Allergies and Natural Alternatives

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KEYWORDS

• Allergic rhinitis • Allergy treatment • Integrative medicine • Complementary medicine

KEY POINTS

- Allergic rhinitis (AR) is a treatable disease with the typical otolaryngologist often using many conventional approaches including antihistamines, corticosteroids, decongestants, and immunotherapy.
- Complementary and integrative therapies have been investigated to varying degrees, and nutritional supplements, herbal medications, traditional medicines, and other techniques have shown varying efficacy in treating AR.
- Certain risks are associated with the use of complementary and integrative medicine and include risks of bleeding and drug interactions.
- Obtaining a thorough history of the use of complementary and integrative therapies is the responsibility of the otolaryngologist treating this condition.

INTRODUCTION

Complementary and integrative medicine (CIM) is defined as "diagnosis, treatment, and/or prevention which complements mainstream medicine by contributing to a common whole, by satisfying a demand not met by orthodoxy or by diversifying the conceptual frameworks of medicine."[1] It is a broad category of practices and treatments that is outside the realm of conventional medicine, including nutritional supplements, herbal treatments, acupuncture, traditional or cultural practices, homeopathy, naturopathy, mind–body medicine, and chiropractic or osteopathic manipulations. This discussion explores the role of CIM in the treatment of allergic rhinitis (AR).

The pathophysiology of AR centers on defining this condition as a systemic inflammatory process associated with inflammatory disorders of the mucous membranes including asthma, rhinosinusitis, and allergic conjunctivitis. It is a state of hypersensitivity that occurs when the body reacts to an allergen. Modern treatment of AR began with the emergence of antihistamine therapy in the 1930s. Topical corticosteroids were developed in the 1950s which, when added to antihistamines, became the

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mainstay of therapy. Since this time, decongestants, mast cell stabilizers, and leukotriene receptor antagonists have offered additional options for treatment. Throughout this time, the use of complementary and integrative therapies has paralleled during this surge of therapies. CIM therapies that target atopic conditions, such as AR, are second only to therapies for back pain.[2] CIM therapies are not unpopular as approximately 40% of adults in the United States[3] have used at least one type of CIM therapy.

The prevalence of AR in the United States has been estimated to be as high as 36%, and before the age of 6 years, 40% of children are affected by AR.[4,5] Subsequently, AR is a major cause of school and work absences, therefore, creating a high cost to the health care system.[6] As a result, it is not surprising that most patients and parents who adopt CIM therapies use it as a complement to conventional care.[7,8] The reasons why patients use natural alternatives are complicated; they include a distrust in conventional medicine and the belief that CIM is more natural and safer.[9] Even with natural alternatives and conventional care, many patients do not believe that their symptoms are well controlled.[10] The negative motivation for using CIM emphasizes the important role of the physician in advising patients on these methods. However, a significant portion (40%–70%) of patients does not disclose the use of CIM therapies to their physicians.[11–13]

Physicians play an integral role in advising patients on the use of natural alternatives. Maintaining an awareness of the efficacy and contraindications of these alternatives is a critical responsibility. However, physicians face a challenge; there is a void of randomized controlled trials and experimental data to support the routine use of these alternatives. It is therefore, the responsibility of the physician to diligently review the data that are available, and then offer advice and recommendations to his or her patients. Many physicians are intimated by CIM because they are unaware of the clinical evidence and feel uncomfortable advising their patients on its efficacy.[9] An obstacle that cannot be understated is that herbal remedies are usually not standardized and most, to varying degrees, contain a mixture of substances. This lack of standardization potentiates the possibility of toxicity, drug-to-drug interactions, and a discrepancy even within what may be marketed as the same supplement. Knowledge of CIM therapies that impact the bleeding time is vital for the perioperative period.[14] Compared with proprietary marketing drugs, herbal remedies carry the risk of impurities, incorrect collection of plants, wrong preparation, and inappropriate/incorrect dosing.[15] Regardless of the obstacles that may limit a physician's knowledge of these alternatives, many patients are using or have used these therapies. Consequently, there is a need for physicians to inquire and discuss these alternatives with their patients while maintaining an understanding of the available data on these natural alternatives. This discussion addresses each natural alternative that has played a role in the treatment of AR, discusses the evidence behind the remedy, and offers recommendations for the physician.

