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## Complementary Medicine in Allergy and Immunology

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### OVERVIEW

Complementary and alternative medicine (CAM) therapies such as Traditional Chinese Medicine (TCM), Ayurvedic (traditional Indian) medicine, acupuncture, yoga, homeopathy, chiropractic medicine, and massage therapy are gaining widespread popularity in the United States and throughout the world for the treatment of asthma and allergies due to their reputed effectiveness, low cost, and favorable safety profiles. CAM is commonly defined as a group of diverse medical and health care systems, practices, and products that are not generally considered part of the conventional allopathic medical practices. Complementary medicine commonly reflects “in addition to” rather than “a substitute for” clinical interventions, whereas “alternative medicine” refers to therapies used in place of traditional medicine.

Patients are often interested in CAM for chronic conditions either because conventional therapies are unsatisfactory or because of concerns about side effects of synthetic drugs. The increasing prevalence and chronic nature of allergic diseases and lack of preventive and curative therapy influence allergy and asthma patients in Western societies to sometimes seek CAM remedies.

In most Western countries, the dichotomy between CAM and the dominant medical therapeutic culture leads to difficulties integrating the best therapeutic interventions based on “evidence-based approaches” with CAM, with the goal of guiding and optimizing patient health care outcomes. In the past, CAM interventions have been marginalized because allopathic medical health care providers who are educated in “pharmaceutical-based medicine” offer patients the most effective and scientifically validated form of medicine based on primary pharmaceutical interventions.

### I. EPIDEMIOLOGY

#### A. Use in the United States

1. The use of CAM in the United States is increasing; in 1991, approximately 33.8% of the US adult population used at least 1 of 16 different types of CAM therapy (“prayer” included as CAM therapy), and by 1997, the usage had increased to 42.1% (83 million people). The typical users of CAM are college-educated white women, between the ages of 40 and 60. In 2007, 38% of adults and 12% of children had used CAM in the past year (not including “prayer,” the most common CAM therapy) consisting of natural products (18%), deep breathing exercises (13%), meditation (10%), chiropractic or osteopathic manipulation (9%), massage (9%), and yoga (6%). Of those using natural products, Echinacea (20%), Ginkgo biloba (14%), and combination herbal pills (13%) were the most commonly used.

**B. Why Patients May Use CAM**

1. Chronic unrelenting diseases where CAM is often employed include musculoskeletal disorders, asthma, allergies, and immunodeficiencies. CAM interventions for the treatment of allergic disorders concentrate on herbal remedies derived from medicinal plants, homeopathy, acupuncture, and Ayurvedic interventions.

**C. Patient Populations Likely to Use CAM**

1. Use of CAM, especially natural products for chronic diseases, is nothing new. In the 1940s and 1950s, pharmacists sold a product known as “Asthmador,” which contained belladonna, an anticholinergic-containing herb. Ma huang was commonly used in herbal preparations marketed for use in asthma, until the FDA banned sales of ephedra-containing products in 2003. Patients most likely to use CAM in the United States and Europe are middle-class (economically) adults between the ages of 30 and 69, women more likely than men, and those more likely to hold graduate degrees (55%) when compared with those with less than high school education (21%). The most important patient information sources regarding CAM include current medical practitioner (40%) or friends and family (37%). Of note, much of the cost of CAM in Europe is paid for in part or in total by the public health insurance system, while in the United States, it is primarily paid “out of pocket” by the patient.

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**II. CATEGORIES OF CAM****A. Acupuncture**

1. Acupuncture is a cornerstone of the **Traditional Chinese Medicine (TCM)** system. It is widely used to treat many chronic illnesses, including asthma, depression, and arthritis. Acupuncture is used by practitioners to restore the balance of “vital flows” by inserting needles at exact points (acupoints) to stimulate specific subcutaneous sites of the body. **Well-controlled trials have demonstrated that acupuncture can be effective for the treatment of chronic migraines, nausea secondary to chemotherapy, and chronic lower back pain.** Although acupuncture is often used to treat allergic rhinitis, most studies investigating this treatment are of poor quality, not randomized, or not controlled. In a well-designed crossover, two-phase, single-blind, randomized trial of acupuncture versus sham acupuncture treatment for seasonal allergic rhinitis, a statistically significant reduction in the severity of nasal and nonnasal symptoms of allergic rhinitis in the acupuncture group was demonstrated, though the use of conventional antiallergic medications was not significantly different between groups. Another study similarly demonstrated acupuncture significantly decreased total nasal symptom scores and rhinorrhea, but not other symptoms, nor the use of relief medications. In a randomized, double-blind, sham-controlled study of pediatric patients with persistent allergic rhinitis, a statistically significant decrease in daily rhinitis score and more symptom-free days in the acupuncture treatment group were seen, while there was no significant difference between the groups for daily relief medication scores, blood eosinophil counts, serum IgE levels, and nasal eosinophil counts. There

are also well-controlled studies that demonstrate no difference in clinical symptoms of allergic rhinitis between active and control groups.

