

Medical Herbalism

A Journal for the Clinical Practitioner

Volume 14, Number 3

Spring 2005

Antiviral Botanicals in Herbal Medicine

by Paul Bergner

Abstract: The human organism is an ecological domain naturally inhabited by microorganisms including bacteria, fungi, and virus. The majority of viruses known to infect humans cause no symptoms or known disease. The organism possesses multiple mechanisms of host defense to maintain ecological balance in the presence of viruses. Except for the occasional use of herbal medicines as topical agents in viral infections of the skin, plant medicines probably do not exhibit direct virucidal properties within the organism. Many plants have been used traditionally to enhance host resistance to viral infection, and recent advances in immunology have uncovered possible novel mechanisms for their action. These include effects on TH-1/TH-2 balance, on expression of heat shock protein, and interaction with toll-like receptors. These mechanisms are reviewed, along with the effect on them of various lifestyle factors. A variety of effects of the following plants on the viral life-cycle or antiviral host defenses are discussed:

Allium sativum; *Astragalus spp*; *Calendula officinalis*; *Chamomilla recutita*; *Curcuma longa*; *Echinacea spp*; *Eleutherococcus senticosus*; *Eupatorium spp*; *Ganoderma lucidum*; *Glycyrrhiza glabra*; *Ligusticum spp*; *Lomatium dissectum*; *Melissa officinalis*; *Paeonia spp*; *Panax ginseng*; *Platycodon grandiflorum*; *Sambucus spp.*; *Saussurea spp.*; *Schisandra chinensis*.

Introduction

Viral organisms are “obligate host cell parasites” – small pieces of genetic material packaged in various ways that must infect and take over the processes of a living cell in order to reproduce. Viruses are ubiquitous in both the plant and animal kingdoms. Their forms, genetic content, and patterns of infection and replication are radically varied. Some produce symptoms of various well-known diseases in humans, such as influenza, herpes, warts, chicken pox, smallpox, and

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Grapefruit Seed Extract

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The ubiquitous and widespread usage of grapefruit seed extract (GSE) within the health food industry, including its use by supposedly knowledgeable practitioners, is an issue of serious concern for me as a herbalist, researcher and clinician. GSE in various forms is used by hundreds of thousands of consumers all over the world, all of whom praise the virtues of this “natural” antibiotic. In 1999 a study authored by Sakamoto, Sato, Maitani, and Yamada details an analysis of a commercially available GSE and compared this to an ethanol extract of grapefruit seeds (*Citrus paradisi*). The researchers report that two chemicals found in GSE and not in the ethanol extract were methyl-p-hydroxybenzoate and triclosan, two commonly used preservative compounds (Sakamoto). This study was followed up in 1999 by von Woedtke, Schluter, Pfliegel, Lindequist and Julich, who analyzed the antimicrobial efficacy of six commercially available GSEs and one self-made extract from the seed and juiceless pulp of grapefruit (*Citrus paradisi*). The researchers found that five of the commercially available extracts had significant antimicrobial activities, all of which contained the preservative benzethonium chloride. Three of these same extracts were also found to contain the preservatives triclosan and methyl parabene. The researchers found that only one of the commercial GSEs tested had no preserving agent, but that this extract as well as the self-made extract had no antimicrobial activity. The researchers concluded that the antimicrobial activity being attributed to GSE is “...merely due to the synthetic preservative agents contained within”(von Woedtke).

While on the one hand the marketing of GSE could be nothing more than a kind of charlatanism, there are additional concerns about the long term safety of ingesting the aforementioned preservatives. I am quite sure that many of the people currently using GSE, who espouse the value of natural alternatives over commonly

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so on. The majority of viruses known to infect humans, however, produce no visible effects at all, and viruses must be viewed as natural components of the human ecology, as natural as bacteria on the skin or in the gut. Viral infection in the human organism is opposed by sophisticated host response mechanisms, including non-specific immune defenses, humoral and cell-mediated immunity. Non-specific immunity includes the activity of complement system chemicals, of macrophages and dendritic cells, and the expression of heat-shock proteins.

The term “antiviral” is commonly applied to medicinal herbs by practitioners, but the term is imprecise. As an empirical term, “antiviral” means “an herb used for viral infections” and many herbs are known in herbal traditions to be effective for various types of viral disease, for prevention or for acute or chronic infection. Unfortunately the term implies that all such herbs or their constituents somehow kill viruses directly, rather than enhancing host response. The term as commonly used also implies that the herb has some sort of universal activity, and that an antiviral herb good for one condition will automatically be of benefit in others. Such

action, if it could be demonstrated, should designated *virucidal*.

