**GINKGO (GINKGO BILOBA L.), A MEDICINAL TREE**

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**Abstract:** *Ginkgo biloba* is a member of family Ginkgoaceae. The ginkgo tree, known to be among the oldest living species on this planet, has flourished in forests for over 150 million years and hence it is called a “living fossil”. The best growing conditions are found on deep sandy and well-drained soils. Active substances are predominantly produced in the roots and then translocated to the leaves. The two main pharmacologically active groups of compounds present in the ginkgo leaf extract are the flavonoids and the terpenoids. Standard *Ginkgo biloba* extract, EGb 761, contains 22-27% flavonoids (ginkgo flavone glycosides) and 5-7% terpenoids (ginkgolides and bilobalides). The extract of ginkgo uses in the treatment of poor circulation, heart disease, eye disease, short term memory loss, brain trauma and depression.

**Key words:** Ginkgo, Medicinal plants, Active substances, Ginkgolides, Bilobalides.

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**INTRODUCTION**

The Ginkgo tree (*Ginkgo biloba* L.; from Japanese ginkyo, meaning silver apricot) or maidenhair tree, is characterized by fan-shaped leaves and fleshy, yellow, foul-smelling seeds, enclosing a silvery, edible inner kernel. *G. biloba* is the only surviving member of a family of trees, Ginkgoaceae, which appeared in the Jurassic period 170 million years ago and for this reason, is called the “living fossil.” There is a gap of 100 million years between the current and ancient tree in the fossil record but recent paleontological findings of a fossil over 121 million years old have shown that the tree has barely changed since the days of the dinosaurs (Stromgaard and Nakanishi, 2004).

The ginkgo tree, known to be among the oldest living species on this planet, has flourished in forests for over 150 million years and hence it is called a “living fossil” (McKenna et al., 2001)

Initially this plant was found in China and it is estimated that it was brought to Europe around the 18th century. At present there are many commercially available preparations made from *Ginkgo biloba* leaves, which results from the broad spectrum of its advantageous action on the human organism (Kobus et al. 2009; Kobus-Cisowska et al., 2010).

It is distinct from all other living plants and is often categorized in its own division, Ginkophyta, by botanical taxonomists. *G. biloba* is believed to be the oldest living tree species and is capable of reaching ages in excess of one thousand years. Recent investigations have used this “living fossil” to evaluate CO$_2$ levels in prehistoric times. stem up to 10 meters in girth. The tree is a resilient survivor in polluted environments, growing where other trees find it difficult, and is exceptionally resistant to attacks by fungi and insects (Stromgaard and Koji Nakanishi, 2004).

Both the leaves and the nuts of this tree have been in use for the past several centuries in traditional Chinese medicine. In fact, the nuts are known to have a longer history of usage, being first mentioned in herbas in the Yuan
The best growing conditions are found on deep sandy and well-drained soils with pH values between 5 and 6. Additional irrigation is necessary to obtain optimal yields if rainfall is insufficient during summer months. In Central Europe, temperatures are too low for an optimal production and late frost may damage sprouting leaves in springtime (Schmid and Balz, 2005).

Germination of untreated seed planted in a soil medium varied from 32 to 85% (Davis and Henery 1942; Swingle 1939). A stratification period has been recommended (Ponder et al., 1981), however 1- to 2-months of warm stratification before cold stratification is also advised to allow seeds to fully mature (Dirr and Heuser, 1987; Willan, 1985). Ginkgo seedlings grown in artificial growth chambers were able to grow continuously for a 20 week period under a 32 to 25 °C day/night regime (16-hour day-length) (Flesch et al., 1991). Ginkgo can also be propagated in the nursery from cuttings treated with 8,000 ppm indolebutyric acid (IBA) and misted for 7 to 8 weeks (Dirr and Heuser, 1987).

Depending on climatic conditions, green ginkgo leaves are harvested in July (USA), August (China) or September/October (France). Leaves are harvested mechanically using modified cotton pickers. In China, leaves are hand picked involving thousands of smallholders and their family members. Yields are between 2 and 4 t of dry leaves per ha depending on site and pruning stage (Schmid and Balz, 2005).

