Active Components and Applications of *Ginkgo Biloba* Leaves

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Abstract. The pharmacological relevance of *Ginkgo biloba* extract lies in its well-characterized composition and broad therapeutic spectrum. This review highlights the biological activities of its principal phytochemicals—flavonoids and terpenoid lactones—emphasizing their roles in oxidative stress reduction, platelet aggregation inhibition, inflammation modulation, and neuroprotection. Clinical utility is supported by both monotherapy and combinatory regimens, especially in cerebrovascular and neurodegenerative conditions. The extract's standardized formulation, EGb 761, demonstrates consistent efficacy and tolerability, though careful consideration is needed regarding anticoagulant interactions. This paper synthesizes current evidence on the compound's mechanisms of action and practical applications, contributing to a more integrative understanding of plant-based therapeutics.

Keywords: Ginkgo biloba; flavonoids, terpenoids, antioxidant, neuroprotection, cardiovascular diseases.

1. Introduction

Ginkgo biloba, one of the oldest living tree species, has a long-standing history in traditional Chinese medicine, where its leaves have been used to promote blood circulation, enhance memory, and manage respiratory disorders. Contemporary pharmacological studies have identified a range of bioactive constituents in ginkgo leaves, notably flavonoids and terpenoids, which possess potent antioxidant, anti-inflammatory, neuroprotective, and microcirculatory-enhancing properties [1]. Owing to these multifaceted biological effects, ginkgo leaf extract has been increasingly incorporated into adjunctive therapeutic strategies for cardiovascular conditions and neurodegenerative diseases.

2. Main Active Components of Ginkgo biloba Leaves

The pharmacologically active constituents of *Ginkgo biloba* leaves are primarily categorized into two major classes: flavonoids and terpenoid lactones. In addition, small quantities of other bioactive compounds—such as organic acids, sugars, polysaccharides, polyphenols, and aromatic substances—are also present and have demonstrated certain physiological effects [1] (Figure 1).

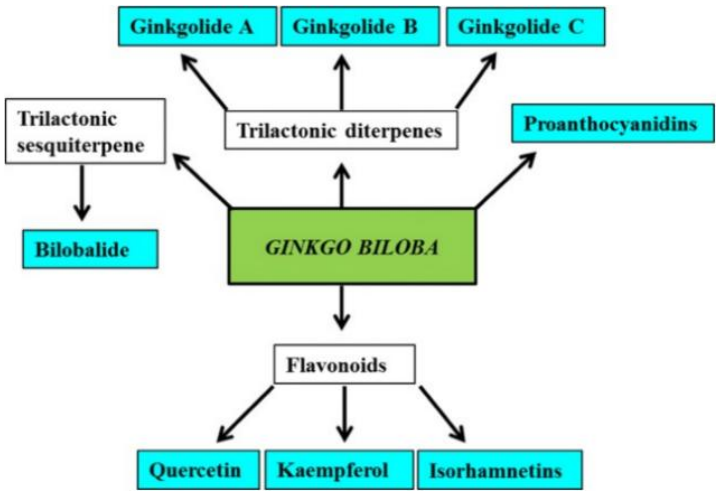

Figure 1. Classification of major active components in *Ginkgo biloba* leaves and their representative compounds. [2]

2.1. Flavonoids

Flavonoids represent the most abundant group of polyphenolic compounds in *Ginkgo biloba* leaves, mainly consisting of flavonoid glycosides and their corresponding aglycones. Major representatives include quercetin, kaempferol, isorhamnetin, and their glycosidic forms. These molecules exhibit potent antioxidant and anti-inflammatory properties, which contribute to scavenging reactive oxygen species (ROS), stabilizing cellular membranes, and maintaining capillary integrity. Moreover, ginkgo flavonoids have been shown to regulate cholesterol metabolism, enhance microvascular circulation, and alleviate vasospasm.

Their antioxidant effects are attributed to several mechanisms: (1) direct neutralization of free radicals to inhibit lipid peroxidation; (2) upregulation of endogenous antioxidant enzymes, including glutathione peroxidase (GSH-Px), superoxide dismutase (SOD), and catalase (CAT); and (3) activation of the Nrf2/ARE signaling pathway, which promotes the expression of phase II detoxification enzymes [3].

