

# Role of Ginkgo Biloba in Alzheimer Disease

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**Abstract:** *Alzheimer's disease is a deadly neurodegenerative disease, with a complex etiology with many potential drug goals. Ginkgo biloba leaf extract has shown beneficial effects in the treatment of memory impairment, cognitive function of daily living (ADL) edema, inflammation and free toxins associated with traumatic brain injury (TBI). Alzheimer's dementia Flavonoid glycosides may have antioxidant effects that may reduce endothelial cell damage due to free radical oxidation thereby reducing the development of atherosclerosis. In addition, extraction of ginkgo may play an important role in treating minor dementia. The purpose of this article is to review the role of Ginkgo Biloba in Alzheimer's disease(AD).*

**Keywords:** Ginkgo biloba, Dementia, Free radical, Alzheimer disease.

## I. INTRODUCTION

Alzheimer's disease (AD) is characterized by senile plaques and neurofibrillary tangles with ongoing involvement of cognitive changes that mainly involve memory loss. The above-mentioned sign of AD therefore illustrates the need to clarify some important questions about how to understand the etiology of the disease. For example, what factor / event causes changes in the processing of amyloid- $\beta$  protein precursor (A $\beta$ PP) that lead to plaque formation and hyper phosphorylation of tau protein leading to seizures? The prevalence of AD varies between several different factors, including age, genetics, associated disease, and level of education. There is no cure for AD; however, promising research and advances in early detection and treatment are ongoing. In addition, developing effective treatment for AD remains an important clinical challenge. Many therapies are available to help prevent various symptoms of the disease, and researchers around the world are focused on finding better treatments, prevention strategies, and finally a cure. Researchers use a variety of synthetic and / or pharmaceutical compounds to test their effectiveness against AD. In this case, polyphenolic compounds from medicinal plants are a major source of neuroprotective agents against AD. Identifying the composition of these bioactive ingredients as synthetic pharmaceuticals provides a variety of potential neuroprotective compounds. Natural polyphenolic compounds give their antioxidant effect by reducing free radical forms, binding to iron, and / or producing endless antioxidant doses. Therefore, antioxidant properties have a positive effect on their neuroprotective effect. Ginkgo's hometown is believed to be the remote mountain valleys in the eastern Chinese province of Zhejiang. A common extract of Ginkgo biloba (GBE) found in dried leaves of Ginkgo is used as a therapeutic drug in the treatment of memory impairment and dementia including Alzheimer's disease (AD). Numerous clinical studies have shown improvements in cognitive function in the elderly and AD patients; however, some reports do not support ginkgo extracted from AD.

The ginkgo tree (Fig.1) has a ripe, apricot-shaped fruit. Thus, the name ginkgo comes from the Chinese word sankyo or yin-kuo. The family name of the ginkgo tree is Ginkgoaceae, from the genus Ginkgoatae. Englbart Kaempfer, a German surgeon, first used the term "Ginkgo" in 1712, but it was Linnaeus who referred to it as Ginkgo in 1771.

### 1.1 Botanical Information



Fig.1 Ginkgo biloba

*Ginkgo biloba* L. belongs to the botanical family of Ginkgoaceae. The common names are Ginkgo, Kew tree, Ginkyo, Yinhsing (Silver Apricot-Japanese), Maidenhair tree, Fossil Tree, Ginkgo Folium, *Salisburia Adiantifolia*. The synonyms are *Salisburia adiantifolia*, *Salisburia macrophylla*, and *Pterophylla salisburiensis*. Today, nearly 500 scientific papers now documenting Ginkgo's effects make it the well-researched botanical medicine available. While firmly rooted in antiquity, GB is today the most frequently prescribed herbal preparation in Germany and one of the most commonly used over-the-counter (OTC) herbal preparations in the United States. The German Commission (equivalent to the US Food and Drug Administration for botanicals) has approved GB for symptomatic treatment of deficits in memory, concentration, and depression from organic brain disease.

