

Ginkgo (*Ginkgo biloba* L.)

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While some complementary and alternative techniques have been studied scientifically, high-quality data regarding safety, effectiveness, and mechanism of action are limited or controversial for most therapies. Whenever possible, it is recommended that practitioners be licensed by a recognized professional organization that adheres to clearly published standards. In addition, before starting a new technique or engaging a practitioner, it is recommended that patients speak with their primary healthcare provider(s). Potential benefits, risks (including financial costs), and alternatives should be carefully considered. The below monograph is designed to provide historical background and an overview of clinically-oriented research, and neither advocates for or against the use of a particular therapy.

Related Terms:

- Arbre aux quarante écus, adiantifolia, baiguo, bai guo ye, BN-52063, duck foot tree, EGb, EGb 761, Elefantenoehr, Eun-haeng, facherblattbaum, Fossil tree, GBE, GBE 24, GBX, ginan, gin-nan, Ginkgoaceae (family), ginkgo balm, ginkgoblätter, *Ginkgo biloba* blätter, Ginkgo folium, ginkgogink, ginkgold, ginkgopower, ginkyo, icho, ityo, Japanbaum, Japanese silver apricot, kew tree, kung sun shu, LI 1370, maidenhair tree, noyer du Japon, oriental plum tree, pei kuo, pei-wen, Pterophyllus, *Pterophyllus salisburiensis*, Rokan, salisburia, *Salisburia adiantifolia*, *Salisburia macrophylla*, silver apricot, sophium, tanakan, tanakene, tebofortan, tebonin, tempeltrae, temple balm, tramisal, valverde, vasan, vital, ya chio, yin-guo, yin-hsing.

BACKGROUND

- *Ginkgo biloba* has been used medicinally for thousands of years. Today, it is one of the top selling herbs in the United States.
- Ginkgo is used for the treatment of numerous conditions, many which are under scientific investigation. Available evidence demonstrates ginkgo's efficacy in the management of intermittent claudication, Alzheimer's/multi-infarct dementia, and "cerebral insufficiency" (a syndrome thought to be secondary to atherosclerotic disease, characterized by impaired concentration, confusion, decreased physical performance, fatigue, headache, dizziness, depression, and anxiety).
- Although not definitive, there is promising early evidence favoring use of ginkgo for memory enhancement in healthy subjects, altitude (mountain) sickness, symptoms of premenstrual syndrome (PMS), and reduction of chemotherapy-induced end-organ vascular damage.
- Although still controversial, a recent large trial has shifted the evidence against the use of ginkgo for tinnitus.
- The herb is generally well tolerated, but due to multiple case reports of bleeding, should be used cautiously in patients on anti-coagulant therapy, with known coagulopathy, or prior to some surgical or dental procedures.

SCIENTIFIC EVIDENCE

<p>Uses <i>These uses have been tested in humans or animals. Safety and effectiveness have not always been proven. Some of these conditions are potentially serious, and should be evaluated by a qualified healthcare provider.</i></p>	<p><u>Grade</u> *</p>
<p><u>Claudication (painful legs from clogged arteries)</u></p> <p>Numerous studies suggest that <i>Ginkgo biloba</i> taken by mouth causes small improvements in claudication symptoms (leg pain with exercise or at rest due to clogged arteries). However, ginkgo may not be as helpful for this condition as exercise therapy or prescription drugs. Additional evidence is needed.</p>	<p>A</p>
<p><u>Dementia (multi-infarct and Alzheimer's type)</u></p> <p>The scientific literature overall does suggest that ginkgo benefits people with early stage Alzheimer's disease and multi-infarct dementia, and may be as helpful as acetylcholinesterase inhibitor drugs such as donepezil (Aricept®). Well-designed research comparing ginkgo to prescription drug therapies is needed.</p>	<p>A</p>
<p><u>Cerebral insufficiency</u></p> <p>Multiple clinical trials have evaluated ginkgo for a syndrome called "cerebral insufficiency." This condition, more commonly diagnosed in Europe than the United States, may include poor concentration, confusion, absent-mindedness, decreased physical performance, fatigue, headache, dizziness, depression, and anxiety. It is believed that cerebral insufficiency is caused by decreased blood flow to the brain due to clogged blood vessels. Some research reports benefits of ginkgo in patients with these symptoms, but most have been poorly designed without reliable results. Better studies are needed before a strong recommendation can be made.</p>	<p>B</p>
<p><u>Acute hemorrhoidal attacks</u></p> <p>In early study ginkgo was shown to be effective in the treatment of patients with acute hemorrhoidal attacks. Further research is needed to confirm these results.</p>	<p>C</p>
<p><u>Age-associated memory impairment (AAMI)</u></p> <p>Age-associated memory impairment (AAMI) is a non-specific syndrome, which may be caused by early Alzheimer's disease or multi-infarct dementia (conditions for which ginkgo has been shown to have benefit). There is preliminary research showing small improvements in memory and other brain functions in patients with AAMI, although some studies disagree. Overall, there is currently not enough clear evidence to recommend for or against ginkgo for this condition.</p>	<p>C</p>
<p><u>Altitude (mountain) sickness</u></p>	

