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Biocidin – Scientific Validation of Botanical Ingredients

Bilberry extract (*Vaccinium myrtillus*)

Medicinal Actions:
Antiinflammatory, antimicrobial, antioxidant, urinary antiseptic.[1-3]

Scientific Evidence:
Bilberry is rich in phenolic compounds which possess bacteriostatic and antimicrobial properties.[4] In animal models, bilberry has been shown to protect the small intestine from ischemia-reperfusion induced inflammation and oxidative stress. Subsequent to their findings, the authors concluded bilberry as a dietary supplement "may be used to prevent or suppress oxidative stress."[5, 6] As natural antiinflammatory agents, bilberry polyphenols help reduce lipopolysaccharide (LPS)-induced nuclear factor kappa-beta (NF-Kβ) activation.[7]

Based on *in vitro* research, bilberry possesses antiadhesive and antimicrobial properties against the respiratory pathogens *Streptococcus pneumoniae* and *Neisseria meningitidis*.[8, 9] Other organisms bilberry has demonstrated strong antibacterial activity against include *Bacillus cereus*, *Citrobacter freundii*, *Enterococcus faecalis*, *Helicobacter pylori, Salmonella* and *Staphylococcus aureus*.[4, 10-13]

Safety Summary:
Considered safe at the recommended dose.[1] No adverse effects expected during pregnancy and breastfeeding.[2]

Noni (*Morinda citrifolia*)

Medicinal Actions:
Antiinflammatory, antimicrobial, antioxidant.[3, 14]

Scientific Evidence:
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 and antiinflammatory properties.[14] *In vitro* research has shown that noni is highly effective at inhibiting hydroxyl radicals which are known to cause oxidative damage to proteins, lipids and deoxyribonucleic acid (DNA).[14]

As a natural antiinflammatory agent, noni inhibits LPS-induced activation of a number of chemical mediators including cycoloxygenase (COX)-1 and COX-2, nitric oxide and prostaglandins E2 (PGE2) in a dose dependent manner.[15] Noni possess natural immune stimulating properties and based on *in vivo* and *in vitro* studies, enhances both cellular and humoral-mediated immunity.[16]
The active compounds acubin, L-asperuloside and alizarin isolated from noni have demonstrated antibacterial activity against a number of pathogens including *Pseudomonas aeruginosa*, *Proteus morganii*, *Stapylococcus aureus*, *Bacillis subtilis*, *Escherichia coli*, *Salmonella* and *Shigella*.[17] Noni has also been shown to inhibit the activity of enterohemorrhagic *E. coli* (0157) and *Heli1cobacter pylori*.[18]

Traditionally noni was used for tuberculosis infections, which has now been substantiated by *in vitro* studies indicating noni is nearly as effective as Rifampcin (with inhibition rates of 89% and 97% respectively).[19, 20]

Noni has demonstrated antifungl activity against *Candida albicans* in a dose dependent manner.[21] 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. Similarly, noni has been shown to inhibit the germination of spores from the filamentous fungi *Aspergillus nidulans*.[22]

Safety Summary:
No known warnings, precautions or contraindications at the dose recommended.[3, 23] No adverse effects expected during pregnancy and breastfeeding.[3, 24]

Milk Thistle (*Silybum marianum*)

Medicinal Actions:
Antimicrobial, antioxidant, choleretic, hepatic trophorestorative, hepatotprotective.[1, 2]

Scientific Evidence:
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.[1] 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.[25]

Silibinin (an equal extract of silybin A and silybin B) has demonstrated antibacterial activity against methicillin-resistant strains of *Staphylococcus aureus*.[1, 26] When silibinin was combined with the antibiotics oxacilin or ampicillin there was a more than four-fold reduction in the minimum inhibitory bactericidal concentrations. Based on *in vitro* research, silibinin's antimicrobial properties are due to its ability to inhibit ribonucleic acid (RNA) and protein synthesis of Gram-positive organisms (as opposed to attacking the bacterial membrane).[26] Ethanol extracts of silibin have also demonstrated antibacterial activity against *Campylobacter jejuni*.[27]

Silibinin has also demonstrated antioxidant and antiinflammatory properties on LPS-stimulated human monocytes through an inhibitory effect on hydrogen peroxide release and tumor necrosis-alpha (TNF-α) production.[28]

