

A NOVEL APPROACH OF GINKGO BILOBA: PHARMACOGNOSTIC REVIEW WITH PHARMACOLOGICAL ACTIONS, CURRENT USES AND FUTURE PROSPECTS

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Received date: 21 October 2021

Revised date: 11 November 2021

Accepted date: 01 December 2021

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1. INTRODUCTION

Ginkgo biloba is a “living fossil” that has existed for about 200 million years on the earth. It is one among the most widely used medicinal plants in the world. Terpenoids, polyphenols, allyl phenols, organic acids, carbohydrates, fatty acids and lipids, inorganic salts, and amino acids are among the secondary metabolites produced by the plant.^[1] The world’s oldest tree has been shown to have “anti-aging” characteristics. Even if you disagree with Mother Nature’s creative licence, the use of ginkgo as a cure for age-related and other ailments is backed by a large body of scientific evidence. According to a Chinese source, ginkgo leaves have been used medicinally since 1505.

In modern Chinese medicine, ginkgo biloba is utilised to improve brain function and relieve stress.^[2] Although Alzheimer’s disease has no cure, promising research and development for early detection and therapy is presently underway. Furthermore, deciding on an acceptable treatment method is a challenging undertaking. However, there is still a significant clinical difficulty in combating Alzheimer’s disease. Several medication treatments are available to aid in the prevention of certain diseases. Researchers from all over the world are focusing on new therapies and prevention measures to discover a cure for the disease’s symptoms.^[3] Glaucoma is a neurodegenerative eye disease that results in visual loss due to the death of retinal ganglion cells. Elevated intraocular pressure is the most common recognised cause of retinal ganglion cell damage (IOP). Alternative medical treatments, particularly Ginkgo Biloba extract, have been proposed as a possible treatment option for normal-tension glaucoma. In 1965, Dr. Willmar Schwabe’s preparation, EGb 761, was the first to introduce GBE to the European market, and it is still used as a criterion standard today.^[4] Annual sales of ginkgo are expected to reach approximately \$500 million in Europe, where it is approved as a prescription drug. Standardised ginkgo extracts were first launched in the United States in the mid-1980s, and they are now available without a prescription. Ginkgo is said to help with a wide range of medical conditions, many of which

are chronic. Their pathophysiology and aetiology appear to be unrelated.^[2] Ginkgo seeds have been used in Chinese medicine for thousands of years to cure cough, asthma, enuresis, alcoholism, pyogenic skin infections, and intestinal worm infections (van Beek and Montoro, 2009). Chinese and Japanese cuisines have used the seeds.^[5]

2. Scientific classification of ginkgo biloba pharmacognostic profile^[6,7,8]

- ❖ Plantae is the kingdom of plants.
- ❖ Ginkgophyta is a division of the Ginkgophyta family of plants.
- ❖ Ginkgopsida is a subclass of Ginkgopsida.
- ❖ Ginkgoales is a genus of ginkgo trees.
- ❖ Ginkgoaceae is a family of plants.
- ❖ Ginkgo biloba or G.biloba is the name of the species.

Source: Botanical

Ginkgo biloba leaves are a type of Ginkgo plant that belongs to the Ginkgoaceae botanical family. Some common names are Ginkgo, Kew tree, Ginkyo, Yinhsing (Japanese Silver Apricot), Maidenhair tree, Fossil Tree, and Salisburia Adiantifolia.^[6,7,8] The leaves of the “Maidenhair fern” are referred to as “Maidenhair tree” in

English (adiantum).^[10] Due to its millions of years of existence, it is called a living fossil.^[9]

Geographical source^[6,7,8]

The leaves are bilobed, with each lobe having a delicate radiating, fan-like venation; it is native to China and Japan and is grown as an ornamental in many temperate countries. The leaf is completely margined, glabrous, and petiolate. Synonyms and Common Names Ginkgo biloba, often known as ginkgo or gingko and also referred to as ginkgo, is a tree species endemic to China. Ginkgo is a misspelling of the Japanese word Yin-Kwo, which means Silver Fruit or Silver Apricot. The bilobed shape of the plant leaves is referred to as biloba. Ginkgo biloba L is a unique plant that has no living relatives. Latin name: Ginkgo biloba English: Maiden hair tree called Living Fossils, Kew tree, Fossil tree, Japanese silver apricot Hindi: Balkuwari Trade name: Ginkgo.

