

Creative Review



Ginkgo biloba: a medicinal plant with clear effects and many indications

Abstract

There are not many herbal remedies that are as well known worldwide as the extract from the leaves of the Ginkgo biloba tree. This remedy has not only been used as a folk remedy in East Asia for thousands of years, but its effectiveness has also been proven in all recent studies. The emphasis is on improvements in blood circulation with blood thinning and improvements in brain performance. It therefore meets a large number of current needs in outpatient therapy, especially for older people. It is postulated that the drug (EGb 761®) should generally be used in older people.

Volume 12 Issue 3 - 2023

Manfred Doepp

HolisticCenter, Justus-Liebig-University, Giessen, Switzerland

Correspondence: Doepp Manfred, Holistic Center, 13 Haupt St., Abtwil 9030, Justus-Liebig-Univ. Giessen, Switzerland, Tel 0041799240088, Email holisticcenter@yahoo.de

Received: December 06, 2023 | Published: December 21, 2023

Introduction

There is hardly an herbal remedy for which there is as much positive evidence of efficacy and publications as for ginkgo (actually ginkyo) biloba. The artificially and chemically determined pharmaceutical industry has had to recognize this and admit that it has not been possible to extract a single active substance from it that could imitate the effects of the plant extract from the leaves of the Ginkgo biloba tree. Apparently, it is the complexity of the extract that is necessary to produce its manifold effects.^{1–6}

If we take a look at the history of this tree, it is striking that it is one of the oldest plant varieties still in existence today, the Japanese temple tree Ginkgo biloba is one of the oldest trees in the world. Its valuable ingredients have been appreciated for thousands of years. These are mainly found in the leaves of the tree and can be concentrated into an extract using a multi-stage process. Ginkgo biloba, also known as the fan tree, is the last living representative of the Ginkgoales, a plant order that dates back almost 270 million years. Originally native to China, the ginkgo tree is now found all over the world. It is known for its unique fan-shaped leaves and impressive resilience (Figures 1 & Figure 2). In fact, ginkgo trees were some of the few living organisms to survive near the epicenter of the atomic bomb in Hiroshima.



Figure I A bonsai ginkgo in the fall, 90 years old.



Figure 2 The fan-shaped leaf of the ginkgo tree.

The leaves and seeds of the ginkgo tree are edible. Ginkgo nuts, the seeds of the tree, have a sweet, slightly bitter taste and are often used in Asian cuisine. The leaves, on the other hand, have a bitter taste and are usually not eaten raw, but in the form of tea or extracts. Ginkgos are normally dioecious-separate-sexed - the flowers of a male and a female specimen must come together to reproduce. However, female trees are less common due to the unpleasant smell of their fruit in the fall. The ginkgo tree can grow up to 40 meters high and live for hundreds of years (Figures 1 & Figure 2).

Goethe, the poet

The famous German poet J. W. von Goethe had a special relationship with the ginkgo tree and its leaves. He studied it in detail and wrote a poem about it (Figure 3).

Here is the poem by Goethe:

This tree's leaf, coming from the east

- Entrusted to my garden,
- Gives secret meaning to taste,

MOJ Public Health. 2023;12(3):174-177.



©2023 Doepp. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and build upon your work non-commercially.

How it edifies the knowledgeable.

Is it a living being

That separates into itself,

Are there two who choose each other?

That they are known as one.

To answer such a question

I think I found the right meaning;

Do you not feel my songs

That I am one and double?

The poem is dated September 15, 1815, for which Goethe's friend Boisserée noted in his diary: "Cheerful evening; Goethe had sent Mrs. Willmer a leaf of the Ginkgo biloba as a symbol of friendship from the city (Frankfurt)." In 1815, the court gardener J. C. Sckell planted a ginkgo tree behind the Princely House in Weimar at Goethe's request, and it is still there today. Weimar is also home to the only ginkgo museum in Germany.⁷⁻¹²



Figure 3 Goethe's poem "Ginkgo biloba".

