



Review on Immunomodulatory Activity of the Plant *Ginkgo biloba*

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ABSTRACT

Ginkgo biloba is a member of the single-order Ginkgoales, family Ginkgoaceae, and the single extant genus Ginkgo. The tree is deciduous, reddish-colored, and can reach a height of four meters. Female trees are low and spreading, while male specimens have an uneven and upright shape. Fan-shaped, glossy green leaves with unevenly spaced upper margins, akin to those of the Adiantum or maidenhair fern. It has many veins and a split in the middle, giving the appearance of having two lobes. Before they fall, the leaves turn a golden yellow color.

The flowers grow on short spurs and are not very noticeable. After, 20 to 35 years, trees begin to flower, with the females showing an abundance of ovules in pairs on stalks that each contain an egg cell. Very green at first, but subsequently becoming greenish-yellow, orange, and brown. A single, nude ovule develops into a drupe-like seed with a thin, smooth, horny inner layer and an unpleasant, fleshy, acrid outer layer. Oftentimes, the fleshy, coated seeds are mistakenly classified as either nuts or fruits. The word ginkgo, which means "silver apricot" in Chinese and later Japanese, is the source of the generic name Ginkgo.

Keywords: *Ginkgo biloba*, Ginkgoales, Ginkgo, Apricot, Adiantum

Introduction

Traditional Chinese medicine has been using the fruits and seeds of the *Ginkgo biloba* tree for over 5,000 years to treat a variety of ailments, including cough and asthma.

The use of *G. biloba* leaves internally for medicinal purposes was first documented in a publication in 1505 A.D. The standardized *G. biloba* leaf extract, or EGb761, has grown to be one of the most well-liked memory-enhancing supplements in the United States since the early 1990s. One of the most popular herbs in the United States, *g. biloba* is typically taken as tablets, capsules, or teas. The quantity of each component in *G. biloba* can vary greatly depending on the country of origin, harvesting period, and other variables. Therefore, for the purposes of drug regulation, clinical trials, human consumption, and reproducibility, it is crucial to have a standardized preparation with known composition. French and German companies have approved a standardized form of *G. biloba* leaf extract (EGb 761) that has less than 5 ppm of ginkgolic acid (a component that may cause allergies), 6% terpene lactones, and 24% flavonoid glycosides. Based on available data, *G. biloba* may be beneficial in the following conditions: Cardiovascular disease is a condition affecting the heart and blood vessels that may include hypertension. It is characterized by high blood lipid levels, artery hardening, and plaque development. Unstable A stroke is a condition where a blood clot blocks a blood vessel supplying the brain, injuring a portion of the brain. The damage may be minor or major. Dementia is a disorder that causes changes in behavior and memory, making it difficult for a person to cope and socialize. Claudication is a circulatory condition that typically results from peripheral artery disease and hurts the lower legs during exercise.

Extract from *ginkgo biloba* has been used extensively to treat acute ischemic stroke. According to a survey on common treatments used in China, 75% of physicians thought that Chinese herbal products were a good way to treat acute stroke, and 66% of physicians regularly used them for the majority of their patients. Herbs are frequently used in Chinese medicine, but it's still unclear how beneficial they are as medicines. Growing data points to *G. biloba* extract's (GBE) possible use in treating and postponing the onset of chronic illnesses like cardiovascular disease (CVD). It's unclear exactly how the action works at its foundation. Studies on patients with peripheral vascular diseases, particularly intermittent claudication—pain in the legs brought on by peripheral artery disease (PAD)—have shown some of the therapeutic benefits of GBE.



Figure 1: *Ginkgo biloba* branch picture

Morphological Character

The Ginkgo's fan-shaped leaves have uneven notches and are flat. The name *Ginkgo biloba* (two lobes) comes from the fact that they frequently have a deep groove in the center of the leaf, resulting in two separate lobes. As you can see below, there is variation in the leaves' degree of division between the two lobes. The veins in leaves have an open dichotomous venation pattern, meaning they split in pairs at the base of the leaf rather than connecting crosswise. The cuticle is hypostomatic, or has recessed pores; the abaxial side of the cuticle has many more stomatal complexes than the adaxial side, where only a small number of these stomata are found. Water loss from evaporation is decreased by the pores' retraction and restricted quantity on the leaf's upper surface. The leaf's petiole is relatively flexible and thin. The plant is known as the "maidenhair tree" because of its clustered leaves that grow on short shoots that can reach a length of 3 inches. The leaves have a shape similar to a maidenhair fern's leaflets. Longer horizontal or drooping branchlets give rise to the shoots. Older trees' trunks produce leafy branches above and peg-like structures that grow into the ground to form roots. The yellow wood within the trunk of the tree contrasts with the grey, deeply furrowed bark of older trees. Before they fall off the tree in the fall, the leaves turn a stunning gold.



