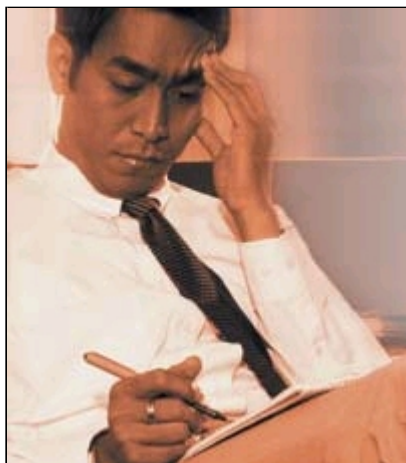


REPORT

Ginkgo
Fails to Enhance Memory in Short-Term Trial

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New studies of dietary supplements are published every day. While these studies often confirm what is already known, inconsistencies inevitably arise. If a new study contradicts previous research findings, then further scrutiny is deserved. Such is the case in a study reported in the Journal of the American Medical Association (JAMA)[1] about the short-term effects of ginkgo.

In this JAMA study, a group of healthy adults were given 40 mg of ginkgo extract three times a day or placebo for six weeks. The results showed no difference in memory scores, self-reported perception, or rating by spouses, friends and relatives after six weeks. The implication from the study is that ginkgo provides no short-term benefits in people with healthy cognitive function.

The JAMA report contradicts a similar study conducted on healthy people who received 180 mg a day of ginkgo for six weeks.[2] This study showed that, compared to placebo, ginkgo improved memory scores and significantly improved self-perception of memory. Those who

received ginkgo rated their overall ability to remember as "improved" compared to those receiving placebo. This correlates well with previous studies indicating a potential short-term benefit for ginkgo supplementation.

The JAMA article was highly critical of a ginkgo supplement maker who claimed a perceivable benefit would occur within four weeks of using its (Ginkoba) product. Due to ginkgo's enormous popularity (\$310 million annual sales in U.S. alone), the media made headline news out of this negative JAMA study. The question the media raised for consumers is whether ginkgo is a worthwhile supplement to take.

In this article, Life Extension reviews what the scientific literature says about ginkgo biloba extract, a potential flaw in the JAMA study, and why people seeking to slow brain aging are taking ginkgo.

An inevitable consequence of aging is reduced flow of blood to the brain. Common causes are chronic inflammation, arteriosclerosis and increased blood stickiness. The result of cerebral vascular disease can range from mild cognitive impairment to ischemic stroke. The third leading cause of death in the United States is stroke. This crippling disease causes many otherwise healthy people to become institutionalized.

Ginkgo biloba extract has demonstrated specific mechanisms of action that counteract age-related vascular disorders. Human clinical studies have shown that ginkgo helps to slow cognitive dysfunction and restores cognitive function in those suffering from vascular dementia or Alzheimer's disease.

The first large-scale American clinical study on ginkgo was published in the 1997 issue of the Journal of the American Medical Association (JAMA).[3] This study showed that, compared to placebo, ginkgo helped prevent short-term memory loss in patients with early-diagnosed Alzheimer's disease. The researchers concluded that ginkgo improved cognitive performance and social functioning in these patients.

Ginkgo is a popular prescription drug in Europe and a dietary supplement in the United States. Hundreds of scientific studies demonstrate ginkgo's favorable effects in the human body. The primary benefit of ginkgo, however, may be to help prevent the consequences of premature brain aging.

Ginkgo and the brain

The brain depends on a steady supply of oxygen and glucose to function properly. It uses 20% of all the oxygen taken in through

the lungs. Without enough oxygen, brain cells are irreparably damaged.

In a critical review of 40 clinical studies using ginkgo extract for "cerebral insufficiency" or age-related dementia, virtually all trials reported positive results.[4] The methodological quality of the eight best designed studies were found to be comparable to the evidence for an FDA-approved pharmaceutical used for the same indication.

In most of these studies, a daily dose of 120 mg to 160 mg of the ginkgo extract was given over a period of four to twelve weeks. Significant improvement compared to the placebo group was observed in typical symptoms such as memory difficulties, confusion, fatigue, anxiety, dizziness, tinnitus and headaches.

