



Cognitive Vitality Reports[®] are reports written by neuroscientists at the Alzheimer's Drug Discovery Foundation (ADDF). These scientific reports include analysis of drugs, drugs-in-development, drug targets, supplements, nutraceuticals, food/drink, non-pharmacologic interventions, and risk factors. Neuroscientists evaluate the potential benefit (or harm) for brain health, as well as for age-related health concerns that can affect brain health (e.g., cardiovascular diseases, cancers, diabetes/metabolic syndrome). In addition, these reports include evaluation of safety data, from clinical trials if available, and from preclinical models.

Ginkgo biloba

Evidence Summary

Ginkgo biloba may improve memory in people with cognitive impairment but in clinical trials, it failed to prevent cognitive decline or dementia. Ginkgo is generally considered safe.

Neuroprotective Benefit: In a recent meta-analysis and in multiple clinical trials, Ginkgo improves memory where some cognitive impairment already exists. However, Ginkgo does not seem to enhance cognitive function or lower the risk of dementia in healthy individuals.

Aging and related health concerns: Previous studies in isolated cells and insects hinted that Ginkgo might slightly slow cellular aging or delay death but these results have never been replicated in mammals or humans.

Safety: Ginkgo is generally considered safe for use even though a couple of health risks have been noted.



What is it?

Ginkgo biloba is a tree native to China whose leaves have been used for centuries in traditional Chinese medicine to treat the brain, heart, and lungs. While Ginkgo teas and tinctures are most typical in Eastern medicine, the modern pharmaceutical industry produces extracts of Ginkgo leaves that are standardized to contain reliable specified amounts of the most beneficial chemicals.

Neuroprotective Benefit: In a recent meta-analysis and in multiple clinical trials, Ginkgo improves memory where some cognitive impairment already exists. However, Ginkgo does not seem to enhance cognitive function or lower the risk of dementia in healthy individuals.

Types of evidence:

- 3 meta-analyses and systematic reviews on cognitively healthy adults
- 8 meta-analyses and systematic reviews on cognitively impaired to severely demented patients
- Numerous laboratory studies on possible mechanisms of action

Prevention of dementia/cognitive aging (human research):

Despite some promising results from animal experiments, multiple [clinical trials](#) involving thousands of patients have conclusively shown that treatment with Ginkgo biloba for up to 5-6 years does not prevent [cognitive decline](#) or [dementia](#), including Alzheimer's disease [[Vellas, 2012](#), [Snitz, 2009](#), [Dodge, 2008](#), [DeKosky, 2008](#)]. Ginkgo biloba extract (60 mg EGB 761 given twice daily) also failed to prevent the effects of chemotherapy on cognitive function in a Phase III (i.e. large and rigorous) clinical trial of women being treated for breast cancer [[Barton, 2013](#)].

Treatment of dementia or mild cognitive impairment (human research):

In a couple of systematic reviews, Ginkgo biloba extract treatment appeared to have stabilized and slowed decline in cognition for both mild cognitively impaired and Alzheimer's disease patients [[Weinmann, 2010](#), [Herrschaft, 2012](#), [Yang, 2015](#), [Tan, 2015](#), [Hashiguchi et al., 2015](#); [Yang et al., 2016](#)]. However some studies show mixed results and inconsistent patterns of effectiveness and a 2009 Cochrane meta-analysis concluded that results from these studies were inconsistent and unreliable. Clinical guidelines are similarly mixed. Although the World Federation of Societies of Biological Psychiatry guidelines [[Ihl, 2014](#)] suggest that EGb761 ginkgo biloba extract may be used to treat dementia symptoms, the British Association for Psychopharmacology and guidelines published by the

[American Academy of Family Physician \[Winslow, 2011\]](#) concluded that the putative benefits from ginkgo extracts are also inconsistent and unreliable.

Mechanism of action for neuroprotection:

Pre-clinical studies in animal models suggest Ginkgo treatment may positively impact multiple aging-related pathways, such as ameliorating oxidative damage from reactive oxygen species and protecting against mitochondrial dysfunction.

Mitochondrial function: Mitochondria are organelles that are essential in generating energy for a cell. In Alzheimer's disease, mitochondrial dysfunction is an early event, which triggers cell degradation and death. In laboratory animal experiments, Ginkgo Biloba extract (EGb761®) was observed to protect against [amyloid-β](#) induced mitochondrial dysfunction, improving mitochondrial function and energy metabolism [[Shi, 2009](#), [Eckert, 2012](#)].

Cerebral Blood Flow: Alzheimer's disease is a vascular disorder where therapies that improve cerebral vasodilation have been shown to lower Alzheimer's disease symptoms [[De la Torre, 2004](#)]. In an observational study, Ginkgo Biloba extract reduced the major symptoms of cerebral vascular insufficiency by increasing blood flow [[Mashayekh, 2011](#)].

Oxidative Stress: Evidence has shown that the presence of extensive oxidative stress, the imbalance between [free radical](#) formation and detoxification, is characteristic of Alzheimer's disease. In a preclinical animal study, Ginkgo biloba improved cognitive function by decreasing oxidative damage [[Belviranli, 2015](#)].