East Asia

In Asia, ginkgo has always been a symbol of hope, long life, fertility, vitality and invincibility. Ginkgo biloba is often used there as a medicinal plant - among other things, it is used to treat circulatory disorders, dizziness and tinnitus. However, it is said to be particularly effective for poor concentration and memory disorders.

In East Asia, especially in China, the "miracle tree" has long been used for beauty care and above all as a medicinal plant. The seeds or fruits, as well as the roots, leaves and bark, are used as medicine for asthma, bronchitis, circulatory disorders and skin diseases. Ginkgo is also said to prevent skin ageing and have a positive effect on the psyche and brain, including anxiety, poor concentration and memory problems.¹⁻⁶

How does the «miracle tree» work?

The health-promoting effect of the tree is due to the substances contained in its leaves, seeds and roots. $^{13-15}$

- I. Flavonoids (quercetin and kaempferol)
- II. Terpenoids (ginkgolide A, B and C and bilobalide)
- III. Ginkgolic acid.

The flavonoids quercetin and kaempferol act against oxidative stress. They have the ability to neutralize free radicals and thus counteract the development of numerous diseases. Over a longer period of time, oxidative stress can contribute to cardiovascular diseases, inflammation, cancer and dementia, among other things.^{1,16,17}

As the two flavonoids are also considered phytoestrogens, leaf extracts can be used for menopausal symptoms if these are due to an oestrogen deficiency. On the other hand, due to the possible estrogen-like effect, ginkgo extracts are not recommended if estrogen-dependent breast cancer is present.¹⁸

Ginkgolides A, B and C and bilobalide all have a circulationpromoting effect. They dilate the blood vessels, improve blood flow and oxygen supply to the tissue. The secondary plant substances, the flavonoids and terpenoids, which are only found in ginkgo in this special form and composition as ginkgolides and bilobalides, are therefore particularly effective. Ginkgolic acid is said to have a celldamaging effect in large quantities, which is why a maximum of 5 $\mu g/g$ of it may be contained in high-quality food supplements.^{19,20,21,22}

The "miracle tree" for Alzheimer's: good research situation

Ginkgo extract is one of the best researched and most widely used herbal remedies for the treatment of Alzheimer's disease. Several clinical studies show that the miracle tree can actually improve the brain performance of patients with dementia.^{23,24,25}

A meta-analysis conducted by Chinese researchers in 2015 examined nine studies with a total of 2561 patients. The standardized leaf extract EGb 761® (Tebonin®) was used.²²⁶

Taken at a dosage of 240 mg per day for 5 to 6 months, this extract led to a slowing of cognitive decline in patients with mild to moderate dementia. This is attributed to the improved blood flow to the brain, which improves memory and concentration. The researchers emphasized the good tolerability of the extract.

The mental capacity of dementia patients is usually assessed in such studies using many different tests and scales. For example, they have to memorize pictures, solve concentration tasks or it is evaluated how well they can cope with everyday tasks.

In 2019, a panel of experts from Asian countries came to the conclusion that ginkgo extract EGb 761® deserves a place in Alzheimer's therapy. The extract is comparable in its effect to conventional Alzheimer's therapies such as the use of acetylcholinesterase inhibitors. However, it is better tolerated and could therefore be an effective alternative for patients who cannot tolerate conventional medical therapy.^{1,27}

Ginkgo preparations are often taken for tinnitus and are even recommended by many doctors in Europe as the first treatment option. The cause of tinnitus can be a circulatory disorder of the inner ear. The standardized extract EGb 761® was also used in studies. The authors of the above-mentioned Cochrane review came to the conclusion that there were just as few side effects when taking ginkgo as when taking placebos.

Dizziness

Extracts from the miracle tree are also taken to treat dizziness.⁵ Dizziness can occur, for example, as a result of ageing or in connection with a circulatory disorder.

Citation: Doepp M. Ginkgo biloba: a medicinal plant with clear effects and many indications. *MOJ Public Health.* 2023;12(3):174–177. DOI: 10.15406/mojph.2023.12.00428

A European research group investigated the effect of ginkgo extract EGb 761® in a meta-analysis.⁵ They used five clinical studies with a total of 1927 dementia patients, 1040 of whom also suffered from dizziness. The test subjects took 240 mg of the extract daily over a period of 22 to 26 weeks.⁵ In addition to the positive effect on memory and concentration, taking the extract led to an improvement in dizziness of 18 to 31 percent - compared to the people who took a placebo.