2.2. Terpenoid lactones

Terpenoid lactones are another hallmark group of bioactive compounds found in *Ginkgo biloba*, notably including ginkgolides A, B, and C, as well as bilobalide. These molecules are structurally unique to ginkgo and rarely found in other botanical species. Their pharmacological effects are primarily associated with anti-platelet aggregation, modulation of central nervous system activity, and neuroprotection.

Ginkgolides A–C act as antagonists of platelet-activating factor (PAF), thereby inhibiting platelet aggregation, reducing thrombus formation, and preventing the development of atherosclerosis. Additionally, these compounds promote vasodilation and improve cerebral blood flow and microcirculation [4]. Bilobalide, in particular, demonstrates pronounced neuroprotective effects through modulation of GABA_A receptor function, stabilization of neuronal membrane potential, inhibition of glutamate-induced excitotoxicity, and prevention of mitochondrial dysfunction and calcium overload [5].

2.3. Other components

Beyond the principal classes, *Ginkgo biloba* leaves also contain minor constituents with biological significance. Organic acids and polysaccharides, for instance, have demonstrated immunomodulatory activity, including enhancement of macrophage phagocytic function. Polyphenolic compounds contribute further to antioxidant defense mechanisms through effective free radical scavenging, thereby supporting cellular protection and anti-aging processes.

3. Pharmacological Mechanisms of Active Components in Ginkgo biloba Leaves

Extracts from *Ginkgo biloba* leaves have attracted extensive clinical and pharmacological interest due to the diverse biological activities of their natural constituents, particularly flavonoids and terpenoids. These compounds exhibit a wide range of therapeutic effects—including antioxidative, antiplatelet, anti-inflammatory, immunomodulatory, and neuroprotective actions—which form the mechanistic foundation for the clinical application of ginkgo extracts in neurological and cardiovascular diseases.

3.1. Antioxidant Effects of Flavonoids

Flavonoids such as quercetin and kaempferol are key contributors to the antioxidant potential of ginkgo leaves. These compounds efficiently neutralize reactive oxygen species (ROS) and nitrogen-based radicals, thereby mitigating lipid peroxidation and preserving cellular membrane integrity. Moreover, they support endogenous antioxidant defense by modulating the glutathione (GSH) system and enhancing the activity of enzymes such as superoxide dismutase (SOD) and catalase (CAT).

Recent studies have also highlighted the ability of ginkgo flavonoids to activate the nuclear factor erythroid 2-related factor 2 (Nrf2) and antioxidant response element (ARE) signaling pathways, thereby inducing the expression of phase II detoxifying enzymes and offering systemic protection against oxidative stress [3, 6] (Figure 2).