### B. Homeopathy

1. Homeopathy is based on the belief that substances distinct from any disease-causing agent that can create symptoms similar to that specific disease can be used to cure the disease. This concept is known as the “**Law of Similars**,” and it was first used in the treatment of malaria when it was noted that the bark of the Cinchona tree caused fevers and rigors similar to the malaria it treated. True homeopathy requires “potentiation” of the substance through serial dilutions, which at times are so extensive as to make it mathematically impossible for the dilution to contain any of the actual substance.
2. Homeopathy in allergic diseases has been extensively studied through numerous rigorous trials conducted in allergic rhinitis. As a form of treatment for allergic diseases, homeopathy is quite popular. A retrospective (uncontrolled) study of people with hypersensitivity illnesses who choose treatment with general practitioners versus classical homeopaths found that those patients who sought care from homeopaths self-reported a significantly greater improvement in their overall health.<sup>1</sup> One double-blind, placebo-controlled trial study of patients with allergic rhinitis showed a significant difference in favor of homeopathy, while another well-controlled study comparing cromolyn and an intranasal homeopathic remedy, *Luffa compositum Heel*, found no significant difference between the active and control groups. In several double-blind controlled studies in patients with seasonal or perennial allergic rhinitis, homeopathic treatments either have been shown to be marginally effective or demonstrated mixed efficacy, such as an effect in nasal flow measurements, but not necessarily in symptoms. Interestingly, in one randomized, double-blind trial, homeopathic preparations showed significantly better quality of life questionnaire scores compared to placebo. Although there is published literature suggesting that some beneficial effect of homeopathy exists, in many cases, this effect may be a placebo effect. An analysis of 100 clinical trials of homeopathy when compared to conventional allopathic medicine, matched for disease and outcome, concluded that the beneficial effects of homeopathy on allergic rhinitis were inconclusive and more rigorous studies are required.

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### C. Phytotherapy

1. Herbal preparations are becoming increasingly popular among patients looking for CAM therapies. Treatments based on herbs cannot all be considered as alternative or unconventional, as more than 60% of allopathic medications are derived from plants. However, in allopathic medicine, when an active and beneficial ingredient in an herb becomes isolated, its chemistry may be altered slightly to improve pharmaceutical characteristics or allow for patent protection; the pharmacokinetic and pharmacodynamic qualities are defined, and the absorption, distribution, metabolism, and elimination are characterized before a dose form for humans is created. This dose leads to a reproducible blood level with defined and reproducible characteristics. Rarely is such precision possible in herbal preparations. Most herbal preparations are sold by weight of the parent herb, not the active ingredients, which can fluctuate widely

depending on growing, harvesting, and storage conditions. This is an effect where, similar to the cultivation of wine, small differences in farming location and practice can have big effects on the end product.

2. **Phytotherapy** can be divided into traditional and nontraditional herbal preparations. Traditional preparations from Chinese, Japanese, and Ayurvedic medicines often use groups of different herbs in fixed mixtures (i.e., *ma huang* and *saiboku-to*) to treat diseases including allergic rhinitis and asthma. Problems with herbal remedies can arise when hand-made mixtures are used or when herbs are used in combination with other CAM therapies. A trend seen in nontraditional herbal preparations involves using single herbs in fixed doses rather than mixtures of multiple herbs; examples include *Echinacea*, butterbur, and stinging nettle. Some physicians and nutrition centers are developing their own proprietary herbal mixes using both traditional and nontraditional data to create products that may or may not be reproducibly effective.

3. Phytotherapy: traditional therapies

- a. The literature on herbal remedies for allergic rhinitis is extensive because of the large variety of herbs and their combinations. Some of the most known and most commonly used herbs for allergic rhinitis and asthma are listed in Tables 22-1A and 22-1B. In general, the studies with herbal remedies are of low quality, but in many cases, a clinical effect can be measured in allergic rhinitis. A mixture of 18 traditional Chinese herbs, called **RCM-101**, shows significant differences in quality of life scores as well as its effect on various inflammatory mediators, such as decreased the production of prostaglandin E2 and nitrous oxide production in murine macrophages. In an animal model using rat peritoneal mast cells, RCM-101 inhibits the release and/or synthesis of histamine, leukotriene B4, and prostaglandin E2, which may account for some of its activity in allergic rhinitis.

Tables 22-1

- i. **Biminne**, is composed of 11 Chinese herbs, used in perennial allergic rhinitis patients showed an improvement trend over time in mean weekly symptom scores and physician overall evaluation; however, only sneezing was significantly reduced, and there was no effect on nasal obstruction. Q3

- iii. **ASHMI** and **FAFH-2** are two preparations based on TCM. **ASHMI** is a mixture of three herbs (*Ganoderma lucida*, *Glycyrrhiza uralensis*, and *Sopborae flavescens*), which are common herbs used in China for patients with asthma. A randomized clinical trial comparing prednisone to ASHMI in 91 moderate to severe asthmatics showed no significant symptom or  $\beta$ -agonist use difference between the groups; however, the prednisone group showed slight improvement in PEF and FEV<sub>1</sub>. **FAFH-2** and **FAFH-1** are proprietary blends of herbs being studied for treatment of food anaphylaxis. Murine studies show that administration of **FAFH-1** significantly attenuates anaphylaxis in mice previously sensitized to peanut. Q4

4. Phytotherapy: nontraditional preparations

- a. **Urtica dioica (stinging nettle)** is a common ingredient in homeopathic pharmacopeias for allergies. In a randomized controlled trial, *U. dioica* was superior to placebo for the treatment of allergic rhinitis.

