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A COMPREHENSIVE REVIEW OF GINKGO BILOBA: BOTANICAL CHARACTERISTIC, ETHNOMEDICINAL USES, AND PHARMACOLOGICAL ACTIVITIES

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ABSTRACT

Ginkgo biloba, one of the oldest tree species and is also known as the “living fossil”, it has been used in traditional medicine in Asia, Europe, Cannada, Brazil and the Americas for thousands of years. Its diverse phytochemical profile, mostly consisting of terpene tri-lactones and flavonoids, is believed to contribute to its therapeutic properties. This paper summarizes its phytoconstituents, pharmacological activity, mechanisms of action, and ethnomedical importance. *Ginkgo biloba* has strong neuroprotective, cardioprotective, antioxidant, anticancer, anti-inflammatory, antifungal, antibacterial, antiviral, and antiplatelet properties. The traditional Chinese medicine has employed the leaves and seed(nuts) to treat kidney, bladder, and lungs problem for a long time. The leaves are used in various region for lowering the cholesterol levels Labyrinthitis, and cerebrovascular insufficiency. And people in Greece have utilized its fruit and leaves for treating headaches, depression, coronal sickness arteriosclerosis. Some of the ways these actions happen include by boosting antioxidant defenses, protecting dopaminergic neurons, stopping inflammatory mediators, stopping platelet-activating factor, and stopping topoisomerase II in cancer cells. It also cross the blood brain barrier, enhance synaptic plasticity, lower lipid peroxidation, and protect neuron, liver and heart from oxidative damage. The extract is beneficial to treat Alzheimer's disease, cardiovascular insufficiency, dementia, Parkinson's disease, respiratory diseases,

infections, and problems with circulation. *Ginkgo biloba* is still a useful medicinal plant with a wide range of pharmacological effects that make it a good choice for treating a wide range of conditions. *Ginkgo biloba* can enhance therapeutic accuracy and clinical reliability by integrating traditional herbal advantages with modern pharmacological innovations. To fully exploit its medicinal potential, further research and development are essential.

KEYWORDS: *Ginkgo biloba*, Anti-Cancer, Neuroprotective, Anti hyperlipidemic.

INTRODUCTION

Ginkgo biloba leaves, commonly referred to as ginkgo, represent the sole surviving species of Ginkgoaceae and are among the most ancient trees globally. Many people call it a "living fossil".[1] The leaves of the Ginkgo biloba plant are from China and have been grown all over Asia. Ginkgo trees grow best in full sun and soil that is not too dry.[2] According to the earliest records, the tree originated in an area south of the Yangtze River. It wasn't until the middle and late 1700s that *ginkgo biloba* was brought to North America and Europe. The tree is currently grown as an ornamental shade tree in Europe, Japan, Australia, Southeast Asia, and the United States because of its exceptional beauty and fan-shaped bilobed leaves.[3] Additionally, China, France, Korea, and the US all commercially grow it.[4] Traditional Chinese medicine has used leaf extracts for more than 5,000 years. These days, many people grow it for its nuts and leaves. The Materia Medica, a Chinese herbal encyclopedia written around 2800 BC, talks about how ginkgo can be used to treat illnesses. Ginkgo leaves were used in traditional Chinese medicine to treat asthma, vertigo, tiredness, tinnitus, and problems with the circulatory system. People have long used ginkgo nuts to cure coughs, fevers, sputum, diarrhea, gonorrhea, toothaches, and skin problems, and to make it less common for people to urinate.[5] Ginkgo seeds were used to cure leucorrhea, coughs, bladder irritation, alcohol misuse, and asthma. *Ginkgo biloba* leaves were added to contemporary Chinese pharmacopoeias to treat lung and heart conditions.[6]