**ACTIVE SUBSTANCES AND UTILIZATION**

Investigation regarding the biochemistry of ginkgo showed that active substances are predominantly produced in the roots and then translocated to the leaves. The extent of production depends on plant age. Cell cultures are unsuitable for in vitro production of relevant terpenes (Balz, 1999).

The two main pharmacologically active groups of compounds present in the ginkgo leaf extract are the flavonoids and the terpenoids (Smith and Luo, 2004). Flavonoids, also called phenylbenzopyrones or phenylchromones, are a group of low molecular weight substances that are widely spread in the plant kingdom. Flavonoids present in the Ginkgo leaf extract are flavones, flavonols, tannins, biflavones (amentoflavone, bilobetol, 5-methoxybilobetol, ginkgetin, isoginkgetin and sciadopitysin), and associated glycosides of quercitin and kaempferol attached to 3-rhamnosides, 3-rutinosides, or p-coumaric esters (McKenna et al., 2001).

The most important substances are flavonoids (ginkgo flavone glycosides) and terpenoids (ginkgolides and bilobalide) (Kleijnen and Knipschild, 1992).

Standard Ginkgo biloba extract, EGb 761 (commercial name), contains 22-27% flavonoids (ginkgo flavone glycosides) and 5-7% terpenoids (ginkgolides and bilobalides), which are the most important active substances in the extract. The most important flavonoids are glycosides of kaempferol, quercetin, and isorhamnatin with glucose or rhamnose (Chao and Chu, 2004).

The most important constituents of the standardized extracts of dried leaves of Ginkgo biloba are flavone glycosides (quercetin, kaempferol, isorhamnetin) and terpene lactones (ginkgolides and bilobalide) (Blecharz-Klin et al., 2009).

Ginkgo biloba extract has been mentioned in the traditional Chinese pharmacopoeia, and used for the treatment of asthma and bronchitis (Kleijnen and Knipschild, 1992; Chao and Chu, 2004).

For over 5000 years, the seeds (nuts) have been known to treat pulmonary disorders (like asthma, cough, and enuresis), alcohol abuse, and bladder inflammation while the leaves have been mainly used to treat heart and lung dysfunctions and skin infections (Mahady, 2002; Smith and Luo, 2004). However, it was only in the last 20 to 30 y that the use of the ginkgo leaf and its standardized extract formulation, EGb 761, originated in Germany, and now is the most used form of supplement for cognitive ailments in the United States (Smith and Luo, 2004).

Ginkgetin or isoginkgetin, is a biflavonoid from Ginkgo biloba extract (Lee et al., 1995). Ginkgetin selectively inhibited the proliferation of human ovarian carcinoma OVCAR-3 cells via the induction of apoptosis in a dosedependent Manner (Su et al., 2010).

An investigation showed the effect of administration of the standardized extract of Ginkgo biloba leaves (EGb 761) on learning, memory and exploratory behavior in water maze and hole-board tests. Rats (18-month old) received for three months EGb 761 at doses: 50, 100 and 150 mg/kg b.w. per day. After completion of the behavioral experiment, concentrations of neurotransmitters were estimated in selected brain regions. The increased level of 5-hydroxytryptamine (5-HT)
in the hippocampus and 5-HIAA (5-HT metabolite) in the prefrontal cortex correlated positively with the retention of spatial memory (Blecharz-Klin et al., 2009).

Clinical studies indicate use of the standardized extract of ginkgo in the treatment of poor circulation, impotence, heart disease, eye disease, tinnitus, chronic cerebral insufficiency, short term memory loss, brain trauma, depression, dementia, and conditions associated with senility (Foster, 1996).

Ginkgo has been used extensively in China to treat kidney infections, kidney stones and other urinary tract disorders. It is considered valuable because it has a tonifying effect on the urinary system (Elkins, 1994).

The added ethanol extracts from Ginkgo biloba leaves limited the rate of oxidation of the fats in the product; however, their efficacy was similar as that obtained with the usage of the BHT synthetic antioxidant used for comparative purposes (Kobus et al., 2010).