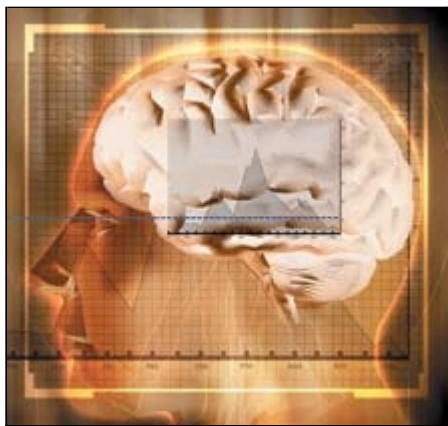
No serious side effects were reported in any of the 40 trials and the non-serious side effects were no different from those reported in patients treated with placebo. This satisfying fact confirms DeFeudis' conclusion in his summary of the ginkgo literature. He points out that there is generally very little risk associated with products containing a properly standardized ginkgo extract.[5]

In European studies, progressive degenerative dementia, such as Alzheimer's disease, has been treated with ginkgo extract. The results of these European trials were so impressive that the German government approved ginkgo biloba extract for treatment of dementia.

Free radicals are considered to be the reason for the excessive lipid peroxidation and cell damage observed in Alzheimer's disease.[6] The main effect of ginkgo extract in these conditions appears to be related to its potent antioxidant properties.

In the 1997 JAMA report,[7] the efficacy and safety of ginkgo extract was tested in patients with Alzheimer's disease and multi-infarcts (vascular) dementia. This 52-week, randomized double-blind, placebo-controlled multicenter study included 202 patients with mild to moderately severe cognitive impairment. The daily dose given was 120 mg. Measures of outcome included the Alzheimer's Disease Assessment Scale-Cognitive subscale (ADAS-Cog), Geriatric Evaluation by Relative's Rating Instrument (GERRI), and Clinical Global Impression of Change (CGIC).

Whereas the ginkgo group maintained its cognitive baseline over the year-long study and improved slightly in social functioning, the placebo group worsened over time in both aspects. The conclusion was that ginkgo appears capable of stabilizing and, in a substantial number of cases, improving the cognitive performance and the social functioning of demented patients. This corresponds to a delay of six months to a year in the progression of the disease. Regarding the safety of ginkgo, there were no significant differences compared with placebo in either the number of patients reporting side effects or in the severity of these effects.



A German double-blind placebo-controlled study[8] provides further support. In this study, 20 outpatients aged 50 to 80 who were suffering from mild to moderate dementia of Alzheimer's type were treated with a daily dose of 240 mg of ginkgo extract for three months. The patients' attention and memory performance (measured by SKT test) showed significant improvement after three months of treatment. The extract was well tolerated with no adverse effects.

Ginkgo biloba has consistently shown that it can help protect against a variety of insults associated with restricted blood supply to the brain (cerebral vascular insufficiency). Ginkgo's three major pharmacological features are improving blood supply by dilating and toning blood vessels; reducing blood-clotting through antagonism of platelet-aggregating factor (PAF); and preventing membrane damage by means of its antioxidant activities.

Can ginkgo boost memory in healthy people?

We know that ginkgo has improved clinical conditions in those diagnosed with severe neurological disease. Based on its multiple mechanisms of action, ginkgo may reduce the risk of developing senile dementia both of the vascular and Alzheimer's type. The question raised by the recent JAMA study is whether ginkgo can help improve memory in healthy people. Most research shows a benefit, but the most important effect of ginkgo for healthy aging people may be in preserving cognitive function.

It should be pointed out that there is scientific support for memory enhancement even in young healthy people. Following just a



A Leading Prescription Drug in Europe, Ginkgo extract has a remarkably broad spectrum of pharmacological effects, which makes many clinical applications possible. It is most widely prescribed, however, for age-related deterioration of mental function due to insufficient blood flow to the brain, and also used for peripheral vascular disease. Ginkgo is a widely prescribed drug in Europe.

single dose of 600 mg of ginkgo extract, significant memory improvement was demonstrated in a randomized, double-blind crossover study[9] using Sternberg's memory scanning test. The effect lasted for several hours.

Another study in healthy volunteers[10] investigated the effects of ginkgo extract on memory and psychomotor function. In this randomized, double-blind and placebo-controlled crossover study, 31 volunteers aged 30 to 59 years were given multiple doses of 50 mg or 100 mg, a single dose of 120 mg or 300 mg, or placebo during the day of testing. A psychometric test battery was administered before the first dose and at frequent intervals during the day until 11 hours after the last dose.