Table 22-1A Selected Herb-derived Substances Used in the Treatment of Allergic Rhinitis

Safety vs. Efficacy	Likely Safe	Possibly Safe	Insufficient Evidence	Possibly Unsafe	Likely Unsafe	Unsafe
Effective	Nasal lavage					
Likely effective						
Possibly effective						
Insufficient evidence	Echinacea, vitamin C	Capsaicin, butterbur, quercetin		Bitter orange		Ephedra
Possibly ineffective		Tinospora, cordifolia				
Likely ineffective		Goldenseal, Cat's claw, stinging nettle, spirulina				
Ineffective		Grape seed extract				

This assumes use of high-quality, uncontaminated products and the use of typical doses. Some products are never appropriate for specific patients due to concomitant disease states, potential drug interactions, or other clinical factors. Use good clinical judgment before recommending any product.

**Table 22-1B** Some Herb-derived Substances Used in the Treatment of Asthma

Safety vs. Efficacy	Likely Safe	Possibly Safe	Insufficient Evidence	Possibly Unsafe	Likely Unsafe	Unsafe
Effective	Nasal lavage					
Likely effective						
Possibly effective						
Insufficient evidence	Grapefruit, Kiwi, Pyridoxine, Sweet orange, vitamin C, vitamin E	Pycnogenol, eucalyptus, menthol Butterbur, Indian frankincense, Perilla		Noni Juice		
Possibly ineffective	Yoga					
Likely ineffective						
Ineffective						

This assumes use of high-quality, uncontaminated products and the use of typical doses. Some products are never appropriate for specific patients due to concomitant disease states, potential drug interactions, or other clinical factors. Use good clinical judgment before recommending any product.

When combined with acupuncture, a Chinese herbal mixture similarly showed significant improvement in symptoms and quality of life scores, but the herbal treatment and acupuncture were not studied alone; therefore, no conclusions can be drawn about the efficacy of the individual components. A double-blind randomized, placebo-controlled trial showed that **grape seed** extract was no more effective than placebo in patients with ragweed-induced allergic rhinitis.

- b. Because the mechanisms of action of most herbal treatments are unknown, there is the potential for herb–drug interactions if traditional and conventional medicines are used simultaneously. For example, **glycyrrhizin**, a Chinese herbal remedy for allergic rhinitis, interacts with angiotensin-converting enzyme inhibitors and is associated with pseudoaldosteronism (metabolic alkalosis and severe hypokalemia). **Reverse herbology**, which examines the effect of the herb or herbal mixture on the cytochrome P450 (CYP) enzymes and thus potential herb–drug interactions, demonstrates that sho-seiryu-to, a traditional mixture of eight herbs used to treat allergic rhinitis in Japan, has minimal effect on the CYP enzymes, xanthine oxidase, or *N*-acetyltransferase.
- c. The potential mechanisms through which herbal medicines might affect allergic rhinitis have been studied. *Lycopus lucidus* (rough bugleweed) demonstrated inhibition of mast cell–derived immediate-type allergic reactions through downregulation of proinflammatory cytokines, including NF- $\kappa$ B. ***Shu-Bi-Lin***, a traditional Chinese herbal formula consisting of six herbs, was tested in a guinea pig model of allergic rhinitis comparing it to an antihistamine and found decreased eosinophil infiltration and endothelial nitric oxide synthase (NOS) activity, as well as decreased sneezing and nasal scratching in the treatment group when compared to untreated controls. The same herbal preparation was also found to inhibit the release of IL-4, TNF- $\alpha$ , and IL-6 from human mast cell lines.
- d. **Butterbur**, *Petasites hybridus*, a perennial shrub found throughout Europe as well as parts of Asia and North America, shows mixed results when studied in allergic rhinitis. Butterbur root compounds, known as petasins, are used to treat a variety of conditions including back pain, asthma, topical wound healing, and allergic rhinitis. Compared to cetirizine, treatment with butterbur is equally effective in decreasing symptom scores and improving quality of life, and both treatments are significantly better than placebo in decreasing symptoms of allergic rhinitis. Fexofenadine and butterbur were equivalent in decreasing symptom scores of allergic rhinitis patients; however, in a rigorous double-blind, placebo controlled, crossover study in patients with intermittent rhinitis, there was no significant effect of butterbur on symptoms and nasal inspiratory peak flow. In uncontrolled postmarketing surveillance, 90% of patients self-reported improved seasonal allergic rhinitis symptoms while on butterbur treatment. The initial enthusiasm for butterbur was tempered, however, by the discovery that unprocessed butterbur extracts contained high levels of pyrrolizidine alkaloids, which are hepatotoxic and carcinogenic.

Many commercially available preparations of butterbur have had the pyrrolizidine alkaloids removed.

- e. *Arthrospira platensis* is an oxygenic, photosynthetic bacterium found in both fresh and salt water. **Spirulina**, which refers to the dried biomass of *A. platensis* used as a high-protein food throughout the world, inhibits histamine release from mast cells and exhibits some anti-inflammatory properties such as increased interferon- $\gamma$  production and natural killer cell activity. In a randomized, double-blind, placebo-controlled trial, the spirulina group significantly reduced IL-4 levels. There are no large scale, controlled trials of spirulina in patients with allergic rhinitis.