Further effects

Many other positive effects of the miracle tree are described, but these have so far only been insufficiently proven or only in animal studies. Complaints for which the intake of ginkgo extracts could have a positive effect include:^{28,29,30,31}

- Improving mental performance, increasing concentration and memory problems^{28,29,30,31}
- Prevention of age-related dementia or slowing down a process that has already begun^{2,3,5,32,33}
- Improvement of the blood supply in the legs
- Improvement in tinnitus or sudden hearing loss^{4,5}
- Preventing the formation of blood clots
- Reduction of dizziness⁵
- Prevention of migraines
- · Influence of multiple sclerosis on cognitive impairments
- Relief of premenstrual symptoms (PMS) in women^{21,23}
- Improvement of the metabolic syndrome (high blood pressure, elevated blood sugar, high blood lipid levels, overweight)^{22,34}
- · Relief from anxiety
- Prevention of altitude sickness
- Reduction of visual impairment in glaucoma¹⁷
- Lowering high blood pressure

What does ginkgo extract do?

In Asia, especially in China, the "miracle tree" has long been used for beauty care and above all as a medicinal plant. The seeds or fruits, as well as the roots, leaves and bark, are used as medicine for asthma, bronchitis, circulatory disorders, skin diseases and urinary incontinence. Ginkgo is also said to prevent skin ageing and have a positive effect on the psyche and brain, including anxiety, poor concentration and memory problems.

There are two reasons why extracts of the leaves are used:

The valuable ingredients of the leaves are only slightly soluble in water and can therefore only be insufficiently utilized by the body. Eating the leaves can cause allergies (due to the ginkgolic acids).

A distinction must be made between medicines containing ginkgo and dietary supplements. Approved medicines contain only highquality extracts that are produced in accordance with the specifications and whose efficacy has been scientifically proven for the respective application. Food supplements, on the other hand, may contain differently produced extracts containing the ingredients in different concentrations and for which there is usually no evidence of efficacy.

Studies of the ginkgo extract

Ginkgo is said to have various mechanisms of action, although these have not yet been fully researched. The following effects are attributed to ginkgo extract:^{2-5,28-33,35}

It is intended to improve blood flow, i.e. the flow properties of the blood. The blood vessels are to be widened and the blood flow in the arteries, veins and fine vessels (microcirculation) improved - and thus also the oxygen and nutrient content of the «gray cells».

It is intended to prevent platelets from sticking together and thus reduce blood clotting (blood-thinning effect).

Ginkgo is a so-called radical scavenger and can neutralize aggressive molecules that have an electron deficit, such as free oxygen radicals.

The nerve cells are to be protected, as ginkgo is said to counteract the breakdown of nerve cells and increase the performance of the existing cells by improving the transmission of stimuli in the nerves.

Ginkgo biloba promotes neuronal plasticity, inhibits the aggregation of amyloid beta proteins, thus improving subjective brain dysfunction (SCD) and can therefore be used to prevent Alzheimer's disease.

Even if not all of these effects have been scientifically proven, there are approved medicines containing ginkgo extract for the treatment of certain forms of dementia or brain disorders, poor concentration and memory, circulatory disorders and for the supportive treatment of tinnitus or dizziness.

The «Dementia» guideline published in 2016, for example, attributes a possible effect to the special extract EGb 761® (Tebonin®). Treatment with a dose of 240 mg daily could therefore be considered for dementia, while a dose of 120 mg is probably not sufficient.³⁶

After a stroke

Recently, a study from China caused a stir.³⁷ It was a randomized prospective study from seven centers in China, again with the extract EGb 761[®]. It looked at changes in the cognitive status of stroke patients. Significant improvements were found in memory (p < 0.001), orientation (p < 0.001) and language (p < 0.05). There were no side effects. The authors write: "Ginkgo extract contains several compounds that improve blood flow to the brain, reduce oxidative stress and promote the activity of neurotransmitters such as acetylcholine, which is particularly important for functions related to attention and learning. Therefore, the neuroprotective properties of EGb 761[®] may provide a moderate but consistent benefit in slowing or even halting cognitive decline."