The results showed that the memory-enhancing effect of ginkgo in healthy volunteers was most evident with the 120 mg dose, more apparent in the oldest age group of 50 to 59 years, and more pronounced for short term memory than for other aspects of cognitive function. This study is interesting in that it showed that a single daily dose of 120 mg was more effective than smaller multiple doses given throughout the day. In the most recent JAMA study, only 40 mg of ginkgo was given three times a day. Perhaps taking a 120 mg ginkgo capsule once a day, rather than dividing it up into smaller 40 mg doses, would have yielded short-term memory improvement in the JAMA study.

Ginkgo and depression

Because patients treated with ginkgo extract for cerebral insufficiency often show general mood improvement, it made sense to take a closer look at the antidepressive effects of ginkgo. Schubert et al.[11] conducted a study with 40 patients aged 51 to 78 diagnosed with depression, who had not fully responded to standard antidepressant treatment. They were given either placebo or 80 mg ginkgo extract three times daily. After eight weeks of treatment, the assessment on the Hamilton Depression Scale showed a drop from 14 to 4.5 in the ginkgo-treated group, compared to 14 to 13 in the placebo group. These results suggest that ginkgo may be of significant value as an antidepressant.



Peripheral vascular insufficiency

Leg cramps and reduced walking capacity due to atherosclerosis in the arteries of the leg- claudicatio intermittens-occurs in about 3% of the population over age 50. The symptoms are caused by reduced blood flow and oxygen delivery to the muscles, which results in production of free radicals and other toxic metabolites. Ginkgo biloba extract is approved as a drug treatment in Germany for this condition. Several clinical studies have confirmed the effect of long-term (six to twelve months) treatment with ginkgo extract, showing statistically significant improvement in walking performance measured by standardized treadmill exercise.[12]

Ginkgo for the heart

There is a great deal of evidence that oxygen-derived free radicals contribute to the progress of ischemia-reperfusion injury of the heart by inducing an accumulation of lipid peroxidation products.

In one in vivo study Ginkgolide B infusion suppressed arrhythmias (irregular heart rhythm) caused by ischemia. The anti-arrhythmic effect of Ginkgolide B was comparable to standard antiarrhythmic drugs.[13]

Cardiac-protecting mechanisms of ginkgo extract were demonstrated in several other experimental (animal) studies. Shen et al[14] and Haramaki et al.[15] studied the effects of ginkgo on myocardial ischemia followed by reperfusion. Ginkgo treatment significantly inhibited the increase of lipid peroxidation during reperfusion compared to a placebo group.

In a study by Akiba et al.,[16] it was demonstrated that ginkgo extract caused a dose-dependent inhibition of platelet aggregation induced by oxidative stress. The authors suggest that this effect is related to ginkgo's protective effect on myocardial as well as cerebral injuries.

These results indicate that ginkgo protects the heart by its antioxidant properties as well as by its suppressive effect on platelet aggregation.

Impotence

There are many possible causes of impotence (erectile dysfunction), including emotional stress, fatigue and anxiety. Most cases of chronic (long-term) impotence, however, have an organic origin, including circulatory problems, nerve damage, side effects of medication and hormone imbalance. Some studies indicate that ginkgo biloba extract can be beneficial when the cause is impaired blood flow.

A study by Sikora et al.[17] involved 60 patients with erectile dysfunction, who had not responded to other treatments. After six to eight weeks of treatment with ginkgo biloba extract at 60 mg/day, signs of improved blood supply could be seen. After six months of therapy, in spite of the small dose, 50% of the patients had regained potency. No change in systemic blood pressure was observed.

Ginkgo for the eyes and ears

Senile macular degeneration and diabetic retinopathy are the leading causes of blindness among the elderly in the United States. Experimental studies have found reasons to believe that ginkgo extract might be useful in the prevention and treatment of macular degeneration, diabetic retinopathy and glaucoma,[18-20] thanks to its increased blood flow and free radical scavenging actions. The ear, like the eye, is a delicate organ that is sensitive to oxygen deprivation and other injuries. For a certain kind of hearing loss, acute cochlear deafness, ginkgo extract has been effective in restoring hearing.[21] The extract has also shown a protective effect against toxic injury from the ototoxic drug gentamicin.[22]

Tinnitus (ringing in the ear) is a common symptom in the elderly population. It is considered a symptom of poor circulation and very difficult to treat. Ginkgo biloba treatment has been successful in cases with recent onset (less than one year) of tinnitus.[23]

How ginkgo improves circulation

A main reason why ginkgo biloba has such a broad variety of effects on the body is that it makes the whole circulatory system more efficient. By improving both the elasticity and the tone of the blood vessels, it enhances blood flow.

