Herbs for Viral Respiratory Infections

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Abstract

Herbal medicines have long been used to treat and prevent viral respiratory infections (VRI). Here, a broad survey of these herbs is provided. The effects and benefits of a wide array of antiviral herbs are discussed in depth. The benefit of most of these herbs having built-in immune-stimulating and inflammation-modulating effects means that they can help prevent immune overreaction ("cytokine storm") to VRI while still helping the immune system cope better with the infections. The scientific basis supporting these contentions are discussed. Major herbs with clinical trial evidence that they help resolve VRI reviewed in detail include *Sambucus nigra* (black elder) fruit, BNO 1016 (Sinupret®) formula, *Andrographis paniculata* (kalmegh), *Pelargonium sidoides* (African geranium), má huáng tāng (maō-tō, ephedra decoction), and antiwei formula. The failure of research on *Echinacea angustifolia* (narrow-leaved purple coneflower), particularly by using far too low of doses, is reviewed. An individualized approach to formulating for VRI patients is presented, followed by a review of the evidence that various herbs, notably *Panax ginseng* (Asian red ginseng), *Panax quinquefolius* (American ginseng), *Camellia sinensis* (green tea), and *Allium sativum* (garlic), can prevent VRI.

Keywords: herbal medicine, influenza, *Echinacea angustifolia*, *Sambucus nigra*

Introduction

Viral respiratory infections (VRI) continue to be one of the most common human illnesses. Herbal medicine has much to offer for patients with the common cold, viral pharyngitis, acute bronchitis, and influenza.

While influenza vaccines are available and recommended for use each year, they have unfortunately low levels of uptake in the population and variable efficacy (depending on the degree of accuracy of strain matching, viral mutation including during production, and other factors).[1] Also, this vaccine has no effect on other viruses. Conventional treatments for cold and influenza only mask the symptoms, and are often not even effective for that purpose (as in the case of nonsteroidal anti-inflammatory drugs).[2] Conventional treatments that directly target these viruses are few and far between, and even in the case of neuramidase inhibitors (oseltamivir, zanamivir) for influenza that do, efficacy is marginal and adverse effects are substantial.[3,4]

Herbal medicines continue to play an important role in preventing and treating VRI. Here, herbs for treating such infections will be considered first, including both traditional treatments and those that have been scientifically researched. Then, research-based preventative measures will be discussed. These measures are particularly important to provide clinicians with evidence-based alternatives to antibiotics, which have no place in the treatment of purely viral infections.[5]

Antiviral Herbs

Generally, no single herb is a solution to VRI, but instead a range of herbs with diverse actions are needed (see Table 1). Perhaps most important among these are herbs to attack the invading viruses directly. Rhinovirus, metapneumovirus, coronavirus, adenovirus, parainfluenza, enterovirus, respiratory syncytial virus (RSV), and influenza viruses, as the major causes of VRI, will be the focus here.

It is beyond the scope of this article to address every one of the numerous antiviral herbs in detail. Evidence that various of the herbs listed have activity against causes of VRI are given in Table 2. However, it is likely most of these herbs have very broad activity against respiratory viruses, as their clinical efficacy is broad, and those that have been studied against a wide range of organisms show good activity against most. Most of the herbs noted as being anviral in Table 1 that are not included in Table 2 have simply never been studied for this effect. They are listed as such in Table 1 based on their clinical effects and because they have documented antimicrobial effects against other organisms not related to VRI. No research could be found on any of these herbs as to whether they affected metapneumovirus, which is surprising, as this is a very common cause of VRI.

There are many ways to choose between these herbs for an individual patient besides trying to match to a specific virus infecting a patient. Because there is still no affordable, rapid test available to determine what virus a patient has (except influenza), this is rarely an option anyhow. Also, a lack of systematic research on which herbs are effective for infections by which organism hampers this type of matching by infecting organism.