DISCUSSION

The use of CIM therapies in allergy can be split into the broad categories of nutritional supplements, herbal supplements, Ayurvedic medicine, and Chinese traditional medicine.

NUTRITIONAL SUPPLEMENTS

Various nutritional supplements have been reported to improve the symptoms of allergy and AR or hasten recovery of upper respiratory infections. **Table 1** details the active ingredients, intended use, and mechanism of action of each of these

Table 1
Nutritional supplements used in the treatment of allergy and allergic rhinitis

Supplement	Active Ingredient	Uses and Mechanism of Action	Adverse Effects	Drug–Drug Interactions
Vitamin C	Ascorbic acid	Acute viral or bacterial rhinitis Inhibit histamine secretion by lymphocytes[16] Decrease nasal secretions, congestion. and edema[16]	Kidney stones Diarrhea Delayed wound healing Increase iron absorption in blood-iron disorders (thalassemia, hemochromatosis) Worsen sickle cell disease	Decrease effectiveness of HIV/AIDS medications Decrease effectiveness of warfarin (Coumadin) Delay metabolism of aspirin
Capsaicin	8-methyl-N-vanillyl-6-nonenamide	Allergic rhinitis Inhibit release of substance P from nasal mucosal cells, decreasing IL-6 production[17]	Localized irritation at application site	Unknown
Fish Oil	Eicosapentaenoic acid and docosahexaenoic acids, ω-3 fatty acids	Allergic rhinitis Anti-inflammatory properties Reduce production and effectiveness of prostaglandins[17]	Dose-related increase in bleeding time Hypotension by increasing the effects of antihypertensive medications	Unknown
Spirulina	Filamentous cyanobacteria, blue-green algae *Arthrospira platensis, Aporosa fusiformis, and Aristolochia maxima*	Allergic rhinitis Anti-inflammatory Inhibition of histamine release from mast cells Reduce IL-4, enhances IgA production[18,19]	Hepatotoxicity Heavy metal contamination	Unknown

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Table 1
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Supplement	Active Ingredient	Uses and Mechanism of Action	Adverse Effects	Drug–Drug Interactions
Manuka/Tualang honey	Methylglyoxal	Allergic rhinitis Anti-inflammatory Modulates mast cell response[20] Suppresses antigen-specific IgE levels[21]	Unknown	Unknown

HIV/AIDS, Human immunodeficiency virus/acquired immunodeficiency syndrome; IgA, Immunoglobulin A; IgE, Immunoglobulin E; IL, interleukin; MIC, minimum inhibitory concentration; OTC, over-the-counter.

supplements, as well as the adverse effects and known drug–drug interactions. Unfortunately, much is still unknown about the side effects and interactions of these supplements.

Vitamin C, also known as ascorbic acid, has been used for the treatment of acute bacterial and viral rhinitis by inhibition of histamine secretion by lymphocytes.[16] It has been shown to decrease nasal secretions, congestion, and edema.[16] The most common adverse effects include kidney stones, diarrhea, delayed wound healing, increased iron absorption in diseases like thalassemia and hemochromatosis, and it may worsen sickle cell disease. Vitamin C also decreases the effectiveness of HIV/AIDS medications including amprenavir, nelfinavir, ritonavir, and saquinavir. It also decreases the effectiveness of warfarin and delays the metabolism of aspirin.

Capsaicin contains the active ingredient 8-methyl-N-vanillyl-6-nonenamide and is used as a topical treatment of AR by blocking neuropeptide substance P, thereby reducing IL-6 production.[16] However, one study has shown no therapeutic effect in the treatment of AR.[17] Side effects are relatively benign, mainly limited to localized irritation at application site.

