Nutritional Supplements: Too Much of a Good Thing

A look at ocular complications that can develop in patients who misuse nutritional supplements.

August L. Reader III, MD, FACS
San Francisco

THROUGHOUT THE CENTURIES, herbal and vitamin supplements have prevented, treated and cured various health problems and diseases. But mixing, matching and taking megadoses of natural remedies can harm ocular health.

In the following article, I'll discuss a number of nutritional supplements that studies have shown can cause serious–and sometimes irreversible –ocular complications in patients who abuse them.

Licorice

For more than 4,900 years, licorice (*Glycyrrhiza glabra*) has been commonly used in Chinese medicine as an anti-inflammatory for sore throat, abscesses and dermatitis. It's also been used in Europe for catarrh of upper respiratory infections and gastritis. But if you take more than 50 grams a day, licorice becomes toxic.

In a recent study, five patients who consumed 0.5 to 2 pounds of licorice daily developed transient monocular or binocular vision loss with scintillating scotomata, headaches and/or hypertension.[1] Symptoms resolved with cessation of licorice ingestion.

Yohimbe

The African herb yohimbe (*Pausinystilia yohimbe*) is a selective alpha-2 antagonist that has been shown to combat male impotence. It increases genital blood flow, raises genitalia nerve impulses and cord reflexes.

Unfortunately, megadoses of this herb can cause severe ocular complications and other serious health problems. A recent poster presentation reported that a 51-year-old man developed bilateral vision loss with disc edema after using yohimbe for impotence for three weeks.[2] His visual evoked potentials were markedly delayed, and his MRI showed bilateral optic nerve enlargement. Symptoms, however, resolved once he stopped taking the herb, although his VEPs remained abnormal.

Ginkgo

Ginkgo (*Ginkgo biloba)* extract is a powerful antioxidant for the retina and brain. Studies have reported that it increases retinal and brain circulation up to 30 percent. But when it's combined with aspirin in certain instances, ocular complications can arise. A 1997 study reported an incident of hyphema in a 71-year-old man who was taking ginkgo and aspirin.[3] The hyphema resolved once the man stopped taking the herb. The problem is that ginkgo extract inhibits platelet-activating factor; aspirin inhibits platelet adhesion factor. So you get a synergistic effect that can increase bleeding.

Some laboratory studies have shown that ginkgo protects nerve cells during periods of ischemia and stimulates nerve regeneration. The herb is the most recommended drug in Europe, where it requires a prescription. It's covered by insurance in Germany. It's also used to treat dementia, vascular hearing loss in the elderly, intermittent claudication and erectile dysfunction secondary to atherosclerosis.

Patients taking Coumadin, warfarin or heparin should not take ginkgo because of a high risk of bleeding diathesis.

Chamomile

Consumed as a tea to promote relaxation, chamomile (*Matricaria recutita*) has been used for 2,000 years to soothe stomach problems, protect against ulcers and ease muscle spasms. But it can cause severe allergic conjunctivitis along with an allergy attack in hyperallergenic patients with a history of hay fever.[4] People allergic to ragweed, daisies and chrysanthemums may also develop an allergic reaction to chamomile.

Cayenne

Cayenne (*Capsicum frutescens*) contains antioxidant vitamins A and C along with the alkaloid capsaicin. It's commonly known as a stimulant and irritant that, when rubbed onto the skin, increases blood circulation and causes a warm, burning sensation. It's used in over-the-counter skin-cream preparations to relieve arthritis pain. It's also used in several herbal eye preparations for blepharitis and conjunctivitis. Yet, because it's an irritant, it can severely worsen the symptoms of conjunctival irritation. There have been several cases reported of corneal ulcerations when used in high concentrations. The herbal preparation can literally eat a hole in the cornea, starting an ulcer.

Euphorbia

Called *E. kansui* (*gan sui*) in Chinese medicine, euphorbia is a purgative that contains carcinogens and irritants. A recent article reported that a patient accidentally rubbed his eye after pruning euphorbia leaves and developed a severe case of keratitis that required steroid drops for several weeks to resolve symptoms.[5] No reports indicate a link between keratitis and internal intake of euphorbia. But external use isn't recommended.