A study on the positive effects of ginkgo on post-Covid syndrome has also recently been registered.³⁸

Conclusion

There is hardly any other medicinal plant with such a good and broad spectrum of action as Ginkgo biloba. It would be worth considering and is not presumptuous to use it in general for people over the age of 60. It should be a high-quality extract such as EGb 761[®] in a dosage of 240 mg/day.

Acknowledgments

None.

Conflicts of interest

The author declares there is no conflict of interest.

References

- Singh SK, Srivastav S, Castellani RJ, et al. Neuroprotective and antioxidant effect of ginkgo biloba extract against AD and Other neurological disorders. *Neurotherapeutics*. 2019;16(3):666–674.
- Tan MS, Yu JT, Tan CC, et al. Efficacy and adverse effects of ginkgo biloba for cognitive impairment and dementia: a systematic review and meta-analysis. *J Alzheimers Dis.* 2015;43(2):589–603.
- Kandiah N, Ong PA, Yuda T, et al. Treatment of dementia and mild cognitive impairment with or without cerebrovascular disease: Expert consensus on the use of Ginkgo biloba extract, EGb 761[®]. CNS Neurosci Ther. 2019;25(2):288–298.
- Sereda M, Xia J, Scutt P, et al. Ginkgo biloba for tinnitus. *Cochrane Database Syst Rev.* 2022;11(11):CD013514.
- Spiegel R, Kalla R, Mantokoudis G, et al. Ginkgo biloba extract EGb 761[®] alleviates neurosensory symptoms in patients with dementia: a meta-analysis of treatment effects on tinnitus and dizziness in randomized, placebo-controlled trials. *Clin Interv Aging*. 2018;13:1121– 1127.
- Ihl R, Tribanek M, Bachinskaya N; GOTADAY Study Group. Efficacy and tolerability of a once daily formulation of Ginkgo biloba extract EGb 761[®] in Alzheimer's disease and vascular dementia: results from a randomized controlled trial. *Pharmacopsychiatry*. 2012;45(2):41–46.
- http://www.ginkgomuseum.de/content/ginkgomuseum/goethe-undginkgo.
- Carola Schüren: Thuringia: Homage to the world tree. In: DIE WELT. November 21, 2009.
- Wolfgang-Hagen Hein, Dietrich Andernacht: Der Garten des Apothekers Peter Saltzwedel und Goethes Ginkgo biloba. In: Annaliese Ohm/Horst Reber: Festschrift für Peter Wilhelm Meister zum 65. Geburtstag am 16. Mai 1974. Hamburg, 1975, pp. 303–311.
- Siegfried Unseld: Goethe and the ginkgo. A tree and a poem. Insel-Verlag IB 1188, Frankfurt/Main 1998. 20th edn. 2006.
- 11. Reiner Wild: "*This tree's leaf*". On Goethe's poem Gingo biloba. Edition Literaturhaus, Heidelberg 2016.
- Bernd Witte (Ed.): Poems by Johann Wolfgang Goethe (Interpretations). Philipp Reclam jun., Stuttgart 1995.
- Wichtl M: *Tea drugs and phytopharmaceuticals*. Wissenschaftliche Verlagsgesellschaft mbH Stuttgart. 2016.
- ESCOP Monograph: Ginkgo folium. European Scientific Cooperative on Phytotherapy. Thieme, Stuttgart, 2nd edn. 2003.
- Diamond BJ, Shiflett SC, Feiwel N, et al. Ginkgo biloba extract: mechanisms and clinical indications. *Archives of Physical Medicine and Rehabilitation*. 2000;81(5):668–678.
- Achete de Souza G, de Marqui SV, Matias JN, et al. Effects of Ginkgo biloba on diseases related to oxidative stress. *Planta Med.* 2020;86(6):376–386.
- Kang JM, Lin S. Ginkgo biloba and its potential role in glaucoma. *Curr Opin Ophthalmol*. 2018;29(2):116–120.
- Mei N, Guo X, Ren Z, et al. Review of Ginkgo biloba-induced toxicity, from experimental studies to human case reports. *J Environ Sci Health C Environ Carcinog Ecotoxicol Rev.* 2017;35(1):1–28.

