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Review Article

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An Overview on The Phytochemical and Therapeutic Potential of *Ginkgo Biloba*

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Abstract

Background: Ginkgo biloba leaf extract (GBLE) contains flavone glycosides and terpenoids and is widely studied for its pharmacological potential. Key Pharmacological Effects: GBLE exhibits antioxidant activity by scavenging free radicals and reduces inflammation by suppressing reactive oxygen and nitrogen species. It improves vascular relaxation, blood flow, and microcirculation, antagonizes platelet-activating factor, and modulates neurotransmitter activity. GBLE protects mitochondria from oxidative damage, reduces neuronal cell death, and shows neuroprotective effects in experimental models. Clinical Relevance: In ischemia-reperfusion injury models, GBLE demonstrates cardioprotective and antioxidant effects in vivo. Clinical trials report beneficial outcomes in patients with memory disorders, arteriosclerosis, and dementia. Conclusion: GBLE's strong antioxidant and anti-inflammatory properties suggest its potential as a therapeutic agent for oxidative stress-related diseases, including ischemic heart disease, cerebral infarction, chronic inflammation, and aging.

Introduction

Ginkgo, also called the Maidenhair Tree, belongs to the Ginkgoaceae family. Its uses include the management of anxiety, dementia, Alzheimer's disease, tinnitus, glaucoma, premature aging syndrome, and hypertension. Ginkgo biloba is a highly versatile plant that thrives in diverse climatic conditions, including Mediterranean environments. It plays a unique role in both plant evolution and human culture. In Europe and the United States, it is one of the top-selling herbal supplements. Historically, ginkgo has been used to address blood irregularities and memory problems, and today its most well-known use is for preserving cognitive function.The order Ginkgoales (division Ginkgophyta) comprises around 15 genera that originated during the Permian Period. Fossilized leaves of extinct genera, such as *Ginkgoites* and *Baiera*, closely resemble those of living trees. Various components of the immune system participate in the inflammatory response to repair damaged tissues or combat foreign invaders. Chronic inflammation, even in the absence of illness or injury, can cause irreversible tissue and DNA damages. *Ginkgo* has been shown to reduce inflammation associated with several ailments, contributing to its wide range of health benefits. Previous studies have indicated that ginkgo supplementation can increase blood flow to multiple organs in patients with cardiovascular disease, partly due to a 12% increase in circulating nitric oxide, a vasodilator. Although the evidence is mixed, some studies suggest that ginkgo may enhance cognitive function in healthy individuals. In patients with post-stroke depression, supplementation with *Ginkgo biloba* extract alongside an antidepressant for eight weeks significantly reduced depressive symptoms compared to antidepressant treatment alone. Preliminary research also suggests that ginkgo may improve ocular blood flow, although its direct effects on vision remain unclear. Certain types of headaches may respond to ginkgo's anti-inflammatory and circulation-enhancing properties; however, caution is advised in specific populations, such as pregnant or nursing women, individuals with epilepsy, patients taking anticoagulants (such as aspirin), or those with diabetes, who should consult a physician before use. Ginkgo may increase the risk of serotonin syndrome when combined with SSRIs (e.g., sertraline and fluoxetine) and may interact with monoamine oxidase inhibitors (MAOIs). Additionally, long-chain alkylphenols in Ginkgo leaves can trigger allergic reactions, particularly in individuals sensitive to alkylphenol-containing plants, such as poison ivy. The seeds (nuts) have traditionally been used for cardiovascular health, skin infections, respiratory disorders (including asthma and cough), bladder irritation, and alcohol abuse management. [1, 2]

History

In the late 1600s, Engelbert Kaempfer became the first European to describe *Ginkgo*. The tree was eventually named *Ginkgo biloba* by Linnaeus in 1771, which means "silver plume with two lobes." The most widely used phytomedicine derived from this species is *Ginkgo biloba* leaf extract, which is used to treat vascular dementia, peripheral claudication, early stage Alzheimer's disease, and vascularly induced tinnitus. EGb 761 is a standard preparation of *Ginkgo biloba* extract. In the United States, Ginkgo is classified as a dietary supplement. Brands such as Ginkoba, Ginkgold, and Ginkai have completed clinical testing and are comparable to EGb 761. Standardized formulations typically contain a maximum of 5 parts per million (ppm) ginkgolic acids, 24% ginkgo flavonoid glycosides, and 6% terpene lactones. [1,2]

