Serican Journal of Medicine
2025, VOL. 2, NO. 3, 23966
https://doi.org/10.17161/sjm.v2i3.23966

A Review of the Pharmacological Effects of Ginkgo Biloba Extract

Shanwen You

Chinese Materia Medica, School of Pharmacy, Jining Medical University, Rizhao, Shandong Province 276800, China
***Correspondence**: youshanwen@163.com; Tel: +86-13689651452.

ABSTRACT
As an extract from a traditional medicinal plant, ginkgo biloba extract (GBE) has complex chemical components and diverse pharmacological activities that have always been a research hotspot in the medical field. This article systematically reviews the main components and extraction processes of GBE. From multiple aspects such as cardiovascular and cerebrovascular protection, neural regulation, intervention in metabolic diseases, and respiratory system protection, this review explores GBE's pharmacological effects and mechanisms of action, combined with clinical research and experimental data. Further, this review analyzes the research progress of GBE in antibacterial activity, drug interactions, and safety evaluation, aiming to provide a comprehensive theoretical reference for clinical application and subsequent research of GBE.

ARTICLE HISTORY
Received: May 12, 2025
Revised: June 3, 2025
Accepted: June 23, 2025

KEYWORDS
Ginkgo Biloba extract, pharmacological effects, clinical application, mechanism of action, safety

1. Introduction

Ginkgo biloba, commonly known as ginkgo or ginkgo, also known as the maidenhair tree, is a species of gymnosperm tree native to East Asia. It is one of the oldest tree species on Earth and has a long-recorded history of its medicinal value in traditional medicine. In ancient China, ginkgo biloba leaves were used to treat symptoms such as cough and asthma. With the development of modern medicine, ginkgo biloba extract (GBE) has gradually become the focus of research. GBE contains a variety of bioactive components and shows potential therapeutic effects in multiple diseases. In recent years, research on GBE has been continuously advanced, covering multiple aspects such as component analysis, exploration of pharmacological mechanisms, and evaluation of clinical applications. This article aims to comprehensively review the research on the pharmacological effects of GBE to provide a reference for its further development and clinical application.

2. Chemical Components and Extraction Processes of GBE

2.1 Main Chemical Components

The chemical components of GBE are extremely rich, mainly including flavonoids, terpene lactones, phenolic acid components, and other active substances. It was found through color reaction and high-performance liquid chromatography that the extract of Ginkgo biloba leaves contains polysaccharides, organic acids, flavonoids, terpene lactones, tannins, and anthraquinone compounds, but no alkaloids and saponins [1]. Among them, flavonoid components such as quercetin, kaempferol, Isorhamnetin, and their glycoside derivatives are the main active ingredients of GBE. Flavonoids can reduce inflammatory responses, enhance antioxidant capacity, and delay aging [2]. Terpene lactones, including ginkgolide A, B, C, J, and ginkgolide, are characteristic components that distinguish GBE from other plant extracts and play a key role in neuroprotection and anti-platelet aggregation.

Flavonoids have multiple phenolic hydroxyl structures, which endow them with strong antioxidant capacity. They can eliminate excessive free radicals in the body, such as superoxide anions and hydroxyl radicals, and reduce the damage of oxidative stress to cells. Quercetin possesses a variety of beneficial biological activities such as antioxidation, anti-inflammatory, antibacterial, antiviral, anticancer, immunomodulatory, and neuroprotective properties [3]. Studies have shown that quercetin mainly exerts antioxidant effects by regulating cancer-related pathways, the advanced glycation end-product receptor (AGE-RAGE) signaling pathway, blood lipids, and atherosclerosis pathways [4]. Quercetin can enhance the antioxidant defense system of cells by regulating the activities of intracellular antioxidant enzymes, such as superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), etc. Flavonoids can inhibit the release of inflammatory cytokines. For instance, flavonoids can suppress the production of inflammatory factors such as tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), and interleukin-1 β (IL-1β), affect cytokines and their receptors, stabilize anti-inflammatory factors, and exert anti-inflammatory effects [5].

Among terpene lactones, ginkgolides have a unique chemical structure. Ginkgolide B is a platelet-activating factor (PAF) antagonist and has the strongest effect. Platelet-activating factor binds to the corresponding receptor (platelet-activating factor receptor: PAFR) to exert biological functions. The main principle by which ginkgolide exerts its antiplatelet effect is that it inhibits the binding of platelet-activating factors and antibodies through competition [6]. Ginkgolide has a protective effect on central nervous system injury as it can promote the growth and differentiation of nerve cells and enhance the anti-injury ability of nerve cells [7].

It is worth noting that GBE also contains ginkgolic acids, which are a type of alkylphenol compound with strong sensitization and cytotoxicity. Shao et al. pointed out that even trace amounts of residual ginkgolic acid may cause adverse reactions such as rashes and anaphylactic shock [8], thus becoming the core indicator for the safety evaluation of GBE. The toxic mechanism of ginkgolic acid may be the uncoupling effect of mitochondrial oxidative phosphorylation reactions. Meanwhile, studies have shown that ginkgolic acid and related alkyl acids can cause chromosome breaks in sperm, leading to embryo mutations [9].

2.2 Extraction and Purification Processes

The extraction process directly affects the composition and quality of GBE. Therefore, the extraction process was gradually optimized. Different concentrations of ethanol were used for extraction, and macroporous resin column treatment was carried out after extraction to better retain the effective components and remove the toxic components [10]. This process enriches flavonoids and terpenoids through ethanol extraction and then removes impurities such as ginkgolic acid through macroporous resin adsorption, which can make the content of ginkgolic flavonoid glycosides reach more than 24%. The content of ginkgolide is over 6%, while the content of ginkgolide acid is controlled below 5 μg/g, which complies with the standards of the Chinese Pharmacopoeia [11]. During the ethanol extraction process, factors such as temperature, time, and ethanol concentration will all affect the quality of the extract. Appropriately increasing the temperature and extending the extraction time can enhance the extraction rate of the active ingredients. However, excessively high temperatures and overly long extraction time may lead to the degradation of the components. Studies show that the optimal extraction process conditions are as follows: the ratio of material to liquid is 1:15, the ethanol concentration is 70%, the time is 2 hours, and the temperature is 50°C. The greatest advantage of this method is that it can achieve the efficient separation of shikimic acid, chlorogenic acid, total lactones, and total flavonoids in ginkgo biloba leaves, thereby providing a reference for the comprehensive utilization of the four active components in ginkgo biloba leaves and playing an important guiding role in the comprehensive utilization of ginkgo biloba leaves [12].