#### D. Overview of Herbs

1. The traditional uses of herbal medicines are for the prevention and treatment of a variety of self-limiting to life-threatening illnesses, and herbal medicines are the most commonly consumed health care products. Scientific evaluation of herbal products is limited, but due to inherent toxicity of many herbal remedies and because nearly all these remedies contain multiple, biologically active constituents, herb–drug interactions are a concern. Clinicians need to be aware of which herbs can cause toxicity and to be cognizant of potential herb–drug interactions. In many countries, herbal medicines are poorly regulated, may be neither registered nor controlled, and are rarely monitored by national surveillance systems for adverse events. However, the increasing popularity of herbal medicines raises concerns over their safety, quality, and efficacy on the part of health authorities and the general public. In response to these concerns, the World Health Organization publishes formal monographs on selected medicinal plants to establish quality standards of herbal products and outline the parameters for their safe and effective use. These monographs are highly correlated with the special expert committee of the German Federal Institute for Drugs and Medical Devices known as the Commission E monographs and ESCOP (European Scientific Cooperative on Phytotherapy) (<http://www.escop.com/>).
2. **Drug interactions**
  - a. Many of the constituents of herbal remedies compete with allopathic drugs for cytochrome P450 metabolism. Therefore drug interactions are a primary concern when patients are using herbal formulations.
3. **Herbals having antiallergic effects**
  - a. Natural medicines with antihistamine effects include **grape seed extract** (*Vitis vinifera*), B (*Pinus pinaster*) and B; those with decongestant potential include **bitter orange** (*Citrus aurantium*) and **ephedra** (*Ephedra* spp.); those with mast cell–stabilizing effects include **Indian frankincense** (*Boswellia serrata*), **picrorhiza** (*Picrorhiza kurroa*), **quercetin**, **spirulina**, and **stinging nettle** (*U. dioica*); those with leukotriene modifier effects include **butterbur** (*P. hybridus*), **fish oil**, **Indian frankincense** (*B. serrata*), **New Zealand green-lipped mussel** (*Perna canaliculus*), **perilla** (*Perilla frutescens*), and **pycnogenol** (*P. pinaster*). Natural antioxidants include grapefruit (*Citris paradisi*), kiwi (*Actinidia chinensis*), noni juice (*Morinda citrifolia*), sweet orange (*Citrus sinensis*), vitamin C, and vitamin E. Other agents with reported effects on allergies with various mechanisms not listed above include choline, eucalyptus (*Eucalyptus globulus*), magnesium, pyridoxine (vitamin B6), soy (Glycine max), capsaicin, cat's claw (*Uncaria*



*guianensis*, *Uncaria tomentosa*), goldenseal (*Hydrastis canadensis*), methylsulfonylmethane (MSM), and nasal irrigation.

4. **Herbal Agents.** The agents listed below are provided by their English, Latin, and pharmacopeial names followed by their common uses (not necessarily approved by any health authorities), contraindications, drug interactions and assorted reactions (allergic and idiosyncratic) (C = Common; R = Rare; U = Unlikely).

a. **Garlic (*Allium sativum*) Bulbus Allii Sativi**

- i. **Common uses:** for cardiovascular health (hypertension, cholesterol and lipid lowering, atherosclerosis), relief of cough, cold symptoms, and rhinitis
- ii. **Adverse effects:** gastrointestinal disturbances (C), hypoglycemia (R), change in body odor through the sweat and breath (C), and allergic reactions (R)
- iii. **Contraindicated** in patients undergoing surgery since it can prolong bleeding time
- iv. **Drug interactions:** increasing the anticoagulant effects of warfarin (C), bleeding times have been noted to be double in patients on warfarin and garlic supplements; changes pharmacokinetic variables of paracetamol (R); produces hypoglycemia when taken with chlorpropamide (R); may cause large increases in the MIC to ampicillin over baseline values (R)
- v. **Contraindications:** none known

b. **Angelica (*Angelica archangelica*) Radix Angelicae Sinensis**

- i. **Common uses:** as an expectorant for bronchial illnesses, colds, and coughs; treatment of mild spasms of gastrointestinal tract, loss of appetite (anorexia nervosa), flatulence, and feeling of fullness; used in liqueurs such as Benedictine, Boonekamp, and Chartreuse
- ii. **Adverse effects:** skin sensitization to sunlight due to the furanocoumarins causing photodermatitis and phototoxicity (R). Prolonged sunbathing and exposure to intense UV radiation must be avoided. Bleeding can occur when used with other anticoagulants (U).
- iii. **Drug interactions:** none known
- iv. **Contraindications:** use during pregnancy

c. **Chamomile flower, German (*Chamomilla recutita*, *Matricaria recutita*) Flos Chamomillae**

- i. Name originates from the low-lying (chamos—ground) flower that has an apple scent (melos—apple).
- ii. **Common uses:** for gastrointestinal inflammatory disorders, peptic ulcers, and spasms; topical cutaneous inflammation and bacterial infections; oral, throat, and mouth mucosal irritation; inhalations for the respiratory tract; baths for anogenital inflammation
- iii. **Adverse effects:** exacerbation of allergic symptoms in ragweed-sensitive patients who have cross-reactivity with hazelnut, kiwi, birch, several Compositae (*Ambrosia*, *Chrysanthemum*, *Matricaria*, *Solidago*), and grass allergens (oral allergy syndrome primarily) (C); contact dermatitis (R); and anaphylaxis (R)
- iv. **Drug interactions:** none known
- v. **Contraindications:** none known

