Broad-Spectrum Botanical Medicines
The Uniquely Synergistic Complex in Biocidin®

A Safe and Effective Treatment Strategy Addressing Bacterial, Viral, Fungal, and Parasitic Infection

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Broad-Spectrum Biocidal Botanical Medicines –

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In 300 B.C. The Inner Classic of the Yellow Emperor, considered to be the bible of Chinese medicine, describes how external pathogenic factors, what we know as bacteria and viruses manifest, and the subsequent progression of the disease process. For several thousand years, Chinese medicine has documented the effectiveness of botanical therapies and maintains the most highly developed herbal Materia Medica. Thousands of plants have been categorized according to their medicinal properties, and a basic set of principles in formulation of remedies has been developed. In a typical formula, an "Emperor" herb is chosen as the main thrust of treatment, and several "Minister" are selected which support the activity of the main herb. Other herbs then are used as "Assistants" to carry the treatment to specific channels and organs, and also balance the effects of the stronger herbs. Supportive herbs are also chosen to bolster the weakened systems and to lessen the chance of side effects of the treatment.

With the availability of medicinal plants from around the world, formulas have now been developed using the same therapeutic model, without being restricted to the use of plants from only one country of origin. Using the anti-pathogenic properties of more than one botanical in a combination or formula provides a broader spectrum of activity against infections. The resulting formulations which I have dubbed "Biocidals" are powerful alternatives to some of the potentially toxic agents that may be used in the treatment of infectious diseases. The addition of herbs used for immune support and to assist the drainage pathways of the liver and kidneys increases the overall effectiveness in promoting a healing response.

The following test of one such combination, Biocidin®, containing Bilberry extract, Noni, Milk Thistle, Echinacea (purpurea & angustifolia), Goldenseal, Shiitake, White Willow, Garlic, Grape Seed extract, Black Walnut (hull and leaf), Raspberry, Fumitory, Gentian, Tea Tree oil, Galbanum oil, Lavender oil, Oregano oil shows a remarkable broad spectrum of activity.

A & L Analytical Laboratories, in Memphis, TN, performed USP Effectiveness Tests, in which this botanical combination was injected with large numbers of disease causing organisms, and then cultured for 28 days. The results below demonstrate the bacteria and yeast pathogens are completely eliminated in a matter of hours, and do not recur over a 28 day period of being cultured.

Organisms Tested

Aspergillus niger
Candida albicans
Escherichia coli
Pseudomonas aeruginosa
Staphylococcus aureus

USP Effectiveness Test

Organisms	Initial concentration cfu/ml	O day (2-3 hours) cfu/ml	7 days cfu/ml	14 days cfu/ml	28 days cfu/ml
Aspergillus niger	19750	6900	0	0	0
Candida albicans	12750	100	0	0	0
Escherichia coli	402500	100	0	0	0
Pseudomonas aeruginosa	765000	100	0	0	0
Staphylococcus aureus	515000	50	0	0	0

The selection criteria for the Biocidin® combination includes plants that demonstrate the following characteristics:

A broad-spectrum of activity against a wide range of pathogens, including gram positive and gram negative bacteria, yeast, parasites and viruses.

Inhibition of biofilms through more than one mechanism of action.

Act both systemically and in the digestive system.

May be used in acute or chronic infection.

Contain immune system modulators to up-regulate the body's own defenses.

Support removal of toxins through activation of drainage pathways.

Reduce inflammation and promote healing of tissues.

When researching some of the individual ingredients in this particular combination, we find a wealth of data demonstrating the inhibitory effect on various pathogens. Most recently many of these ingredients have been lauded for the ability to inhibit *biofilm* encapsulated infections such as MRSA and C. Difficile that may be resistant to antibiotics. Some of the most complex infections are caused by *biofilms*. Prior to the late 1970's, microbiologists were not looking at the relationship of pathogens and the micro-environment they create.

We now understand that these infections are made of communities of microbial cells surrounded by a secreted polymer, called the extracellular polymeric substance, hence the term biofilm. Biofilms are composed of multiple types of organisms, including both aerobic and anaerobic bacteria and/or fungal species. According to the NIH, more than 80% of all microbial infections have developed biofilms beginning in as little as two weeks from the onset of infection. Biofilms related infections cause 2 million HAI infections and 100,000 deaths annually. In 2011 the NIH identified a specific protein in S. epidermidis named phenol soluble modulin beta (PSM-beta) that is implicated in the growth, development and dissemination of S. epidermidis biofilm.

Biofilm bacteria can resist up to 100 times the antibiotic concentration that would normally be needed to resolve infections. These biofilm encapsulated drug-resistant infections are occurring more frequently among the healthy population.

For example, chronic sinusitis is a common upper respiratory infection where biofilms of both yeast and/or bacteria are found. Biopsies from patients undergoing sinus surgery show that 80% have biofilm communities present. Bacterial and fungal biofilms can cause chronic pulmonary infection such as pneumonia, cystic fibrosis, and tuberculosis. A newly discovered antibiotic resistant tuberculosis strain in India has a 50% mortality rate, due to the resistant nature of this biofilm.

The majority of ear infections (Otitis Media) are caused by biofilm bacteria and or fungal pathogens. OM is the most common illness for which children visit a physician, receive antibiotics, or undergo surgery in the US. 70% of post-operative tissue cultures contain biofilms.

Biofilms also play critical roles in persistent and resistant renal and urinary tract infections. In clinical nephrology, biofilms influence the development of kidney stones and affect dialysis systems, including peritoneal and central venous catheters. These biofilms are composed of both bacterial/fungal components and mineralized stone deposits.

