Dentalcidin LS (Liposomal Oral Care Solution with Biocidin®) – Scientific Validation of Botanical Ingredients

Liposomal Technology

Liposomal technology involves a specific drug delivery system that has been extensively used in cosmetic and pharmaceutical industries.[1,2] Liposomes as drug carriers have been researched since the 1970s for improving the delivery of therapeutic agents to specific sites within the body.[1]

Liposomes are spherical, microscopic phospholipid vesicles, consisting of an aqueous core entrapped by one or more natural (or synthetic) phospholipid bilayers.[2] Liposomes can be made from cholesterol, non-toxic surfactants, sphingolipids, glycolipids, long chain fatty acids and membrane proteins.[3] Predominantly, the lipid components of liposomes are phosphatidylcholine derived from egg or soybean lecithin.[4] Liposomes have been studied extensively as a carrier system for therapeutically active compounds due to their unique characteristics.[4] These characteristics include the ability to incorporate hydrophilic, lipophilic and amphiphilic compounds, high biocompatibility, low toxicity, lack of immune system activation, and targeted delivery of bioactive compounds to the site of action.[4,5]

Liposomes can be classified on the basis of structure (size and number of lipid layers), method of preparation, composition and application.[3] According to size, liposomes can be composed of unilamellar vesicles which consist of a single bilayer with a size range of 50–250 nanometres (nm), or multilamellar vesicles comprised of two or more lipid bilayers with a size ranging between 500–5000 nm.[4] Classification can also be based upon conventional or speciality liposome technology. Examples of conventional liposomes include; 1) stabilized natural lecithin (phosphatidyl choline) mixtures, 2) synthetic identical, chain phospholipids, and 3) glycolipids containing liposome. Examples of speciality liposomes include; 1) bipolar fatty acid, 2) antibody directed liposome, 3) methyl/methylene x- linked liposome, 4) lipoprotein coated liposome, 5) carbohydrate coated liposome, and 6) multiple encapsulated liposome.[3] Because liposomes form a barrier around their contents, they provide protection against oxidation and degradation within the body. Encased in their protective barrier, medicinal actives are impervious to digestive enzymes in the mouth and stomach, alkaline secretions from the pancreas, bile acids, intestinal flora, and free radicals.[2]

Given liposomes are non-toxic, flexible, biocompatible, biodegradable, non-immunogenic, and suitable for systemic and non-systemic administration, they offer a number of distinct advantages including[2]:

- Increased efficacy and therapeutic index of drugs or medications
- Increased stability (via encapsulation technology)
- Reduced toxicity of the encapsulated agent
- Reduced exposure of sensitive tissues to toxic drugs
- Flexibility to bind with site-specific ligands for active targeting

Although herbal medicine has been used since ancient times and studied extensively in present days, its application can present with certain limitations. These may include instability in a highly acidic pH environment, pre-systemic metabolism in the liver, as well as solubility and absorption problems. Such challenges can lead to lower therapeutic concentrations of botanicals in plasma, resulting in a reduction or absence of therapeutic effects.[6] Furthermore, the majority of plant actives are polar molecules, which are poorly absorbed due to their large molecular size, which limits their absorption via passive diffusion and their ability to cross the lipid-rich biological membranes. These factors can lead to reduced bioavailability and low therapeutic index of phytochemicals.[6]

AUTHORS: Corene Humphreys, ND, BHSc, Dip Med Herb, Dip Hom, QTA (Microbiology). | Anita Kasa, BNat, Dip Herb Med, Dip Nutr, Dip Yoga.

NUTRITIONALMEDICINENZ.COM / BIOCIDIN.NZ.

PHONE: NZ: 09 425 4250 / 021 941 556. AUST: 001169 425 4250 /00116 21 941 556.

Incorporation of liposomal drug delivery system and herbal medicine can improve stability, bioavailability, and minimize the pre-systemic metabolism and degradation of phytochemicals in the gastrointestinal tract. It can also lessen the distribution and accumulation of phytochemicals in the non-targeted tissues and organs, thereby reducing toxicity and possible side effects as well as improving therapeutic efficacy and patient compliance.

Dentalcidin™ LS utilizes advanced Etheric Delivery™ phospholipid encapsulation technology, which provides unilamellar vesicles of 100 nm or smaller particle size, for enhanced therapeutic application. Because these liposomes are smaller and more stable, the vesicles are able to be absorbed as soon as they enter the oral cavity for maximum bioavailability. Delivery of Dentalcidin™ LS in liposomal format enables the botanicals to cross the blood-brain barrier, be delivered intracellularly, and also improve lymphatic circulation of the actives. Given phospholipids represent the basic building blocks of all cellular membranes, their inclusion in Biocidin LSF helps nourish and enhance cell membrane function, which in turn supports nutrient absorption and enhances the excretion of toxins and cellular waste products.

Dental caries and periodontal diseases, including gingivitis and periodontitis, are the most prevalent dental diseases.[7] Numerous pharmaceutical agents such as mouth rinses and dentifrices have been developed for the prevention and local therapy of dental ailments. The disadvantage of conventional methods includes short retention time in the oral cavity due to salivation (secretion of an average of 620 ml/day), the intermittent swallowing, food and beverage intake as well as abrasion by soft tissue movements. The use of liposomes as a dental agent to overcome these issues is a new strategy with promising research.[7,8] Liposomes can be designed to be bioadhesive so that they are retained on enamel surfaces, thereby increasing contact time and extending retention time within the oral cavity. In addition to its encapsulating ability of therapeutic agents to combat cariogenic microorganisms, liposomes may also protect the enamel against deterioration by covering the enamel surfaces, which in turn prevents the adsorption of bacteria to dental enamel.[7]

The use of Dentalcidin™ Liposomal Oral Care Solution for four weeks has been evaluated in a periodontal pilot study by Dr John Rothchild. His research demonstrated a marked reduction of oral pathogens from an average of 35 species down to 3 species, with many of the remaining species being considered as normal oral bacteria.[9,10]

Bilberry (*Vaccinium myrtillus*)

Medicinal Actions:
Antibiofilm,[11] antiinflammatory, antimicrobial,[12] antioxidant.[13-15]

Scientific Evidence:
Traditionally bilberry as a herbal medicine has been used externally for inflammation of the mouth and mucous membranes as they possess significant astringent activity.[16] Bilberry is rich in phenolic compounds which possess strong bacteriostatic and antimicrobial properties.[12] This herb is renowned for its exceptionally high levels of anthocyanins, which are responsible for bilberry's diverse antioxidant effects.[17,18] As natural antiinflammatory agents, bilberry polyphenols help reduce lipopolysaccharide (LPS)-induced nuclear factor kappa-beta (NF-Kβ) activation.[19]

Based on *in vitro* experiments, bilberry may affect the coaggregation capabilities of oral pathogens, which is an interspecies adhesion process essential for the development of dental plaque. Polyphenol constituents in the high molecular size fractions of bilberry have been shown to exhibit antiaggregation (inhibit and reverse coaggregation) activity against the pairs of common bacteria causing dental biofilm

accumulation including *Streptococcus mutans* with *Fusobacterium nucleatum* or *Actinomyces naeslundii*.[11]

Phenolic compounds found in berries provides bioactive molecules for the prevention and/or treatment of inflammatory diseases, including gingival inflammation.[20] Consumption of bilberry has been shown to demonstrate ameliorating effect on markers of gingival inflammation by reducing interleukin (IL)-1β, IL-6 and vascular endothelial growth factor (VEGF) and therefore reducing gingivitis to a similar extent compared to standard of care.[20]

Safety Summary:
Considered safe at the recommended dose.[13] No adverse effects expected during pregnancy and breastfeeding.[14]

Noni (*Morinda citrifolia*)

Medicinal Actions:
Antibacterial,[21] antiinflammatory, antimicrobial, antioxidant,[15,22] immunomodulatory.[21]

Scientific Evidence:
Noni fruit has been used throughout Southeast Asia and Polynesia for more than 2000 years as an important food source, as well as a medicinal plant.[16,21] To date, over 160 different phytochemical compounds have been identified in the noni plant. The major secondary metabolites include phenolic compounds, organic acids and alkaloids which give rise to noni's potent antioxidant, antiinflammatory and immune enhancing properties.[21,22]

Based on *in vitro* research, aqueous extract of noni fruits are capable of inhibiting the growth of dental caries-causing oral pathogens including *Streptococcus mutans* and *Streptococcus mitis*.[21] Noni has demonstrated antifungl activity against *Candida albicans* in a dose-dependent manner.[23] Aqueous extracts of noni may also help protect against the conversion of cellular *Candida albicans* into the hyphenated or filamentous form of the yeast. Germ tube formation or hyphenation from blastoconidia by Candida species is thought to be a virulence factor in their pathogenesis.[24]

Safety Summary:
No known warnings, precautions or contraindications at the dose recommended.[15,25] No adverse effects expected during pregnancy and breastfeeding.[15,26]

Milk Thistle (*Silybum marianum*)

Medicinal Actions:
Antimicrobial, antioxidant.[13,14]

Scientific Evidence:
Milk thistle, also known as St. Mary's thistle, has been used as a traditional herbal medicine since ancient times.[16] Milk thistle is rich in flavanolignans which comprise of silybin A and silybin B (diastereoisomers), silydianin, silychristin and diastereoisomers isosilybin A and isosilybin B. These polyphenolic molecules are collectively referred to as silymarin.[13]

Research has shown that the flavanolignans from milk thistle possess potent antibacterial activity against Gram-positive bacteria, but no antimicrobial activity against Gram-negative bacteria or fungi. Silybin affects the growth of Gram-positive organisms by inhibiting ribonucleic acid (RNA) and protein

AUTHORS: Corene Humphreys, ND, BHSc, Dip Med Herb, Dip Hom, QTA (Microbiology). | Anita Kasa, BNat, Dip Herb Med, Dip Nutr, Dip Yoga.

NUTRITIONALMEDICINENZ.COM / BIOCIDIN.NZ.

PHONE: NZ: 09 425 4250 / 021 941 556. AUST: 001169 425 4250 /00116 21 941 556.

synthesis (as opposed to attacking the bacterial membrane).[27] Silibinin has also demonstrated antioxidant and antiinflammatory properties on LPS-stimulated human monocytes through an inhibitory effect on hydrogen peroxide release and TNF-α production.[28]

Based on *in vitro* research, the combination of silymarin and resveratrol has demonstrated antiinflammatory effects by decreasing IL-6 and IL-8 secretion by lipopolysaccharide-induced inflammatory responses in human gingival fibroblasts (which are one of the key cell lines involved in gingival inflammatory processes and periodontal diseases).[29]

Safety Summary:
Contraindicated in persons allergic to plants from the Compositae family.[30] No other known warnings, precautions or contraindications.[30] No adverse effects expected during pregnancy and breastfeeding.[30]

Echinacea (*Echinacea purpurea* & *Echinacea angustifolia*)

Medicinal Actions:
Antiinflammatory, antimicrobial, depurative, immune enhancing, immune modulating, lymphatic.[14,15,30]

Scientific Evidence:
Echinacea has been used as herbal medicine by Native American Indians for centuries.[16] Echinacea possesses both antiinflammatory and immunostimulating properties.[31] Alkylamides, one of the active constituents of echinacea are thought to be responsible for the herb's antiiflammatory activity. Emerging research suggests that bacterial lipoproteins and lipopolysaccharides within echinacea (endophytes) represent the major source of immune enhancing properties of this herb.[32,33] Human cells of the innate immune system detect Braun-type lipoproteins and LPS through Toll-like receptor 2 and 4 pathways, macrophage activation and upregulation of natural killer cell activity in the body.[34,35]

Echinacea has demonstrated antimicrobial activity against a number of respiratory pathogens including *Streptococcus pyogenes*, *Staphylococcus aureus*, *Haemophilus influenzae*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, *Legionella pneumophila* and *Candida albicans*.[36,37] Based on *in vitro* research, echinacea has both antiinflammatory and direct killing activity against *Streptococcus pyogenes, Haemophilus influenzae and Legionella pneumophila.* Echinacea has been shown to inhibit the production of the following cytokines: IL-4, IL-6, IL-8, monocyte chemoattractant protein (MCP)-1, VEGF, and growth-regulated protein alpha (GROα).[38]

Based on salivary incubation bioassays, echinacea may inhibit oral malodor production, also known as halitosis. Using an *in vitro* model for oral malodor production, echinacea has demonstrated antibacterial activity against Gram-positive streptococci and significant antimalodorous activity.[39]

