

# Chapter 6



## General Medicine

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### Anxiety

Approximately 4%-15% of Americans meet DSM-IV criteria for generalized anxiety disorder (GAD), with milder forms of anxiety being even more common. Many people with GAD also have other psychiatric conditions such as major depression, phobias, post-traumatic stress disorder, obsessive-compulsive disorder and/or panic disorder. The economic costs associated with anxiety approach \$46 billion annually in the United States.

People presenting initially with GAD should be evaluated for coexisting psychiatric conditions and those underlying conditions should be treated aggressively. Mainstay treatment for GAD includes exercise, medications, and psychological counseling including cognitive behavioral therapy (1,2). Medications include anti-depressants (tricyclic anti-depressants, selective serotonin reuptake inhibitors, selective serotonin and norepinephrine reuptake inhibitors), buspirone, and benzodiazepines.

CAM therapies are used as monotherapy as well as combination therapy in the treatment of GAD (2). A 2004 review of these therapies found the best evidence for kava, exercise, and relaxation therapies. They report limited evidence for acupuncture, music, autogenic training, and meditation. The more widely used CAM therapies are described below.

### Dietary Supplements

#### *Kava*

Kava is a member of the pepper family and grows as a shrub in the South Pacific. Kava has been used for ceremonial purposes throughout the Pacific islands for centuries. Traditionally the root is pulverized with a mortar and pestle and mixed with water or coconut milk. Kava is typically ingested as a drink in ceremonial bowls and is used socially as a mild intoxicant like alcohol. The active ingredients are called kavalactones including kavain, dihydromethysticin,

and methysticin. Dietary supplement extracts can be standardized to specific kavalactone concentrations, with most clinical trials using 100 mg kavalactones three times daily.

More than a dozen randomized blinded trials have been conducted that suggest kava is effective in treating anxiety, although one large internet-based randomized blinded trial found kava no more effective than placebo (3). Multiple systematic reviews have reported favorable therapeutic benefits and found kava to be associated with mild and transient side effects (4-6).

In March 2002, however, the FDA issued a Consumer Advisory after Germany, Switzerland and the United States identified 11 patients who used kava-containing products and experienced fulminant liver failure requiring liver transplantation (7,8). Nonetheless, some reviews suggest the benefits of Kava when used in otherwise healthy individuals on a short-term basis outweigh the remote risk of liver toxicity (4). Until there is better understanding of the mechanisms, products, and populations at-risk for hepatotoxicity, we believe risks outweigh the benefits particularly given the myriad of pharmaceutical, psychological, and mind-body interventions available to manage this condition (see Evidence Summary table at end of chapter).

### ***Passionflower***

Passionflower is commonly found in dietary supplement products purporting to relieve stress and anxiety. One randomized trial enrolled 36 people with GAD to passionflower extract 45 drops/day plus placebo tablet or oxazepam 30 mg/day plus placebo drops for 4 weeks. Both were effective in the treatment of anxiety, and no significant differences were observed between groups. Oxazepam was found to have a more rapid onset but also to be associated with impaired job performance (9). While this preliminary research is promising, there is currently insufficient evidence to refute or recommend passionflower for the treatment of anxiety (see Evidence Summary table at end of chapter).

### ***Hops (Humulus lupulus)***

Hops is commonly found in stress and anxiety dietary supplement products; however, there is a paucity of clinical trial data available to evaluate its effectiveness. Consequently, at this time, there is insufficient evidence to refute or recommend Hops for the treatment of anxiety (see Evidence Summary table at end of chapter).

### ***Bach Flower Remedy***

A systematic review identified four controlled clinical trials of Bach Flower remedy that met inclusion criteria for their review. Two of these trials reported positive benefits; however, after controlling methodological issues, Bach flower remedy was no better than placebo (10). Two of the more rigorous randomized trials found no benefit over placebo (11,12). At this time, the evidence suggests

that Bach Flower remedy appears not to have therapeutic benefit over placebo for the treatment of anxiety (see Evidence Summary table at end of chapter).

## Acupuncture

As described in more depth in Appendix 1, acupuncture is frequently associated with neurophysiologic and biochemical changes such as increases in endomorphin-1, beta endorphin, enkephalin, and serotonin levels. Many of these physiologic effects are associated with relaxation and analgesia. In clinical practice, most patients will describe feeling a sense of calm and well-being after acupuncture treatments. Two reviews have found limited evidence suggesting that acupuncture has increasing promise as an effective treatment for anxiety (13,14). Specifically, there are several randomized clinical trials reporting reductions in anxiety symptoms for procedure-related anxiety among those treated with acupuncture compared with controls, including subjects undergoing extracorporeal shock wave lithotripsy (15), colonoscopy (16), dental procedure-related anxiety (17), pre-operative anxiety (18), and pre-hospital transport (19). Other trials have examined anxiety symptoms among people living with chronic conditions such as chronic neck and shoulder pain (20) and fibromyalgia (21). One trial found acupuncture was not better than sham control for anxiety related to oocyte retrieval (22), and another found similar results for anxiety related to alcohol withdrawal symptoms (23).

There are only a few randomized trials evaluating the effects of acupuncture for people diagnosed with GAD or anxiety related to other psychiatric illness. One study randomized 43 patients with minor depression and 13 patients with GAD to 10 sessions of real versus sham acupuncture. Treatment was associated with statistically significant improvement on the Clinical Global Impression Scale (primary outcome) compared with controls. Multivariate analysis demonstrated a trend toward lower anxiety scores using the Hamilton Anxiety Rating scale compared with sham. Investigators concluded that acupuncture was associated with reductions in anxiety symptoms in people with minor depression and among people with GAD (24). A multi-center trial randomized 241 inpatients with depression to electroacupuncture + placebo, amitriptyline alone, or electroacupuncture + amitriptyline. Based on results from the Hamilton Rating Scale for Depression, and Clinical Global Impression scales, investigators report electroacupuncture was superior to amitriptyline for depressive disorders, including anxiety somatization and cognitive process disturbance with a reduced side effect profile (25). Finally, one study randomized 55 healthy volunteers to sham acupuncture, shenmen ear acupuncture point (the 'relaxation' ear acupuncture point) and found reduced anxiety among volunteers randomized to the 'relaxation' point compared with sham acupuncture at 30 minutes, 24 hours post-treatment (26).

In summary, there is moderate evidence that acupuncture may be effective for procedure-related anxiety, and limited evidence for anxiety symptoms related to selected medical conditions. There is insufficient evidence to support or refute recommending acupuncture for treating GAD (13) (see Evidence Summary table at end of chapter).

## Aromatherapy

Aromatherapy involves the use of fragrant essential oils for healing purposes. It frequently is applied on the skin or inhaled in dilute form through a vaporizer. A 2000 review identified 6 randomized trials evaluating the effect of aromatherapy on relaxation measures pertaining to a range of conditions and issues. Five of the six trials reported positive benefits; however, all were of poor methodological quality. Consequently, the authors concluded that aromatherapy likely provides transient and mild anxiolytic effects that are likely not strong enough to be beneficial for the treatment of anxiety. They did not identify evidence to suggest aromatherapy provides any long-term health benefits. (27). There are no randomized trials evaluating its effectiveness for people with GAD.