Over 500 microbial biofilm species colonize the human mouth, causing tooth decay and chronic gum disease, and these bacteria can migrate throughout the body causing a variety of infections. In many cases of periodontal infection, C. albicans and S. aureus co-colonization makes it difficult to treat.

Biofilms have been implicated in chronic wounds, including antibiotic resistant Staph such as Methicillin Resistant Staphylococcus Aureus (MRSA). Pathogenic biofilms are also commonly found on medical devices such as joint prostheses. Septic failure following joint replacement is a leading cause of revision surgery. Slow-growing phenotypic variants often remain undetected using hospital microbiological analyses. SCVs make the infection difficult to eradicate. They often lead to recurrence since they respond poorly to standard antibiotic treatment and can sometimes survive intra-cellularly. Another example of intracellular bacteria is with biofilm components is Rickettsia. One species causes typhus, while another causes Rocky Mountain Spotted Fever, a tick born disease that may be a co-infection with Lyme disease.

Research has demonstrated links to infective agents in many conditions including cardiovascular disease, Alzheimer's, Arthritis, Cancers, CFS, and Autoimmune diseases. Using Organic Acid urine testing, metabolic byproducts of pathogenic yeast and bacteria have been found in many cases of Autism and Pervasive Developmental Delay (PDD). Reports from parents of autistic children being treated with the Biocidin® botanical combinations have been very positive. Many children have shown improved cognitive function, verbal and motor skills, as well as normalization of bowel function. This improvement has been concurrent with the reduction or elimination of Candida, Clostridia, Klebsiella and other pathogens as noted in before and after lab testing.

Over 70% of the population has some degree of inbalance in intestinal flora due to poor food and water quality, antibiotics, and other causes that suppresses the beneficial organisms needed to keep unfriedly species at bay. Consequently, many people now suffer from yeast and bacterial overgrowth called intestinal dysbiosis, and the resulting inflammation to the intestinal tract in dysbiosis leads to “leaky gut” syndrome. When particles of food or bacteria and yeast that should stay in the digestive tract escape to the blood stream, a immune cascade is triggered that can lead to Autoimmune diseases such as Rheumatoid arthritis, food allergies, and systemic inflammation.

Candida is one of the most problematic conditions affecting millions of people. The hyphal form of Candida yeast invades epithelial cells and causes tissue damage. In addition to primary tissue damage, secondary insult is caused by toxic by-products of yeast such as acetaldehyde, which may be carried to distant parts of the body including the brain. AH damages the red blood cells and impairs oxygen transport. Since 20% of oxygen intake is used by the brain, it is no wonder that people that have high levels of Candida complain of “brain fog”, learning disabilities, poor memory and fatigue. Candida biofilms may cause a systemic infection that can be fatal. 90,000 people a year are hospitalized with C. albicans infection and the mortality rate is 40-50%.

C. difficile is another intestinal pathogen that is on the rise. Clostridia are anaerobic, spore-forming rod type bacteria. C. difficile is the most serious cause of antibiotic-associated diarrhea (AAD) and can lead to

pseudomembranous colitis, a severe inflammation of the colon, often resulting from eradication of the normal gut flora after use of antibiotics such as Clindamycin and Cephalosporins.

In a very small percentage of the adult population, C. difficile bacteria naturally reside in the gut. Other people accidentally ingest spores of the bacteria while they are patients in a hospital, nursing home, or similar facility. When the bacteria are in a colon in which the normal gut flora has been destroyed (usually after a broad-spectrum antibiotic such as clindamycin has been used), the gut becomes overrun with C. difficile. This overpopulation is harmful because the bacteria release toxins that can cause bloating and diarrhea, with abdominal pain, which may become severe. C. difficile infections are the most common cause of pseudomembranous colitis, and in rare cases this can progress to toxic megacolon, which can be life threatening. 3 million cases of C. difficile have been reported in hospitals in the US, one study found 20% of nurse's uniforms contaminated by the bacteria at the end of a workday. Not killed by alcohol or soap and water, high concentration of bleach is needed to remove the contagious spores from surfaces.

In one clinical test, a patient with positive lab results for C. difficile and ongoing symptoms of morbid diarrhea was given the Biocidin® botanical combination. After 6 weeks her lab results were negative for the bacteria. More studies are warranted given the indication for success in treating C. difficile with broad-spectrum botanicals.

Chronic inflammation of the GI tract is commonly seen in acid reflux, GERD, colitis, and Crohn's disease. In order to combat inflammation, application of anti-inflammatory herbs such as Morinda (Noni) and Bilberry along with anti-pathogenic botanicals has proven a valid approach to treatment. Systemic inflammation seen in Autoimmune disease, including Rheumatoid Arthritis, MS, and Lupus may benefit from the combination of anti-pathogen and anti-inflammatory ingredients in Biocidin®.

Dysbiosis also affects neurotransmitter production, as the majority of serotonin and other neurotransmitters are found in the gut. Patients with sleep and mood disturbances that are given Selective Serotonin Re-uptake Inhibitors (SSRI's) such as Prozac, Zoloft, and Paxil may be also treated by rebalancing intestinal ecology and adjusting diet to reduce inflammation. Often these very patients will show a diminished absorption of nutrients such as B vitamins that play an important role in mental health. Once the GI tract is healthy, patients may no longer have the need for ongoing pharmaceutical treatment of depression, as proper production of serotonin and increased absorption of nutrients is established. One new test for dysbiosis is for Lipopolysaccharides, or LPS. LPS are endotoxins comprised of structural components of Gram-negative bacteria that may be discovered in plasma though an Intestinal Antigenic Permeability Screen. The presence of LPS is an indicator of intestinal permeability, or "Leaky Gut Syndrome". Use of Biocidin® is recommended if LPS is found lab results.