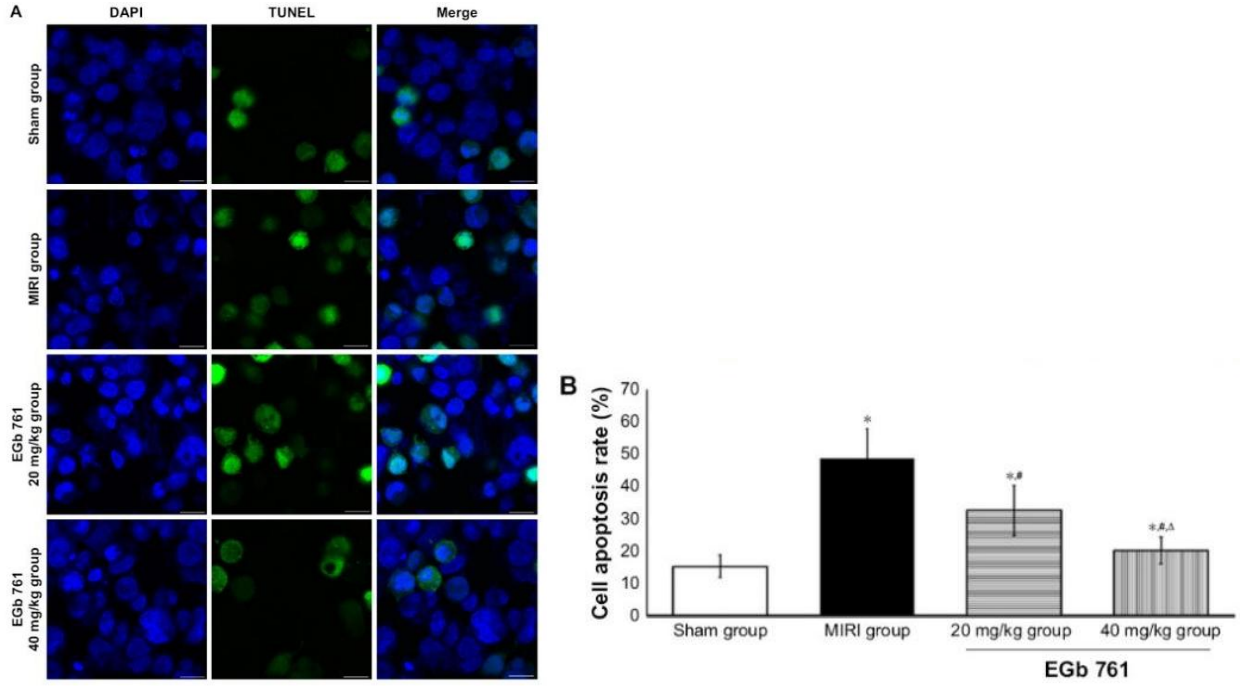

Figure 2. Effect of EGb 761 on MIRI-induced cell apoptosis detected by TUNEL assay. (A) Representative images showing apoptotic nuclei (green, TUNEL) and total nuclei (blue, DAPI); (B) Quantification shows dose-dependent reduction of apoptosis by EGb 761. [3, 6]

3.2. Antiplatelet and Microcirculatory Effects of Terpenoids

The terpenoid lactones—namely ginkgolides A, B, C, and bilobalide—exert prominent antiplatelet effects. Their mechanism involves competitive antagonism of platelet-activating factor (PAF), resulting in inhibition of platelet aggregation and degranulation, which helps prevent thrombus formation. In addition, these compounds facilitate vasodilation, improve cerebral blood flow, and enhance microcirculation, making them particularly effective in treating ischemic conditions such as cerebral infarction and peripheral vascular disease [4].

3.3. Other components

Both flavonoids and polysaccharides in *Ginkgo biloba* exhibit marked anti-inflammatory and immunoregulatory activities. They suppress the synthesis and release of key inflammatory mediators such as tumor necrosis factor-α (TNF-α) and interleukin-1β (IL-1β), thereby reducing tissue damage. Additionally, they inhibit activation of the nuclear factor κB (NF-κB) signaling pathway, leading to downregulation of proinflammatory gene expression [7]. Polysaccharides further modulate immune cell function, including macrophages, T lymphocytes, and dendritic cells, thereby contributing to immune homeostasis.

3.4. Neuroprotective Role of Bilobalide

Bilobalide, a unique terpenoid lactone found in ginkgo, demonstrates multitarget neuroprotective effects. It enhances inhibitory neurotransmission by regulating GABA_A receptors and counteracts excitotoxicity mediated by glutamate [5]. Bilobalide also maintains calcium homeostasis through modulation of ion channels and protects mitochondrial integrity, thereby attenuating apoptosis. Notably, it has been shown to mitigate β-amyloid (Aβ)-induced neurotoxicity, suggesting potential utility in the treatment of neurodegenerative diseases such as Alzheimer's disease [2].

In summary, the active constituents of *Ginkgo biloba* exert broad pharmacological effects through multiple molecular targets and signaling pathways. Their actions—ranging from antioxidant and antiplatelet activity to inflammation regulation and neuroprotection—provide a comprehensive theoretical framework for the therapeutic application of ginkgo extracts in cardiovascular, cognitive, and neurodegenerative disorders.

4. Applications of Ginkgo biloba Leaf Extract

Ginkgo biloba leaf extract has been extensively applied in a wide range of pharmaceutical products and health supplements. Common formulations include ginkgo tablets, flavonoid capsules, extract liquids, and ginkgolide ester injections. These products are primarily used to enhance cerebral blood flow, alleviate cognitive dysfunction, and assist in the prevention and treatment of vascular diseases. Notably, ginkgo extract is recognised as an important adjunct therapy for improving circulatory and neurological function, particularly in middle-aged and elderly populations.