In clinical research, herbal-based toothpaste composed of sodium bicarbonate and herbal extracts including chamomile, echinacea, sage, myrrh, rhatany and peppermint oil have been shown to be as effective as the conventionally formulated dentifrice for the control of plaque and gingivitis.[40] *Echinacea purpurea* in combination with *Centella asiatica* and *Sambucus nigra* applied as a topical gingival patch and mouth rinse has been shown to reduce and stabilize gingival recession, without the need for surgery.[41] In a pilot study, a mouth rinse that contained *Echinacea purpurea*, *Centella asiatica* and *Sambucus nigra* reduced gingival inflammation in an experimental gingivitis model.[42] Topical application of the transmucosal herbal periodontal patch containing plant extracts derived from *Echinacea purpurea*, *Centella asiatica* and *Sambucus nigra* have also been shown to reduce gingival inflammation.[43]

Safety Summary:

Contraindicated in persons allergic to plants from the Compositae family.[14] No other known warnings, precautions or contraindications.[44] No adverse effects expected during pregnancy or breastfeeding.[14,30]

Golden Seal (*Hydrastis canadensis*)

Medicinal Actions:
Antihistamine, antiinflammatory, antimicrobial,[45] mucous membrane trophorestorative.[13,15,30,46,47]

Scientific Evidence:
The root and rhizomes of goldenseal has been used traditionally by Native American Indians for mouth inflammation and general ulceration.[16] Goldenseal root contains a number of alkaloids, of which the most abundant is berberine. Both *in vitro* and *in vivo* studies have revealed that berberine possesses antimicrobial activity against bacteria and fungi.[14,48] Goldenseal leaves are rich in flavonoids (specifically sideroxylin, 8 desmethyl-sideroxylin and 6 desmethyl-sideroxylin).[49] While the flavonoids from golden seal have no inherent bactericidal properties, they enhance the antimicrobial activity of berberine by acting as efflux pump inhibitors.[49] It should be noted that one of the major mechanisms by which bacteria become resistant to antibiotics is by over expression of efflux pumps.[50] One of the key mechanisms by which golden seal inhibits microbial growth is through quenching of the agr quorum sensing (QS) system.[49,51] QS is a bacterial cell-to-cell communication that controls genes and influences a number of processes including bioluminesence, sporulation, competence, antibiotic production, biofilm formation and virulence factor secretion.[52]

Based on *in vitro* experiments, berberine possesses antimicrobial activity against the oral pathogens *Streptococcus mutans* and *Fusobacterium nucleatum.*[45] Berberine in combination with C-methyl flavonoids exhibited an additive antimicrobial effect when tested against *Streptococcus mutans*.[45] When compared with sterile saline irrigation, berberine was found to be more effective at eradicating the endodontic pathogens in a biofilm tooth model using *Fusobacterium nucleatum, Enterococcus faecalis* and *Prevotella intermedia*. [53]

Safety Summary:
No known warnings, precautions or contraindications at the dose recommended.[14] Contraindicated during pregnancy in therapeutic doses.[15] Discouraged during breastfeeding in therapeutic doses.[13]

Shiitake Mushroom (*Lentinula edodes*)

Medicinal Actions:
Antibacterial, antifungal, antioxidant, immune modulating.[15,54]

Scientific Evidence:
Shiitaki mushrooms have long been used as a traditional medicine and health food in East Asian countries.[55] Active constituents of shiitake mushroom include the polysaccharide lentinan, shiitake mushroom mycelium, culture media extracts (LEM, LAP and KS-2) and eritadenine, all of which have demonstrated antimicrobial, antiviral and antitumour activity.[55,56] As an antimicrobial agent, lentinan works by activating macrophages and the cytokines tumor necrosis factor (TNF)-α and interferon (IFN)-γ with resultant stimulation of T lymphocytes and enhanced immunity.[55]

Shiitake may be effective against oral pathogens associated with dental caries and dental plaque accumulation.[57-59] In clinical research, low molecular mass fraction of a shiitake extract formulated in a mouth rinse has been shown to be effective in reducing dental plaque deposition.[58] Low molecular

AUTHORS: Corene Humphreys, ND, BHSc, Dip Med Herb, Dip Hom, QTA (Microbiology). | Anita Kasa, BNat, Dip Herb Med, Dip Nutr, Dip Yoga.

NUTRITIONALMEDICINENZ.COM / BIOCIDIN.NZ.

PHONE: NZ: 09 425 4250 / 021 941 556. AUST: 001169 425 4250 /00116 21 941 556.

weight fraction of shiitake extract applied as a mouth rinse has been shown to possess caries-preventive properties by reducing the metabolic activity of the dental plaque.[59]

In vitro studies have demonstrated antigingivitis and anticaries activities of Shiitake against the following oral pathogens: *Streptococcus sanguinis, Streptococcus mutans, Fusobacterium nucleatum*, *Prevotella intermedia, Veillonella dispar, Neisseria subflava, Actinomyces naeslundii* and *Lactobacillus casei*.[57,60-62] Shiitake protects against gingivitis and caries through a number of mechanisms including inhibition of cell division, prevention of coaggregation and biofilm formation as well as disruption of preexisting biofilms.[57,60] These effects are explained in part by Shiitake's alpha-glucan content. Shiitake mushroom is rich in alpha-gluconase, an enzyme that has been shown to inhibit sucrose-induced formation of oral biofilms from *Streptococcus mutans* and *Streptococcus sobrinus* species.[63,64]

Safety Summary:
Considered safe and well tolerated at doses of up to 2.5 mg per day for 6 weeks.[65] No adverse effects expected during pregnancy and breastfeeding at the dose recommended.[66]

White Willow Bark (*Salix alba*)

Medicinal Actions:
Analgesic, antiinflammatory.[13]

Scientific Evidence:
Willow bark has been used traditionally as an antiinflammatory and analgesic agent since ancient times.[16] The key active constituents of white willow bark comprise of phenolic glyosides including the salicylates salicortin and salicin.[13] Other important medicinal actives include the flavonoids naringenin and isosalipurpuroside (also known as eriodictyol) and condensed tannins.[67-69]

In vitro studies assessing LPS activated monocytes show that *Salix alba* is able to block nitric oxide release and reduce IL-6 and TNF-α production.[68,70] While the underlying mechanisms have not been fully elucidated, white willow bark appears to induce monocyte apoptosis and block transcription factor NF-Kβ activation.[68,69] This multifactorial effect is thought to be an innate protective mechanism to control local and systemic inflammatory responses in the body.[68]

Safety Summary:
Contraindicated in people with salicylate sensitivity.[15] No other known warnings, precautions or contraindications at the dose recommended.[15] No adverse effects expected during pregnancy and breastfeeding.[15]

Garlic (*Allium sativum*)

Medicinal Actions:
Antiinflammatory, antimicrobial, antioxidant.[13]

Scientific Evidence:
Garlic has been used as both a food and a medicine for thousands of years throughout the world. Traditionally garlic has been used as a warming and blood-cleansing herb to prevent and treat colds, flu, coughs and to fight infections as well as to expel worms and other parasites.[16] The main active antimicrobial constituent of garlic is allicin (allyl 2-propene thiosulfinate), which is formed when the herb is crushed and alliinase (an enzyme from the bundle sheath cells) combines with the substrate allin.

AUTHORS: Corene Humphreys, ND, BHSc, Dip Med Herb, Dip Hom, QTA (Microbiology). | Anita Kasa, BNat, Dip Herb Med, Dip Nutr, Dip Yoga.

NUTRITIONALMEDICINENZ.COM / BIOCIDIN.NZ.

PHONE: NZ: 09 425 4250 / 021 941 556. AUST: 001169 425 4250 /00116 21 941 556.

Crushed garlic contains a number of QS compounds such as ajoene and other organosulfides that are produced as degradation products of allicin.[71,72]

In clinical research garlic has been shown to be effective in the treatment of denture stomatitis, the most common form of chronic oral candidiasis.[73] Based on *in vivo* experiments, a garlic mouthwash solution has demonstrated significant antibacterial activity against *Streptococcus mutans*, with a maintenance of reduced salivary levels of microorganisms during the study period.[74,75]

Garlic has demonstrated antibacterial activity against several oral microbes associated with dental plaque and caries including *Streptococcus mutans, Streptococcus sanguis, Streptococcus salivarius, Pseudomonas aeruginosa*, and *Lactobacillus* spp.[76,77] Other periodontal pathogens for which garlic has demonstrated antimicrobial activity include *Porphyromonas gingivalis* and *Aggregatibacter actinomycetemcomitans*. Garlic appears to inhibit the growth of these organisms through antiproteolytic activity and by inhibiting total protease activity.[78,79]

Other *in vitro* experiments using crude garlic extract show that it possesses greater antibacterial activity against *Streptococcus mutans*, than chlorhexidine.[80] Garlic extract has also demonstrated inhibitory activity on multidrug-resistant strains of *Streptococcus mutans* isolated from human carious teeth, suggesting that toothpastes or mouthwashes containing garlic extract may be used for prevention of dental caries.[81]

Garlic allicin has been shown to inhibit Gram-positive oral bacteria including *Streptococcus mutans*, *Streptococcus sobrinus*, and *Actinomyces oris*. Allicin was also bactericidal to *Streptococcus mutans* grown in mature biofilms (*in vitro* research).[82]

Safety Summary:
No known warnings, precautions or contraindications at the dose recommended.[30] No adverse effects expected during pregnancy and breastfeeding.[30]

Grape Seed (*Vitis vinifera*)

Medicinal Actions:
Antibacterial,[83,84] antibiofilm, antiinflammatory, antioxidant.[15]

Scientific Evidence:
Grape has been used medicinally to treat a variety of ailments, including skin and eye irritation since the time of Ancient Greece. Oligomeric proanthocyanidin complexes extracted from grapeseed extract are considered a superior source.[16] Grape seed contains over 95% flavonols, which are predominately comprised of oligomeric proanthocyanins (~82%) and active monomeric proanthocyanins (~12%).[85]

The proathocyanidins found in grape seed have also demonstrated a protective effect against endotoxin-induced experimental periodontitis (animal research).[86] Based on *in vitro* research, grape seed has demonstrated antiplaque and antibiofilm activity against oral microbes associated with periodontitis and other acute periodontal diseases. The antimicrobial activity of grape seed has been documented for the following organisms: *Porphyromonas gingivalis, Fusobacterium nucleatum, Streptococcus mutans, Streptococcus sobrinus, Lactobacillus rhamnosus* and *Actinomyces viscosus*.[84] Other *in vitro* studies indicate grape seed extract supports healthy remineralization of teeth and may be more effective than oral fluoride or calcium glycerophosphate.[87,88]
In an oral bacteria biofilm model, gape seed extract rich in flavan-3-ols demonstrated strong antimicrobial activity against *Actinomyces oris*, *Fusobacterium nucleatum* and *Streptococcus oralis*, and resulted in a decrease in cell viability of the whole biofilm.[83]

AUTHORS: Corene Humphreys, ND, BHSc, Dip Med Herb, Dip Hom, QTA (Microbiology). | Anita Kasa, BNat, Dip Herb Med, Dip Nutr, Dip Yoga.

NUTRITIONALMEDICINENZ.COM / BIOCIDIN.NZ.

PHONE: NZ: 09 425 4250 / 021 941 556. AUST: 001169 425 4250 /00116 21 941 556.