<p>A small amount of poorly designed research reports benefits of ginkgo for the treatment of altitude (mountain) sickness. Additional study is needed before a recommendation can be made.</p>	<p><u>C</u></p>
<p><u>Chemotherapy side effects reduction</u></p> <p>In limited human study, ginkgo has been examined in addition to 5-fluorouracil (5-FU) in the treatment of pancreatic and colorectal cancer, to measure possible benefits on side effects. At this time, there is not conclusive evidence in this area.</p>	<p><u>C</u></p>
<p><u>Deafness (cochlear)</u></p> <p>Preliminary clinical study has been conducted on the effect of ginkgo in chronic cochleovestibular disorders. Further research is needed before a recommendation can be made.</p>	<p><u>C</u></p>
<p><u>Depression and seasonal affective disorder (SAD)</u></p> <p>Preliminary study of seasonal affective disorder (SAD) suggests that ginkgo is not effective in preventing the development of winter depression. Other research in elderly patients with depression shows possible minor benefits. Overall, there is not enough evidence to form a clear conclusion.</p>	<p><u>C</u></p>
<p><u>Gastric cancer</u></p> <p><i>Ginkgo biloba</i> exocarp polysaccharides (GBEP) capsule preparation has been studied for upper digestive tract malignant tumors of middle and late stage with positive results. However, further research is needed before a recommendation can be made.</p>	<p><u>C</u></p>
<p><u>Glaucoma</u></p> <p>Several small human studies report ginkgo may be associated with mild increases in blood flow to the eyes, vision and intraocular pressure. Well-designed research is needed before a recommendation can be made.</p>	<p><u>C</u></p>
<p><u>Macular degeneration</u></p> <p>Preliminary research suggests that ginkgo may improve eye blood flow, although it remains unclear if macular degeneration is significantly affected by ginkgo. More research is needed in this area before a conclusion can be drawn.</p>	<p><u>C</u></p>
<p><u>Memory enhancement (in healthy people)</u></p> <p>It remains unclear if ginkgo is effective. Further well-designed research is needed</p>	<p><u>C</u></p>

<p>as existing study results conflict.</p>	<p><u>C</u></p>
<p><u>Multiple sclerosis</u></p> <p>Based on laboratory study, it has been suggested that ginkgo may provide benefit in multiple sclerosis (MS). Human research is limited to several small studies, which have not found consistent benefit. Additional research is needed before a recommendation can be made.</p>	<p><u>C</u></p>
<p><u>Premenstrual syndrome (PMS)</u></p> <p>Initial study in women with premenstrual syndrome or breast discomfort suggests that ginkgo may relieve symptoms including emotional upset. Further well-designed research is needed before a recommendation can be made.</p>	<p><u>C</u></p>
<p><u>Pulmonary interstitial fibrosis</u></p> <p>Based on early study, ginkgo may be effective in treating pulmonary interstitial fibrosis. Further research is needed to confirm these results.</p>	<p><u>C</u></p>
<p><u>Quality of life</u></p> <p>Early studies suggest that ginkgo may aid in quality of life. More randomized controlled trials are needed before a conclusion can be made.</p>	<p><u>C</u></p>
<p><u>Raynaud's disease</u></p> <p>Results from one clinical trial suggest that <i>Ginkgo biloba</i> may be effective in reducing the number of Raynaud's attacks in patients suffering from Raynaud's disease. In order to confirm these results, further clinical trials are required.</p>	<p><u>C</u></p>
<p><u>Retinopathy (diabetes mellitus type II)</u></p> <p>Early study suggests <i>Ginkgo biloba</i> extract may offer benefit to individuals with retinopathy. Further clinical trials are required to determine efficacy.</p>	<p><u>C</u></p>
<p><u> ringing in the ears (tinnitus)</u></p> <p>There is conflicting research regarding the use of ginkgo for tinnitus. Additional well-designed research is needed in order to resolve this controversy.</p>	<p><u>C</u></p>
<p><u>Sexual dysfunction</u></p> <p>Ginkgo has been used and studied for the treatment of sexual dysfunction in men</p>	