Virucidal action

The usual measure of virucidal activity of herbal medicines or other agents is to incubate the virus with a host cell in a lab dish, and to measure the effect of the herb or constituent on viral replication. A number of herbal medicines or their constituents have been studied and found effective in their activity against viral/host-cell colonies in the lab dish. In some cases, the mechanism of inhibition – the point at which the substance interferes with the viral life cycle – is identified, but usually not. Such research does little to predict the activity of the herb when taken orally in the human body, a radically different ecological system than the lab dish. Assimilation and distribution of the antiviral constituents of a plant must occur, with delivery to the specific cell host in sufficient quantities in the surrounding extracellular fluid. I have been unable to identify any line of research of herbal medicines or their constituents which demonstrates an inhibition of viral replication in vitro, and then demonstrates that similar levels of the substance is possible in the blood, and in fact inhibits viral replication in the body. A problem with this type of research is that even if an

Ecological factors in viral resistance

Herbal medicines may constitute one portion of an ecological approach to preventing or treating viral illness. Other ecological factors include:

Nutrition.

Many micronutrients that are commonly deficient in a modern diet are involved in viral resistance. These include copper, iron, magnesium, manganese, selenium, zinc, vitamin A, folic acid, vitamin B complex, vitamin C, vitamin D, vitamin A, and essential fatty acids.

Exercise

Exercise in moderation (30-40 minutes per session) stimulates immunity, while lack of exercise or over-exercise (exercising to exhaustion twice or more in a week) are immunosuppressive. Of the factors discussed in this article, exercise induces a heat-shock protein response. It also profoundly enhances circulation and lymphatic flow, with even light walking exercise stimulating lymphatic flow by a factor of ten.

Dietary factors

High sugar or high glycemic content is immunosuppressive. Two ounces of added sugar –the amount of sweetener in an average soft drink or sports drink – reduces phagocyte activity by about 40% and the effect can last for up to 5 hours. Sports drinks may also completely negate the beneficial effects of exercise on heat shock protein expression. Contemporary North Americans consume about six ounces of added sugars per capita per day.

Rest

A state of sleep-debt (sleeping time chronically below that necessary to maintain normal endocrine balance) results in chronically elevated cortisol, which directly suppresses antiviral mechanisms. The TH-1 system is dominant during the deep sleep phase while DHEA is being secreted from the adrenals, and loss of deep sleep may imbalance the system toward TH2 dominance,

herb or constituent inhibits virus in vitro, and even if similar levels were attainable without drastic side effects in vivo, the herb or its other constituents may also have effects to enhance host resistance, and the actual mechanism in the human being may never be proven.

Hypericum

The herbal world was understandably excited in 1988 when an animal trial appeared which indicated that hypericum, and specifically its constituent hypericin, might be active against the HIV virus. The article suggested that hypericin had potent anti-HIV activities at doses that were completely non-toxic (Meruelo et al.) Subsequently it has been established that hypericin is active against a subset of viruses called enveloped viruses, but not against other types of virus (Tang et al.) This raised speculation that it might be clinically effective against HIV, hepatitis-C virus, influenza-A, herpes-simplex (HSV), and many others.

Subsequently, a clinical trial of intravenous hypericum in HIV infected patients showed almost universal phototoxicity at doses that were completely ineffective against the virus, according to several methods of detection (Gulick). Similarly, patients treated with hypericin for hepatitis C (HCV) infection demonstrated a high rate of phototoxicity, and no detectable effect on the virus (Jacobson). It was later found that hypericin only exhibited its antiviral properties when exposed to light (Lopez-Bazzocchi), which is unlikely to occur in the human body. And later trials of the pharmacokinetics of hypericin in typical oral antidepressant doses showed that the blood levels achieved were on the order of 1/1000 of the levels that showed antiviral activities in-vitro (Kerb et al.) The case of hypericin and its in-vitro virucidal properties may be viewed as an archetype for a large amount of misinformation and misconception among contemporary herbalists in North America. In the case of hypericum, following the original in-vitro and mouse trials of hypericin, herbalist, herb companies, authors, and others began to state that hypericum had antiviral properties, implying clinical properties. Even after the failed clinical trials, hypericum is still listed in most herbals as an antiviral herb, and the herb student is likely to be misguided in the appropriate clinical use of the herb.

As a further example, an elderberry (*Sambucus nigra*) syrup has been shown in clinical trials to be active against influenza infection, and its constituents have been shown to be active against 10 different strains of influenza virus in the lab dish (Zakay-Rones, 1995) The same researchers found that the syrup resulted in

higher host immune response to the influenza virus; other authors have demonstrated that Sambucus products have a general immune enhancing effect (Barak et al. 2002; Barak et al 2001). A strengthening of the host resistance, rather than a virucidal action is more likely in light of the historical use of Sambucus in acute febrile illness of many types, not just viral illnesses, and also as an alternative in chronic systemic illness. Any specific virucidal or virus-inhibiting action in the human remains to be demonstrated.