Macroporous resin adsorption technology is a key step in purifying GBE. Different types of macroporous resins have different adsorption and desorption properties for the components in ginkgo biloba leaves. For instance, studies have shown that non-polar macroporous resins have a strong adsorption capacity for flavonoids [13], while polar macroporous resins have a better adsorption effect on total ginkgolic acid and can effectively remove total ginkgolic acid from GBE [14]. In actual production, two or more macroporous resins are usually selected for combined use to achieve a better purification effect.

In addition, new technologies such as supercritical CO_2 extraction and microwave-assisted extraction have also been used to increase the yield of active ingredients. However, due to their high costs, they have not yet been widely applied. Supercritical CO_2 extraction technology uses CO_2 in a supercritical state as the extractant and has the advantages of high extraction efficiency, good selectivity, and no pollution. It can be extracted at a lower temperature, avoiding the loss of heat-sensitive components. Microwave-assisted extraction utilizes the thermal and non-thermal effects of microwaves to accelerate the dissolution of active ingredients, shorten the extraction time, and enhance the extraction efficiency. However, these new technologies have certain limita-

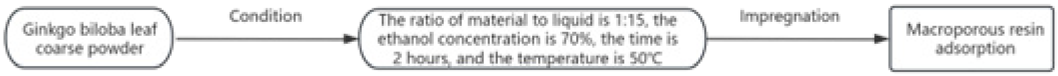

Figure 1, GBE production flowchart.

tions in terms of equipment cost, operation requirements, etc., which restrict their large-scale promotion and application [15]. In terms of operation, microwave pretreatment + resin purification can be used, which shortens the extraction time by 50%, reduces energy consumption by 30%, and maintains the yield, thereby reducing the cost-benefit ratio of the extraction method [16].

3. Pharmacological Effects and Clinical Applications of GBE

3.1 Protective Effects on the Cardiovascular and Cerebrovascular System

3.1.1 Anti-ischemic Stroke and Brain Protection

GBE has a definite therapeutic effect in the treatment of ischemic stroke (IS). The administration method of GBE pretreatment can increase the proliferation activity of lymphocytes in acute ischemic stroke [17]. Ginkgolide and ginkgolide A can regulate the activity of NOS to increase the production of nitric oxide (NO), and NO has the effects of dilating blood vessels and inhibiting platelet aggregation, which helps improve cerebral blood circulation and alleviate ischemic brain injury. In animal experiments, the total organic acids of ginkgo biloba leaves may reduce ischemic brain injury by alleviating oxidative stress rather than by anti-apoptotic effects [18]. Studies have shown that platelet-activating factor receptor antagonist in GBE has the functions of dilating blood vessels, increasing cerebral blood circulation flow, antioxidation, and anti-free radical, changing the state of cerebral ischemia, thus protecting the brain [19]. GBE can also prevent platelet aggregation, reduce fibrinogen, and inhibit thrombosis, which can accelerate the recovery of patients and improve their memory. The therapeutic effect is obvious and effective [20].

GBE combined with pentoxifylline affects the coagulation and fibrinolysis system of patients with acute cerebral infarction. After acute cerebral infarction occurs, the brain tissue will experience ischemia and hypoxia, leading to damage and death of nerve cells. GBE combined with pentoxifylline can improve neurological deficits, cerebral circulation, and coagulation and fibrinolysis systems in patients with acute cerebral infarction, showing good clinical efficacy and high safety [21].

3.1.2 Improving Microcirculation and Vascular Protection

Ginkgolide components can affect the fibrinolytic system of the body, enhance fibrinolytic activity, and further improve blood fluidity. These effects work in synergy with each other to jointly improve the blood circulation of the body, which has important clinical significance for the prevention and treatment of cardiovascular and cerebrovascular diseases [22]. In diabetic vascular lesions, hyperglycemia can lead to an increase in the level of oxidative stress in the body, generating a large number of free radicals and damaging vascular endothelial cells. Studies have shown that treatment of diabetic patients with GBE showed that the blood glucose and insulin levels in the treatment group decreased significantly and various indicators of hemorheology and microvascular circulation improved significantly, suggesting a role in preventing and reducing diabetic complications. Moreover, this drug had no obvious side effects during the treatment period and could be widely used in clinical practice [23].

In terms of retinal microcirculation disorders, GBE can increase blood perfusion to the retina, improve the nutrient supply to the retina, and prevent and treat retinopathy. Studies suggest that GBE can counteract retinal cell injury induced by ischemia-reperfusion [24]. In addition, GBE can also regulate the dilation and constriction function of retinal blood vessels and maintain the stability of retinal microcirculation. GBE protects the retina by increasing blood flow, counteracting platelet-activating factors, and preventing membrane damage caused by free radicals. The beneficial effects of GBE on retinal and choroidal contusion have been reported in clinical trials on patients [25].

3.2 Neural System Regulation

3.2.1 Intervention in Neurodegenerative Diseases

For Alzheimer's disease (AD), multiple clinical trials have shown that GBE can improve the memory and cognitive functions of Alzheimer's patients, especially in the early and middle stages of the disease. Compared with other drugs, the effect of GBE was more lasting and the side effects were relatively small with mild digestive discomfort and headache or allergic reactions [26]. Meanwhile, excessive phosphorylation of Tau protein can lead to the formation of neurofibrillary tangles, and GBE can regulate the phosphorylation level of Tau protein. Reducing the occurrence of neurofibrillary tangles, GBE can prevent and treat learning and memory impairment and tau hyperphosphorylation caused by homocysteine in rats by regulating the activities of GSK-3β and PP2A [27].

In the clinical study by Qin Wang on Alzheimer's disease [28], 220 patients aged 65 to 87 (mean 74 ± 1.2 standard deviation) years were included for a six-month treatment with GBE or placebo. The results showed that the memory functions of AD patients in terms of time and place orientation, attention calculation, immediate language memory, and short-term memory were significantly improved compared with those before medication. In addition, the conditions of insufficient cerebral blood flow in the left and right parietal lobes, the right temporal lobe, and the left frontal lobe of patients treated with GBE were also significantly improved.