Silymarin also works as a potent antiviral agent. In the trial by Song and Choi, silymarin demonstrated strong antiviral activity against influenza A/PR/8/34 virus when compared with the pharmaceutical agent Oseltamivir (98% vs. 52% respectively).[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, antifungal, antiviral, depurative, immune enhancing, immune modulating, lymphatic.[2, 3, 30]

Scientific Evidence:
Echinacea possesses both antiinflammatory and immuno-stimulating 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 (NK) cell activity in the body.[34, 35]

Echinacea has demonstrated antimicrobial activity against a number of common pathogens including *Streptococcus pyogenes*, *Staphylococcus aureus*, *Haemophilus influenzae*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, *Propionibacterium acnes*, *Legionella pneumophila*, *Clostridium difficile* and *Candida albicans*.[36, 37]

As a natural antiviral agent, echinacea has demonstrated efficacy against a number of viruses including influenza viruses (A and B strains), respiratory synctial virus, rhinovirus, herpes simplex virus (HSV-1), calcivirus and coronavirus.[36, 38-41] Based on *in vitro* research, possible antiviral mechanisms of action for echinacea include proinflammatory cytokine inhibition (specifically interleukin (IL)-6 and IL-8) and upregulation of inducible nitric oxide synthase (i-NOS).[39, 42-44]

Safety Summary:
Contraindicated in persons allergic to plants from the Compositae family.[2] Exercise caution with patients taking immunosuppressant medications (short term use only).[2] No other known warnings, precautions or contraindications.[45] No adverse effects expected during pregnancy and breastfeeding.[2, 30]

Golden Seal (*Hydrastis canadensis*)

Medicinal Actions:
Antibacterial, antihistamine, antiinflammatory, antimicrobial, mucous membrane trophorestorative.[1, 3, 30, 46, 47]

Scientific Evidence:
Golden seal root contains a number of alkaloids, the most abundant of which is berberine. Both *in vivo* and *in vitro* studies have revealed that berberine possesses antimicrobial activity against bacteria, fungi and parasites.[2, 48]

Golden seal 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]

The combined effects of the active constituents in golden seal make this herb a potent antimicrobial agent for a number of Gram-positive and Gram-negative organisms including methicillin-resistant *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus sanguis*, *Bacillus subtilis*, *Mycoplasma mycoides capri*, *Escherichia coli*, *Neisseria gonorrhoeae* isolates (including antibiotic-resistant strains), *Campylobacter jejuni, Vibrio cholera* and *Helicobacter pylori*.[27, 48, 49, 51-54]

One of the key mechanisms by which golden seal inhibits microbial growth is through quenching of the agr quorum sensing (QS) system.[49, 54] 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.[55]

Berberine has demonstrated antifungal activity against non-albicans Candida species (specifically *Candida krusei*, *Candida Kefyr*, *Candida glabrata*, *Candida tropicalis* and *Candida parapsilosis).* When combined with the antimycotic drugs Miconazole or Fluconazole, berberine was able to reduce biofilm formation of pathogenic *C. albicans*.[56]

In vitro studies have shown that berberine possesses significant antimicrobial activity against a number of protozoans including *Giardia lamblia*, *Entamoeba histolytica*, *Trichomonas vaginalis* and *Leishmania donovani*. The mechanism by which golden seal inhibits parasitic growth appears to be through lysis of the trophozoite forms.[57]

Berberine has also been shown to inhibit the growth of several viruses including cytomegalovirus, HSV-I and human H1N1 stains of influenza A viruses. As an antiinflammatory agent, berberine works by inhibiting influenza A-induced production of TNF-α and PGE2 from infected macrophages.[58]

Safety Summary:
Exercise caution in patients with kidney disease.[3] No other known warnings, precautions or contraindications at the dose recommended.[2] Contraindicated during pregnancy in therapeutic doses.[3] Discouraged during breastfeeding in therapeutic doses.[1]

Shiitake mushroom (*Lentinula edodes*)

Medicinal Actions:
Antibacterial, antifungal, antioxidant, immune modulating.[3, 59]

Scientific Evidence:
Shiitake mushroom contains activated hexose correlated compound (AHCC), which possesses immune-modulating properties.[60] Another mechanism by which Shiitake enhances immune function is by increasing IL-2, a T helper (Th)-1 cytokine.[61] In human trials, Shiitake mushroom has also been shown to increase the number of circulating B cells in healthy elderly adults.[62]