The recently discovered *Ginkgo yimaensis* differs from *Ginkgo biloba* in having more widely divided leaves and significantly smaller ovules grouped together on branching peduncles. Due to the similarities in ovule structure and leaf morphology, many experts consider *Ginkgo adiantoides* to be the ancestor of *Ginkgo biloba*. A decline in diversity and geographical distribution was observed in the fossil record of Ginkgo between 98 and 65 million years ago during the Upper Cretaceous period. This decline is likely associated with a decrease in temperature. By the end of the Miocene, this genus had disappeared from the polar regions.

Extract of Ginkgo Biloba Leaves

The chemical composition of *Ginkgo biloba* leaves varies depending on the species, geographical origin, and harvest season. As with many other plants, the standardization of *Ginkgo* leaf extract is essential to ensure consistent and reproducible bioactivity. Based on the recognized active components of the leaves, the cultivation, harvesting, and extraction processes are strictly standardized and regulated. Leaves are harvested while they are still green, typically during summer and fall (July to September). After harvesting, the dried leaves were examined for contaminants and hazardous materials, including heavy metals and aflatoxins. The coarse dried leaves are then extracted using an acetone:water mixture (35:1 to 67:1) ratio. Recent advancements have introduced an innovative method for tracking various *preparations of Ginkgo* leaf extracts. High-performance liquid chromatography (HPLC) fingerprinting has been proposed as a reliable technique to evaluate the quality and consistency of *Ginkgo* leaf extracts.[3]

Active Ingredients of Ginkgo biloba Leaves

The pharmacologically active substances in *Ginkgo biloba* leaf extract are primarily flavonoids and terpenoids. Flavonoids, also known as phenylchromones or phenylbenzopyrones, are a broad class of low-molecular-weight plant-derived compounds. Flavonoid glycosides, including kaempferol and quercetin linked to 3-rhamnosides, 3-rutinosides, and/or p-coumaric esters, are commonly present. Biflavones such as amentoflavone, isoginkgetin, bilobetin, 5-methoxybilobetin, ginkgetin, sciadopitysin, and related compounds are also found in the leaves. These compounds primarily function as cation chelators, enzyme inhibitors, and antioxidants or free radical scavengers. Flavonoids exhibit rapid elimination and limited absorption, resulting in relatively poor bioavailability. Unabsorbed flavonoids that reach the colon may be metabolized by bacterial enzymes prior to absorption. In the liver, flavonoids are converted into conjugated derivatives following ingestion. In some cases, the biological activities of flavonoid metabolites differ from those of their parent compounds. Terpenoids in *Ginkgo biloba* include ginkgolides and bilobalides, which are lactones and non-saponifiable lipids

in the form of cyclic esters. Five types of ginkgolides (A, B, C, J, and M) are known, with ginkgolides A, B, and C constituting approximately 3.1% of the leaf extract weight. Bilobalide, a sesquiterpene trilactone, accounts for approximately 2.9% of the standardized *Ginkgo biloba* leaf extract.

Chemical Constituents of Ginkgo biloba

Several chemical compounds with therapeutic properties have been identified in *Ginkgo biloba*, including newly discovered lignans and terpenoids.[6]

A. Flavonoids

Flavonoids from *Ginkgo biloba* can be classified into several categories:

- Flavonols and flavonol glycosides
- Flavones and flavone glycosides
- Flavanones and isoflavone glycosides
- Flavan-3-ols
- Biflavonoids
- Biginkgosides

Among these, flavonols—such as quercetin, kaempferol, isorhamnetin, syringetin, myricetin, and myricetin 3',4'-dimethyl ether—are the major constituents.