Safety Summary:
No known warnings, precautions or contraindications at the dose recommended.[15] Exercise caution during pregnancy and breastfeeding as safety has not been scientifically established during these times.[15]

Black Walnut (*Juglans nigra*)

Medicinal Actions:
Antimicrobial.[13]

Scientific Evidence:
Traditionally the bark of black walnut has been used as a toothbrush.[89] The main active constituents of black walnut include naphthoquinones (juglone and plumbagin), tannins (ellagic acid) and flavanoids.[13,30,90] Tannins comprise approximately 45% of the medicinal actives and exert an astringent effect on mucosal tissue by dehydrating mucosal secretions and protecting the outer layer of mucosal cells.[91]

Antimicrobial, antifungal and antiviral actions have also been attributed to the plumbagin and juglone content of black walnut. *In vitro* studies suggest these quinones exert their cytotoxic effects on microorganisms through redox cycling and the oxidation of glutathione.[92]

Based on *in vitro* research, black walnut extract exerts a broad spectrum antimicrobial activity by inhibiting the growth of several species of pathogenic micro-organisms including Gram-positive bacteria (*Staphylococcus aureus* and *Streptococcus mutans*), Gram-negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*) and pathogenic yeast (*Candida albicans*), which under certain circumstances are thought to play an important role in the etiology of oral and dental diseases.[89]

Safety Summary:
No known warnings, precautions or contraindications at the dose recommended.[30] Contraindicated during pregnancy and breastfeeding in therapeutic doses.[93]

Raspberry (*Rubus idaeus*)

Medicinal Actions:
Antiinflammatory, antimicrobial, antioxidant.[13,15]

Scientific Evidence:
Traditionally raspberry has been used as an astringent herb to treat inflammations of the mucous membranes of the mouth and throat.[16] Raspberry is rich in anthocyanins (mainly cyanidin-3-sophoroside) and phenolic compounds (primarily ellagitannins and ellagic acid). Raspberry also contains quercetin and kaempherol-based flavanols.[94-96] Research shows that the antioxidant properties of raspberry speak to the polyphenolic compounds (specifically ellagitannins) which are highly effective free radical scavengers.[94,96] Results of an *in vitro* study indicate that raspberry's phenolic compounds are able to protect deoxyribonucleic acid (DNA) and decrease lipid peroxidation of lymphocytes in a concentration-dependent manner.[94] Phenolic compounds also possess antimicrobial properties. The mechanism by which phenolic compounds affect the growth of different bacterial species include destabilization of the cytoplasmic membrane, permeabilization of plasma membranes and inhibition of extracellular microbial enzymes. Phenolic compounds also have direct actions on microbial metabolism by depriving bacterial cells of the substrates necessary for growth.[97] Adherence

of bacteria to epithelial surfaces is a prerequisite for colonization of many pathogens, therefore the antimicrobial activity of raspberry may be related in part to the antiadherence activity.[12]

Assay studies reveal that raspberry is effective against oral pathogens associated with dental caries and gingivitis. Raspberry has demonstrated antigingivitis and anticaries activities against *Streptococcus sanguinis, Streptococcus mutans, Fusobacterium nucleatum*, *Prevotella intermedia, Veillonella dispar, Neisseria subflava, Actinomyces naeslundii* and *Lactobacillus casei*.[60,62] Mechanisms by which raspberry protects against oral pathogens include: preventing bacterial coaggregation and biofilm formation, disruption of preexisting biofilms and reducing the expression of genes involved in gingival cellular proliferation and differentiation.[62]

Safety Summary:
No known warnings, precautions or contraindications at the dose recommended. No adverse effects expected during pregnancy and breastfeeding.[30]

Fumitory (*Fumaria officinalis*)

Medicinal Actions:
Antimicrobial, antioxidant.[98]

Scientific Evidence:
Fumitory is a well-known traditional herbal medicine rich in biochemically active compounds. It has been used since the Middle-Ages as a tonic and a blood cleanser agent and to treat digestive and kidney diseases.[99] The active constituents of fumitory include alkaloids, flavonoids and organic acids.[13] The biological activities of this herb are mainly associated with the isoquinoline alkaloids, in particular protopine.[100,101]

To date the scientific evaluation of fumitory as an antimicrobial agent is somewhat limited. Results of an *in vitro* study assessing a methanol extract of fumitory have demonstrated significant antimicrobial activity against the following respiratory-associated microorganisms: *Pseudomonas aeruginosa, Staphylococcus aureus* and *Cladosporium herbarum*.[98] The isoquinoline alkaloids from fumitory have also demonstrated significant antifungal activity against *Candida albicans*.[102]

Safety Summary:
No known warnings, precautions or contraindications at the dose recommended.[103] Exercise caution during pregnancy and breastfeeding as safety has not been scientifically established during these times.[104]

Gentian (*Gentiana lutea*)

Medicinal Actions:
Antiinflammatory, antimicrobial, antioxidant.[13,15,105]

Scientific Evidence:
Gentian has been used in European and Eastern herbal medicine for more than 3000 years due to its bitter properties. Externally it has been used to heal wounds, and internally as a bitter tonic, to treat a sore throat, for arthritic inflammation and jaundice.[106] Gentian contains a number of secoiridoid bitter compounds including; gentiopicrin, amarogentin, gentianine, gentianadine, swerosid and swertiamarin. The medicinal constituents also include a group of xanthones (isovitexin and isogentisin) as well as phenolic acids and phytosterol flavanoids.[13,105,107,108] These active constituents give rise to the herb's

potent antioxidant, antiinflammatory and antibacterial properties.[105,108] The antioxidant and cytoprotective action of gentian is due to the herb's ability to scavenging reactive oxygen species such as hydroxyl radicals, thereby reducing free radical injury to cells.[107-109]

Based on *in vitro* trials, the antiinflammatory activity arises from gentian's ability to inhibit myeloperoxidase enzymes which are released during degranulation of neutrophils and monocytes. Myeloperoxidase upregulation is known to contribute to the development of inflammatory and immune-mediated conditions.[105]

The bitter compounds in gentian include gentiopicrin and xanthone isogentisin. These substances possess antimicrobial properties and have been shown to inhibit the growth of a number of respiratory-associated pathogens including *Streptococcus pyogenes, Staphylococcus aureus*, *Pseudomonas aeruginosa, Sarcina lutea, Micrococcus flavus, Micrococcus luteus* and *Candida albicans.*[110,111]

Safety Summary:
No known warnings, precautions or contraindications at the dose recommended.[14] No adverse effects expected during pregnancy and breastfeeding.[30]

Tea Tree (*Melaleuca alternifolia*) Essential Oil

Medicinal Actions:
Antiinflammatory, antimicrobial, antiseptic.[112,113]

Scientific Evidence:
Tea tree has been used in traditional Aborigines medicine for hundreds of years to treat burns, cuts and insect bites. In Western Herbal Medicine it has been used for wound healing and for skin infections.[16] Tea tree oil is composed of a complex mixture of compounds, mainly monoterpene and sesquiterpene hydrocarbons and their associated alcohols such as pinene, sabinene, α-terpinene, limonene; p-cymene, 1,8-cineole, γ-terpinene, terpinolene, terpinen-4-ol, α-terpineol, aromadendrene, ledene, δ-cadinene, globulol and viridiforol.[114-117] The diverse active constituents give rise to tea tree's antimicrobial activity against a broad range of Gram-positive and Gram-negative bacteria and fungi.[115,118] Mechanisms of antimicrobial and antiinflammatory action of tea tree oil can also be attributed to its hydrocarbon structure and lipophilicity.[112]

Research shows tea tree oil is capable of killing oral pathogens. In a clinical setting, topical application of tea tree oil containing gel has demonstrated antiinflammatory properties when applied to inflamed gingival tissue in subjects with severe chronic gingivitis.[113] Topical application of tea tree oil in a gel format has also demonstrated efficacy in controlling microbial biofilms associated with salivary *Streptococcus mutans* in orthodontic patients.[119] Antibacterial effects of mouthwash-containing tea tree oil have demonstrated significant antibacterial activity against *Streptococcus mutans* and other oral microorganisms. Reduced levels of microorganisms were maintained throughout the five week study period.[74]

Based on *in vitro* research, tea tree oil has demonstrated growth-inhibiting and bactericidal effects as well as adhesion-inhibiting effects against a number of oral organisms including *Porphyromonas gingivalis, Actinobacillus actinomycetemcomitans, Fusobacterium nucleatum, Streptococcus mutans*, and *Streptococcus sobrinus*.[120] Tea tree oil has also demonstrated inhibitory activity against the Gram-positive bacillus *Solobacterium moorei,* an oral microbe associated with halitosis.[118] *In vitro* susceptibility experiments have shown that a wide range of oral bacteria are susceptible to, and rapidly killed by tea tree oil.[121]

AUTHORS: Corene Humphreys, ND, BHSc, Dip Med Herb, Dip Hom, QTA (Microbiology). | Anita Kasa, BNat, Dip Herb Med, Dip Nutr, Dip Yoga.

NUTRITIONALMEDICINENZ.COM / BIOCIDIN.NZ.

PHONE: NZ: 09 425 4250 / 021 941 556. AUST: 001169 425 4250 /00116 21 941 556.

Safety Summary:
Considered safe and well tolerated at the dose recommended. Tea tree oil is generally regarded as non-toxic, and non-irritating.[117] Exercise caution during pregnancy and breastfeeding as safety has not been scientifically established during these times.[122]

Galbanum (*Ferula galbaniflua*) Essential Oil

Medicinal Actions:
Antiinflammatory, antimicrobial, antiseptic.[117,123]

Scientific Evidence:
Galbanum oil has been used for many centuries in the east Mediterranean and central Asia.[123] Traditional applications include inflammatory and skin disorders, wound healing and for ailments of the respiratory, digestive and nervous systems.[117,123] The oil is mainly composed of monoterpene and sesquiterpene hydrocarons and their associated alcohols including tricyclene, α-pinene, camphene, β-pinene, myrcene, δ-3-carene, limonene, cis-ocimene, trans-ocimene and terpinolene.[117,124] It is the high concentrations of monoterpenes and sesquiterpenes that give rise to galbanum's antiinflammatory, antimicrobial and antiseptic properties.[117,123]

To date, few scientific studies have been conducted with galbanum oil. Based on experimental reserach, terpenes have been shown to be active against bacteria, fungi and viruses. The mechanism by which terpenes exert their antimicrobial properties involves disruption of the lipophilic compounds of the cellular membranes of pathogens.[125]

Safety Summary:
Galbanum oil is generally regarded non-toxic, non-irritating and non-sensitizing.[117] Exercise caution during pregnancy and breastfeeding as safety has not been scientifically established during these times.[126]

Lavender (*Lavandula officinalis*) Essential Oil

Medicinal Actions:
Antibacterial,[120] antifungal, antiinflammatory, antimicrobial.[117,127-130]

Scientific Evidence:
Essential oils of lavender have a long-standing history of traditional use for a wide range of conditions. Lavender was used as an antiseptic in ancient Arabian, Greek and Roman medicines, as a bath additive as well as an antiseptic and antibacterial agent.[16] Lavender oil contains a complex mixture of aromatic compounds including terpenes and sesquiterpenes (which include linalyl acetate), linalool, caryophyllene, terpinen-4-ol, 2-myrcene, trans-ocimenel, borneol, 1,8-cineole, camphor and limonene.[117,129,131]

Based on *in vitro* research, lavender essential oil can inhibit the growth of Gram-negative oral bacteria associated with periodontal disease including: *Porphyromonas gingivalis*, *Actinobacillus actinomycetemcomitans*, and *Fusobacterium nucleatum*. Although lavender oil did not demonstrate bactericidal activity, minimum inhibitory concentration values showed that lavender oil works as a natural bacteriostatic agent.[120]

In other *in vitro* experiments, lavender demonstrated protection against LPS-induced inflammation from Gram-negative bacteria. Exposure to LPS in tissues induces an inflammatory reaction which triggers

the release of proinflammatory cytokines and subsequent free radical pathology. Research by Huang et al. verified lavender oil was able to inhibit LPS-dependent superoxide anion generation, NF-Kβ activation and IL-1β production.[127]

Lavender oil has also demonstrated both fungistatic and fungicidal activity against *Candida albicans*, including oropharyngeal strains. In the study by D'Auria et al., lavender oil inhibited both germ tube formation and hyphal elongation of *Candida albicans.*[128]

Safety Summary:
Lavender oil is generally regarded as non-toxic, non-irritant and non-sensitizing.[117] No adverse effects are expected during pregnancy and breastfeeding at the dose recommended.[132]

Oregano (*Origanum vulgare*) Essential Oil

Medicinal Actions:
Antibacterial, antifungal, antiinflammatory.[133-135]

Scientific Evidence:
The use of oregano in traditional medicine dates back to the ancient Greek and Roman times. It has been to treat skin sores, to relieve aching muscles as well as an antiseptic agent. Oregano also has been used in traditional medicines for asthma, cramping, diarrhea, indigestion and general health.[136] Active constituents of oregano oil include phenolic monoterpenes and sesqueterpenes such as carvacol, thymol, p-cymene, cis-ocimene, caryophyllene and linalool.[117] Research shows that antimicrobial activity of oregano oil is predominantly attributed to carvacrol and thymol.[137,138] The bacteriostatic and bactericidal properties of oregano oil are thought to be due to its effects on cell membrane and membrane components of microorganisms. Based on *in vitro* trials, oregano oil and its constituents impair cell membrane integrity and damage intracellular nucleic acids by stimulating potassium and phosphate ion leakage and changes to the internal pH of the cell.[133]

In vitro experiments show that oregano oil is highly active against *Streptococcus mutans* and *Candida albicans* and also demonstrated moderate activity against *Lactobacillus acidophilus*.[135] Oregano oil has also demonstrated antibacterial activity against the following respiratory pathogens: *Staphylococcus aureus* (including methicillin-resistant strains), *Klebsiella pneumonia, Pseudomonas aeruginosa*, *Mycoplasma mycoides* subsp. *carpi*, *Micrococcus flavus* and *Mycobacterium terrae*.[133,138-142]