GBE can also protect nerves by reducing Aβ deposition, alleviating neuroinflammation, antioxidation, anti-apoptosis, improving mitochondrial function and energy metabolism, etc. Through these mechanisms, it will provide new ideas for the development of targeted drugs for neurodegenerative diseases [29]. Experimental results show that ginkgo biloba flavonoids can inhibit the apoptosis of nerve cells by down-regulating the expression levels of TNF-α, caspase-3, and HIF-1α in the serum of mice with acute cerebral infarction, thus playing a role in protecting the nerves [30].

3.2.2 Protection of the Auditory System

In the treatment of sudden deafness, studies have adopted intravenous GBE injection combined with low molecular weight dextran amino acid injection for treatment. Experiments were conducted on patients admitted within fifteen months and forty samples were divided into the experimental group and the control group. The clinical therapeutic effects and the occurrence of adverse reactions of the two groups of patients were compared. After treatment, it was found that the effective rate of the experimental group was 97.5%, significantly higher than that of the control group (82.5%) [31]. Meanwhile, GBE can also inhibit the apoptosis of hair cells and protect auditory function. Huang et al. found that GBE can inhibit the apoptosis of hair cells by regulating intracellular apoptotic signaling pathways, such as the Bcl-2/Bax pathway, etc., and significantly increase the activity of cochlear hair cells [32]. In the treatment of tinnitus, ginkgo biloba leaves can dilate the blood vessels in the inner ear, improve the blood circulation in the inner ear, and increase the oxygen-carrying capacity of the inner ear blood vessels, thereby alleviating cellular hypoxia [33]. At the same time, GBE can also reduce cochlear inflammation and the release of inflammatory cytokines and relieve tinnitus symptoms [34].

3.3 Intervention in Metabolic Diseases

3.3.1 Protection of Diabetic Nephropathy [DN]

Due to its rich pharmacological effects, GBE can intervene in the occurrence and development of DN through multiple pathways and targets and has certain therapeutic effects on blood glucose, blood lipids, urinary microalbumin, renal function, etc. of DN patients [35]. Oxidative stress plays an important role in the occurrence and development of diabetic nephropathy. Studies have shown that GBE has high safety in the treatment of children with diabetic nephropathy. It improves renal function by regulating the levels of serum TGF-β1 and HGF, significantly enhancing clinical efficacy [19].

Liu et al. found that GBE can activate the Nrf2/ARE signaling pathway and act on the oxidative stress process, thereby alleviating the inflammatory response, improving renal function, and ultimately inhibiting the development of diabetic nephropathy in rats [36]. GBE can regulate the secretion of adipokines such as tumor necrosis factor - α, leptin, and adiponectin and regulate the expression of PKB, GLUT4 in skeletal muscle and PPARγ mRNA in adipose tissue, showing a certain dose correlation. That is, the improvement effects of medium and high-dose GBE on insulin sensitivity and related indicators are better than those of the low-dose group [37]. Meanwhile, in animal experiments, after GBE was given to diabetic model rats, it was found that the levels of serum creatinine and urea nitrogen were significantly decreased, and the pathological changes in renal tissues, such as glomerular hypertrophy and mesangial hyperplasia, were also significantly improved. However, the results of animal experiments cannot be completely equated with the clinical application effects. More clinical studies are needed to verify the safety and efficacy of GBE in the treatment of diabetic nephropathy [36].

Liu et al. [38] selected 62 patients with early DN admitted from January 2010 to December 2012 and divided them into two groups. Patients in the control group only received conventional hypoglycemic treatment and the patients in the treatment group were treated with GBE in addition to conventional hypoglycemic treatment. The results showed that GBE delayed the progression of early DN and had a renal protective effect.

3.3.2 Lipid Regulation and Antioxidation

He et al [39] studied 92 patients with hypertension complicated with hyperlipidemia and randomly divided them into a control group and a study group (46 cases in each group). The control group received the treatment of amlodipine combined with Simvastatin, while the study group adopted the treatment plan of amlodipine combined with ginkgo biloba leaves. The results showed that the research group presented significant advantages in lipid regulation, confirming that the combined application of ginkgo biloba leaves and lipid-lowering drugs has better clinical efficacy. Xiao et al. demonstrated that the antioxidant effect of GBE was stronger than that of a single flavonoid or lactone component, and its ability to scavenge free radicals was closely related to the synergistic effect among its components [10]. HMG-CoA reductase is a key enzyme for cholesterol synthesis. The flavonoid components in GBE can inhibit the activity of this enzyme and reduce the synthesis of cholesterol. Meanwhile, GBE can also promote the degradation of LDL and reduce the level of LDL in the blood, thereby lowering blood lipids [30].

The antioxidant effect of GBE is the result of the synergistic action of its multiple components. In the study by Feng et al., it was shown that flavonoids from ginkgo biloba leaves had a very good antioxidant effect. Sodium benzoate, sucrose, as well as Na^+ and K^+, did not affect the content of flavonoids.

3.4 Protection of the Respiratory System

In the treatment of idiopathic pulmonary interstitial fibrosis, GBE is mainly chosen for treatment. The therapeutic effect of the observation group was higher than that of the control group, and the incidence of adverse reactions was lower than that of the control group. The blood gas analysis, adverse reactions, and pulmonary function indicators of the observation group were all better in the observation group ($P<0.05$) [41]. GBE can effectively alleviate inflammatory infiltration and the degree of pulmonary fibrosis [42]. Wu et al. found that the specific mechanism may be for GBE to activate autophagy by up-regulating Beclin-1 and inhibiting p62, thereby reducing inflammatory cell infiltration and the deposition of collagen fibers and finally slowing down the process of pulmonary fibrosis [42].