Ginkgo flavonoids exhibit a wide range of biological activities, including antioxidant, antibacterial, anticancer, anti-inflammatory, antiviral, and neuroprotective effects. For instance, research has shown that biginkgosides possess anti-neuroinflammatory and neuroprotective properties (insert reference). Additionally, *Ginkgo* bioflavonoids have demonstrated promising effects against metabolic, cardiovascular, and neurodegenerative disorders.

B. Terpenoids Terpenoids are plant secondary metabolites produced during secondary metabolic activities. They are often species-specific, stored in particular organs or tissues, and play crucial roles in signaling and stress tolerance in plants. In *Ginkgo biloba*, seeds contain ginkgolides and bilobalides, which are important for the prevention and management of cardiovascular and neurological disorders.[8]

C. Alkylphenolic Acids Alkylphenols in *Ginkgo biloba* are classified into five main groups:

- Alkyl phenolic acids
- Urushiols
- Isourushiols
- Cardols
- α-Hydroxycardanols

Although ginkgolic acids are known for their toxicity, they have been suggested to possess potential therapeutic benefits.[9]

D. Carboxylic Acids *Ginkgo biloba* contains a variety of carboxylic acids, including

- Ferulic acid
- p-Coumaric acid
- Protocatechuic acid
- Caffeic acid

These acids may form glycosidic or covalent linkages with other molecules, contributing to the plant's bioactivity.[6]

E. Lignans Lignans found in *Ginkgo biloba* roots and seeds exhibit significant antioxidant activity. The bioactivity of Ginkgo biloba extract (GBE) containing lignans has been studied; for instance, pinoresinol contains 1.05–1.87 mg/mL of total lignan glycosides. [6,10,11]

F. Proanthocyanidins Proanthocyanidins in *Ginkgo biloba* occur in a ratio of approximately 85:15 and comprise two main types: procyanidins and prodelphinidins. Epigallocatechin units polymerize to form prodelphinidins, while epicatechin units form procyanidins.[6]

G. Polyprenols Polyprenols, long-chain molecules composed of 14–24 isopentenyl units, are active constituents of *Ginkgo biloba*. They resemble S-polyterpene alcohols found in mammals, including humans.[12]

H. Polysaccharides Polysaccharides in *Ginkgo biloba* have been found to consist of mannose, glucose, galactose, arabinose, and rhamnose.[13]

Nutraceutical Value of Ginkgo biloba

Nutraceuticals are naturally occurring bioactive compounds that provide health benefits, including disease prevention and therapeutic effects. These compounds, sometimes referred to as phytochemicals or functional foods, are widely utilized by the pharmaceutical, food, and herbal/dietary supplement industries, as well as in emerging intersections of pharmaceutical and agricultural sectors.[14] Blumenthal (2000) reported that *Ginkgo biloba* products were among the most popular herbal supplements marketed in U.S. health-food stores. While *Ginkgo* nuts were first mentioned in herbal literature around 1350 AD, they have been used as both food and medicine long before the widespread use of *Ginkgo* leaves.[15] The seeds of *Ginkgo biloba* are rich in proteins, vitamin C, carbohydrates, riboflavin, and other essential nutrients. In traditional Chinese medicine, *Ginkgo biloba* seeds are used as dietary supplements to treat skin disorders, gonorrhea, toothaches, overactive bladder, fever, cough, and increased sputum production.

Despite their benefits, *Ginkgo biloba* seeds are not considered staple foods due to potential vitamin B6 deficiencies and adverse effects such as allergic reactions to ginkgolic acids.[16] Various processing methods have been explored to reduce the levels of harmful compounds in *Ginkgo biloba* seeds. For instance, ginkgolic acid can be effectively removed by incubating the seeds in three volumes (v/w) of a 5 g/L Na_2CO_3 solution at 15°C for three hours.[Conventional food preparation

techniques, including baking, boiling, and microwave cooking, may also help reduce seed toxicity [17].