<p>and women. In general, studies are small and not well designed. Additional research is needed before a recommendation can be made.</p>	<p><u>C</u></p>
<p><u>Stroke</u></p> <p>Laboratory studies suggest that ginkgo may be helpful immediately following strokes because of possible antioxidant or blood vessel effects. However, initial study of ginkgo in people having strokes found no benefits. Further research is needed in this area.</p>	<p><u>C</u></p>
<p><u>Vertigo</u></p> <p>A small amount of poorly designed research reports benefits of ginkgo for the treatment of vertigo. Additional study is needed before a recommendation can be made.</p>	<p><u>C</u></p>
<p><u>Vitiligo</u></p> <p>Early study using oral <i>Ginkgo biloba</i> extract reports that ginkgo appears to arrest the progression of this disease. Better-designed studies are needed to confirm these results.</p>	<p><u>C</u></p>
<p><u>Cocaine dependence</u></p> <p>One small study reports no benefit of ginkgo for cocaine independence.</p>	<p><u>D</u></p>
<p><u>Mental performance (after eating)</u></p> <p>The results of one study investigating the effect of <i>Ginkgo biloba</i> on post-prandial mental alertness are unclear. Ginkgo may benefit some but not all endpoints. Further clinical trials are required before recommendations can be made.</p>	<p><u>D</u></p>
<p><u>Mood and cognition in post-menopausal women</u></p> <p>Based on early study of chronic administration, Gincosan appears to have no beneficial effects on mood, anxiety, or sleepiness in post-menopausal women.</p>	<p><u>D</u></p>
<p><i>*Key to grades: A: Strong scientific evidence for this use; B: Good scientific evidence for this use; C: Unclear scientific evidence for this use; D: Fair scientific evidence against this use (it may not work); F: Strong scientific evidence against this use (it likely does not work).</i></p>	

TRADITION/THEORY

The below uses are based on tradition, scientific theories, or limited research. They often have not been thoroughly tested in humans, and safety and effectiveness have not always been proven. Some of these conditions are

potentially serious, and should be evaluated by a qualified healthcare provider. There may be other proposed uses that are not listed below.

- Acidosis, acute cerebral infarction, aging, alcoholism, allergies, angina, anti-bacterial, anti-fungal, antioxidant, anti-parasitic, anti-rheumatic, anti-tumor, anxiety, asthma, atherosclerosis (clogged arteries), attention deficit hyperactivity disorder, autoimmune disorders, blood vessel disorders, blood clots, breast disease, breast tenderness, bronchial asthma, bronchitis, cancer, cardiac rhythm abnormalities, cataracts, chilblains (inflammation of toes, fingers, ears, or face with exposure to cold), chronic rhinitis, congestive heart failure, coronary heart disease, cough, dermatitis, diabetes, diabetic nerve damage (neuropathy), diabetic eye disease, diabetic peripheral neuropathy, digestion, dysentery (bloody diarrhea), eczema, enhancing learning, enhancing memory, enhancement of female sexual function, fatigue, filariasis, freckle-removing, genitourinary disorders, heart disease, heart attack, headache, hepatitis B, high cholesterol, high blood pressure, hypoxia (lack of oxygen), immunomodulator, insomnia, labor induction, menstrual pain, migraine, mood disturbances, oral cavity cancer, respiratory tract illnesses, scabies (ginkgo cream), schizophrenia, seizures, sepsis, skin sores (ginkgo cream), swelling, traumatic brain injury, ulcerative colitis, varicose veins.

DOSING

The below doses are based on scientific research, publications, traditional use, or expert opinion. Many herbs and supplements have not been thoroughly tested, and safety and effectiveness may not be proven. Brands may be made differently, with variable ingredients, even within the same brand. The below doses may not apply to all products. You should read product labels, and discuss doses with a qualified healthcare provider before starting therapy.

Adults (18 years and older)

- 80-240 milligrams of a 50:1 standardized leaf extract taken daily by mouth in two to three divided doses has been used and studied (standardized to 24% to 25% ginkgo flavone glycosides and 6% terpine lactones). Other forms used include tea (bags usually contain 30 milligrams of extract), 3 to 6 milliliters of 40 milligrams per milliliter extract daily in three divided doses, and "fortified" foods. Ginkgo seeds are potentially toxic and should be avoided. The German ginkgo product Tebonin®, given through veins (IV), was removed from the German market due to significant side effects.