Similarly, glycyrrhizin from Licorice root has been shown clinically to reduce viral infection in hepatitis C infection (van Rossum 2001; van Rossum 1999), viral encephalitis (Sekizawa), and influenza (Utsunomiya), with numerous trials showing an inhibition of the viral cycle in vitro. However, it has also been shown to stimulate interferon-gamma production from T-Cells (Utsunomiya). At this time it is impossible to say whether its clinical effects are due to specific viral inhibition or to general strengthening of the host response to viral infection.

In vitro research into the antiviral properties of plants demonstrates that plants may inhibit one type of virus, but have no activity against most others. In one trial of 100 medicinal plants from British Columbia, researchers identified twelve plants with antiviral properties at doses that were not toxic to the cells in the lab dish. These plants were tested against seven different viruses, and most were active against one of the seven, but not the other six. For instance, of the twelve antiviral plants, only two (*Sambucus* and *Oplopanax*) were active against respiratory syncytial virus, one (*Ipomopsis aggregata*) was active against parainfluenza. One plant best known for its empirical activity in influenza (*Lomatium dissectum*) had no activity against parainfluenza virus, suggesting that it acts through effects on host resistance in clinical influenza (McCutcheon).

Heat-shock proteins

One recent area of research in immunity may explain the action of herbal medicines to protect against viral infection. Heat-shock proteins (HSP) are produced in abundance within the cell in response to various stressors. See the review by Welch for a historical overview of the research and some specific roles of these proteins. Heat shock proteins greatly enhance the efficiency of intracellular protein manufacture and transport and may enhance immunity against viruses by improving immune surveillance of virally infected cells. The HSP expression is enhanced by extremes of hot or cold, either

locally or systemically, by exercise, and by viral infection, and by various other forms of stress. Their expression may be one of the mechanisms to explain the beneficial effect of fever therapy on immunity against chronic viral or spirochete infection, as well as various methods of alternating hot and cold, locally or systemically, in hydrotherapy. Elevated serum glucose or insulin inhibit the HSP response – sports drinks inhibit the normal effect of exercise on HSP (Febbraio) — which may in part explain the decreased immune response after ingestion of various sugars, and chronic immune problems in Type II diabetes.

A number of herbs or their chief constituents have been observed to induce or to facilitate HSP response, and such herbs may strengthen the systemic response to viral infection. All have been traditionally use as tonics, adaptogens, or immuno-modulators. They include: *Allium savitum* (Sumioka), *Curcuma longa* (Dunsmore; Bath), *Schisandra chinensis* (Chiu), *Glycyrrhiza spp.* (Yan), *Paeonia spp.* (Yan), and the Chinese medicinal herbs *Panax notoginseng* (Yao), *Platycodon grandiflorum* (Lee) and *Saussurea lappa* (Matsuda).

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Toll-like receptors

Until very recent years, the non-specific side of the immune system, characterized by tissue macrophages, dendritic cells, and complement system has been viewed as the poor-cousin of the specific immunity produced by the humoral and cell-mediated systems. It was thought that non-specific immunity was primarily a local immune response, and that the specific immunity, characterized by B-Cell and T-Cells must be directly activated to elicit a systemic response. The recent discovery of the role of *toll-like receptors* (TLR) in macrophages and dendritic cells has shown that these non-specific defense cells can also initiate a systemic response by previously unknown pathways. The various types of specialized TLR, which are present on the membranes and nuclear membranes of the immune cells, detect specific chemicals that are characteristic of specific types of organisms, such as virus, gram-negative and gram-positive bacteria, and fungi. Research shows that some polysaccharides from medicinal plants can trigger the expression and activity of the some TLR, and plants containing polysaccharides may assist in the initiation of system wide enhanced immune surveillance.

Plants or plant-derived polysaccharides which have been shown to initiate or enhance TLR response and immune activation are: *Astragalus membranaceus* (Shao et al; 2004b), *Ganoderma lucidum* (Shao et al, 2004a), *Panax ginseng* (Nakaya; Pugh) *Panax quinquefolius* (Pugh), *Echinacea angustifolia* and *purpurea* (Pugh), *Eleutherococcus senticosus* (Han), and the Chinese herb *Platycodon grandiflorum* (Yoon). Polysaccharides from *Eupatorium perfoliatum*, *Chamomilla recutita*, *Calendula officinalis*, and *Baptisia tinctoria*, have been shown to increase phagocytosis (Wagner), but specific connections to TLR have not been identified. Note that polysaccharides are insoluble in alcohol, and are not present in tinctures with greater than about 35% alcohol. These plants must be taken as powders, infusions, or decoctions for these effects on TLR to occur.