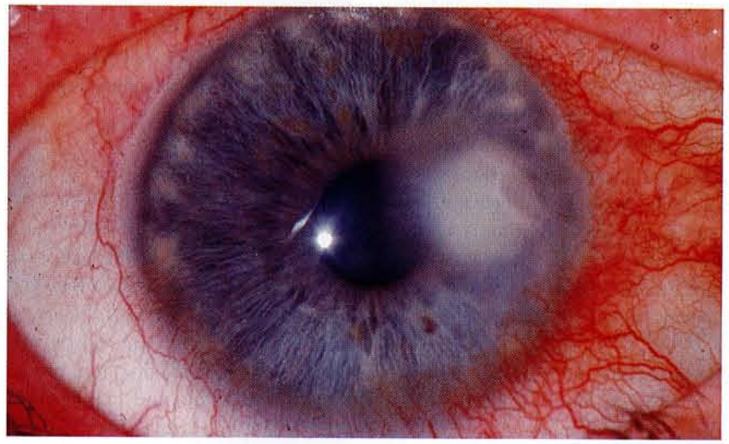
Citral

Citral is the main, volatile ingredient in the herb lemon balm (*Melissa officinalis*) and in may chang (*Litsea cubeba*). Used externally in Chinese medicine, citral is contraindicated in patients with glaucoma. Studies of monkeys have shown that taking low doses of 2 to 5 mcg raises intraocular pressure. Whether or not citral has any effect in humans is theoretical.

Herbs that could potentially precipitate angle-closure glaucoma include scopolia root (*Scopolia carniolica*) and tansy flower (*Chrysanthemi vulgaris*), because they can cause mild-to-moderate pupil dilation. The Chinese herb ma huang (*Ephedra sinensis*) is another one, though it was recently banned by the U.S. Food and Drug Administration. Until a year ago, however, ephedra was commonly used in herbal ecstasy and dietary products.

Male Fern

Male fern (*Filicis maris*) is used in Europe for the treatment of tapeworm, but it's not approved for use here in the United States. It's extremely poisonous when taken orally. Cases of optic neuritis and blindness have been reported in Europe from taking this herb. Common side effects include headaches, tremor, nausea and vomiting, convulsions, cardiac and respiratory failure and death.



Herbal eye preparations containing the herb cayenne (*Capsicum frutescens*) can cause corneal ulcers such as this when used in high concentrations.

Carrot-family Herbs

No studies have been conducted to determine a link between excessive carrot intake and cataract, but it's possible that if you eat too much of this vegetable you can develop them. Carrots contain furocoumarins, types of psoralens that change into a toxic agent when exposed to ultraviolet light. Since UV light is cataractogenic, there is theoretical concern that these sensitizers may increase the risk for cataract development.

Chinese herbs in the carrot family such as angelica root (*Angelica archangelica/atropurpurea*), dong quai root (*Angelica sinensis, A. acutiloba*) and du huo root (*Angelica pubescens*) are found in many postmenopausal symptom-relief formulas. Other carrot-family herbs include celery seed, cumin fruit, dill, fennel, parsley leaves and parsnip root, khella fruit, lomatium root, lovage root, masterwort and Queen Ann's lace.

Phototoxic herbs outside the carrot family that are associated with cataractogenesis include St. John's Wort (*Hypericum perforatum*), an antidepressant; haronga bark and leaf (*Harunganae madagascariensis*), bitter orange peel (Aurantii pericarpium) and bishop's weed fruit (*Ammeos visnagae*), herbs for heart problems; bergamot peel (*Citrus bergamia*), an infection-fighter; lemon peel (*Citrus limonum*), used for swollen lymph glands, and yarrow plant (*Achillea millefolium*), an herb that soothes menstrual cramps, controls heavy menstrual bleeding, cools menopausal hot flashes and helps heal wounds.

According to a Poison Control Centers Study of dietary supplements from California, a prostate-cancer patient de-

veloped an atypical brown cataract within three months of consuming a concoction of barberry, chrysanthemum, gentian, grape skin, celery seed, corn silk, cucumber powder, watermelon powder, pumpkin seed and many other herbs.