The broad antimicrobial effects of oregano oil also extend to other Candida species and fungal organisms.[134,143] In the study by Pozzatti et al., oregano inhibited the growth and hyphenation of both *Candida albicans* and *Candida dubliniensis*.[144] The main mechanism of the antifungal activity is associated with the lipophilicity of oregano oil and consequent interaction with the microbial cell membrane. The lipophilic nature of the oil results in changes and losses of enzymatic and structural components of fungal cells such as adenosine triphosphatase, 1,3-β-D-glucan synthases, chitin and mannans, which are also components involved in germ tube formation.[144] Oregano oil may also exert its antifungal effects through the inhibition of chain respiration through interactions with mitochondrial membranes with resultant decreased energy production and inhibition of germ tube formation and/or cell growth.[143-145] Antifungal activity has been documented for the following species: *Candida tropicalis, Candida krusei, Candida guillermondii*, *Candida parapsilosis, Cryptococcus neoformans, Trichophyton mentagrophytes, Trichophyton rubrum, Microsporum canis, Epidermophyton floccosum, Aspergillus niger, Aspergillus fumigatus* and *Aspergillus flavus*.[146]

Safety Summary:

Generally considered safe and well tolerated at the dose recommended. Active phenolic compounds such as thymol and cavacrol in oregano oil may in some sensitive individuals cause skin and mucus membrane irritation.[117] Exercise caution during pregnancy and breastfeeding as safety has not been scientifically established during these times.[147]

Quercetin

Medicinal Actions:
Antioxidant, antihistamine, antiinflammatory, antimicrobial, immune modulating.[16,148,149]

Scientific Evidence:
Quercetin is a flavanol which belongs to a group of polyphenolic substances known as flavonoids or bioflavonoids.[16] It can be found in a wide variety of fruits and vegetables such as apples, berries, grapes, citrus fruit, onions, broccoli and other green leafy vegetables.[148] Quercetin is also naturally present in black and green tea, red wine as well as many seeds and nuts, flowers, barks and leaves.[16,150]

A systematic review established that quercetin exhibits beneficial effects in oral health via its broad pharmacological properties as a preventive and therapeutic agent in dental caries with anti-inflammatory effects against oral pathogens.[151] In clinical research, topical application of quercetin has demonstrated accelerated healing properties to minor aphthous ulcers when compared to topical benzydamine hydrochloride mouthwash.[152] Toothpaste containing quercetin has been shown to significantly inhibit plaque formation by reducing the accumulation of microorganisms and by preventing the bacterial adhesion on the tooth surface.[153,154]

In vitro experiments show that quercetin possesses antimicrobial activity against *Actinobacillus actinomycetemcomitans* and *Porphyromonas gingivalis* bacteria which are associated with early onset, progressive and refractory periodontal disease.[148] In another study quercetin has demonstrated antibacterial activity by inhibiting the growth of periodontal disease-causing bacteria including *Actinobacillus actinomycetemcomitans, Actinomyces viscosus, Porphyromonas gingivalis, Fusobacterium nucleatum* and *Actinomyces naeslundii*.[155] Quercetin has also been shown to reduce the biofilm formation of *Streptococcus mutans* by inhibiting the expression of the related genes, while exhibiting no cytotoxicity for human dental pulp cells, indicating a potential use of quercetin in oral health.[156] Quercetin also demonstrated antibacterial properties against *Streptococcus mitis*, by inhibiting adhesion, biofilm formation and maturation.[157]

The antiinflammatory properties of quercetin have also been evaluated through *in vitro* research using human gingival fibroblasts and human mesenchymal stem cells.[158,159] Quercetin decreased the release of the inflammatory mediator prostaglandin E2,[158] downregulated IL-6 messenger RNA levels, reduced the expression of profibrotic markers during wound healing and decreased reactive oxygen species levels.[159]

Safety Summary:
Quercetin is considered safe and well tolerated with no interactions expected at the recommended dose.[160] Safety of quercetin has been established in numerous clinical trials.[161-174] Contraindicated in persons with a known hypersensitivity to quercetin. Adverse effects are rare and may include nausea, dyspnoea, headache and mild tingling of the extremities.[16,175] Not recommended during pregnancy and breastfeeding as safety has not been scientifically established during these times.[161]

Coenzyme Q10 (Ubiquinone)

Medicinal Actions:
Antiinflammatory, antioxidant, immune stimulating, immune modulating, tissue protection.[16,176]

Scientific Evidence:
CoQ10 is a fat soluble antioxidant vitamin used in every cell of the body. It is necessary for cellular integrity and intracellular energy production[16] and serves as an essential co-factor in mitochondrial electron transport chain reactions.[177] CoQ10 is required as a key component for adenosine triphosphate (ATP) production and cellular respiration.[177] It also acts as a powerful antioxidant in the inner mitochondrial membrane.[16] At the mitochondrial level, CoQ10 is essential for the optimal function of the immune system.[178] Metabolically active cells such as heart, immune system, gingiva and gastric mucosa are susceptible to CoQ10 deficiency due to their greater requirements for normal cellular function.[176,179] A deficiency of CoQ10 has been found in the gingiva of individuals with periodontal disease.[176,180] People with gum disease have also been found to have lower circulating levels of CoQ10 when compared with those without the disease.[181]

In clinical research CoQ10 has been used both topically and internally for the treatment of periodontal disease.[182-184] As a sole treatment, topical application of CoQ10 to the periodontal pocket has been shown to significantly reduce gingival crevicular fluid flow, probing depth and attachment loss, and improve the gingival index, bleeding on probing and peptidase activity of periodontopathic microorganisms.[182] Topical application of CoQ10 gel alone and as adjunct with mechanical debridement has been shown to improve periodontal parameters including the plaque index and gingival index, bleeding on probing, probing pocket depth and clinical attachment level.[185-187]

Oral administration of CoQ10 has been shown to increase the concentration of CoQ10 in the diseased gingiva and effectively suppress advanced periodontal inflammation.[176] Supplementation of CoQ10 in patients with periodontal disease has also demonstrated faster tissue repair and healing of the gums when compared with placebo.[183]

Safety Summary:
Supplementation with CoQ10 is considered safe and well tolerated.[16] Adverse effects such as dizziness, nausea, epigastric discomfort, anorexia, diarrhoea, photophobia, irritability and skin rash may occur with higher doses (> 200 mg per day).[16,188] Considered safe in pregnancy during the final trimester.[16] Doses of 200 mg per day of CoQ10 have been safely used for five months during pregnancy (from weeks 16 to 20) in women at risk of developing preeclampsia.[189] Avoid using during breastfeeding due to a lack of safety data.[190]

Myrrh Resin

Medicinal Actions:
Antiinflammatory,[16] antimicrobial, astringent, vulnerary.[191,192]

Scientific Evidence:
Myrrh resin is a sticky, water-insoluble substance extracted from the bark of the *Commiphora* plant. Traditionally it has been considered an important herbal medicine throughout the Middle East, China and India since biblical times.[16] The use of myrrh in traditional Western herbal medicine includes mouth ulcers, inflammations of the gums and oral mucosa (including gingivitis and stomatitis), as well as pharyngitis, laryngitis and respiratory infections.[191,192] The three main active compounds of myrrh include the resin, the gum, and the volatile oil.[191,192] Myrrh resin has strong antimicrobial, antiinflammatory, vulnerary and astringent properties and has a soothing effect on inflamed tissues in the mouth and throat.[191,192]

AUTHORS: Corene Humphreys, ND, BHSc, Dip Med Herb, Dip Hom, QTA (Microbiology). | Anita Kasa, BNat, Dip Herb Med, Dip Nutr, Dip Yoga.

NUTRITIONALMEDICINENZ.COM / BIOCIDIN.NZ.

PHONE: NZ: 09 425 4250 / 021 941 556. AUST: 001169 425 4250 /00116 21 941 556.

Myrrh is often used as a component of gargles, mouthwashes, toothpastes or paints for prevention and treatment of dental ailments.[16] In clinical research, herbal-based toothpaste composed of sodium bicarbonate and herbal extracts including chamomile, echinacea, sage, myrrh, rhatany and peppermint oil have been shown to be as effective as the conventionally formulated dentifrice in the control of plaque and gingivitis.[40] In another study using the 4-day plaque regrowth model, the use of mouth rinse made up of eugenol, thymol, chamomile, myrrh, and rhatany demonstrated significant plaque inhibitory effects.[193]
In vitro research shows that the sesquiterpene fractions extracted from myrrh resin possess antibacterial and antifungal activity by inhibiting the growth of standard pathogenic strains of *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Candida albicans*.[194]

Safety Summary:
Considered safe at the recommended dosage.[14] Contraindicated in persons with known hypersensitivity to myrrh.[192] Side effects may include a burning sensation on the skin or mucous membranes. Contraindicated during pregnancy and breastfeeding.[14]

Clove (*Syzygium aromaticum*) Essential Oil

Medicinal Actions:
Analgesic, antiinflammatory, antimicrobial,[195-197] antioxidant,[198] antiseptic.[117]

Scientific Evidence:
Clove essential oil has been used traditionally as an anaesthetic for toothache, skin infections, digestive upsets, parasite eradication, as well as a natural flavouring agent. Due to its eugenol and other polyphenolic components clove oil exerts potent antimicrobial, antiinflammatory and antioxidant properties.[198]

Based on *in vitro* research, clove essential oil may be a potential natural antibacterial agent against cariogenic bacteria and a natural agent for the prevention of periodontitis. The eugenol extracted from clove has been shown to exhibit antibacterial activity against *Porphyromonas gingivalis* (*in vitro* research). Other therapeutic effects of eugenol include its ability to damage to the cell membrane and destroy the integrity of plasmatic membranes of bacteria. In addition, eugenol has been shown to supress biofilm formation, reduce preformed biofilms and down-regulate the expression of virulence factor genes related to the biofilm of *Porphyromonas gingivalis*.[195] Clove essential oil and its main compounds have demonstrated antibacterial activity *in vitro* against the following oral pathogens: *Streptococcus mutans*, *Streptococcus sanguinis*, *Streptococcus sobrinus*, *Streptococcus ratti*, *Streptococcus criceti*, *Streptococcus anginosus*, *Streptococcus gordonii*, *Actinobacillus actinomycetemcomitans*, *Fusobacterium nucleatum*, *Prevotella intermedia*, and *Porphylomonas gingivalis* either alone or in combination with the antibiotic ampicillin.[196,199]

Based on further *in vitro* experiments, clove essential oil may also exhibit antimicrobial properties against bacteria involved in dental caries such as Gram-positive *Streptococcus salivarius*, *Lactobacillus* sp., *Bacillus* sp., *Micrococcus* sp., *Staphylococcus aureus* and Gram-negative *Halobacterium* sp., *Veilonella* sp. and *Pseudomonas* sp. including *Pseudomonas aeruginosa*.[197]

Safety Summary:
Clove essential oil is considered safe at the dose recommended. In sensitive individuals, the oil may cause dermal irritation.[200] Exercise caution during pregnancy and breastfeeding as safety has not been scientifically established during these times, avoid using in amounts greater than those typically found in food.[201]

AUTHORS: Corene Humphreys, ND, BHSc, Dip Med Herb, Dip Hom, QTA (Microbiology). | Anita Kasa, BNat, Dip Herb Med, Dip Nutr, Dip Yoga.

NUTRITIONALMEDICINENZ.COM / BIOCIDIN.NZ.

PHONE: NZ: 09 425 4250 / 021 941 556. AUST: 001169 425 4250 /00116 21 941 556.

Peppermint (*Mentha x piperita)* Essential Oil

Medicinal Actions:
Anticariogenic,[202] antimicrobial,[203] antiseptic.[117]

Scientific Evidence:
Peppermint oil has been extensively used in food favoring, toothpastes and mouthwashes, soaps, detergents and perfumes.[117] Its main active chemical composition is predominantly composed of menthol, menthone, 1.8-cineole, methyl acetate, methofuran, isomethone, limonene, α-pinene and ß-pinene.[117]

In clinical research, herbal-based toothpaste composed of sodium bicarbonate and herbal extracts including chamomile, echinacea, sage, myrrh, rhatany and peppermint oil has been shown to be as effective as the conventionally formulated dentifrice in the control of plaque and gingivitis.[40] Peppermint essential oil has also demonstrated antimicrobial activity against cariogenic oral pathogens by inhibiting the growth of *Streptococcus mutans* and *Lactobacillus casei* (*in vitro* research).[202]

Based on other *in vitro* experiments, peppermint essential oil may be considered a safe natural agent in the prevention of dental biofilm formation.[203,204] It has been shown to exert significant antimicrobial effects against *Streptococcus mutans* and *Streptococcus pyogenes.*[203,204] When compared with chlorhexidine, peppermint essential oil significantly decreased bacterial adhesion and reduced bacterial viability in biofilms.[203,204] *In vivo* research shows that peppermint essential oil blended toothpaste is significantly more effective at reducing the formation of biofilms when compared to chlorhexidine.[204]

Safety Summary:
Peppermint essential oil is considered safe, nontoxic and nonirritating.[117] It may occasionally be sensitizing and should not be used on the face of infants and small children.[117] No adverse effects are expected during pregnancy and breastfeeding at the dose recommended.[14]

AUTHORS: Corene Humphreys, ND, BHSc, Dip Med Herb, Dip Hom, QTA (Microbiology). | Anita Kasa, BNat, Dip Herb Med, Dip Nutr, Dip Yoga.