Researchers have been interested in G. biloba for decades, looking at how it works and finding novel ways it can help people. Terpenoids and flavonoids are two active ingredients in Ginkgo biloba extract that have antioxidant, anti-asthmatic,[7] skin-regenerating, and wound-healing capabilities.[8] Some studies also demonstrate that *Ginkgo biloba* extract can help blood flow, stop clots from forming, strengthen the walls of capillaries and their flexibility, and protect nerve cells from damage that might happen when they don't get enough oxygen.[9] *Ginkgo biloba* is widely used to treat different stages of Alzheimer's

disease, concentration problems (or even concentration deficit disorder).[10,11] dementia and memory loss, cerebral insufficiency, and intermittent claudication, which causes pain and cramps in the legs due to blocked arteries and usually leads to hearing loss. It is important to note that each component of *Ginkgo biloba* extract possesses a distinct therapeutic mechanism, and the collective action of these mechanisms contributes to the extract's distinctive pharmacological efficacy.[12]

TAXONOMY

Ginkgo biloba is a survivor species since it is the only living member of the Ginkgophyta plant lineage.[13] As a result, it belongs to a unique group called the Ginkgophyta. The reproductive traits of this taxon set it apart from conifers.[2]

Table 1: Taxonomical Classification of *Ginkgo Biloba*.[14]

S.No	Taxonomic Rank	Classification
1.	Domain (Area)	Eukaryote
2.	Kingdom	Plantae
3.	Division	Ginkgophyte
4.	Section	Gymnospermae
5.	Class	Ginkgospida
6.	Order	Ginkgoales
7.	Family	Ginkgoaceae
8.	Genus	Ginkgo
9.	Species.	Ginkgo biloba

Figure 1: Tree of *Ginkgo biloba.*

Figure 2: *Ginkgo biloba.*

ETHNOBOTANICAL AND ETHNOMEDIC

Ginkgo biloba is a tree that looks appealing and has health benefits.[15] Many cultures have employed it for healing, including in Asia, North America, South America, Europe, and

Australia. There are fascinating anecdotes of how people in Asia, especially China, have used ginkgo plants in the past.

- For many generations, Traditional Chinese Medicine (TCM) has employed the leaves and seeds (nuts) of this tree to treat a wide range of illnesses.[16]
- People have used its nuts to treat alcoholism, bladder discomfort, and lung problems like asthma and bronchitis.
- Traditional Chinese Medicine (TCM) has used its raw nuts, which have had their fleshy pulp removed, to cure kidney, bladder, and lung problems for a long time.[17]
- Doctors have given its leaves to many people to help with lung difficulties, skin infections, and heart problems.[18]
- The seed, called Eunhaengnamu, is used in Korea to treat a multitude of diseases, such as asthma, high blood pressure, and the common cold.[19]
- Traditional Indian medicine often uses G. biloba leaves extract to help with memory issues like Alzheimer's illness.[20]
- In the US, it has been used to treat brain problems, angina pectoris, asthma, erectile dysfunction, vertigo, and tinnitus.[21]
- In Iran, people use its leaves, which are often called Jinko, a lot to help with earaches and tinnitus.[22]
- In Brazil, some have said that the leaves of this plant can help with labyrinthitis. Also, it is a well-known plant in traditional European medicine.[23]
- Traditional healers in Canada say that it is one of the top 20 herbs for enhancing memory and blood and circulation problems.[12]
- In Argentina, its leaves have been suggested as a way to lower cholesterol, lower lipids, and lower cholesterol levels.[24]
- People in Greece have utilized its fruits and leaves to treat headaches, depression, coronal sickness, arteriosclerosis, and ear difficulties.[18]
- In France and Germany, its leaf extract works quite well to treat peripheral vascular and cerebrovascular insufficiency and atherosclerotic illnesses.[25]
- Mabed agaci, a tea produced from its leaves, has been used in Turkey to help people remember things better. People in Edo State, Nigeria, think that its leaves can help with high blood pressure. In addition, G. biloba is commonly used in Australia's herbal stores to help people with dementia and Alzheimer's disease.[19] The most popular uses of G.

biloba in ethnomedicine seem to be for treating respiratory problems, heart disease, nervous system ailments, urinary problems, and memory problems.[26]

PARTS OF GINKGO BILOBA

Figure 3: This are the parts of ginkgo biloba tree.

PHYTOCHEMICALS

Phytochemical investigations on Ginkgo biloba resulted in the extraction of various secondary metabolites, such as iso-flavonoids, flavones, anthocyanidins, terpenes, steroids, phytosterols, carotenoids, polyphenols, and additional categories of secondary metabolites from its distinct components. There are phenolic chemicals, especially flavonoids, in practically all of Ginkgo biloba's sections.