- Leistner E, Drewke C. Ginkgo biloba and ginkgotoxin. J Nat Prod. 2010;73(1):86–92.
- Jang HS, Roh SY, Jeong EH, et al. Ginkgotoxin induced seizure caused by vitamin B6 Deficiency. J Epilepsy Res. 2015;5(2):104–106.
- Ozgoli G, Selselei EA, Mojab F, et al. A randomized, placebo-controlled trial of Ginkgo biloba L. in treatment of premenstrual syndrome. J Altern Complement Med. 2009;15(8):845–851.
- Eisvand F, Razavi BM, Hosseinzadeh H. The effects of Ginkgo biloba on metabolic syndrome: A review. *Phytother Res.* 2020;34(8):1798–1811.
- Oh SM, Chung KH. Estrogenic activities of Ginkgo biloba extracts. *Life* Sci. 2004;74(11):1325–1335.
- Lejri I, Grimm A, Eckert A. Ginkgo biloba extract increases neurite outgrowth and actvates the Akt/mTOR pathway. *PLoS ONE*. 2019,14(12):e0225761.
- 25. Alzheimer Switzerland, Dementia in Switzerland 2022.
- https://kfn-ev.de/meldungen/2015-2/307-neue-metaanalyse-bestaetigtguenstige-therapie-effekte-von-ginkgo-spezialextrakten-bei-demenz-1?format=html.
- https://www.schwabe.de/ginkgo-spezialextrakt-egb-761r-leichtekognitive-stoerungen.
- Jessen F. Subjective and objective cognitive decline at the pre-dementia stage of Alzheimer's disease. *Eur Arch Psychiatry Clin Neurosci*. 2014;264(Suppl 1):53–57.
- 29. Swissmedic authorized human medicinal products.
- Gruenwald, J, Eckert A, Kressig RW, The Effects of standardized ginkgo biloba extracts (GBE) on subjective cognitive decline (SCD) in Middle-Aged Adults. A Review. *Advances in Aging Research*. 2020;09(23)45– 65.
- Kressig R. Dementia of the Alzheimer type. Non-drug and drug therapy. *Therapeutic Review*. 2015;72(4):233–238.
- Livingston A, Huntley J, Sommerlad A, et al. Dementia prevention, intervention, and care. 2020 report of the Lancet Commission. Lancet. 2020 ;396 :413–446.
- 33. Scherrer B AS, Andrieu S, Ousset PJ, et al, Analyzing time to event data in dementia prevention trials : the example of the guidage study of EGb761. J Nutr Health Aging. 2015,19(10):1009–1011.
- 34. Yu Fan, Xin Jin, Changfeng Man, et al. Does ajuvant treatment with Ginkgo biloba to Statins have additional benefits in Patients with Dyslipidemia? *Front Phar.* 2018;9:659.
- Savaskian E, Bopp-Kistler I, Buerge M, et al. Recommendations for the diagnosis and treatment of behavioral and psychological symptoms of dementia (BPSD). *Praxis (Bern 1994)*. 2014;103(3):135–148.
- Deuschl G, Maier W. S3-Guideline Dementia-2016. in: German Society of Neurology. Edn. Guidelines for diagnostics and therapy in neurology.
- 37. Cui Mei, Tongyao You, Yuwo Zhao, et al. Ginkgo extract EGb761® improves cognition and overall condition after ischemic stroke: Results from a pilot randomized trial. *Front Pharm.* 2023;14:1147860.
- Al-Kuraishy HM, Al-Gareeb AI, Kaushik A, et al. Ginkgo biloba in the management of the COVID-19 severity. *Arch Pharm (Weinheim)*. 2022;355(10):e2200188.