One randomized trial found aromatherapy no more effective than smelling a pleasant odor among people scheduled for a medical procedure (28). A large trial randomized 313 patients undergoing cancer radiation treatment and found no benefit of inhalation aromatherapy compared to controls (29). Another trial did not find benefit to adding aromatherapy to massage among 42 palliative care cancer patients who were randomized to receive four weekly massages with lavender essential oil or massage only or no intervention (30). A Cochrane review evaluated the effect of massage or aromatherapy massage for symptom relief in cancer patients (31). Anxiety measures were evaluated in four trials involving 207 patients with 19%-32% reduction in symptoms reported. There was conflicting evidence on the benefit of the addition of aromatherapy to massage on anxiety measures. Another trial found short-term benefits associated with aromatherapy massage among cancer patients diagnosed with clinical anxiety and/or depression. In this multi-center trial, they randomized 288 patients to aromatherapy massage or usual care and found improvements in self-reported anxiety at 10 weeks (OR 3.4), and in clinical anxiety scores at 6 weeks (OR 1.4) without sustained benefit at 10 weeks (32).

In summary, there is no evidence to suggest that aromatherapy is an effective treatment for anxiety disorders. Therefore, there is insufficient evidence to support or refute the use of aromatherapy for these conditions (see Evidence Summary table at end of chapter). However, there is moderate evidence to suggest that aromatherapy massage may confer short-term anxiolytic benefits among hospitalized patients; there is conflicting evidence on the additional benefit that aromatherapy itself has when provided in the context of a therapeutic massage.

## Meditation

Meditation enables people to consciously regulate their attention or “moment to moment” awareness. The two major types of meditation commonly practiced in the United States are concentration meditation and mindfulness meditation. The primary goal of concentration meditation is to focus attention on a single object such as a sound, image, or one’s breath. The most popular practices include the Relaxation Response and Transcendental Meditation. When the natural tendency of the mind to wander occurs, the practitioner gently redirects attention back to the object of focus time and time again. Practitioners purport the mind gently settles into a relaxed and aware state of consciousness that is incompatible with high states of arousal such as anxiety or agitation. Mindfulness meditation focuses on cultivating a moment-to-moment awareness of thoughts and perceptions in the absence of self-ridicule or judgment. As the mind wanders, the practitioner gently brings attention back to the present moment including the corresponding thoughts and perceptions. Primary examples of this technique include Mindfulness-Based Cognitive Therapy and Mindfulness-Based Stress Reduction. Over time, practitioners are said to become much more accepting of themselves and also more aware of their psychological processes. Given the importance of directing attention in the psychotherapeutic encounter, one trial evaluated the effect of training psychotherapists in mindfulness meditation. Eighteen psychotherapists in training (treating 124 inpatients) were randomized to a 9-week Zen meditation course or usual care. The intervention group received significantly higher evaluations, and patients reported greater symptom improvement across multiple measures including the Global Severity Index and 8 scales of the Symptom Checklist (SCL-90-R) including Somatization, Insecurity in Social Contact, Obsessiveness, Anxiety, Anger/Hostility, Phobic Anxiety, Paranoid Thinking and Psychoticism (33).

The scientific literature in this area of study, however, is quite limited. A 2006 Cochrane review identified only two randomized clinical trials evaluating the effect of meditation on anxiety conditions and concluded there was insufficient evidence to render an opinion on the effectiveness of meditation therapy for anxiety disorders (34). Another review identified five randomized trials on the effect of meditation on GAD and high trait anxiety (2). Four of these trials found that meditation was no different than relaxation therapies and biofeedback and was superior to wait list control. In conclusion, there is limited evidence suggesting that meditation may be effective for reducing anxiety symptoms among people with GAD or high-trait anxiety; however, further research is needed before making a recommendation (see Evidence Summary table at end of chapter).

## Relaxation Therapies

Relaxation therapies include a range of therapies that promote a sense of calm and well-being. The two most common forms are progressive muscle relaxation

and the “relaxation response” as defined by Herbert Benson. Relaxation techniques teach patients to recognize symptoms of anxiety, as well as triggers and cues. These techniques are said to induce a state of consciousness that is incompatible with elevated states of arousal such as anxiety and agitation (2). A 2007 review found muscle relaxation techniques effective for GAD (35). A 2007 meta-analysis found relaxation therapies superior to control and as effective as cognitive behavior therapy, meditation, autogenic training and biofeedback for GAD (36). In summary, there is strong evidence supporting the effectiveness of relaxation therapies for the treatment of GAD (see Evidence Summary table at end of chapter). This class of interventions is well-tolerated and generally safe.

## Common Cold

Upper respiratory infections are the leading reason for primary care visits in the United States. Unfortunately, antibiotics are still routinely prescribed for the treatment of this viral infection despite widespread education on the lack of efficacy and the safety concerns regarding the growing emergence of antibiotic resistance partly secondary to over-prescribing practices. There are no effective mainstay treatments to prevent or treat the common cold. There are numerous dietary supplements sold over-the-counter that purport to prevent or treat the common cold. We will review four of the more widely used products: zinc, Echinacea, vitamin C, and garlic.

### Dietary Supplements

#### *Zinc*

Sufficient serum levels of zinc are required for an optimally functioning immune system. There are more than nine clinical trials demonstrating that adequate zinc levels are associated with fewer respiratory, gastrointestinal and other infections in children and in elderly nursing home residents (37-45). For the treatment of the common cold, however, it is the topical application of zinc onto mucosal surfaces such as the buccal or nasal mucosa that seems to provide benefit. Zinc lozenges or nasal gel when applied to the mucosa have been found to inhibit cold viruses, such as rhinovirus, from adhering to the mucosal epithelium, thereby limiting infection or preventing it all together.

There are multiple randomized blinded trials evaluating zinc for the treatment of the common cold, with the balance showing beneficial effects and a good safety profile (46). One trial randomized 100 people to 13.3 mg zinc gluconate or placebo at onset of cold symptoms and found statistically significant reduction in duration of cough, sore throat, and rhinorrhea (47). Zinc as a treatment for the common cold comes in nasal and oral preparations, multiple formulations, and flavorings. The greatest scientific evidence is for zinc gluconate and zinc acetate lozenges without flavorings (48). Nasal gel formulations should

be avoided due to the risk of insomnia and pain with use. Overall, there is sufficient evidence to support a weak recommendation for zinc gluconate or zinc acetate lozenges for the treatment the common cold (see Evidence Summary table at end of chapter). For optimal effect, however, these products should be taken in the first 24 hours of cold symptoms. Frequent dosing requirements may limit its use. Patients should be informed that favorable results require lozenges to be taken every 2 hours. These products are generally well-tolerated.

### ***Echinacea***

*Echinacea* comes in many species (*E. purpurea*, *E. pallida*, *E. angustifolia*), formulations, dosages, active ingredients, and routes of administration. Over the past several decades, studies have shown conflicting results, largely because investigators use different preparations. For example, a well-conducted trial by Turner et al randomized 437 healthy volunteers to receive prophylaxis *Echinacea angustifolia* root extract after experimental inoculation with rhinovirus type 39. They found no statistically significant benefits in preventing or shortening infection (49).

Overall, the best evidence for the therapeutic benefit of *Echinacea* is with the above-ground preparations of *Echinacea purpurea* (stems, flowers, and leaves). A Cochrane review identified 16 trials, including 22 comparisons using a variety of *Echinacea* preparations (50). Nineteen comparisons evaluated its effect for the treatment of the common cold, and three comparisons evaluated its efficacy for cold prevention. None of the prevention trials showed benefit over placebo. Among the treatment comparisons, nine reported statistically significant benefit over placebo, one reported a trend, and six showed no benefit. They concluded that *Echinacea* preparations differed greatly in therapeutic benefit and the most promising evidence was for above-ground preparations of the *Echinacea purpurea* for the early treatment of colds. The evidence is inconclusive for other *Echinacea* preparations (50). Other systematic reviews have suggested that *Echinacea* when taken immediately after exposure or at first onset of symptoms may abort infection by the common cold (51) and reduce the duration and severity of symptoms among people suffering from the common cold (52).