Shiitake mushroom also contains the polysaccharides lentinan, LEM, KS-2 and eritadenine, which have demonstrated antimicrobial and antiviral activity.[63] As an antimicrobial agent, lentinan works by activating macrophages and the cytokines TNF-α and IFN-γ with resultant stimulation of T lymphocytes and enhanced immunity.[63]

Based on *in vitro* research, Shiitake mushroom has demonstrated antibacterial activity against a number of organisms including; *Bacillus* sp, *Escherichia coli*, Enterobacter/*Klebsiella* sp., *Serratia* sp., *Pseudomonas aeruginosa*, *Listeria monocytogenes, Salmonella poona, Cupriavidis* sp., *Staphylococcus* sp. (including methicillin-resistant *Staphylococcus aureus* (MRSA)), *Staphylococcus epidermidis*, *Streptococcus pyogenes* and *Enterococcus faecalis*.[64-68]

Shikate has also demonstrated antifungal activity against the following microbes; *Candida albicans*, *Candida glabrata*, *Candida parapsilosis*, *Aspergillus fumigatus*, *Aspergillus niger*, and *Scedosporium apiospermum*.[66-68] Unlike antibiotics, the probiotic strains Bifidobacterium and Lactobacteria are not affected by the antimicrobial activities of Shiitake mushroom.[67]

Safety Summary:
Considered safe and well tolerated at doses of up to 2.5mg per day for 6 weeks.[62] Doses of 9 grams per day of liquid AHCC have also been trailed for two weeks in healthy adults with no changes in blood chemistry markers or significant adverse events.[69] No adverse effects expected during pregnancy and breastfeeding at the dose recommended.[70]

White willow bark (*Salix alba*)

Medicinal Actions:
Analgesic, antiinflammatory.[1]

Scientific Evidence:
The key active constituents of white willow bark comprise of phenolic glyosides including the salicylates salicortin and salicin.[1] Other important actives include the flavonoids naringenin and isosalipurpuroside (also known as eriodictyol) and condensed tannins.[71-73]

Initially it was thought that salicin (converted to salicylic acid *in vivo*) was responsible for the antiinflammatory effects of this herb.[73] More recent evidence suggests that the potent antiinflammatory effect is derived the sum total of the medicinal actives given white willow bark's effects are much broader acting than non-steroidal antiinflammatory drugs (NSAIDs) which contain acetyl salicylic acid.[1, 72] Unlike NSAIDs, white willow bark is not associated with unwanted side effects of gastric erosion.[73]

The synergistic effect of the salicylates, flavonoids and tannis found in white willow bark have been shown to inhibit COX-2 and subsequent generation of free radicals by converting arachidonic acid to prostaglandins.[74] Other downstream products of COX activity include nitric oxide release and up-regulation of proinflammatory cytokines.[72]

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.[72, 75] While the underlying mechanisms have not been fully elucidated, white willow bark appears to induce monocyte apoptosis and block transcription factor NF-Kβ activation.[72, 73] This multifactorial effect is thought to be an innate protective mechanism to control local and systemic inflammatory responses in the body.[72]

Safety Summary:
Contraindicated in people with salicylate sensitivity.[3] No other known warnings, precautions or contraindications at the dose recommended.[3] No adverse effects expected during pregnancy and breastfeeding.[3]

Garlic (*Allium sativum*)

Medicinal Actions:
Anthelmintic, antiinflammatory, antimicrobial, antioxidant.[1]

Scientific Evidence:
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.[76] Crushed garlic contains a number of QS compounds such as ajoene and other organosulfides that are produced as degradation products of allicin.[77, 78]

Both *in vitro* and *in vivio* studies have identified ajoene as the major QS component of garlic that is able to inhibit the expression of 11 virulence genes controlled by QS – these genes are considered crucial for *Pseudomonas aeruginosa* pathogenicity.[77, 79] In addition to *P. aeruginosa*, ajoene has demonstrated antimicrobial activity against the following organisms; *Escherichia coli, Klebsiella pneumoniae*, *Salmonella typhimurium*, *Xanthomonas maltophilia*, *Neisseria gonorrhoea*, *Moraxella cattarhalis*, *Staphylococcus aureus*, *Enterococcus facealis*, *Candida albicans*, *Aspergillus niger* and *Paracoccidioides brasiliensis*.[76, 77, 80, 81]