Ginkgo is unique because it affects all parts of the circulatory system, arteries, veins and capillaries. A healthy circulatory system will provide nutrients including oxygen to all parts of the body and thus improve its function. This is particularly critical in the brain, where the cells are extremely susceptible to a lack of oxygen (hypoxia, cerebral ischemia).

In vitro studies (on isolated blood vessels) and in vivo studies (animal studies) are important to obtain basic information on mechanisms of action that cannot be acquired in human clinical studies. Such studies⁵ have revealed that standardized ginkgo biloba extract:

- Has a spasmolytic (relaxing) action on the arterial wall, which dilates the blood vessels. This vasodilating effect is due to release of endothelium-derived relaxing factor (EDRF).
- Increases capillary perfusion without increasing capillary permeability, thus preventing edema.
- Enhances venous tone and mobility, and thus supports the return of the venous blood and helps clear toxic metabolites that accumulate in the tissues when oxygen supply is insufficient.

Ginkgo biloba has a demonstrated capacity to simultaneously reduce vascular spasm in one area and restore tone in another area when needed. This is an extremely beneficial feature that vasodilating drugs lack. Those drugs may sometimes worsen a condition of constricted circulation by dilating mainly the healthy vessels and leaving the constricted vessels with even less blood and oxygen.

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Mitochondrial antioxidant

According to the free radical theory of aging, oxygen-derived free radicals are responsible for the age-associated decline in cellular function. Mitochondria have recently been shown to play a key role in cellular aging since these "energy factories" of the cell are major targets for free radical attack. Mitochondrial DNA (mtDNA) is particularly vulnerable and accumulates genetic damage over time. There is abundant experimental evidence that oxidative damage to mtDNA accumulates within both liver and brain mitochondria.

Ginkgo biloba extract is a potent antioxidant and scavenger of most free radical species, such as hydroxyl and peroxy radicals and superoxide anions, which is likely to enhance its wide-ranging therapeutic benefits. It is known to protect the energy-producing mitochondria within the cells,²⁴ thus enhancing oxygen utilization and cellular respiration.

The aim of an experimental study by Sastre et al.^[25] was to test whether ginkgo extract could prevent age-associated changes in mitochondria and, if so, to determine whether this effect was due to protection against oxidative stress. In this study, the brain and liver mitochondria of old mice fed ginkgo extract in their drinking water was compared to those of young and old control mice.

The results confirmed that ginkgo prevents age-related changes in mitochondria. Mitochondria from the rats given ginkgo exhibited significantly less genetic damage, peroxide generation and oxidation of the crucial antioxidant glutathione than the untreated old rats. In addition, mitochondria from the old rats given the ginkgo extract resembled those of the young rats much more closely, being similar in size and morphology. The study concluded that standardized ginkgo extract prevents age-related decline in mitochondrial structure and function by protecting mitochondria from oxidative damage.

Membrane-stabilizing activities are also important in the prevention of cell damage and aging, as the health and stability of cell membranes are crucial to the function of the cell. The membranes are vulnerable to lipid peroxidation induced by free radicals.

Oxygen deprivation produces free radicals that can overwhelm the body's own free radical scavengers, such as superoxide dismutase (SOD) and glutathione peroxidase. This leads to peroxidation and damage of membrane lipids. PAF (platelet-activating factor), which also accumulates in the brain during ischemia, stimulates production of additional free radicals. The reperfusion stage, when blood comes back to the oxygen-deprived area, has been shown to cause even more cell damage due to increased lipid peroxidation.

Preventing brain damage from lack of oxygen

Brain cells are more susceptible to free radical damage than other cells because their membranes have a higher content of unsaturated fatty acids (phospholipids) and are particularly vulnerable to peroxidation.

Brain cells are also more susceptible to hypoxia (cerebral ischemia) than any other cells. They require large amounts of energy to function, and when blood supply is restricted there is not enough oxygen and glucose for membrane function and energy production. The result is usually a variety of metabolic changes, such as acidosis, electrolyte shifts, free radical production and increased release of free fatty acids, prostaglandins and neurotransmitters.

