

Continuing Education for Pharmacists



Thomas A. Gossel, R.Ph., Ph.D.
Professor Emeritus
Ohio Northern University
Ada, Ohio

Gossel



J. Richard Wuest, R.Ph., PharmD
Professor Emeritus
University of Cincinnati
Cincinnati, Ohio

Wuest

Natural Products:

Ginkgo, Ginseng, Glucosamine

Goal. The goals of this lesson are to present information on the claims, mechanisms of action, typical dosages used and other items of interest on natural products and nutraceuticals alphabetically from ginkgo to glucosamine, and to provide background information for assisting others on their proper selection and use.

Objectives. At the conclusion of this lesson, successful participants should be able to:

1. exhibit knowledge of the claims, mechanisms of action, and typical dosages for natural products and nutraceuticals presented;
2. select from a list, the synonyms for these products; and
3. demonstrate an understanding of information that can be used when discussing these products with consumers.

This lesson is part of a series that presents an overview of the common uses, proposed mechanisms of action, typical dosage regimens and other information of interest on natural products and nutraceuticals.

Since natural products are somewhat controversial, the authors

restate that the information presented is neither a promotion of nor a condemnation against their use. It is merely an overview of what has been reported in both the public and scientific literature, and certainly not an in-depth treatise. Additional sources (websites) of information on natural products are provided in Table 1. Some of these websites require subscription.

GINKGO

Ginkgo (*Ginkgo biloba*), also known as adiantifolia, baiguo, fossil tree, ginkgo folium, Japanese silver apricot, kew tree, maidenhair tree, and yinhsing, is reported to be the oldest living tree species on the planet. Fossils have been found that are more than 200 million years old. Individual trees may live as long as 1000 years. Their leaf system is unique among all other trees. The stem branches out like a fan reaching the entire edge of each leaf. All other species have an artery-like configuration in which the stem extends through the middle of the leaf and branches out into smaller and smaller channels throughout the leaf. The ginkgo leaf appears to be the most successful version of the

evolution of the separate pine needles of conifers to the broad leaves of most trees seen today.

The ginkgo is also unique in that it survived the last ice age in China, where it was cultivated as a sacred tree. Preparations made from its leaves have been used for medicinal purposes since the beginning of recorded Chinese history. However, ginkgo did not become a popular natural product in the Western World until the 1960s.

Ginkgo is used for Alzheimer's dementia, vascular and mixed dementias; cerebral vascular insufficiency conditions including memory loss, dizziness, vertigo, headache, difficulty concentrating, mood disturbances, tinnitus and hearing disorders; ischemic stroke and intermittent claudication; cognitive problems related to depression and Lyme disease; angina pectoris; and diabetic retinopathy. It is also used for attention-deficit/hyperactivity disorder, premenstrual syndrome, sexual dysfunction, arteriosclerosis, hypercholesterolemia, heart disease, thrombosis, allergies, asthma and bronchitis.

Ginkgo, one of the most prescribed agents in Europe, is

approved by the German Commission E (a European agency that oversees the promotion and use of natural products) for symptomatic relief of organic brain dysfunction; intermittent claudication; and vertigo and tinnitus of vascular origin.

As with most natural products, there is a lack of clinical proof of therapeutic benefits for ginkgo sufficient to gain FDA approval of its effectiveness. The following represents a review of those conditions for which there are citations in the literature, reporting some evidence that ginkgo may possibly be effective.

Age-related Memory Impairment. There are reports that ginkgo leaf extract improves cognitive function in some elderly people with mild to moderate, age-related memory impairment, especially short-term visual memory, and possibly speed of cognitive processing. However, taking ginkgo does not seem to improve memory in persons over the age of 60 with normal mental function.

Cognitive Function. Taking ginkgo leaf extract reportedly improves some measurements of cognitive function in healthy young to middle-aged individuals. It might modestly improve memory and speed of cognitive processing, including increasing speed of performance on factors used to assess increased attentiveness in individuals with no complaints of memory impairment.