3.5 Other Pharmacological Effects

3.5.1 Antibacterial Activity

Numerous studies have shown that GBE has antibacterial effects on various plant pathogenic fungi (such as persimmon leaf spot pathogen, rice blast pathogen, pear rust pathogen, corn anthracis pathogen, citrus scab pathogen, citrus penicillium pathogen, etc.), and the magnitude of the antibacterial effect varies depending on the method of extracting the antibacterial active components of ginkgo biloba and is related to the concentration of the antibacterial active components in GBE [43]. Among different extraction methods, the antibacterial effect of ethanol extract is superior to that of water extract. In the study by Li et al., ethanol extract of ginkgo biloba leaves had varying degrees of inhibitory effects on fungi, the mechanism by which flavonoids and terpene lactones have antibacterial activity may include destroying the cell membrane structure of bacteria and fungi and inhibiting the synthesis of their proteins and nucleic acids [44]. Ethanol extracts contain more lipophilic components, which are more likely to penetrate the cell membranes of bacteria and fungi, thereby exerting a stronger antibacterial effect. GBE has certain antibacterial properties against Escherichia coli, Staphylococcus aureus, and Porphyromonas gingivalis [45]. Studies show that as the concentration of GBE increases and the duration of action prolongs, its antibacterial effect will be enhanced. The sensitivity of different types of microorganisms to GBE also varies. Gram-positive bacteria

Table 1: Monitoring recommendations during the combination period based on INR values.

Stage	Monitoring frequency	Action threshold	Clinical intervention measures
Use in combination for 1 to 2 weeks at the beginning	Test once every three days	The INR increases by more than 0.5 or exceeds the target range	Reduce the dose of warfarin immediately
Use in combination for 3 to 4 weeks	Test once a week	The INR keeps rising or fluctuates >1.0	Suspend GBE and adjust warfarin to the original dose until INR stabilizes
Long-term combination period	At least once every two weeks	INR >5.0 or bleeding symptoms occur	Discontinue warfarin and GBE, give vitamin K antagonism, and seek emergency medical attention.

are usually more sensitive to GBE than Gram-negative bacteria. The higher the concentration of GBE, the more obvious the antibacterial effect [45].

3.5.2 Drug Interactions

Ginkgo biloba extract has an impact on the pharmacokinetics of clopidogrel in the human body. Clopidogrel is an antiplatelet drug whose function is to inhibit platelet aggregation and prevent thrombosis. The experimental results of Wang DY et al. show that long-term consumption of ginkgo biloba leaves can help increase the utilization and total absorption of clopidogrel in the human body. The results of this pharmacokinetic experiment suggest that long-term use of Ginkgo biloba leaves can increase the total absorption of clopidogrel in the human body. The increase in the total absorption of clopidogrel in the human body may be related to the inhibition of P-gp by Ginkgo biloba leaves [46]. Clinically, attention should be paid to the influence of such interactions on the risk of bleeding. However, this drug interaction may also increase the risk of bleeding.

In addition to clopidogrel, GBE may also interact with other drugs. For example, GBE may affect the metabolism of warfarin. Warfarin is a commonly used anticoagulant drug with a narrow therapeutic window. Even minor changes in dosage can lead to significant differences in anticoagulant effects. GBE may slow down the metabolism of warfarin in the body, increase the blood drug concentration, and increase the risk of bleeding [47]. Therefore, when using GBE warfarin simultaneously, the International Normalized Ratio (INR) needs to be monitored more carefully, and the dose of warfarin should be adjusted according to the monitoring results. The monitoring recommendations for INR are shown in Table 1.

Meanwhile, GBE can also accelerate the metabolism of Tolbutamide, phenobarbital, and propranolol, and reduce their efficacy [48]. The extract of ginkgo biloba leaves can significantly induce the enzymatic activity of cytochrome P450 enzyme CYP1A2 in rats and significantly affect the blood concentration of propranolol and its metabolites in rats [49]. Kubota et al. [50] fed Wistar rats with food containing three concentrations of ginkgo biloba extract: 0.1%, 0.5%, and 1.0%. A week later, the effects on the pharmacokinetics and pharmacodynamics of phenobarbital were determined. The results showed that ginkgo biloba extract significantly shortened the sleep time of rats, suggesting that ginkgo biloba extract reduced the efficacy of phenobarbital by enhancing the expression of CYP. Sugiyama et al. [51] investigated the effect of ginkgo biloba extract on the hypoglycemic effect of Tolbutamide (metabolized by CYP2C9) in rats. The results showed that in the ginkgo biloba extract pretreatment group, the total amount of liver CYP was increased by three times and the activity of CYP2C9 was increased by four times. The effect on the induction of enzymes was obvious, the metabolism of Tolbutamide was accelerated, and the efficacy was reduced.

Yin et al. [52] administered 140 mg of ginkgo biloba extract twice a day for 12 days and then took 40 mg of omeprazole once again. The results showed that ginkgo biloba extract induced CYP2C19-mediated omeprazole hydroxylation and simultaneously reduced the renal clearance rate of 5-hydroxy omeprazole.

In addition, GBE may also interact with antihypertensive drugs, hypoglycemic drugs, etc. GBE has a certain vasodilatory effect. When used in combination with antihypertensive drugs, it may enhance the

Table 2. Drug Interactions.

Drug combination	Drug interactions	Mechanism of action
GBE + Warfarin	The metabolism of warfarin in the body slows down and the blood drug concentration increases.	Efficacy is affected by influencing the activity of the CYP1A2 enzyme.
GBE + Pioglitazone Hydrochloride Tablets	It will enhance the antihypertensive effect and lead to the occurrence of hypotension.	Reduce angiotensin, aldosterone, and oxidized low-density lipoprotein in the serum.
GBE + dipyridamole	In the early treatment of DN, urinary microalbumin can be significantly reduced.	Inhibit the formation of lipid peroxides and protect cell membranes from free radical damage.
GBE + Tolbutamide pulse	It accelerates the metabolism of drugs and reduces their efficacy	Induce the enzymatic activity of cytochrome P450 enzyme CYP1A2.
GBE + omeprazole	Reduce the renal clearance rate of 5-hydroxy omeprazole	Induce the hydroxylation of omeprazole mediated by CYP2C19.
GBE + phenobarbital	It accelerates the metabolism of drugs and reduces their efficacy	Enhance the expression of CYP.
GBE + Propranolol	It accelerates the metabolism of drugs and reduces their efficacy	Induce the enzymatic activity of cytochrome P450 enzyme CYP1A2.
GBE+ clopidogrel	Improve the utilization and total absorption of clopidogrel in the human body.	It is related to the inhibition of P-gp by Ginkgo biloba leaves.

antihypertensive effect and lead to the occurrence of hypotension [53]. When used in combination with hypoglycemic drugs, since GBE may affect blood glucose levels through mechanisms such as improving insulin resistance, it may increase the risk of hypoglycemia. Therefore, when diabetic patients use GBE and hypoglycemic drugs simultaneously, they need to strengthen blood glucose monitoring and adjust the dosage of hypoglycemic drugs in a timely manner [54]. The addition of GBE to dipyridamole injection in the early treatment of DN can significantly reduce urinary microalbumin [55].