Figure 2: Picture of *Ginkgo biloba* Plant

Distribution

One of the earliest trees to arrive in Europe in 1730 is the *G. biloba* tree that is still alive in the Utrecht botanical garden. On the western summit of Tianmu Mountain in Zhejiang province, China, there is rumored to be one of the last wild specimens of *G. biloba*. Around 1730, ginkgo was brought to

Europe and is now commonly grown as an ornamental tree in parks and streets. It was discovered that there are fourteen *G. biloba* plants growing throughout India, the majority of which are found in hilly regions spanning the country's northwest and northeast.

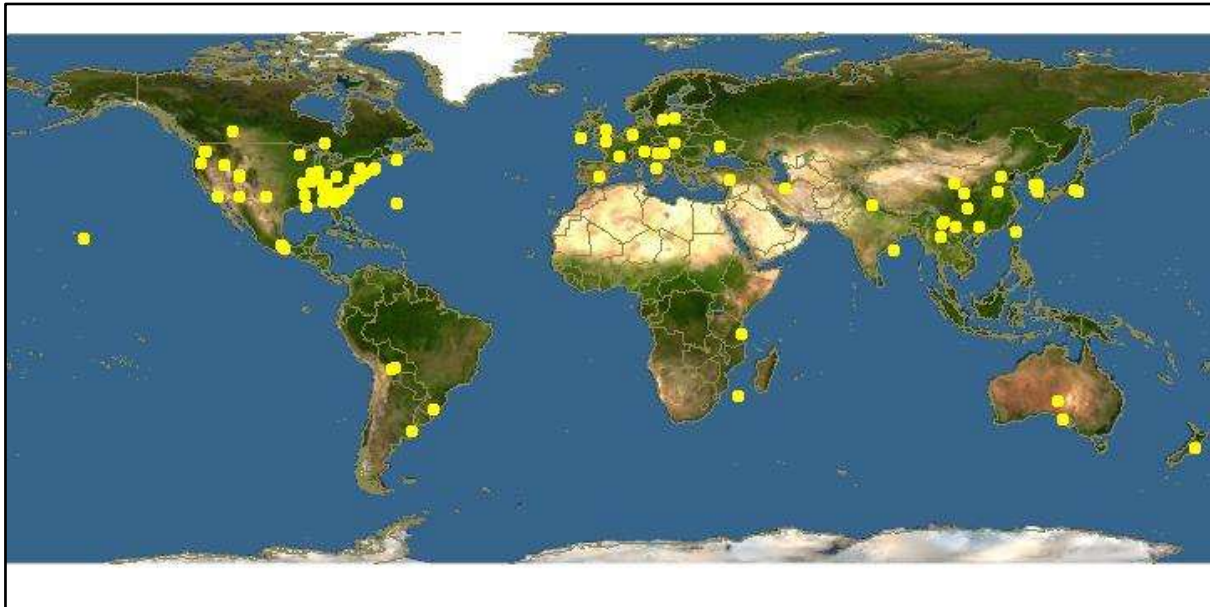


Figure 3: Geographical distribution of the plant Ginkgo

Soil

G. biloba typically grows with a pH value ranging from 5.11 to 8.05, and it prefers clayey loam soil that is rich in organic matter. Soil should have an electrical conductivity of 0.07M mhos/cm to 1.965M mhos/cm. The range of the organic matter content should be 0.974 to 15.02%. Available potassium, phosphorus, and nitrogen in the soil must range from 45.89 to 456.10 ppm, 12.30 to 846.89 ppm, and 191.29 to 686.78 kg/ha, respectively.

