Ginkgo biloba (Maidenhair tree)

Ginkgo biloba

Description

Ginkgo biloba, also known as Maidenhair Tree, is the oldest living tree species, dating back approximately 200 million years. It is extremely resistant to pollution and disease, and is often planted as an ornamental tree. Because of its hardiness, Ginkgo trees can live as long as 1,000 years and grow to a height of 120 feet. Ginkgo seeds and leaves have been used in traditional Chinese medicine for over 5,000 years. In modern botanical medicine, extracts are made from the distinctive, fan-shaped leaves.

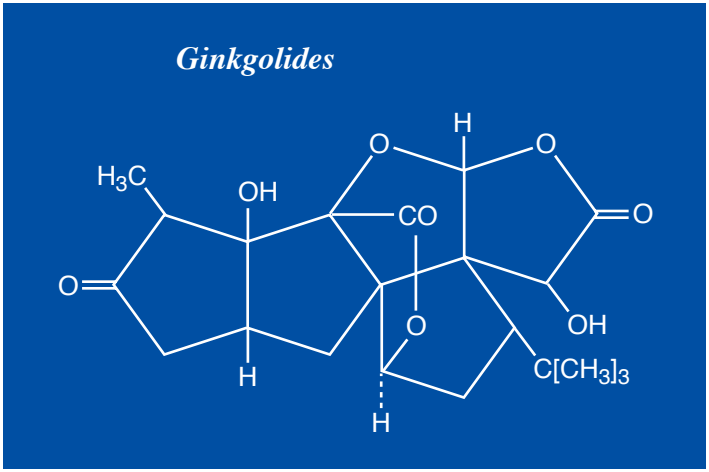
Active Constituents

Ginkgo biloba extracts utilized in clinical trials (EGb 761 and LI1370) are standardized in a multi-step procedure designed to concentrate the desired active principals from the plant. These extracts contain approximately 24-percent flavone glycosides (primarily composed of quercetin, kaempferol, and isorhamnetin) and 6-percent terpene lactones (2.8-3.4% ginkgolides A, B, and C, and 2.6-3.2% bilobalide). Other constituents include proanthocyanadins, glucose, rhamnose, organic acids (hydroxykinurenic, kynurenic, protocatechic, vanillic, shikimic), D-glucaric acid and ginkgolic acid, and related alkylphenols.

Mechanisms of Action

Ginkgo biloba extracts exhibit potent antioxidant activity,[1-4] and are capable, *in vitro*, of scavenging various reactive oxygen species,[5,6] and inhibiting or reducing the functional and morphological impairments observed after lipoperoxide release.[7,8] Animal and human studies note that Ginkgo extracts reduce clastogenic (chromosome-breaking) activity in the plasma after radiation exposure.[9] It is also possible that a large part of Ginkgo's anti-ischemic effect involves inhibition of free radical formation.[10]

One of the components of *Ginkgo biloba*, ginkgolide B, is a potent platelet-activating factor antagonist.[11] It is also likely that the flavonoid fraction, containing free radical scavengers, is important in this respect.[12] Extracts from the leaves of *Ginkgo biloba* are reported to be effective at increasing vascular relaxation via a nitric oxide pathway.[12] Ginkgo extracts (specifically the bilobalide component) can suppress hypoxia-induced membrane breakdown in the brain.[13]



Oral administration can prevent the decline in muscarinic (cholinergic) receptor density in the hippocampus of rats,[14] and might inhibit degradation of acetyl-choline by acetyl-cholinesterase.[15]

Experimental evidence indicates Ginkgo's effect on the central adrenergic system might also be involved in its therapeutic actions,[16] since the extract appears to reactivate noradrenergic activity,[17] particularly in aged animals.[18] Extracts of *Ginkgo biloba* leaves produce reversible inhibition of rat brain monoamine oxidase (MAO). Both MAO-A and -B types were inhibited to a similar extent.[19] The anti-stress and neuroprotective effects of *Ginkgo biloba* extract might also be related to its effect on glucocorticoid biosynthesis. Ginkgo extract – and specifically its components ginkgolide A and B – decreases corticosteroid synthesis.[20] *Ex vivo* treatment with Gingko extract has resulted in a 50-percent reduction of ACTH-stimulated corticosterone production by adrenocortical cells.[21]