Dementias. Several studies have reported that taking ginkgo leaf extract seems to moderately improve symptoms of Alzheimer's dementia, and vascular and mixed dementias. Studies lasting from three months to a year have shown that ginkgo improves some measurements of cognitive function and social behavior in individuals with multiple types of dementia. The majority of studies found in researching this topic report that ginkgo leaf extract can be modestly helpful in delaying the disease from worsening, but there is a lack of evidence that verifies ginkgo has an effect on the disease's progression.

Other Conditions. There is some evidence that ginkgo leaf extract can improve measurements of color vision in patients with early diabetic retinopathy; improve preexisting damage to the visual field in patients with normal tension glaucoma; increase pain-free walking distance in patients with intermittent claudication; relieve breast tenderness and psychological symptoms in women with premenstrual syndrome (PMS); decrease painful attacks in patients with Raynaud's syndrome; and alleviate symptoms of vertigo.

Ginkgo leaf contains several constituents that are claimed to have pharmacologic activity. These include flavonoids, terpenoids and organic acids, which are thought to protect tissues in the body from oxidative damage, due to antioxidant and free-radical scavenger properties.

Claims are made that these flavonoids protect neurons and retinal tissue from oxidative stress and injury following ischemic episodes (temporary inadequate blood flow). This might prevent progression of tissue degeneration in patients with dementia and other conditions. Patients with certain central nervous system disorders such as dementia and peripheral arterial disease, and allergies, asthma and bronchitis might benefit from the anti-inflammatory effects of the extracts from *ginkgo biloba*.

Ginkgo leaf constituents seem to improve blood flow to capillaries throughout the body, especially to the brain, eyes and extremities, both by decreasing blood viscosity and relaxing the vascular smooth muscle. This might benefit central nervous system and vascular disorders by improving circulation.

Another proposed, but unproven, activity of ginkgo leaf extract that might be helpful for patients with Alzheimer's dementia is the ability to inhibit toxicity and cell death induced by beta-amyloid peptides. It is a build-up of these peptides that is linked with destruction of cholinergic

neurons in the brain that can lead to Alzheimer's dementia.

Ginkgo leaf extract is well tolerated in typical doses, but there are reports that, rarely, it causes mild gastrointestinal upset, headache, dizziness, irregular heart beat, constipation and allergic skin reactions. Large doses can cause nausea, vomiting and diarrhea, restlessness, weakness and lack of muscle tone. There have been reports of spontaneous bleeding, including intracerebral and ocular bleeding.

The typical dose of ginkgo leaf extract for dementias is 120 to 240mg daily, divided into two or three doses. The same or higher doses are used to relieve walking pain in patients with intermittent claudication. For cognitive function improvement in healthy, young to middle-aged persons, doses of 120 to 160mg daily have been used.

Ginkgo leaf extract, in a dose of 80mg twice daily beginning on the sixteenth day of the menstrual cycle until the fifth day of the next cycle, is recommended for PMS symptoms. For vertigo or tinnitus, dosages of 120 to 160mg daily, divided into two or three doses, have been used. For the treatment of Raynaud's syndrome, 120mg three times a day is the typical dose. These doses are often started at lower amounts and increased to the recommended doses to avoid adverse gastrointestinal effects.

GINSENG

Ginseng (*Panax ginseng*), also known as Asian ginseng, Chinese ginseng, ginseng radix alba, jenshen, jinsao, Korean ginseng, Korean panax ginseng, oriental ginseng, radix rubra, red ginseng, renshen, renxian, shen-seng, sheng shai shen, and white ginseng, is possibly the most widely recognized plant used in folk medicine. It plays a major role in the herbal healthcare marketplace.

Various forms of ginseng have been used for more than 2000 years. The name *Panax* is derived from the Greek word *all healing*. The

medicinal part of the plant is its whole root, which is considered to be shaped like a man. Its oriental name is shen-seng, which means *man-root*. Because of its shape, the root was thought to have properties that could strengthen any part of the body.