The most recent meta-analysis reviewed 14 trials including 1600 people and found that *Echinacea* reduced the odds of getting a cold by 58% and shortened the duration of symptoms by 1.4 days compared to placebo. Subgroup analysis limited to Echinaguard/Echinacin use or controlling for concomitant supplement use, method of cold exposure, Jadad scores less than 3, or use of a fixed-effects model did not effect the benefits seen (53).

There has been controversy over whether immune-compromised patients should be using *Echinacea* for the long-term due to theoretical immune-stimulating effects. Recent research suggests that short-term use of *Echinacea* may have immune-stimulating effects, but long-term use appears not to have these effects (54-56).

In summary, Echinacea comes in varied preparations with varying clinical benefits. The best evidence is for above-ground preparations of *E. purpurea*. Overall, there is sufficient evidence to make a weak recommendation in favor of using this specific species and plant part for the treatment of the common cold (see Evidence Summary table at end of chapter). People with allergies to ragweed, chrysanthemums, marigolds, and daisies should not take this herb because there is cross reactivity.

### ***Vitamin C***

There has been significant controversy as to whether vitamin C is effective in the prevention or treatment of the common cold. A recent Cochrane systematic review evaluated the effect of vitamin C prophylaxis and treatment for the common cold. They identified 30 trials involving 11,350 subjects for vitamin C prophylaxis and found a 4% reduction in incident colds episodes which achieved borderline statistical significance (RR= 0.96, 95% CI 0.92 to 1.00) and questionable clinical significance. Among a subgroup of trials in which subjects were exposed to brief periods of severe physical or environmental stress (marathon runners, skiers, and soldiers on sub-artic exercises), they identified 50% reduction in incident cold infection when compared to placebo. Furthermore, vitamin C when taken prophylactically reduced cold symptom duration across all subgroups by 8% in adults and 13% in children when compared with placebo. Vitamin C when taken after the onset of symptoms, however, failed to shorten duration or severity of symptoms compared to placebo (57).

Overall, there is moderate evidence to suggest that vitamin C is not effective in reducing cold symptom severity or duration of symptoms when taken at onset of symptoms (see Evidence Summary table at end of chapter). There is moderate evidence to suggest that taking vitamin C prophylactically appears effective in reducing symptom duration (see Evidence Summary table at end of chapter). There is moderate evidence to suggest taking vitamin C prophylactically does not provide clinically meaningful benefits in preventing the common cold, except in subjects placed under severe stress, in which case it does appear to be quite effective (see Evidence Summary table at end of chapter).

### ***Garlic***

Folklore has portrayed garlic as the wonder herb, conquering infections and evil spirits. The only randomized trial identified enrolled 146 people and reported fewer colds (24 vs 65,  $p < 0.001$ ), and shorter symptom duration (1.5 vs 5,  $p < 0.001$ ) compared with placebo (58). There is promising preliminary data on the possible therapeutic benefit of garlic for the prevention and treatment of the common cold; however, there is insufficient evidence to refute or recommend the use of garlic for this indication at this time (see Evidence Summary table at end of chapter).

## Diabetes

Type 2 diabetes mellitus affects many people worldwide. Although it has traditionally been considered a disease of adulthood, it is occurring with increasing incidence in young people, particularly as more and more youngsters develop obesity. The estimated number of new cases of diagnosed diabetes in people aged 20 years or older in 2005 in the United States was 1.5 million, with a total prevalence of 20.8 million people. Total costs (direct and indirect) for diabetes care in 2002 were approximately \$132 billion (59).

Although some type 2 diabetics are able to improve their conditions with physical activity, dietary changes and weight loss, many patients have difficulty with these lifestyle changes, and they look for solutions both within and outside of the conventional medical setting (60). A regional analysis of 2474 adult patients with diabetes at Medical University of South Carolina revealed that 48% of adults with diabetes used some form of CAM (in a broad definition) (61). Use of CAM was independently associated with receipt of pneumonia vaccination (but not influenza vaccination), visits to the emergency department, and six or more visits to a primary care office. Whereas previous studies suggested that diabetic patients might use CAM independent of the conventional medical system, this study suggested that most diabetics use CAM in addition to conventional medicine.

Use of CAM and conventional treatments simultaneously was also found in a broader demographic in a national survey study discussed in Chapter 1, in which the vast majority of diabetic patients who used CAM were also under the care of a medical doctor (62). This means that medical doctors have an excellent opportunity to determine what remedies their patients are using, to offer guidance, and to follow their patients' progress.

CAM therapies have been tried for a number of manifestations of diabetes, including glycemic control, peripheral neuropathy, quality of life, lipid parameters, leg ulceration, and others.

### Dietary Supplements

#### *Cinnamon*

Cinnamon is a delightful and exotic spice that became a popular supplement for diabetes after the publication of a clinical study performed in Pakistan (63). This study reported that cinnamon powder (*Cinnamomum cassia*), taken over a 40-day period, reduced mean fasting serum glucose, LDL cholesterol, and total cholesterol. Three doses were studied, and all reported to be effective. There are no validated studies of western populations at that time.

By 2006 Dugoua and colleagues performed a systematic review of the effects of cinnamon for type 2 diabetes, surveying nine databases along with the Complete German Commission E Monographs, Natural Database and Natural Standard (64). They also hand searched relevant review papers and reference

lists of original research publications. They found three randomized clinical trials of aqueous cassia extract.

The first used 3 gm vs placebo for 4 months in 79 people. They found a significantly greater reduction in fasting glucose in the cinnamon group, but no difference was seen in hemoglobin A1c (HbA1c) or cholesterol levels. In the second study 60 participants were given 1 gm, 3 gm or 6 gm vs placebo for 40 days. The authors found significant improvement in blood glucose control and reductions in cardiovascular risk factor biomarkers. They did not follow HbA1c levels. Fasting baseline glucose levels were noted to be quite high. The third study used 1.5 gm daily vs placebo for 6 weeks in 25 postmenopausal patients. No improvements were seen in fasting glucose, plasma insulin, or lipid parameters.

In 2006 a clinical trial of 60 patients randomized to 1.5 gm cassia powder or placebo for 12 weeks showed HbA1c to be similarly decreased in both groups. There were no significant differences in lipid profiles. The mean start fasting plasma glucose was 154 +/- 24 mg/dL (65).

More recently, Solomon looked at the effects of short-term cinnamon ingestion on in vivo glucose tolerance in seven lean, healthy male volunteers in their mid 20's. They underwent three oral glucose tolerance tests, supplemented with 5 gms of placebo, 5 gms of cinnamon, or 5 gms of cinnamon taken 12 hours before a randomized cross-over design. Use of cinnamon was associated with improvement in total plasma glucose responses and insulin sensitivity by the Matsuda model, with sustained effects seen after 12 hours (66).

A 2008 meta-analysis of randomized controlled trials of cinnamon supplementation evaluated five prospective, randomized controlled trials with 282 patients and did not find a difference in A1c, fasting blood glucose or lipid parameters. Subgroup and sensitivity analyses also showed no significant changes (67).