With the continuous in-depth research on the drug interactions of GBE, it has been found that it may also interact with some psychotropic drugs. Some studies have pointed out that GBE may affect the metabolism of benzodiazepines, which are often used to treat symptoms such as anxiety and insomnia [56]. This is a matter that requires high attention for patients who simultaneously suffer from neurological diseases and other diseases and need combined medication. To gain a more comprehensive understanding of the interaction mechanisms between GBE and other drugs, researchers are currently conducting in-depth explorations at multiple levels, including cells, animal models, and clinical studies. These studies will provide a more reliable basis for rational clinical drug use to reduce the adverse consequences caused by drug interactions. The chart of drug interactions is shown in Table 2.

4. Safety and Quality Control of GBE

4.1 Safety Evaluation

The overall safety of GBE is good, but the toxicity of ginkgolic acid cannot be ignored. Shao et al. pointed out that ginkgolic acid can trigger mast cell degranulation by activating the transient receptor potential vanalic acid subtype 1 (TRPV1) channel, leading to allergic reactions [8]. Furthermore, animal experiments have shown that high-dose GBE may have

Table 3. International Regulatory System.

Region	Standard basis	Differences in core requirements
China	Chinese Pharmacopoeia 2020	Quantification of flavonoids/lactones, strict limit of ginkgolic acid
European Union	EMA	The requirement is 24% flavonoids +6% terpene lactones
The United States	FDA	There are no mandatory quantification standards and it is certified as GRAS.
Japan	The Japanese pharmaceutical company	The total flavonoids should be ≥26%, including the detection of ginkgolic acid.

a slight impact on liver and kidney functions, and the safety of long-term medication needs to be considered. The allergic reaction mechanism of ginkgolic acid is rather complex. The adverse reactions caused by ginkgolic acid are related to the cellular immune and humoral immune status. He et al [57] found that ginkgolic acid may act as an allergen to enhance the body's sensitivity, induce cell division and proliferation, enhance the cellular immune response, and simultaneously promote cell proliferation and differentiation into antibody-producing cells.

In addition, the potential impact of GBE on the nervous system has gradually attracted attention. Although GBE has a certain effect on neuroprotection, studies have reported [58] that in some cases, high doses or long-term use of GBE may cause neurological symptoms such as headache, dizziness, and insomnia. The specific mechanism is still unclear. It may be related to the regulatory effect of GBE on the neurotransmitter system, or it may be due to different responses caused by individual differences.

4.2 Key Points of Quality Control

Xiao et al. emphasized that the quality control of GBE should take into account both effectiveness and safety. In terms of active ingredients, it is necessary to ensure that the contents of ginkgo flavonoids and terpene lactones meet the standards [10]. For example, the Chinese Pharmacopoeia stipulates that flavonoids ≥24.0% and terpene lactones ≥6.0%) and the content of ginkgolic acid should be strictly limited (≤5 μg/g) [11]. At present, ultra-performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS) has been used to simultaneously determine the contents of 19 main components in GBE, providing technical support for precise quality control.

To ensure the quality stability of GBE, quality control during the production process is of vital importance. From the collection of ginkgo biloba leaves, it is necessary to strictly control their sources to ensure that the varieties of ginkgo biloba leaves are pure and the growth environment is suitable, avoiding contamination [59]. Under the same technological conditions, the flavonoid content in the extracts obtained from ginkgo biloba leaves of different qualities can vary by 10% to 20%, suggesting that different purification technological conditions should be designed for ginkgo biloba leaves of different qualities [60]. In addition to the control of chemical composition, the microbial limit of GBE is also an important part of quality control. Microbial contamination may cause product deterioration, affecting its safety and effectiveness. In terms of the research on quality control methods, in addition to the UPLC-MS/MS technology, new analytical methods are constantly emerging. However, in the current quality control process, the traditional preparation method is still adopted [61]. The international standards are shown in Table 3. In terms of solutions, cooperation on the revision of monographs should be carried out among the Chinese Pharmacopoeia, the European Pharmacopoeia (EP), and the United States Pharmacopeia (USP) to reduce trade technical barriers and promote the global unification of key indicators (such as the limit of ginkgolic acid and the threshold of bioactive components).

5. Research Prospects

5.1 Correlation Mechanism of Components - Targets - Efficacy

Most of the existing studies are based on network pharmacology and animal experiments. The specific targets and signaling pathways of the components in the human body still need to be further clarified through techniques such as isotope tracing and gene knockout. Although network pharmacology can predict the potential targets of drugs, the actual effects of these targets in the human body still require more experimental verification [62]. Isotope tracer technology can visually observe the distribution and metabolic process of drug components in the body and determine their target sites of action. However, although network pharmacology can predict many potential key targets, in actual animal experiments, only some of these key targets are often verified [63]. Gene knockout technology, on the other hand, can remove a specific gene to study its role in the mechanism of drug action [64]. Through the application of these technologies, a deeper understanding of the component-target-therapeutic effect association mechanism of GBE can be achieved.

5.2 Standardization of Clinical Applications

The differences in components of different preparations, the optimal dosage, and treatment course (for example, the onset time of GBE in the treatment of AD should be ≥12 weeks) have not yet formed a unified standard, and more multi-center, double-blind controlled trials are needed for support. At present, there are numerous types of GBE preparations on the market, and the component contents and proportions of different preparations vary, which brings certain confusion to clinical medication [65].

5.3 Development of New Preparations

Aiming at the problem of low bioavailability of liposoluble components in GBE, new delivery systems such as nanoparticles and liposomes can be explored to improve drug targeting. New delivery systems such as nanoparticles and liposomes have the advantages of small particle size, good targeting, and high biocompatibility. They can improve the solubility and stability of liposoluble components of GBE and enhance their bioavailability [66]. By encapsulating GBE in nanoparticles or liposomes, targeted drug delivery can be achieved, reducing damage to normal tissues and improving therapeutic effects [67].