- d. Black cohosh (root) (*Cimicifuga racemosa*) Cimicifugae racemosa rhizome**
- i. Used for premenstrual discomfort or menopausal symptoms
  - ii. Use during pregnancy is, in theory, contraindicated but has been used during first trimester to decrease uterine spasms; not to be given to children or during lactation
  - iii. **Drug interactions:** increases the action of antihypertensives; interacts with other hormone replacement therapies
- e. Echinacea herb and root (*Echinacea angustifolia/Pallida/Purpurea*) Herba/Radix *E. angustifolia/Pallida/Purpurea***
- i. **Common uses:** At one time, the most common alternative herbal treatment, now is used by itself or in preparations for the common cold, flu-like illness, sore throat, and HSV-1.
  - ii. **Adverse effects:** Echinacea may cause increases in the MIC to ampicillin. Can cause allergic reactions, exacerbation of asthma, and anaphylactic reactions.
  - iii. **Drug interactions:** No significant herb–drug interactions are known for Echinacea (*E. angustifolia*, *E. purpurea*, *E. pallida*); there is a potential risk of hepatotoxicity (R) and therefore this herb should not be used with other known hepatotoxic drugs, such as anabolic steroids, amiodarone, methotrexate, and ketoconazole.
  - iv. **Contraindications:** Although no specific contraindications are known, it is not recommended for use in patients with chronic systemic disease such as AIDS, tuberculosis, and other autoimmune disorders.
- f. Ephedra (*Ephedra sinica*) Herba Ephedrae**
- i. **Common uses:** known as *ma huang*; used to treat asthma, bronchitis, and nasal congestion; as diet aids for weight loss; for enhancement of athletic performance; and for stimulation of the central nervous system due to its high content of ephedrine
  - ii. **Adverse effects:** hypertension (C), insomnia (C), tremor (C), heart palpitations (C), headache (C), nausea (C), loss of appetite (C), prostatism (C), cardiac arrhythmias (R), and even fatalities (R)
  - iii. **Drug interactions:** cardiac glycosides and halothane anesthetics, leading to arrhythmias (C); guanethidine enhances sympathomimetic effect; MAO inhibitors increase the sympathomimetic actions of ephedrine
  - iv. **Contraindications:** none known
- g. Ginkgo (*Ginkgo biloba*) Folium Ginkgo**
- i. **Common uses:** for cerebral insufficiency, memory loss, concentration difficulties, fatigue, anxiety, headaches and depressed mood, peripheral arterial insufficiency, vertigo, and tinnitus
  - ii. **Adverse effects:** gastric or intestinal upsets (C), headaches (U), morbilliform (R), and other allergic skin reactions (R) due to sensitization to the ginkgolic acid
  - iii. **Drug interactions:** bleeding when combined with warfarin (U), elevated blood pressure when combined with a thiazide diuretic (U), and coma when combined with trazodone (R). Chronic use is associated with increased bleeding time (R) and spontaneous

hemorrhage (R). Use with caution in patients receiving aspirin, NSAIDs, anticoagulants, or other platelet inhibitors.

iv. **Contraindications:** none known

**h. Licorice root (*Glycyrrhiza glabra*) Radix Glycyrrhizae**

i. **Common uses:** Latin name derived from its common use as a sweetener (glukos—sweet) (riza—root) containing glycyrrhizin (or glycyrrhizic acid) that is 50 times sweeter than sucrose. Used for treatment of gastric and duodenal ulcers, rhinoconjunctivitis, bronchitis, impaired digestion, bloating, and flatulence; as a demulcent for sore throats; as an anti-inflammatory in treating allergies and adrenocortical insufficiency.

ii. **Adverse effects:** Excessive ingestion (>20 g/d) produces excessive levels of aldosterone (pseudoaldosteronism) (U) resulting in headache (C), lethargy (C), sodium and water retention (C), hypertension (C), potassium loss (C), and myoglobinuria (R).

iii. **Drug interactions:** include agents that cause potassium loss, for example, thiazide diuretics; offsets the pharmacologic effect of spironolactone; interferes with cardiac glycosides, for example, digoxin, pharmacodynamically

iv. **Contraindications:** in patients with cholestatic liver disorders, cirrhosis, hypokalemia, and renal insufficiency

**i. St. John's wort (*Hypericum perforatum*) Herba Hyperici**

i. **Common uses:** available in the United States as an alcoholic tincture, oral aqueous infusion, topical oil infusion, and dry capsules and tablets; in Germany, used as a tea (Hyperforat<sup>®</sup>), coated tablet (Jarsin<sup>®</sup>), juice (Kneipp<sup>®</sup>) and tincture (Psychotonin<sup>®</sup>), and in combination with valerian (Sedariston<sup>®</sup>). Used for neuralgia, anxiety, neurosis, micturition (Incontinuria<sup>®</sup>), and depression.