Medicinal Use

Since the 1960s, standardized ginkgo leaf extract has been used in research and clinical studies throughout the world. Laboratory research and clinical studies over the past three decades have validated the ancient use of the ginkgo tree as a medicinal remedy. Ginkgo biloba extract has demonstrated effectiveness in improving circulation, particularly in the brain. It is a registered drug in Germany where its major therapeutic applications are "cerebral insufficiency," degenerative dementia, such as Alzheimer's disease, neurosensory problems (e.g. ringing ears, dizziness and impaired vision) and peripheral circulatory disturbances (e.g. leg cramps). It has also been found to be useful in a variety of other conditions, such as impotence due to impaired blood circulation, and fluid retention and breast tenderness in premenstrual syndrome (PMS). Ginkgo is also known to prevent damage from radiation exposure (tested in Chernobyl) and has demonstrated exceptional effectiveness in preventing acute mountain sickness and vascular reactivity to cold exposure and high altitudes.* Besides being used as a prescription drug in Europe, ginkgo is also sold over the counter in lower dosages and used in the prevention of various symptoms of aging, such as decline of hearing,

Ginkgo Is A Multi-Component Extract

Ginkgo leaf extract is a complex mixture containing substances with several active components: flavone glycosides (flavonoids with attached sugar molecules unique to ginkgo), terpenes (Ginkgolides and bilobalides), and organic acids. Flavonoids are a group of substances common in the plant kingdom, occurring as pigments in flowers and fruits. They have a wide range of biochemical functions as antioxidants, free radical scavengers, enzyme inhibitors, enzyme inducers and more. Flavonoids are known to make vitamin C more effective, to increase the strength of capillary walls, and to improve microcirculation. The three major flavonoids in ginkgo are quercetin, kaempferol and isorhamnetine. In addition there are some proanthocyanidins, which can also be found in grape seed, pine bark and bilberry extract. The bilobalides and Ginkgolides have not been found in any other plants. Their unique molecular structure was discovered by the Japanese chemist Nakanishi in 1966, and it has so far been impossible to synthesize them in the lab. The range of their biochemical actions include anti-aggregatory blood platelet activity and reduction of blood viscosity.



Ginkgo extract has shown a remarkable ability to prevent such metabolic disturbances in experimental studies of insufficient oxygen supply to the brain.[26]

An interesting study on the biochemical events in the rat brain after ischemia[27] suggests that lack of oxygen alone cannot initiate peroxidation. This process requires restoration of oxygen supply. It is therefore concluded that the more severe brain damage happens during the reperfusion phase (restoration of circulation) after ischemia. It was shown that administration of ginkgo extract before the ischemic injury prevented reduction of SOD activity and reduced lipid peroxide contents of the mitochondria in the rat brain. This was a clear indicator of the extract's protective effect against post-ischemic injury due to free radical production.

Additional neuroprotective actions

A condition common to many chronic and acute neurological disorders is excitotoxicity-oversensitivity of neurons to the excitatory neurotransmitter glutamate. A series of laboratory experiments[28-30] suggests that ginkgo extract can protect neurons from excitotoxicity, preventing glutamate-induced calcium influx leading to cell death.

A study[31] showed the protective effect of ginkgo extract on mice injected with a neurotoxin known as MPTP. This neurotoxin brings about a close approximation of Parkinson's disease in humans, monkeys and mice. When the mice were pretreated with ginkgo, the neurotoxicity of MPTP was prevented in a dose-dependent manner.

MPTP selectively damages the dopamine system in the nigrostriatal region affected by Parkinson's disease. When the mice were treated with ginkgo extract after exposure to the toxin, dopamine levels recovered more rapidly. Other studies have shown that ginkgo improves dopamine uptake under conditions of oxidative stress.

Brain metabolism generates hydrogen peroxide, a cytotoxic agent that generates oxidative stress in the brain, contributes to cerebral injury and edema following ischemia, and causes programmed cell death (apoptosis) in cortical neurons (nerve cells). Hydrogen peroxide damages DNA and oxidizes lipids and proteins through reactions that have not been entirely clarified but are thought to involve iron and copper ions.

Interesting studies by Oyama et al.[32] and Ni et al.[33] demonstrated that ginkgo extract is able to protect neurons from oxidative stress induced by hydrogen peroxide. When neurons were treated with ginkgo extract for one hour before adding hydrogen peroxide, it was highly effective in protecting nerve cells from damage and death.