Children (younger than 18 years)

- There is not enough scientific evidence to recommend use of ginkgo in children.

SAFETY

The U.S. Food and Drug Administration does not strictly regulate herbs and supplements. There is no guarantee of strength, purity or safety of products, and effects may vary. You should always read product labels. If you have a medical condition, or are taking other drugs, herbs, or supplements, you should speak with a qualified healthcare provider before starting a new therapy. Consult a healthcare provider immediately if you experience side effects.

Allergies

- Allergy/hypersensitivity to *Ginkgo biloba* or members of the Ginkgoaceae family may occur. A severe reaction called Stevens-Johnson syndrome, which includes skin blistering and sloughing-off, has been reported with use of a combination product. There may be

cross-sensitivity to ginkgo in people allergic to urushiols (mango rind, sumac, poison ivy, poison oak, cashews), and an allergic cross-reaction has been reported in a person allergic to poison ivy.

- If administered into a vein (IV), ginkgo may cause a skin allergy, blood vessel irritation and damage. Ginkgo fruit or pulp has caused strong allergic reactions after skin contact, and severe skin reactions and intestinal spasms have occurred after direct contact with fleshy fruit pulp.

Side Effects and Warnings

- Overall, ginkgo leaf extract (used in most commercial products) appears to be well tolerated in most healthy adults at recommended doses for up to six months. Minor symptoms including headache, nausea, and intestinal complaints have been reported.
- Bleeding has been associated with the use of ginkgo taken by mouth, and caution is advised in patients with bleeding disorders or taking drugs/herbs/supplements that may increase the risk of bleeding. Dosing adjustments may be necessary. Ginkgo should be stopped prior to some surgical or dental procedures. Reports of bleeding range from nose bleeds to life-threatening bleeding in several case reports. In some of these reports, ginkgo has been used with other agents that may also cause bleeding.
- Eating the seeds is potentially deadly, due to risk of tonic-clonic seizures and loss of consciousness.
- Based on human study, ginkgo may theoretically affect insulin and blood sugar levels. Caution is advised in patients with diabetes or hypoglycemia, and in those taking drugs, herbs, or supplements that affect blood sugar. Serum glucose levels may need to be monitored by a healthcare professional, and medication adjustments may be necessary.
- There have been uncommon reports of headache, dizziness, stomach upset, nausea, diarrhea, vomiting, muscle weakness, loss of muscle tone, restlessness, heart racing, rash, and irritation around the mouth with the use of ginkgo. There is a case report of "coma" in an elderly Alzheimer's patient taking trazodone and ginkgo, although it is not clear that ginkgo was the cause. Based on laboratory and human research, ginkgo may decrease blood pressure, although there is one report of ginkgo possibly raising blood pressure in a person taking a thiazide diuretic ("water pill"). Based on theory, high concentrations of ginkgo may reduce male and female fertility. Contamination with the drug colchicine has been found in commercial preparations of *Ginkgo biloba*.
- Ginkgo may affect the outcome of electroconvulsive therapy (ECT). Adverse effects on the eyes have also been reported.
- Another study reported vomiting and convulsions from large quantities of MPN (4-O-methylpyridoxine), which is contained in *Ginkgo biloba* seeds.

Pregnancy and Breastfeeding

- Use of ginkgo is not recommended during pregnancy and breastfeeding due to lack of reliable scientific study in this area. The risk of bleeding associated with ginkgo may be dangerous during pregnancy.

INTERACTIONS

Most herbs and supplements have not been thoroughly tested for interactions with other herbs, supplements, drugs, or foods. The interactions listed below are based on reports in scientific publications, laboratory experiments, or traditional use. You should always read product labels. If you have a medical condition, or are taking other drugs,

herbs, or supplements, you should speak with a qualified healthcare provider before starting a new therapy.