TH-1/TH-2 Balance

The T-Helper (TH) cells are like the “quarterbacks” of the specific immune system, and they coordinate the escalation of both the humoral (antibody) and cell-mediated (macrophages, T-killer cells) responses. The TH cells may be undifferentiated, or may differentiate into TH-1 cells, favoring cell-mediated immunity, or TH-2 cells, favoring antibody production. The composition of the TH pool of cells may become un-

balanced, favoring one side of the immune equation over the other. A common dysregulation that can lead to *viral overload* is a dominance of TH-2 cells. In this case, many antibodies are produced which can tag the virus and other antigens, but the cells to actually clear the antigens are deficient. This condition has been demonstrated in many cases of chronic fatigue and accompanying chronic viral infection, such as Epstein-Barr virus. For a complete review, see Kidd.

Some proven causes of Th-2 dominant imbalance are: certain immunizations, depletion of the cell-produced antioxidant glutathione, corticosteroid drugs or stress-induced endogenous cortisol excess with corresponding DHEA deficiency. Herbal medicines may be used to help restore the TH1/TH2 balance, but evidence for consistent effects on either system in humans is scarce, and it is difficult to predict clinical effects from the suggestive in-vitro and in-vivo evidence that exists. The five herbal medicines with some evidence of being to restore balance in a TH-2 dominant system are *Allium sativum*, *Astragalus membranaceus*, *Ganoderma lucidum*, *Grifola frondosa*, and *Panax ginseng*. (Bergner 2004a)

TH1/TH2 imbalance may also explain the common aggravating effects of echinacea in chronic fatigue syndrome, fibromyalgia, and some autoimmune disorders. Echinacea has a acute effect of increasing the white blood cells, including the lymphocytes. If the system is already unbalanced, with an excess of TH2 cells, then echinacea could acutely aggravate the condition.

Circulatory factors in acute infection

The expectorant and diaphoretic activity of herbs, commonly employed in acute respiratory viral infection, may also directly increase host resistance at the surface level. In North American vitalist herbal traditions, it is the practice to keep the mucous membranes and the skin at least slightly moist during acute febrile illness. Expectorants, by promoting the free flow of mucous increase surface immunity because the mucous is laden with IgA-type anti bodies. Diaphoretics are used to gently cool a fever by shifting blood to the capillaries of the vessel-rich dermis, allowing for increased heat loss through ventilation. This action also promotes circulation of immune components at the surface. Some traditional herbs used in febrile viral illness which possess either expectorant or diaphoretic actions, include *Allium sativum*, *Eupatorium perfoliatum*, *Glycyrrhiza spp.*, *Ligusticum porteri*, *Melissa officinalis*, and *Sambucus nigra*.

Traditional indications

The most useful definition of the term *anti-viral* for the clinician may be “traditionally used for people with viral infections” without undue concern paid to an identified mechanism. They are probably only indirectly virucidal, by enhancing host resistance. The most important of these herbs for acute conditions, based on traditional indications, are: *Echinacea spp.*; *Melissa officinalis*; *Allium sativum*; *Ligusticum porteri*; *Eupatorium spp.*; and *Sambucus spp.* The most important preventives or strengtheners for those with chronic infection are: *Astragalus spp.*; *Eleutherococcus senticosus*; *Schisandra chinensis*; *Glycyrrhiza glabra*; and *Ganoderma lucidum*.

Allium sativum

Garlic (*Allium sativum*) and its many varied constituents have a wide array of medicinal effects. Notable among the effects on the immune system are stimulation of the cell-mediated immunity (TH-1) (Bergner 2004a). This is the cell-set which attacks virally infected cells. *Allium* may also enhance immunity in respiratory infection through its expectorant or diaphoretic actions. One peculiarity of the pharmacodynamics of garlic may also assist in resistance to respiratory route viral infection – some of its immune-enhancing constituents are excreted through the lung, directly reaching infected mucosa in the respiratory tract.

While garlic must be freshly chopped or powdered to optimize its direct antimicrobial effects, it may be aged somewhat for maximize its effects on host resistance. The allicin constituent of garlic, released upon crushing, rapidly degrades into a number of constituents which can enhance host resistance; more than half of allicin is converted in this way within 24 hours. A method used since the time of the Roman Galen is to crush garlic in wine and let it sit overnight. Another method of delivery, which allows high doses in the fragile individual is to deliver a well-strained garlic preparation via bulb enema. This may be very useful in the patient with post-influenza syndrome. Garlic may also be eaten with food, raw or lightly cooked, during viral epidemics, as a preventive.