Table 1. Herbal Treatment of Viral Respiratory Infections

Desired action	Indicated herbs
Antiviral	*Glycyrrhiza* spp., *Sambucus* spp. fruit, *Allium sativum*, *Pelargonium sidoides*, *Geranium sanguineum*, *Populus* spp., *Tilia* spp., *Lonicera japonica*, *Forsythia suspensa, Usnea* spp., *Andrographis paniculata*
	Apiaceae group: *Ligusticum* spp., *Lomatium dissectum, Osmorhiza occidentalis, Hedera helix*
	Lamiaceae group: *Salvia apiana*, *Thymus vulgaris*, *Rosmarinus officinalis, Prunella vulgaris*
	Evergreen group: *Pinus* spp., *Abies* spp., *Picea* spp., *Thuja* spp., *Juniperus* spp.
Immune stimulator	*Echinacea angustifolia*, *Ligusticum* spp., *Lomatium dissectum*, *Andrographis paniculata*, *Eupatorium perfoliatum*, *Thuja* spp., *Astragalus membranaceus*, *Allium sativum*, *Pelargonium sidoides*
Analgesic	*Echinacea angustifolia*, *Ulmus fulva*, *Althaea officinalis*, *Alcea rosea*, *Calendula officinalis*, *Salix* spp., *Populus* spp., *Aconitum* spp.
Diaphoretic	*Eupatorium perfoliatum*, *Achillea millefolium*, *Encelia farinosa*, *Salvia apiana*, *Asarum canadense*, *Zingiber officinale*, *Aristolochia watsonii*, *Monarda fistulosa*, *Tilia* spp., *Verbesina encelioides*, *Asclepias tuberosa*
Inflammation modulator	*Glycyrrhiza* spp., Solidago *canadensis*, *Euphrasia* spp., *Achillea millefolium*, *Grindelia* spp., *Lomatium dissectum*, *Eriodictyon* spp., *Pinus* spp., *Abies* spp., *Picea* spp., *Populus* spp., *Tilia* spp., *Forsythia suspensa*, *Andrographis paniculata*, *Hedera helix*
Lymphagogue	*Phytolacca americana*, *Galium aparine*, *Calendula officinalis*, *Asclepias tuberosa*, *Asclepias asperula*

Instead, secondary properties of the antiviral herbs are used to choose among them, and a selection of herbs from two or three different families and with different chemistries are recommended. This helps maximize antiviral synergy and avoid resistance.

Antiviral Herbs with an Edge

Three particular groups of antiviral herbs within botanical families deserve specific mention, as indicated in Table 1. Three herbs from the Apiaceae family—*Ligusticum* spp. (oshá, oshala), *Lomatium dissectum* (desert parsley, lomatium), and *Osmorhiza occidentalis* (western sweet Cicely)—are all clinically potent respiratory-tract antivirals that are also immune stimulant and inflammation modulating. The root is the part used with each herb. *Ligusticum porteri* (oshá) from the mountainous regions of the desert southwestern United States and northern Mexico, *L. grayi* (Gray's lovage) from the Pacific Northwest, and *L. striatrum* = *L. chuanxiong* (chuān xiōng) are three notable species used around the world for colds and influenza, among other uses.[6] Ligustilides, other phthalides, and furanocoumarins are believed to be the major active compounds in these herbs, such as the only confirmed antiviral compound identified in *Ligusticum* spp., (Z)-ligustilide.[7] Oshá has been greatly overharvested in the wild near cities, but it is still abundant in outlying areas. Nevertheless, work continues on cultivating this valuable herb to insure its long-term sustainability.

None of these herbs have been much studied in the modern era, with chuān xiōng having received the most attention, and has been confirmed at least to be inflammation modulating.[8,9] As previously argued, herbs do not act like drug anti-inflammatories (i.e., potently inhibiting one major pathway). Instead, they act on multiple pathways more mildly, and thus there is the need for distinctive terminology.[10] (Z)-Ligustilide has been shown to be inflammation modulating as well, supporting this effect across the genus.[11] While oshá, chuān xiōng, and desert parsley have fairly strong, objectionable tastes, western sweet Cicely is quite pleasant tasting, with a mild licorice-like flavor. The unusual chemistry and strong activity of these herbs, along with the fact that they are active at low doses, recommends their widespread use. There is a rarely observed potential for these herbs causing photosensitivity dermatitis, but otherwise they are very safe.