### 1.2 Active Ingredients

*Ginkgo biloba*, like many herbal medicines contains many active ingredients, which are believed to have joint effects. Flavonoids include quercetin, kaempferol, and isorhamnetins; trilactonic diterpenes: Ginkgolide A, Ginkgolide B, Ginkgolide C; trilactonic sesquiterpene: bilobalide; and proanthocyanidin is thought to be able to compensate Ginkgo for its therapeutic effects. Other nutrients such as glucose, rhamnose, hydroxykinurenic, kynurenic, protocatechic, vanillic, and shikimic acid, D-glucaric acid, ginkgolic acid and related alkyphenols are isolated. The main active ingredients of ginkgo biloba extract (GbE) are:

- Flavonol and Flavone glycosides
- Ginkgolides
- Catechin
- Diterpene lactones
- Ascorbic acid
- Iron-based superoxide dismutase
- Sesquiterpenes
- P-hydroxybenzoic acid

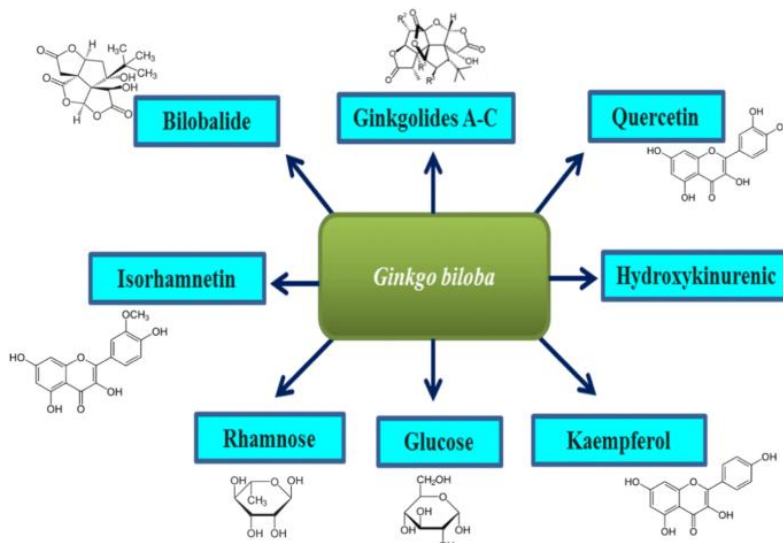


Fig.2 active constituents

GBE combines different elements (Figure 2) such as Trilactonic diterpenes, ginkgolides A, B, and C (ginkgolides J and M, not shown, are present in low concentrations). Flavonoids include quercetin, kaempferol, isorhamnetins, trilactonic sesquiterpene, and proanthocyanidins. Other nutrients such as glucose, rhamnose, hydroxykynurenic, kynurenic, protocatechuic, vanillic, and shikimic acid, D-glucaric acid, ginkgolic acid and related alkyphenols are isolated. Ginkgolides have been specifically shown to act as antagonists of platelet-activating factor (PAF), inhibiting platelet aggregation and promoting blood flow. Flavonoids are known to act as major antioxidants among various polyphenols and also act as heavy metal chelators due to their phenolic properties. They have been clinically tested for inflammatory

diseases and heart disorders. In addition, GBE has shown neuroprotection and anti-inflammatory properties in preclinical models of AD and Stroke.

### 1.3 Mechanism of Action

Ginkgo shows anti-inflammatory effects by disrupting the release of flammable chemicals by competing with inhibiting platelet-activating factor (PAF). Ginkgo contains ginkgolides A and B antagonists that effectively suppress PAF binding to membrane receptor potential potentially neuroprotective and antithrombotic effects. In addition, flavonoid glycosides and gold B may inhibit lipoprotein formation, platelet aggregation, and platelet aggregation which may reduce the incidence of atherosclerosis and vascular injury. In addition, resistance to PAF may prevent cyclosporine-induced nephrotoxicity, and reduce coronary blood flow and myocardial contractility. Additionally, this method may provide beneficial effects on circulatory disorders, hypersensitivity reactions, and bronchospasm. Flavonoid glycosides may have antioxidant effects that can reduce endothelial cell damage due to free oxidation thus reducing the development of atherosclerosis. In addition, the ginkgo extract may result in intestinal mucosa protection against ischemic injury by decreasing neutrophil infiltration and lipid peroxidation, stimulate choline uptake and prevent declension of age-related muscarinic receptors, and decrease blood Viscosity. Further, there is capability restriction effect of ginkgo on monoamine oxidase activity; however, the mechanism of action is unclear.