Habitat

Ginkgo was first transported to Europe around 1730, and it is now widely planted in China, Korea, France, Germany, and the United States as an ornamental tree in streets and parks as well as a medicinal plant. The Ginkgo biloba tree has divided leaves and is tall, sturdy, and extremely long-lived.^[10]

General description^[6,7,8]

The tree is a deciduous, resinous, dioecious deciduous tree.

It has a dichotomously veined petiole and a lengthy petiole. Only one of the two ovules on a long peduncle in the female reproductive system matures most of the time. Height - Trees can grow up to 60 metres tall. The inflexible branches are adorned with elongated and spur shoots.

Shape - Seeds are plum-like in shape, yellowish and drupe-like in appearance, up to 2.5cm long, long peduncled, with a fleshy outer coat and a stony inner coat, with a fleshy outer coat and a stony inner coat.

Odour - If the pulp is taken from the seeds, it can cause dermatitis, or skin irritation, and the smell might stay for a long time on their hands.

Taste -Plum, and hence the nut, can have a delicate texture and a slightly bitter flavour with undertones of the tree's signature aroma.

Size- 50 to 80 feet tall and 30 to 40 feet wide are the dimensions.

Shape- The leaves in the centre are alternately clustered, fan-shaped, and cut.

Lifespan- G. biloba may be a beautiful tree with a long lifespan, and it is highly resistant to insects, bacterial, and viral infections. Ginkgo has a long juvenile phase, usually taking 20 to 30 years to attain sexual maturity.

History of cultivation

Ginkgo trees have been cultivated in China for generations, with some temple trees dating back over

1,500 years. Europeans first noticed the tree in Japanese temple gardens in 1690, when German botanist Engelbert Kaempfer discovered it. The ginkgo is commonly planted in Korea and parts of Japan due to its position in Buddhism and Confucianism; some naturalisation has occurred in both areas, with ginkgo seeding into natural woods. Ginkgo trees are male cultivars (cultivated species) that are grafted onto seedlings since male trees do not produce the foul-smelling seeds. "Autumn Gold," a popular cultivar, is a clone of a male plant. Female cultivars include "Liberty Splendor," "Santa Cruz," and "Golden Girl," which gets its name from the bright yellow hue of its leaves in the fall. It's also a PLANT FOR THE GARDEN otherwise called ORNAMENTAL PLANT. Even in metropolitan environments, they are rarely afflicted by disease and are only occasionally attacked by insects. Ginkgo trees are popular as urban and shade trees for this reason, as well as their general attractiveness. Spring leaves have a larger content of flavonol glycosides, while fall leaves have a higher quantity of biflavones. In cell cultures, glycosides have been discovered.^[12]

Chemical constituents

Root-bark: Ginkgolides A, B, C & M

Plant: bilobalide, bilobanone sesquiterpene

Fruit: anacardic acids, ginnol, bilobols, cardanols.

Leaf: Flavonoids glycosides, terpenoids^[7,8] flavonols, biflavonoids, diterpenes, sesquiterpene bilobalide A, β -sitosterol, ginkgolides A, B & C, shikimic acid, sequoyitol, 1,5-Me Obilobetin About 40 flavonoids, including kaempferol glycosides, quercetin derivatives, and isorhamnein derivatives, have been extracted from the leaves. A number of biflavonoids based on amentoflavone are also synthesised by the tree. Long chain hydrocarbons and derivatives, as well as long chain phenols having anti-tumor, anti-microbial, and toxic effects, have been identified from the leaves.^[11]

3. Mechanism of action of Ginkgo biloba and its active chemical constituents

Pharmacological activity

Ginkgo, which has a wide range of pharmacological activity, is an excellent therapeutic target.