The Lamiaceae group of herbs have a completely different chemistry, primarily monoterpenoids. *Salvia apiana* (white sage), *S. officinalis* (garden sage), *Thymus vulgaris* (thyme), *Rosmarinus officinalis* (rosemary), and *Prunella vulgaris* (heal-all) are among the many other mints with antiviral and other beneficial effects relevant to VRI. Generally, these are received well by patients based on taste. A combination of thyme and *Hedera helix* (English ivy) leaf was shown to reduce cough significantly compared to placebo in a double-blind, randomized trial in 361 German adults with acute bronchitis.[12]

Trees from two evergreen families, the Pinaceae and Cupressaceae, make up the third family group of antivirals. *Pinus* spp. (pine), *Abies* spp. (true firs), *Picea* spp. (spruces), *Thuja* spp. (cedars), and *Juniperus* spp. (junipers) resin and branch tips are all antiviral and inflammation modulators with a respiratory tract affinity. These herbs are extremely sustainable sources of

Table 2. Antiviral Activity Reported for Herbs Against Major Respiratory Viruses

Herb	Virus affected	Reference
Allium sativum	Parainfluenza, rhinovirus	Weber 1992[a]
Forsythia suspensa	RSV	Chen 2009[b]
Geranium sanguineum	Influenza	Serkedjieva 2008[c]; Gegova 1993 (synergy with rimantidine)[d]
Glycyrrhiza spp.	Influenza Rhinovirus RSV	Dao 2011[e]; Chen 2015 (synergy with ribavirin)[f] Yamaya 2007[g] Feng Yeh 2013[h]
Lonicera japonica	Influenza	Ding 2017[i]
Pelargonium sidoides	Influenza Coronavirus, Coxsackie, parainfluenza Rhinovirus, RSV	Theisen 2012[j] Michaelis 2011[k] Fal 2016[l]
Pinus spp.	Influenza	Won 2013[m]; Watanabe 1995[n]
Prunella vulgaris	Influenza	Tian 2011[o]
Rosmarinus officinalis	RSV	Shin 2013[p]
Salvia spp.	Influenza	Bang 2017[q]
Sambucus spp.	Influenza (fruit) Rhinovirus (fruit) RSV (branch tip) Parainfluenza, adenovirus, Coxsackie virus (flower)	Zakay-Rones 1995[r] Fal 2016[l] McCutcheon 1995[s]; Fal 2016[l] Glatthaar-Saalmüller 2011[t]
Thuja spp.	Influenza	Won 2013[m]

[a]Weber ND, Andersen DO, North JA, et al. In vitro virucidal effects of *Allium sativum* (garlic) extract and compounds. Planta Med 1992;58:417–423; [b]Chen Y, Li X, Zhou JY, et al. Effect of an active component from *Forsythia suspensa* (Thunb) Vahl against respiratory syncytial virus in vitro. Wei Sheng Yan Jiu 2009;38:733–735 [in Chinese]; [c]Serkedjieva J, Gegova G, Mladenov K. Protective efficacy of an aerosol preparation, obtained from *Geranium sanguineum* L, in experimental influenza infection. Pharmazie 2008;63:160–163; [d]Gegova G, Manolova N, Serkedzhieva Iu, et al. Combined effect of selected antiviral substances of natural and synthetic origin. II. Anti-influenza activity of a combination of a polyphenolic complex isolated from *Geranium sanguineum* L and rimantadine in vivo. Acta Microbiol Bulg 1993;30:37–40; [e]Dao TT, Nguyen PH, Lee HS, et al. Chalcones as novel influenza A (H1N1) neuraminidase inhibitors from *Glycyrrhiza inflata*. Bioorg Med Chem Lett 2011;21:294–298; [f]Chen XX, Zhou HX, Qi WB, et al. Antiviral effects of the combination of glycyrrhizin and ribavirin against influenza A H1N1 virus infection in vivo. Yao Xue Xue Bao 2015;50:966–972 [in Chinese]; [g]Yamaya M, Sasaki T, Yasuda H, et al. Hochu-ekki-to inhibits rhinovirus infection in human tracheal epithelial cells. Br J Pharmacol 2007;150:702–710; [h]Feng Yeh C, Wang KC, Chiang LC, et al. Water extract of licorice had anti-viral activity against human respiratory syncytial virus in human respiratory tract cell lines. J Ethnopharmacol 2013;148:466–473; [i]Ding Y, Cao Z1, Cao L, et al. Antiviral activity of chlorogenic acid against influenza A (H1N1/H3N2) virus and its inhibition of neuraminidase. Sci Rep 2017;7:45723; [j]Theisen LL, Muller CP. EPs® 7630 (Umckaloabo®), an extract from *Pelargonium sidoides* roots, exerts anti-influenza virus activity in vitro and in vivo. Antiviral Res 2012;94:147–156; [k]Michaelis M, Doerr HW, Cinatl J Jr. Investigation of the influence of EPs® 7630, a herbal drug preparation from *Pelargonium sidoides*, on replication of a broad panel of respiratory viruses. Phytomedicine 2011;18:384–386; [l]Fal AM, Conrad F, Schönknecht K, et al. Antiviral activity of the "virus blocking factor" (VBF) derived i.a. from *Pelargonium* extract and *Sambucus* juice against different human-pathogenic cold viruses in vitro. Wiad Lek 2016;69:499–511; [m]Won JN, Lee SY, Song DS, Poo H. Antiviral activity of the plant extracts from *Thuja orientalis*, *Aster spathulifolius*, and *Pinus thunbergii* against influenza virus A/PR/8/34. J Microbiol Biotechnol 2013;23:125–130; [n]Watanabe K, Momose F, Handa H, Nagata K. Interaction between influenza virus proteins and pine cone antitumor substance that inhibits the virus multiplication. Biochem Biophys Res Commun 1995;214:318–323; [o]Tian L, Wang Z, Wu H, et al. Evaluation of the anti-neuraminidase activity of the traditional Chinese medicines and determination of the anti-influenza A virus effects of the neuraminidase inhibitory TCMs in vitro and in vivo. J Ethnopharmacol 2011;137:534–542; [p]Shin HB, Choi MS, Ryu B, et al. Antiviral activity of carnosic acid against respiratory syncytial virus. Virol J 2013;10:303; [q]Bang S, Li W, Ha TKQ, et al. Anti-influenza effect of the major flavonoids from *Salvia plebeia* R Br via inhibition of influenza H1N1 virus neuraminidase. Nat Prod Res 2017;1–5; [r]Zakay-Rones Z, Varsano N, Zlotnik M, et al. Inhibition of several strains of influenza virus in vitro and reduction of symptoms by an elderberry extract (*Sambucus nigra* L) during an outbreak of influenza B Panama. J Altern Complement Med 1995;1:361–369; [s]McCutcheon AR, Roberts TE, Gibbons E, et al. Antiviral screening of British Columbian medicinal plants. J Ethnopharmacol 1995;49:101–110; [t]Glatthaar-Saalmüller B, Rauchhaus U, Rode S, et al. Antiviral activity in vitro of two preparations of the herbal medicinal product Sinupret® against viruses causing respiratory infections. Phytomedicine 2011;19:1–7.

