Pharmacognosy, phytochemistry, pharmacology and clinical application of *Ginkgo biloba*

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GSC Biological and Pharmaceutical Sciences, 2021, 16(02), 229–240

Publication history: Received on 19 July 2021; revised on 24 August 2021; accepted on 26 August 2021

Article DOI: https://doi.org/10.30574/gscbps.2021.16.2.0249

Abstract

In the present review, we are highlighted various pharmacognostic and pharmacological aspects of the different parts of plant *Ginkgo biloba*. Leaves are mainly potential source of phytochemical constituents. The plant encompasses variety of pharmacological activities namely antioxidant, hypolipidemic, antibacterial, etc. The pharmacological profile of plant is mainly attributed to the presence of chemicals such as Ginkgolide A, Ginkgolide B, Ginkgolide C, Bilobalide, Ginkgotoxin, ginkgolides and bilobalide are the major constituents. The pills with the highest concentration of plant extract (100 mg) allow the intake of the highest antioxidants concentration. It is also used along with 5-flurouracil in cancer treatment. There is need to explore more activities of the plant.

Keywords: *Ginkgo biloba*; Pharmacognosy; Ginkgolide A; Tinnitus

1. Introduction

Herbal medicines have been used for over 5000 years and they are one of the most promising sources of new medicines. *Ginkgo biloba* is one is the medicinal plants widely used in treatment of various diseases and disorders [1]. *Ginkgo biloba* has identity as a valuable plant for mankind since more than 2000 years. The name *Ginkgo* is derived from a wrong transcription of the Japanese name Yin-Kwo (silver fruit), while the epithet *biloba* refers to the bilobed shape of leaves; the English name “maidenhair tree” is due to a resemblance of the leaf shape and veins to maidenhair fern [2-4].

2. Geographical distribution

The *G. biloba* tree, which is native to China, Japan, and Korea, is distributed through cultivation in many parts of Europe, America, and the temperate regions of New Zealand, Argentina, and India [5-6]. Tree also found in other regions (Table 1).

3. Taxonomy

Plant taxonomy is the science that finds, identifies, describes, classifies, and names plants. Taxonomy of *Ginkgo biloba* is given in Table 1. *Ginkgo biloba* is both the Latin binomial and common name of the species. It is also known as "maidenhair tree," owing to its resemblance to the maidenhair fern. The phylum Ginkgophyta catagorizes seed pollen-bearing deciduous plants lacking flowers and fruiting structures. The seed is only found on the female plant, and is surrounded by a fleshy covering. *Ginkgo* is derived from the Chinese and Japanese name for the plant, meaning "silver
apricot,” or "silver fruit," referring to the female seed structure. *Ginkgo* is a translation error; it should be *Ginkyo biloba* is Latin for "two-lobed," referring to the leaf shape [5-7] (Table 2).

**Table 1 Geographical distribution**

| Country | Region                                      |
|---------|---------------------------------------------|
| China   | Zhejiang province, Guangxi, Guizhou, Sichuan province, etc |
| Japan   | Tsukuba, Ibaraki, Okayama, Tokyo, Fukuoka    |
| Korea   | Seoul, Incheon                              |
| Netherlands | Utrecht                             |
| Austria | Vienna University                          |
| France  | Montpellier                                 |
| Germany | Hannover                                    |
| Italy   | Padua                                       |
| North America | Pennsylvania |
| India   | Uttarakhand                                 |

**Table 2 Taxonomy of *Ginkgo biloba***

| Classification | Name       |
|----------------|------------|
| Botanical name | *Ginkgo biloba* L. |
| Kingdom        | Plantae    |
| Division       | Pinophyta  |
| Phylum         | Ginkgophyta|
| Class          | Ginkgoopsida|
| Order          | Ginkgoales |
| Family         | Ginkgoaceae|
| Genus          | Ginkgo     |
| Species        | *Biloba*   |
| Plant part     | Leaf       |
| Common names   | Fossil tree, Kew tree, Maidenhair tree.    |

4. **Morphology**

The plant body of *Ginkgo biloba* is sporophytic, and the sporophyte resembles several conifers in general habit. The trees have a pronounced ex-current habit of growth and attain a height up to 30 meters. The branches are dimorphic i.e. bear long shoots which are of unlimited growth with scattered leaves and dwarf shoots which are short branches of limited growth. A dwarf shoot of 2-3 cm length may be several years old.