Brain and nerve cell loss due to chronic neuro-excitotoxicityis seen in both Autism and MS. 70% of MS

patients test positive for infection while 80-100% of autistic children have abnormal yeast and bacterial loads. Infections found in chronic neuro-excitotoxicity may include yeast, bacteria, viruses, parasites, Lyme disease and other co-infections. These chronic infections need to be treated to stop persistent activation of microglia and subsequent nerve and brain cell loss.

Bacteria may also play a major role in cardiovascular disease. In Circulation (1998:628-633), investigators note that Chlamydia pneumonia, an obligate intracellular parasite, has been found in diseased coronary tissues. Inflammation of the smooth membranes which line the inside of the heart is caused by a complex biofilm composed of both bacterial and host components. Biofilms have been found on stents and other cardiac prosthetics. Numerous studies have revealed the presence of bacterial biofilms within fatty deposits of damaged arteries (but rarely in healthy arteries), and have established a significant association between infection and coronary heart disease.

Epidemiologists from Johns Hopkins and other universities tested for the presence of C. pneumonia infection in a group of Alaska Natives--a population with a relatively low risk for developing heart disease--and, years later, compared these results with a forensic examination of each individual's cardiovascular system at the time of death. The researchers found that early serological evidence of infection with C. pneumonia was predictive of the presence of this bacteria in atherosclerotic tissue many years later, clearly supporting the notion of its pivotal role as an initiating trigger in the early stages of CVD, rather than as an associated late-stage event. This strongly supports the use of C. pneumonia as a powerful early warning indicator of CVD, even in young, low-risk individuals, and sheds a completely new light on the bio-mechanisms underlying the pathogenesis of cardiovascular disease.

Researchers have also identified this same bacterial agent inside the damaged brain tissue of patients with Alzheimer's disease. Infection with C. pneumonia is known to trigger an inflammatory cascade - one that often occurs inside the brain and other areas of the body. Clinical research has also forged a link between the Apo E4 gene, arteriosclerosis, and late-onset Alzheimer's.

Spurred by this series of connections, a team of investigators sought to more clearly elucidate the role of C. pneumonia infection in late-onset Alzheimer's. They examined post-mortem brain tissue in patients who had suffered from Alzheimer's disease (AD) and compared it with brain tissue from individuals who had never developed the disease. A surprising 17 out of 19 of the former AD patients tested positive for the organism, while only 1 of the 19 patients in the control group exhibited similar signs of infection. Significantly, evidence of C. pneumonia infection occurred exactly in those areas of the brain that showed specific neurological damage. In another study, published in Medical Microbiology and Immunology (1998;187:23-42), AD patients with both C. pneumonia and the Apo E-4 allele typically exhibited the most severe neurological damage.

The scientific evidence of the role of infection in seemingly unrelated diseases has prompted many practitioners to consider using broad-spectrum anti-microbial formulations as part of a base line treatment protocol where pathogens and biofilms mauy be implicated. The role of broad spectrum combination formulas such as Biocidin® has continued to increase, as practitioners and patients seek out treatments that are safe and effective for long-term use.

Novel methods of Biofilm Control In Biocidin®

The botanicals in the Biocidin® combination accomplish control of biofilms through several methods. The first method is by the inhibition of *Quorum Sensing*. Quorum Sensing is cell signaling by bacteria and other organisms using auto inducers to determine gene expression, virulence, resistance, and development of biofilms. Botanicals shown to inhibit Quorum Sensing such as Garlic and Oregano are well known for their anti-microbial ability. This new understanding of how they can combat biofilms highlights their clinical and historical significance.

Another method of biofilm control is by the inhibition of efflux pumps within cells called *Multi-Drug Resistance Pumps*. Plants containing tannins, berberine, and certain phenolics have useful effects as efflux pump inhibitors, demonstrating marked synergy when combined with conventional antibiotics against a variety of both Gram positive and Gram-negative organisms. Goldenseal, Black Walnut, White Willow, Raspberry Leaf and Garlic are a few that have been studied.

Bacteriostatic agents inhibit the reproduction of biofilm organisms and so help to control the spread of infection. Berberine has been proven bacteriostatic for S. epidermidis. One study showed that sub-minimal inhibitory concentrations blocked the formation of S. epidermidis biofilms. Both Gentian and Goldenseal contain berberine and are most useful additions to Biocidin® for biofilm control. Grape Seed and Bilberry contain condensed tannins that prevent adherence of biofilms, and may inhibit swarming motility of bacteria.

Essential oils have long played an important role in healing. From the preservation of mummies of ancient Egypt, to gifts of Frankincense and Myrrh for the infant Jesus, to the Middle Ages where Thieves oil was used to protect from the bacteria Yersinia pestis, essential oils contain powerful antimicrobial components. Oregano, Tea Tree, Galbanum, and Lavender have been added to Biocidin® to improve the overall activity against pathogens. Phenolics such as thymol and carvacrol in Oregano interact with surface proteins of bacteria, leading to an alteration of the cell surface and thereby compromising the initial attachment phase of biofilm formation. Hydrophobic in nature, carvacrol and thymol interact with the lipid bilayer of cytoplasmic membranes causing loss of integrity and leakage of cellular material such as ions,

ATP and nucleic acid, destroying the Biofilm components. Essential oils may prove to be most useful in treating the latest superbugs, which are multi drug-resistant Gram-negative bacteria such as Pseudomonas, Escherichia and Acinetobacter. Used correctly, the wealth of the plant kingdom is one of our greatest allies in optimizing our health, and provides a strong defense in the ongoing war against infectious diseases.