RSV, respiratory syncytial virus.

medicine, available year-round and with little negative impact on the trees from harvesting reasonable amounts of medicine.

All three of these groups are inflammation modulators, which is important for two reasons. The symptoms of VRI are significantly due to immune responses to the infecting virus. More importantly, severe influenza is in part due to what has been dubbed "cytokine storm": a hyperreaction of the immune system to certain influenza strains.[13] Thus, inflammation-modulating herbs are important to decrease symptoms and to prevent severe consequences, at least in the case of influenza infection. Additionally, these herbs frequently have immune-stimulating effects, running the risk of increasing symptoms of VRI or making cytokine storms worse. With concomitant inflammation-modulating effects, this potential problem is avoided.

Research on some of the antiviral herbs noted here supports the importance of their inflammation-modulating effects. Desert parsley has been shown to decrease CXCL10 production, a cytokine highly associated with dangerous cytokine storms in severe influenza, in an in vitro model.[14] It may well be that desert parsley simultaneously increases other cytokines that do not promote cytokine storm, but do beneficially inhibit the

virus, though this has not been well-studied. Chuān xiōng, as well as *Forsythia suspensa* (forsythia, lián qiào) and *Glycyrrhiza uralensis* (Chinese licorice, gān cǎo), inhibited production of CCL5 (also known as RANTES), another participant in cytokine storms.[15] Diterpenoids from rosemary and garden sage have been shown to inhibit production of multiple cytokines associated with cytokine storms.[16] Heal-all has repeatedly been shown to have inflammation-modulating effects.[17] Human studies are lacking, but these results support what is seen clinically: mitigation of severity and lethality of influenza and other VRI in patients who take these herbs in sufficient doses.

Clinical Trials in Acute VRI

Many of the herbs discussed here have been shown to be effective in treatment of VRI. One of the most famous is the fruit of *Sambucus nigra* (black elder). The original double-blind trial was conducted among 40 adults and children in southern Israel confirmed to have influenza B, randomizing them to black elderberry syrup or placebo 1 tbsp b.i.d. (for children) or 2 tbsp b.i.d. (for adults).[18] Symptom severity and duration (mean 1.3 days shorter with black elder) were significantly lower in the black elder group compared to placebo. A similar double-blind trial randomized 60 adult Norwegians with influenza A or B to 15 mL of black elder syrup or placebo.[19] Again, symptom severity was significantly less with black elder compared to placebo, and in this case recovery was on average four days quicker with black elder. Use of rescue medication was also significantly less in the black elder group versus placebo. There were no adverse effects in either of these trials.