Interactions with Drugs

- Overall, controlled trials of ginkgo report few adverse effects and good tolerance, with rates of complications similar to placebo. However, use of ginkgo with drugs that may cause bleeding may further increase the risk of bleeding, based on multiple case reports of spontaneous bleeding in patients using ginkgo alone, with warfarin (Coumadin®), or with aspirin. One case report documents a possible increase in bleeding risk with ticlodipine (Ticlid®) and ginkgo. Examples of drugs that may increase the risk of bleeding include aspirin, anticoagulants ("blood thinners") such as warfarin (Coumadin®) or heparin, anti-platelet drugs such as clopidogrel (Plavix®), and non-steroidal anti-inflammatory drugs such as ibuprofen (Motrin®, Advil®) or naproxen (Naprosyn®, Aleve®). However, not all studies agree with the existence of this risk, and it is not clear if particular types of patients may be at greater risk.
- Based on preliminary research, ginkgo may affect insulin and blood sugar levels. Caution is advised when using medications that may also lower blood sugar. Patients taking drugs for diabetes by mouth or insulin should be monitored closely by a qualified healthcare professional. Medication adjustments may be necessary.
- Ginkgo has been found to decrease blood pressure in healthy volunteers, although some studies disagree. Theoretically, ginkgo may add to the effects of medications that also lower blood pressure, although raised blood pressure has been reported in a patient taking a thiazide diuretic ("water pill") with ginkgo. It has been suggested that *Ginkgo biloba* leaf extract (GBE) and nifedipine should not be ingested at the same time.
- Monoamine oxidase (MAO) inhibition by ginkgo was reported in one animal study, but has not been confirmed in humans. In theory, if taken with MAOI drugs, such as isocarboxazid (Marplan®), phenelzine (Nardil®), or tranylcypromine (Parnate®), additive effects and side effects may occur. Based on laboratory research, ginkgo may also add to the effects of SSRI antidepressants such as sertraline (Zoloft®), with an increased risk of causing serotonin syndrome, a condition characterized by stiff muscles, fast heart rate, hyperthermia, restlessness, and sweating.
- Based on human use, ginkgo may decrease side effects of antipsychotic drugs, although scientific information in this area is limited. There is a case report of "coma" in an elderly Alzheimer's patient taking trazodone and ginkgo, although it is not clear that this reaction was due to ginkgo. In theory, ginkgo may increase the actions of drugs used for erectile dysfunction such as sildenafil (Viagra®).
- There may be a risk of seizure when taking ginkgo, particularly in people with a history of seizure disorder. Although most reports of seizures have been due to eating ginkgo seeds (not leaf extract which is found in most products), an animal study found that the anti-seizure properties of sodium valproate or carbamazepine were reduced by giving ginkgo. In theory, drugs such as donepezil (Aricept®) and tacrine (Cognex®) may have an additive effect when used at the same time as ginkgo, potentially increasing cholinergic effects (such as salivation and urination).
- 5-fluorouracil induced side effects and cyclosporine kidney toxicity may in theory be improved by ginkgo, although evidence is not conclusive in these areas. Colchicine has been found in commercial preparations of ginkgo, and may increase blood concentrations in patients using colchicine.
- Ginkgo may alter the way the liver breaks down certain drugs.

Interactions with Herbs and Dietary Supplements

- Use of ginkgo with herbs or supplements that may cause bleeding may increase the risk of bleeding, although some studies disagree. Several cases of bleeding have been reported with the use of garlic, and two cases with saw palmetto. Numerous other agents may theoretically increase the risk of bleeding, although this has not been proven in most cases.
- Ginkgo has been found to decrease blood pressure in healthy volunteers, although some studies disagree. Theoretically, ginkgo may have additive effects when used with herbs or supplements that also decrease blood pressure. However, high blood pressure was reported in a patient taking a thiazide diuretic ("water pill") plus ginkgo. Although it remains unclear if ginkgo has clinically significant effects on blood pressure, caution may be warranted when ginkgo is used with other agents that affect blood pressure.
- Based on human study, ginkgo may theoretically affect insulin and lower blood sugar levels. Caution is advised when using herbs or supplements that may also affect blood sugar. Blood glucose levels may require monitoring, and doses may need adjustment.
- Effects on monoamine oxidase (inhibition) by ginkgo are reported in animals but not confirmed in humans. In theory, ginkgo may add to the side effects of herbs or supplements that also inhibit monoamine oxidase, such as 5-HTP (5-Hydroxytryptophan).
- Based on laboratory research, ginkgo may add to the effects of herbs or supplements that affect levels of serotonin in the blood or brain, and could increase the risk of serotonin syndrome (a condition characterized by muscle stiffness, increased heart rate, hyperthermia, restlessness, and sweating).
- Ginkgo may alter the way the liver breaks down herbs and supplements.

AUTHOR INFORMATION

- This information is based on a systematic review of scientific literature edited and peer-reviewed by contributors to the Natural Standard Research Collaboration (www.naturalstandard.com).

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Natural Standard developed the above evidence-based information based on a thorough systematic review of the available scientific articles. For comprehensive information about alternative and complementary therapies on the professional level, go to www.naturalstandard.com. Selected references are listed below.

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