Bioactive Ingredients in Ginkgo biloba

Ginkgo biloba leaves contain flavonoids and terpenoids, which are the primary active chemical constituents of G. biloba. Ginkgo extracts exhibit a wide range of pharmacological activities, including antioxidant, anti-inflammatory, antibacterial, cytotoxic, anticancer, and anti-allergic effects. [18,19]

In addition to flavonoids and terpenoids, several other bioactive compounds have been identified in *Ginkgo biloba*, including polyphenols, organic acids, and bioflavonoids. Terpenoids, such as ginkgolides and bilobalides, are also present and are associated with significant pharmacological effects. Glycoside derivatives of flavonoids, such as isorhamnetin, kaempferol, and quercetin, are key contributors to the therapeutic potential of *Ginkgo biloba*.

Table 1: Important bioactive ingredients of ginkgo biloba

S.No	Class	Plant Parts	Major chemical constituents	Bioactivity	References
1.	Polyphenols	Leaves	Di-trans-poly-cis-octadecaprenol	Anti-bactrial properties and safety against Aβ25-35 attack.	20
2.	Flavonoids	Leaves	Quercetin, Kaempferol, isohamnetin	Antioxidant, antibacterial, antiviral and anticancer	21
3.	Organic acids	Leaves	Benzoic acid derivatives [ginkgolic acid, N- containing acid]	Inhibitory effects of Xanthine oxidase [XOD] and its potential anti-tumor properties.	22
4.	Biflavanoids	Leaves	Sciadopitysin, ginkgetin, isogenkgetin, amentoflavone	Anti-adipogenesis, anti-obesity properties and significant inhibitory effects on thrombin activity	22
5.	Terpenoids	Roots	Teriterpines; sterols	Protective effectsto cerebral	23, 24

Pharmacology

Ginkgo biloba is believed to exert its effects primarily through the terpene ginkgolide B, which acts as a neuroprotective agent by inhibiting the platelet-activating factor, scavenging free radicals, providing antioxidant activity, and stabilizing cell membranes. [28–31]

Additional pharmacological effects of *Ginkgo biloba* include the following:

- Inhibition of 3',5'-cyclic GMP (guanosine monophosphate) phosphodiesterase. [32,33]
- Prevention of age-related loss of α-adrenoceptors.
- Modulation of muscarinic cholinergic receptors.
- Stimulation of choline uptake in the hippocampus.

Moreover, *Ginkgo biloba* extract prevents the accumulation of beta-amyloid, a hallmark of neurodegenerative disorders such as Alzheimer's disease. [34,35]

Effects of Ginkgo biloba on the Body

Ginkgo biloba leaf extract has demonstrated potential benefits in managing various health conditions, including age-related macular degeneration, vertigo, cancer, cardiovascular diseases, stress, memory loss, tinnitus, and neurodegenerative disorders such as Alzheimer's disease.

The diverse pharmacological effects of *Ginkgo biloba* leaf extract are mediated through multiple mechanisms.

- Reduction of beta-amyloid peptide (Aβ) accumulation, which may slow the progression of Alzheimer's disease, was also observed.
- Antioxidant activity protects cells from oxidative stress.
- Anti-platelet activating factor (Anti-PAF) activity is beneficial for cardiovascular and cerebrovascular health.
- Decreased expression of peripheral benzodiazepine receptors (PBR) contributes to stress relief.
- Stimulation of endothelium-derived relaxing factors, improving blood circulation.[36]

Therapeutic and Antioxidant Activities of Ginkgo biloba

Ginkgo biloba leaf extract exhibits therapeutic activity against chronic illnesses, including cancer, cardiovascular disease, and neurological disorders. Its mechanisms of action involve both direct scavenging of free radicals and indirect inhibition of free radical formation.

The extract can directly scavenge reactive oxygen species (ROS), including

- Hydrogen peroxide (H_2O_2)
- Hydroxyl radicals ($OH\cdot$)
- Peroxyl radicals ($ROO\cdot$)
- Superoxide anion radicals
- Ferrous ion species.[37]

Indirectly, *Ginkgo biloba* leaf extract can enhance the activity of several antioxidant enzymes, such as:

- Glutathione
- Peroxidase
- Catalase
- Superoxide dismutase (SOD)
- Heme-oxygenase-1

Additionally, *Ginkgo biloba* may improve the function of mitochondrial enzymes, such as NADH dehydrogenase, thereby regulating ROS production within the mitochondria. By preventing the uncoupling of oxidative phosphorylation, it helps maintain ATP levels, which are critical for energy metabolism.[38]