A more recent trial randomized 312 Australian adults who were undertaking international travel by coach to black elder capsules 300 mg b.i.d. before travel and t.i.d. during travel and after arrival, or placebo.[20] Each participant took their assigned medicine for a total of 14 days. About half had been vaccinated against influenza. There was no difference between the groups in terms of incidence of clinical VRIs. However, duration of these colds were significantly shorter and severity significantly less in the black elder group compared to placebo. There was no difference in adverse effects between the two groups, suggesting no significant danger from black elder.

A proprietary German formula BNO 1016 (known by the trade name Sinupret®; Bionorica, Neumarkt, Germany) has been fairly extensively studied for VRI since its creation by Josef Popp in 1933. Its ingredients are listed in Table 3; they are fairly unusual, with only black elder flower still enjoying wide use for VRI in Western herbal medicine. The mixture has been shown to be active against parainfluenza, RSV, rhinovirus, and adenovirus in vitro.[21] It has also demonstrated inflammation-modulating activity in rodents.[22] The usual dose of the dry extract is 160 mg t.i.d.

Table 3. BNO 1016 (Sinupret) Herbal Formula

Verbena officinalis (vervain) flowering tops 23%
Primula veris (cowslip) flower 23%
Sambucus nigra (black elder) flower 23%
Rumex spp. (yellow dock) leaf 23%
Gentiana lutea (yellow gentian) root 8%

Numerous clinical trials have demonstrated efficacy of BNO 1016 in patients with VRI. The most recent two double-blind trials randomized a total of 589 German adults with VRI to either BNO 1016 or placebo for 15 days.[23] Symptom severity was significantly reduced by BNO 1016 compared to placebo in both trials. There were minimal adverse effects with the formula. Another double-blind trial in 386 German adults with acute VRI found that BNO 1016 relieved symptoms significantly compared to placebo.[24,25] The number needed to treat with BNO 1016 to achieve a clinically significant reduction in symptoms was seven. Again, the formula was very safe. An earlier open trial investigated 40 Russian children with suppurative otitis media already undergoing treatment with antibiotics, nasal decongestants, and some surgical treatment, some of whom were also treated with BNO 1016.[26] Exudate cleared significantly faster in the group that took the herbal formula compared to those who did not. Finally, the formula is also helpful in treating allergies, which can sometimes be clinically indistinguishable from upper VRIs.[27]

Andrographis paniculata (kalmegh) is a tropical species in the Acanthaceae family native to South Asia, with a strong reputation for treating VRI in Ayurvedic and other traditional Asian medical systems. It is also intensely bitter, and indeed is sometimes called king of bitters. It is best administered as a capsule to avoid its unpleasant taste. A meta-analysis evaluated seven double-blind, randomized clinical trials of various kalmegh preparations in patients with upper VRIs.[28] Kalmegh significantly reduced severity of cold symptoms compared to placebo. It did so without adverse effects. The dose of a tablet or encapsulated extract of kalmegh is 1–3 g t.i.d.

Pelargonium sidoides (African geranium) is native to South Africa (particularly the Eastern Cape region including Lesotho) and is part of the Geraniaceae family. It is notable that other species in this family, particularly *Geranium sanguineum*, also have antiviral activity (see Table 2). A meta-analysis of 10 trials of African geranium root extracts for VRI in children and adults found evidence they are more effective than placebo, but the quality of the trials was generally low.[29] Though more rigorous trials are needed, it still has a place in clinical use given the great safety profile of this herb. A typical dose of the tincture (which is the most effective form in studies, at least compared to encapsulated extracts) is 1–2 mL t.i.d.