Echinacea spp.

Echinacea is the top-selling botanical medicine in North America today, and some forms and dosing strategies may be useful in viral infections. Results of scientific trials of echinacea have been mixed, however (Bergner 2004b), and in the majority of recent randomized-controlled clinical trials for prevention or treatment of colds, echinacea has failed to show signif-

icant benefit. The Eclectics did not consider it a primary remedy in influenza, but noted that in very weak individuals it may contribute to recovery. High doses of well-made products that include the root, repeated frequently, may be necessary to obtain benefit.

The Eclectics also considered that *Echinacea angustifolia* was the medicinal species, and considered *E. purpurea* to be inferior. Contemporary herbalists report mixed opinions, with about half of those surveyed expressing the opinion that *E. angustifolia* is the superior medicine (Bergner 1997). Two of three randomized clinical trials that contained *E. angustifolia* along with *E. purpurea* have been positive, a much better track record for such trails that those using *E. purpurea* alone (Barret; Kim; Lindenmuth). The failed trial used a non-traditional form of echinacea – a mixture of *E. purpurea* and *-angustifolia* as powder in capsules. Notably, in a trial of immune activation, mixtures of the two species had a positive effect, while *E. purpurea* alone did not.

Contemporary herbalists, like the Eclectics, prefer a tincture of Echinacea, but antiviral effects may be enhanced by using a strong decoction in place of, or along with treatment by the tincture. Traditional Native American use was to chew the root, or to make a decoction (Moerman), and this method allows contact of echinacea polysaccharides with the oral and gut-associated lymphatic tissues. A large body of research in Germany shows immune-enhancing activity of these polysaccharides, possibly through activation of immune surveillance via toll-like receptors. One of the recent successful clinical trials of echinacea used the tea form (Lindenmuth). Note that tincture with greater than about 35% alcohol contain no polysaccharides. A practical method of extracting and delivering a dose of polysaccharide-rich echinacea is to put one to two ounces of echinacea root in quart of water and simmer it for forty minutes. The dose can be two ounces repeated frequently (a tincture dose may be added to this), or up to the entire quart consumed over several hours in critical cases. Adjuvant herbs may be used to cover the bad taste. I have case reports of this method being rapidly and remarkably effective in copperhead bite, pelvic inflammatory disease, and acute kidney infection, especially in high doses. I also have direct experience with it in West Nile fever, strep pharyngitis, and gum infection after oral surgery.

Another method of delivering a polysaccharide-rich dose of echinacea is to prepare honey pills from freshly powdered echinacea. Hot honey is mixed with the pow-

dered root (add powdered osha root for extra potency), allowed to cool, and then shaped into pills the diameter of a U.S. ten-cent piece. These can be rolled in licorice root powder for stability and stored in the refrigerator. One pill is chewed as needed, usually about four times per day in acute infection.

Eupatorium spp.

Boneset (*Eupatorium perfoliatum*) has been considered as the primary herbal treatment for acute influenza in the Eastern United States at least since the mid-1700s, and was the favorite of American physician-herbalists in the great influenza epidemic of 1916-1918. Boneset has also been used traditionally as a topical treatment for herpes viral infection. Despite its fame, little scientific investigation of the plant has been conducted. Two trials have shown an increase in phagocytosis from various extracts of boneset, including the water-soluble polysaccharides (Wagner et al; Wagner and Jurcic). In the latter trial, Eupatorium polysaccharides were more potent than those of Echinacea.

In addition to acute influenza, boneset was a primary remember for intermittent fever from the late 18th through the early 20th centuries in North American medicine. Because such fevers can have many causes or infectious agents, this suggests an effect to enhance host resistance.

The earliest use of boneset by European colonists was of the decoction, either hot in acute illness, or room temperature in chronic conditions. Later in the 19th century tinctures were introduced. The traditional water extract contains the polysaccharides of the plant, which may be important for full effects on host resistance against virus. Note that higher doses can cause nausea, and the plant was traditionally used in large doses as an emetic.

The plant has been used historically as a preventive during influenza epidemics with at least some success, and may also be very useful for post-influenza syndrome. It combines well with Echinacea or Ceanothus in formulas.

Ligusticum porteri

The primary medicinal use of North American species of Ligusticum, especially *L. grayi* and *L. porteri* is for upper respiratory infections. There is very little investigation of North American species for antiviral or immune-enhancing effects, with one in-vitro trial demonstrating only a weak antiviral effect of one constituent (Beck). The Chinese species is not used for respiratory conditions and is not considered an immune-enhancer.

Despite its reputation in contemporary herbalism, this herb probably should not be considered as having specific antiviral activity. Its circulatory stimulating, diaphoretic, and expectorant activities may confer indirect resistance against respiratory viruses. Future research into the furanocoumarin compounds in *Ligusticum* may uncover immune-enhancing or antiviral effects (Tower).