NUTRITIONALMEDICINENZ.COM / BIOCIDIN.NZ.

PHONE: NZ: 09 425 4250 / 021 941 556. AUST: 001169 425 4250 /00116 21 941 556.

References

1. Kulkarni PR, Yadav JD, Vaidya KA. Liposomes: A Novel Drug Delivery System. *International Journal of Current Pharmaceutical Research.* 2011;3(2):10-18.
2. Akbarzadeh A, Rezaei-Sadabady R, Davaran S, et al. Liposome: classification, preparation, and applications. *Nanoscale research letters.* 2013;8(1):102.
3. Samad A, Sultana Y, Aqil M. Liposomal drug delivery systems: an update review. *Curr Drug Deliv.* 2007;4(4):297-305.
4. Mufamadi MS, Pillay V, Choonara YE, et al. A Review on Composite Liposomal Technologies for Specialized Drug Delivery. *Journal of Drug Delivery.* 2011;2011:939851.
5. Amol K, Pratibha P. Novel Drug Delivery System in Herbal's. *International Journal of Pharmaceutical, Chemical and Biological Sciences.* 2014;4(4):910-930.
6. Kulkarni GT. Herbal Drug Delivery Systems: An Emerging Area in Herbal Drug Research. *Journal of Chronotherapy and Drug Delivery.* 2011;2(3).
7. Nguyen S, Hiorth M, Rykke M, Smistad G. The potential of liposomes as dental drug delivery systems. *Eur J Pharm Biopharm.* 2011;77(1):75-83.
8. Nguyen S, Hiorth M, Rykke M, Smistad G. Polymer coated liposomes for dental drug delivery--interactions with parotid saliva and dental enamel. *Eur J Pharm Sci.* 2013;50(1):78-85.
9. Rothchild D, J. Preliminary Report of Activity of Dentalcidin LS in Oral Cavitation Pathogens as evidenced by DNA Analysis. Durango, Colorado2018.
10. Rothchild D, J. Preliminary Report of Activity of Dentalcidin LS on dental plaque as evidenced by Phase Contrast Microscopy. Durango, Colorado2018.
11. Riihinen K, Ryynanen A, Toivanen M, Kononen E, Torronen R, Tikkanen-Kaukanen C. Antiaggregation potential of berry fractions against pairs of Streptococcus mutans with Fusobacterium nucleatum or Actinomyces naeslundii. *Phytother Res.* 2011;25(1):81-87.
12. Puupponen-Pimia R, Nohynek L, Alakomi HL, Oksman-Caldentey KM. The action of berry phenolics against human intestinal pathogens. *BioFactors (Oxford, England).* 2005;23(4):243-251.
13. Fisher C. *Materia Medica of Western Herbs.* Nelson, New Zealand: Vitex Medica; 2009.
14. Bone K. *A Clinical Guide to Blending Liquid Herbs: Herbal Formulations for the Individual Patient.* Edinburgh, Scotland: Churchill Livingstone; 2003.
15. Braun L, Cohen M. *Herbs and Natural Supplements an Evidenced Based Guide.* 3rd ed. Chatswood, NSW: Churchill Livingstone; 2010.
16. Braun L, Cohen M. *Herbs and Natural Supplements an Evidenced Based Guide.* Vol 2. 4th ed. Chatswood, NSW: Elsevier Australia; 2015.
17. Jakesevic M, Xu J, Aaby K, Jeppsson B, Ahrne S, Molin G. Effects of bilberry (Vaccinium myrtillus) in combination with lactic acid bacteria on intestinal oxidative stress induced by ischemia-reperfusion in mouse. *Journal of agricultural and food chemistry.* 2013;61(14):3468-3478.
18. Jakesevic M, Aaby K, Borge GI, Jeppsson B, Ahrne S, Molin G. Antioxidative protection of dietary bilberry, chokeberry and Lactobacillus plantarum HEAL19 in mice subjected to intestinal oxidative stress by ischemia-reperfusion. *BMC complementary and alternative medicine.* 2011;11:8.
19. Karlsen A, Paur I, Bohn SK, et al. Bilberry juice modulates plasma concentration of NF-kappaB related inflammatory markers in subjects at increased risk of CVD. *European journal of nutrition.* 2010;49(6):345-355.

AUTHORS: Corene Humphreys, ND, BHSc, Dip Med Herb, Dip Hom, QTA (Microbiology). | Anita Kasa, BNat, Dip Herb Med, Dip Nutr, Dip Yoga.

NUTRITIONALMEDICINENZ.COM / BIOCIDIN.NZ.

PHONE: NZ: 09 425 4250 / 021 941 556. AUST: 001169 425 4250 /00116 21 941 556.

20. Widen C, Coleman M, Criten S, Karlgren-Andersson P, Renvert S, Persson GR. Consumption of bilberries controls gingival inflammation. *International journal of molecular sciences.* 2015;16(5):10665-10673.
21. Kumarasamy B, Manipal S, Duraisamy P, Ahmed A, Mohanaganesh S, Jeevika C. Role of aqueous extract of morinda citrifolia (Indian noni) ripe fruits in inhibiting dental caries-causing streptococcus mutans and streptococcus mitis. *Journal of dentistry (Tehran, Iran).* 2014;11(6):703-710.
22. Serafini MR, Santos RC, Guimaraes AG, et al. Morinda citrifolia Linn leaf extract possesses antioxidant activities and reduces nociceptive behavior and leukocyte migration. *Journal of medicinal food.* 2011;14(10):1159-1166.
23. Jainkittivong A, Butsarakamruha T, Langlais RP. Antifungal activity of Morinda citrifolia fruit extract against Candida albicans. *Oral surgery, oral medicine, oral pathology, oral radiology, and endodontics.* 2009;108(3):394-398.
24. Banerjee S, Johnson AD, Csiszar K, Wansley DL, McGeady P. An extract of Morinda citrifolia interferes with the serum-induced formation of filamentous structures in Candida albicans and inhibits germination of Aspergillus nidulans. *The American journal of Chinese medicine.* 2006;34(3):503-509.
25. West BJ, White LD, Jensen CJ, Palu AK. A double-blind clinical safety study of noni fruit juice. *Pacific health dialog.* 2009;15(2):21-32.
26. Wang MY, Hurn J, Peng L, Nowicki D, Anderson G. A multigeneration reproductive and developmental safety evaluation of authentic Morinda citrifolia (noni) juice. *The Journal of toxicological sciences.* 2011;36(1):81-85.
27. Lee DG, Kim HK, Park Y, et al. Gram-positive bacteria specific properties of silybin derived from Silybum marianum. *Arch Pharm Res.* 2003;26(8):597-600.
28. Bannwart CF, Peracoli JC, Nakaira-Takahagi E, Peracoli MT. Inhibitory effect of silibinin on tumour necrosis factor-alpha and hydrogen peroxide production by human monocytes. *Natural product research.* 2010;24(18):1747-1757.
29. Shahidi M, Vaziri F, Haerian A, et al. Proliferative and Anti-Inflammatory Effects of Resveratrol and Silymarin on Human Gingival Fibroblasts: A View to the Future. *Journal of dentistry (Tehran, Iran).* 2017;14(4):203-211.
30. Mills S, Bone K. *The Essential Guide to Herbal Safety.* Philadelphia, U.S.A.: Churchill Livingstone; 2005.
31. Gan XH, Zhang L, Heber D, Bonavida B. Mechanism of activation of human peripheral blood NK cells at the single cell level by Echinacea water soluble extracts: recruitment of lymphocyte-target conjugates and killer cells and activation of programming for lysis. *International immunopharmacology.* 2003;3(6):811-824.
32. Tamta H, Pugh ND, Balachandran P, Moraes R, Sumiyanto J, Pasco DS. Variability in in vitro macrophage activation by commercially diverse bulk echinacea plant material is predominantly due to bacterial lipoproteins and lipopolysaccharides. *Journal of agricultural and food chemistry.* 2008;56(22):10552-10556.
33. Pugh ND, Tamta H, Balachandran P, et al. The majority of in vitro macrophage activation exhibited by extracts of some immune enhancing botanicals is due to bacterial lipoproteins and lipopolysaccharides. *International immunopharmacology.* 2008;8(7):1023-1032.
34. Pugh ND, Jackson CR, Pasco DS. Total bacterial load within Echinacea purpurea, determined using a new PCR-based quantification method, is correlated with LPS levels and in vitro macrophage activity. *Planta medica.* 2013;79(1):9-14.
35. Sullivan AM, Laba JG, Moore JA, Lee TD. Echinacea-induced macrophage activation. *Immunopharmacology and immunotoxicology.* 2008;30(3):553-574.
36. Hudson JB. Applications of the phytomedicine Echinacea purpurea (Purple Coneflower) in infectious diseases. *Journal of biomedicine & biotechnology.* 2012;2012:769896.
37. Bany J, Siwicki AK, Zdanowska D, Sokolnicka I, Skopinska-Rozewska E, Kowalczyk M. Echinacea purpurea stimulates cellular immunity and anti-bacterial defence independently of the strain of mice. *Polish journal of veterinary sciences.* 2003;6(3 Suppl):3-5.
38. Sharma SM, Anderson M, Schoop SR, Hudson JB. Bactericidal and anti-inflammatory properties of a standardized Echinacea extract (Echinaforce): dual actions against respiratory bacteria. *Phytomedicine.* 2010;17(8-9):563-568.
39. Sterer N, Rubinstein Y. Effect of various natural medicinals on salivary protein putrefaction and malodor production. *Quintessence international (Berlin, Germany : 1985).* 2006;37(8):653-658.
40. Mullally BH, James JA, Coulter WA, Linden GJ. The efficacy of a herbal-based toothpaste on the control of plaque and gingivitis. *Journal of clinical periodontology.* 1995;22(9):686-689.
41. Levine WZ, Samuels N, Bar Sheshet ME, Grbic JT. A novel treatment of gingival recession using a botanical topical gingival patch and mouthrinse. *The journal of contemporary dental practice.* 2013;14(5):948-953.
42. Samuels N, Grbic JT, Saffer AJ, Wexler ID, Williams RC. Effect of an herbal mouth rinse in preventing periodontal inflammation in an experimental gingivitis model: a pilot study. *Compend Contin Educ Dent.* 2012;33(3):204-206, 208-211.
43. Grbic J, Wexler I, Celenti R, Altman J, Saffer A. A phase II trial of a transmucosal herbal patch for the treatment of gingivitis. *Journal of the American Dental Association (1939).* 2011;142(10):1168-1175.
44. Brendler T, Grünwald J, Jänicke C. Echinaceae angustifoliae herba. In: Heilpflanzen - Herbal Remedies. Medpharm Scientific Publishers; 2003. Accessed March 1st, 2011.
45. Hwang BY, Roberts SK, Chadwick LR, Wu CD, Kinghorn AD. Antimicrobial constituents from goldenseal (the Rhizomes of Hydrastis canadensis) against selected oral pathogens. *Planta medica.* 2003;69(7):623-627.
46. Mills S, Bone K. *Principles and Practice of Phytotherapy.* London, England: Churchill Livingstone; 2000.
47. Natural Standard. Bottom Line Monograph: Goldenseal (*Hydrastis canadensis*). http://www.naturalstandard.net. Accessed March 1st, 2011.
48. Scazzocchio F, Cometa MF, Tomassini L, Palmery M. Antibacterial activity of Hydrastis canadensis extract and its major isolated alkaloids. *Planta medica.* 2001;67(6):561-564.

AUTHORS: Corene Humphreys, ND, BHSc, Dip Med Herb, Dip Hom, QTA (Microbiology). | Anita Kasa, BNat, Dip Herb Med, Dip Nutr, Dip Yoga.

NUTRITIONALMEDICINENZ.COM / BIOCIDIN.NZ.

PHONE: NZ: 09 425 4250 / 021 941 556. AUST: 001169 425 4250 /00116 21 941 556.