Blevins et al, evaluated 60 patients with 1 gm cinnamon daily versus placebo for 3 months. Forty-three patients completed the study, dropouts were accounted for appropriately and adherence was high. The participants were of mixed ethnicity. 77% of the cinnamon group also used diabetes medications, whereas 91% of the placebo group used medication. There were no significant differences between the cinnamon and placebo groups in the change in any measure (fasting glucose, lipid A1C or insulin levels) from baseline to 1, 2, or 3 months (68).

In summary, although there is an increasing number of well-designed clinical trials, there is currently insufficient evidence to recommend use of cinnamon for treatment of diabetes, particularly not as an alternative to medications with well-established hypoglycemic effects (see Evidence Summary table at end of chapter). Both common and cassia cinnamon have been studied and, as with all dietary supplements, the exact composition of cinnamon might have varied significantly in the different trials.

## **Omega-3 Fatty Acids**

Omega-3 fatty acids are found in a number of foods, such as fish, walnuts, certain seeds, wheat germ and several vegetable oils. They are commonly purchased as dietary supplements in the form of fish oil capsules.

In the original Cochrane evaluation in 2001 of 18 randomized, double-blind, placebo-controlled trials, patients with type 2 diabetes who consumed fish oils lowered triglyceride and slightly raised LDL cholesterol, but had no significant effect on fasting blood glucose, HbA1c, total cholesterol, or HDL cholesterol (69). In the last substantive update in 2008, Hartweg et al concluded that supplementation lowered triglycerides and VLDL cholesterol, had no effect on blood glucose or fasting insulin levels, and might slightly raise LDL cholesterol (although these findings did not achieve statistical significance). There were no adverse effects (70).

The Agency for Healthcare Research and Quality published an independent analysis in 2004 of 18 studies on omega-3 fatty acids for a number of measurable outcomes in type 2 diabetes. The authors concurred with the Cochrane authors' findings, except for finding no significant effect on LDL cholesterol (71). See the Evidence Summary table at the end of the chapter.

While consumers should be aware of the theoretical risk of poorly manufactured supplements that contain mercury, two studies conducted random testing of omega-3 dietary supplements and found no evidence of high levels of mercury in the brand names tested (72). Nonetheless, we recommend that consumers identify companies that abide by the FDA final rule for current Good Manufacturing Practices to ensure supplements are free of toxic levels of mercury. Even better, consumers can look for the NSF, USP seal of approval of good manufacturing practices or go to [consumerlab.com](http://consumerlab.com) to identify products that have passed their quality-control testing.

## **Chromium**

Chromium has been studied more extensively than other complementary treatments for type 2 diabetes with mixed results. It is abundant in the earth's crust and found in numerous foods, such as vegetables, beef, potatoes with skin, brewer's yeast, cheese and others. Chromium is required for normal glucose metabolism. It may play a role in helping insulin bind to insulin receptors, theoretically augmenting carbohydrate and lipid metabolism. The recommended daily allowance for healthy adults is 50-200 mcg (73). Supplemental chromium does not cause hypoglycemia in healthy people. It may be that chromium is helpful for some patients who are deficient in it, or for certain other populations. Kleefstra et al found no benefit to adding chromium 400 mcg (in the form of chromium yeast) for 6 months beyond usual care, including oral hypoglycemic agents, to Western patients with type 2 diabetes (74).

This is in contrast to the study performed by Anderson et al in China, which found that patients treated with 1000 mcg of chromium picolinate dropped their HbA1C levels more than patients who took placebo, in a study of 180 patients over 4 months (75).

In 2002 Althuis et al looked at 20 clinical trials, including 15 randomized trials with enough data for evaluation. Trials used chromium chloride, chromium nicotinate, chromium niacin, chromium “rich” yeast, Brewer’s yeast and chromium picolinate. The dose ranged from 10.8 to 1000 mcg. There were several different controls. Glucose and insulin concentration were assessed after fasting and at 120 minutes after an oral glucose tolerance test. The effects of chromium were studied in diabetic patients (193 patients with type 2 diabetes) and non-diabetic patients (425 patients). The reviewers concluded that there is no evidence that chromium has any effects on glucose or insulin levels in non-diabetic patients, and there was insufficient evidence to determine the effect of chromium on diabetic patients. This analysis looked at only two databases, and patient populations may have differed considerably between studies. The authors recommend further safety testing (76). See the Evidence Summary table at the end of the chapter for a summary of the evidence.

### ***Chinese Herbs***

A Cochrane review of Chinese herbs for diabetes identified 66 trials involving 8302 participants that met their criteria for inclusion. Methodologic quality was generally low. Sixty-nine different herbal medications were evaluated compared to placebo, hypoglycemic drugs or herbal medications plus hypoglycemic drugs. Compared with placebo, holy basil leaves, Xianzhen Pian, Qidan Tongmai, traditional Chinese formulae Huoxue Jiangtang Pingzhi, and Inolter showed a significant hypoglycemic response. No high-quality trials were identified.

In conclusion, some Chinese herbal medications show hypoglycemic effects in type 2 diabetes. However, these findings should be carefully interpreted because of the low methodological quality of these trials. The authors felt that in light of some positive findings, some herbal medicines deserve further examination (77). The safety of these herbs also needs further evaluation. Given that Chinese herbal treatments (albeit unrelated to the ones studied for diabetes) have been associated with liver and kidney adverse effects (78-81), the safety issues should be more fully evaluated as part of any clinical program evaluating the efficacy of these treatments. If patients intend to take Chinese herbs, they should limit themselves to products that have been independently certified for good manufacturing practices by the NPA, USP, or NSF. Alternatively, they can go to [consumerlab.com](http://consumerlab.com) and verify which specific brand names passed their quality-assurance testing.

### ***Other Agents***

Other agents, such as aloe vera and ginseng, have been used for diabetes without strong evidence based upon clinical investigation (82,83).

### **2003 Summary of Dietary Supplements for Diabetes**

Yeh et al summarized available clinical data for dietary supplement treatments of diabetes in 2003, which is now somewhat dated. The systematic review of multiple databases selected studies that looked at glycemic control. The authors concluded that there was insufficient evidence to draw definitive conclusions about the efficacy of individual herbs and supplements, but that several supplements, including *Coccinia indica* and American ginseng, deserve further study. Other supplements judged to have “positive preliminary results” include *Gymnema sylvestre*, Aloe vera, vanadium, *Momordica charantia* and nopal (84).

### **Acupuncture for Diabetic Neuropathy**

Peripheral neuropathy is a painful complication experienced by some diabetic patients. Safe, effective alternative therapies would be a welcome addition to the physician’s armamentarium of treatments. Although much has been written about use of acupuncture for diabetic neuropathy, high-quality clinical trials are lacking. One pilot study treated 46 diabetic patients with diabetic peripheral neuropathy with acupuncture and found 77% reporting significant improvement and 67% reduced their related medications (85). Currently there is insufficient evidence to recommend or refute the use of acupuncture for treatment of diabetic peripheral neuropathy (see Evidence Summary table at end of chapter).

### **Ayurvedic Interventions for Diabetes Mellitus**

As noted in the Appendix, Ayurvedic medicine is a medical system that uses single or multiple modalities simultaneously in the treatment of disease. With respect to the treatment of patients with diabetes, a summative analysis has been published by the Agency for Healthcare Research and Quality. The reviewers identified 54 articles containing 62 clinical trials of Ayurvedic therapy for diabetes that met their inclusion criteria. Meta-analysis was not possible owing to the heterogeneity of the trials.