There are several other members of the same plant family as *Panax ginseng*. These include *Panax japonicus* (Japanese ginseng), *Panax notoginseng* (Western five-finger ginseng), *Panax pseudoginseng* (Himalayan ginseng or zhuzishen), *Panax quinquefolius* (American or Canadian ginseng), and *Panax vietnamensis* (Vietnamese ginseng).

The major components of the various types of ginseng are saponins (ginsenosides), steroid-like compounds linked to glycosides. Over 20 ginsenosides have been identified to date, and each variety of ginseng contains similar but different combinations. Only two of these components are common to American, Chinese, Japanese and Korean ginsengs. Major variants in saponin content for any of these forms are the age of the root, where it was grown, in what season it was harvested, and what processing method was used in its preparation.

Since saponins are difficult to isolate and purify on a large scale, the whole root is generally used in herbal preparations. Other minor compounds that have been isolated from ginseng root include biotin, caffeine, choline, flavonoids, peptides, polysaccharides, starch, steroids, theophylline, and volatile oils, as well as a number of enzymes, minerals and several B vitamins.

Today, *Panax ginseng* is used for its "adaptogenic" effects. This term refers to products that are believed to provide strengthening effects to the body for increasing resistance to environmental stress, and as a tonic for improving well-being. Ginseng is also used to stimulate immune function; improve physical stamina, cognitive function, concentration, memory and efficiency at work; to treat anxiety, chronic fatigue syndrome, and depression; and for

American Botanical Council	www.herbalgram.org
Facts and Comparisons	www.factsandcomparisons.com
Food and Drug Administration	www.fda.gov (click on Food)
National Center for Complementary and Alternative Medicine of the National Institutes of Health	www.nccam.nih.gov
PDR for Herbal Remedies	
PDR for Nutritional Supplements	www.pdr.net
Pharmacist's Letter	www.naturaldatabase.com

various cancers, including breast, liver, lung, ovarian and skin.

Additionally, ginseng is used for anemia, asthma, chronic bronchitis, convulsions, cystic fibrosis, diabetes, dizziness, dysentery, erectile dysfunction and impotence, gastritis, headache, insomnia, loss of appetite, menopausal symptoms, and to slow the aging process.

Among the claims made for the benefits of ginseng, because one of its components has demonstrated a stimulation activity on nicotine receptors in the CNS, the herb is alleged to be beneficial for neuroprotection against age-associated cognitive disorders.

Ginseng reportedly exerts antineoplastic effects by inhibiting proliferation of adenocarcinoma cells resistant to cisplatin, inducing apoptotic cell death (the normal, programmed phagocytic destruction) of malignant tumor cells. Conversely, it also exerts antioxidant effects that are claimed to protect normal cells against oxidative DNA and protein damage caused by free radicals.

The herb is reported to decrease intravascular blood clot formation by inhibiting aggregation and thromboxane activity of platelets. It is said to induce production of interferon, enhance natural killer cell and antibody-dependent cytotoxic activities, and stimulate cell-mediated immunity.

Components of ginseng reportedly activate lipoprotein lipase, an enzyme that reduces

chylomicrons and very low-density lipoproteins (VLDL), thus decreasing serum triglyceride and cholesterol levels; stimulate insulin release and increase the production of insulin receptors to exert a hypoglycemic effect; and enhance penile erectile capacity mediated by endothelium-derived relaxing factor.

There is evidence that ginseng may improve abstract thinking, mental arithmetic skills and reaction time in otherwise healthy persons; decrease fasting blood sugar and hemoglobin A1c in some people with type 2 diabetes; and improve sexual function in some men with erectile dysfunction. However, there is a lack of strong confirmation supporting the effectiveness of ginseng for these conditions. Nonetheless, ginseng is approved by the German Commission E for use in persons with a lack of stamina.

Ginseng is usually well tolerated. One reference estimates that more than six million people ingest ginseng regularly in the United States with few reports of severe reactions. The adverse effects noted most often are nervousness, excitation and insomnia. Lesser reported adverse effects are amenorrhea and vaginal bleeding, decreased appetite, diarrhea, edema, euphoria, fever, headache, hypertension, hypotension, irregular heart beats, itching, mania and vertigo.

