

**A SHORT REVIEW: POTENTIAL USE OF MEDICINAL PLANT GINKGO BILOBA****Ghotekar Tejaswini Ambadas\*, Bhandare Siddhi Vijay and Pawar Dipali Ishwar**

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**❖ ABSTRACT**

The Ginkgo tree, scientifically known as Ginkgo biloba, it is a oldest seed plants, commonly known as a “living fossil. And which is used to improve blood flow, prevent the formation of clots, bolster capillary structures, and safeguard neural cells in situations of reduced oxygen availability The active compounds in Ginkgo biloba extract, including terpenoids and flavonoids, exhibit anti-inflammatory and anti-asthmatic effects, aiding in the relief of bronchospasm. These compounds also possess skin-regenerative and wound-healing abilities, and studies have shown that they can enhance blood circulation, strengthen capillary walls and their elasticity, and protect nerve cells from damage caused by oxygen deficiency. This blend of ancient lineage, unique physiological attributes, and growth versatility contributes to the Ginkgo biloba’s status as a remarkable specimen in the plant kingdom, cherished by both scientists and nature enthusiasts alike. The purpose of this publication is to examine research findings primarily from 2015 to 2022 regarding the chemical makeup of Ginkgo biloba, along with its biological effects, toxicity, and potential drug interactions. In summary, Ginkgo biloba stands out not only as a traditional medicinal herb but also as a symbol of the enduring wisdom of herbal medicine. Its leaves and nuts serve as valuable resources for addressing a wide array of health concerns, ranging from respiratory and cardiovascular issues to skin infections and alcoholism, underscoring its significance across centuries of therapeutic practice. Among its numerous applications, GBE is frequently employed in the treatment of respiratory conditions such as asthma and bronchitis, providing relief to those suffering from these chronic ailments. The leaves of the G. biloba plant are rich in flavonoids and terpenoids, compounds known for their anti-inflammatory and antioxidant effects, which contribute to the herb’s ability to enhance respiratory function

**❖ KEYWORD:** Plant Description, Pharmacological Activities, Phytochemical Constituents Of Ginkgo Biloba’s, Bio Activities Of Ginkgo Biloba.

**❖ INTRODUCTION**

The term ginkgo, which translates to “hill apricot” or “silver fruit” in Chinese, comes from the apricot-shaped, mature, yellow fruits of the ginkgo tree.<sup>[1]</sup> The definition of complementary and alternative medicine is “diagnosis, treatment and/or prevention which complements mainstream medicine by contributing to a common whole, by satisfying a demand not met by orthodoxy, or by diversifying the theoretical frameworks of medicine” (Ernst 2000).<sup>[2]</sup> Ginkgo biloba (Gb) is among the oldest seed plants, commonly known as a “living fossil.” This towering tree can survive for more than 1000 years and can grow up to 40 m tall. Although it is originally from China, Gb is now grown globally. The extract from Gb leaves has been utilized in traditional Chinese medicine for hundreds of years to address circulatory issues, asthma, tinnitus, dizziness, and cognitive difficulties.<sup>[3]</sup> Ginkgo biloba, commonly referred to as the “maidenhair tree” or a “living fossil,” is an ancient species of tree characterized by its unique fan-shaped leaves, recognized for its therapeutic applications and aesthetic appeal, and

is the only extant representative of its botanical family.<sup>[4]</sup> Ginkgo extracts include active compounds that offer numerous health benefits. These extracts improve blood flow, prevent the formation of clots, bolster capillary structures, and safeguard neural cells in situations of reduced oxygen availability.<sup>[5]</sup> The Ginkgo Biloba L. tree species has a rich history of medicinal usage due to its numerous health advantages. Even after decades of research, scientists continue to explore G. biloba, focusing on its mechanisms and discovering new beneficial properties. The active compounds in Ginkgo biloba extract, including terpenoids and flavonoids, exhibit anti-inflammatory and anti-asthmatic effects, aiding in the relief of bronchospasm. These compounds also possess skin-regenerative and wound-healing abilities, and studies have shown that they can enhance blood circulation, reduce clot formation, strengthen capillary walls and their elasticity, and protect nerve cells from damage caused by oxygen deficiency.<sup>[6]</sup> The purpose of this publication is to examine research findings primarily from 2015 to 2022 regarding the

chemical makeup of Ginkgo biloba, along with its biological effects, toxicity, and potential drug interactions. Additionally, this publication includes a

section that analyzes patents related to the innovative uses of Ginkgo biloba in the food and beverage industry.<sup>[7]</sup>