Fish oil contains eicosapentaenoic acid and docosahexaenoic acids (omega-3 fatty acids), which are used in the treatment of AR via anti-inflammatory properties of reducing the production and effectiveness of prostaglandins. However, the efficacy of fish oil has not been overly positive, with some studies showing no benefit, and another showing an increase in the prevalence of AR in those with reduced intake of fish oil.[17] Fish oil has a dose-related increase in bleeding time and has been shown to decrease blood pressure by increasing the effect of antihypertensive medications, thereby causing hypotension.

Spirulina is a filamentous cyanobacteria or blue-green algae of the genus *Arthrospira*. It has been used in the management of AR by inhibiting the release of histamine from mast cells and reducing IL-4 in the IgE-mediated allergy pathway, thereby enhancing IgA production.[19] Spirulina has been shown to decrease IL-4 and improve nasal symptoms in patients with AR after 6 months of spirulina dosing.[18,19] In addition, spirulina has been cited as inhibiting histamine release from mast cells and increased interferon (INF)-gamma levels.[19] On the negative side, spirulina has been shown to cause hepatotoxicity and reaction from heavy metal contamination.

Manuka honey and Tualang honey contain the active ingredient of methylglyoxal and are used in the treatment of AR. They have been shown to modulate mast cell response and suppress IgE levels.[20,21] Clinically, they have been shown in clinical trials to improve the symptoms of AR, and the findings state that ingestion of honey along with standard antihistamines is beneficial in relieving the AR symptoms without any reported adverse effect.[22] However, another study showed no decrease in allergy symptoms when compared with placebo.[23]

HERBAL SUPPLEMENTS

Various herbal supplements have been used in the treatment of allergy and AR. **Table 2** details the active ingredients, intended use, and mechanism of action, as well as adverse effects and drug–drug interactions.

Angelica, also known as Danggui, is from the *Angelica archangelica* plant. It is an expectorant used for bronchial illnesses, allergies, colds, and coughs, as well as for treatment of mild spasms of the gastrointestinal tract, loss of appetite (anorexia nervosa), flatulence, and satiety. Isolated forms of the various furanocoumarins have shown to have an inhibitory effect on the lipopolysaccharide-induced prostaglandin E2 production with decreased expressions of cyclooxygenase-2 and microsomal

Table 2
Herbal supplements used in the treatment of allergy and allergic rhinitis

Supplement	Active Ingredient	Uses and Mechanism of Action	Adverse Effects	Drug–Drug Interactions
Angelia (*A archangelica*) Danngui	Furanocoumarins	Allergic rhinitis, upper respiratory infections Inhibitory effect on prostaglandin E2[24]	Photodermatitis and phototoxicity[25,26]	Inhibition of cytochrome P450
Bromelain (*A comosus*)	Proteolytic enzyme of the pineapple plant	Allergic rhinitis, sinusitis, anti-inflammatory Mucolytic; thins nasal mucus secretion Inhibits production of prostaglandin E1[16]	Gastrointestinal upset Allergic reactions overlap with allergies to pineapple, wheat, celery, papain, carrot, fennel, and cypress pollen or grass pollen	Unknown
Butterbur (*Petasites hydridus*)	Petasin	Allergic rhinitis Inhibits leukotrienes, mast cell degranulation, and nasal levels of histamine[27–29]	Removal of pyrrolizidine alkaloids is essential Pyrrolizidine alkaloids are hepatotoxic and carcinogenic Petasin is a processed butterbur extract with alkaloids removed[30–32] Gastrointestinal upset	Unknown
Cineole	Eucalyptol, 1,8-cineole, an extract from eucalyptus oil	Acute rhinosinusitis, anti-inflammatory Increased beat frequency of cilia[33]	Reflux, headache, and nausea Undiluted eucalyptus oil is toxic (3.5 mL of undiluted oil can be fatal) Symptoms of poisoning include dizziness, weakness, mydriasis, shortness of breath and abdominal pain/burning	Unknown