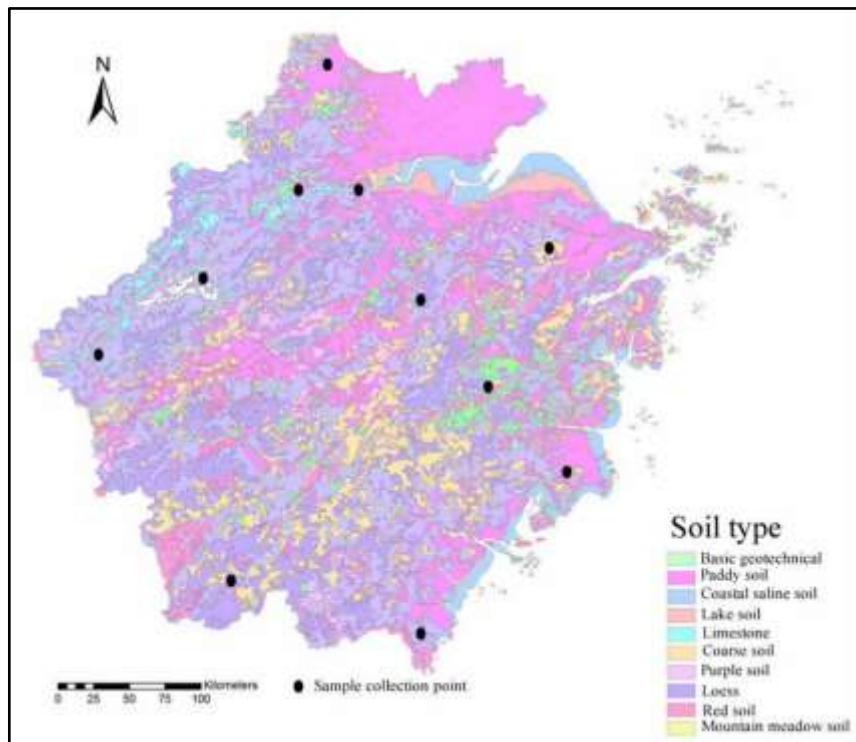


Figure 4: Soil where Ginkgo can be grown

Climate

G. biloba prefer temperature ranging from 10°C to a maximum of 25°C, relative humidity 60-85%, rainfall 1800-3200 mm and it likes bright sunshine. It is observed to grow well at the altitude of 500-3600 m. During the growing season drought, hail storms, excessive rainfall, etc., affect the quality of the leaves.

Cultivation

Plants of *G. biloba* are perennials and should be spaced 3 to 6 meters apart from one another. Its ideal soil temperature ranges from 15 to 27°C, with full sunlight and well-drained soil being preferred. It has been established through research on how physical treatment affects *G. biloba* seed germination that the viability of the seeds diminishes over time.



Figure 5: Seeds of the plant *G. biloba*

Medicinal Uses

One of the earliest known medicinal plants, the ginkgo tree has been of use to humans for over 2,000 years. According to "Pen Ts'ao Kang MLL," *G. biloba* seeds have therapeutic benefits. It is used to treat a variety of conditions, including multiple sclerosis, allergies, headaches, asthma, tinnitus, impotence, circulatory disorders, eye disorders, diabetes, and brain trauma. The cardioprotective mechanism, myocardial ischemia and reperfusion injury, and environmental pollution tolerance to SO₂ and sulfur accumulation have all been addressed by *G. biloba* leaf extract. The ginkgo tree is a very beautiful tree that grows for a long time and is extremely resistant to insects, bacteria, viruses, and air pollution in China, Korea, France, Germany, and the United States. One of the top 10 commercial products in the world is *G. biloba* leaf extract. Its leaves have pharmacological qualities such as enhanced blood flow, anti-platelet activating factor activity, and radical scavenging. Additionally well-known for its anti-ischemic, antioxidant, and anticonvulsant qualities is ginkgo extract. Furthermore, a growing body of research indicates that the bioactive components of ginkgo extract have important therapeutic effects on cerebral vascular insufficiency, which includes Alzheimer's and cardiovascular disease, as well as age-related physical and mental decline.

