, *Streptococcus salivarius* and *Streptococcus mutans*, microorganisms found in the saliva and teeth of people suffering from dental caries (19). Green tea in combination with the synthetic antioxidant butylated hydroxyanisole (BHA) reduced the hydrophobicity of *S. mutans* and greatly inhibited ($p<0.001$) the formation of hyphae in *Candida albicans*. The increased antimicrobial activity of green tea is related to an impairment of the barrier function in microorganisms and a depletion of thiol groups (20).

Miswak (*Salvadora persica*)

Salvadora persica, often called chewing sticks or miswak, is a common oral hygiene tool in Asia, Middle East, and Africa. *Salvadora persica* chewing stick called miswak is frequently used in Saudi Arabia. The antimicrobial effects of miswak have been well documented. The antimicrobial effects of miswak are attributed to the high content of sodium chloride, potassium chloride, salvadourea, salvadorine, saponins, tannins, vitamin C, silica, resin, cyanogenic glycosides, and benzylisothiocyanate. Miswak is most effective against *S. faecalis, P. aeruginosa* and *Staph. aureus*, which is likely due to the nitrate content of miswak (22). The organic parts of the sticks of *Salvadora persica* are comprised mainly of cellulose, hemicellulose, and lignin (23). In one study, by using GC-MS analysis of the volatile oil extracted from *Salvadora persica* L. leaves, benzyl nitrile, eugenol, thymol, isothymol, eucalyptol, isoterpinolene, and beta-caryophyllene were identified (24). Other biological activities include anti-ulcer activity; a decocting of the plant is protective against stress-induced ulcers (25), indicating anti-inflammatory wound healing effects. *In vitro* studies examined the effects of aqueous extracts of miswak on healthy and periodontally involved human dentine with Scanning Electron Microscopy (SEM). Twenty-five percent aqueous extract of freshly prepared miswak solution was used for the study. Twelve human premolars teeth, (six healthy and six with periodontal disease), that were recently extracted for orthodontic and periodontal reasons were used in the study. Twenty-four SEM specimens were prepared and treated with miswak extract with different conditions, such as soaking. Soaking the healthy and periodontally diseased root dentine in miswak extract resulted in partial removal of smear layer and occlusion of dentinal tubules was observed in dentine specimens burnished with miswak solution (26).

Probiotics and Oral Care

A clinical study in Finland revealed that long-term consumption of a probiotic bacterium, *Lactobacillus rhamnosus* GG, in milk had beneficial effects in dental caries and in reducing caries risk in children (27). Other studies similarly report the effectiveness of probiotics in preventing gum disease and halitosis. Decreased gum bleeding and reduced gingivitis effected by the probiotic *Lactobacillus reuteri* is reported in literature (28). Colonization of the oral environment with probiotic cultures is reported to be effective in reducing bad breath as well. Replacement of bacteria implicated in halitosis by colonization with competitive bacteria such as *Streptococcus salivarius* K12, in a mouthwash for example, may potentially provide an effective strategy to reduce the severity of halitosis (29).

EMERGING TRENDS

The above summary of natural ingredients constitutes only a small fraction of the plethora of ingredients available for use in oral care products. Recent approaches to maintaining oral health target preventing bacterial biofilm (plaque) formation through molecular approaches and insight into quorum sensing mechanisms. Quorum sensing is the regulation of gene expression in bacteria in response to fluctuations in cell-population density. Although the nature of the chemical signals, their relay mechanisms, and the target genes controlled by bacterial quorum sensing systems vary, in every case the ability to communicate with one another allows bacteria to coordinate the gene expression, and therefore the behavior, of the entire community. Therefore disrupting such communication between bacteria presents a practical means of preventing plaque formation (30). A number of natural molecules have shown promising results in this area, and could well become the future guardians of oral health.

REFERENCES

1) Demmer R.T., Desvarieux M.J. J Am Dent *Assoc*. **2006**, *137* (Oct) Suppl, 14S-20S
2) Misra L.N. *et al. J. Essential Oil Res.* **1994**, *6*, 243-247
3) Majeed M., Prakash S. "Composition and methods containing an antimicrobial essential oil extended from *Coleus forskohlii*" United States Patent 6,607,712, Aug. 19, 2003
4) Kiuchi F., Nakamura N., Tsuda Y. *Phytochemistry* **1987**, *6*, 3350
5) Gupta S.K., Banerjee A.B., Achari B. *Lloydia* **1976**, *39* (4), 218-22
6) Research Report (unpublished); Sabinsa Corporation, 2003
7) Goldig B.T., Pombo E., Samuel C.J. *J. Chem. Soc. Chem. Commun.* **1982**, 363-364
8) Chopra R.N., Gupta J.C., Chopra G.S. *Ind. J. Med. Res.* **1971**, *29* (4), 769-772
9) Ramprasad C., Sirsi M. *J. Sci. Ind. Res.* **1956**, *15c*, 239-241
10) Iyengar M.A., Rao M.P.R., Bairy I., Kamath M.S. *Indian Drugs* **1984**, *31*, 54-49
11) Bhavani Shankar T.N., Sreenivas Murthy V. *J. Food. Sci. Tech.* **1978**, *15*, 152-153
12) Soler-Rivas C. *et al. J. Sci. Food Agric.* **2000**, *80*, 1013-1023
13) Renis H. "*In vitro* antiviral activity of calcium elnolate" in *Antimicrobial Agents and Chemotherapy*; 1969 (printed 1970), pp.167-279
14) Juven B., Henis Y., Jacoby B. *J Appl Bacteriol* **1972**, *35*, 559-567
15) Khan M., Schneider B., Wassilew S.W., Splanemann V. *Z. Hautkrankheiten* **1988**, *63* (6), 499-502
16) Pai M.R., Acharya L.D., Udupa N. *J. Ethnopharmacol.* **2004**, *90* (1), 99-103
17) Yam T.S. *et al. J Antimicrob Chemother* **1998**, *42* (2), 211-6
18) Shiota S. *et al. Biol Pharm Bull* **1999**, *22* (12), 1388-90
19) Rasheed A., Haider M. *Arch Pharm Res* **1998**, *21* (3), 348-52
20) Simonetti G., Simonetti N., Villa A. *J Chemother.* **2004**, *16* (2), 122-7
21) Majeed M., Badmaev V., Shivakumar U., Rajendran R. *Curcuminoids Antioxidant Phytonutrients* NutriScience Publishers, Inc: Piscataway, New Jersey, 1995
22) Darout I.A. *et al. Indian J of Pharmacology* **2000**, *32*, 11-14
23) Bahabri F.S. *Physica A* **2000**, *276*, 346-351
24) Alali F., Al-Lafi. *Nat Prod Res* **2003**, *17*, (3), 189-94
25) Sanogo R, *et al. Phytomedicine* **1999**, *6* (5), 363-6
26) Almas K. *Indian J Dent Res* **2001**, *12* (3), 127-32
27) Nase L. *et al. Caries Res.* **2001**, *35* (6), 412-20
28) Krasse P. *et al. Swed Dent J.* **2006**, *30* (2), 55-60
29) Burton J.P. *et al. J Appl Microbiol.* **2006**, *100* (4), 754-64
30) ten Cate J.M. *Odontology* **2006**, *94* (1), 1-9