49. Cech NB, Junio HA, Ackermann LW, Kavanaugh JS, Horswill AR. Quorum quenching and antimicrobial activity of goldenseal (Hydrastis canadensis) against methicillin-resistant Staphylococcus aureus (MRSA). *Planta medica.* 2012;78(14):1556-1561.
50. Junio HA, Sy-Cordero AA, Ettefagh KA, et al. Synergy-directed fractionation of botanical medicines: a case study with goldenseal (Hydrastis canadensis). *Journal of natural products.* 2011;74(7):1621-1629.
51. Wang X, Yao X, Zhu Z, et al. Effect of berberine on Staphylococcus epidermidis biofilm formation. *International journal of antimicrobial agents.* 2009;34(1):60-66.
52. Rutherford ST, Bassler BL. Bacterial quorum sensing: its role in virulence and possibilities for its control. *Cold Spring Harbor perspectives in medicine.* 2012;2(11).
53. Xie Q, Johnson BR, Wenckus CS, Fayad MI, Wu CD. Efficacy of berberine, an antimicrobial plant alkaloid, as an endodontic irrigant against a mixed-culture biofilm in an in vitro tooth model. *Journal of endodontics.* 2012;38(8):1114-1117.
54. Zhong M, Liu B, Wang X, et al. De novo characterization of Lentinula edodes C(91-3) transcriptome by deep Solexa sequencing. *Biochem Biophys Res Commun.* 2013;431(1):111-115.
55. Jung BG, Lee JA, Lee BJ. Immunoprophylactic effects of shiitake mushroom (Lentinula edodes) against Bordetella bronchiseptica in mice. *Journal of microbiology (Seoul, Korea).* 2012;50(6):1003-1008.
56. Lee KH, Morris-Natschke SL, Yang X, et al. Recent progress of research on medicinal mushrooms, foods, and other herbal products used in traditional Chinese medicine. *J Tradit Complement Med.* 2012;2(2):84-95.
57. Signoretto C, Marchi A, Bertoncelli A, et al. Effects of mushroom and chicory extracts on the shape, physiology and proteome of the cariogenic bacterium Streptococcus mutans. *BMC complementary and alternative medicine.* 2013;13:117.
58. Signoretto C, Burlacchini G, Marchi A, et al. Testing a low molecular mass fraction of a mushroom (Lentinus edodes) extract formulated as an oral rinse in a cohort of volunteers. *Journal of biomedicine & biotechnology.* 2011;2011:857987.
59. Lingstrom P, Zaura E, Hassan H, et al. The anticaries effect of a food extract (shiitake) in a short-term clinical study. *Journal of biomedicine & biotechnology.* 2012;2012:217164.
60. Spratt DA, Daglia M, Papetti A, et al. Evaluation of plant and fungal extracts for their potential antigingivitis and anticaries activity. *Journal of biomedicine & biotechnology.* 2012;2012:510198.
61. Ciric L, Tymon A, Zaura E, et al. In vitro assessment of shiitake mushroom (Lentinula edodes) extract for its antigingivitis activity. *Journal of biomedicine & biotechnology.* 2011;2011:507908.
62. Canesi L, Borghi C, Stauder M, et al. Effects of fruit and vegetable low molecular mass fractions on gene expression in gingival cells challenged with Prevotella intermedia and Actinomyces naeslundii. *Journal of biomedicine & biotechnology.* 2011;2011:230630.
63. Yano A, Kikuchi S, Yamashita Y, Sakamoto Y, Nakagawa Y, Yoshida Y. The inhibitory effects of mushroom extracts on sucrose-dependent oral biofilm formation. *Applied microbiology and biotechnology.* 2010;86(2):615-623.
64. Shouji N, Takada K, Fukushima K, Hirasawa M. Anticaries effect of a component from shiitake (an edible mushroom). *Caries research.* 2000;34(1):94-98.
65. Gaullier JM, Sleboda J, Ofjord ES, et al. Supplementation with a soluble beta-glucan exported from Shiitake medicinal mushroom, Lentinus edodes (Berk.) singer mycelium: a crossover, placebo-controlled study in healthy elderly. *International journal of medicinal mushrooms.* 2011;13(4):319-326.
66. Natural Medicines Comprehensive Database. Shitake Mushroom Monograph. http://naturaldatabase.therapeuticresearch.com. Accessed December 22nd, 2013.
67. Poblocka-Olech L, van Nederkassel AM, Vander Heyden Y, Krauze-Baranowska M, Glod D, Baczek T. Chromatographic analysis of salicylic compounds in different species of the genus Salix. *Journal of separation science.* 2007;30(17):2958-2966.
68. Bonaterra GA, Heinrich EU, Kelber O, Weiser D, Metz J, Kinscherf R. Anti-inflammatory effects of the willow bark extract STW 33-I (Proaktiv((R))) in LPS-activated human monocytes and differentiated macrophages. *Phytomedicine.* 2010;17(14):1106-1113.
69. Bonaterra GA, Kelber O, Weiser D, Metz J, Kinscherf R. In vitro anti-proliferative effects of the willow bark extract STW 33-I. *Arzneimittel-Forschung.* 2010;60(6):330-335.
70. Drummond EM, Harbourne N, Marete E, et al. Inhibition of proinflammatory biomarkers in THP1 macrophages by polyphenols derived from chamomile, meadowsweet and willow bark. *Phytother Res.* 2012;27(4):588-594.
71. Jakobsen TH, van Gennip M, Phipps RK, et al. Ajoene, a sulfur-rich molecule from garlic, inhibits genes controlled by quorum sensing. *Antimicrob Agents Chemother.* 2012;56(5):2314-2325.
72. Bhardwaj AK, Vinothkumar K, Rajpara N. Bacterial quorum sensing inhibitors: attractive alternatives for control of infectious pathogens showing multiple drug resistance. *Recent patents on anti-infective drug discovery.* 2013;8(1):68-83.
73. Bakhshi M, Taheri JB, Shabestari SB, Tanik A, Pahlevan R. Comparison of therapeutic effect of aqueous extract of garlic and nystatin mouthwash in denture stomatitis. *Gerodontology.* 2012;29(2):e680-684.
74. Groppo FC, Ramacciato JC, Simoes RP, Florio FM, Sartoratto A. Antimicrobial activity of garlic, tea tree oil, and chlorhexidine against oral microorganisms. *International dental journal.* 2002;52(6):433-437.
75. Groppo FC, Ramacciato JC, Motta RH, Ferraresi PM, Sartoratto A. Antimicrobial activity of garlic against oral streptococci. *Int J Dent Hyg.* 2007;5(2):109-115.
76. Chavan SD, Shetty NL, Kanuri M. Comparative evaluation of garlic extract mouthwash and chlorhexidine mouthwash on salivary Streptococcus mutans count - an in vitro study. *Oral health & preventive dentistry.* 2010;8(4):369-374.

AUTHORS: Corene Humphreys, ND, BHSc, Dip Med Herb, Dip Hom, QTA (Microbiology). | Anita Kasa, BNat, Dip Herb Med, Dip Nutr, Dip Yoga.

NUTRITIONALMEDICINENZ.COM / BIOCIDIN.NZ.

PHONE: NZ: 09 425 4250 / 021 941 556. AUST: 001169 425 4250 /00116 21 941 556.

77. Houshmand B, Mahjour F, Dianat O. Antibacterial effect of different concentrations of garlic (Allium sativum) extract on dental plaque bacteria. *Indian J Dent Res.* 2013;24(1):71-75.
78. Shetty S, Thomas B, Shetty V, Bhandary R, Shetty RM. An in-vitro evaluation of the efficacy of garlic extract as an antimicrobial agent on periodontal pathogens: A microbiological study. *Ayu.* 2013;34(4):445-451.
79. Bakri IM, Douglas CW. Inhibitory effect of garlic extract on oral bacteria. *Archives of oral biology.* 2005;50(7):645-651.
80. Jain I, Jain P, Bisht D, Sharma A, Srivastava B, Gupta N. Use of traditional Indian plants in the inhibition of caries-causing bacteria--Streptococcus mutans. *Brazilian dental journal.* 2015;26(2):110-115.
81. Fani MM, Kohanteb J, Dayaghi M. Inhibitory activity of garlic (Allium sativum) extract on multidrug-resistant Streptococcus mutans. *Journal of the Indian Society of Pedodontics and Preventive Dentistry.* 2007;25(4):164-168.
82. Bachrach G, Jamil A, Naor R, Tal G, Ludmer Z, Steinberg D. Garlic allicin as a potential agent for controlling oral pathogens. *Journal of medicinal food.* 2011;14(11):1338-1343.
83. Munoz-Gonzalez I, Thurnheer T, Bartolome B, Moreno-Arribas MV. Red wine and oenological extracts display antimicrobial effects in an oral bacteria biofilm model. *Journal of agricultural and food chemistry.* 2014;62(20):4731-4737.
84. Furiga Chusseau A, Roques C, Badet C. Preventive effects of an original combination of grape seed polyphenols with amine fluoride on dental biofilm formation and oxidative damage by oral bacteria. *Journal of applied microbiology.* 2013.
85. Su X, Howell AB, D'Souza DH. Antibacterial effects of plant-derived extracts on methicillin-resistant Staphylococcus aureus. *Foodborne pathogens and disease.* 2012;9(6):573-578.
86. Govindaraj J, Emmadi P, Deepalakshmi, Rajaram V, Prakash G, Puvanakrishnan R. Protective effect of proanthocyanidins on endotoxin induced experimental periodontitis in rats. *Indian journal of experimental biology.* 2010;48(2):133-142.
87. Xie Q, Bedran-Russo AK, Wu CD. In vitro remineralization effects of grape seed extract on artificial root caries. *Journal of dentistry.* 2008;36(11):900-906.
88. Benjamin S, Sharma R, Thomas SS, Nainan MT. Grape seed extract as a potential remineralizing agent: a comparative in vitro study. *The journal of contemporary dental practice.* 2012;13(4):425-430.
89. Alkhawajah AM. Studies on the antimicrobial activity of juglans regia. *The American journal of Chinese medicine.* 1997;25(2):175-180.
90. Amarowicz R, Dykes GA, Pegg RB. Antibacterial activity of tannin constituents from Phaseolus vulgaris, Fagoypyrum esculentum, Corylus avellana and Juglans nigra. *Fitoterapia.* 2008;79(3):217-219.
91. McGuffin M, Hobbs C, Upton R, Goldberg A eds. *American Herbal Products Association's Botanical Safety Handbook.* Boca Raton, FL: CRC Press, LLC; 1997.
92. Inbaraj JJ, Chignell CF. Cytotoxic action of juglone and plumbagin: a mechanistic study using HaCaT keratinocytes. *Chemical research in toxicology.* 2004;17(1):55-62.
93. Natural Medicines Comprehensive Database. Black Walnut Monograph. http://naturaldatabase.therapeuticresearch.com. Accessed July 17th, 2012.
94. Godevac D, Tesevic V, Vajs V, Milosavljevic S, Stankovic M. Antioxidant properties of raspberry seed extracts on micronucleus distribution in peripheral blood lymphocytes. *Food Chem Toxicol.* 2009;47(11):2853-2859.
95. Mullen W, McGinn J, Lean ME, et al. Ellagitannins, flavonoids, and other phenolics in red raspberries and their contribution to antioxidant capacity and vasorelaxation properties. *Journal of agricultural and food chemistry.* 2002;50(18):5191-5196.
96. Kahkonen M, Kylli P, Ollilainen V, Salminen JP, Heinonen M. Antioxidant activity of isolated ellagitannins from red raspberries and cloudberries. *Journal of agricultural and food chemistry.* 2012;60(5):1167-1174.
97. Puupponen-Pimia R, Nohynek L, Alakomi HL, Oksman-Caldentey KM. Bioactive berry compounds-novel tools against human pathogens. *Applied microbiology and biotechnology.* 2005;67(1):8-18.
98. Sengul M, Yildiz H, Gungor N, Cetin B, Eser Z, Ercisli S. Total phenolic content, antioxidant and antimicrobial activities of some medicinal plants. *Pakistan journal of pharmaceutical sciences.* 2009;22(1):102-106.
99. Sajjad S, . B, Aghajanshakeri S, Anousheh D, Mikaili P. Ethno-botanical, Bioactivities and Medicinal Mysteries of Fumaria officinalis (Common Fumitory). *2015.* 2015;5(11).
100. Hentschel C, Dressler S, Hahn EG. [Fumaria officinalis (fumitory)--clinical applications]. *Fortschritte der Medizin.* 1995;113(19):291-292.
101. Rakotondramasy-Rabesiaka L, Havet JL, C. Porte, Faucet H. Solid–liquid extraction of protopine from Fumaria officinalis L.—Kinetic modelling of influential parameters. *Industrial Crops and Products.* 2009;29(2-3):516-523.
102. Orhana I, Ozcelik B, Karaoglu T, Sener B. Antiviral and antimicrobial profiles of selected isoquinoline alkaloids from Fumaria and Corydalis species. *Zeitschrift fur Naturforschung.* 2007;62(1-2):19-26.
103. Brinkhaus B, Hentschel C, Von Keudell C, et al. Herbal medicine with curcuma and fumitory in the treatment of irritable bowel syndrome: a randomized, placebo-controlled, double-blind clinical trial. *Scandinavian journal of gastroenterology.* 2005;40(8):936-943.
104. Newall CA, Anderson LA, Philpson JD. *Herbal Medicine: A Guide for Healthcare Professionals.* London, UK: The Pharmaceutical Press; 1996.
105. Nastasijevic B, Lazarevic-Pasti T, Dimitrijevic-Brankovic S, et al. Inhibition of myeloperoxidase and antioxidative activity of Gentiana lutea extracts. *Journal of pharmaceutical and biomedical analysis.* 2012;66:191-196.
106. Prakash O, Singh R, Kumar S, Srivastava S, Ved A. Gentiana lutea Linn. (Yellow Gentian): A comprehensive review. 2017;3:175-181.