One study suggests that hydrogen peroxide activates nuclear factor kappa beta in bovine endothelial cells, thus contributing to atherosclerosis, and demonstrates that ginkgo extract blocks this activation.[34]

vision and memory.



Roncin JP, Schwartz F, D'Arbigny P. EGb 761 in control of acute mountain sickness and vascular reactivity to cold exposure. *Aviat Space Environ Med* 1996;May;67(5):445-52.

Preventing abnormal blood clotting

Another interesting action of ginkgo extract is its inhibition of platelet aggregation and adhesion, which may reduce the risk of thrombus formation. This effect is at least partly exerted by the Ginkgolide terpenes in the extract, which have been shown to be potent inhibitors of platelet-activating factor (PAF). Platelet-activating factor is known to be involved in many inflammatory and allergic processes including bronchial constriction, besides being an activator of platelet aggregation and release of inflammatory components.

A stress antidote

Imagine the potential in our modern world for a compound that reduces the negative effects of stress on the body with no side effects. Ginkgo biloba shows great promise in this direction.

Stress give rise to stress hormones that are both good and bad for us. They are essential for adaptation to acute physical stressors-as in fight or flight situations. [35,36] In our mental and emotional stress situations today, however, we usually do not have much use for these hormones. They therefore accumulate in the body and give rise to disease through their immunosuppressive and neurotoxic effects. One of the detrimental effects of glucocorticoid excess is its ability to damage the hippocampus area of the brain. This area is a structure in the limbic system that is critical to cognitive functions such as learning and memory.

Behavioral studies in rats and mice (whose response patterns are very similar to humans) demonstrated that repeated oral administration of ginkgo extract had significant anti-stress effects, determined in several kinds of stress tests.[37-39]

One study demonstrated that treatment with ginkgo extract decreased serum corticosteroid levels by 50%.[40] The remaining 50% may be the normal level in conditions without stress. This theory is supported by the fact that no detrimental effects on either animal or human health were observed. The results indicate that ginkgo does not affect basal adrenal function but controls the stress-induced excess of corticosteroid levels.

In vivo findings that ginkgo extract can enhance adaptation under stressful conditions supports its extensive use in the elderly to improve their capacity to cope with the demands of everyday living.[41] An interesting "side effect" of chronic ginkgo treatment in rats[42] was the observation that these animals lived significantly longer than the animals that received placebo.

Prevention. . . ginkgo's most important benefit!

Hundreds of scientific studies have confirmed ginkgo's beneficial effects in the human body. Due to its multiple mechanisms of action, ginkgo provides enormous potential protection against our most feared diseases. Aging humans have much to gain from using ginkgo biloba extract as a preventative measure to help maintain neurological and circulatory health.

The fact that one study failed to show improved memory in healthy people who received 40 mg of ginkgo (three times a day) for only six weeks is not relevant to those seeking long-term anti-aging effects. The authors of the JAMA study acknowledge that higher doses of ginkgo for longer periods of exposure might produce the desired effects.



Hundreds of scientific studies have confirmed ginkgo's beneficial effects on the human body. Due to its multiple mechanisms of action, ginkgo provides enormous potential protection against our most feared diseases.