The following are some of the properties that recent research has brought to light for the individual components of Biocidin®:

Bilberry (*Vaccinium myrtillus*)

Anti-inflammatory and Antioxidant

Bilberries contain one of the highest levels of OPC's (Oligomeric Proanthocyanidin) found in nature. OPCs are a class of polyphenols, which have significant antioxidant and anti-inflammatory properties, as well as antibacterial, antiviral, anticarcinogenic, anti-allergic, and vasodilatory action. They have been found to inhibit lipid peroxidation, platelet aggregation, capillary permeability and fragility, and to affect enzyme systems, making Billberry useful for a number of conditions[1]. One study's findings suggests that supplementation with bilberry polyphenols may modulate the inflammation processes, and it can be used as a potential strategy in the prevention and treatment of chronic inflammatory diseases[2]. Bilberry was identified as one of nine plants in a review of 1000 plants as having significant evidence of therapeutic effect and anti-inflammatory activity.[3] Bilberry's anthocyanin helps the formation of and strengthening of connective tissue and capillaries, and is used for ocular health. The anti-inflammatory properties have also been helpful in GI Dysbiosis. Bilberries inhibit or kill fungi, bacteria, and protozoans.

Noni (*Morinda citrifolia*)

The Noni plant is a small evergreen tree that grows in the tropical regions of Polynesia and Australasia. It was believed to have been carried by the Polynesians when they migrated from Southeast Asia 2000 years ago[4]. It has been used traditionally for a wide variety of illnesses. In alternative medicine, it is still used for a myriad of conditions, such as arthritis, diabetes, high blood pressure, muscle aches and pains, menstrual difficulties, headaches, heart disease, AIDS, cancers, gastric ulcers, sprains, depression, senility, poor digestion, atherosclerosis, blood vessel problems, and drug addiction, with evidence of its use in colds and influenza[1].

Noni is considered to be an adaptogen due to its unusually high nutritive and medicinal components, which provide numerous health benefits. Recent research has indicated Noni to be an analgesic, anti-

inflammatory, immunostimulant and immunomodulator, antioxidant, and antimicrobial (bacteria, viruses, parasites, fungus). This combination of medicinal properties make it an excellent choice in fighting infection. Its analgesic properties may also help provide relief from pain and discomfort that accompany infection.

Immunomodulator (immunostimulant)

Noni enhances the immune system. It has been found to be an overall strong cellular and humoral immunostimulant, which confirms its traditional use in treating infection. It stimulates T lymphocyte, B lymphocyte and splenocyte activity, thus increasing the cell-mediated immune response.[5] Noni has also been found to activate the cannabinoid 2 (CB2) receptor in a concentration-dependent manner. The CB2 receptor is expressed in the immune system, brain, gastrointestinal system, and peripheral nervous system. In the immune system, CB2 is primarily responsible for mediating cytokine release, which has an essential role in the immune system response, such as communication between white blood cells. *In vivo*, Noni suppresses the Interleukin 4 (IL-4), reducing the activation of T and B lymphocytes; but Noni also increases the production of interferon-gamma cytokines (IFN), which are responsible for innate and adaptive immunity against intracellular bacterial and viral infections. Overall, Noni exerts beneficial immunomodulation effects in conditions involving inadequate immune responses.[6]

Antibacterial

Noni has been shown to fight against infectious bacterial strains, *Pseudomonas aeruginosa, Proteus morgaii, Staphylococcus aureus, Baciillis subtilis, Escherichia coli, Salmonella*, and *Shigela*; this makes Noni useful against skin infections, colds, fevers, and other bacterial-caused health problems[7]. Noni is also moderately effective against *Ps. aeruginosa, M. pyrogenes and E. coli*, *Salmonella typhosa*, *Salmonella Montevideo*, *Salmonella schottmuelleri*, *Shigella paradys* BH, and *Shigella paradys* III-Z[8]. Noni not only has curative properties against these infectious diseases[9] it also addresses *H. Pylori*, which helps treat infection-related stomach ulcers[10]. It has also shown to be effective against *Vibrio cholorae* (Cholera)[11].

Antiviral

Recent studies have shown Noni to be antiviral. The fruit juice displayed a significant cytotoxic activity in lymphocyte (MT-4) cells, inhibiting HCV (Hep-C Virus) replicon replication and Huh 5-2 cell proliferation, thus effective against Hepatitis C[12]. Noni also shows pronounced antitubercular activity[13] and moderate inhibitory effects against the Epstein-Barr virus (member of herpes virus family)[14]. One of its major biochemical components, damnacanthal (an anthraquinone), inhibits Vpr, an accessory protein of HIV-1, thus an effective anti-HIV therapy, which is applicable to other viruses[15] .

Antifungal

Noni demonstrates anti-fungal activity, including action against *Candida albicans*. It was shown to interfere with the serum-induced morphological conversion of *Candida* from a cellular yeast to a filamentous form in vitro, as well as inhibited the germination of *Aspergillus nidulans*[16]. The juice extract of Noni was found to be fungicidal against Candida, showing greater effect with increased concentration and contact time[17].

Anthelminthic

Noni has even shown anthelmenthic activity in a recent study of the use of its aqueous and ethanolic extracts against *Ascaridia galli* in chickens affected with this parasite[18]. It has also been traditionally used by native cultures in the South Pacific for body or intestinal worms[19].