Fig. 1



Fig. 2

### ❖ PLANT DESCRIPTION

The Ginkgo tree, scientifically known as *Ginkgo biloba*, boasts a rich and fascinating lineage that stretches back millions of years. Fossil evidence has been uncovered in rock formations that date as far back as the Triassic period, an era that began approximately 250 million years ago. Some experts suggest that evidence of this remarkable plant may be found even earlier, in the Permian and Carboniferous layers of earth, which are known to contain numerous traces of ancient flora. Today, *Ginkgo biloba* continues to thrive in various environments, which has led botanists and paleobotanists alike to affectionately refer to it as a "living fossil." This designation highlights its unique status as one of the oldest surviving seed-bearing plants on the planet. The longevity of *Ginkgo* is particularly notable, as it offers a living snapshot of the Earth's botanical history and evolution.<sup>[8]</sup>

The anatomy of the *Ginkgo* plant is quite distinctive, with its saprophytic body structure resembling that of several conifer species, yet it exhibits characteristics all its own. *Ginkgo* trees typically grow in an ex-current manner, whereby their central stem or trunk continues to extend upward, allowing them to achieve impressive heights that can reach up to an astounding 30 meters.

One of the key features of *Ginkgo* trees is their unique branching pattern, which can be quite irregular and uneven. The branches are classified as dimorphic, signifying the existence of two different types. The long shoots showcase unlimited growth potential and are often adorned with widely spaced leaves that help capture sunlight. In contrast, the dwarf shoots exhibit limited growth potential, appearing more compact and dense. These long shoots are capable of remarkable growth rates, yielding up to 50 centimeters of new growth in just one year, a testament to the *Ginkgo*'s resilience and adaptability. Conversely, the maturity process for dwarf shoots is considerably prolonged, with the small shoots—measuring only 2-3 centimeters in length—potentially being several years old before they reach full development. Interestingly, the distinction between these two types of shoots is not always sharply defined. In fact, environmental factors or changes in the plant's growth conditions can lead to a long shoot gradually evolving into a dwarf shoot over time, demonstrating the *Ginkgo*'s remarkable capacity to adapt to its surroundings. This blend of ancient lineage, unique physiological attributes, and growth versatility contributes to the *Ginkgo biloba*'s status as a remarkable specimen in the plant kingdom, cherished by both scientists and nature enthusiasts alike.<sup>[7]</sup>

### *Ginkgo biloba*: The Living Fossil

#### Pharmacological Effects

##### Nervous system

Memory Enhancing  
Alzheimer's Disease  
Parkinson's Disease  
Neuropathic Pain  
Epilepsy  
Depression

##### Cardiovascular system

Ischemic arrhythmia  
Hypertension  
Hypertrophy  
Atherosclerosis

##### Endocrine system

##### Muscular and skeletal system

##### Renal system

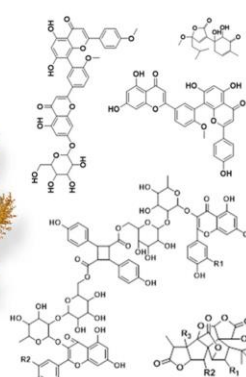
##### Respiratory system

##### Gastrointestinal system

##### Immunity system and cancer



Fig. 3



### ❖ Phytochemical Constituents of Ginkgo biloba's

Flavonoids, glycosides and terpene lactones are said to be the main bioactive components of Ginkgo biloba leaves. 3 Differences in the quantity and arrangement of -OH groups account for variations across ginkgolide subtypes. The four five-member ringed species known as bilobalides include a carbocycle, three lactones, and a tert-butyl group. Chloride channel blockers, ginkgolides, and bilobalides are strong, selective GABA receptor antagonists that reduce inhibitory synaptic transmission in the adult central nervous system because of their structural resemblance to picrotoxinin.