Garlic has also been shown to be effective against a number of multidrug resistant strains of Gram-negative and Gram-positive bacteria including *Pseudomonas aeruginosa*, *Escherichia coli*, *Bacillus* sp., *Proteus* sp. and *Staphylococcus aureus*.[82, 83]

QS inhibitors such as garlic have demonstrated a synergistic effect when combined with antibiotics. Based on *in vitro* research, the addition of ajoene to a Pseudomonas biofilm plus tobramycin killed more than 90% of the bacteria (compared with no effect when tobramycin was tested in isolation).[77] Synergistic effects have been observed between garlic and gentamicin for infectious diseases caused by *Escherichia coli* strains.[84]

Research shows that garlic has a temporal effect on commensal flora – when initially exposed to the herb, probiotic strains such as lactobacillus are transiently inhibited, followed by a resurgence of growth with bacterial counts comparable to levels preceding garlic intervention.[76]

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, antiinflammatory, antioxidant.[3]

Scientific Evidence:
Grape seed contains over 95% flavonols, which are predominately comprised of oligomeric proanthocyanins (~82%) and active monomeric proanthocyanins (~12%).[85]

Grape seed extracts have demonstrated anitmicrobial activity against a number of respiratory pathogens including *Moraxella cattarhalis*, *Staphylococcus aureus*, *Enterococcus facealis, Streptococcus* sp. Group F*, Streptococcus pneumoniae and Pseudomona aeruginosa*.[86]

Grape seed extract has also demonstrated antibacterial activity against MRSA strains when assayed through *in vitro* experiments. While the underlying mechanism has not been fully elucidated, grape seed appears to reduce microbial growth by disrupting or breaking down cell wall surfaces.[85]

Based on *in vitro* experiments, grape seed extract may improve microbial composition in the gastrointestinal tract by promoting the growth of beneficial bacteria such as *Lactobacillus* sp. and reducing bacterial counts of undesirable organisms such as Clostrida.[87]

Safety Summary: No known warnings, precautions or contraindications at the dose recommended.[3] Exercise caution during pregnancy and breastfeeding as safety has not been scientifically established during these times.[3]

Black Walnut (*Juglans nigra*)

Medicinal Actions:

Anthelmintic, antimicrobial, depurative.[1]

Scientific Evidence:
The main active constituents of black walnut include naphthoquinones (juglone and plumbagin), tannins (ellagic acid) and flavanoids.[1, 30, 88] Tannins comprise ~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 themselves.[89]

Presently, there is little scientific research on this herb regarding its antimicrobial and anthelminthic effects, rather most of the understanding of this herb stems from traditional and folklore use. Based on *in vitro* research, black walnut has demonstrated broad spectrum antimicrobial activity against the following organisms; *Escherichia coli*, *Streptococcus aureus*, *Fusarium oxysporum*, *Bacillus cereus, Erwinia carotovora*, *Micrococcus luteus, Proteus vulgaris*, *Listeria monocytogenes* and *Brochothrix thermosphacta*.[88, 90]

Yeast and fungal organisms susceptible to black walnut comprise of *Candida albicans, Trichophyton rubrum, Aspergillus niger, Penicillium notatum, Pythium ultimum, Rhyzopus nigricans* and *Sacchromyces cerevisiae*.[90]

Safety Summary:
No known warnings, precautions or contraindications at the dose recommended.[30] Contraindicated during pregnancy and breastfeeding in therapeutic doses.[91]

Raspberry (*Rubus idaeus*)

Medicinal Actions:
Antiinflammatory, antimicrobial, antioxidant.[1, 3]
Scientific Evidence:
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.[92-94] Research shows that antioxidant properties of raspberry are attributed to the polyphenolic compounds specficially ellagitannins which are highly effective free radical scavengers.[92, 94] Results of an *in vitro* study indicate that raspberry's phenolic compounds are able to protect DNA and decrease lipid peroxidation of lymphocytes in a concentration-dependent manner.[92]