Ligusticum combines well with licorice, which can balance its harsh effects and reinforce its expectorant properties. It also combines well with honey for the respiratory tract. Consider making honey-pills of freshly powdered *Ligusticum*.

Lomatium dissectum

Botanical varieties of *Lomatium dissectum* have wide use in the ethnobotany of the Native American tribes in its range. Uses for bacterial or viral respiratory infections or allergic conditions are present in most native groups. The plant drew national attention in medical circles after the influenza pandemic of 1916-1918 when a physician from Nevada reported a complete lack of influenza mortality in a Native American group taking the preparation (Krebs). The traditional form is the decoction, taken in large quantities, or inhalation of the steam of the decoction (Moerman; Krebs). More common in modern herbalism is the use of the tincture, but with this method a whole-body rash is a common side effect. The rash has been observed with even modest doses of the tincture, as a component of a larger formula. This effect has also been observed very commonly with the freeze-dried form. The nature of the rash is not clear. It does not respond to steroidal suppression. Some herbalists have suggested that it is due to the waste products of killed bacteria or virus, but in the absence of some positive confirmation this must be considered speculation. It is also possible that the rash is due to constituents which otherwise would have been driven off by the traditional method of long decoction – resins may be responsible.

Other than its traditional use in respiratory viral infections, there is no evidence that *lomatium* or its constituents have any general antiviral activity. One trial found a *lomatium* extract active in-vitro against rotavirus, but not active against six other viruses tested, including parainfluenza (McCutcheon). The fact that it was also used traditionally in bacterial and allergic respiratory problems suggests either a local or a systemic enhancement of host resistance, and possibly an antispasmodic or anti-inflammatory effect. The decoction is a stimulating expectorant, and may enhance

immunity in the mucosa indirectly by increased secretions of IgA antibodies inherent in the mucous.

Melissa officinalis

Melissa officinalis has traditionally been used as a diaphoretic in a variety of fevers. It has gained a reputation as a specific antiviral after in-vitro research led to it effective topical application in herpes infections, popular in Europe. A review of the research fails to show unique or broad antiviral effects of the herb. In vitro research showing activity against herpes virus (Allahverdiyev; Dimitrova), supports the topical use for herpes also demonstrated in a human trial (Koytchev). One trial showed *Melissa* to have anti-HIV activities in-vitro, but in this screening of 51 herbal extracts, *Melissa* was in no way unique. Forty-five other plants also showed activity. *Melissa* was among those most effective, but 5 other plants, including *Mentha piperita*, *Ocimum basilicum*, and *Prunella vulgaris* – none of them usually considered to have specific clinical antiviral activity – were equally effective. The effective dose of these extracts, at sixteen micrograms per ml, may not be practically attainable in the human with oral doses. Some authors have speculated that anti-viral activity is due at least in part to caffeic acid, rosmarinic acid and ferulic acid, but these constituent are widely distributed in the plant world, and are common constituents of a variety of medicinal herbs. One trial showed that *Melissa* increased general immunity in mice, including both humoral and cell-mediated immunity (Drozd and Anuszevska).

The most common traditional use of *Melissa* is as a tea. The suspected active constituents are soluble both in hot water and in alcohol. The common traditional practice of sniffing the hot tea of aromatic herbs may be an effective way to deliver *Melissa* constituents to the site of respiratory infections. The tea also has circulatory-stimulating, diaphoretic, and febrifuge effects.

Sambucus spp.

Elderberry and elder flower have long traditional use in febrile illness, including influenza. They have also been used as an alterative or blood purifier in chronic conditions. Recent research on an elderberry syrup (*Sambucol*) has shown it to be very effective clinically against influenza. It also inhibits at least ten strains of influenza virus in-vitro (Zakay-Rones 2004; Zakay-Rones 1995). Its actual mechanism in the body remains unknown, but enhancement of host resistance are probably more important than any virucidal activity. In one clinical trial of *Sambucol* in influenza, the

researchers found higher antibody activity against the virus in patients treated with Sambucol. In research with healthy volunteers, they found that the product increased the production of the immune-enhancing cytokine tumor-necrosis-factor-alpha by nearly 5000% (Barak).

Sambucus is traditionally taken as a tea, 2-4 cups per day for elder flower tea, or as a tea or syrup of the berries. Either form taken to excess can cause queasiness or nausea.