Beta Carotene

Megadoses of beta carotene can cause hypercarotenemia, a condition characterized by peripheral pigmented corneal rings or a yellowish-orange deposition at the peripheral cornea. In a recent study, three patients who ingested 9 to 54 mg of beta carotene a day, equivalent to 15,000 to 90,000 IUs, developed parafoveal crystals in the macula.[6] One patient, in particular, had some pigmentation on the anterior lens capsule. The palms of the patients' hands were orange-yellow. No one should take more than 15,000 IUs of beta carotene a day. In fact, 10,000 IUs is probably enough.

Canthaxanthine

Canthaxanthine is a tanning agent that you can either rub onto your skin or take orally. Excessive amounts can cause what's called canthaxanthine retinopathy, characterized by crystalline deposits in the retina and visual-acuity loss.[7] It's commonly found in salmon, used to deepen the pink color of the meat, as well as in other cold-water fish. So if you eat too much farm-raised fish, canthaxanthine toxicity can develop. The poultry industry adds canthaxanthine to eggs to deepen the yellow pigment of the yolks. The recommended daily intake is .003 mg/kg. Some farm-raised salmon have as much as 25 mg/kg; some eggs contain 8 mg/kg. Ingesting more than 80 mg/kg is toxic.

Selenium

Selenium is a mineral that has antioxidant properties. It's an essential cofactor for glutathione peroxidase, which

Chamomile (*Matricaria recutita*) can cause severe allergic conjunctivitis in hyperallergenic patients.

is one of the major enzyme systems responsible for detoxifying environmental toxins. The optimal dose for selenium is 200 to 400 mcg per day. Megadoses of the mineral can wreak havoc on the eyes. When I was in the U.S. Navy, a medical corpsman recommended that a 20-year-old male suffering from psoriasis wash his whole body with Selsun Blue shampoo three times a day for three months. After three months, the young man's vision in both eyes was 20/200. He had very severe toxic optic neuropathy that never recovered. We figured out that his skin absorbed about 3 to 5 g of selenium per day by washing his body three times a day with the shampoo.

What Can Physicians Do?

Currently, many people consume excessive amounts of herbs, vitamins and other nutritional supplements and are not telling their doctors. As eye-care practitioners, we need to take detailed histories of our patients. Ask them specifically what herbs, vitamins and other nutrients they're taking. Document how much they're consuming and list the dosages.

If you suspect there's potential for systemic or ocular toxicities, counsel the patient, take him off the supplement or reduce the dosage. Then, contact his primary physician.

As ophthalmologists, we need to educate ourselves about the efficacy and safety of natural therapies and the complications that can result. More and more patients are using them all of the time. And over the next several years, we will see more toxicities pop up as people continue to use nutritional supplements. So be on the lookout for new complications that haven't been documented. We never know what's going to happen with herbs and vitamins. New syndromes may evolve over the next few years as more people use these products.

To learn more about herbal medicines, you can purchase the *German Commission E Monograph*, a comprehensive reference book that lists 175 approved herbs for the treatment of various diseases. It describes preparations, dosing, indications, side effects, drug interactions, and lists unapproved herbs and their interactions. It's published by the American Herbal Council, Austin, Texas. RO

Dr. Reader is a neuro-ophthalmologist who utilizes alternative therapies to promote ocular health at Pacific Eye Associates in San Francisco. Contact him at (415) 923-3007.

1. Dobbins KRB, Saul RF. Transient visual loss after licorice ingestion. J Neuro-Ophthal 2000;20:38-41.
2. Weinstock RJ, Selhorst JB. Toxic optic neuropathy secondary to yohimbine use. Poster presentation, NANOS, 2000.
3. Rosenblatt M, Mindel J. Spontaneous hyphema associated with ingestion of Ginkgo biloba extract. (letter). N Engl J Med 1997;336:1108.
4. Subiza J, Subiza JL, Alonso M, et al. Allergic conjunctivitis to chamomile tea. Ann Allergy 1990;65:127-132.
5. Eke T, Al-Husainy S, Raynor MK. The Spectrum of ocular inflammation caused by euphorbia plant sap. Arch Ophthalmol 2000;118:1:13-16.
6. Rahmani B, Jampol LM, Feder RS. Clinicopathologic reports, case reports, and small case series: peripheral pigmented corneal ring: a new finding in hypercarotenemia. Arch Ophthalmol 2003;121:3:403-407.
7. Espaillat A, Aiello LP, Arrigg P, et al. Canthaxanthine retinopathy. Arch Ophth 1999;117:412-413.