Clinically, ginkgo extract is widely used in the treatment of cerebral hypoperfusion, cerebral arteriosclerosis, transient ischemic attacks (TIAs), and Alzheimer's disease. Its therapeutic mechanisms involve vasodilation, enhancement of cerebral perfusion, and inhibition of platelet aggregation, collectively improving ischemic symptoms and promoting cognitive function. Beyond central nervous system conditions, ginkgo is also employed in managing peripheral vascular disorders, such as intermittent claudication, Raynaud's phenomenon, and retinal microcirculation impairment. Furthermore, due to its potent antioxidant and neuroprotective properties, ginkgo extract holds promise as an adjunct in the management of neurodegenerative diseases, including Alzheimer's and Parkinson's disease.

Among the available formulations, the most widely adopted internationally is the standardised extract EGb 761, which typically contains 22–27% flavonoids and around 6% terpenoids. This formulation is valued for its clinical stability and reproducible pharmacological effects (Figure 3). EGb 761 has been approved as a prescription medication in several countries, including Germany and France, and has demonstrated efficacy in alleviating memory impairment, mood disturbances, and behavioral symptoms in patients with mild to moderate Alzheimer's disease [8].

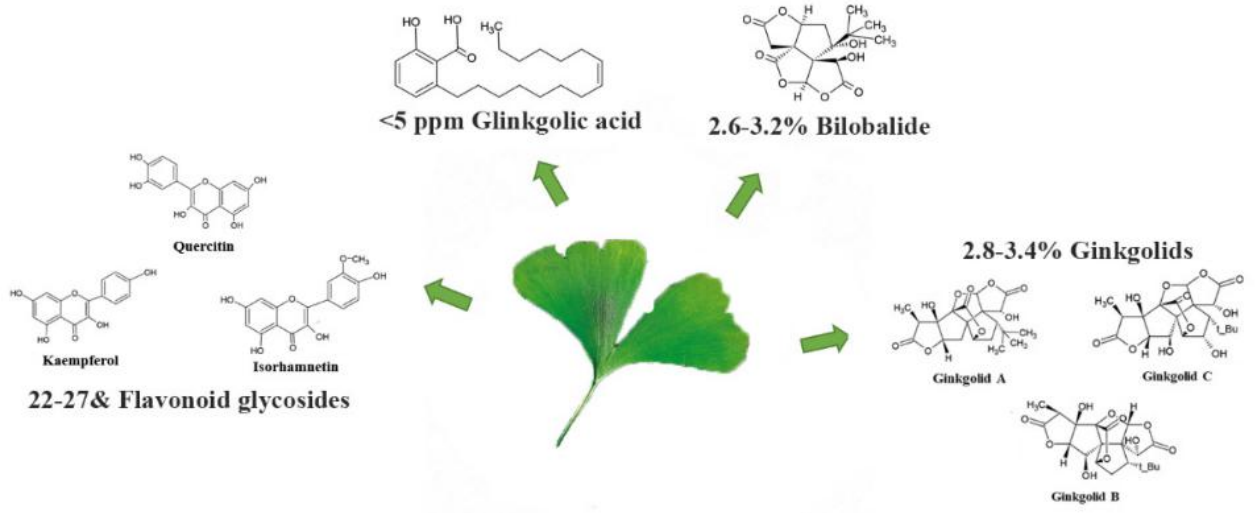

Figure 3. Standard composition of EGb 761, including flavonoids (22–27%) and terpenoids (6%), with ginkgolides (2.8–3.4%) and bilobalides (2.6–3.2%) as the main components; ginkgolic acid is controlled to <5 ppm to ensure safety and quality stability. [9]

In recent years, ginkgo extract has also been increasingly studied for its use in combination therapy. When co-administered with cholinesterase inhibitors such as donepezil, it has been shown to improve the overall clinical response in Alzheimer's disease patients [10] (Figure 4). In patients with coexisting hypertension and cognitive impairment, combination with antihypertensive agents may

further enhance cerebral perfusion, demonstrating synergistic benefits. Additionally, ginkgo extract has been shown to significantly inhibit platelet aggregation and modulate prostaglandin metabolism in individuals with type 2 diabetes, suggesting its potential utility in treating metabolic syndrome and diabetic neuropathy [11].