Echinacea (E angustifolia, E pallida, and E purpurea)	Alkamides, chicoric acid, and polysaccharides	Acute infectious rhinitis Activates T and B lymphocytes in vitro[35]	Gastrointestinal upset, tongue numbness, headache, muscular aches, and dizziness Associated with hepatotoxicity, especially after 8 wk of use	May delay metabolism of caffeine, causing tachycardia and nervousness
Ephedra *(E sinica)* Ma huang	Ephedrine	Nasal congestion, asthma, bronchitis, and nasal congestion, weight loss aid and stimulant Central nervous system stimulant via noradrenaline on adrenergic receptors[36,37]	Tachycardia, palpitations, hallucinations, hypertension, paranoia, and potentially death[38–42] Banned for OTC use as a dietary supplement[45]	Interactions with glycosides and halothane, may cause arrhythmias and potentiation of monoamine oxidase inhibitors (MAOIs)[43–45]
Esberitox *(T occidentalis, E purpurea,* and *B tinctoria)*	Alkamides, chicoric acid, and polysaccharides	Acute sinusitis Immune stimulant	Rashes, retching, facial swelling, vertigo, and hypotension	Unknown
Garlic *(A sativum)*	Allicin (diallyl-thiosulfinate)	Acute infectious rhinitis, cough Inhibition of prostaglandins, thromboxanes	Rare allergic reactions, hypoglycemia, prolonged bleeding time Decreased platelet aggregation within 5 d of oral dosing via inhibition of epinephrine-induced platelet aggregation[12] Recommend discontinuation 1 wk before surgery	Inhibits cytochrome P450[2] May interfere with paracetamol and chlorpropamide Hypoglycemia Increase MIC of ampicillin
Ginkgo (*Ginkgo biloba*)	Ginkgolides Terpene lactones and ginkgo flavone glycosides	Inhibits development of bronchial hyperreactivity Inhibits eosinophil influx into animal airways induced by platelet activating factor or antigen exposure[46,47]	Unknown	Inhibition of cytochrome P450 Increase in blood pressure when combined with thiazide diuretics[48] and coma with trazodone[49,50]

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Table 2
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Supplement	Active Ingredient	Uses and Mechanism of Action	Adverse Effects	Drug–Drug Interactions
Grape seed extract	Proanthocyanidins	Chemoprevention of cellular damage[51]	Unknown	Unknown
Licorice root (*G glabra)*	Glycoside glycyrrhizin	Allergic rhinitis, conjunctivitis, and bronchitis Anti-inflammatory and antiviral Inhibit 11-beta-hydroxysteroid dehydrogenase and the classic complement pathway	Hypokalemia, muscle pain, extremity numbness, pseudo-aldosteronism which may lead to hypertension, headaches, and cardiac events[12]	Interferes with ACE inhibitors, diuretics, corticosteroids, insulin and other diabetic drugs, MAOIs, oral contraceptives, and digoxin, and can dangerously increase the toxicity of digoxin[43]
Myrtol (*Pinus spp* (pine), *C aurantifolia* (lime) and *Eucalyptus globulus*)	Monoterpenes, D-limonene, 1,8-cineole, alpha-pinene	Acute rhinosinusitis, chronic rhinosinusitis, anti-inflammatory Secretolytic and secretomotoric effects, increase upper and lower airway patency[52]	Gastrointestinal disturbance, facial swelling, allergic reactions, and taste disturbances	Unknown
N-acetylcysteine	N-acetylcysteine	Sinusitis Mucolytic Cleavage of disulfide bonds in mucoproteins by its sulfhydryl group resulting in less viscous mucus[16]	Gastrointestinal upset	Unknown
P frutescens	Phenolic acids, flavonoids, anthocyanins	Upper respiratory infections, asthma, allergic rhinitis Antioxidant, anti-	Pulmonary toxicity in animal studies, no evidence to support toxicity in humans[53,54]	Unknown