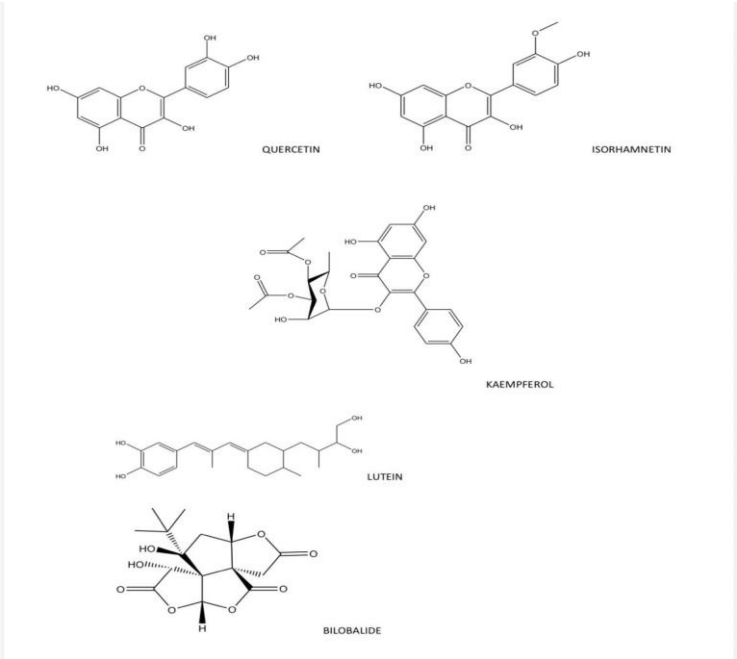


Figure 4: Phytoconstituent of *Ginkgo biloba.*

FLAVONOID

Flavonoids are a large group of secondary metabolites that plants make. They are polyphenolic compounds with low molecular weights that help plants grow and protect them in many ways. Some of them are proanthocyanidins, flavones, flavonol and its glycosides, acylated flavonol glycosides, bi-flavonoids, and flavan-3-ols. Many of these flavonoids are derived from the aglycones quercetin, kaempferol, and isorhamnetin.[27]

Ginkgoaceae

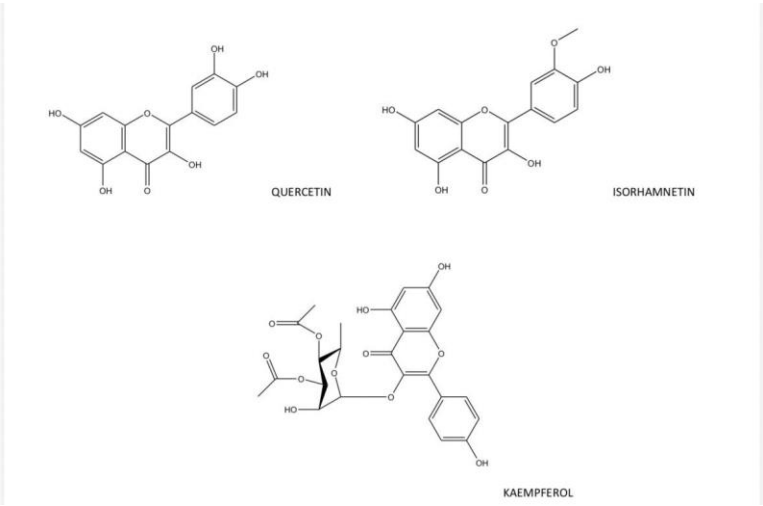


Figure 5: Chemical structure of flavonoids

TERPENES

Terpenes diterpenes and sesquiterpenoids are the two main terpenoids that scientists have found and isolated from Ginkgo biloba. Ginkgolides, also known as diterpenes, are the most important parts of Ginkgo biloba. The ginkgolide structure has six rings: three lactones, a tetrahydrofuran, and a spiro.[4.4] nonane carbocyclic ring. Ginkgolides are very stable and have a caged structure, even though they have numerous oxygen functions. The sole thing that makes ginkgolides different is the number and arrangement of hydroxyl groups.[2] So far, ten ginkgolides have been taken out of Ginkgo biloba. Ginkgolide K (GK), L (GL), and N (GN) are dehydration derivatives (between C-3 and C-14). Ginkgolide A (GA), B (GB), C (GC), J (GJ), M (GM), P (GP), and Q (GQ) are different because they have different hydroxyl substitutions at C-1, C-3, and C-18. Bilobalide (BB) is a monoterpene discovered in Ginkgo biloba that has a sesquiterpenoid structure. Ginkgolides and bilobalide are both types of terpene tri-lactones (TTLs).[13]