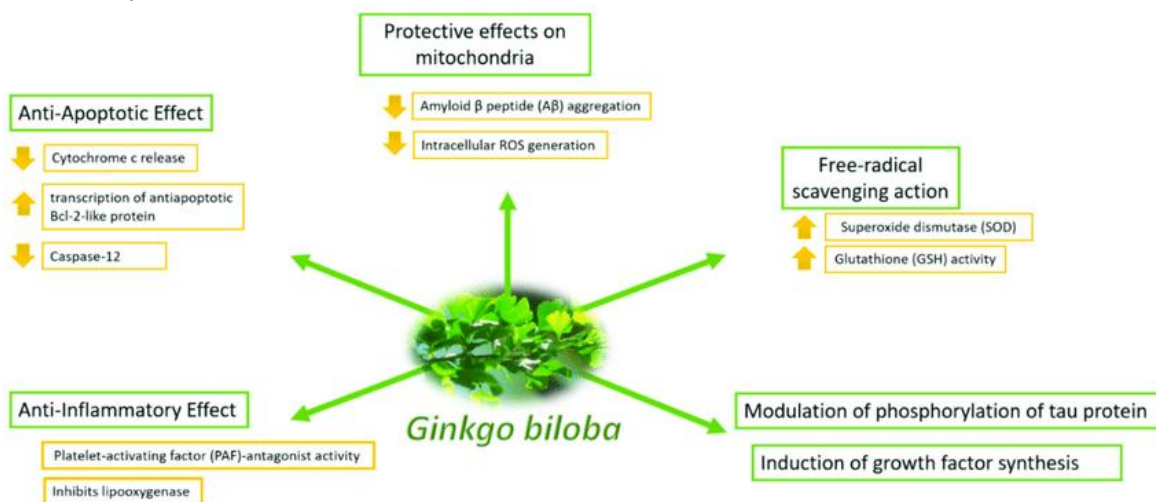


Fig.3 Mechanism of action

### 1.4 Neuroprotective Effects of Ginkgo biloba Extract

The neuroprotective effect of GBE has been confirmed in several in vitro and in vivo studies. In vitro studies have revealed that GBE protects enhanced neurons from death caused by hydrogen peroxide hypoxia glutamate, verapamil, amyloid- $\beta$ , 1-methyl -4-phenyl-1,2,3,6 tetrahydropyridine (MPTP), nitric oxide (NO), and Cyanide. Also, in vivo effect, a reduction in neuronal damage by EGb761 (10-100 mg / kg, p.o. (per os), or i.p. (intraperitoneally)) was observed behind a transient central nervous system. Occlusion (MCAO) in mice and gerbils, focalcerebral ischemia in rats and mice; hypoxia heat stress; chronic cold depression and amphetamine-induced behavioral sensitivity, as well as the transgenic mouse model of amyotrophic lateral sclerosis. Ginkgolides (1–100  $\mu$ M in vitro or 50–100 mg / kg in vivo), bilobalide (25–100  $\mu$ M in vitro or 10 mg / kg in vivo), and in some cases also a fraction of flavonoid (25–100  $\mu$ g / ml in vitro or 40–100 mg / kg in vivo) has been shown to contribute to the neuroprotective effect of EGb 761. Outside. In addition the EGb 761 free radical-scavenging property has also been shown to affect the gene expression of several genes associated with oxidative stress-induced stress. This is important EGB 761 property as it can help to better tolerate cells against oxidative stress thus protecting the neuronal cell from oxidative damage commonly associated with neurodegenerative infectious diseases such as AD and PD status.