Neurogenesis: The hippocampus is an area of the brain most responsible for learning and memory. Dysfunctional neurogenesis of the hippocampus contributes to memory loss, characteristic of Alzheimer's disease. In a preclinical animal model, mice treated with Ginkgo biloba extract had a decrease in apoptotic cells, increased cellular proliferation, along with the creation of new neurons and neural stem cells [[Osman, 2015](#)]. All of which help to repair the brain and improve cognitive impairment.

APOE4 interactions: There is very limited evidence on how Ginkgo biloba treatment affects ApoE4 positive and negative patients. However in one combination drug trial, both the ApoE4 non-carrier (-) and ApoE4 carrier (+) groups who had supplementation showed improvements in cognitive function [[Yasuno, 2012](#)].



Aging and related health concerns: Previous studies in isolated cells and insects hinted that Ginkgo might slightly slow cellular aging and delay death but those results have never been replicated in mammals or humans.

Types of evidence:

- 1 meta-analysis of clinical trials
- 2 randomized controlled trial
- Numerous preclinical studies

A [meta-analysis](#) of clinical trials in 2014 reported major flaws in the few available trials that used ginkgo as a treatment for hypertension [[Xiong, 2014](#)].

When Ginkgo treatment was given for 6 years to over 3,000 patients, it failed to lower the risk of death or major cardiovascular events like stroke or heart attack [[Kuller, 2010](#)]. Treatment for 6 years also failed to reduce blood pressure or the risk of hypertension in over 3,000 elderly men and women [[Brinkley, 2010](#)].

In animal models, Ginkgo Biloba treatment increased mean lifespan, as well as, delayed cell death by activating telomerase [[Wu, 2002](#), [Dong, 2007](#)].

Safety: Ginkgo is generally considered safe for use even though a couple of health risks have been noted.

Types of evidence:

- 1 meta-analysis (based on 18 RCTs)
- Some systematic reviews and observational studies

Side Effects and Warnings:

Some clinical trials suggested Ginkgo might raise the risk of stomach bleeding in older adults, yet a meta-analysis of numerous clinical trials found no such association [[Heinonen, 2015](#)]. Because Ginkgo can dilate blood vessels, it may not be safe in patients taking medication for high blood pressure. It may also be unsafe for children, people with [diabetes](#), and women trying to become pregnant.



A [recent toxicology report](#) from the National Institutes of Health (NIH) found high doses of Ginkgo caused cancer in laboratory mice; the doses were 560-1120 times higher than the doses people normally take. There is currently no evidence that Ginkgo causes cancer in humans. As with all dietary supplements, the safety of Ginkgo supplements depends on the actual content of the pill and the manufacturing practices of the supplier.

Sources and Dosing:

Ginkgo Biloba extract is available as an oral pill, powder, liquid extract and tea from a variety of manufacturers. An independent rating of popular over the counter USP-certified [dietary supplements](#) available has been generated by [Consumer Labs](#) [[Rapaka, 2006](#)]. Most clinical trials on dementia treatment have used EGb761®, a prescription-based standardized ginkgo biloba extract. Evidence suggests that Ginkgo biloba is safe when properly used by healthy adults [[Birks, 2009](#), [Kellerman, 2011](#)]. Standardized Ginkgo biloba extract appears to be well tolerated by most people who take it at oral doses of 120-240 mg per day.

Future Research:

On-going [clinical trials](#) will provide more information on whether Ginkgo is a useful treatment for brain aging and other diseases. A clinical trial testing Ginkgo in patients with [mild-cognitive impairment](#) was completed in 2015 but the results are not published yet ([NCT01046292](#)). A phase III trial is testing the effectiveness of Ginkgo in combination with ginseng in treating dementia ([NCT01637168](#)). Additionally, clinical trials are testing the effects of Ginkgo in [Parkinson's disease](#) ([NCT01416818](#)), osteoarthritis ([NCT02604381](#)), diabetes ([NCT01038050](#)) and in children with [attention deficit hyperactivity disorder \(ADHD\)](#) ([NCT01536210](#)). More information about these and other trials can be found at [clinicaltrials.gov](#) (U.S.) and [clinicaltrialsregister.eu](#) (Europe).

Search terms:

Pubmed, Google, Cincaltrials.gov:

- Ginkgo Biloba; GBE; Ginkgolide B; EGb761; Ginkoba; Fossil tree; Tanakan; Tebonin; Gingio; Tebokan plus the following terms in separate searches: extract, amyloid, blood pressure, cancer, hypertension, dementia, Alzheimer's, aging, mortality, cognitive function, telomere, gait, lifespan, USP certified supplements



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If you have suggestions for drugs, drugs-in-development, supplements, nutraceuticals, or food/drink with neuroprotective properties that warrant in-depth reviews by ADDF's Aging and Alzheimer's Prevention Program, please contact INFO@alzdiscovery.org. To view our official ratings, visit [Cognitive Vitality's Rating page](#).