Clinical trials were limited almost exclusively to herbal preparations, and no other modalities could be assessed. Unfortunately, there were no studies that tested multiple simultaneous Ayurvedic interventions, or Ayurveda as a whole system. Several clinical trials from India (published in English) could not be located, and several trials in India written in other languages were not reviewed.

Based on the current evidence, the reviewers note that the single herbs *Coccinia indica*, holy basil, fenugreek and *Gymnema sylvestra*, and the herbal formulas Ayush-82 and D-400 show preliminary evidence of glucose-lowering effect and should be studied further. There are currently too few randomized controlled trials of sufficient quality to make firm conclusions, and therefore there is insufficient evidence to recommend or refute the effect of these treatments for

active treatment of diabetes (see Evidence Summary table at end of chapter). The authors recommend field studies to determine how Ayurvedic medicine is used in real-life clinical practice, and they encourage investigation of the interaction between botanicals and other Ayurvedic modalities, such as yoga (86).

NCCAM is currently sponsoring research into the effects of chromium, yoga, ginkgo, vitamin C, and the safety of glucosamine on diabetes.

## Herpes Infection

Genital herpes infection is a sexually transmitted disease caused by both herpes simplex virus 1 (HSV-1) and herpes simplex virus 2 (HSV-2) viruses. HSV-1 predominately causes mouth sores and HSV-2 infection can cause both genital and mouth sores. Approximately 20% of the US population is infected with genital herpes infection with a greater predominance among women. More than 371,000 initial visits to physician offices occurred in 2006 related to herpes infection. Approximately 200,000 to 500,000 new cases of herpes infection occur annually. Transmission occurs through release of the virus during a “herpes outbreak” (when blisters are present) but can also occur when no skin lesions are identified. Herpes infection can facilitate transmission of HIV virus, particularly when skin lesions are present.

There is no cure for herpes infection and therefore people carry the virus throughout the duration of their life. Mainstay therapy includes anti-viral medications such as valcyclovir and acyclovir. These medications can prevent and shorten the duration of outbreaks. When taken regularly as a daily prophylactic, these medications can reduce the frequency of symptomatic herpes for individuals prone to recurrent outbreaks, as well as reduce transmission rates to uninfected partners.

## Dietary Supplements

### *L-Lysine*

L-lysine is an amino acid widely used by consumers for the prevention and treatment of herpes infection. A review of several randomized blinded clinical trials using 1.25 to 3 grams daily dose reported reductions in recurrent episodes (87). One trial randomized 52 people with genital herpes to 3 grams daily or placebo for 6 months and found a statistically significant reduction of 2.4 fewer recurrences than the control group (88). An earlier multi-center study by the same author also found benefit (89). McCune conducted a randomized blinded cross-over trial of 42 patients taking 1.25 grams of lysine and found reduced recurrence rates. Of note, they found no benefit using the lower dose of 624 mg daily. They also noted lysine did not appear to heal lesions more quickly than placebo (90). DiGiovanna randomized 21 people to 400 mg three times daily of lysine hydrochloride compared to placebo and found no benefit (91). Milman randomized 65 people with recurrent herpes simplex labialis infections

to 12 weeks of 1000 mg lysine daily in a randomized, blinded, crossover study. Investigators found no effect on the recurrence rates; however, significantly more people were recurrence-free during the lysine intervention period than during the placebo treatment period. They found no effect of lysine on healing of skin lesions (92). Overall, there is limited evidence to suggest that 3 grams daily of L-lysine monohydrochloride may reduce recurrence rates of symptomatic herpes infection among at-risk populations (93). Overall, there is sufficient evidence to make a weak recommendation in favor of L-lysine for this indication (see Evidence Summary table at end of chapter).

There is significant discussion among consumers and in media regarding the benefits of a high-lysine and low-arginine diet to prevent recurrent symptomatic herpes outbreaks. Foods containing more arginine than lysine include whole wheat, oats, chocolate, peanuts, walnuts, orange juice, and blueberries, for example. Foods containing more lysine than arginine include meats and dairy products.

There are no clinical trials or large cohort studies evaluating these claims. There are in vitro studies, however, suggesting that arginine-rich environments are critical for herpes virus function and growth (94,95). At this time there is insufficient evidence to support or refute using this modified diet as effective treatment for herpes.

### ***Lemon Balm (Melissa officinalis)***

Topical lemon balm is sold in Europe as a topical cream for the treatment of oral and genital herpes. In one study, 116 people with oral or genital herpes were randomized to lemon balm or placebo cream for 10 days, and the treatment group experienced a more rapid recovery than controls (96). Another trial evaluated 66 people with oral herpes and reported similar findings on day 2 (97). At this time, there is insufficient evidence to support or refute the use of lemon balm for the treatment of genital herpes (see Evidence Summary table at end of chapter).

## **Migraine Headaches**

Migraine headaches can be unilateral or bilateral and may or may not involve prodromal symptoms. The cause remains unclear but is thought to be mediated by neurotransmitters such as serotonin and dopamine, which are thought to initiate an inflammatory cascade leading to vasodilation and secondary perivascular changes. The International Headache Society recently redefined migraines such that “classic migraine” is now defined as a migraine with aura and “common migraine” is now defined as a migraine without aura. The latter accounts for 80% of all migraine episodes.

Approximately 17% of women and 6% of men in the United States have suffered from migraine headaches. Migraines are the second most common headache following tension headaches. Surprisingly, less than half of migraine

sufferers are diagnosed by their doctors. Overall, this condition remains largely undertreated and underdiagnosed. Symptoms include intense pain, as well as nausea, visual disturbances, and, in cases of complicated migraines, neurological deficits. Some people experience early warning signs such as changes in energy or mood, fatigue, food cravings, or visual disturbances such as flashing lights, colors, and transient loss of peripheral vision.

Many people benefit from keeping a journal in order to identify factors that may trigger their migraines. Examples of triggers include lack of sleep, skipping meals, birth control pills or hormonal changes including menstrual cycle, smoking tobacco, intense physical activity or emotional reactivity. Specific foods that trigger migraines in certain people include aspartame, monosodium glutamate, cured or processed meats, alcohol (particularly red wine), caffeine, chocolate, nuts and peanuts, preserved or pickled foods, and soy sauce, among others.

Treatments for migraine headaches fall into two categories: prevention and acute treatment. If migraines are interfering with daily functioning or occur more than twice monthly, daily medication to prevent recurrent migraines is recommended. Medications for prevention of migraines include beta-blockers, tricyclic anti-depressants, ergot derivatives, antihistamines, and anti-convulsants. Management of acute migraines includes a range of effective medications including simple analgesics (acetaminophen, aspirin, codeine), non-steroidal anti-inflammatory drugs, 5-HT<sub>1</sub> serotonin receptor agonists (sumatriptans, zolmitriptan, and Rizatriptan), ergot alkaloids and their derivatives (ergotamines, dihydroergotamines), and combination drugs (isometheptene/dichloralphenazone/acetaminophen, and acetaminophen/butalbital/caffeine). In addition, people benefit from stress management therapies such relaxation techniques, breathing practices, lying down in a quiet and dark room, and self-massage to the scalp.