Astragalus spp

Astragalus is one of the primary tonic herbs in Chinese medicine, and recent research has shown a number of mechanisms of immune system enhancement. It has no direct antiviral activity. It is traditionally taken as a tea in China, or often cooked in soups, stews, or medicinal rice gruel. Traditionally the Chinese may take an alcohol preparation of Astragalus, but then in large doses – ½ to 1 ounce – when the heating and blood-moving effects of the alcohol are also required. The Astragalus tincture products widely sold in North America are likely to be devoid of immune enhancing or tonic effects in normal tincture doses. Astragalus may make an excellent preventive in the weak patient who is prone to colds or flu, if taken regularly during seasons or periods of susceptibility.

Eleutherococcus senticosus

Eleutherococcus (Acanthopanax) senticosus, or Siberian ginseng, enhances host resistance to multiple possible stressors, including infection (Deyama; Davydov). In one experiment, it was found to have direct antiviral effect against all RNA-type virus tested (Glatthaar-Saalmuller). Two clinical trials have shown a preventive effect against complications of respiratory viral infections, and one has shown activity reducing the frequency and severity of herpes outbreaks (ESCOP). *Eleutherococcus* enhances host antiviral defenses, especially cell-mediated immunity (TH1) (Szolomicki; Bohn). *Eleuthero* may effect general immunity via its action on the toll-like receptors (Han).

Most of the *Eleutherococcus* products in the North American marketplace are of little value. The original research bringing this medicine into medical use occurred in the former Soviet Union. The Russian Pharmacopoeia product is a 1:1 fluid extract in 30% alcohol, taken in doses of 2-15 ml. The low alcohol content, compared to standard tinctures, likely conserves constituents in the plant that are lost in the standard tinctures mostly available in this country. By

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extrapolation, even if all the constituents were present, the dose of a standard 1:5 tincture would have to be 10-75 ml, or 1/3 to 2.5 ounces. The HerbPharm company of Williams, Oregon, markets a product made according to the Russian specifications, and further concentrated to 2:1 in strength. Other companies offer encapsulated products based on 2:1, 10:1, or in one case, 50:1 concentrates. Regarding the inefficiency of other contemporary products, one herbalist-author states that the plant must be taken for thirty days to show any benefit, and another says that patients can take as much as they want. The Russian preparation results in noticeable activity within 1-2 doses, and overdose symptoms of anxiety, insomnia, and tension occur readily. It is the latter sort of product that must be taken to prevent viral infection.

Ganoderma lucidum.

Reishi mushroom is clinically one of most important of the herbs discussed here for treatment for chronic viral infection, or as a preventive during periods of threatened viral infection. Investigation shows that the polysaccharide, water-soluble fraction of this medicinal mushroom increases both the numbers and the cytokine secretion of the monocytes, macrophages, and lymphocytes. In one trial, production of interferon, which protects cells from viral infection, was increased by a factor of thirty (Wang). Reishi may act to stimulate systemic immunity via the action of its polysaccharides on toll-like receptors. Various constituents of ganoderma have been found to have antiviral properties in-vitro, especially against herpes simplex virus and Epstein Barr virus (Eo; Iwatsuki). However, a trial of six constituents found none of them active against influenza or several other viruses (Eo). Reishi may be especially helpful in chronic viral conditions with dominance of the humoral immunity (TH2) (Bergner 2004a).

Two problems exist in finding effective forms of reishi. The traditional Chinese form is a decoction, but the taste is very unpleasant, and patient compliance is very poor. Some extracts formed from the residue of evaporated water extracts are available. Some also have alcohol constituents mixed. Note that although the Chinese have traditionally used many herbs in alcohol form, there is no traditional use of reishi in alcohol extract form in China. Alcohol preparations also do not contain the plant polysaccharides, which are important to its action. Much of the encapsulated reishi on the market in North America today is from the mycelium, which must be considered inferior until some medicinal activity is demonstrated in clinical trials.

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Grapefruit seed extract from page one

used synthetic drugs and spend their hard earned money to buy “all-natural” products, would be shocked to learn the mechanism of GSE’s biological activity.

Benzethonium chloride is commonly used as a disinfectant in cosmetic products. In Switzerland benzethonium chloride is classified as a “...disinfectant categorized as a class 2 poison because of its teratogenicity and caustic effects” (kantonslabor-bs.ch). The amount found in some GSE products is upwards of 8% (Takeoka), considerably more than many cosmetic products. The Environmental Defense Fund describes benzethonium chloride as a “suspected endocrine toxicant” that “lacks...data required for safety assessment” (scorecard.org). According to the National Institute For Occupational Health and Safety the internal ingestion of benzethonium chloride could cause “...diarrhoea, nausea, vomiting, collapse, convulsions (and) coma” (cdc.gov). Some sources suggest that benzethonium chloride is a by-product produced from grapefruit flavonoids by ammoniation, but researchers at the USDA regard this as “unlikely” (Takeoka). Regardless of its origin, benzethonium chloride is clearly stated to be a potentially harmful compound, and is not approved for internal use in the United States.