6. Conclusion

GBE with its multi-component and multi-target action characteristics shows broad application prospects in disease treatment. From cardiovascular and cerebrovascular protection to neural regulation, from intervention in metabolic diseases to antibacterial activity, the pharmacological effects of GBE cover multiple medical fields. However, its complex mechanism of action, long-term medication safety, and uniformity of preparation quality still need in-depth research. In the future, by combining new technologies such as systems biology and artificial intelligence, it is expected to comprehensively reveal the medicinal value of GBE and promote its precise application in clinical practice. Through measures such as in-depth research on the correlation mechanism of components-targets-efficacy, formulation of clinical application standards, and development of new preparations, the clinical efficacy and safety of GBE will be further improved, making greater contributions to human health.

Conflicts of interest: The author has no conflicts of interest to declare.

References

[1] Luo XM, Lei F, Chen W, et al. **Components in ginkgo biloba extract qualitative detection and content measurement.** *Journal of Chemical Reagents***,** 2021,43(02): 191-195. The DOI: 10.13822/j.carolcarrollnkihxsj.2021007861.

[2] Huang YL **Research progress of plant flavonoids**. *Chinese Fruit*, 2025 ,45(01): 71-79. The DOI: 10.19590/j.carolcarrollnki.1008-1038.2025.01.012.

[3] Zhang SN, Ye C, Lan QH et al. **Research progress on the crude drug resources, pharmacological effects and main dosage forms of quercetin**. *Journal of Wenzhou Medical University*, 2025, 55(01): 66-74.

[4] Xi YX, An LX, Zhang YY, et al. **Quercetin antioxidant effect of network pharmacology study**. *Journal of Modern Animal Husbandry and Veterinary*, 2024, 01(01): 25-28, DOI: 10.20154/j.carolcarrollnkiissn1672-9692.2024.01.005.

[5] Su YY, Wang XY, Li CL, et al. **Advances in the pharmacological effects of flavonoids from Chinese traditional medicine**. *Chinese Veterinarian Medicine Journal*, 2023, 52(06): 42-46. DOI: 10.13823/j.carolcarrollnkiJTCVM.2023.114.

[6] Cai L, Du Y, Peng P. **Research progress on the extraction methods and pharmacological effects of Ginkgolide from Ginkgo Biloba**. *Anhui Chemical Industry*, 2022, 48(03): 18-19+22.

[7] Qiao SL, Zhang LH, Zhao JF. **Research status of the Effects of Ginkgo Biloba Extract on the Central Nervous System**. *Chinese Journal of Geriatric Cardiovascular and Cerebrovascular Diseases*, 2009, 11(06): 477-478.

[8] Shao ZY, Jiang YQ. **Research progress on the Pharmacological Effects of Ginkgic acid and the Deacidification methods of Ginkgo Biloba Extract**. *Rural Science and Technology*, 2018, 11(11): 111-113. DOI:10.19345/j.cnki.1674-7909.2018.11.068.

[9] Zhang SJ. **Research Progress on the Pharmacological and Toxicological Effects and Deacidification Methods of Ginkgolic Acid**. *Chinese Community Physician*, 2019, 35(08):16-17

[10] Xiao ST, Cao CR, Liu HY, et al. **Pharmaceutical Research Progress of Ginkgo Biloba Extract**. *China Pharmaceutical Affairs*,2022, 36(04):429-443. DOI :10.16153/j.1002-7777.2022.04.008.

[11] National Pharmacopoeia Commission. **Chinese Pharmacopoeia** [2020 Edition] (Volume I). Beijing: China Medical Science Press, 2020: 483-485.

[12] Dong RH, Wang QY, Li QL, et al. **Analysis of the Extraction process and Progress of Active Components from Ginkgo Biloba Leaves**. *Chemical Engineering Design Communication*, 2023, 49(10): 91-93+102.

[13] An XD, Jia QC, Wang HL, et al. **Macroporous adsorption resin to remove pesticide residues in ginkgo biloba extract study**. *Journal of Food Additives in China*, 2021, 32 (12): 97-103. The DOI: 10.19804/j.i ssn1006-2513.2021.12.013.

[14] Bi YY, Liu J, Nie ZH, et al. **Research on Resin Column Chromatography Deacidification Process of Ginkgo Biloba Extract**. *Modern Medicine and Clinical Practice*, 2023, 38(08): 1929-1934.

[15] Xu R, Wei S. **Progress in the Extraction and Separation Technology of Chemical Components in Traditional Chinese Medicine over the Past 20 Years**. *Chinese Patent Medicine,* 2006, 28(11):1646-1651.

[16] Li J, You Y, Lu HL, et al. **Study on Microwave-Assisted Extraction of Flavonoids from Ginkgo Biloba Leaves and Its Antibacterial Effect**. *China Condiments*, 2020, 45 (08): 143-146.

[17] Liu XD. **The effect of Ginkgo biloba extract on the reactivity of T lymphocyte subsets in acute ischemic stroke**. *Dalian Medical University*, 2006:29.

[18] Yao JB **Analysis of Organic Acid Components in Ginkgo Biloba Extract and Study on Its Protective Effect against Cerebral Ischemic Injury.** *Zhejiang University*, 2022:74. DOI: 10.27461/dcnki.GZJDX.2022.000251.

[19] Wang YX, Wu ZQ, Du Si S, et al. **The effect of Ginkgo biloba extract on TGF-β1 and HGF levels in children with diabetic nephropathy**. *Molecular Diagnosis and Treatment of Journal,* 2024,16(04): 721-724 + 729. DOI: 10.19930/j.carolcarrollnkiJMDT.2024.04.034.

[20] Chen Y. **Research on the Protective Effect and Mechanism of Ginkgo Biloba Extract on Retinal Photodamage**. *Nanjing Medical University*, 2022:40. DOI: 10.27249/dcnki.Gnjyu.2022.000262.

[21] Guan X, Sun DG, Zhao R, et al. **Clinical study on the Treatment of Acute Cerebral Infarction with Ginkgo Biloba Extract combined with hexanone theobromine**. *Journal of Practical Hospital Clinical Practice*, 2023, 20(06):80-83

[22] Ha JL. **The physiological basis of the pharmacological effects of Ginkgo Biloba Extract and its clinical application**. J*ournal of Hubei Polytechnic College*, 2024, 27(03): 102-106. DOI:10.16347/j.cnki.cn42-1742/z.2024.03.003.