Typical doses of ginseng include: for cognitive dysfunction, 400mg daily; for treating type 2 diabetes, 200mg

daily; for erectile dysfunction, 600 to 900mg three times a day; and for lack of stamina, 100mg twice a day.

GLUCOSAMINE

Glucosamine (2-amino-2-deoxyglucose), also known as chitosamine, glucosamine hydrochloride, glucosamine sulfate, glucose-6-phosphate, and *N-acetyl glucosamine*, is an amino-sugar that is naturally produced in humans. It is a building block in the synthesis of glycosaminoglycans, hyaluronic acid and proteoglycans.

These substances are the foundation of many of the body's tissues, including tendons, ligaments, cartilage, collagen, basement membranes (membranes separating various cavities and spaces throughout the body), mucous membranes of the digestive system, membranes in the respiratory tract and synovial fluid in joints. Proteoglycans are proteins that make up the connective tissue of cartilage, which gives joints their elasticity, strength, and resilience.

Tissues in the joints become damaged when the lubricating synovial fluids in the joint spaces lose their viscosity. The amount of glucosamine synthesized by an individual may not be in sufficient quantity to allow for repair. The resulting loss of cushioning for the long bones connected in the joint may allow degeneration of the bones and cartilage to begin, along with reduced flexibility of the joint. Advocates of the use of glucosamine state that supplementation helps make the synovial fluid thick and elastic.

Glucosamine is not found in food to an appreciable extent, with the exception of its commercial source, chitin. Chitin is the processed exoskeleton of shellfish, such as shrimp, crabs and lobsters. Commercial glucosamine is also manufactured synthetically.

Glucosamine is used orally to treat osteoarthritis, alone and with chondroitin and/or magnesium salts. Claims are made that glucosamine

significantly improves symptoms of pain and functionality in patients with osteoarthritis, especially in their knees. Some evidence suggests that it is comparable with and even better than NSAIDs or placebo. Glucosamine may have disease-modifying activity and may slow joint degeneration in patients with osteoarthritis. It has been reported that patients taking glucosamine for up to three years seem to have significantly less knee joint degeneration, less joint space narrowing and symptom improvement when compared with placebo.

A single report suggests that although glucosamine may decrease pain and improve joint functionality, it might not prevent disease flare-ups and patients are likely to need a rapid-acting analgesic for these flare-ups. While most studies have evaluated glucosamine for the treatment of osteoarthritis of the knee, there are reports that it might also help in patients with osteoarthritis of the hip and lumbar spine.

Opponents of the claims made for the use of glucosamine argue that there are deficiencies in studies reporting beneficial effects. These include their short duration (sometimes only one to two months); the exclusion of obese patients and those with severe forms of osteoarthritis; the use of different, and sometimes unstandardized, formulations of glucosamine as well as different dosages; study sponsorship by manufacturers of glucosamine products; concurrent use of analgesics in some trials; and the use of different outcome measurements of arthritis pain relief and patient mobility.

Currently, there is lack of evidence that combining glucosamine with chondroitin is any more effective than using the individual ingredients alone. Also, while claims are made that the sulfate salt of glucosamine is more effective than the hydrochloride form, there is lack of proof that this is true. Opponents

point out that since glucosamine is cleaved from both its sulfate salt and hydrochloride moiety in the stomach, neither form can be any more or less effective than the other.

Glucosamine is well tolerated by most persons, with the most often reported problem being difficulty in swallowing the large tablet. The majority of adverse effects reported have been mild and include gastric discomfort, heartburn, diarrhea, constipation, nausea, vomiting and itching.

The typical dose of glucosamine for osteoarthritis is 1500mg once daily, although 500mg three times a day has also been used.