Nevertheless, bilobalides' strong effects are marginally less pronounced than those of ginkgolides. The pharmacological effects of ginkgo biloba extracts and ginkgolide B are diverse. However, one of their main functions is to serve as antagonists of platelet-activating factor (PAF), and they have also shown notable effects on disorders connected to dementia.<sup>[27]</sup>

### ❖ Bio activities of Ginkgo Biloba

#### Nephroprotection

Severe tubular cell damage and acute kidney malfunctions due to systemic and intrahepatic inflammation are diagnostic indicators of nephron inflammation. A significant increase in renal ROS levels indicated that oxidative damage was involved in hypertension-induced nephropathy. When given EGb

extracts for its Ginkgetin aglycone fraction, 8–12 weeks old healthy adult C57BL/6 female mice showed reduced pro-inflammatory responses mediated by LPS (bacterial endotoxin), decreased incidence of renal injury, and inhibited renal cell apoptosis. Additionally, SIRT1 protein levels were elevated, and the activation of the pro-inflammatory NF- $\kappa$ B pathway was inhibited, concluding its alluring therapeutic roles in inducing nephroprotection.<sup>[28]</sup>

EGb 761's crucial role as an effective and noticeable antioxidant in hypertensive rats was confirmed when 180–200 g healthy adult Wistar male l-NAME-mediated hypertensive rat models were pre-treated with EGb extract at 100 mg/kg per day for four weeks. These models showed a gradual decrease in systolic blood pressure, renal tissue MDA (lipid peroxidation biochemical marker), and TNF- $\alpha$  levels in comparison to the control groups.<sup>[29]</sup>

Ginkgo biloba's preclinical studies as an anti-inflammatory, anti-platelet, neuroprotective, and anti-neoplastic drug are summarized in Table 2.

The table shows preclinical research on EGb 761, a Ginkgo biloba extract, in a variety of animal models, showing its intended activity and outcomes at the specified dose rate/concentration.

Ginkgo Biloba Preparations	Model for study	Dose rate/concentration	Targeted Activity	Result	Reference
Nephroprotection					
EGb 761 Extract	MCAO filament model in wild type knockout and Ho-Iknockouts	100 mg/kg/d EGb 761; 7 days	Transient ischemia, nephroprotection	Increased HO-I protein levels; Inhibitory effect on H <sub>2</sub> O <sub>2</sub> , Glutamate-induced excitotoxicity were observed in primary neuronal cultures of mouse.	[30]
EGb 761 Extract	Adult C57BL/6 male mice, 14 day adult C57BL/6 female mice	100 mg/kg/d E6b761; 6 mg/kg GA; 6 mg/kg GB; 10 mg/kg/d TFM; 6 mg/kg BB	Nrf2/HOI induction of CRMP2 pathway, neuroprotection	33% and 49% reduction in infarct volumes, enhanced sensory behavior	[31]
EGb 761 Extract	Sprague-Dawley (SD) rats	N = 44; 50-200 mg/kg EGb 761	Permanent focal and transient cerebral Ischemia	Increases protein expressions of HOI, Nrf2, GAPDH, CRMP2, B-actin. Neuritogenic effects.	[32]
Anti-neoplastic					
EGb 761 Extract	(200-250 gm) white albino rat	Single dose; 100 200 mg/kg/d EGb 761	Cisplatin drug induced cardiotoxicity and hepatotoxicity	Reduced cisplatin induced toxicity; substantial down regulation of CK, ALT, LDH	[33]
EGb 761 Extract	Experimental Guinea pig	100 mg/kg/d E6b761 for 8 days	Cisplatin drug induced ototoxicity	Reduced cisplatin induced ototoxicity	[34]

	Animal model				
EGB 761 Extract	Excision and dead space wound male rat model	50 mg/kg/d E6b761	Effect of cyclophosphamide	Reversal of wound healing suppressant activities of Cyclophosphamide	[35]
Ginkgo biloba seed polysaccharide (GSBP)	SMMC-7721 cell cultures	50 mg/kg/d 65BP (for 36h)	HepG2 cell lines, SMMC-7721 cells (Tumour cells)	Cyclophosphamide Induction of apoptotic effects on SMMC-772) cells by GBSBP	[36]