[23] Liu RX. **The effects of Ginkgo biloba Extract on hemorheology and microvascular circulation in diabetic patients**. *Pharmacology and Clinical Practice of Traditional Chinese Medicine*, 2015, 31(4): 239-241. The DOI: 10.13412/j.carolcarrollnkizyyl.2015.04.079.

[24] Li XN, Li X, Zhang X, et al. **The protective effect of Ginkgo biloba extract on retinal ischemia-reperfusion injury in rats**. *Chinese Journal of Gerontology*, 2012, 32(07): 1424-1426.

[25] Yao LW. **Ginkgo biloba injection clinical observation on treatment of 30 cases of choroid retinal contusion**. *Journal of Traditional Chinese Medicine*, Zhejiang 2014, 49 (09): 689. DOI: 10.13633/j.carolcarrollnkiZJTCM.2014.09.099.

[26] Yin L, Luo Y. **The Application of Traditional Chinese Medicine in the Treatment of Alzheimer's Disease**. *Famous Doctor*, 2024 ,37(06): 84-86

[27] Zeng K, Huang F, Bao J, et al. **The preventive and therapeutic effects and mechanisms of Ginkgo biloba extract on Alzheimer's disease**. *Chinese Journal of Pathophysiology*, 2015, 31(10):1898.

[28] Wang Q. **Research on the Effect of Ginkgo Biloba Extract on Memory Function in Alzheimer's Disease**. *Medical Review*, 2013, 19 (10): 1898-1899+1905.

[29] Zhang H, Wang SJ, Yuan TY, et al. **The mechanism and research progress of Ginkgo Biloba extract on neurodegenerative diseases**. *Pharmaceutical Research*, 2020, 39(01):37-40. DOI: 10.13506/j.cnki.jpr.2020.01.008.

[30] Yu HH, Wu MN**. The effects of flavonoids from Ginkgo biloba leaves on the expressions of serum TNF-α, Caspase-3 and HIF-1α and neuronal apoptosis in mice with acute cerebral infarction**. *General Medicine and Education*, 2024, 22 (07): 600-603. The DOI: 10.13558/j.carolcarrollnkiissn1672-3686.2024.007.006.

[31] Wang Y. **Analysis of the Efficacy and Pharmacological Effects of Ginkgo Biloba Extract Injection in the Treatment of Sudden Deafness**. *Chinese Medical Abstracts (Otorhinolaryngology)*,2021, 36(02): 124-125+130. DOI:10.19617/j.issn1001-1307.2021.02.124.

.[32] Huang SB Gao WM, Chen X, et al. **Study on the Protective Mechanism of Ginkgo Biloba Extract Injection on Noise-induced Hearing Loss**. *Chinese Journal of Drug Application and Monitoring*, 2024, 21(01): 42-46.

[33] Lin H. **Observation on the Therapeutic Effect of Mecobalamin Combined with Ginkgo Biloba Leaf in the Treatment of Neurogenic Tinnitus**. *Chinese Journal of Misdiagnosis,* 2008, 8(24): 5889-5890.

[34] Jiang XE. **Ginkgo biloba extract of pharmacological action and clinical application**. *Journal of Inner Mongolia Medicine*, 2010, 29 (14): 108-109. The DOI: 10.16040/j.carolcarrollnkicn15-1101.2010.14.047.

[35] Zhao HX, Fei Y. **Research Progress of Ginkgo Biloba Extract in Diabetic Nephropathy**. *Zhejiang Practical Medicine,* 2022, 27(04): 357-360. DOI:10.16794 /j cnki.cn33-1207/r.2022.04.006.

[36] Liu SY, Yang B, Zhang X et al. **To explore the regulation of oxidative stress in diabetic nephropathy rats by Ginkgo biloba extract based on the Nrf2/ARE signaling pathway**. *Chinese Journal of Gerontology*, 2024, 44(11):2723-2727.

[37] Wang J. **Study on the Effect of Ginkgo Biloba Extract on Insulin Sensitivity in Rats with a High-fat Diet and Its Related Mechanism**. *Hebei Medical University*, 2008:27-110.

[38] Liu DJ, Liu HH, Li JF et al. **Clinical Observation of Ginkgo Biloba Extract on Improving Endothelial Function in Patients with Early Diabetic nephropathy**. *Western Medicine*, 2015, 27(01): 80-82.

[39] He YD. **Ginkgo leaf with amlodipine therapy curative effect observation of hypertension with hyperlipidemia**. *Journal of Traditional Chinese and Western Medicine Combined with Cardiovascular Disease the Electronic Magazine*, 2015, 3 (02): 52-53. DOI: 10.16282/j.carolcarrollnkicn11-9336/r.2015.02.072.

[40] Feng J, Peng XM Li CQ, et al. **The oxidation resistance and the stability of the ginkgo biloba flavonoids research**. *Journal of Food Science and Technology*, 2019, 44 (4): 244-249. The DOI: 10.13684/j.carolcarrollnkiSPKJ.2019.04.044.

[41] Liu CY, Liu C, Cai YH. **Analysis of the pharmacological effects and therapeutic Effects of Ginkgo Biloba Extract combined with prednisone Tablets in the treatment of idiopathic pulmonary interstitial Fibrosis.** *Systems Medicine,* 2022, 7(23): 183-186.DOI: 10.19368/j.cnki.2096-1782.2022.23.183.

[42] Wu YC. **The difference in the expression of autophagy-related proteins beclin-1 and p62 in the treatment of pulmonary fibrosis experiment with Ginkgo biloba extract**. U*niversity of Chinese Medicine in Guangx*i, 2023:48. DOI: 10.27879/dcnki.Ggxzy.2023.000541.

[43] Mo XN, Pan HY, Li A, et al. **Study on the Antibacterial Activity of Ginkgo Biloba Extract**. *Grain Science and Technology & Economy,* 2019, 44(04):97-99+105. DOI:10.16465 /j. gste.cn431252ts.20190423.

[44] Li QR, Lu CM, Jiang YJ. **Study on the Inhibitory Effect of Ethanol Extract of Ginkgo Biloba Leaves on Mold (Part Two) - Antibacterial Effects and Chemical Components of Ethanol Crude and Refined Isolates of Ginkgo Biloba Leaves.** *Zhengzhou Grain College Journal*, 2000, 21(03): 15-20. The DOI: 10.16433/j.carol carrollnkiissn1673-2383.2000.03.004.