The active ellagitannin constituents (sanguiin H-6 and lambertianin C) have also demonstrated antiinflammatory properties. Based on *in vitro* research, they inhibit the increase of NF-Kβ driven nuclear transcription and resultant TNF-α production in a dose-dependent manner.[95] Raspberry actives also been shown to reduce inflammation by inhibiting the release of the enzyme elastase secreted by neutrophils, which is considered a major component of the inflammatory cascade.[96]

Phenoclic compounds also possess antimicrobial properties and have been shown to inhibit the growth of both Gram-positive and Gram-negative pathogenic bacterial strains including *Staphylococcus aureus* and *Salmonella enterica* sp., as well as *Staphylococcus epidermidis, Helicobacter pylori, Bacillus cereus, Campylobacter jejuni* and *Candida albicans*.[4, 11, 97, 98] The mechanism by which phenolic compounds affect the growth of different bacterial species include destabilization of cytoplasmic membrane, permeabilisation of plasma membrane and

inhibition of extracellular microbial enzymes. They also have direct actions on microbial metabolism by depriving the cells of the substrates necessary for growth.[12] 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 antiadherence activity suggested by Puupponen et al.[4]

Growth of the probiotic strain *Lactobacillus rhamnosus* does not appear to be inhibited by the phenolic properties of raspberry.[11, 97]

Safety Summary:
No known warnings, precautions or contraindications at the dose recommended. Take away from alkaloid-containing medications, metal ion supplements and vitamin B1 (thiamine).[30] No adverse effects expected during pregnancy and breastfeeding.[30]

Fumitory (*Fumaria officinalis*)

Medicinal Actions:
Antimicrobial, antioxidant.[99]

Scientific Evidence:
The active constituents of fumitory include alkaloids, flavonoids and organic acids.[1] The biological activities of this herb are mainly associated with the isoquinoline alkaloids, in particular protopine.[100, 101] Protopine, has also demonstrated antihistamine effects.[102] The antioxidant capacity of fumitory is thought to be due to the synergistic effect of the medicinal constituents.[99]

While the scientific evaluation of this herb somewhat limited, an *in vitro* study assessing a methanol extract of fumitory demonstrated significant antimicrobial activity against the following microorganisms; *Pseudomonas aeruginosa, Staphylococcus aureus* and *Cladosporium herbarum*.[99]

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.[102]

Gentian (*Gentiana lutea*)

Medicinal Actions:
Antiinflammatory, antimicrobial, antioxidant.[1, 3, 104]

Scientific Evidence:
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.[1, 104-106] These active constituents give rise to the herb's potent antioxidant, antiinflammatory and antibacterial properties.[104, 106]

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.[105-107]

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 up-regulation is known to contribute to the development of inflammatory and immune-mediated conditions.[104]

The bitter compounds in gentian include gentiopicrin and xanthone isogentisin. These substances possess antimicrobial properties and have been shown to inhibit the growth of Gram-positive and Gram-negative organisms including *Streptococcus pyogenes, Staphylococcus aureus*, *Salmonella typhimurium, Escherichia coli, Psuedomonas aeruginosa* and *Micrococcus luteus.*[108, 109]

Safety Summary:
No other known warnings, precautions or contraindications at the dose recommended.[2] No adverse effects expected during pregnancy and breastfeeding.[30]

Tea Tree oil (*Melaleuca alternifolia*)

Medicinal Actions:
Antifungal, antimicrobial.[110-116]

Scientific Evidence:
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.[113, 114, 116, 117] The diverse active constituents give rise to tea tree's antimicrobial activity against a wide range of Gram-positive and Gram-negative bacteria as well as yeast and fungi.[114, 118]

The main antibacterial constituents of tea tree oil are terpinen-4-ol and γ-terpinene. It has been indicated, that terpene compounds found in tea tree oil act on the phospholipid layer of the microbial cell membrane destroying its normal structure and function.[115]