		inflammatory, antibacterial		
Quercetin (3,3′,4′5-7-pentahydroxyflavone)	Bioflavonoid	Anti-inflammatory Inhibition of inflammatory enzymes (cyclooxygenase and lipoxygenase, regulators of leukotrienes and prostaglandins) Mast cell stabilizer, inhibits release of histamine	Unknown	May lessen the effects of quinolone antibiotics Not recommended in those with hypertension, immunosuppression, or kidney stones[34]
Sinupret Elder flower (*Sambucus nigra)*, cowslip flowers (*Primula veris*), common sorrel (*Rumex acetosa*) European vervain (*Verbena officinalis*), and gentian (*Gentiana lutea)* root	Unknown	Allergic rhinosinusitis Mucolytic, antiviral, anti-inflammatory[33]	Kidney stones, allergic reactions, gastrointestinal symptoms, numbness, and mild dermatitis	Interacts with therapeutic monoclonal antibodies, hypertensive medications, and immunosuppressants (tacrolimus, methotrexate, corticosteroids, mycophenolate, etanercept, and cyclosporine)
Stinging nettle (*U dioica*)	Unknown	Allergic rhinitis[55]	Application to mucosal surfaces causes burning and itching, contact dermatitis, GI disturbances[2]	Unknown

prostaglandin E synthetase.[24] It also has inhibitory effects on cytochrome P450. Adverse effects include skin sensitization to sunlight due to the furanocoumarins causing photodermatitis and phototoxicity.[25,26]

Bromelain is an extract from the pineapple plant *Ananas comosus.* It contains a proteolytic enzyme used in the treatment of AR, sinusitis, and for anti-inflammatory properties. It is a mucolytic, which thereby thins nasal mucus and inhibits the production of prostaglandin E1.[26] It has been shown to aid in a faster symptomatic recovery from sinusitis.[16] An adverse side effect is gastrointestinal upset. It should not be used in those with allergies to pineapple, wheat, celery, papain, carrot, fennel, cypress pollen, or grass pollen because of an allergic reaction overlap with the pineapple plant.

Butterbur (*Petasites hybridus*) is a perennial shrub found in Europe and parts of Asia and North America which contains petasin, a compound believed to have anti-inflammatory and leukotriene inhibitory properties.[32,56,57] Petasin inhibits the biosynthesis of cysteinyl leukotrienes in vitro[27–29] and decreases nasal levels of histamine and cysteinyl leukotrienes in vivo.[56] In a randomized clinical trial, butterbur was shown to relieve symptoms, attenuate peak nasal inspiratory flow recovery, and reduce maximum percentage of peak nasal inspiratory flow decrease from baseline.[58,59] When compared against fexofenadine, it has been shown to be non-inferior in relieving symptoms of AR.[60] Trials suggest that *P hybridus* is superior to placebo or similarly effective when compared with nonsedative antihistamines.[60,61] Butterbur contains pyrrolizidine alkaloids which have been shown to cause acute hepatotoxicity, DNA damage, and neurologic damage.[30–32] Only butterbur with pyrrolizidine alkaloids removed should thus be considered for use.

Cineole is an herbal supplement containing eucalyptol (1,8-cineole), which is an extract from the eucalyptus plant. It has been used for the treatment of acute rhinosinusitis by increasing cilia beat frequency.[33] Clinical trials have shown efficacy when used with decongestants; it improves the effectiveness of nasal decongestants for the treatment of acute rhinosinusitis compared with placebo when dosed early in the course of an infection.[34] The known side effects include reflux, headache, and nausea. Importantly, undiluted eucalyptus oil is toxic, with a fatal dose of 3.5 mL. The symptoms of eucalyptus poisoning include dizziness, weakness, mydriasis, shortness of breath, and abdominal pain/abdominal burning.

Echinacea has been used for the treatment of the common cold and upper respiratory tract allergies. It reportedly has antiviral and immunomodulating properties.[35] Three species of *Echinacea* commonly used are *Echinacea angustifolia, Echinacea pallida,* and *Echinacea purpurea.* Studies to date have shown no benefit in the prevention of acute otitis media in children.[62] In treatment of the common cold, most recent randomized clinical trials have shown that *Echinacea* provides no detectable benefit or harm.[63] Older studies reported a reduction in severity and duration of upper respiratory tract disorders such as a cold, but more recent literature has not supported these claims.[64–66] Regardless, there are no clinical trials to support the use of *Echinacea* in the management of AR.