In addition, ginkgo increases oxygen transport at the blood-brain barrier site, while inhibiting the permeability of toxins into brain tissue. As well as boosting blood supply to the brain, ginkgo has demonstrated the ability to increase the rate at which information is transmitted at the nerve cell level (Hindmarch and Subhan, 1984).

Stress involves a rise in the levels of glucocorticoids, and a subsequent memory dysfunction, increased anxiety, decreased immunity, gastrointestinal tract disturbances, myocardial infarction, or effects such as increased vigilance (Walesiuk et al., 2005). Since mood and emotion are related to stress, the alleviating effects of Ginkgo leaf extract may result in improving mood, thus resulting in antidepressant activity (DeFeudis and Drieu, 2004).

Evidence suggests that ginkgo may prevent illness due to high altitude hypoxemia (Ajasse, 1984; Roncin et al., 1996; Leadbetter et al., 2001).

Ginkgo biloba Extract (EGB), a natural antioxidant, has recently attracted considerable attention for preventing oxidative stress-related diseases including cancers, cardiovascular diseases, degenerative diseases and central neural system disorders. EGB is a well-known and inexpensive herb that has been used without side effects for centuries. It is an extract from green leaves of the Ginkgo biloba tree. EGB has been showed to have hydroxyl scavenging property, lipid peroxidation restraining capacity and antioxidant enzyme-like activity (Liu et al., 2006).

Treatment with Ginkgo biloba extract lowers fibrinogen levels and decreases plasma viscosity (Witte et al., 1992).

The most unique components of the extracts are the terpene trilactones, that is, ginkgolides and bilobalide. These structurally complex molecules have been attractive targets for total synthesis. Terpene trilactones are believed to be partly responsible for the neuromodulatory properties of Ginkgo biloba extracts (Stromgaard and Koji Nakaniishi, 2004)

Laboratory tests performed on aged rats showed that ginkgo extract works to protect neuronal membranes in the brain. In addition, these tests also showed that the herb has a restorative effect which can help to pre vent the decrease in cerebral receptors that occurs with aging (Juguet et al., 1994).

Ginkgo biloba extract is well known for its antioxidant property, which may result from its ability to scavenge free radicals (Gardès-Albert et al., 1993; Chao and Chu, 2004), and to neutralize ferryl ion-induced peroxidation (Deby et al., 1993; Chao and Chu, 2004).

The antioxidant effect is determined by the presence of flavonoids, capable of free radical scavenging (Kobus et al. 2009; Kobus-Cisowska et al., 2010). Antioxidant potential of extracts from Ginkgo biloba leaves is comparable to that of ascorbic acid, glutathione or alphatocopherol (Kalisch et al. 2006; Kobus-Cisowska et al., 2010).

The compounds in ginkgo act to varying degrees as scavengers for free radicals, which have been considered the mediators of the excessive lipid peroxidation, decline of membrane fluidity, and cell damage observed in Alzheimer’s disease (Stoll et al., 1996; Le Bars et al., 1997).

Several studies have reported that the antioxidant activity of Ginkgo biloba extract could be helpful in the prevention and therapy of diseases and degenerative processes associated with oxidative stress (Chao and Chu, 2004).

The therapeutic mechanisms of action of the Ginkgo leaf extract are suggested to be through its antioxidant, antiplatelet, antihypoxic, antiedemic, hemorrhheologic, and microcirculatory actions, where the flavonoid and the terpenoid constituents may act in a complementary manner. Toxicity studies show that the Ginkgo leaf extract is relatively safe for consumption, although a few side effects have been reported, that is, intracerebral hemorrhage, gastrointestinal disturbances, headaches, dizziness, and allergic skin reactions (Mahadevan and Park, 2008).
The various compounds found in ginkgo may play a protective role in different stages of the decline of intellectual function via several mechanisms of action: vasoregulating activity of arteries, capillaries, and veins (increased blood flow); platelet activating factor (PAF) antagonism; homeostasis of inflammation and oxidative stress; prevention of cell membrane damage caused by free radicals; and neurotransmission modulation (Kleijnen and Knipschild, 1992; Turan and Martorano, 1995).

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