### **1.5 Effect of GBE against A $\beta$ Aggregation**

The accumulation of A $\beta$  plaque is a hallmark of AD. Recently, the use of GBE in neuroprotection against A $\beta$ -induced neurotoxicity has gained considerable attention among science community. Several recent studies have shown that GBE protects A $\beta$ -induced neurotoxicity by inhibiting A $\beta$ -induced events, such as glucose uptake, active oxygen. Types (ROS) accumulation, AKT activation, mitochondrial dysfunction, JNK and ERK 1/2 pathways, and apoptosis. It has been reported that GBE inhibits the production of A $\beta$  in the brain by reducing the levels of free circulating cholesterol, as A $\beta$ PP processing and amyloidogenesis should be influenced by free circulation and intracellular cholesterol levels. Despite this evidence, further research is needed to identify the major genes responsible for this anti-amyloidogenic effect. GBE may also disrupt the oligomer formation of A $\beta$ . It is known that the  $\beta$ -sheet structure of A $\beta$  oligomers is primarily responsible for A $\beta$  neurotoxicity and may also aid A $\beta$  release in proteolytic cleavage. A $\beta$  oligomers can also be a very effective strategy to prevent A $\beta$  poisoning. In addition to A $\beta$  self-oligomerization, A $\beta$  interactions with different metal ions, in particular. Copper, iron, and zinc, may contribute to the oligomerization use of A $\beta$ . GBE has iron chelating properties that can also prevent the formation of A $\beta$  fibril. Collectively, we can say that GBE is very effective and outstanding against. Although studies show promising effects of GBE against A $\beta$ -induced toxicity, further research is needed to refine the performance of individual components of GBE against A $\beta$  toxicity in AD.

### **1.6 Antioxidant Activity**

Oxidative stress disequilibrium has been one of the most significant symptoms involved in AD pathogenesis. A few in vitro and in vivo studies support the beneficial action of GBE in particular due to its free radical-scavenging action, as shown in a study in which cerebellar granule cells with GBE effectively reduce oxidative damage. H<sub>2</sub>O<sub>2</sub> / FeSO<sub>4</sub>. In addition, in studies from AD models, A $\beta$ -expressing transgenic *Caenorhabditis elegans* and A $\beta$ -expressing neuroblastoma cell line N2a, GBE was found to significantly reduce basal and induced levels of active H<sub>2</sub>O<sub>2</sub>-related oxygen. (ROS). In addition to the direct reduction of ROS, GBE may also be helpful in regulating antioxidant enzymes and protein levels. For example, superoxide dismutase (SOD) and catalase activity have been found to be elevated in rat hippocampus and rat ileum combined with GBE. Glutathione (GSH) reductase and gamma-glutamylcysteineyl synthetase, two important enzymes used in the reduction process of GSH synthesis, are also enhanced by GBE. The main active and responsible component of antioxidant activity in the extraction of GBE flavonoids. Previous studies have suggested that the flavonoid antioxidant component of the flavonoid component is ROS scavenging, an increase in antioxidant proteins such as SOD and GSH, and chelating prooxidant transitional metal ions. Quercetin and myricetin are two flavonoid structures that effectively inhibit tert-butylhydroperoxide oxidation. In contrast, the antioxidant activity of terpene lactones remains to be determined. Differences in the antioxidant activity of terpene lactones may be attributed to differences in the type of oxidative stress used and experimental models bilobalide.

## **II. CONCLUSION**

The ginkgo biloba extract is the herbal medicine with low cost and no side effect supplement to treat the primarily neurodegenerative dementia. Also ginkgo extract used in treatment of various diseases due to flavonoid, ginkgetin, bilobetin, ginkgolides and diterpenes present in it. Various studies were conducted on Ginkgo biloba extract. and found its phytochemical properties and its function under many disease conditions. Numerous studies report effective use of GBE in cerebrovascular dysfunction, peripheral artery dysfunction, multi-infarct dementia, memory impairment in the elderly, Alzheimer's disease, chronic depression, asthma, and venous dysfunction. GBE for schizophrenia, tinnitus, brain syndrome, vertigo of undiagnosed origin, and PMS, although less established, still require further research. Various in vivo and in vitro preclinical studies support a simplified hypothesis Ginkgo biloba extract EGb761 may be effective in treating and preventing AD and other age-related, neurodegenerative disorders. Anti-oxidation, anti-inflammation, antiapoptosis, immunity against mitochondrial dysfunction, amyloidogenesis and A $\beta$  aggregation, modification of tau protein phosphorylation, ion homeostasis, and even implantation of growth factors are possible forms of GBE action. However, the clinical efficacy of EGb761 is still difficult. Many factors such as demographic sensitivity, severity of malignancy, type of test used to measure efficacy, dosages were elevated to potentially interfere with EGb761 efficacy in clinical practice. In relation to these factors, basic scientific reports provide useful information that can help reverse the clinical efficacy of this drug. Overall, a better understanding of the mechanisms underlying the neuroprotective effects

of EGb761 may contribute to a better understanding of the efficacy and complexity of this drug and may also be helpful in designing treatment strategies for future clinical practice.

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