## Dietary Supplements

### ***Butterbur (Petasites hybridus)***

Butterbur (*Petasites hybridus*) can be found in southwest Asia, North Africa, and Western Europe. The unprocessed herb contains pyrrolizidine alkaloids (PAs), which can cause hepatotoxicity. Consequently, a special Butterbur root extract that is free of PAs has been used for clinical trials. The most widely evaluated compound is called Petadolex, which is manufactured by high-pressure carbon dioxide extraction. This special extract has been evaluated in three randomized double-blind clinical trials. A systematic review analyzed two of the larger studies in which the proprietary product, Petadolex, was evaluated. They concluded that there is moderate evidence for effectiveness (98). One trial randomized 245 patients meeting the International Headache Society criteria for migraine to 4 months of twice daily specialized Petasites extract at 75 mg, 50 mg, or placebo. Over the course of the study, per-protocol analysis found the 75 mg dosage reduced migraine frequency by 48% ( $p=0.001$  vs placebo), compared with 36% for the 50 mg dosage ( $p=0.13$  vs placebo), and 26% for the

placebo group. In addition, 68% of the high-dose group, compared with 49% of the placebo group, had a 50% or greater reduction in migraine frequency ( $p < 0.05$ ) at 4 months (99). An earlier trial randomized 60 people to 3 months of 50 mg twice daily Butterbur PA-free extract or placebo and found a statistically significant reduction in migraine frequency compared with placebo. 75% of patients reported improvement compared with 25% taking placebo (100). Another trial, not included in the systematic review, randomized 33 people to 50 mg butterbur twice daily or placebo and found reductions in monthly migraine frequency from 3.4 at baseline to 1.8 after 3 months compared to a reduction from 2.9 to 2.6 reported for the control group. In addition, 45% of the verum group compared with 15% of the placebo group had a 50% or greater reduction in migraine frequency (101).

In summary, there is moderate evidence suggesting pyrrolizidine alkaloid (PA)-free butterbur extracts such as Petadolex appear effective and safe for the prevention of migraine headaches at 75 mg and 50 mg twice daily dosing. Animal and human research suggest the PA-free product is generally well-tolerated (102). There is sufficient evidence to support a strong recommendation for this treatment (see Evidence Summary table at end of chapter).

### ***Feverfew***

A recent Cochrane systematic review identified five randomized clinical trials (including 343 people) and reported inconsistent evidence on the beneficial effect of feverfew for migraine prevention. Only transient and mild adverse effects were reported (103). Overall, the best evidence can be found among the trials evaluating a liquid carbon-dioxide extraction.

One trial randomized 170 people who met criteria according to the International Headache Society criteria for migraines to a liquid carbon-dioxide extraction of 6.25 mg three times daily of feverfew or placebo in a multi-center, parallel-group, double-blind, placebo-controlled trial. At the end of 4 months, migraine frequency was reduced by 1.9 attacks per month in the feverfew group compared with 1.3 attacks per month in the placebo group ( $p = 0.046$ ). There were no differences in adverse events between groups (104). An earlier trial using the same formulation found benefit limited to a sub-group with more frequent attacks (105).

Two other randomized trials, both published in the 1980s, used whole feverfew leaf and found feverfew to be safe and effective (106,107); however, a trial evaluating feverfew in combination with riboflavin and magnesium compared to low-dose riboflavin found no benefit (108).

Overall, there is conflicting evidence regarding the effectiveness of feverfew for the prevention of migraines. In general, feverfew appears generally safe with mild and transient side effect profile. There is insufficient evidence to refute or support feverfew for the prevention of migraine headaches at this time (see Evidence Summary table at end of chapter).

## **Magnesium**

One study enrolling 60 people with migraines found intravenous magnesium sulphate was an effective treatment for acute migraines with aura for treating pain and for associated symptoms in subjects compared to placebo (109). Cete et al enrolled 120 people presenting to an emergency department who met International Headache Society criteria and randomized them to 10 mg intravenous metoclopramide, 2 grams intravenous magnesium, or normal saline and found neither treatment more effective than placebo (110). Another trial randomized 44 people to intravenous 20 mg metoclopramide with or without 1 gram intravenous magnesium sulfate and found magnesium was associated with worsened symptoms (111).

Two multi-center trials examined the use of oral magnesium for migraine prophylaxis. In one multi-center trial, investigators randomized 81 people who met International Headache Society criteria for migraine to 600 mg oral trimagnesium dicitrate daily or placebo for 12 weeks and found a marked reduction in headache frequency of 42% compared with 16% in the placebo group; however, these differences did not achieve statistical significance. Duration and intensity of migraine episode also decreased compared with placebo but also did not achieve statistical significance (112). A second multi-center trial randomized 118 children and adolescents with moderate to severe migraines to 3 mg/kg of magnesium oxide three times daily or placebo. Magnesium was associated with a reduced number of headache days and severity compared with placebo (113).

Overall, there is conflicting evidence regarding the effect of intravenous magnesium sulfate for the acute treatment of migraine headaches; consequently there is insufficient evidence to refute or support its use (see Evidence Summary table at end of chapter). There is limited evidence suggesting that oral magnesium oxide may prevent migraines; however, the evidence is too limited to render a recommendation at this time (see Evidence Summary table at end of chapter).

## **Coenzyme Q10**

One trial randomized 42 people with migraines to receive 100 mg three times daily of coenzyme Q10 or placebo and found 48% experienced at least a 50% reduction in attack frequency in the treatment group compared with 14% in the placebo group. Based on these findings, only three people would need to be treated to prevent one migraine (NNT= 3) (114). Coenzyme Q10 was well tolerated. These findings are very promising and suggest larger clinical trials are warranted. At this time, however, there is insufficient evidence to refute or support Co-Q10 for the treatment of migraines at this time (see Evidence Summary table at end of chapter).

## Acupuncture

A 2001 Cochrane review identified 26 randomized or quasi-randomized trials involving 1151 patients evaluating the effect of acupuncture for the treatment of idiopathic (primary) headaches. Sixteen of these trials were conducted among migraine sufferers, six among patients with tension-type headaches, and four among patients with miscellaneous headache-types. Among the eight trials comparing real to sham acupuncture, real acupuncture was superior; in four trials there was a trend favoring real acupuncture; and in two studies real acupuncture provided no additional benefit over sham. They concluded that the evidence suggests a clinical benefit of acupuncture for idiopathic headache, including migraine headaches, but called for more studies to confirm these findings under real-life circumstances and for cost-effectiveness studies to affirm its utility (115).

Several large clinical trials were subsequently published. One trial randomized over 400 primary care patients with predominantly migraine headaches to 12 weekly sessions of acupuncture or usual care (116). Compared with controls, patients randomized to acupuncture had 22 fewer headache days per year, scored better on the SF-36, used 15% less medication, made 25% fewer visits to general practitioners and took 15% fewer days of sick leave. Overall, acupuncture was more expensive than usual care; however, there was a 0.021 QALY gain in that group associated with a cost of GBP9180 per QALY gained. The investigators concluded that acupuncture is associated with clinically relevant and persistent benefits for primary care patients that are cost-effective compared with other interventions provided by conventional care. A 2008 clinical trial randomized 3182 headache patients to acupuncture or usual care and also found costs were higher in the acupuncture group compared with usual care (117). Investigators performed a cost-effectiveness analysis and determined that acupuncture was associated with a cost of 11,657 Euro per 1 Quality-Adjusted Life Year (QALY) gained. The authors report that according international cost-effectiveness threshold values is a cost-effective treatment for this population.