The content of this lesson was developed by the Ohio Pharmacists Foundation, UPN: 129-000-08-006-H01-P. Participants should not seek credit for duplicate

Natural Products:

Ginkgo, Ginseng, Glucosamine

1. All of the following statements about ginkgo are true EXCEPT:

- a. it is reported to be the oldest living tree species on the planet.
- b. its leaf system is unique among all other trees.
- c. its leaf is an artery-like configuration extending through the middle of the leaf.
- d. its leaf appears to be the most successful version of the evolution from pine needles to broad leaves.

2. The German Commission E approves the use of ginkgo for all of the following EXCEPT:

- a. Alzheimer's dementia.
- b. intermittent claudication.
- c. organic brain dysfunction.
- d. tinnitus of vascular origin.

3. Which of the following statements about ginkgo leaf extract is FALSE?

- a. There is some evidence it can improve measurements of color vision in patients with early diabetic retinopathy.
- b. It seems to moderately improve symptoms of Alzheimer's, vascular and mixed dementias.
- c. It might modestly improve memory and speed of cognitive processing in individuals with no complaints of memory impairment.
- d. It seems to improve memory in persons over the age of 60 with normal mental function.

4. The components of ginkgo that are claimed to protect neurons and retinal tissue from oxidative stress and injury following ischemic episodes are:

- a. alkaloids.
- b. flavonoids.
- c. organic acids.
- d. terpenoids.

5. Ginkgo leaf constituents seem to improve blood flow to capillaries throughout the body by:

- a. increasing cardiac output.
- b. stimulating alpha-adrenergic receptors.
- c. inhibiting platelet aggregation.
- d. relaxing vascular smooth muscle.

6. All of the following statements about ginseng are true EXCEPT:

- a. various forms of ginseng have reportedly been used for more than 2000 years.
- b. the medicinal part of ginseng is its whole root.
- c. the name Panax is derived from the Greek word all natural.
- d. the oriental name of ginseng is shen-seng which means man-root.

7. The major components of ginseng are:

- a. saponins.
- b. polysaccharides.
- c. flavonoids.
- d. alkaloids.

8. The typical dose of ginseng for lack of stamina is:

- a. 50mg once a day.
- b. 1 00mg twice a day.
- c. 250mg 3 times a day.
- d. 500mg 4 times a day.

9. Glucosamine is a building block in the synthesis of all the following EXCEPT:

- a. chondroitin.
- b. glycosaminoglycans.
- c. hyaluronic acid.
- d. proteoglycans.

10. Chitin, the commercial source of glucosamine, is the processed:

- a. bones of slaughtered animals.
- b. exoskeleton of shellfish.
- c. by-products from the dairy industry.
- d. residue of mining dolomite.



The Georgia Pharmacy Association is accredited by the Accreditation Council for

Pharmacy Education as a provider of continuing pharmacy education.

Natural Products: Ginkgo, Ginseng, Glucosamine

Volume XXVI, No. 6

GPhA Code J08-10

Program Number: 142-999-08-006-H01-P

CE Hours: 1.5 (0.15 CEUs)

Release Date: 10/5/2008

Expiration: 06/15/2011

1. Select one correct answer per question and circle the appropriate letter below using blue or black ink (no red ink or pencil).
2. Members submit \$4, Non-members must include \$10 to cover the cost of grading and issuing statements of credit. Please send check or money order only. Note: GPhA Members will receive priority in processing CE. Statements of credit for GPhA members will be mailed within four weeks of receipt of the course quiz.

- | | |
|------------|-------------|
| 1. A B C D | 6. A B C D |
| 2. A B C D | 7. A B C D |
| 3. A B C D | 8. A B C D |
| 4. A B C D | 9. A B C D |
| 5. A B C D | 10. A B C D |

Mail completed quiz to: GPhA, 50 Lenox Pointe NE, Atlanta, GA 30324

A passing grade of 70% is required for each examination. A person who fails the exam may resubmit the quiz only once at no additional charge.

Please check here if you are indicating a change of address _____ Phone # _____

Name _____ License Number(s) and State(s) _____

Address _____

City _____ State _____ Zip _____

How long did this program take to complete? _____