Clinical Uses

Alzheimer's Disease/Senile Dementia

Research indicates Ginkgo extract may be efficacious in the treatment of a wide array of conditions associated with age-related physical and mental deterioration. Ginkgo extracts appear to be capable of stabilizing and, in some cases, improving cognitive performance and social functioning of patients with dementia.[22-25]

Cardiovascular Disease

Treatment with *Ginkgo biloba* extract lowers fibrinogen levels and decreases plasma viscosity.[26] Ginkgo administration might improve the clinical outcome following cardiopulmonary bypass by limiting oxidative stress.[27,28]

Cerebral Vascular Insufficiency and Impaired Cerebral Performance

Administration of *Ginkgo biloba* extracts has been shown to improve a variety of conditions associated with cerebral insufficiency,[29,30] including visual field disturbances associated with chronic lack of blood flow,[31] oculomotor and complex choice reaction,[32] vigilance and

reaction times,[33] depressive mood,[34] memory and mental performance,[35,36] dizziness,[36] circulatory encephalopathy,[37] and decreased blood flow.[38]

Premenstrual Syndrome

Ginkgo extract is effective for the treatment of congestive (particularly breast symptoms) and neuropsychological symptoms of PMS,[39] and the alleviation of idiopathic cyclic edema.[40]

Antidepressant-Induced Sexual Dysfunction

Ginkgo extract has been used successfully to treat impotence and sexual dysfunction secondary to antidepressant medication use.[41] This includes selective serotonin reuptake inhibitors, serotonin and norepinephrine reuptake inhibitors, monoamine oxidase inhibitors, and tricyclics.[42]

Vascular Diseases

Research has shown positive findings in vascular complications such as intermittent claudication,[43-45] peripheral arterial occlusive disease,[46,47] chronic venous insufficiency,[48] and hemorrhoids.[49]

Liver Fibrosis

In a preliminary study, *Ginkgo biloba* was shown to be effective in arresting the development of liver fibrosis associated with chronic hepatitis B.[50]

Macular Degeneration

In spite of the small population sample, a statistically significant improvement in long distance visual acuity was observed in patients with macular degeneration after treatment with *Ginkgo biloba* extract.[51]

Tinnitus

Studies have shown contradictory results in the treatment of tinnitus, which might be due to the diverse etiology of this condition.[52-57]

Vertigo/Equilibrium Disorders

In a placebo-controlled, multi-center study, Ginkgo provided statistically and clinically significant relief of vertigo symptoms, with 47 percent of Ginkgo patients having total symptom relief, compared to 18 percent of those taking placebo.[58] Other studies have confirmed these results.[59-60]

Memory

Studies have shown improvements in attention, speed of memory, and quality of memory in healthy human subjects.[61-64]

Cancer

Phase two clinical trials have shown a good benefit-risk ratio of the combination of 5-fluorouracil and parenteral Ginkgo extract in the treatment of advanced colorectal and pancreatic cancer.[65,66]

Drug-Botanical Interactions

Ginkgo biloba should be avoided in patients with known hypersensitivity to the plant. The use of Ginkgo preparations during pregnancy and lactation has not been studied in humans.

The combined use of aspirin and *Ginkgo biloba* extracts has been reported to cause subdural hematoma in a few individuals.[67] Although the bleeding resolved after discontinuation of *Ginkgo biloba* extract, this combination, or the use of *Ginkgo biloba* extract with other blood thinners should be done with caution.[68,69] At least one case of retinal hemorrhage associated with Ginkgo and aspirin use has been reported.

Side Effects and Toxicity

Side effects are uncommon; however, gastrointestinal disturbances (nausea, vomiting, increased salivation, loss of appetite), headaches, dizziness, tinnitus, and hypersensitivity reactions, such as skin rash, have been reported to occur in some individuals.

The LD_{50} of *Ginkgo biloba* extract is 15.3 g/kg. No mutagenicity has been detected for the extract.

Dosage

The generally recommended daily dosage is 40-80 mg of a standardized extract two to three times daily. Recommended dosage for Alzheimer's disease is at the higher end of this range, or around 240 mg daily. In chronic conditions the extract should be administered for at least 6-8 weeks before evaluation of efficacy.

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