Anti-inflammatory and Anti-oxidative

Noni is a very strong natural anti-inflammatory substance. It is well known that one of its historical uses in Polynesia, eastern Asia, and Australia is for painful inflammatory conditions, such as arthritis[20]. Noni has been shown to reduce pain sensitivity comparably to tramadol, an analgesic drug, and to have effects comparable to hydrocortisone. These findings suggest that noni fruits are effective in decreasing pain and join destruction caused by arthritis[21]. A major bioactive component of Noni, damnacanthal, was shown to be highly anti-inflammatory and is useful in the treatment of inflammatory-related diseases[22]. Noni is comparable in use to NSAIDS, and shows COX-2 inhibition comparable to Celebrex, without any side effects[23]. Its anti-oxidant properties have become of great interest to researchers. It is hypothesized that its antioxidant activity may protect individuals from oxygen free radicals and consequent lipid peroxidation[1]. One study led to the isolation of two new iridoid glucosides and 17 known anti-oxidant compounds, with the neolignan, americanin A, found to be a potent anti-oxidant in the study's assays.[24]

A later study on its anti-inflammatory and anti-oxidative effects found several polyphenols belonging to the coumarin, flavanoid, and phenolic adic groups, as well as two iridoids (type of secondary metabolite). It demonstrate a mean range free radical scavenging capacity and reduced carrageenan-induced paw edema. Its anti-oxidant properties are most likely due to its high polyphenol content, iridoids and ascorbic acid, which is also likely to strengthen its anti-inflammatory action[25]. One study indicates that its anti-inflammatory activity may reflect a more extensive action against several inflammatory mediators, such as histamine, hydroxytryptamine, bradykinin, prostaglandin, and nitric oxide, which are reported to be involved in carrageenan-induced edema[17].

Wound-healing

One study specifically investigated Noni's wound-healing abilities. It was found to significantly enhance wound contraction, decrease epithelialization time, and increase hydroxyproline content[26].

Milk Thistle (*Silybum marianum*)

Milk Thistle has been traditionally used as an herbal medicine for over 2000 years[27]. Known as a liver, kidney, and gallbladder tonic, it shows anti-inflammatory, anti-cancer, and anti-diabetic activity. It is particularly used for hepatitis of the liver, showing marked antiviral activity. Other reported uses of Milk Thistle include it as a treatment for malarial fever, bronchitis, gallstones, jaundice, peritonitis, uterine congestion, varicose veins, and milk production stimulant for nursing mothers[28].

Silymarin, Milk Thistle's liver-protecting active ingredient repair liver cells damaged by alcohol and other toxic substances, as well as protects the liver from being destroyed by toxins. Recently in Santa Cruz, CA, a family that had accidently ingested poisonous mushrooms had been hospitalized and were in critical condition due to acute liver damage. In 2007 Dr. Todd Mitchell and Dr. Wendy Knapp treated a family of six who had eaten tacos made of death cap mushrooms they picked at Wilder Ranch State Park. Searching Google, Mitchell found a treatment used in Europe, an intravenous milk thistle preparation called Legalon-Sil. He had persuaded the Food and Drug Administration to allow its use as an emergency investigational new drug. He arranged for an air courier to deliver the medication to the San Francisco hospital where four of the six patients had been taken after developing liver failure and needed transplants. None of the patients underwent transplants once the IV solution of Milk Thistle arrived from Germany and was administered, the family members recovered.

Antiviral

Several trials have found Milk thistle to be effective against hepatitis C and HIV[1]. Silibinin, a compound found in silymarin, was found to be well tolerated and showed substantial antiviral effect against hepatitis C when administered intravenously.[29] Treatment with a milk thistle (silybin), vitamin E and phospholipid formula improves the conditions of patients with hepatitis C infection[30]

Echinacea (*Echinacea purpurea*, *E. angustifolia*)

E. purpurea and *E. angustifolia* contain substances that enhance the activity of the immune system, relieve pain, reduce inflammation, and have antiviral and antioxidant effects. Echinacea preparations have a long history of medicinal use for infections, being among the best-selling herbs in several developed countries[31]. Several clinical trials of *E. angustifolia* and *E. purpurea* preparations have reported effects superior to those of placebo in the prevention and treatment of upper respiratory tract infections[32].

Immunomodulator

E. purpurea is widely used as an immunomodulator to fight infections, such as the common cold. An

overwhelming amount of studies, including pharmacological and clinical trials, have been conducted on Echinacea spp., reporting its immune system stimulating and modulating effects[1]. Results of another recent study found *E. angustifolia* to be useful for improving the immune response subsequent to the influenza vaccine[33].

Antiviral

Echinacea has been traditionally used for viral infections, including the common cold and influenza, and this use has now been supported by science. Clinical studies have shown that *E. purpurea* preparations can diminish the severity and length of common colds significantly, and can be used for the treatment of children[34]. E. *purpurea* has even been found to be effective against the flu virus, without producing resistant virus strains such as is the case with antiviral drugs like Tamiflu; this is useful in cases when antiviral vaccines are not readily available[35]. Recently, in a randomized, double-blind, placebo-controlled clinical trial with *E. purpurea*, the herb inhibited viral colds and especially prevented enveloped virus infections, and it showed maximal effects on recurrent infections[36]. Echinacea also reduced the duration of the common cold[37]

Anti-inflammatory and Analgesic

Many classes of chemicals naturally present in Echinacea species have been isolated, which are responsible for its anti-inflammatory and analgesic properties; extracts from the roots had potent activity against TRPV1, a mammalian pain receptor that is responsible for inflammatory pain and hyperalgesia, which is a prime therapeutic target for analgesic and anti-inflammatory drugs[38].

Antioxidant

Echinacea was found to exhibit free-radical scavenging and transition metal chelating activities, and suppressed the oxidation of human low-density lipoprotein[39], which is important in for cardiovascular health.