AUTHORS: Corene Humphreys, ND, BHSc, Dip Med Herb, Dip Hom, QTA (Microbiology). | Anita Kasa, BNat, Dip Herb Med, Dip Nutr, Dip Yoga.

NUTRITIONALMEDICINENZ.COM / BIOCIDIN.NZ.

PHONE: NZ: 09 425 4250 / 021 941 556. AUST: 001169 425 4250 /00116 21 941 556.

107. Calliste CA, Trouillas P, Allais DP, Simon A, Duroux JL. Free radical scavenging activities measured by electron spin resonance spectroscopy and B16 cell antiproliferative behaviors of seven plants. *Journal of agricultural and food chemistry.* 2001;49(7):3321-3327.
108. Singh A. Phytochemicals of gentianaceae: a review of pharmacological properties. *nt J Pharm Sci Nanotechnol.* 2008;1:33-36.
109. Kusar A, Zupancic A, Sentjurc M, Baricevic D. Free radical scavenging activities of yellow gentian (Gentiana lutea L.) measured by electron spin resonance. *Human & experimental toxicology.* 2006;25(10):599-604.
110. Weckesser S, Engel K, Simon-Haarhaus B, Wittmer A, Pelz K, Schempp CM. Screening of plant extracts for antimicrobial activity against bacteria and yeasts with dermatological relevance. *Phytomedicine.* 2007;14(7-8):508-516.
111. Savikin K, Menkovic N, Zdunic G, Stevic T, Radanovic D, Jankovic T. Antimicrobial activity of Gentiana lutea L. extracts. *Zeitschrift fur Naturforschung.* 2009;64(5-6):339-342.
112. Kanth MR, Prakash AR, Sreenath G, Reddy VS, Huldah S. Efficacy of Specific Plant Products on Microorganisms Causing Dental Caries. *J Clin Diagn Res.* 2016;10(12):Zm01-zm03.
113. Soukoulis S, Hirsch R. The effects of a tea tree oil-containing gel on plaque and chronic gingivitis. *Australian dental journal.* 2004;49(2):78-83.
114. Thomsen NA, Hammer KA, Riley TV, Van Belkum A, Carson CF. Effect of habituation to tea tree (Melaleuca alternifolia) oil on the subsequent susceptibility of Staphylococcus spp. to antimicrobials, triclosan, tea tree oil, terpinen-4-ol and carvacrol. *International journal of antimicrobial agents.* 2013;41(4):343-351.
115. Flores FC, de Lima JA, Ribeiro RF, et al. Antifungal activity of nanocapsule suspensions containing tea tree oil on the growth of Trichophyton rubrum. *Mycopathologia.* 2013;175(3-4):281-286.
116. Kurekci C, Padmanabha J, Bishop-Hurley SL, Hassan E, Al Jassim RA, McSweeney CS. Antimicrobial activity of essential oils and five terpenoid compounds against Campylobacter jejuni in pure and mixed culture experiments. *International journal of food microbiology.* 2013;166(3):450-457.
117. Battaglia S. *The Complete Guide to Aromatherapy.* Brisbane, Australia: The perfect potion (Aust) Pty Ltd; 2003.
118. Forrer M, Kulik EM, Filippi A, Waltimo T. The antimicrobial activity of alpha-bisabolol and tea tree oil against Solobacterium moorei, a Gram-positive bacterium associated with halitosis. *Archives of oral biology.* 2013;58(1):10-16.
119. Santamaria M, Jr., Petermann KD, Vedovello SA, Degan V, Lucato A, Franzini CM. Antimicrobial effect of Melaleuca alternifolia dental gel in orthodontic patients. *American journal of orthodontics and dentofacial orthopedics : official publication of the American Association of Orthodontists, its constituent societies, and the American Board of Orthodontics.* 2014;145(2):198-202.
120. Takarada K, Kimizuka R, Takahashi N, Honma K, Okuda K, Kato T. A comparison of the antibacterial efficacies of essential oils against oral pathogens. *Oral microbiology and immunology.* 2004;19(1):61-64.
121. Hammer KA, Dry L, Johnson M, Michalak EM, Carson CF, Riley TV. Susceptibility of oral bacteria to Melaleuca alternifolia (tea tree) oil in vitro. *Oral microbiology and immunology.* 2003;18(6):389-392.
122. Natural Standard. Professional Monograph: Tea tree oil (*Melaleuca alternifolia*). http://www.naturalstandard.net. Accessed December 24th, 2013.
123. Nazari ZE, Iranshahi M. Biologically active sesquiterpene coumarins from Ferula species. *Phytother Res.* 2011;25(3):315-323.
124. Kanani MR, Rahiminejad MR, Sonboli A, Mozaffarian V, Kazempour Osaloo S, Nejad Ebrahimi S. Chemotaxonomic significance of the essential oils of 18 Ferula species (Apiaceae) from Iran. *Chemistry & biodiversity.* 2011;8(3):503-517.
125. Cowan MM. Plant products as antimicrobial agents. *Clinical microbiology reviews.* 1999;12(4):564-582.
126. Natural Medicines Comprehensive Database. Professional Monograph: Galbanum. http://naturaldatabase.therapeuticresearch.com. Accessed December 25th, 2013.
127. Huang MY, Liao MH, Wang YK, Huang YS, Wen HC. Effect of lavender essential oil on LPS-stimulated inflammation. *The American journal of Chinese medicine.* 2012;40(4):845-859.
128. D'Auria FD, Tecca M, Strippoli V, Salvatore G, Battinelli L, Mazzanti G. Antifungal activity of Lavandula angustifolia essential oil against Candida albicans yeast and mycelial form. *Medical mycology.* 2005;43(5):391-396.
129. Roller S, Ernest N, Buckle J. The antimicrobial activity of high-necrodane and other lavender oils on methicillin-sensitive and -resistant Staphylococcus aureus (MSSA and MRSA). *J Altern Complement Med.* 2009;15(3):275-279.
130. de Rapper S, Kamatou G, Viljoen A, van Vuuren S. The In Vitro Antimicrobial Activity of Lavandula angustifolia Essential Oil in Combination with Other Aroma-Therapeutic Oils. *Evid Based Complement Alternat Med.* 2013;2013:852049.
131. Evandri MG, Battinelli L, Daniele C, Mastrangelo S, Bolle P, Mazzanti G. The antimutagenic activity of Lavandula angustifolia (lavender) essential oil in the bacterial reverse mutation assay. *Food Chem Toxicol.* 2005;43(9):1381-1387.
132. Brendler T, Gruenwald J, Jaenicke C. Comm. E Monograph: Lavandulae flos In: Heilpflanzen - Herbal Remedies. In: Publishers MS, ed2003. Accessed December 25th, 2013.
133. Lambert RJ, Skandamis PN, Coote PJ, Nychas GJ. A study of the minimum inhibitory concentration and mode of action of oregano essential oil, thymol and carvacrol. *Journal of applied microbiology.* 2001;91(3):453-462.
134. Irkin R, Korukluoglu M. Growth inhibition of pathogenic bacteria and some yeasts by selected essential oils and survival of L. monocytogenes and C. albicans in apple-carrot juice. *Foodborne pathogens and disease.* 2009;6(3):387-394.

AUTHORS: Corene Humphreys, ND, BHSc, Dip Med Herb, Dip Hom, QTA (Microbiology). | Anita Kasa, BNat, Dip Herb Med, Dip Nutr, Dip Yoga.

NUTRITIONALMEDICINENZ.COM / BIOCIDIN.NZ.

PHONE: NZ: 09 425 4250 / 021 941 556. AUST: 001169 425 4250 /00116 21 941 556.

135. Miller AB, Cates RG, Lawrence M, et al. The antibacterial and antifungal activity of essential oils extracted from Guatemalan medicinal plants. *Pharmaceutical biology.* 2015;53(4):548-554.
136. Singletary K. Oregano: Overview of the Literature on Health Benefits. 2010;45:129-138.
137. Gilling DH, Kitajima M, Torrey JR, Bright KR. Antiviral efficacy and mechanisms of action of oregano essential oil and its primary component carvacrol against murine norovirus. *Journal of applied microbiology.* 2014;116(5):1149-1163.
138. Sokovic M, Glamoclija J, Marin PD, Brkic D, van Griensven LJ. Antibacterial effects of the essential oils of commonly consumed medicinal herbs using an in vitro model. *Molecules (Basel, Switzerland).* 2010;15(11):7532-7546.
139. Friedman M, Henika PR, Levin CE. Bactericidal activities of health-promoting, food-derived powders against the foodborne pathogens Escherichia coli, Listeria monocytogenes, Salmonella enterica, and Staphylococcus aureus. *Journal of food science.* 2013;78(2):M270-275.
140. Arjoon AV, Saylor CV, May M. In Vitro efficacy of antimicrobial extracts against the atypical ruminant pathogen Mycoplasma mycoides subsp. capri. *BMC complementary and alternative medicine.* 2012;12:169.
141. Eng W, Norman R. Development of an oregano-based ointment with anti-microbial activity including activity against methicillin-resistant Staphlococcus aureus. *J Drugs Dermatol.* 2010;9(4):377-380.
142. Preuss HG, Echard B, Enig M, Brook I, Elliott TB. Minimum inhibitory concentrations of herbal essential oils and monolaurin for gram-positive and gram-negative bacteria. *Mol Cell Biochem.* 2005;272(1-2):29-34.
143. Pozzatti P, Loreto ES, Lopes PG, Athayde ML, Santurio JM, Alves SH. Comparison of the susceptibilities of clinical isolates of Candida albicans and Candida dubliniensis to essential oils. *Mycoses.* 2010;53(1):12-15.
144. Pozzatti P, Loreto ES, Nunes Mario DA, Rossato L, Santurio JM, Aleves SH. Activities of essential oils in the inhibition of Candida albicans and Candida dubliniensis germ tube formation. *Journal de Mycologie Médical.* 2010;20(3):185-189.
145. de Loreto ES, Pozzatti P, Alves Scheid L, Santurio D, Morais Santurio J, Alves SH. Differentiation of Candida dubliniensis from Candida albicans on rosemary extract agar and oregano extract agar. *Journal of clinical laboratory analysis.* 2008;22(3):172-177.
146. Vale-Silva L, Silva MJ, Oliveira D, et al. Correlation of the chemical composition of essential oils from Origanum vulgare subsp. virens with their in vitro activity against pathogenic yeasts and filamentous fungi. *Journal of medical microbiology.* 2012;61(Pt 2):252-260.
147. Natural Medicines Comprehensive Database. Oregano Monograph. 2003; http://naturaldatabase.therapeuticresearch.com. Accessed December 25th, 2013.
148. Geoghegan F, Wong RW, Rabie AB. Inhibitory effect of quercetin on periodontal pathogens in vitro. *Phytother Res.* 2010;24(6):817-820.
149. Anand David AV, Arulmoli R, Parasuraman S. Overviews of Biological Importance of Quercetin: A Bioactive Flavonoid. *Pharmacogn Rev.* 2016;10(20):84-89.
150. Kelly GS. Quercetin. Monograph. *Altern Med Rev.* 2011;16(2):172-194.
151. Corega C, Vaida L, Festila DG, et al. The benefits of Quercitin for dentistry and maxillofacial surgery: a systematic review. *Minerva stomatologica.* 2014.
152. Hamdy AA, Ibrahem MA. Management of aphthous ulceration with topical quercetin: a randomized clinical trial. *The journal of contemporary dental practice.* 2010;11(4):E009-016.
153. Ammar N, Diwany AE, Osman N, Gaafar S, Amin N. Flavonoids as a possible preventive of dental plaque. *Archives of Pharmacal Research.* 1990;13(2):211-213.
154. Palaska I, Papathanasiou E, Theoharides TC. Use of polyphenols in periodontal inflammation. *Eur J Pharmacol.* 2013;720(1-3):77-83.
155. Li M, Xu Z. Quercetin in a lotus leaves extract may be responsible for antibacterial activity. *Archives of Pharmacal Research.* 2008;31(5):640-644.
156. Yue JX, Yang HY, Han L, Zhu MY, Song FF, Huang C. [Inhibitory effect of quercetin on the biofilm formation of Streptococcus mutans]. *Zhonghua kou qiang yi xue za zhi = Zhonghua kouqiang yixue zazhi = Chinese journal of stomatology.* 2016;51(6):368-373.
157. Shahzad M, Millhouse E, Culshaw S, Edwards CA, Ramage G, Combet E. Selected dietary (poly)phenols inhibit periodontal pathogen growth and biofilm formation. *Food & function.* 2015;6(3):719-729.
158. Gomez-Florit M, Monjo M, Ramis JM. Quercitrin for periodontal regeneration: effects on human gingival fibroblasts and mesenchymal stem cells. *Scientific reports.* 2015;5:16593.
159. Gomez-Florit M, Monjo M, Ramis JM. Identification of quercitrin as a potential therapeutic agent for periodontal applications. *Journal of periodontology.* 2014;85(7):966-974.
160. Business Wire. Quercegen Pharmaceuticals LLC Obtains FDA GRAS Notified Status for Its QU995™ Quercetin with Purity Greater Than 99.5% 2011; www.fda.gov/Food/FoodIngredientsPackaging/GenerallyRecognizedasSafeGRAS/GRASListings/ucm235935.htm
161. Natural Medicines Comprehensive Database. Professional Monograph: Quercetin. 2014; http://naturaldatabase.therapeuticresearch.com. Accessed 08/10/2017.
162. Konrad M, Nieman DC, Henson DA, Kennerly KM, Jin F, Wallner-Liebmann SJ. The acute effect of ingesting a quercetin-based supplement on exercise-induced inflammation and immune changes in runners. *International journal of sport nutrition and exercise metabolism.* 2011;21(4):338-346.
163. Knab AM, Shanely RA, Henson DA, et al. Influence of quercetin supplementation on disease risk factors in community-dwelling adults. *Journal of the American Dietetic Association.* 2011;111(4):542-549.
164. Jin F, Nieman DC, Shanely RA, Knab AM, Austin MD, Sha W. The variable plasma quercetin response to 12-week quercetin supplementation in humans. *European journal of clinical nutrition.* 2010;64(7):692-697.