Prevention of Neurodegenerative Diseases Alzheimer's disease (AD), a common form of dementia, affects approximately 4% of individuals over 65 years of age and 50% of those over 80 years of age. The accumulation of amyloid beta peptide (Aβ) is closely associated with AD pathogenesis. *Ginkgo biloba* leaf extract has been shown to inhibit Aβ production, a critical step in disease progression, and compete with free cholesterol to reduce Aβ aggregation. Additionally, the extract regulates reactive oxygen species (ROS) accumulation and prevents neuronal apoptosis, both of which are key contributors to neurodegenerative disorders. [39,40]

Ischemia, or reduced blood flow, is a common underlying cause of cardiovascular and cerebrovascular disorders. During ischemic episodes, increased lipid peroxidation and free radical generation can damage tissues and contribute to the development of chronic diseases. *Ginkgo biloba* leaf extract exerts cardioprotective effects through mechanisms such as antioxidant activity, enhanced nitric oxide and prostaglandin production, and improved blood flow.

Studies have shown that administration of *Ginkgo* leaf extract before heart surgery reduces lipid peroxidation caused by reperfusion, prevents tissue necrosis and ascorbate depletion, and protects against heart failure. Ginkgolide B, a key terpene component, has been found to reduce post-ischemic ROS generation by 50–60%. Hearts reperfused and treated with terpene components alone demonstrated better functional recovery than those treated with EGb 761, suggesting that terpene components specifically decrease the heart's susceptibility to ischemia-reperfusion injury. [36,37]

Anticancer Effects Cancer arises from uncontrolled cell division and tissue invasion. *Ginkgo biloba* leaf extract exhibits chemopreventive, antioxidant, and anti-angiogenic properties. It enhances cellular resilience to oxidative stress and reduces angiogenesis, thereby potentially inhibiting tumor growth, and progression.[41]

Effects on Stress, Mood, and Memory The prevalence of anxiety disorders, stress, mood disturbances, and depression is increasing in modern society. Complementary and alternative medicines, including *Ginkgo biloba* leaf extract, are gaining attention for both preventive and therapeutic use in various diseases. Elevated glucocorticoid levels during stress can lead to memory impairment, anxiety, reduced immunity, gastrointestinal disturbances and cardiovascular events.

Ginkgo biloba leaf extract has calming and neuroprotective effects that may improve mood and exhibit antidepressant activity, as emotional regulation is closely linked to stress responses.[42] Ginkgolides A and B have been shown to reduce the ligand-binding ability, protein levels, and mRNA expression of peripheral benzodiazepine receptors (PBR), contributing to these neuropsychological effects.[36]

Effects on Tinnitus

Tinnitus, a common condition affecting approximately 10% of the population, has been investigated for its potential management using *Ginkgo biloba* leaf extract. Clinical trials have explored its effects not only on tinnitus but also on

senile macular degeneration, vertigo and schizophrenia. While studies support the potential of *Ginkgo biloba* extract in preventing vertigo and senile macular degeneration, its efficacy in alleviating tinnitus remains inconclusive.[43]

Anti-dementia Effects EGb 761, a standardized *Ginkgo biloba* extract, has been the focus of clinical trials targeting dementia, memory enhancement, and cognitive improvement. Its mechanisms include modulation of excitotoxic glutamatergic neurotransmission, free radical scavenging, and prevention of amyloid formation, making it potentially effective against various dementia etiologies.[44]

Antidiabetic effects *Ginkgo biloba* can counteract insulin resistance and hypoxia-induced inflammation in adipose tissue by reducing inflammatory adipokine production, increasing adiponectin secretion, and inhibiting insulin receptor substrate-1 signalling. Oral administration of ginkgolide B in male Sprague Dawley rats has been shown to promote cholinergic vasorelaxation and phenylephrine-induced vasoconstriction while enhancing endothelial nitric oxide synthase (eNOS) and superoxide dismutase (SOD) activities.[46]