Goldenseal (*Hydrastis canadensis*)

Immunostimulant and Antimicrobial

Goldenseal has antibiotic and immunostimulant properties. It is traditionally combined with Echinacea as a cold and influenza remedy. It is used for upper respiratory problems and minor wounds. It demonstrates antibacterial activity against *Staphloccocal*, *Steptococcal*, *E.coli*, and *Pseudomoas aeruginosa* strains in vitro[40]. It even inhibits Helicobacter pylori growth[41]. Goldenseal contains berberine, which has broad antimicrobial activity. Berberine has also been shown to kill a wide range of organisms, such as those that

cause candida (yeast) infections, viruses, and various parasites such as tapeworms and Giardia. One study found berberine extracts and decoctions to have significant antimicrobial activity against bacteria, viruses, fungi, protozoans, helminthes, and chlamydia. Its current predominant uses include bacterial diarrhea and intestinal parasite infections[42]. Berberine may also activate white blood cells, making them more effective at fighting infection and strengthening the immune system[43], in addition to helping to remove biofilms. One study found that berberine blocked the formation of *Staphylococcus epidermidis* biofilm, and that it has the potential application as an adjuvant therapeutic agent for the prevention of biofilm-related infections[44].

Shiitake (*Letinula edodes*)

Shiitake has numerous health benefits. It is used for depressed immune function (including AIDS), cancer, environmental allergies, fungal infection, frequent flu and colds, bronchial inflammation, heart disease, hyperlipidemia (including high blood cholesterol), hypertension, infectious disease, diabetes, and hepatitis[45].

Immunomodulator (immunostimulant)

Shiitake is a strong immunomodulator due in part to its lentinin content, a type of β-Glucan .[46]. Aqueous extracts demonstrated immunostiulatory properties[47]. Lentinin, which increases the number of Th1 lymphocytes, helping protect organisms against allergic reactions, is anticarcinogenic, and has an immunity-stimulating effect; it also participates in physiological processes related to the metabolism of fats in the human body and decreases total cholesterol content in the blood, thus helping to regulate body weight[48]. Shiitake also has potent antibiotic effects against other organisms. It has shown anti-HIV activity[49,50]. An antifungal protein isolated from Shiitake inhibited mycelial groth in a variety of fungal species, including *Physalospora piricola*, *Botrytis cinerea*, and *Mycosphaerells arachidicola*[51]. In one study, aqueous extracts of shiitake showed extensive antimicrobial activity against 85% of the 29 tested bacterial pathogens, and 50% of yeast and mold species ; comparing favorably with Ciprofloxacin[52].

White Willow (*Salix alba*)

White Willow is mainly used for pain, headache, fever, and inflammatory conditions. It contains salicin, a chemical from which aspirin is derived, which is thought to be responsible for the analgesic and anti-inflammatory effects of the herb.

Anti-inflammatory and Analgesic

One recent study found that polyphenols from White Willow had significant activity at reducing IL-6 and TNF-α production, greater than the anti-inflammatory activity of meadowsweet and chamomile[53]. Another recent study showed that White Willow had the greatest anti-inflammatory effect when applied to neutrophils (a granular leukocyte) among 10 other herb extracts[54]. Salicin was found to have significant anti-inflammatory activity in rat hind-paw edema, as well as analgesic and antioxidant activities in another study[55]. Willow Bark extract STW 33-1 and its water-soluble fraction inhibited pro-inflammatory cytokines, COX-2, and induced apoptosis of pro-inflammatorily activated monocytes, which provided further ecidence of its therapeutic use in inflammation-related disorders; this suggests that its anti-inflammatory and uses in treating pain (mainly arthritis and back pain) cannot be explained by solely its salicin content[56]. Its anti-inflammatory processes are even being found to have anti-depressant effects[57]

White Willow has been used in the treatment of pain, including for low back pain. In a placebo study on White Willow for back pain found that it seemed to reduce pain more than placebo[58] . Willow Bark extracts have well-known anti-inflammatory and analgesic effects similar to NSAIDs, with a different influence on the COX-1 and COX-2 mRNA expressions compared to NSAIDs, and without side effects such as gastric erosions[59].

Garlic (*Allium sativum)*

A potent antioxidant and antimicrobial, garlic has been used as medicine for a variety of maladies since antiquity in virtually every known civilization, such as ancient India, Egypt, Rome, China, and Japan, making it a well-established folk medicine, and with modern research increasingly supporting it as a possible alternative or complementary medicine[60]. Recent research points to its cardiovascular and immune system benefits, and anti-cancer activity.

Antimicrobial

Garlic has been traditionally used for its antiviral effects in the common cold. In one clinical trial, the Garlic intervention group experienced fewer days of illness than the placebo group, though more clinical trials need to be conducted to validate this finding[61]. It is effective against bacterial, viral, fungal, and parasitic infections[62]. Recent studies have pointed to significant biological activity of one of Garlic's natural components, the thiosulfinate allicin, and several trisulfides and tetrasulfides found in Allium species, including the antibiotic properties of polysulfides; this research may ultimately form the basis for the development of antibiotics and fungicides with dramatically reduced side effects in humans[63]. Garlic

ointment was found to inhibit certain bacteria species and disrupt partially developed biofilms of other species, and can be used to prevent wound biofilms caused by both Gram-negative and Gram-positive bacteria from forming, and as a potential therapy for disrupting established staphylococcal biofilms[64]. One review highlights Garlic's potential effectiveness against clinical isolates of multi-drug resistant tuberculosis based on research findings of scientific importance[65].

Antioxidant and Cardiovascular benefits

Allicin, is readily absorbed through the cell membrane without inducing any damage to the phospholipid bilayer, then rapidly metabolized, providing cardio-protective effects by inducing vasorelaxation and alleviating various conditions of cardiovascular disease. It also lowers the level of reactive oxygen species and stimulates the production of glutathione[66], making it a potent antioxidant.