A 2007 review concluded that the evidence-base now suggests a 6-week course of acupuncture is not inferior to a 6-month course of prophylactic drug treatment (118). The review also noted the evidence suggests that specific acupuncture point location, stimulation, and needle depth are not as important as previously thought. They concluded the evidence is sufficient such that acupuncture should be added to evidence-based practice guidelines for the prevention of migraine headache.

Overall, there is sufficient evidence to support a strong recommendation favoring the use of acupuncture for the prevention of migraine headaches (see Evidence Summary table at end of chapter).

## Manipulative and Body-Based Practices

A 2005 review found physical therapy to be more effective than massage or acupuncture for tension-type headache and for people with frequent attacks. PT was most effective for migraine when used in combination with other therapies such as exercise, relaxation training, and biofeedback (119). They found no convincing evidence on the benefits of chiropractic or spinal manipulation for the treatment of migraine headaches and this has been confirmed in other reviews (120). These findings contradict a 2004 Cochrane review reporting evidence suggesting that spinal manipulation may be effective for short-term treatment for migraine headache with similar effect to amitriptyline (121).

Overall, the methodological quality of the evidence limits the ability to generalize these findings to everyday clinical practice. Consequently, physical treatments should be considered only within the context of a multi-disciplinary treatment plan at this time (119) (see Evidence Summary table at end of chapter).

## Mind-Body and Behavioral Therapies

There is strong evidence to support mind-body and behavioral interventions such as biofeedback, cognitive behavioral therapy, stress management and relaxation training for the prevention and treatment of migraine headaches (122-125) (see Evidence Summary table at end of chapter). The literature suggests that these interventions are consistently superior to control conditions, providing patients with 35%-55% improvement in symptoms. Consequently, many professional organizations now recommend using these mind-body and behavioral interventions as primary therapeutic options for the management of headache, including migraine headaches.

## Recurrent Urinary Tract Infections

Recurrent urinary tract infections (UTI) are common among young healthy women with normal urinary tract anatomy and function, with approximately one-quarter of college women having a recurrent infection within 6 months of their first UTI (126). Some women have genetic factors that make them prone to recurrent infection such as a cellular defect of the uroepithelial cells or being an ABH blood group antigen nonsecretor, both of which encourage adherence of uropathogenic organisms. Behavioral factors also play a large role in predicting recurrence. Frequent sexual intercourse, use of spermicides, and recent antibiotic use are each independent risk factors. Among post-menopausal women, urinary incontinence, ABH blood group antigen nonsecretor status, and history of UTI are the strongest risk factors for recurrent UTI.

A range of treatments available to women include self-treatment with antimicrobials, post-coital prophylactic use of antimicrobials or continuous

antimicrobial prophylaxis. The decision between these regimens depends on patient preference, identifiable risk factors such as sexual activity, and/or the frequency and severity of episodes. For post-menopausal women, one randomized blinded trial involving 93 women with recurrent UTI reported a 90% risk reduction (5.9 to 0.5 episodes) over 8 months using an intravaginal estriol cream (127). Treated women also demonstrated a marked reduction in *E. coli* and an increase in lactobacilli vaginal colonization when compared with placebo. The most popular supplement for prevention of recurrent UTI is cranberry.

## Dietary Supplements

### **Cranberry (*Vaccinium macrocarpon*) Juice and Supplements**

Cranberry has been used for the prevention of recurrent urinary tract infections by Native Americans for centuries. Because cranberry can acidify the urine and *E. coli* does not proliferate in acidic environments, this was thought to be the mechanism of action for its therapeutic benefits. More recent research indicates that the mechanism of action is likely the decreased adherence of uropathic *E. coli* strains to uroepithelial bladder cells (128).

A recent Cochrane review identified 10 randomized clinical trials including over 1000 people, and reports that cranberry juice (including cranberry-lignonberry juice) and supplements are associated with a 35% reduction in the frequency of urinary tract infections when compared with placebo (129). The greatest effect was seen in women with recurrent UTI. One of the more well-conducted clinical trials randomized 150 women with recurrent *E. coli*-related UTI to 50 cc cranberry-lingonberry juice concentrate daily for 6 months or 100 cc lactobacillus drink 5 days weekly for 1 year or no intervention. At 6 months follow-up, 16% of women assigned to the cranberry group, 39% assigned to lactobacillus and 36% assigned to placebo experienced one or more recurrent UTI. Overall, there was a 20% absolute risk reduction in the cranberry group compared with the control group, which is equivalent to a number needed to treat of 5 (130). Another study evaluated the cost-effectiveness of cranberry products and randomized women with recurrent UTI to cranberry tablets + placebo juice, placebo tablets + cranberry juice, or placebo tablets + placebo juice. Tablets were taken twice daily and 250 mL of juice were taken three times daily. Overall, they found 18% and 20% of patients experienced at least one symptomatic UTI/year for cranberry tablets and cranberry juice, respectively, compared to 32% of patients randomized to the control group. Prophylaxis cost \$624 and \$1400 for cranberry tablets and juice, respectively, for 1 year. Antibiotic use was less annually in both treatment groups compared with placebo. Cranberry tablets provided the most cost-effective therapeutic option in this trial for preventing UTIs (131). In general, cranberry products are well-tolerated and are relatively safe. Overall, there is sufficient evidence to support a strong recommendation in favor of cranberry products for the prevention of recurrent UTIs

(see Evidence Summary table at end of chapter). Evidence indicates the appropriate dose is 400 mg capsule twice daily of cranberry concentrated extract (standardized to contain 11% to 12% quinic acid) or 8 ounces of unsweetened cranberry juice from concentrate taken three times daily. Be sure patients avoid cranberry cocktail, which contains minimal cranberry juice.

**Evidence Summary of CAM Treatments in General Medicine**

Clinical Indication	Category	Specific Therapy	Dose	Outcome	Confidence of Estimate on			Clinical Recommendation‡	Comments
					Effectiveness	Magnitude of Effect*	Safety†		
Anxiety: generalized anxiety disorder	Biologically based practices	Kava	100 mg kava-lactones three times daily	Anxiety	Grade B	Moderate	Single thumbs down*	Weak against	*11 case reports of fulminant liver failure requiring transplantation
Anxiety: generalized anxiety disorder	Biologically based practices	Passion-flower	Variable	Anxiety	Grade C	Unclear	No recommendation	No recommendation	1 small equivalency trial suggesting no different than oxazepam
Anxiety: nonspecific	Biologically based practices	Hops	Variable	Anxiety	Grade D	Unclear	No recommendation	No recommendation	—
Anxiety: nonspecific	Biologically based practices	Bach Flower Remedy	Variable	Anxiety	Grade B	None	No effect	Weak against	—
Anxiety: procedure-related	Whole medical system	Acupuncture	Variable	Anxiety	Grade B	Small	Single thumbs up	Weak in favor	—
Anxiety: generalized anxiety disorder	Whole medical system	Acupuncture	Variable	Anxiety	Grade D	Unclear	Single thumbs up	No recommendation	—
Anxiety: symptoms related to underlying medical conditions	Whole medical system	Acupuncture	Variable	Anxiety	Grade C	Moderate	Single thumbs up	Weak in favor	—

(continued)

## Evidence Summary of CAM Treatments in General Medicine (continued)

Clinical Indication	Category	Specific Therapy	Dose	Outcome	Confidence of Estimate on Effectiveness			Clinical Recommendation‡	Comments
					Grade	Magnitude of Effect*	Safety†		
Anxiety: generalized and body-anxiety disorder	Manipulative and body-based	Aromatherapy	Variable	Anxiety	Grade D	Unclear	Double thumbs up	Weak against	Clinical trials for milder conditions suggest lack of effect
Anxiety: among palliative care	Manipulative and body-based	Aromatherapy Massage	Variable	Anxiety	Grade B	Small	Double thumbs up	No recommendation	Evidence suggests that benefits are mild, and transient (several weeks) and aromatherapy may not provide additional benefit over massage alone.
Anxiety: generalized anxiety disorder and high trait	Mind-body medicine	Meditation	Variable	Anxiety	Grade C	Small	Double thumbs up	Weak in favor	—
Anxiety: generalized anxiety disorder	Mind-body medicine	Relaxation training	Variable	Anxiety	Grade A	Moderate	Double thumbs up	Strong in favor	—
Common cold	Biologically based practices	Zinc gluconate lozenges	13.3 mg	Symptom duration	Grade B	Small	Double thumbs up	Weak in favor	Requires every 2 hour dosing, which may limit its use.