Anti-bacterial activity

The plant's methanolic, ethanolic, chloroform, and hexane extracts were tested in *Agrobacterium tumefaciens*, *Bacillus subtilis*, *E. coli*, *Erwinia chrysanthemi*, and *Xanthomonas phaseoli* strains. Assays for disc diffusion and broth dilution were performed. The following was the order of the activity:

Methanol, Ethanol, Chloroform, and Hexane are the steps from Methanol to Ethanol, Chloroform, and Hexane.^[16,17]

Anti-oxidant activity

In 2015, Fermino et al. showed that the plant extracts (EGb 761) have a strong antioxidant effect. Low toxicity was also confirmed. Flavonoids are polyphenolic compounds that are found in plants. The antioxidant activity of this plant is due to its presence of flavonoids.^[3,16]

For glaucoma treatment

Ginkgo biloba has been demonstrated to improve ocular blood flow in glaucoma sufferers. A placebo-controlled experiment in eleven volunteers is part of the evaluation approach. Doppler imaging was used to assess ocular blood flow before and after the study. The extract increases the end diastolic velocity of the ophthalmic artery but has no effect on systemic arterial blood pressure, intraocular pressure, or heart rate.^[4]

For impotence treatment

A total of sixty impotent patients were investigated. Objective tests had revealed diminished penile arterial blood flow in all of the patients, and they had all failed to respond to papaverine injections. Ginkgo biloba was given to each patient at a dose of 60 mg per day for 12 to 18 months. After six to eight weeks of treatment, improvements in penile arterial blood flow were visible on duplex sonography. A total of sixty impotent patients were investigated. Objective tests had revealed diminished penile arterial blood flow in all of the patients, and they had all failed to respond to papaverine injections. Ginkgo biloba was given to each patient at a dose of 60 mg per day for 12 to 18 months. After six to eight weeks of treatment, improvements in penile arterial blood flow results of improved potency were visible on duplex sonography.^[2]

Anti-coagulant and Memory enhancer

GBE's neuroprotective impact has been proven in a number of in vitro and in vivo investigations. GBE protected cultured neurons from mortality caused by hydrogen peroxide, hypoxia, glutamate, verapamil, amyloid- β , 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), nitric oxide (NO), and cyanide, according to in vitro investigations. In addition, after transient middle cerebral artery occlusion (MCAO) in rats, EGb761 (10–100 mg/kg, p.o. (per os) or i.p. (intraperitoneally) was found to reduce neuronal damage and improves memory enhancer.^[3]

Antidepressant and neuroprotective effects

GBE has the anti depressant property of reversible inhibition of two MAOA and MAOB enzymes, while the flavonoid and terpenoid content in GBE contributes to the antioxidant, anti-inflammatory, and neuroprotective properties. Ginkgo biloba improves cognitive and neurological performance by regulating vascular flow and inhibiting platelet activation, which protects the brain from ischemic injury.^[3]

Anti-inflammatory activity

Purified polysaccharide (p-PGBL) was used to demonstrate the plant's anti-inflammatory activity on a lipopolysaccharide-induced inflammatory response. The experiment was conducted both in vitro and in vivo. The extract has been shown to inhibit the TLR4/NF- κ B signalling pathway.^[16]

Anti-mutagenic activity

5- Fluorouracil with GBE 761 ONC (Special extract of Ecb 761) improves the drug's efficacy and tolerability as a second-line treatment for metastatic colorectal cancer. While the medicine was being tested, the dose of GBE 761 ONC required to cause the effect was discovered to be 350mg. The dose was discovered to be 500mg/m².^[16]