Má huáng tāng (see Table 4) is a traditional Chinese formula first published in the *Shāng Hán Lùn* (*Treatise on Cold Damage Diseases*) written by Zhāng Zhòng-Jǐng in 220 CE. It is known as maō-tō in Japanese and ephedra decoction in English. It is historically used to treat influenza and has been validated in modern times for this purpose. An open trial in 28 Japanese adults with influenza were randomized to either take ephedra decoction in

Table 4. Má Huáng Tāng Formula

Ephedra sinica (má huáng, ephedra) stem 33%
Prunus armeniaca (xìng rén, apricot) seed 33%
Cinnamomum cassia (guì zhī, cassia) branch 22%
Glycyrrhiza uralensis (zhì gān cǎo, Chinese licorice) prepared root 11%

the form of a granulation (basically a dried, granulated form of the decoction) 2.5 g t.i.d. orally, oseltamivir 75 mg b.i.d. orally, or zanamivir 20 mg b.i.d. by inhalation.[30] Median fever duration was significantly shorter in the ephedra decoction group than in the oseltamivir group, and the same as in the zanamivir group. There was no difference between the groups in terms of median duration of total symptoms, duration of viral persistence in nasal secretions, or serum cytokine profiles. Other than one patient taking ephedra decoction and one taking oseltamivir who developed mildly elevated serum transaminases, there were no adverse effects. A similar trial in 150 Japanese children with influenza compared ephedra decoction alone, ephedra decoction plus oseltamivir, ephedra decoction plus zanamivir, oseltamivir alone, and zanamivir alone.[31] Mean duration of fever was significantly shorter in the ephedra decoction plus oseltamivir and zanamivir groups compared to the oseltamivir group in patients with influenza A; there was no difference in those with influenza B. Though double-blind trials are needed to confirm it, these studies provide sufficient evidence that ephedra decoction is as safe and effective as neuramidase-inhibiting drugs, though its mechanisms of action are unknown.

A variant of ephedra decoction called antiwei (see Table 5), of unknown origin, adds three herbs to the mixture. A double-blind trial involving 480 Chinese adults with influenza ($n = 125$) or influenza-like illness ($n = 355$) randomized them to antiwei granulation 6 g b.i.d. or placebo at the same dose for three days.[32] Duration and severity of both confirmed influenza and influenza-like illness were significantly lower in the antiwei group compared to placebo. There was no difference in adverse effects between the groups, which were mild.

Table 5. Antiwei Formula, a Variant of Ephedra Decoction

Imperata cylindrica (bái máo gēn, woolly grass) rhizome 33%
Pueraria montana var *lobata* or *chinensis* (gé gēn, kudzu) root 16%
Ephedra sinica (má huáng, ephedra) stem 11%
Prunus armeniaca (xìng rén, apricot) seed 11%
Cinnamomum cassia (guì zhī, cassia) branch 11%
Glycyrrhiza uralensis (zhì gān cǎo, Chinese licorice) prepared root 11%
Zingiber officinale (gān jiāng, ginger) dry rhizome 7%

The Case for Echinacea

Echinacea angustifolia (narrow-leaved purple coneflower; Fig. 1) root is a good example of how poorly designed research studies can make an herb that is clinically very effective appear ineffective. This herb was and is much heralded in traditional herbalism for VRI.[33] In a famous clinical trial, 437 American young adult volunteers with low antibody titers to rhinovirus type 39 were randomized to one of seven groups.[34] All subjects took their first treatment (one of three extracts of echinacea in three groups, or four different placebo groups) for seven days and then were challenged with the rhinovirus. Then, all groups that initially took echinacea switched to placebo, and three of those previously on placebo switched to one of the three *E. angustifolia* preparations (so one group, the seventh group, took placebo the entire time). No significant difference was found between any group in rates of infection, symptom severity, or viral titers at any point in the study.

The three extracts used were a supercritical carbon dioxide extract, a 60% ethanol tincture, or a 20% ethanol tincture. The

Figure 1. ***Echinacea angustifolia*. Drawing by Meredith Hale and reprinted with permission.**

first and last extracts are not based on traditional use; only the 60% extract mirrors anything particularly known to work prior to the study. An even bigger problem was the dose: just 1.5 mL (equivalent to 300 mg of *E. angustifolia* root) t.i.d. were given of each extract. This is at least one third the effective dose (typically a full 5 mL or 1 tsp is given at a time of *E. angustifolia* tincture), and not nearly of sufficient frequency (during an acute cold, a typical dose is at least six times per day). The duration of treatment for prevention was simply too short to be realistic. *E. angustifolia* was not given continuously in any group, ruling out any possibility of finding an effective dose regimen from continuous treatments. Based on all this, the most that can be concluded is that extremely low and infrequent doses of *E. angustifolia* (sometimes in extracts with historical basis for use) are ineffective, which hardly required a very expensive, large clinical trial to determine. This study is often cited as proof that *E. angustifolia* does not work, when it should be used to argue for higher, more frequent doses at a minimum.