Ephedra (*Ephedra sinica*), also known as ma huang, is commonly used to treat asthma, bronchitis, and nasal congestion. It is also used as a diet aid for weight loss, enhancement of athletic performance, and as a central nervous system stimulant.[36,37] It has been used for nasal congestion, asthma, bronchitis, and nasal congestion, as well as a weight loss aid and stimulant. It works by simulating adrenergic receptors via norepinephrine. Therefore, common adverse side effects include hypertension, insomnia, tremor, heart palpitations, stroke, and even fatalities[38–42] There are also known drug interactions, including arrhythmias with cardiac glycosides and

halothane, enhanced sympathomimetic effect with guanethidine, and monoamine oxidase inhibitors.[42–45] Ephedra was banned in 2004 for its over-the-counter use as a dietary supplement by the US federal government due to increasing reports of adverse effects.[45]

Esberitox is an herbal supplement derived from three species of plants, *Thuja occidentalis, E purpurea,* and *Baptisia tinctoria.* The active ingredients include alkamides, chicoric acid, and polysaccharides which are reported to be immune stimulants used to treat acute sinusitis. It has been shown to have a positive effect as an adjunct to doxycycline for treatment of acute sinusitis.[34] Significant side effects include rashes, retching, facial swelling, vertigo, and hypotension.

Garlic (*Allium sativum*) contains allicin (diallyl-thiosulfinate). It is used in the treatment of acute infectious rhinitis and cough via the inhibition of prostaglandins and thromboxanes. There are rare side effects including hypoglycemia, prolonged bleeding time due to decreased platelet aggregation prompting the recommendation for discontinuation 1 week before surgery.[12] Garlic inhibits cytochrome P450, thereby potentiating warfarin.[2] It may also interfere with paracetamol and chlorpropamide and may increase the minimum inhibitory concentration of ampicillin.

Ginkgo (*Ginkgo biloba)* and ginkgo derivatives containing ginkgolides are commonly used for decreased vascular perfusion type syndromes, such as peripheral arterial insufficiency, cerebral insufficiency associated with memory loss, difficulties in concentration, fatigue, anxiety, headaches, and depressed mood. In asthmatic patients, it has been shown to inhibit the development of bronchial hyperreactivity.[46,47] However, drug interactions include increased bleeding when combined with warfarin and spontaneous hemorrhage, which has led to its cautious use in patients receiving aspirin, nonsteroidal anti-inflammatory drugs, anticoagulants, or other platelet inhibitors. An increase in blood pressure when combined with thiazide diuretics[48] and coma when combined with trazodone have also been reported.[49,50]

Grape seed extract contains proanthocyanidins, which have been reported to prevent cellular damage.[67] In vivo studies have showed that grape seed extract may generate possible beneficial effects in the chemoprevention of cellular damage, chemotherapy-induced toxic effects of anthracycline, tissue damage in acute and chronic pancreatitis, acetaminophen-induced hepatotoxicity, and b-cell lymphoma (bcl) and cellular myelocytomatosis (c-myc) oncogene expression and had some cardioprotective effect with red wine consumption.[51,68–70] In the treatment of AR, clinical trials have shown no improvement.[67]

Licorice root (*Glycyrrhiza glabra*) contains glycoside and glycyrrhizin which are used in the treatment of AR, conjunctivitis, and bronchitis. It inhibits 11-beta-hydroxysteroid dehydrogenase and the classic complement pathway. Owing to the mechanism of action, side effects are primarily hypokalemia and pseudo-aldosteronism, which leads to hypertension, headaches, and cardiac events.[12] It is known to interfere with angiotensin-converting enzyme (ACE) inhibitors, diuretics, corticosteroids, insulin, monoamine oxidase inhibitors , and oral contraceptives and may dangerously increase the toxicity of digoxin.[45]

Myrtol is a combination of extracts from pine (*Pinus spp*), lime (*Citrus aurantifolia*), and eucalyptus. It contains monoterpenes, D-limonene, 1,8-cineole, and alpha-pinene. It is used for its secretolytic and secretomotoric properties in the treatment of AR and chronic rhinosinusitis (CRS).[52] Research has only shown a modest benefit in one study, but the data were insufficient to draw any significant conclusions.[35] Primary side effects include gastrointestinal disturbance, facial swelling, allergic reactions, and disturbance of taste.