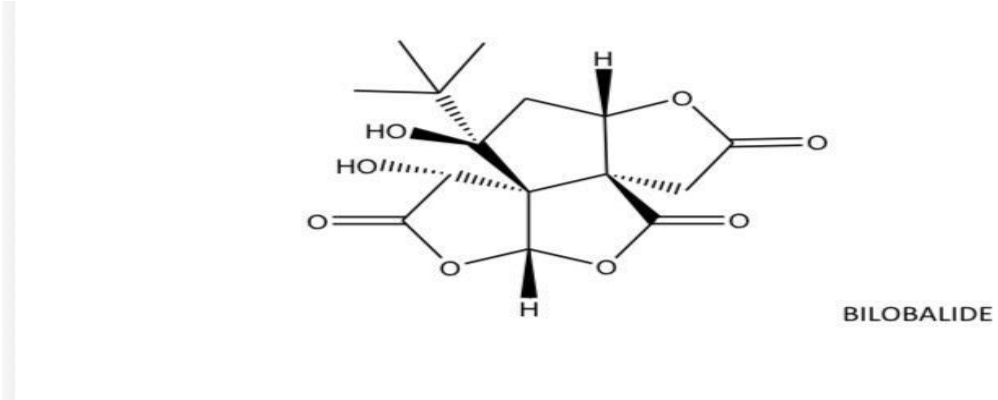


Figure 6: The chemical structure of bilobalide.

STEROL

Researchers have found many steroids and phytosterols in different parts of G. biloba. Campe-sterol, dauco-sterol, stigmasterol, β-sitosterol, ergosterol, stigmast-3,6-dione, and stigmast-4-ene-3,6-dione are some of these.[28]

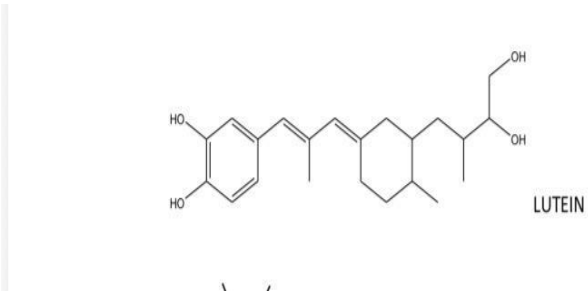


Figure 7: The chemical structure of lutein.

CAROTENOID

In G. biloba leaves, the carotenoids are either xanthophylls, which have oxygen, like lutein and zeaxanthin, or carotenes, which are pure hydrocarbons without oxygen, like α-carotene.[29]

PHARMACOLOGICAL EFFECT

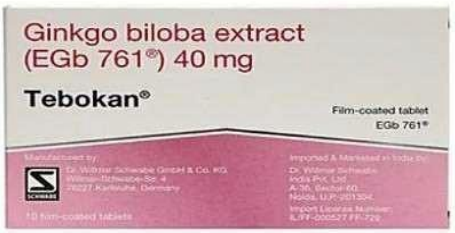
Table No. 2: Table for the pharmacological action of Ginkgo biloba.