Cardiovascular Disease and Hypolipidemic activity

Ginkgo biloba extract can be employed as a hypolipidemic activity, according to a study conducted by Dubey et al (2005). The albino white rats were divided into four groups: normal control, cholesterol control, group fed cholesterol and lovastatin, and three other groups fed cholesterol and ginkgo biloba doses of 25mg/kg, 50mg/kg, and 100mg/kg. As the trial progressed, it was discovered that the groups given ginkgo biloba extract saw a decrease in cholesterol from 9.51 to 16.31 percent, despite the fact that the decrease was not proportional to the increased doses of the plant extract.^[16] Herbal medicines may contain antioxidant, vasodilator, anti-inflammatory, anti-proliferative, or diuretic properties. It can also inhibit endothelial dysfunction, platelet activation, lipid peroxidation, ROS generation, and macrophage atherogenicity, as well as prevent VSMC phenotypic flipping reduce CVDs.^[17]

Hepatoprotective activity

Ginkgo biloba composite (GBC) was found to be effective in preventing the development of liver fibrosis in chronic hepatitis in a preliminary study. Ginkgo biloba can also be utilised to protect the liver from carbon tetrachloride damage by giving protection against the oxidative damage caused by carbon tetrachloride, according to a study conducted by K. Ashok Shenoy et al.^[16]

Anti-diabetic (Hyperglycaemic) activity

The plant extract was found to be useful in modulating the hypoglycemic action of the medication tolbutamide in a study conducted by T Sugiyama et al. Sulfonylureas of the first generation include tolbutamide and sulfonylureas of the second generation include tolbutamide and tolbutamide. The hepatic cytochrome P450-mediated mechanism was responsible for the change in tolbutamide's efficacy.^[16]

Alzheimer's disease

GBE helps to reduce A β fibrillogenesis and A β induced toxicity simultaneously increase mitochondrial function. It suppress oxidative imbalance, decrease mental dyshomeostasis, reduce caspase 3 & 12 and inhibit apoptosis. Improve the quality of Alzheimer's disease patient's life.^[2,3]

Vertigo

For three months, 70 individuals with recent-onset idiopathic vertigo were given either ginkgo or a placebo. Ginkgo was found to be much more helpful than placebo in terms of symptom intensity, frequency, and duration.

After three months, 47 percent of ginkgo patients were symptom-free, compared to 18 percent of placebo patients.^[2]

4. Phyto-Chemical tests

Phytochemical analysis: Ginkgo biloba extracts were utilised to identify antioxidant components in addition to antioxidant analysis. Using high-performance liquid chromatography, several phytochemicals from Ginkgo biloba extracts, such as phenolic acids and flavonoids, were examined.^[11]

Macular degeneration

As people get older, they are more likely to lose their vision. The most prevalent cause of vision loss in the elderly is age-related macular degeneration, which is considered to be caused in part by oxidative damage to the retina. Ginkgo was found to reduce the decrease in retinal function in rats with alloxan-induced diabetes in one investigation. Ginkgo's benefit appears to be attributable to a decrease in free-radical damage.

5. Traditional use

Ginkgo biloba is a popular supplement that contains an extract from a tree. It has the potential to improve cognitive function. Soothing a bladder infection and enhancing sexual vigour are two traditional uses. This supplement should not be taken by those who are on certain antidepressants.^[2,3,11,16]

6. Scope of ginkgo biloba as a medicine in the future

The current state of Ginkgo biloba leaf exploration and utilisation in China. We stress the importance of further research into Ginkgo biloba's intra-specific genetic variety, as genetic variation within this species might lead to significant changes in chemical and pharmacological qualities among sub-species. As a result, it's critical that we document the intraspecific variation of Ginkgo biloba L., and we emphasise the need of preserving this diversity because distinct subspecies may have different pharmacochemical properties, resulting in diverse medical applications.^[18]

7. CONCLUSIONS

Apart from showing a potential therapeutic role in cardiovascular disease-related circulation difficulties and ageing damages in central nervous system illnesses, ginkgo biloba offers a variety of other positive effects. Intermittent claudication, male impotence, and sexual dysfunction have all been cured with it. Ginkgo biloba has been shown to help with diabetes, macular degeneration, premenstrual syndrome (PMS), tinnitus, and stress relief. As a result, ginkgo is an ideal therapeutic target because it has a wide range of pharmacological activities.

Financial disclosure statements

The author received no specific funding for this work.

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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