4.1. **Leaves**

Leaves may be pale yellow, golden yellow or dark green in colour. Foliar epidermis also exhibits some distinguishable characters in *Ginkgo biloba*. The leaves are hypostomatic (i.e., bear stomata only on the lower surface of the leaf). The *Ginkgo biloba* tress has long and short branches growing at right angles. The leaves grow alternate on the long branches
during spring. They are fan-shaped, leathery and smooth. They are often deeply grooved in the middle of the leaf, producing two distinct lobes, hence the name *Ginkgo biloba* (two lobes) (Fig. 1).

![Figure 1 Leaves](image)

*Ginkgo* leaf is also used orally for preventing acute mountain sickness and aging, regulating gastric acidity, improving liver and gallbladder function, regulating bacterial flora, controlling blood pressure. It is also used orally to treat asthma, allergies, bronchitis, and for various disorders of the central nervous system [8-9]

### 4.2. Trunk

A *Ginkgo biloba* tree can reach 30-40m in height and a spread of 8meters. Trunk can become about 3-4 meters wide in diameter. It is straight columnar and sparingly branched. Young trees have usually a central trunk, pyramidal in shape, with regular, lateral, ascending, asymmetrical branching. It fissures rough furrows with the age [10] (Fig. 2).

![Figure 2 Trunk](image)

### 4.3. Fruits

Female ginkgo tree bears oval to round, 2.5–3.5 × 1.6–2.2 cm fleshy fruits about the size of small jujube (Chinese date). Fruit is normally green when young turning to pale yellow when mature. Its outer, nasty smelling pulp (exocarp) is known botanically as sarcotesta.

![Figure 3 Fruits](image)
A single hard shelled seed enclosing edible embryo (kernel) is situated at the center of fruit. Ginkgo kernels measure about 1.5-2 cm in length and 1 cm in diameter and feature light jade green hue (Fig. 3).

4.4. Flowers
Female flower display an abundance of ovules in pairs on stalks each containing an egg cell, initially very green, but later turning greenish yellow, then orange and brown. The male flowers are ivory-colored, catkin-like pollen cones (microsporangia), 3–6 on each short shoot containing boat-shaped pollen sacs with widely gaping slit (Fig. 4).

4.5. Seeds
The mature seed of Ginkgo is relatively large (20–30 mm x 16-24 mm) and consists of an embryo embedded in the tissue of the female gametophyte surrounded by a thick seed coat. This seed coat consists of a soft, fleshy outer layer (sarcotesta), a hard, stony middle layer, and a thin, membranous inner layer. The seed, devoid of the fleshy sarcotesta, is generally referred to as the Ginkgo “nut,” with dimensions of 19-30 mm x'll-14 mm [9-14] (Fig. 5).

5. Phytoconstituents of plant
The major bioactive compounds of Ginkgo are reported to be terpenoids, flavonoids, biflavonoids, organic acids, polyprenols, and many others. Of these, Ginkgolide A, Ginkgolide B, Ginkgolide C, Bilobalide, Ginkgotoxin, ginkgolides and bilobalide are the major constituents. Ginkgolides can be classified in five forms (A, B, C, J, and M), all having the same molecular geometrical skeleton but different numbers and geometric locations of hydroxyl functional groups. Ginkgolides A, B, and C, and bilobalide have been shown to increase circulatory perfusion, antagonize platelet activating factor (PAF), have neuroprotective effects, and serve as cognitive activators. The flavone glycosides possess antioxidant and mild platelet aggregation inhibiting activities [15-16].