S.NO.	Pharmacological Effect	Parts of plant used	Major Phytoconstituent	Mechanism of Action
1.	Neuroprotective	leaves	flavonoids (quercetin, kaempferol, isorhamnetin), terpene trilactones (ginkgolides A, B, & C & bilobal).	Crosses the blood-brain barrier, reduces Aβ aggregation,[30] diminishes neuronal death, enhances synaptic plasticity, stabilizes the mitochondrial membrane,[31] and safeguards dopaminergic neurons.[32]
2.	Antioxidant	leaves	Flavonoids, terpenoids	get rid of reactive oxygen species (ROS), lower superoxide dismutase (SOD), raise glutathione peroxidase (GPx),[33] raise catalase, lower lipid peroxidation, and protect neurons, liver, and heart from oxidative damage.[34]
3.	Anti-inflammatory	leaves	flavonoids, terpenoids,	decrease cyclooxygenase 2 (COX-2).[35] prostaglandin E 2 (PGE 2), nuclear factor (NF)-κB activation,[36] leukocyte adhesion, and interleukin IL-1β-induced mucus secretion.[37]
4.	Anti-asthmatic/airway protection	leaves	Flavonoids, ginkgolides.	Reducing mucus formation and bronchodilation caused by interleukin IL-1β lowers inflammation in the airways.[38]
5.	Anti-cancer	leaves	Quercetin, kaempferol, terpene tri-lactones	Inhibits topoisomerase II, which causes DNA damage in cancer cells, triggers apoptosis,[39] and lowers Tumor necrosis factor TNF-α alters the expression of genes involved in DNA replication.[40]
6.	Cardioprotective	leaves	Flavonoids, terpenoids	terpenoids Reduces oxidative damage to the heart, lowers lipid peroxidation, lowers inflammation in the heart, raises levels of glutathione

				(GSH), and protects the myocardium.[41]
7.	Antiplatelet/Antithrombotic	leaves	Ginkgolides A and B	It stop platelet-activating factor (PAF), raises the level of thrombomodulin.[42] and raises the level of t-PA. This breaks down clots and lowers the level of thromboxane (TXA2) and Ca^{2+} mobilization.[43]
8.	Antimicrobial	leaves	polyphenols, flavonoids	It damages bacterial membranes, interferes with metabolism, tampers with bacterial proteins, and inhibits bacterial growing.[44]
9.	Antiviral	leaves	Flavonoids, Terpenoids	Inhibits SARS-COV-2 3CL pro,[45] it stops the entry of HSV-1 and HSV-2, binds and inactivates viral particles, and lowers the risk of infection.[46]
10.	Antifungal and Antibacterial	leaves	Polyphenols, Terpenoids	It breaks down fungal cell walls, stops Candida from growing, works well against S. aureus, and has a modest effect on both gram-positive and gram-negative bacteria.[47]

COMMON MARKETED FORMULATION OF GINKGO BILOBA

Table No. 3: Table for the most popular Ginkgo biloba products on the market.

S.No.	Name of the formulation	Application	Formulation
1.	Tebokan (40 mg)	It makes it easier to think, remember, and learn new things.	
2.	INLIFE since 1973 GINKGO BILOBA (120 mg)	To help the brain work properly and make you more mentally attentive	

3.	Ginkgo biloba (230 mg)	To help with memory, thinking, and mental clarity	
4.	Hering Pharma Ginkgo Biloba (30 ml)	It helps blood flow to the brain.	
5.	Ginkgo 60 (60 mg)	It helps the heart and mind work normally.	
6.	Ginkgo Biloba Tablets IP (40 mg)	To help their memory, focus, and cognitive performance by getting more blood to the brain.	
7.	Organic Ginkgo Biloba extract powder (50–500 mg)	It helps blood flow better, especially to the brain, and to reduces stress.	

8.	Ginkgo Biloba (60 mg) Dietary Supplement	It used to help the brain work well, remember things, and keep blood flowing.	

CONCLUSION

The review demonstrated that ginkgo biloba is a medicinal plant with many medicinal properties that show pharmacological action. Flavonoids and terpenoids are the major phytoconstituents of the plant. They have many bioactivities, such as protecting the brain, reducing inflammation, and fighting cancer, bacteria, fungi, viruses, and platelets. These mechanisms could potentially be used to treat heart disease, neurological conditions, oxidative stress, infections, and inflammatory disorders and stop tumors from growing. However, poor solubility, short half-life, and low gastrointestinal absorption continue to constrain its clinical efficacy. Microspheres are a novel drug delivery system that helps overcome the limitation by enhancing the gastro-retention time, which improves sustained release and increases the bioavailability of the active constituents. There is evidence that ginkgo biloba can help with health problems, but there isn't enough research on a large scale to fully use its medicinal properties. More research and development are needed.

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