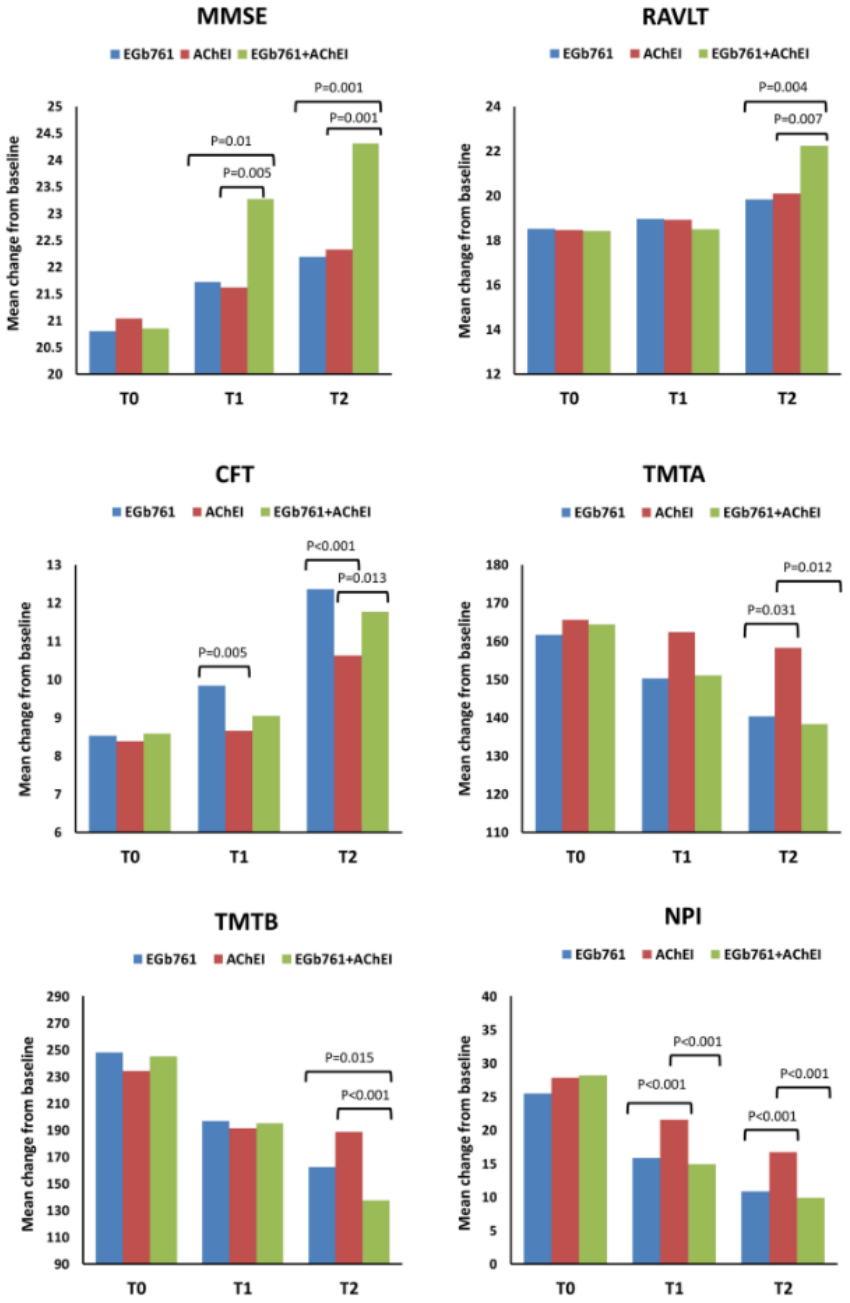

Figure 4. Quantitative assessment of the effects of combination therapy on cognitive function in patients with mild Alzheimer's disease. The figure shows the performance of the EGb 761 monotherapy group, the AChEI (cholinesterase inhibitor) monotherapy group, and the combination therapy group in multiple cognitive function tests, including the MMSE, RAVLT, CFT, TMTA, TMTB, and NPI. The combination therapy group showed significant improvements in multiple metrics, suggesting that the combination of *Ginkgo biloba* extract and AChEI can enhance overall therapeutic efficacy. [10]

Although ginkgo extract is generally well tolerated, caution is warranted when used alongside antiplatelet agents (e.g., aspirin, clopidogrel) or oral anticoagulants (e.g., warfarin). A study by Mai et al. (2025) reported a statistically significant association between concurrent use and increased risk of bleeding and coagulation abnormalities, with a reported bleeding incidence of approximately 4.15%

(Figure 5) [12]. Similarly, Stoddard et al. (2015) found that co-administration with warfarin significantly elevated the risk of haemorrhagic adverse events (HR ≈ 1.38, P < 0.001) [13]. Common side effects include mild to moderate gastrointestinal discomfort, headache, and skin rash. Therefore, in patients undergoing surgery or those on polypharmacy regimens, careful risk-benefit evaluation is recommended before initiating ginkgo therapy.