ii. **Adverse effects:** Photosensitization (R) can occur with 30 to 50 times the 900-mg recommended dose; a variety of other cutaneous eruptions.

iii. **Drug interactions:** lowers blood concentrations (C) of cyclosporin, amitriptyline, digoxin, warfarin, phenprocoumon, and theophylline; intermenstrual bleeding (U) when used concomitantly with oral contraceptives (ethinylestradiol/desogestrel); delirium when used with loperamide or mild serotonin syndrome (C) when used with amphetamines, MAO, or selective serotonin-reuptake inhibitors (sertraline, paroxetine, nefazodone, trazodone, and other tricyclic antidepressants). Decreases antiretroviral action of indinavir (R). Increased sedation with paroxetine use

iv. **Contraindications:** none known

**j. Peppermint oil and leaf (*Mentha piperitae*) Aetheroleum Menthae Piperitae and Folium Menthae Piperitae**

i. **Common uses:** available as an oral and topical oil, inhalant, liniment, ointment, and tincture. Used for symptoms of indigestion, flatulence, irritable colon, and other gastrointestinal tract (spasmodic) complaints, including those of the gallbladder and bile ducts. Also used for colds, rheumatic complaints, allergies, pruritus, urticaria, and pain in irritable skin conditions

- ii. **Drug interactions:** no known drug interactions
  - iii. **Contraindications:** in patients with biliary obstruction, gallstones, and gallbladder inflammation (U); use on the face of infants and children due to risk of respiratory spasms (U)
- k. Ginseng root (*Panax ginseng*) Radix Ginseng**
- i. **Common uses:** as an aphrodisiac and a stimulant
  - ii. **Adverse effects:** headache (U), tremulousness (U), and manic episodes (R) in patients treated with phenelzine sulfate. Chronic use associated with vaginal bleeding (R), mastalgia (R), mental status changes (R), and Stevens-Johnson syndrome (R).
  - iii. **Drug interactions:** interference with digoxin and hypoglycemic agents; lowers blood concentrations of alcohol and warfarin (R) and induces mania (R) if used concomitantly with phenelzine; possible additive effect on estrogens or corticosteroids (U)
  - iv. **Contraindications:** in patients with diabetes
- l. Kava kava rhizome (root) (*Piper methysticum*) Piperis methystici rhizome**
- i. **Common uses:** for the short-term treatment for anxiety
  - ii. **Adverse effects:** severe hepatotoxicity including liver failure (R), dizziness (C), drowsiness (C), stomach upset (R), and allergic reactions (R)
  - iii. **Drug interactions:** potentiation of the sedative effect of anesthetics inducing a semicomatose state when given concomitantly with alprazolam (R); increasing “off” periods in Parkinson’s patients taking levodopa (R)
  - iv. **Contraindications:** none known
- m. Saw palmetto (berry) (*Serenoa repens*) Sabal fructus**
- i. **Common uses:** for urinary problems associated with benign prostatic hypertrophy
  - ii. **Adverse effects:** headache, nausea, vomiting, urinary retention (R), impotence (R), and hypersensitivity reactions (R)
  - iii. **Drug interactions:** anticoagulants (increased bleeding time) and from anti-inflammatory agents (aspirin and other nonsteroidal agents) (C); oral contraceptives (antiestrogen effect) (U)
  - iv. **Contraindications:** in pregnancy secondary to antiandrogenic properties, should be avoided during lactation or given to children
- n. Stinging nettle root, herb, and leaf (*U. dioica*) Radix Urticae, herba/folium**
- i. **Common uses:** The Latin genus name comes from the term “burn” due to the urticate (stinging) nature of its hairs. Available as a freeze-dried powder, extract, and juice; or combined with saw palmetto (PRO®). Homeopathically used for the treatment of allergic rhinitis; natural product used for benign prostatic hypertrophy; for in general use for its anti-inflammatory effects in acute arthritis; as a diuretic
  - ii. **Drug interactions:** none known
  - iii. **Contraindications:** none known, although collection of fresh leaves can cause urticaria (C), burning and itching upon application to mucosal surfaces (C); is known to cause mild gastrointestinal disturbances and diarrhea (R)

**o. Valerian root (*Valeriana officinalis*) Radix Valerianae**

- i. **Common uses:** for insomnia, restlessness, anxiety, and appetite stimulation
- ii. **Adverse effects:** nephrotoxicity (R), headaches (R), chest tightness (R), mydriasis (R), abdominal pain (R), and tremor (R) of the hands and feet
- iii. **Drug interactions:** can occur with concomitant barbiturate use resulting in excessive sedation
- iv. **Contraindications:** none known

**E. Ayurvedic Remedies**

1. **Common uses:** The first aim of Ayurveda is to reduce the occurrence of disease through breathing exercises, yoga, and herbal intervention.
2. **Adverse effects:** The breathing exercises and yoga are unlikely to cause serious harm if done under proper supervision. Some ayurvedic medications have been adulterated with heavy metals and even corticosteroids. Those that contain arsenic or mercury can produce typical skin lesions and arsenical neuropathy (R).
3. **Drug interactions:** depends on the herbal preparation used; as many of the herbs listed above are used in Ayurveda.