Antiobesity Effects High-fat diets contribute to insulin resistance, weight gain, and metabolic disorders. Administration of *Ginkgo biloba* extract (GBE) has been reported to reduce body weight by lowering tumor necrosis factor-alpha (TNF-α) levels in retroperitoneal fat deposits. The bioactive components of GBE, including ginkgetin, isoginkgetin, bilobetin, and sciadopitysin, exhibit anti-obesity effects and potentially act as bioflavonoid-type pancreatic lipase inhibitors. [37,48–50]

Anti-Lipid Effects Dyslipidemia, characterized by elevated LDL-C, triglyceride (TG), and altered HDL-C levels, is closely associated with obesity and insulin resistance. Treatment with *Ginkgo biloba* has been shown to significantly reduce cholesterol and TG levels, increase HDL-C, and elevate glutathione (GSH) levels, thereby contributing to improved lipid profiles.[51]

Wound healing is a vital biological process for maintaining skin integrity and repairing damaged tissues. Cytokines contribute to this process by promoting basement membrane formation, preventing dehydration, and enhancing granulation tissue formation and inflammation. The antioxidant properties of *Ginkgo biloba* play a protective role; for example, in rats, *Ginkgo biloba* extract has been shown to prevent radiation-induced cataract development in lenses by increasing the activity of glutathione S-transferase (GST), glutathione reductase (GRD), non-protein sulfhydryl acids (NSSA), and total sulfhydryl acids (TSSA). [19,52]

Anti-Platelet Activity Platelet-activating factor (PAF), a phospholipid mediator, helps the immune system respond to infection, ischemia, and brain injury. It activates inflammatory proteins through the PAF receptor (PAFR) and is linked to the JAK/STAT signalling pathway. Treatment with ginkgolide B, a key terpene component of *Ginkgo biloba*, reduces CD40L production and modulates platelet activation, contributing to its antiplatelet effects. [19,53,54]

Anti-Inflammatory Effects Inflammation caused by mechanical, chemical, or physical factors disrupts tissue homeostasis through the release of mediators such as

- Histamine
- Prostaglandins
- Leukotrienes
- Bradykinin
- Platelet-activating factor (PAF)
- Interleukins (IL) from tissues and migrating cells

Flavonoids present in *Ginkgo biloba* possess significant anti-inflammatory properties, making them useful for treating respiratory and other inflammatory diseases. [55–57]

Hepatoprotective Effects *Ginkgo biloba* exhibits hepatoprotective activity by increasing glutathione levels, reducing lipid peroxidation, and restoring antioxidant enzyme activities, including superoxide dismutase (SOD), glutathione peroxidase (GPX), and catalase, as observed in rat models of obstructive jaundice.[58,59,81] Pretreatment with GBE reduces liver histological damage, modulates blood transaminase levels, decreases TNF-α, and upregulates IL-6 mRNA. These effects demonstrate GBE's hepatoprotective and antioxidant qualities, which prevent liver fibrosis in experimental models.

Antidepressant Effects Depression, a chronic mental disorder, contributes to global socioeconomic loss. Gut microbiota, particularly probiotics, play a role in the onset and recovery of depression. Polysaccharides from *Ginkgo biloba* have demonstrated antidepressant effects by inhibiting serum S100B expression and alleviating depressive symptoms, thereby improving neurological function in older adults. The combination of GBE with conventional antidepressants produces a synergistic effect, accelerating therapeutic outcomes. Additionally, water-soluble *Ginkgo biloba* polysaccharides reduce stress-induced depression and correct intestinal dysbiosis in mice. [60–62]

Anti-Aging Effects Oxidative stress accelerates skin aging, resulting in wrinkles, dryness, and impaired skin desquamation. Both *Ginkgo biloba* leaf and ethanol extracts exhibit skin-protective properties, including antioxidant and antiaging effects. Topical application improves skin penetration and retention, while EGb 761 protects against frostbite and reduces tissue peroxidation.[63]

Anti-Hypertensive Effects Hypertension, a progressive condition contributing to heart failure and stroke, can be

mitigated with *Ginkgo biloba*, which reduces inflammatory mediators, such as IL-6 and TNF-α. [64,65]