References

1. Solomon PR, Adams F, Silver A, Zimmer J, Deveaux R. Ginkgo for memory enhancement: a randomized controlled trial. *Journal of the American Medical Association* 2002;288(7):835-40.
2. Mix, JA., Crew WD. A double-blind, placebo controlled randomized trial of Ginkgo Biloba extract EGb761 in a sample of cognitively intact older adults: neuropsychological findings. *Human Psychopharmacology Clin Exp* 2002; 17:267-77.
3. Lebars PL, et. al. Ginkgo biloba for dementia. *Journal of the American Medical Association* 1997;278:1327-1332.
4. Kleijnen J, Knipschild P. Ginkgo biloba for cerebral insufficiency. *Br J Clin Pharmacol* 1992;Oct;34(4):352-8.
5. DeFeudis FV. Coronary atherosclerosis: current therapeutic approaches and future trends. *Life Sci* 1991;49(10):689-705 .
6. Blass, Metabolic alterations common to neural and non-neural cells in Alzheimer's disease. *Hippocampus* 1993;3;Spec No:45-53.
7. LeBars PL, Katz MM, Berman N, et al. A placebo-controlled, double-blind, randomized trial of an extract of ginkgo biloba for dementia. *JAMA* 1997;278:1327-1332.
8. Maurer K, Ihl R, Dierks T, Frolich L. Clinical efficacy of ginkgo biloba special extract EGb 761 in dementia of the Alzheimer type. *J Psychiatr Res* 1997;Nov-Dec;31(6):645-55.
9. Subhan, Hindmarch. The psychopharmacological effects of ginkgo biloba extract in normal healthy volunteers. *Int J Clin Pharmacol Res* 1984;4(2):89-93.
10. Rigney U, Kimber S, Hindmarch I. The effects of acute doses of standardized ginkgo biloba extract on memory and psychomotor performance in volunteers. *Phytother Res* 1999;Aug;13(5):408-15.
11. Schubert et al. Depressive episode primarily unresponsive to therapy in elderly patients: efficacy of ginkgo biloba extract (EGB 761) in combination with antidepressants. *Geriatr Forsch* 1993;3:45-53.
12. Schneider B. Ginkgo biloba extract in peripheral arterial diseases. Meta-analysis of controlled clinical studies. *Arzneimittelforschung* 1992;Apr; 42(4): 428-36.
13. Koltai M, Tosaki A, Hosford D, Braquet P. . Ginkgolide B protects isolated hearts against arrhythmias induced by ischemia but not reperfusion. *Eur J Pharmacol* 1989;May 19;164(2):293-302.
14. Shen J-G, Zhou D-Y. Efficiency of Ginkgo biloba extract (EGb 761) in antioxidant protection against myocardial ischemia and reperfusion injury. *Biochem Mol Biol Int* 1995;35:125-134.
15. Haramaki N, Aggarwal S, Kawabata T, Droy-Lefaix MT, Packer L. Effects of natural antioxidant ginkgo biloba extract (EGB 761) on myocardial ischemia-reperfusion injury. *Free Radic Biol Med* 1994; Jun;16(6):789-94.
16. Akiba S, Kawauchi T, Oka T, Hashizume T, Sato T. Inhibitory effect of the leaf extract of ginkgo biloba L. on oxidative stress-induced platelet aggregation. *Biochem Mol Biol Int* 1998;Dec;46(6):1243-8.
17. Sikora R, et al. Ginkgo biloba extract in the therapy of erectile dysfunction. *J Urol* 1989;141:188A.
18. Doly M, Droy-Lefaix MT, Bonhomme B, Braquet P. Effect of ginkgo biloba extract on the electrophysiology of the isolated retina from a diabetic rat. *Presse Med* 1986;Sep 25;15(31):1480-3.
19. Baudouin C, Pisella PJ, Ettaiche M, Goldschild M, Becquet F, Gastaud P, Droy-Lefaix MT. Effects of EGb761 and superoxide dismutase in an experimental model of retinopathy generated by intravitreal production of superoxide anion radical. *Graefes Arch Clin Exp Ophthalmol* 1999;Jan;237(1):58-66.
20. Chung HS, Harris A, Kristinsson JK, Ciulla TA, Kagemann C, Ritch R. Ginkgo biloba extract increases ocular blood flow velocity. *J Ocul Pharmacol Ther* 1999;Jun;15(3):233-40.
21. Bascher V and Steinert W: Differential diagnosis of sudden deafness and therapy with high dose infusions of ginkgo biloba extract. In: *Vertigo, Nausea, Tinnitus and Hypoacusia in Metabolic Disorders*, Amsterdam, 1988, pp. 575-582.