**F. Homeopathy**

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1. NasalEase™, used in allergy relief; contains hydroxymethylcellulose as a carrier for various homeopathic remedies with a decrease in allergen diffusion and increase in therapeutic retention on nasal mucosal surface.
2. In general, many homeopathic preparations contain highly diluted metals that theoretically could cause heavy metal systemic toxicity when used in the highest (least therapeutic concentration) (U).

**G. Aromatherapy**

1. **Common uses:** Aroma therapy is used to reduce anxiety and stress, promote healing and reduce pain.
2. **Adverse effects:** Phototoxic dermatitis from 5-methoxypsoralen; photo-contact dermatitis, immediate contact reactions, and pigmentary changes (R); cutaneous reactions to fragrances (C) affects approximately 1% of the general population with axillary dermatitis, dermatitis of the face (including the eyelids) and neck, well-circumscribed patches in areas of “dabbing-on” perfumes (wrists, behind the ears), and exacerbation of hand eczema. Frequent use of lavender oil can cause a contact dermatitis (C).
3. **Drug interactions:** Eucalyptus oil can decrease blood levels of pentobarbital and amphetamines.
4. **Contraindications:** theoretically can cause bronchoconstriction (R). Oils should never be taken by mouth, and one must avoid any open flames while using aromatherapy.

**H. Moxibustion**

1. **Common use:** chronic fatigue, malaise, depression, ulcerative colitis, parasitic infection, and breach birth
2. **Adverse effects:** third-degree burns that are directly related to burning the various materials (C)
3. **Drug interactions:** none
4. **Contraindications:** none

**I. Acupuncture**

- 1. Common uses:** chemotherapy-induced nausea, back pain, osteoarthritis, addiction, asthma, bronchitis, fibromyalgia, headaches, IBS, and menstrual pain
- 2. Adverse effects:** Acupuncture needles can reach vulnerable structures and cause adverse effects such as pneumothorax (R), cardiac tamponade (R), direct injury to nerve roots and spinal cord (R), as well as infectious complications such as hepatitis, staphylococcal septicemia, bacterial endocarditis, and HIV infection. Contact dermatitis can occur from the nickel-based acupuncture needles (C).
- 3. Contraindications** include an unstable spine, severe clotting disorder, valvular heart disease, neutropenia, and lymphedema (R).

**J. Vitamins and Minerals**

1. These agents are unlikely to cause allergic or pseudoallergic reactions although vitamin K and iron dextran can cause anaphylactoid reactions (R) upon rapid infusion, and chondroitin and dextran infusions can cause serum sickness reactions (R).
2. Dietary supplements used in CAM interventions at times can restrict intake of specific nutrients resulting in cases of nutritional rickets (lack of vitamin D) and protein deficiency (“kwashiorkor”).
3. Vitamin E reduces oxidative damage in vivo and is associated with lower IgE levels and lower frequency of allergen sensitization. Vitamin E was no better than placebo in allergic rhinitis symptom severity scores and serum IgE levels. Gamma-tocopherol, a specific component of vitamin E, blocks enhancement by ozone in an allergen-induced asthma model, attenuating both ovalbumin or ozone-stimulated eosinophilic infiltration and increases of bronchial alveolar lavage fluid cystinyl leukotrienes, MCP-1, IL-6, IL-5 and IL-13 mRNA.

**K. Antioxidants**

1. The term “oxidative stress” refers to the imbalance between reactive oxygen species, which can be harmful, and antioxidants. Examples of endogenous antioxidants include **superoxide dismutase (SOD), catalase, glutathione peroxidase, and glutathione S-transferase**. Oxidative stress occurs as a result of environmental factors as well as inflammation and plays a role in the development and exacerbation of allergic diseases, including allergic rhinitis.
2. **Nitric oxide (NO)** regulates many molecular and cellular functions. It is produced in vivo in part due to the presence of NOS. NO is present in exhaled air, and concentrations of exhaled NO increase with allergic rhinitis. The NOS inhibitor, L-NAME, is no better than controls for the treatment of allergic rhinitis.<sup>2</sup>
3. **Superoxide dismutase (SOD)** is an antioxidant found in the epithelial-lining fluid and epithelial cells of the airways that protects cells against oxidative stress by converting superoxide radicals to hydrogen peroxide. However, exogenous SOD fails to attenuate allergic nasal congestion symptoms in a canine model of allergic rhinitis.
4. **Rosmarinic acid** use in allergic rhinitis significantly decreases symptom scores, numbers of neutrophils and eosinophils in nasal lavage fluid, and decreases reactive oxygen radical production.

5. **Aller-7/NR-A2** is a polyherbal formulation consisting of seven herbal extracts, which significantly decreases symptoms of allergic rhinitis. Aller-7, like rosmarinic acid, appears to act through anti-inflammatory and antioxidant pathways.
6. **Quercetin** is a flavonoid aglycone of rutin found in many vegetables, fruits, and herbs, which is a medicinal herb with significant antioxidant and anti-inflammatory properties. Quercetin inhibits the inflammatory process through membrane stabilization of activated neutrophils, perhaps by inhibiting hyaluronidase, which prevents the breakdown of collagen matrix proteins. Quercetin can prevent mast cell and basophil degranulation, neutrophil lysosomal enzyme secretion, and leukotriene production. Quercetin inhibits antigen-stimulated histamine release, more than sodium cromoglycate in perennial allergic rhinitis.