A standardized leaf extract of G. biloba, known as EGb 761, contains 24% flavonoid glycosides, 6% terpenoids, 5%-10% organic acids, and other constituents, and are responsible for numerous health benefits. The flavonoids present primarily as glycosides. Major and minor flavonoids are described below. Standardized extracts of ginkgo leaves are frequently formulated to contain 24% flavonoids and 6% lactones. Other important constituents found in ginkgo include
biflavonoids and traces of alkylphenols, such as ginkgolic acids. Ginkgo also contains ginkgotoxin, which has been reported to be structurally related to vitamin B6 [17-18].

The main active ingredients of *Ginkgo biloba* extract (GbE) are flavones and flavone glycosides ginkgolides, catechin, diterpene, lactones, ascorbic acid, iron-based superoxide dismutase sesquiterpenes p-hydroxybenzoic acid.

- **Major flavonoids**
  
  Major flavonoids are quercetin-3-β-D-glucoside, quercitrin and rutin, etc.

- **Minor flavonoids**
  
  Minor flavonoids are Quercetin, Kaempferol and sorhamnetin

- **Lactone components** [19-22].

### 6. Nutritional value

Other than above phytoconstituents, the plant is rich in nutritional source (Table 3).

**Table 3 Nutritional value of plant**

| Nutrition                  | Amount          |
|----------------------------|-----------------|
| Vitamin B3 (Niacin)        | 6 mg (37.50%)   |
| Copper; Cu                 | 0.274 mg (30.44%) |
| Carbohydrate               | 37.6 g (28.92%) |
| Vitamin B6 (Pyridoxine)    | 0.328 mg (25.23%) |
| Vitamin B1 (Thiamin)       | 0.22 mg (18.33%) |
| Phosphorus, P              | 124 mg (17.71%) |
| Vitamin C (Ascorbic acid)  | 15 mg (16.67%)  |
| Tryptophan                 | 0.071 g (16.14%)|
| Threonine                  | 0.268 g (15.23%)|
| Vitamin B9 (Folate)        | 54 µg (13.50%)  |
| Valine                     | 0.283 g (13.40%)|
| Iron, Fe                   | 1 mg (12.50%)   |
| Isoleucine                 | 0.209 g (12.50%)|
| Potassium, K               | 510 mg (10.85%) |
| Calories in (100g)         | 182 K cal       |

### 7. Pharmacological activities

The plant is reported to show a numerous pharmacological activity.

#### 7.1. Alzheimer’s disease

Ginkgo biloba extract (GBE) standardized to 24% Ginkgo flavon glycosides and 6% terpenoids shows great benefit in senility and AD; increases brain functional capacity; normalizes Ach receptors in hippocampus of aged animals, increasing cholinergic transmission. GBE helps reverse or delay mental deterioration only in early stages of AD; may help patient maintain normal life, avoid nursing home; improves Clinical Global Impression scores, stabilizes AD, and significantly improves mental function without side effects[23].

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7.2. Hepatoprotective effects
In a *Gingko biloba* composite (GBC) was suggested that GBC was effective in halting the development of liver fibrosis of chronic hepatitis. *Gingko biloba* can also be used to protect the liver from carbon tetrachloride damage. Ginkgo has not been specifically linked to liver injury, either in the form of transient serum enzyme elevations or clinically apparent acute liver injury. Indeed, ginkgo is sometimes used to treat acute or chronic liver injury [24].

7.3. Acute pancreatitis
Acute pancreatitis is an inflammatory condition of the pancreas. The plant extract is demonstrated to be highly advantageous in case of acute pancreatitis. The extract reduces serum amylase as well as lipase level. This action of the extract is dependent on the free radical scavenging effect [25].

7.4. Antioxidants effects
Ginkgo contains high levels of flavonoids and terpenoids, which are compounds known for their strong antioxidant effects. Antioxidants combat or neutralize the damaging effects of free radicals. Free radicals are highly reactive particles that are produced in the body during normal metabolic functions, such as converting food to energy or detoxification [26-28].