Triclosan is structurally related to a number of bis-phenyl polychlorinated and bis-phenyl chlorophenol compounds that have come under increasing scrutiny for their health-damaging effects. Triclosan is listed by the Environmental Protection Agency (EPA) as a “pesticide” (epa.gov). It is widely used in the cosmetic industry, especially in antibiotic soaps, and has been fingered as a factor for the emergence of antibiotic-resistant bacteria (Braoudaki). Researchers are finding it wastewater, in the tissues of fish, and even in human breast milk (Adolfsson-Erici). While triclosan is approved for use in topical and oral applications, it is not approved for internal use in the United States.

GSE is marketed as an all natural and perfectly safe health food product, when it is neither. Various Citrus species have been used as a food and medicine in Chinese and Ayurvedic medicine for thousands of years. Although being familiar with the many benefits of Citrus, neither Chinese nor Ayurvedic medicine has ever advocated the use of grapefruit seed or any other Citrus

seed in acute infectious disease: this alone should provide some clue as to its effects or lack thereof.

Todd Caldecott obtained his diploma in Clinical Herbal medicine at the Coastal Mountain College in Vancouver, Canada, and his Ayurvedic education in India at the Arya Vaidya Chikitsalayam. He is the former director of clinical herbal studies at Wild Rose College in Calgary, Canada, and served as a senior practitioner and clinical supervisor at Wild Rose Clinic. He is a professional member of the American Herbalists Guild and serves on the Guild’s admissions committee. His upcoming textbook on Ayurvedic medicine will be published by Elsevier (UK) later this year.

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Clinical Correspondence

Lung cancer

On February 22, 2005, I was giving a lecture on Stress Related Diseases. I couldn't help noticing a man by the name of Charles, sitting in the front row who every once in a while would comment aloud about one treatment or another or some affront of the medical establishment. I must confess that I felt a little annoyed at first because sometimes it would cause me to lose my train of thought. At the end of the lecture, after the number of people who came up with their special questions, Charles came up and delivered a copy of a hand written protocol that he followed to cure himself of medically diagnosed non-small cell carcinoma in his lungs. He said he simply followed the anti-cancer protocol described in the third edition of my book, *The Way of Herbs*. He also referred to *Super Antioxidants* by James F. Balch, *Herbal Medicine, Healing and Cancer* by Donald Yance and *Food: Your Miracle Medicine* by Jean Carper. The cancer that originated in his lungs was beginning to invade the spinal cord at the level of T3 and T4. Doctors recommended both radiation and chemotherapy. He underwent 20 radiation treatments and there was still a trace of cancer. He put himself on the following protocol and on the subsequent visits which included MRI scans the doctors could find no sign of the cancer. Charles then showed them the protocol he had been following and they discounted it as having no merit, although they confessed that they could find no reason for his cancer to have completely disappeared. It's been a number of years now that Charlie has been cancer free which attributes to the rigorous dietary, nutritional and herbal protocol described below. Charlie said he strictly followed the protocol for about 4 years. It consisted of the following:

Nature Life Brand: 25,000 I.U. Beta Carotene
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Now Brand: 100 mg Beta glucan, with Maitake Mushroom
Now Brand 500 mg L-glutamine
Now Brand: 60 mg CO-Q-10
Now Brand: 500 mg N-Acetylcysteine
Now brand: 100 mg grape seed
Nutrabiocotic Brand: Buffered ascorbate Bio-C with bioflavonoids and minerals
American Biologics: Oxy-food forte (a complex antioxidant formula) 1000 mg
Omega 2-6-9 E.P.A 440 mg
Garlic extract wit 200 mg
Astragalus extract 1000 mg
Siberian ginseng
Chlorella or wheat grass
Green tea
Apricot Kernels — one kernel for every 10 pounds of weight divided into two doses daily
Herbal Tea— Burdock, Chaparral, Cat's Claw, Licorice, Pau d'Arco, Red clover, sheep sorrel
A Champion juicer
Crock Pot (3 quart size) to make a half gallon of herbal tea at a time.
Vegetable juice: Made from all organic, fresh juice carrot, bok choy, celery and cabbage
Food: Kale, dandelion, spinach, broccoli, bok choy, cabbage, onion, garlic, tomatoes, shiitake mushroom, bell peppers, potatoes, miso, tempeh, seaweed, brown rice, mung beans or lentils, fish including tuna, salmon, yogurt, organic non-fat rice milk, no cow's milk, no sugar, no processed foods, no coffee, no ice cream, no alcohol, no tobacco.

Michael Tierra R.H., O.M.D.
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