Grape Seed Extract (From *Vitis spp.*)

Grape Seed Extract is rich in flavonoids and OPCs, which helps strengthen and protect cell membranes from oxidative damage. One polyphenol found in Grape Seed Extract is reservatrol, which, along with other Grape Seed polyphenols, was found to strongly protect against oxidative stress, showing antioxidant and genoprotective effects[67]. Extracts from purple grape skins and seeds were found to inhibit platelet function and platelet-dependent responses at pharmacologically relevant concentrations, which suggest potentially beneficial antithrombotic and anti-inflammatory properties of purple grape-derived flavonoids[68]. Proanthocyanidin, a Grape Seed polyphenol, has been reported to have protective properties against vascular injury and ulcers, preventive effects against artherosclerosis, cancer, is antioxidant, improves lipid metabolism, and slows aging. It was found to protect the gastric mucosa and have anti-histamine effects[69]

Black Walnut (*Juglans nigra*)

Containing valuable tannins, Black Walnut is not only anti-parasitic, but also anti-fungal, anti-viral and antimicrobial[70]. In one study, out of 104 botanical species, the extract of Black Walnut was among 10 species extracts that significantly inhibited biofilms in methicillin-resistant Staphylococcus aureus (MRSA)[71]. Extract of black walnut is reported to treat eczema, herpes, psoriasis, fungal infections, and both skin and internal parasites[72].

Raspberry (*Rubus idaeus*)

Raspberry is a stron anti-inflammatory, due mostly to its anthrocyanin content. Anthrocyanins from raspberries were found to have anti-inflammatory activity comparable to ibuprofen and naproxen[73]. Phenolic compounds in Raspberry juice were found to significantly lower levels of inflammatory cytokines in chronic pulmonary disease, and increase antioxidant production[74].

Fumitory (Fumaria spp.)

Gastrointestinal support

Fumitory has been traditionally used for gastrointestinal problems such as indigestion, nausea, constipation, and diarrhea. One study showed that *Fumaria parviflora* is a prokinetic, laxative, and spasmodic, and is therefore useful in indigestion and constipation[75]. Another study of *Fumaria indica* found that the presence of its cholinergic and calcium channel blockade constituents could explain its traditional use for constipation and diarrhea[76].

Anti-inflammatory and antioxidant

In one recent study *Fumaria indica* was found to exhibit dose-dependent and significant anti-inflammatory activity[77]. Another study found that *Fumaria vaillantii* exhibited high antioxidant activity[78].

Antibiotic, Anthelmintic, and Antiplasmodial

In the same aforementioned study on *Fumaria vaillantii*, the plant was found to have antibacterial activity. *Fumaria parviflora* was also found to have anthelmitic activity.[79] Ten *Fumaria* species were found to have the alkaloids protopine and cryptopine[80]. In one study, protopine showed promising in vitro antiplasmodial activities against *Plasmodium falciparum*[81], which is the most deadly cause of malaria. Cryptopine was found to have anthelmintic activity[82].

Tea Tree Oil (*from the Melaleuca alternifolia*)

Tea tree oil is extracted from the leaves of the plant via distillation. It has been shown to be active against a variety of bacteria, fungi, viruses, and mites. It contains terpinen-4-ol, which exhibits broad-spectrum antimicrobial activity[83].

Antiseptic

Tea Tree Oil has been reported to have broad-spectrum antimicrobial activity against bacterial, viral, fungal, and protozoal infections affecting the skin and mucosa. Several studies have suggested its use for

acne, seborrheic dermatitis, and chronic gingivitis. It is as effective as the drug Clotrimazole for treating nail fungus[84]. It accelerates wound healing and shows anti skin cancer activity[85]. Tea tree oil has been used topically against Staph including MRSA; in fact, tea tree topical preparations have been shown to be superior to the standard topical regimen for the clearance of MRSA colonization[86]. It was found to inhibit the growth of Streptococcus pyogenes and enhance the bactericidal activity of macrophages, as well as to inhibit inflammation response[87]. In another study, 84% of children with the dermal viral condition *Molluscum contagiosum* experienced 90% reduction in the number of lesions when treated with Tea Tree Oil[88].

Antifungal and Fungal Biofilms

Among Tea Tree Oil's popular uses are against fungal infection. One study found that Tea Tree Oil is an effective therapy for fluconazole-refractory oropharyngeal candidiasis[89], and is thus effective where drug-resistant strains are present. Another study confirmed this by finding that it has significant anti-fungal activity against azole-resistant forms of *Candida albicans*[90], and yet another study had the same finding with fluconazole-resistant vaginal Candidiasis[91].

Tea Tree Oil and its component terpinin-4-ol exhibit strong antimicrobial properties against fungal biofilms[92]. In fact, in a recent study on the treatment of biofilm infections in cochlear implants, Staphylococcus aureus biofilms were completely eradicated using a 5% Tea Tree Oil solution within 1-hour exposure[93].

Antibiotic

Tea Tree Oil could be considered an active disinfectant against *Legionella pneumophila*[94]. Halitosis-associated bacterium, *Solobacterium moorei* growth was inhibited by Tea Tree Oil in one study[95]. Another recent study demonstrated that Tea Tree Oil was effective against *Pseudomonas aeruginosa* and *Enterococcus faecium*[96].

Galbanum Oil *(from the Ferula spp.)*

Mentioned in the Old Testament, as well as by Hippocrates, Galbanum has one of the oldest recorded histories of beneficial use. It is both antimicrobial and anti-parasitic and is traditionally used for healing wounds and in the treatment of infection both internally and externally. Many studies show that *Ferula* species contain active sequiterpene coumarins, which have various biological activities, such as cytotoxicity, antibacterial, antiviral, P-glycoprotein inhibitory and anti-inflammatory activity[97].