Neuroprotective Effects The increasing prevalence of neurodegenerative diseases highlights the need for effective therapeutic strategies. *Ginkgo biloba*, rich in terpenoids and flavonoids, enhances cerebral blood flow, prevents neuronal hyperactivity, and supports cognitive function, underscoring its potential in managing chronic inflammatory and cerebrovascular conditions.[66]

Table 2: Ginkgo biloba and its extracts prevent and treat various CVD's [cardiovascular diseases]

Atherosclerosis	MI/RI	Hyperlipidemia	Hypertension	Myocardial infraction	Cardiac arrhythmias	Adriamycin cardiotoxicity
↑Angiogenic cells ↓Superoxide anion ↓MMP-1 ↓Cholesterol intake ↓Fat Formation ↓Inflammatory cell ↓Foam cell formation ↓PAF accumulation	↑Cardiac function ↑Coronary blood flow ↑SOD activity ↓Cytochrome C release ↓Caspase-3 activation ↓infarct size ↓Cell apoptosis ↓Inflammatory response ↓FRS damage ↓LDH release ↓PAF accumulation ↓ROS produced	↑HDL-C ↑HMG-Co ↓TG ↓TC ↓LDL-C ↓Cholesterol ↓PL	↑NO synthesis ↑NO release Pathological ↑Circulation Endothelial ↑Cell Ca^{2+} Systolic blond ↓pressure diastolic blond ↓pressure cardiac ↓Hypertrophy Oxidative ↓Stress Platelet ↓Aggregation Blood Clots ↓Inflammation	↑Myocardial contractile ↑Na^{+} /k^{+} atpase ↑Ca^{2+} /Mg^{2+} atpase ↓MDA ↓Cell inflammation ↓Myocardial cell apoptosis ↓Oxidative stress ↓α-SMA expression ↓ERK ½ expression ↓TGF-β1 expression ↓Type 1 collagen	↑ATPase activity ↑Cardiac function ↓DAD ↓APD ↓ICa-L ↓IK ↓HCN2 ↓HCN4 ↓Mayocardial Ca^{2+} ↓OS damage ↓VF incidence ↓VT incidence	↓TNF-a ↓Caspase-3 ↓Oxidative stress ↓Cell apoptosis ↓Oxygen radical ↓Nitrogen oxide ↓Cardiotoxicity ↓Inflammatory ↓Response ↓Ca^{2+} concentration
↓Foam cell formation ↓PAF accumulation	↓Cell apoptosis ↓Inflammatory response ↓FRS damage ↓LDH release ↓PAF accumulation ↓ROS produced		↓Hypertrophy Oxidative ↓Stress Platelet ↓Aggregation Blood Clots ↓Inflammation	↓Myocardial cell apoptosis ↓Oxidative stress ↓α-SMA expression ↓ERK ½ expression ↓TGF-β1 expression ↓Type 1 collagen	↓Mayocardial Ca^{2+} ↓OS damage ↓VF incidence ↓VT incidence	↓Cardiotoxicity ↓Inflammatory ↓Response ↓Ca^{2+} concentratio n

Nomenclature and Systematics

The English name "Maidenhair tree" was coined because of the resemblance of its foliage to the Maidenhair fern (*Adiantum*). In Japan, it is simply referred to as "Ginkgo." The genus *Ginkgo* was previously classified under the Taxaceae family. Although this family has traditionally been considered artificial, it now primarily includes the Podocarpaceae and Cephalotaxaceae.

The unique multi-coated spermatozoid of *Ginkgo* formed the basis for Engler's classification of the distinct Ginkgoopsida family and class, which dates back to the Lower Jurassic. [67,68] This group reached its peak in the Early Jurassic and declined sharply before the end of the Cretaceous. Of the 19 genera and approximately 60 species in the family, most became extinct during the Oligocene epoch. Today, *Ginkgo biloba* is the sole surviving species, making it a classic example of a "living fossil." [69]