AUTHORS: Corene Humphreys, ND, BHSc, Dip Med Herb, Dip Hom, QTA (Microbiology). | Anita Kasa, BNat, Dip Herb Med, Dip Nutr, Dip Yoga.

NUTRITIONALMEDICINENZ.COM / BIOCIDIN.NZ.

PHONE: NZ: 09 425 4250 / 021 941 556. AUST: 001169 425 4250 /00116 21 941 556.

165. Heinz SA, Henson DA, Austin MD, Jin F, Nieman DC. Quercetin supplementation and upper respiratory tract infection: A randomized community clinical trial. *Pharmacol Res.* 2010;62(3):237-242.
166. Egert S, Wolffram S, Schulze B, et al. Enriched cereal bars are more effective in increasing plasma quercetin compared with quercetin from powder-filled hard capsules. *The British journal of nutrition.* 2012;107(4):539-546.
167. Cialdella-Kam L, Nieman DC, Sha W, Meaney MP, Knab AM, Shanely RA. Dose-response to 3 months of quercetin-containing supplements on metabolite and quercetin conjugate profile in adults. *The British journal of nutrition.* 2013;109(11):1923-1933.
168. Shanely RA, Knab AM, Nieman DC, Jin F, McAnulty SR, Landram MJ. Quercetin supplementation does not alter antioxidant status in humans. *Free radical research.* 2010;44(2):224-231.
169. Nieman DC, Williams AS, Shanely RA, et al. Quercetin's influence on exercise performance and muscle mitochondrial biogenesis. *Medicine and science in sports and exercise.* 2010;42(2):338-345.
170. Nieman DC, Henson DA, Maxwell KR, et al. Effects of quercetin and EGCG on mitochondrial biogenesis and immunity. *Medicine and science in sports and exercise.* 2009;41(7):1467-1475.
171. Nieman DC, Henson DA, Davis JM, et al. Quercetin ingestion does not alter cytokine changes in athletes competing in the Western States Endurance Run. *Journal of interferon & cytokine research : the official journal of the International Society for Interferon and Cytokine Research.* 2007;27(12):1003-1011.
172. Nieman DC, Henson DA, Davis JM, et al. Quercetin's influence on exercise-induced changes in plasma cytokines and muscle and leukocyte cytokine mRNA. *Journal of applied physiology (Bethesda, Md : 1985).* 2007;103(5):1728-1735.
173. Nieman DC, Henson DA, Gross SJ, et al. Quercetin reduces illness but not immune perturbations after intensive exercise. *Medicine and science in sports and exercise.* 2007;39(9):1561-1569.
174. Kaushik D, O'Fallon K, Clarkson PM, Dunne CP, Conca KR, Michniak-Kohn B. Comparison of quercetin pharmacokinetics following oral supplementation in humans. *Journal of food science.* 2012;77(11):H231-238.
175. Shoskes DA, Zeitlin SI, Shahed A, Rajfer J. Quercetin in men with category III chronic prostatitis: a preliminary prospective, double-blind, placebo-controlled trial. *Urology.* 1999;54(6):960-963.
176. Prakash S, Sunitha J, Hans M. Role of coenzyme Q(10) as an antioxidant and bioenergizer in periodontal diseases. *Indian journal of pharmacology.* 2010;42(6):334-337.
177. Jain AK, Mehra NK, Swarnakar NK. Role of Antioxidants for the Treatment of Cardiovascular Diseases: Challenges and Opportunities. *Current pharmaceutical design.* 2015;21(30):4441-4455.
178. Folkers K, Wolaniuk A. Research on coenzyme Q10 in clinical medicine and in immunomodulation. *Drugs under experimental and clinical research.* 1985;11(8):539-545.
179. Kadir AKMS, Rabbi AA, Rahman MM. CoEnzyme Q10: A new horizon in the treatment of periodontal diseases. *International Dental Journal of Students Research.* 2017;5(1):1-6.
180. Littarru GP, Nakamura R, Ho L, Folkers K, Kuzell WC. Deficiency of coenzyme Q 10 in gingival tissue from patients with periodontal disease. *Proc Natl Acad Sci U S A.* 1971;68(10):2332-2335.
181. Overvad K, Diamant B, Holm L, Holmer G, Mortensen SA, Stender S. Coenzyme Q10 in health and disease. *European journal of clinical nutrition.* 1999;53(10):764-770.
182. Hanioka T, Tanaka M, Ojima M, Shizukuishi S, Folkers K. Effect of topical application of coenzyme Q10 on adult periodontitis. *Molecular aspects of medicine.* 1994;15 Suppl:s241-248.
183. Wilkinson EG, Arnold RM, Folkers K, Hansen I, Kishi H. Bioenergetics in clinical medicine. II. Adjunctive treatment with coenzyme Q in periodontal therapy. *Res Commun Chem Pathol Pharmacol.* 1975;12(1):111-123.
184. Wilkinson EG, Arnold RM, Folkers K. Bioenergetics in clinical medicine. VI. adjunctive treatment of periodontal disease with coenzyme Q10. *Res Commun Chem Pathol Pharmacol.* 1976;14(4):715-719.
185. Hans M, Prakash S, Gupta S. Clinical evaluation of topical application of perio-Q gel (Coenzyme Q(10)) in chronic periodontitis patients. *Journal of Indian Society of Periodontology.* 2012;16(2):193-199.
186. Taif MS, Maha SM. An Evaluation of the Effectiveness of Coenzyme Q10 Gel in Management of Patients with Chronic Periodontitis (II inter group comparison). *Oral and Maxillofacial Surgery and Periodontics.* 2016;28(1):127-132.
187. Taif MS, Maha SM. Evaluation of the effectiveness of coenzyme Q10 gel in management of patients with chronic periodontitis (I intra group comparison). *Oral and Maxillofacial Surgery and Periodontics.* 2015;27(2):130-135.
188. Food and Nutrition Board, Institute of Medicine, National Acadamies. *Dietary reference intakes (DRIs): Tolerable upper intake levels (UL), Vitamins.* 2004.
189. Teran E, Hernandez I, Nieto B, Tavara R, Ocampo JE, Calle A. Coenzyme Q10 supplementation during pregnancy reduces the risk of pre-eclampsia. *Int J Gynaecol Obstet.* 2009;105(1):43-45.
190. Natural Medicines Comprehensive Database. Professional Monograph: Coenzyme Q10. 2012; http://naturaldatabase.therapeuticresearch.com. Accessed 29/11/2016.
191. Taheri JB, Azimi S, Rafieian N, Zanjani HA. Herbs in dentistry. *International dental journal.* 2011;61(6):287-296.
192. Bone K, Mills S. *Principles and Practice of Phytotherapy: Modern Herbal Medicine.* Second ed: Churchill Livingstone, Elsevier; 2013.
193. Moran J, Addy M, Roberts S. A comparison of natural product, triclosan and chlorhexidine mouthrinses on 4-day plaque regrowth. *Journal of clinical periodontology.* 1992;19(8):578-582.
194. Dolara P, Corte B, Ghelardini C, et al. Local anaesthetic, antibacterial and antifungal properties of sesquiterpenes from myrrh. *Planta medica.* 2000;66(4):356-358.

AUTHORS: Corene Humphreys, ND, BHSc, Dip Med Herb, Dip Hom, QTA (Microbiology). | Anita Kasa, BNat, Dip Herb Med, Dip Nutr, Dip Yoga.

NUTRITIONALMEDICINENZ.COM / BIOCIDIN.NZ.

PHONE: NZ: 09 425 4250 / 021 941 556. AUST: 001169 425 4250 /00116 21 941 556.

195. Zhang Y, Wang Y, Zhu X, Cao P, Wei S, Lu Y. Antibacterial and antibiofilm activities of eugenol from essential oil of Syzygium aromaticum (L.) Merr. & L. M. Perry (clove) leaf against periodontal pathogen Porphyromonas gingivalis. *Microbial pathogenesis.* 2017;113:396-402.
196. Chaudhari LK, Jawale BA, Sharma S, Sharma H, Kumar CD, Kulkarni PA. Antimicrobial activity of commercially available essential oils against Streptococcus mutans. *The journal of contemporary dental practice.* 2012;13(1):71-74.
197. Gupta C, Kumari A, Garg AP, Catanzaro R, Marotta F. Comparative study of cinnamon oil and clove oil on some oral microbiota. *Acta bio-medica : Atenei Parmensis.* 2011;82(3):197-199.
198. Goñi MG, Roura SI, Ponce AG, Moreira MR. Chapter 39 - Clove (Syzygium aromaticum) Oils A2 - Preedy, Victor R. *Essential Oils in Food Preservation, Flavor and Safety*. San Diego: Academic Press; 2016:349-357.
199. Moon SE, Kim HY, Cha JD. Synergistic effect between clove oil and its major compounds and antibiotics against oral bacteria. *Archives of oral biology.* 2011;56(9):907-916.
200. Rowe RC, Sheskey PJ, Quinn ME, Association AP. *Handbook of Pharmaceutical Excipients.* Pharmaceutical Press; 2009.
201. Natural Medicines Comprehensive Database. Professional Monograph: Clove. 2013; http://naturaldatabase.therapeuticresearch.com. Accessed 02/02/2017.
202. Wiwattanarattanabut K, Choonharuangdej S, Srithavaj T. In Vitro Anti-Cariogenic Plaque Effects of Essential Oils Extracted from Culinary Herbs. *J Clin Diagn Res.* 2017;11(9):Dc30-dc35.
203. Rasooli I, Shayegh S, Taghizadeh M, Astaneh SD. Phytotherapeutic prevention of dental biofilm formation. *Phytother Res.* 2008;22(9):1162-1167.
204. Shayegh S, Rasooli I, Taghizadeh M, Astaneh SD. Phytotherapeutic inhibition of supragingival dental plaque. *Natural product research.* 2008;22(5):428-439.

AUTHORS: Corene Humphreys, ND, BHSc, Dip Med Herb, Dip Hom, QTA (Microbiology). | Anita Kasa, BNat, Dip Herb Med, Dip Nutr, Dip Yoga.

NUTRITIONALMEDICINENZ.COM / BIOCIDIN.NZ.

PHONE: NZ: 09 425 4250 / 021 941 556. AUST: 001169 425 4250 /00116 21 941 556.