N-acetylcysteine is a mucolytic used in the treatment of sinusitis via cleavage of disulfide bonds in mucoproteins, thereby reducing the viscosity of mucus.[16] There have been no trials assessing the efficacy of this compound. The only described side effect is gastrointestinal disturbance.

Perilla frutescens is an annual herb native to eastern Asia. It contains phenolic acids, flavonoids, and anthocyanins which are used in the treatment of upper respiratory infections, asthma, and AR. Clinical trials to date have not shown any significant improvement in symptoms of AR.[71] In animal studies, it has been shown to cause pulmonary toxicity, although it has not been studied sufficiency in humans to assess for this side effect.[53,54]

Quercetin contains 3,3′,4′5-7-pentahydroxyflavone, a bioflavonoid, which is used for anti-inflammatory properties via inhibition of cyclooxygenase and lipoxygenase which regulate leukotrienes and prostaglandins. It is reportedly a mast cell stabilizer which inhibits the release of histamine. However, no definitive evidence of its effect has been shown in clinical trials. It may lessen the effects of quinolone antibiotics and is not recommended for use in those with hypertension, immunosuppression, or kidney stones.[34]

Sinupret is a proprietary combination of elder flower, cowslip flowers, common sorrel, European vervain, and gentian root. It is used in the treatment of AR as a mucolytic with antiviral and anti-inflammatory properties. Its efficacy has been tested in three large studies which have shown positive efficacy.[33] Side effects include kidney stones, allergic reactions, gastrointestinal symptoms, numbness, and mild dermatitis. It interacts with therapeutic monoclonal antibodies, hypertensive medications, and immunosuppressants.

Stinging nettle (*Urtica dioica*) is a perennial plant found in Africa, Europe, and North America. Its application to mucosal surfaces causes burning and itching and at times contact dermatitis, whereas its ingestion is known to cause mild gastrointestinal disturbances such as diarrhea.[55] Double-blind randomized studies in the treatment of AR have shown no, or only subjective benefit. [2,55]

AYURVEDIC MEDICINE

The goal of Ayurvedic medicine is to balance body, mind, and spirit through herbal medications, massage, and diet. In Sanskrit, *ayur* means life and *veda* means science. Of the multitude of Ayurvedic herbs and formulas, Aller-7 and Tinofend are both used for the treatment of AR.

Aller-7/NR-A2 is a formulation of herbal extracts including quercetin, stinging nettle, methylsulfonylmethane, turmeric, feverfew, ginger, and vitamin C. Randomized clinical trials testing Aller-7 against placebo in relieving symptoms of AR have shown potentially some benefit in relieving symptoms.[72,73] In animal models, Aller-7 has shown anti-inflammatory effects.[74] Overall, it has shown some improvement in AR symptoms by reducing inflammation.[17]

Tinofend (*Tinospora cordifolia)* or guduchi in Sanskrit has historically *been* used in the treatment of fever, jaundice, chronic diarrhea, cancer, dysentery, bone fracture, pain, asthma, skin disease, poisonous insect, snake bite, and eye disorders.[75] It has been reported to boost the phagocytic activity of macrophages and increase the production of reactive oxygen species in neutrophil cells.[76] It may influence cytokine production, mitogenicity, and stimulation and activation of immune effector cells.[77] In animal models, it has been shown to upregulate IL-6, activate cytotoxic T cells, and affect B cell differentiation.[78] It has been shown to also enhance immune response in mice by inducing secretion of IL-1 and activating macrophages. The(1,4)-

alpha-d-glucan, derived *T cordifolia* has been shown to activate human lymphocytes with downstream synthesis of the pro- and anti-inflammatory cytokines.[79] There has, however, only been one randomized clinical trial in patients with AR, which showed the reduction of symptoms in the test group.[80]

CHINESE TRADITIONAL MEDICINE

Shi-bi-lin is a Chinese herbal medication used in the treatment of AR by inhibiting release of IL-4 and TNF-alpha.[17] Animal trials have shown a decrease in eosinophil infiltration; however, human safety trials have not emerged.