Tea tree oil has demonstrated consistent effective antimicrobial activity against MRSA, vancomycin-resistant *Enterococcus*, multi-resistant *Pseudomonas aeruginosa*, extended-spectrum-beta-lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella pneumoniae*.[119] The antimicrobial effect of tea tree oil against *Pseudomonas aeruginosa* was found to superior to commercially used antibacterial agents (specifically 0.1 % chlorhexidine and 70% ethanol solutions).[119] Tea tree oil has also been shown to decolonize and eradicate biofilms from *Staphylococcus aureus* (both coagulase-negative and coagulase-positive strains).[111]
Numerous *in vitro* studies have demonstrated the potent antifungal activity of tea tree oil against *Candida albicans* in both planktonic and biofilm culture. Tea tree oil has also demonstrated antifungal activity against *Saccharomyces uvarnum* and *Trichophyton rubrum*.[110, 112, 114]

Safety Summary:
Considered safe and well tolerated at the dose recommended. Tea tree oil is generally regarded as non-toxic, and non-irritating.[116] Exercise caution during pregnancy and breastfeeding as safety has not been scientifically established during these times.[120]

Galbanum oil (*Ferula galbaniflua*)

Medicinal Actions:
Antiinflammatory, antimicrobial, antiseptic.[116, 121]

Scientific Evidence:

Galbanum is composed of mainly 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.[116, 122] It is the high concentrations of monoterpenes and sesquiterpenes that give rise to galbanum's anti-inflammatory, antimicrobial and antiseptic properties.[116, 123]

Terpenes have been shown to be active against bacteria, fungi, viruses and protozoa. The mechanism by terpenes exert their antimicrobial properties involves disruption of the lipophilic compounds of cellular membranes of pathogens.[124]

To date, few scientific studies have been conducted with galbanum oil. Traditionally the herb has been used in the treatment of inflammatory and skin disorders, in wound healing and for ailments of the respiratory, digestive and nervous systems.[116, 123]

Safety Summary:
Galbanum oil is generally regarded non-toxic, non-irritating and non-sensitizing.[116] Exercise caution during pregnancy and breastfeeding as safety has not been scientifically established during these times.[125]

Lavender oil (*Lavandula officinalis*)

Medicinal Actions:
Antifungal, antiinflammatory, antimicrobial.[116, 126-129]

Scientific Evidence:
Lavender oil contains a complex mixture of aromatic compounds specifically terpenes and sesquiterpenes which include linalyl acetate, linalool, caryophyllene, terpinen-4-ol, 2-myrcene, trans-ocimenel, borneol, 1,8-cineole, camphor and limonene.[116, 128, 130]

This essential oil has been found to be active against many species of bacteria and fungi. Based on *in vitro* studies, lavender oil has demonstrated antibacterial activity against both methicillin-sensitive and methicillin-resistant strains of *Staphylococcus aureus*.[128, 129, 131]

Lavender oil has demonstrated both fungistatic and fungicidal activity against *Candida albicans.* Research also shows lavender is effective against both vaginal and oropharyngeal strains of *Candida albicans.* In the study by D'Auria et al, lavender oil inhibited both germ tube formation and hyphal elongation of *Candida albicans.*[127]

Based on *in vitro* experiments, lavender helps protect 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.[126]

Safety Summary:
Lavender oil is generally regarded non-toxic, non-irritant and non-sensitizing.[116] No adverse effects expected during pregnancy and breastfeeding at the dose recommended.[132]

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Oregano oil (*Origanum vulgare*)

Medicinal Actions:
Antibacterial, antifungal, antiinflammatory.[112, 133]

Scientific Evidence:
Active constituents of oregano oil include phenolic monoterpenes and sesqueterpenes such as carvacol, thymol, p-cymene, cis-ocimene, caryophyllene and linalool.[116]

Based on *in vitro* research, oregano oil showed high inhibitory effect against a number of organisms including *Listeria monocytogenes, Escherichia coli, Salmonella enteritidis, Proteus mirabilis, Staphylococcus aureus* and *Bacillus cereus*.[112, 134] Due to the broad spectrum antibacterial activity, several studies have suggested that multiple antibacterial compounds may be present in oregano.[51, 133, 135]

Oregano oil has demonstrated antibacterial activity against both *Pseudomonas aeruginosa* and *Staphylococcus aureus*. 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 components 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]

Oregano oil has also demonstrated antifungal activities against Candida species.[136] In the study by Pozzatti et al, oregano inhibited the growth and hyphenation of both *Candida albicans* and *Candida dubliniensis*.[137] 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.[137] 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.[136-138]

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.[116] Exercise caution during pregnancy and breastfeeding as safety has not been scientifically established during these times.[139]

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