7.5. Sexual dysfunction
*G. biloba* extract have shown positive result on sexual dysfunction. Extract is potent in treating sexual dysfunction which is induced due to intake of antidepressant drugs. The impotency is considered to be due to selective serotonin reuptake inhibitors (SSRI), serotonin and nor epinephrine reuptake inhibitors (SNRI), monoamine oxidase inhibitor (MAOIs), and tricyclics. On combination with sex therapy the extract was effective for sexual response arousal [29].

7.6. Glaucoma treatment
The extract elevates the ophthalmic artery end diastolic velocity and do not produce any effect on systemic arterial blood pressure, intra ocular pressure or heart rate. Flavonoids, often found in Ginkgo biloba, had a beneficial impact on glaucoma, particularly in terms of increasing ocular blood flow and potentially halting the progression of visual field loss. More quality research is warranted to determine the role in treating glaucoma [30-31].

7.7. Hypolipidemic activity
*Gingko biloba* extract can be used as hypolipidemic agent though not as effective as the cholesterol lowering agent lovastatin. The flavonoid content of the plant is assumed to be responsible for their hypolipidemic action and the plant is estimated to contain 24% flavonoids [32].

7.8. Antibacterial activity
The compounds of plant showed high antimicrobial activity against Gram-positive and Gram-negative bacteria, including several food-borne pathogens. In particular, compounds 5-7 and 8-10, containing phenolic acids and bilobols, respectively, were highly effective against *Salmonella enteric serovar Typhimurium, Listeria monocytogenes, Listeria innocua, Streptococcus pyogenes, Escherichia coli,* and *Shigella dysenteriae.* On the opposite, compounds 1-4, containing cardanols, showed little antibacterial activity [33-35].

7.9. Platelet activating factor antagonist
Platelet activating factor is a phospholipid which act as activator as well as a mediator in many leucocytes function, platelet aggregation and inflammatory process. Gingolide which is the terpene present in the plant has been reported with unique platelet activating factor antagonist activity [36-37].

7.10. Dementia and cognitive impairment
Ginkgo has been repeatedly evaluated for its ability to reduce anxiety, stress and other symptoms associated with Alzheimer’s disease and cognitive decline associated with aging. Some studies show a marked reduction in the rate of cognitive decline in people with dementia using ginkgo, but others fail to replicate this result [38-39].

7.11. Vertigo
*Ginkgo biloba* extract could reduce the intensity, frequency, and duration of vertiginous syndrome compared (47% in the EGB group compared to 18% in the placebo group). Another randomized controlled trial in 2014 showed that there
was no statistically significant difference in vertigo treatment outcomes between Ginkgo biloba versus betahistine group though EGb had a better tolerance profile. Again, due to the lack of strength of the evidence, more studies are necessary to establish the efficacy of Ginkgo biloba in treating vertigo.

7.12. Tinnitus

*Ginkgo biloba* was effective in patients with a primary complaint of tinnitus. GB extracted data from systematic reviews concluded the use of *Ginkgo biloba* did not alleviate the severity of tinnitus or improve the quality of life of patients [40-42].

8. Analysis of plant’s extract

There are many analytical tools that are used for the analysis of various pharmaceutical and herbal formulations, crude drugs and their extracts [43-65]. These methods include UV-spectrophotometry, gas chromatography, HPLC, HPTLC, etc [65-110].

9. Conclusion

Thus, the plant could be used as an herbal remedy to treat many conditions. It may be best known as a treatment for dementia, Alzheimer’s disease, and fatigue. It’s often used to treat mental health conditions, Alzheimer’s disease, and fatigue. Other conditions it’s used to treat are: anxiety and depression, schizophrenia, insufficient blood flow to the brain, blood pressure problems, altitude sickness, erectile dysfunction, asthma, neuropathy, cancer, premenstrual syndrome, attention deficit hyperactivity disorder (ADHD), macular degeneration.

**Compliance with ethical standards**

**Acknowledgments**

We express our sincere thanks to Shri. Yogendraji Gode and Dr. Yogeshji Gode, IBSS’s Dr. Rajendra Gode Institute of Pharmacy, Amravati and Dr. Rajendra Gode College of Pharmacy, Amravati (India).

**Disclosure of conflict of interest**

The author declares no conflict of interest.

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