Xiao-qing-long-tang, Sho-seiryu-to in Japanese or *TJ-19,* is a granule made from 8 Chinese herbs: *Paeonia lactiflora*, *E sinica*, *Cinnamomum cassia,* calcium sulfate, *Prunus armeniaca*, *Glycyrrhiza uralensis*, *Zingiber officinale*, and *Ziziphus jujube.* It is used for infectious rhinitis, asthma, and AR and shows the inhibition of histamine signaling and IL-4 and IL-5 expression in rat models.[17] One study has shown improvement in symptoms of sneezing, stuffy nose, and running nose, but not for nasal membrane edema.[81]

Biminne (*11-herb CHM*) is a capsule composed of 11 Chinese herbs (*Rehmannia glutinosa*, *Scutellaria baicalensis*, *Polygonatum sibiricum*, *Ginkgo biloba*, *Epimedium sagittatum*, *Psoralea corylifolia*, *Schisandra chinensis*, pulp of *Prunus mume*, *Ledebouriella divaricata*, *Angelica dahurica*, and *Astragalus membranaceus*). In one clinical trial, only one symptom (sneezing) was significantly reduced compared with placebo and there was no improvement in nasal obstruction.[82]

An extract of *18 Chinese herbs* (*Angelica sinensis*; Asari, herba; Astragali, radix; *Atractylodis macrocephalae,* rhizome; Bupleuri*,* radix; Cimicifugae, rhizome; *Codonopsis pilosulae,* radix; Glycyrrhizae, radix; Chuanxiong, rhizome; Magnoliae, flos*;* Menthae, herba; *Citri reticulatae,* pericarpium; Plantaginis, semen; Schisandrae, fructus; Schizonepetae, herba; Saposhnikoviae, radix; Chebulae, fructus; and Xanthii, fructus) has been studied in one small (n = 55) trial in the treatment of AR, which showed improvement in symptoms after 5 to 6 weeks of treatment.[83]

Acupuncture. Please refer to the chapter on acupuncture for further discussion.

ADDITIONAL THERAPIES

Homeopathy uses stimulating active ingredients dosed in ultra-dilution based on an individual's symptomatic response.[17] Homeopathic treatments have varied efficacy but have been shown to worsen symptoms.

Phototherapy uses light wavelengths to stimulate an immunosuppressive response. Phototherapy reduces antigen presentation by dendritic cells and inhibits proinflammatory factors, thereby decreasing levels of IL-5 and eosinophils.[17] Further studies have demonstrated efficacy, especially for patients for who use of other drugs are contraindicated.[84–86]

SUMMARY

CIM therapies in the treatment of allergy and AR are divided broadly into the categories of nutritional supplements, herbal supplements, Ayurvedic, and Chinese traditional medicine. The efficacy of these therapies is varied and under-researched. The therapies with the strongest evidence in the treatment of allergy and AR are Manuka honey, Butterbur, and Sinupret. It is at the discretion of the physician to balance efficacy against risks when advising patients of these treatment options.

CLINICS CARE POINTS

- Maintaining knowledge of complementary and integrative medicine (CIM) therapies is essential in the treatment of allergic rhinitis (AR).
- The otolaryngologist must ask patients about the use of CIM therapies and monitor for adverse effects and drug interactions.
- In the perioperative period, a thorough understanding of CIM therapy's impact on bleeding and interaction with conventional medications is critical.
- American Society of Anesthesiologists recommends the discontinuation all herbal medications 2 to 4 weeks before surgery.
- Research on the efficacy of CIM therapies is lacking for many supplements and herbs; therefore, randomized clinical trials are needed to improve standardization of CIM therapies.

DISCLOSURE

The authors have no relevant disclosures related to this topic.

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