There was prior clinical trial evidence to suggest the dose used in this trial was too low. In a 2002 double-blind trial in an American college population of 148 students, a capsule providing 500 mg of *E. angustifolia* six times per day (along with 250 mg each of *E. purpurea* and *E. pallida*) was not more effective than placebo.[35] Why the researchers in the 2005 trial used even less material is completely inexplicable. Most other trials have used *E. purpurea*, an inferior species for this purpose, and thus not surprisingly most of the trials support that low, infrequent doses of the herb do not help speed recovery from VRIs. It is also notably important that echinacea products be gargled, as they have a topical numbing effect that is very helpful for reducing pharyngeal pain.

Various species of echinacea have been shown to act as inflammation modulators in cells infected with influenza, rhinovirus, and other respiratory viruses.[36–38] This effect may help prevent cytokine storms as well as explain reduction of symptoms.[39]

Formulating for Acute VRI

Putting together an individualized formula is the real art of working with patients with acute VRIs. A proposed base formula is given in Table 6. This should be adjusted to fit the specifics of an individual patient. If they definitively or very likely have influenza, then *Sambucus* spp. fruit should be added. If their oral temperature is $>103^{\circ}$F, then febrifuge herbs such as *Salix* spp. (willow) or *Betula* spp. (birch) bark and/or leaf, or, in the most extreme cases, *Aconitum* spp. (aconite) cooked root should be added. These herbs or other analgesics are also indicated if the patient has particularly severe myalgia. If they have no fever, then not only should they take the diaphoretic tea as directed in Table 6, but also add *Zingiber officinale* (ginger) rhizome or another heating herb to the mix. If they have a sore throat, then the formula should be gargled so the echinacea can have its numbing effect (and it should be 30% of the formula). If the taste of the formula is disagreeable, then *Nepeta cataria* (catnip) glycerite should be substituted for heal-all at 40% of the formula and desert parsley limited to 10%. If the patient has a bothersome wet cough, then a mucolytic herb such as *Grindelia* spp. (gumweed) flower bud, *Eriodictyon* spp. (yerba santa) leaf, or *Populus* spp. (poplar) resin should be added. If the patient has a bothersome dry cough, then in addition to a mucolytic herb an antitussive such as *Tussilago farfara* (coltsfoot) or *Prunus virginiana* (wild cherry) bark should be added.

Preventing VRI

Herbs also have significant potential to help prevent VRI in the first place. Several botanical extracts that have been shown to do so in clinical trials are highlighted here.

Panax ginseng (Asian red ginseng) steamed root and *P. quinquefolius* (American ginseng) root are two immunomodulating plants that have been fairly extensively studied for preventing VRI. In one double-blind trial, 100 Korean adults were randomized to received either a red ginseng extract or placebo at the start of the influenza season.[40] The Asian red ginseng extract was provided at a dose of 1 g t.i.d., and was standardized to contain 7 mg/g of the sum of ginsenosides Rg1 and Rb1. Incidence of VRI was significantly lower in the Asian red ginseng group compared to placebo (reduced by about 45%). Severity and duration of illness was not significantly different between the groups in those who developed VRI. Asian red ginseng was as safe as placebo in this study. A different extract of Asian ginseng at a dose of 100 mg daily was compared to placebo in a double-blind trial in 227

Table 6. Base Formula for Acute VRI

Herb	Extract	Principal action(s)	Percentage
Echinacea angustifolia	Fresh root tincture	Immune stimulating, inflammation modulating	20–30%
Lomatium dissectum	Fresh root rincture	Antiviral, immune stimulating, inflammation modulating	15–20%
Prunella vulgaris	Fresh herb glycerite	Antiviral, inflammation modulating, corrigent	30–40%
Glycyrrhiza glabra	Dry root glycerite	Antiviral, inflammation modulating, corrigent, synergizer	15–30%
Phytolacca americana	Fresh root tincture	Lymphagogue	5–10%

Take 1 tsp every two to four waking hours for three days, then three times per day. Add to hot tea of any one of the diaphoretic herbs listed in Table 1 if fever is >101°F.

Italian adults receiving influenza immunization after four weeks of supplementation.[41] With an additional treatment period of eight weeks, the incidence of total VRI was significantly less in the vaccine + ginseng group compared to vaccine + placebo. Influenza antibody titers and natural killer cell activity were significantly higher with Asian ginseng supplementation compared to placebo. There were minimal, mild adverse effects.