Chemical Constituents

1. Bilobalide
2. Ginkgolide A
3. Ginkgolide B
4. Ginkgolide C
5. Ginkgolide J

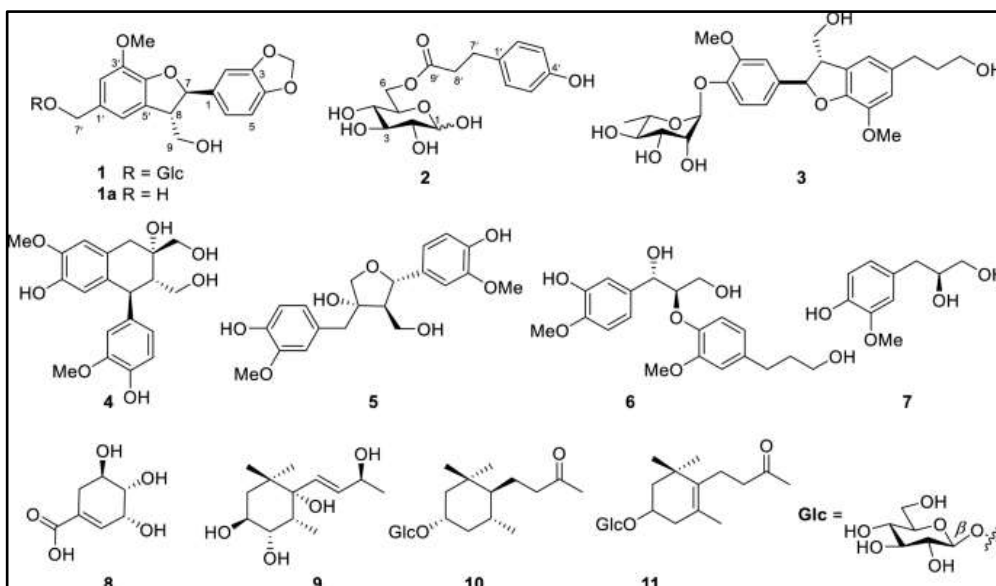


Figure 6: Chemical structure of Ginkgo plant chemical constituents

Clinical Use in Small Vessel Disease

Small vessel-related ischemic vasculopathy can impact several organs and systems. Clinical trials on patients with Raynaud's syndrome, retinopathy, and nephropathy related to different vascular beds' insufficiency have shown *G. biloba* to be clinically effective.

Clinical Use in Venous Insufficiency

It has also been noted that GBE helps patients who suffer from chronic venous insufficiency. *G. biloba* works by blocking the initial stage of the cascade that causes endothelium activation, which in turn causes vessel narrowing and epithelial growth.

Clinical Use in the Prevention of Thrombosis

The development of a clot or thrombus inside a blood vessel, known as thrombosis, impedes blood flow via the circulatory system. Increased platelet function is a known risk factor for thrombotic complications and cardiovascular disease, especially in response to collagen. According to studies, GBE can help avoid thrombosis by lowering blood viscosity and inhibiting platelet aggregation.

Alzheimer's Disease

GBE is approved for use in Europe to treat intermittent claudication, dementia, tinnitus, or ringing in the ears. The most common cause of dementia in the elderly is Alzheimer's disease (AD), which affects 4% of people over 65 and 20% of people over 80. Alzheimer's disease (AD) is a long-term, gradually worsening neurodegenerative illness that impairs cognitive function and memory. It has been demonstrated that a number of nutrients and substances can halt the advancement of AD-related cognitive decline. These include neurotrophic factors, cholinergic agents, anti-inflammatory medications, monoamine oxidase inhibitors (MAOIs), vitamin E, and antioxidants. These chemotherapy medications frequently have adverse effects, some of which are quite serious. Furthermore, none have proven to be completely successful in preventing.

Side Effects and Cautions

Ginkgo biloba side effects could include headaches, dizziness, allergic skin reactions, and gastrointestinal distress like nausea and diarrhea. *G. biloba* may make excessive bleeding more likely. This is especially crucial for people taking anticoagulants, those who have bleeding disorders, and those who are about to undergo surgery or dental work.

Dosage and Duration

Doses of dry extract as a dietary supplement range from 80 mg to 240 mg, split into two or three daily doses, with an average daily suggested dose of 120 mg. For cerebral insufficiency, the German Commission E suggests taking 120–240 mg of extract two or three times a day. Clinical trials have used ginkgo dosages as high as 720 mg/d to treat circulatory disorders, dementia, and memory problems. Doses of 120–300 mg/d for three to twelve weeks

are linked to significant improvements in one or more outcome measures. When ginkgo is taken for disorders of memory, mood, or physiologic function, 12 treatments lasting 4 to 6 weeks are usually required before positive effects can be expected.

Conclusion

It has been discovered that the standardized preparation of Ginkgo leaf extract has a variety of therapeutic benefits, including effects on cancer, cardiovascular disease, neurodegenerative diseases, tinnitus, geriatric complaints, and psychiatric disorders. The antioxidant qualities of the extract have been the primary underlying mechanism of action in each of these instances. Additional mechanisms of action encompass PAF antagonistic effect, peripheral benzodiazepine receptor modulation, and endothelium relaxing factor-mediated enhancement of blood circulation. Consequently, it has been demonstrated that ginkgo leaf extract is a promising herbal dietary supplement with established medical advantages. However, adequate attention must be given to its long-term safety.

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