Common cold	Biologically based practices	Extract from above-ground preparations of <i>Echinacea purpurea</i>	300 mg three times daily	Prevention of incident common cold episodes; symptom duration	Grade B	Moderate	Double thumbs up	Weak in favor	People with allergies to ragweed, daisies, marigolds, and chrysanthemums should avoid this herb.
Common cold	Biologically based practices	Vitamin C prophylaxis	Variable	Symptom duration	Grade B	Small	Double thumbs up	Weak in favor	—
Common cold	Biologically based practices	Vitamin prophylaxis	Variable	Prevention of the common cold	Grade B	No effect	Double thumbs up	No recommendation	Vitamin C appears quite effective among people under severe physical or environmental stress.
Common cold	Biologically based practices	Vitamin C treatment at onset of symptoms	Variable	Symptom duration and severity	Grade B	No effect	Double thumbs up	Weak against	—
Common cold	Biologically based practices	Garlic	Variable	Prevention of the common cold, and symptom duration	Grade C	Small	Double thumbs up	No recommendation	—

(continued)

## Evidence Summary of CAM Treatments in General Medicine (continued)

Clinical Indication	Category	Specific Therapy	Dose	Outcome	Confidence of			Comments	
					Estimate on Effectiveness	Magnitude of Effect*	Safety†		
Type 2 diabetes	Biologically based practices	Cinnamon	1.5 gm to 5 gm, 1 day to 4 months	HbA1C, fasting glucose, glucose tolerance test	Grade B	Conflicting	Double thumbs up	No recommendation	Different kinds of cinnamon; different outcomes tested; healthy and diabetics tested; conflicting results. No hypoglycemic effect. No clinically meaningful effect on LDL levels.
Type 2 diabetes	Biologically based practices	Omega 3 fatty acids	Varied	1. Blood glucose, 2. Triglycerides	1. Grade A 2. Grade A	1. None 2. Small 3. Unclear	No recommendation	1. Strong against 2. Strong in favor	No hypoglycemic effect. No clinically meaningful effect on LDL levels.
Type 2 diabetes	Biologically based practices	Chromium	Different chromium preparations at different doses	Fasting glucose, HbA1c	Grade C	Unclear	No recommendation	No recommendation	May have different effects in different populations.
Type 2 diabetes	Biologically based practices	Chinese herbs	Many herbs, some formulas, varied doses	Mortality, quality of life, long-term diabetic complications, glycemic control, weight or	Grade C	Varied	No recommendation	No recommendation	Some herbs may be beneficial but interpretation of trials limited by poor quality. Evaluation of safety profile is needed.

Diabetic neuropathy	Whole medical systems	Acupuncture	Different techniques	Pain	body mass index, fasting insulin levels	Grade D	Unclear	Single thumbs up	No recommendation	—
Type 2 diabetes	Whole medical systems	<i>Ayurvedic herbal medicines: Coccinia indica, Holy basil, fenugreek and Gymnema sylvestra; Ayush-82, D-400 (29)</i>	Varied doses	Glucose lowering effect and other measurements		Grade C	Small	Side-ways thumb	No recommendation	Agency for Healthcare Research and Quality recommends further study of <i>Coccinia indica</i> , holy basil, fenugreek, <i>Gymnema sylvestra</i> , <i>Ayush-82</i> , D-400.
Genital herpes	Biologically based practices	L-Lysine monohydrochloride	3 grams daily	1. Prevention of recurrent episodes 2. Duration of symptoms		1. Grade C 2. Grade C	1. Moderate 2. No effect	Double thumbs up	1. Weak in favor 2. Weak against	—
Genital herpes	Biologically based practices	Lemon balm topical cream	Variable	Duration of symptoms		Grade C	Small	Double thumbs up	No recommendation	—

(continued)

## Evidence Summary of CAM Treatments for General Medicine (continued)

Clinical Indication	Category	Specific Therapy	Dose	Outcome	Confidence of Estimate on Effectiveness			Clinical Recommendation‡	Comments
					Magnitude of Effect*	Safety†			
Migraine headaches prophylaxis practices	Biologically based	Buterbur extract, liquid-carbon-dioxide PA-free	50-75 mg twice daily	Migraine recurrence	Grade B	Moderate	Double thumbs up	Weak in favor	—
Migraine headaches prophylaxis practices	Biologically based	Feverfew	Variable	Migraine recurrence	Grade B	Conflicting	Single thumbs up	No recommendation	—
Migraine headaches prophylaxis practices	Biologically based	Trimagnesium dicitrate	600 mg oral daily dose	Migraine recurrence	Grade B	Small	Double thumbs up	No recommendation	—
Migraine headaches treatment	Biologically based	Magnesium sulfate	1-2 grams IV	Migraine symptom management	Grade C	Conflicting	Unclear	No recommendation	One trial reported symptom worsening
Migraine headaches prophylaxis practices	Biologically based	Co-enzyme Q10	100 mg three times daily	Migraine recurrence	Grade C	Large	Double thumbs up	No recommendation	One trial which reported NNT=3
Migraine headaches prophylaxis system	Whole medical	Acupuncture	Variable	Migraine recurrence	Grade A	Moderate	Single thumbs up	Strong recommendation	Identified as cost-effective treatment. 6-week acupuncture not inferior to 6-month prophylactic regimen.

Migraine headaches prophylaxis	Manipulative and body-based practices	Physical therapy, massage, chiropractic and spinal manipulation	Variable	Migraine recurrence	Grade C	Conflicting	Single thumbs up	No recommendation	Generally safe excluding precautions with cervical manipulation (See Muscular-Skeletal chapter).
Migraine headaches prophylaxis	Mind-body medicine and behavioral therapies	Biofeedback, cognitive behavioral therapy, stress management and relaxation training	Variable	Migraine recurrence	Grade B	Moderate	Double thumbs up	Strong in favor	—
Urinary tract infection	Biologically based practices	Cranberry, supplements and juice	400 mg bid (11% quinic acid) or 803 unsweetened juice tid	Fewer recurrent episodes, cost-effectiveness	Grade A	Large NNT=5	Double thumbs up	Strong in favor	Avoid juice cocktails that contain minimal quantity of fruit.

\* Small, moderate (OR>1.2-2) or large (OR>2)

†5 categories: Double thumbs up, single thumb up, no recommendation, single thumb down, double thumb down

‡5 categories: Strong (in favor), weak (in favor), no recommendation, weak (against), strong (against)

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\* The complete reference list is to be found on the book's Web site.

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