[45] Tan YZ, Li JP. **Research on the Antibacterial and Fresh-breath Effects of Toothpaste Containing Ginkgo Biloba Extract**. *Oral Care Products Industry*, 2024, 34(05): 35-36.

[46] Wang DY, Huang QL, Chen LF et al. **The pharmacokinetic effect of Ginkgo biloba extract on clopidogrel in the human body**. *Armed Police Medical*. 2018, 29(12): 1133-1137. DOI:10.14010/j.cnki.wjyx.2018.12.007.

[47] Zhou YL, Zeng R. **The effect of Ginkgo biloba extract on the anticoagulant function and blood drug concentration of warfarin in humans**. *Chinese Journal of Traditional Chinese Medicine*, 2011, 36(16): 2290-2293.

[48] Zuo XL, Liu YL, Wu CF et al. **The effect of Ginkgo biloba extract on CYP enzyme and its interaction with other drugs**. *Chinese Journal of New Drugs and Clinical Practice*, 2008, 27(01): 64-69.

[49] Zhao LZ, Ma JF, Deng Y et al. **Experimental Study on Cytochrome P450 Enzyme CYP1A2 by Ginkgo Biloba Extract**. *Chinese Journal of Clinical Pharmacology*, 2005, 21(02): 122-125. DOI: 10.13699/j.carolcarrollnki.1001-6821.2005.02.012.

[50] Kubota Y, Kobayashi K, Tanaka N, et al. **Pretreatment with Ginkgo biloba extract weakens the hypnosis action of phenobarbital and its plasma concentration in rats**. *Pharm Pharmaco*l, 2004, 56(03): 401-405.

[51] Sugiyama T, Shinozuka K, Sano A, et al. **Effects of various Ginkgo biloba extracts and proanthocyanidin on hepatic cytochrome P450 activity in rats**. *Shokuhin Eiseigaku Zasshi*, 2004, 45(06): 295-301.

[52] Yin OQ, Tomi, Inson B, Waye MM, et al. **Pharmacogenetics and herb-drug interactions: experience with Ginkgo biloba and omeprazole**. *Pharmacogenetics*, 2004, 14 (12): 841-850.

[53] Chen YJ, Gong YC. **The effect of Ginkgo biloba Extract Injection combined with pioglitazone Hydrochloride Tablets on patients with essential hypertension**. *Journal of Practical Cardiovascular, Cerebrovascular and Pulmonary Diseases*, 2017, 25(09): 150-152.

[54] Cai DL, Xu CJ, Song YH et al. **Research on the Auxiliary Hypoglycemic Function of Ginkgo Biloba Extract**. *Danone Nutrition Center, Chinese Center for Disease Control and Prevention. Nutrition and Complications of Diabetes - Proceedings of the 16th Academic Conference of Danone Nutrition Center*. Zhejiang Provincial Center for Disease Control and Prevention, 2013: 232-237.

[55] Zhang Y. **Clinical Observation on the Treatment of Diabetic Nephropathy with Ginkgo Damo Injection**. *Zhejiang Journal of Integrated Traditional Chinese and Western Medicine*, 2006, 29(07): 406-407.

[56] Yang GG, Tan YL, Wang ZR, et al. **A randomized double-blind controlled study on the treatment of acute schizophrenia with Celebrex and/or Ginkgo biloba extract**. *The 13th National Conference on Psychiatry of the Chinese Medical Association*, 2015: 224-225.

[57] He JR. S**tudy on the Allergenicity and Allergenic Mechanism of Ginkgolic Acid**. *Huazhong Agricultural University*, 2003:114-116.

[58] Yang L, Du XX, Guo XX, et al. **Literature Analysis of Adverse Reactions of Ginkgo Biloba Extract Injection**. *Chinese Pharmacovigilance*, 2014, 11(03):163-169. DOI:10.19803 /J.1672-8629.2014.03.011.

[59] Jiang W, Yao X, Liu Y. **Analysis of Polysaccharide Composition and Monosaccharide Content in Ginkgo Biloba leaves from Different Origins**. *Chinese Journal of Traditional Chinese Medicine*, 2018, 33(10): 4654-4657.

[60] Ni LJ, Yan WT, Zhang LG. **Study on the Effect of Flavonoid Content in Ginkgo Biloba Leaves on the Purification Process Conditions of Macroporous Resin of Ginkgo Biloba Leaf Extract**. *Research and Development of Natural Products*, 2017, 29(12):2097-2103+2091.DOI:10.16333 /j.1001-6880.2017.12.017.

[61] Mei L, Li Y, Zhang W. **Quality improvement and Application Safety of Ginkgo Biloba extract preparations**. *Chinese Journal of New Drugs*, 2024, 33(04):339-344.

[62] Zhang Q, Chang J, Ji WW, et al. **Research progress in the field of network pharmacology in Chinese medicine**. *Chinese Journal Of Chinese Medicine Information*, 2024, 31 (11): 186-190. The DOI:10.19879/j.carolcarrollnki.1005-5304.202207685.

[63] Wang X. **Investigation on the Effect and Mechanism of Ginkgo Biloba Extract on Sepsis-Associated Encephalopathy Based on Network Pharmacology and Animal Experiments**. *Dali University*, 2024:25-29. DOI: 10.27811/dcnki.gdixy.2024.000729.

[64] Chang HB, Hou ZM. **A Brief Introduction to Gene Knockout Technology**. *Examination Weekly*, 2017, 78(42):194-196.

[65] Wang PX, Sui HX, Qu SJ. **Analysis of Adverse Drug Reaction Reports of 44 Cases of Ginkgo Biloba Preparations**. *Clinical Medicine Mractice*, 2024, 33(03): 198-200. The DOI: 10.16047/j.carolcarrollnkicn14-1300/r.2024.03.014.

[66] Xiao JB. **Research on Temperature-Sensitive Nasal in Situ Gel of Ginkgo Biloba Extract**. Yanbian University, 2013:37-38.

[67] Jin Y. **Research on the Preparation Process of Liposomes Extracted from Ginkgo Biloba Leaves**. *Jilin University*, 2009:87-88.