### ❖ Pharmacological Activities

Ginkgo biloba, often simply referred to as *G. biloba*, is a remarkable and time-honored medicinal herb that has been revered for its diverse range of therapeutic properties. This ancient plant has been an integral part of traditional medicine, particularly within Chinese herbal practices, for thousands of years, showcasing its enduring significance in the realm of natural remedies of the key preparations derived from Ginkgo biloba is Ginkgo Biloba Extract (GBE), which is widely recognized for its potential health.<sup>[9-10]</sup> Among its numerous applications, GBE is frequently employed in the treatment of respiratory conditions such as asthma and bronchitis, providing relief to those suffering from these chronic ailments. The leaves of the *G. biloba* plant are rich in flavonoids and terpenoids, compounds known for their anti-inflammatory and antioxidant effects, which contribute to the herb's ability to enhance respiratory function. Furthermore, the leaves of *G. biloba* have a long history of being utilized to address cardiovascular issues. Traditional practitioners have relied on this herb to improve blood circulation, reduce the risk of heart-related diseases, and support overall heart health. Additionally, *G. biloba* leaves are also employed in the management of various skin infections, utilizing their antibacterial and healing properties to aid in the recovery of affected areas. On the other hand, the nuts of the *G. biloba* plant have also been instrumental in traditional medicine, particularly in treating a variety of respiratory disorders. They have been commonly used to alleviate symptoms associated with asthma, chest pain, and persistent coughs, offering comfort to those who suffer from these conditions. In addition to these respiratory benefits, *G. biloba* nuts have been traditionally utilized to address bladder irritation, demonstrating their versatility in treating urological issues as well. Moreover, they have even found applications in the context of alcoholism, where they have been used as part of a holistic approach to support individuals seeking recovery. In summary, Ginkgo biloba stands out not only as a traditional medicinal herb but also as a symbol of the enduring wisdom of herbal medicine. Its leaves and nuts serve as valuable resources for addressing a wide array of health concerns, ranging from respiratory and cardiovascular issues to skin infections and alcoholism, underscoring its significance across centuries of therapeutic practice.<sup>[9-11]</sup>

### 1. Management Of Respiratory Conditions

Acute respiratory distress syndrome (ARDS), asthma, and chronic obstructive pulmonary disease (COPD) are linked to inflammation in the airways, with inflammatory processes playing a key role in the onset, progression, and prognosis of these diseases. The presence of neutrophils and other inflammatory cells worsens airway inflammation. In inflammatory environments, neutrophils are involved in two critical metabolic reactions: respiratory burst and chemotaxis. Wu et al. found that during pulmonary damage caused by lipopolysaccharide (LPS), both ginkgolide M (GM) and ginkgolide B (GB) were effective in reducing the clustering of inflammatory cells, including lymphocytes, neutrophils, and macrophages, while also alleviating cytological lung damage.<sup>[12]</sup> Tao et al. found that treatment with EGB 761 significantly reduced the production of interleukins (IL)-4, IL-5, IL-6, IL-8, IL-13, and tumor necrosis factor (TNF)- $\alpha$  in allergy model mice. Additionally, EGB 761 modulates the function of leukocyte elastase, a protein linked to blood coagulation issues, lung damage, and chronic bronchitis, while its components effectively diminished lung inflammation.<sup>[13]</sup>

### 2. Anticancer Effects

Cancer is a condition where certain cells in the body start to grow uncontrollably and can eventually spread to other parts. It is a worldwide issue, with the National Institutes of Health reporting that in 2016, 1.7 million new cancer cases were identified in the United States, resulting in 600,000 deaths, highlighting the urgent need for new cancer treatments. In their research, Ahmed et al. examined the effectiveness of Ginkgo biloba extract (GBE) on rats suffering from hepatocellular carcinoma (HCC). They found that GBE significantly improved the histological features of liver tissue, leading to reduced levels of alpha-fetoprotein (AFP), glypican-3 (GPC-3), and carcinoembryonic antigen (CEA) in HCC rats. This was achieved by enhancing the gene expression of inhibitor of growth (ING)-3 and reducing the gene expression of the transcription factor forkhead box protein 1 (FOXP1) in the liver.<sup>[14]</sup> When given to C57BL/6J mice, *G. biloba* exocarp extracts (GBEE) showed similar effects on the expression of various proteins, including Wnt3a, vascular endothelial growth factor (VEGF), and phosphorylated (p)-protein kinase B (Akt)/Akt. Another study by Han et al. showed the anti-Lewis lung cancer (LLC) efficacy of GBEE, which



limited in vitro LLC cell growth by regulating catenin and Wnt3a expression in a dose-dependent manner. Lung cancer metastasis was inhibited by GBEE via lowering the levels of p-Akt/Akt, VEGF, VEGF receptor (VEGFR), and  $\beta$ -catenin protein expression. Similar decreases in VEGF and VEGFR2 mRNA levels imply that GBEE inhibits tumor angiogenesis, which has anticancer benefits. The suppression of the Wnt, catenin, and VEGF signaling pathways was linked to the underlying processes of these results.<sup>[15]</sup>