Scientific name : Ginkgo biloba

Biological Source : leaves of ginkgo biloba tree
Class : Ginkgoopsida

Family : Ginkgoaceace

Distribution
Ginkgo biloba was introduced to Europe in the 18th century, around 1730, reportedly inspiring Goethe's poem about trees. Its use in Chinese medicine dates back to approximately 1505 A.D., with the fruit referred to as "bailo" in Chinese medical texts. [70,71] Originally, *Ginkgo biloba* was part of a mixed mesophytic forest community in the hill regions of China near the Yangtze River Valley. Since its introduction to Europe, it has become a popular medicinal plant and ornamental tree. A recent study reported the presence of approximately 30 *Ginkgo biloba* plants in India. [72–74]

Cultivation and Propagation *Ginkgo biloba* is a long-lived tree with a lifespan exceeding 5,000 years. It is cultivated in countries such as China, France, and the USA (notably South Carolina). The tree thrives in well-drained soil under full sunlight and is resistant to air pollution and disease. Research indicates that seed viability decreases over time, prompting studies on intercropping systems and microclimatic optimization to enhance leaf-yielding crops. [75–81]

Uses and Efficacy

Cerebrovascular Disease Eight randomized studies have reported that *Ginkgo biloba* is as effective as ergoloid mesylates in reducing symptoms of dementia and cerebral insufficiency. A meta-analysis found that ginkgo's effect on cognitive function in patients with Alzheimer's disease showed a substantial overall effect size, comparable to that of donepezil. Various cognitive tests were used to assess the efficacy. [82,83]

Dementia

Six-month trials have indicated that *Ginkgo biloba* extract and second-generation cholinesterase inhibitors are equally effective in treating mild-to-moderate Alzheimer's dementia. Although ginkgo has been shown to improve cognition and daily function, its use has been cautiously recommended, pending further research. Cochrane meta-analyses support these findings but highlight the need for larger studies due to some contradictory results. [84–86]

A Cochrane study involving 214 participants assessed the effects of varying Ginkgo doses over 24 weeks. No significant improvement in neuropsychological or behavioral outcomes was observed, potentially due to the inclusion of participants with age-associated memory impairment, which limited the statistical robustness. [87,88]

Memory Enhancement A six-week study in healthy individuals without dementia found that standard doses of Ginkgo did not improve memory or learning. However, higher doses have been shown to significantly improve cognitive function. [89,90]

Intermittent Claudication Ginkgo's benefits in intermittent claudication due to peripheral vascular disease are modest but statistically significant, improving pain-free walking distance. Higher doses further enhanced walking ability, and patients reported reduced pain and improved mobility. [91,92]

Tinnitus
Although tinnitus is a common condition, ginkgo has shown only modest efficacy in treating it. Some studies have reported that 50% of patients with recent-onset tinnitus experienced improvement after 70 days, whereas placebo-controlled trials showed improvement after 119 days. [93–95]

Interactions
Ginkgo may increase the risk of bleeding when combined with other herbal treatments, such as feverfew, garlic, ginseng, doing quai, and red clover. Potential complications include hyphema, subdural, hemorrhage, subarachnoid hemorrhage, and intracerebral hemorrhage. However, a direct causal relationship has not yet been firmly established. [96]

Adverse Effects *Ginkgo biloba* leaves contain ginkgolic acids that can cause mild allergic reactions. Severe adverse effects are rare in this study. Ginkgo is generally considered safe; however, its use during pregnancy or lactation is not recommended unless specifically approved. [1,2]

Dosage
The recommended daily dose for dementia and memory impairment is 120–240 mg. For peripheral vascular disease and tinnitus, doses up to 160 mg/day are used, typically over an initial treatment period of six–12 weeks. [96]

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Authors Contributions
All the authors made immense effort to the concept and design, acquisition of data, or analysis and interpretation of data.

Conflict of Interest

The authors declare that they have no conflicts of interest related to the content of this manuscript

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Data Availability

All data analyzed in this study were derived from previously published studies cited throughout the manuscript. No new datasets were generated or analyzed in this study.

Ethical Approvals

This study was conducted in accordance with the ethical standards of the institutional and/or national research committee and the 1964 Helsinki Declaration and its later amendments, or comparable ethical standards. As this is a review article, no primary human or animal subjects were involved.

Financial Interests

The authors declare they have no financial interests.

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