An American ginseng extract standardized to contain 80% polysaccharides and 10% protein from roots of the plant has been assessed in several double-blind clinical trials. One randomized 279 Canadian adults to either 400 mg of the American ginseng extract or placebo for four months as the influenza season commenced.[42] Significantly fewer participants in the American ginseng group developed VRI at all than in the placebo group, as well as significantly fewer having more than one VRI. Severity and duration of VRI symptoms were significantly lower in the American ginseng group versus placebo.

In a group of 198 elderly American adults living in nursing homes and assisted-living facilities, the same American ginseng extract at a dose of 200 mg b.i.d. was compared to placebo for 12 weeks.[43] Laboratory-confirmed cases of influenza and RSV infection were significantly reduced in the American ginseng group compared to placebo, with no differences in adverse effects. The same American ginseng extract at the same dose in a very similar trial design was confirmed in a study of 43 elderly American adults living in the community who received the influenza vaccination.[44] The incidence and duration of VRI was cut in half in the American ginseng group compared to placebo in this trial, a very significant difference in both cases. Based on all these studies, Asian and American ginseng look very promising for reducing incidence of VRI during the winter months.

American ginseng has largely not been studied for treating acute VRI. A liquid standardized extract of American ginseng was compared to placebo in a randomized trial of 46 Canadian children (age 3–12 years) with acute VRI.[45] The dose was weight-based and complicated: one group were given 26 mg/kg on day 1, 17 mg/kg on day 2, and 9 mg/kg on day 3 of their VRI; a second group were given half this dose; and the third group were given placebo. All doses were divided into three portions throughout the day. There was no difference between any of the groups in terms of severity or duration of VRI symptoms, but there was also no difference in adverse effects. This is important because of the concern, based on Chinese medical theory, that an adaptogenic/*qi* tonifying herb such as American ginseng might "tonify the pathogen" and make VRI worse. This effect was not seen in practice. However, it also suggests that American ginseng is unlikely to be that useful in resolving VRI, and other herbs as discussed above should be favored for this purpose.

Epidemiologic evidence suggests that higher intake of *Camellia sinensis* (green tea) in Japan is associated with lower incidence of influenza among children.[46] Any level of green tea intake is correlated with a dramatic reduction in risk of dying from influenza in women in Japan, but not men, according to a large epidemiological study.[47]

An open-label trial did not find that gargling green tea three times per day was more effective than water at preventing influenza in 757 Japanese teenagers.[48] In a double-blind trial in 197 Japanese adults providing healthcare to the elderly in medical facilities, a green tea extract providing 378 mg of catechins and 210 mg of theanine per day was significant more effective than placebo at reducing the incidence of VRI.[49] Since laboratory-confirmed influenza rates did not differ between the groups, the green tea product seemed primarily to be preventing other viral infections. Another double-blind trial in 108 American adults compared a different green tea extract combining epigallocatechin gallate and theanine to placebo (milligram dose unstated, one capsule b.i.d.) for three months.[50] Total VRI incidence, severity, and duration were all significantly lower with the green tea extract compared to placebo. Levels of γδ T lymphocytes, considered crucial to fending off influenza, were significantly increased by the green tea extract compared to placebo. The treatment was very safe.

In a double-blind trial, 146 British adults were randomized to a garlic supplement or placebo for 12 weeks during the peak cold and influenza season.[51] The garlic product contained 180 mg of an allicin-containing powder and was taken once per day. Self-reported VRIs were significantly less common in the garlic group versus the placebo group, with approximately one third as many colds in those taking garlic. Severity and duration of VRI symptoms were also significantly reduced in the garlic group compared to placebo. No other trial of garlic for VRI prevention has been published, but given its safety and potential efficacy, this looks like a very easy way to reduce such infections.[52]

Conclusion

There are numerous safe and effective botanical treatments for and preventative measures against VRI. Many have been proven in clinical trials, though more evidence is still needed for quite a few. Mechanisms of action include directly inhibiting various causative viruses, affecting the immune and inflammatory response to infection, and counteracting symptoms. Herbs provide a much-needed alternative to ineffective antibiotics while still helping patients with VRI feel they are receiving useful therapy, thereby reducing their tendency to demand antibiotics. The preventative effects of those herbs reviewed here are particularly exciting, and though more trials are needed, we appear to be more than ready for large-scale adoption to help reduce the significant burden VRI places on society.

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