### 3. Effects of Antidementia

The majority of EGb 761 clinical trials focus on improving memory and cognition, but some focus on dementia, specifically dementia presentations that involve a progressive loss of memory and cognition, such as frontotemporal dementia, Lewy body dementia, and vascular dementia. EGb 761 may be utilized to treat a variety of dementia etiologies due to its ability to inhibit amyloid development and toxicity, regulate excitotoxic glutamatergic neurotransmission, and function as a radical scavenger.<sup>[16]</sup>

### 4. Effects of Anti-Obesity

By changing how the central nervous system (CNS) regulates food consumption and peripheral metabolism, high-fat diets contribute to the pathophysiology of obesity by increasing insulin tolerance, causing weight gain, and causing other metabolic abnormalities.<sup>[17]</sup>

It was discovered that administering GBE helped people lose weight. The difference between the amount of food that was given and the amount that was left over the course of a day was used to calculate the amount of food consumed. Insulin receptor (IR), lipid receptor R1 (Adipo R1), IL-10, and Akt phosphorylation all showed large increases in gene expression, which may have triggered the insulin signaling cascade. On the other hand, NF- $\kappa$ B p65 phosphorylation and TNF- $\alpha$  levels decreased. GBE's anti-inflammatory properties can lessen the adverse consequences of consuming an excessively high-fat diet by lowering TNF- $\alpha$  levels in retroperitoneal fat deposits.<sup>[18]</sup>

### 5. Anti-lipidemic effect

Increased low-density lipoprotein cholesterol (LDL-C), decreased high-density lipoprotein cholesterol (HDL-C), and elevated TG levels are the hallmarks of dyslipidemia. Furthermore, obesity and insulin resistance have been linked to hyperlipidemia. In a different investigation, G. biloba (10 mg/kg/day) therapy considerably raised HDL-C levels while drastically lowering TG and plasma cholesterol levels in male rabbits when compared to the control group. Moreover, G. biloba has been shown to increase glutathione (GSH) levels and decrease MDA levels in aortic tissue.<sup>[19]</sup>

### 6. Cardiovascular Disease Treatment

The effects of G. biloba seeds on cholesterol metabolism were first investigated by Mahadevan et al., who looked

at how different parts of the seeds, such as whole seeds, water-soluble fraction, and lipid-soluble fraction, mediated lipid metabolism and the prevention of cardiovascular disease.<sup>[20]</sup> According to in vitro research, G. biloba seeds can affect the production of apolipoprotein B and the LDL receptor, which can alter the liver's blood cholesterol levels. Whole seeds raised blood cholesterol levels while decreasing hepatic cholesterol levels in vivo. It is possible that the lipid-soluble part of G. biloba seeds could be employed to minimize the risk of heart disease because it decreased hepatic cholesterol levels while increasing serum cholesterol levels. Mice fed a high-fat diet demonstrated the benefits of ginkgo seed ethanol extract. When compared to untreated animals, the ethanolic extract significantly reduced the weight of epididymal adipose tissue and adipocyte size, successfully preventing fat accumulation and lowering mice's overall body weight.<sup>[21]</sup>

### 7. Effects of Antihypertensive

Acute coronary syndromes, persistent heart failure, and stroke are among the major issues that can result from hypertension, a progressive illness.<sup>[22]</sup> Pathophysiological etiologies linked to the development of hypertension include inflammation, oxidative stress, autoimmune vascular dysfunction, and dysregulation of the renin-angiotensin system.<sup>[23]</sup>

Numerous animal models have demonstrated G. biloba's antihypertensive properties. By preventing renal NO overproduction and lowering IL-6 and TNF- $\alpha$  levels in kidney tissue, EGb 761 demonstrated hypotensive and renoprotective effects in a study of rats with damaged kidneys.<sup>[24]</sup>

### 8. Impact on Reduction of Inflammation

Inflammation is a complicated biochemical process that disrupts tissue homeostasis. Numerous chemical, mechanical, or physical causes might result in either acute or chronic inflammation.<sup>[25]</sup> Inflammation is typically brought on by tissues and migratory cells producing substances such as histamine, prostaglandins (PGs), leukotrienes (LTs), bradykinin, PAF, and IL.<sup>[26]</sup>

### ❖ CONCLUSION

Ginkgo Biloba is a potential herbs having immeasurable beneficial quality in different aspect have been used by our anticancer. It has significant role to destroy diseases cancer, asthma as well as other systems. The Ginkgo Biloba take a unique place in the traditional herbs based remedies and also economical growth of the nation.

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