22. Jung HW, Chang SO, Kim CS, Rhee CS, Lim DH. Effects of ginkgo biloba extract on the cochlear damage induced by local gentamicin installation in guinea pigs. *J Korean Med Sci* 1998;Oct;13(5):525-8.
23. Meyer B. A multicenter, double-blind, drug versus placebo study of ginkgo biloba extract in the treatment of tinnitus. *Presse Med* 1986;5:1562-4.
24. Du G, Willet K, Mouithys-Mickalad A, Sluse-Goffart CM, Droy-Lefaix MT, Sluse FE. EGb 761 protects liver mitochondria against injury induced by in vitro anoxia/reoxygenation. *Free Radic Biol Med* 1999;Sep;27(5-6):596-604.
25. Sastre J, Pallardo FV, Garcia de la Asuncion J, Vina J. Mitochondria, oxidative stress and aging. *Free Radic Res* 2000;Mar;32(3):189-98.
26. Schaffler K, Reeh PW. Double blind study of the hypoxia protective effect of a standardized ginkgo biloba preparation after repeated administration in healthy subjects. *Arzneimittelforschung* 1985;35(8):1283-6.
27. Seif El Nasr M; El Fattah AA. Lipid peroxide, phospholipids, glutathione levels and superoxide dismutase activity in rat brain after ischaemia: effect of ginkgo biloba extract. *Pharmacol Res* 1995;Nov;32:5, 273-8.
28. Kobayashi MS, Han D, Packer L. Antioxidants and herbal extracts protect HT-4 neuronal cells against glutamate-induced cytotoxicity. *Free Radic Res* 2000;Feb;32(2):115-24.
29. Zhu L, Wu J, Liao H, Gao J, Zhao XN, Zhang ZX. Antagonistic effects of extract from leaves of ginkgo biloba on glutamate neurotoxicity. *Zhongguo Yao Li Xue Bao* 1997;Jul;18(4):344-7.
30. Oyama Y, Hayashi A, Ueha T. Ca(2+)-induced increase in oxidative metabolism of dissociated mammalian brain neurons: effect of extract of ginkgo biloba leaves. *Jpn J Pharmacol* 1993;Apr;61(4):367-70.
31. Wu WR, Zhu XZ. Involvement of monoamine oxidase inhibition in neuroprotective and neurorestorative effects of ginkgo biloba extract against MPTP-induced nigrostriatal dopaminergic toxicity in C57 mice. *Life Sci* 1999;65(2):157-64.
32. Oyama Y, Chikahisa L, Ueha T, Kanemaru K, Noda K. Ginkgo biloba extract protects brain neurons against oxidative stress induced by hydrogen peroxide. *Brain Res* 1996;Mar 18;712(2):349-52.
33. Ni, Y., Yzhao, B., Hou, J., and Xin, W. Preventive effect of ginkgo biloba on apoptosis in rat cerebellar neuronal cells induced by hydroxyl radicals. *Neurosci Lett* 1996;214: 115-118,.
34. Wei Z, Peng Q, Lau BH, Shah V. Ginkgo biloba inhibits hydrogen peroxide-induced activation of nuclear factor kappa B in vascular endothelial cells. *Gen Pharmacol* 1999;Nov;33(5):369-75.
35. Johnson EO, Kamilaris TC, Chrousos GP, Gold PW. Mechanisms of stress: a dynamic overview of hormonal and behavioral homeostasis. *Neurosci Biobehav Rev* 1992;Summer;16(2):115-30.
36. Munck A, Naray-Fejes-Toth A. Glucocorticoids and stress: permissive and suppressive actions. *Ann N Y Acad Sci* 1994;Nov 30;746:115-30; discussion 131-3.
37. Porsolt RD, Martin P, Lenegre A, Fromage S, Drieu K. Effects of an extract of ginkgo biloba (EGb 761) on "learned helplessness" and other models of stress in rodents. *Pharmacol Biochem Behav* 1990;Aug;36(4):963-71.
38. Rodriguez de Turco EB, Droy-Lefaix MT, Bazan NG. EGb 761 inhibits stress-induced polydipsia in rats. *Physiology and Behavior* 1993;May;53(5):1001-2.
39. Rapin JR, Lamproglou I, Drieu K, DeFeudis FV. Demonstration of the "anti-stress" activity of an extract of ginkgo biloba (Egb 761) using a discrimination learning task. *Gen Pharmacol* 1994;Sep;25(5):1009-16.
40. Amri H, Drieu K, Papadopoulos V. Ex vivo regulation of adrenal cortical cell steroid and protein synthesis, in response to adrenocorticotrophic hormone stimulation, by the ginkgo biloba extract EGb 761 and isolated ginkgolide B. *Endocrinology* 1997;Dec;138(12):5415-26.
41. Rai, G.S., Shovlin, C. and Wesnes, K.A. A double-blind, placebo-controlled study of ginkgo biloba extract in elderly out-patients with mild to moderate memory impairment. *Current Medical Research and Opinion* 1991;12: 350-355.
42. Winter JC. The effects of an extract of ginkgo biloba, EGb 761, on cognitive behavior and longevity in the rat. *Physiol Behav* 1998;Feb 1;63(3):425-33.

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