### III. SKIN TESTING EFFECTS OF HERBALS (ANTIHISTAMINIC POTENTIAL)

- A. In general, herbal agents, when taken as a single dose, demonstrate minimal inhibition of skin testing (see Table 22-2). It is unclear whether extensive use would have effects on skin testing results and thus practitioners need to consider this when abhorrent results occur when testing with herbal agents such as licorice and milk thistle (see Table 22-3).

### IV. MEDICOLEGAL

- A. The medicolegal implications of complementary and alternative therapy are just beginning to be worked out in the legal system, and a complete analysis is beyond the scope of this chapter; however, we provide a basic framework

**Table 22-2** Herbal Supplements that *Do Not Affect* Skin Whealing Response

Herbal Supplement	Typical Dosage
Aloe	25 mg
Bilberry	80 mg
Cascara sagrada	500 mg
Cat's claw	500 mg
Cayenne	500 mg
Devil's claw	150 mg
Echinacea	300 mg
Evening primrose	500 mg
Garlic	810 mg
Ginger	500 mg
Ginkgo	50 mg
Ginseng	500 mg
Goldenseal	500 mg
Gotu kola	500 mg
Grape seed extract	50 mg
Valerian	500 mg

Q6

**Table 22-3** Effects of Commonly Used Herbal Supplements on Histamine Skin Prick Testing

<b>Herbal supplements that decrease skin whealing</b>		
<b>Herbal Supplement</b>	<b>Daily Dosage</b>	<b>% Decrease in Whealing Response</b>
Licorice	500 mg	-21%
Green tea	150 mg	-19%
Saw palmetto	500 mg	-19%
St. John's wort	300 mg	-15%
Feverfew	500 mg	-15%
<b>Herbal supplements that increase skin whealing</b>		
<b>Herbal Supplement</b>	<b>Daily Dosage</b>	<b>% Increase in Whealing Response</b>
Milk thistle	200 mg	+24%
Astragalus	250 mg	+15%

From More DR, Napoli DC, Hagan LL. Herbal supplements and skin testing: the lack of effect of commonly used herbal supplements on histamine skin prick testing. *Allergy* 2003;58(6):492-494. with permission.

for any practitioner who would incorporate CAM in his or her practice. The most basic tenet of malpractice litigation is determining whether a physician failed in his or her duty to provide a patient the "standard of care" as defined by local/regional practitioners, medical experts, and the medical literature. Any deviation from the "standard of care" that subsequently results in actual injury to the patient can be considered grounds for malpractice. The emergence of CAM therapeutics as a medical discipline is still evolving, and therefore, no "standard of care" has been defined and most prescribers of CAM (both allopathic physicians and more traditional CAM practitioners) live in a legal limbo as to the liability risks of their practice.

- B.** Most physicians who work with CAM do not provide it in their own office but refer patients out to more experienced practitioners, such as acupuncturists, naturopaths, or chiropractors. Physicians often take for granted our ability to refer patients who actively seek out CAM to reputable practitioners; however, this was not always the case. It took until 1983 and two lawsuits, requiring the AMA to remove disparaging references to chiropractic practices from the association's position on medical ethics. Until that time, it was considered unethical for a physician to refer any patient for treatment to anyone other than another licensed physician. Many states require CAM practitioners to be licensed and have set up educational requirements to practice. For example, the state of New York requires licensed acupuncturists to undergo 200 classroom hours of anatomy, physiology, and pathology; 600 classroom hours of acupuncture theory, and 650 hours of supervised clinical practice. Naturopathic doctors are licensed mostly in the Western United States, with legislation pending in other states; some states are requiring a passing grade on a state licensing exam. All 50 states require chiropractors to be licensed. Therefore, the liability that exists when





a physician refers a patient to a CAM practitioner may be mitigated by the state's legitimizing CAM therapies through this credentialing process. By creating a licensing board (and in some cases, exams), states are helping to define the "standard of care" for CAM, which has resulted to some insurance companies adding coverage of CAM in some of their products.

- C. The liability risks are higher for those physicians who provide CAM therapy in their office (i.e., integrative medicine practices). Any physician who chooses to offer CAM therapies in her or his practice should seek counsel from a lawyer specializing in CAM therapies as different states have different regulations. Equally important, physicians should discuss any potential usage of CAM with their malpractice provider to ensure adequate coverage in case of poor outcome.

## SUGGESTED READINGS

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## Queries

- [Q1] Please check if the sentence beginning "The patients most likely to use CAM..." is OK as edited.
- [Q2] Please check the superscript numbers 1 and 2 in the text.
- [Q3] Please check the sentence beginning "Biminne is composed of 11 Chinese herbs..." for clarity.
- [Q4] Please provide expansion for abbreviations "ASHMI, FAFH, PEF, FEV, NF-KB, TNF, MIC, HSV, MAO, NSAID, IBS, MCP, AMA", if necessary.
- [Q5] Please check if edit to 'NasalEase™ – used in allergy relieve...' is ok.
- [Q6] The term "Gota Kola" was changed to "Gotu kola". Please check if appropriate.
- [Q7] We have followed the Spec for outline numbering. Please confirm if this is correct.