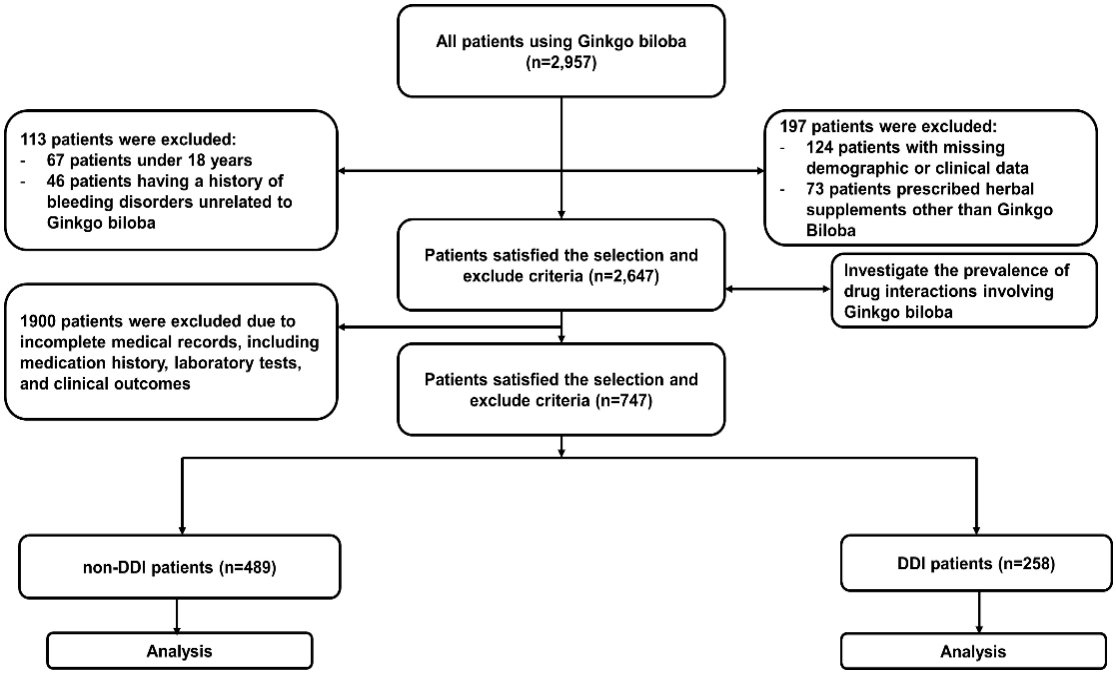

Figure 5. Flowchart of inclusion and grouping for drug-drug interaction (DDI) studies in users of *Ginkgo biloba* leaf extract. [12]

Given the broad pharmacological effects and encouraging clinical evidence, *Ginkgo biloba* leaf extract presents promising prospects for integrative medical approaches.

5. Conclusion

In conclusion, *Ginkgo biloba* extract represents a well-characterized phytopharmaceutical with a stable chemical profile and multifaceted pharmacological activity. Its principal constituents—flavonoids and terpenoid lactones—exert a broad spectrum of biological effects, including antioxidant, anti-inflammatory, antiplatelet, and neuroprotective actions. These mechanisms underpin its utility as an adjunctive therapy in the management of various chronic disorders, particularly those involving neurovascular dysfunction.

Supported by a favourable safety record and growing clinical evidence, *Ginkgo biloba* extract has been widely incorporated into therapeutic strategies for conditions such as Alzheimer's disease, vascular dementia, and peripheral circulatory disorders. Nevertheless, caution remains necessary in special populations or when used concurrently with anticoagulant therapies.

Future research should continue to refine the understanding of its pharmacokinetics and pharmacodynamics, identify optimal patient populations, enhance formulation bioavailability, and explore synergistic effects through rational combination with other agents. With ongoing clinical validation, *Ginkgo biloba* is poised to play an increasingly integrated role in evidence-based complementary medicine.

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