Antibacterial and Antifungal

One study showed that the oil of *Ferula vesceritensis* contains components that exhibited antimicrobial activity against *Staphylococcus aureus*, *Escherichia coli*, and *Klebsiella pneumonia,* which reinforces previous studies that show that the genus Ferula is considered a good source of essential oils for antibacterial use[98]. The oil of *Ferula lutea* also exhibits significant antibacterial activity against E. Coli, *S. aureus* and *S. epidermidis*, as well as against eight Candida species, making it antifungal[99]. One study showed that components of the aqueous extracts of *Ferula hermonis* were significantly effective against *Microscporum gypseum*, *Tricophyton mentagrophytes*, *Candida lactis-condensi*[100], *Pseudomonas aeruginosa, Bacillus subtilis, Mycobacterium bovis* BCG Pasteur*, and Staphylococcus aureus*[101]. Galbanic acid from *Ferula szowitsiana* showed antibacterial activity against S. aureus[102].

Antiparasitic

Ferula asafoetida L. was found to be effective against *Blastocystis sp,* demonstrating its potential as a natural alternative for the treatment of *Blastocystis sp*. infection[103]. *Blastocystis* is one of the cyst type parasites commonly found patients that have traveled in Mexico, South America, India , and Nepal and present with chronic diarrhea. It was also found to be effective against *Schistosoma mansoni* in experimentally infected mice[104]

Anti-inflammatory

*Ferula hermoni*s was found to have two components, ferutinin and teferin, demonstrated significant anti-inflammatory activity [105].

Gentian (*Gentianella spp.)*

Used to purify the blood since discovered around 167 B.C., Gentian is a digestive bitter and a liver tonic, traditionally administered for GI disorders, such as dyspepsia, gastritis, and peptic ulcer disease (PUD)[106]. It also increases the activity of the liver and gall bladder to improve their function, and is used to improve absorption of nutrients, especially iron.

Antimicrobial

Both the extracts of *Gentiana lutea* L. and three of its isolated compounds (mangiferin, isogentisin, and gentiopicrin) exhibited antimicrobial activity against Gram-positive and Gram-negative bacteria, as well as *Candida albicans*. This study indicated that the synergistic activity of the pure compounds may be responsible for high antimicrobial activity[107].

Wound Healing

Three components of *Gentiana lutea* (gentiopicroside, sweroside, and swertiamarine) were evaluated, results indicate the Gentian may be used to stimulate the production of collagen and mitotic activity . These components also exhibited cytoprotective effects, demonstrating its wound healing activity. This research backs up uses that had been previously based only on ethnomedical data[108].

Antioxidant

Gentiana lutea exhibits free radical scavenging activity[109] with extracts of their leaves and roots exhibiting considerable antioxidant properties[110].

Lavender Oil (from *Lavandula angustifolia)*

Essential oil of lavender has antiseptic and anti-inflammatory properties. It was even used to disinfect hospitals during WWI. Lavender oil is extensively used for various respiratory infections, and has a calming effect on the nervous system.

Antibiotic

Lavender oil has antimicrobial activity against methicillin-sensitive and methicillin-resistant Staphylococcus aureus (MSSA and MRSA, respectively)[111]. In conjunction with other herbal oils, it was used in a Naturopathic treatment for children with ear pain in a double-blind study, and was demonstrated to be superior to antibiotic treatment (amoxicillin)[112]. It was found to significantly inhibit the growth of detrimental bacteria that cause intestinal dysbiosis, without harming beneficial bacteria[113].

Antifungal

In the abstract of one study on Lavender oil's antifungal properties, researchers wrote, "Lavender oil shows both fungistatic and fungicidal activity against C. albicans strains. At lower concentrations, it inhibits germ tube formation and hyphal elongation, indicating that it is effective against *C. albicans* dimorphism and may thus reduce fungal progression and the spread of infection in host tissues"[114]. Its vapor has antifungal activity against Trichophyton mentagrophytes[115].

Anti-inflammatory

Lavender oil's vapor increases free radical scavenging and decreases cortisol level in saliva, preventing oxidative stress, and making it a significant anti-inflammatory[116].

Oregano oil (from *Origanum vulgare*)

Antimicrobial

Oil of Oregano is a powerful antimicrobial. It contains two key compounds, carvacrol and thymol[117]. It has broad-spectrum fungicidal activity, with increased concentrations of carvacrol in Oregano oil correlated with its potency. This activity confirms it's use in the treatment of superficial or mucosal fungal infections[118]. In another study, Oregano oil had the highest and broadest activity against human pathogenic bacteria *Bacillus* subtilis, *Enterobacter cloacae, Escherichia coli, Micrococcus flavus, Proteus mirabilis, Pseudomonas aeruginosa, Salmonella enteritidis, S. epidermidis, S. typhimurium, and Staphylococus aureus* among the oils of ten commonly consumed herbs; of all the main medicinal components of each of these oils, carvacrol had the highest antibacterial activity[119]. Thymol has been shown to be an effective fungicide, particularly against fluconazol (Difucan)-resistant strains. This is especially relevant given that opportunistic Candida can cause severe systemic infections. It also has antimalarial activities[120]. In addition, thymol and carcavrol can reduce bacterial resistance to common drugs such as penicillin.[121]

Anti-inflammatory and Anti Ulcer

In one study, carvacrol reduced edema and showed healing capacity on gastric lesions induced by acetic acid, and therefore may be used in the healing process for gastric ulcers.[122]

Conclusion

The wealth of data available on the individual ingredients in the Biocidin® formula definitavely demonstrates the usefullness of this conbination as a safe and effective treatment strategy addressing Bacterial, Viral, Fungal, and Parasitic infection. Futhermore, there is ample evidence to suggest that many biofilm encapsulated infections will also repond to use of these antimicrobial botanicals.

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