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Health benefits and future perspectives of Ginkgo biloba

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Abstract. The aim of the review is to discuss *Ginkgo biloba* and its health benefits with future perspectives. Despite the paucity of scientific studies, *G. biloba*, commonly referred to as "Gingko," is a plant abundant in antioxidants that may mitigate inflammation and enhance cardiovascular, cognitive, and ocular health. *G. biloba* presents possible health advantages such as cognitive enhancement, decreased anxiety, and management of glaucoma. *G. biloba* is an old plant species that is good for your health in many ways, including fighting bacteria, cancer, dementia, diabetes, obesity, high cholesterol, and protecting brain. People with respiratory, cardiovascular, and neurological problems often use it. Nonetheless, its therapeutic potential is limited by its capacity to act as free radical scavengers. More study is needed to make sure it is safe and works.

Keywords: Antioxidant, antibacterial activity, antiviral activity, heart health, cancer.

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1. Introduction

The medicinal properties, cognitive benefits, and asthma relief of *Ginkgo biloba*, an East Asian gymnosperm tree, were initially utilized in Ancient China (Atef et al., 2025; Salam et al., 2025; Yang et al., 2025; Nordqvist, 2023; Shahrajabian et al., 2022). Additionally, its nuts were employed for the prevention of bedwetting, sexual energy, bladder irritation alleviation, intestinal worm treatment, and gonorrhea (Chillemi & Chillemi, 2011; Nordqvist, 2023).

G. biloba leaf derivatives, such as glycosides and ginkgolides, are becoming increasingly popular as food additives due to their potential medicinal benefits. Ligin, which is copious and possesses exceptional antioxidant properties, is present in ginkgo shells, which are manufactured as industrial byproducts (Tabassum et al., 2022). Ginkgo seeds have been employed to alleviate symptoms such as coughs, sputum, fever, diarrhea, toothaches, skin diseases, gonorrhea, and overactive bladder (Isah, 2015). *G. biloba* seeds have a hypocholesterolemic effect on lipid metabolism (Kushwaha et al., 2014).

G. biloba, a supplement with therapeutic properties for blood disorders, memory issues, cardiovascular function, and eye health, is a widely used herbal medication (Nordqvist, 2023; Tabassum et al., 2022; Diamond et al., 2000). It safeguards against oxidative cell injury by containing flavonoids and antioxidants (Singh et al., 2019; Li et al., 2022; Nordqvist, 2023). *G. biloba*, available in capsules, tablets, and teas, is recommended for adults, taking 4-6 weeks for improvement (Shahverdian & Jafari, 2025; Nordqvist, 2023; Tabassum et al., 2022; Diamond, et al., 2000). Not recommended for children, pregnant women, epilepsy patients, blood thinners, and diabetes patients (Trabert & Seifert, 2024; Dincel et al., 2023; Nordqvist, 2023).

Ginkgo medication should be administered with caution to prevent interactions with other medications, risks such as internal hemorrhage, blood circulation disorders, serotonin syndrome, and exacerbation of monoamine oxidase inhibitor effects, and to avoid poisonous ginkgo seeds (Nordqvist, 2023; Sahoo et al., 2018; Sultan et al., 2018). The fundamental aim of this review is to discuss *G. biloba* and its health benefits with future perspectives.

2. Health benefits

2.1. Anti-aging effects

Oxidative stress causes skin aging, leading to increased wrinkles, dryness, and dullness, characterized by collagen loss and poor desquamation (Tabassum et al., 2022). Treating rats with EGb 761 stopped them from getting frostbite and may also slow down the aging process (Aizawa et al., 2019). Total lactones of Ginkgo reduced lipid breakdown, nitric oxide (NO) levels, and cell death in the brains of old mice (Nowak et al., 2021). EGb 716 stops inflammation, lowers oxidative stress, and makes insulin intolerance better (Liu et al., 2020).

2.2. Anti-bacterial activity

Ginkgo extracts are excellent at killing different kinds of germs. This might be because they contain biflavonoids that are antibacterial (Ražná et al., 2021; Menezes & Diederich, 2021). The most studied biflavonoid, amentoflavone, effectively combats a variety of bacteria, including *Enterococcus faecium*, *Staphylococcus aureus*, *Streptococcus mutans*, *Escherichia coli* O-157, *Escherichia coli*, and *Pseudomonas aeruginosa* (Hwang et al., 2013). It might also be able to treat dangerous cyanobacterial blooms, which are a problem for the environment around the world (Šamec et al., 2022). Mentoflavone and ginkgetin can kill *Streptococcus suis*, potentially leading to economic costs and public health issues (Shen et al., 2018).

2.3. Anti-depressant effects

Research has shown that *G. biloba* extract (GBE) can alleviate feelings of sadness and diminish signs of brain impairment in elderly individuals (Dai et al., 2018; Liang et al., 2019). Nonetheless, additional research is required to comprehend its effects on depression within the general populace. The gut microbiota, especially probiotics, can affect the onset and recovery of depression (Tabassum et al., 2022). Polysaccharides, especially those from *G. biloba*, can help with depression by changing the relationship between microbiota and the brain (Ganesan et al., 2018; Vaghef-Mehrabany et al., 2020). GBE can alleviate depressive symptoms and diminish serum S100B levels, thereby reinstating neurological function in older people (Tabassum et al., 2022). Diterpene ginkgolides (DGs) found in GBE protect neurons, which could make it easier to treat major depressive disorders (Tabassum et al., 2022). Chronic DG therapy enhances depressive traits in mice with cardiac illness (Wang et al., 2020).

2.4. Anti-diabetic effects

When taken by mouth, ginkgolide B can protect lipid cells from insulin resistance and inflammation caused by oxygen deficiency. It does this by increasing the release of adiponectin, blocking insulin receptor substrate 1 receptors, lowering the production of inflammatory adipokines, and lowering NF- κ B/JNK activation (Wang et al., 2015; Priyanka et al., 2017; Tabassum et al., 2022). It also enhances cholinergic vasorelaxation, phenylephrine vasoconstriction, and improves enzyme expression (Wang et al., 2015).

2.5. Anti-fungal activity

Ginkgo biflavonoids are excellent at killing fungi. Alternaria alternata, Cladosporium oxysporum, and Fusarium culmorum are the fungi that bilobetin kills the best (Krauze-Baranowskaa and Wiwart, 2003). Krauze-Baranowska and Wiwart (2003) also reported that Ginkgetin and 7-O-methylamentoflavone show greater efficacy against Alternaria alternata. The bisflavonoids were not able to kill Alternaria alternate and Cladosporium oxysporum because they did not have a methoxyl group (Šamec et al., 2022). Amentoflavone works well against Candida albicans by causing cell death and mitochondrial dysfunction (Hwang et al., 2013).

2.6. Anti-hypertensive effects

Hypertension gets worse over time and can cause serious health problems like acute coronary attacks, chronic heart failure, and stroke (Tabassum et al., 2022). *G. biloba* has anti-hypertensive effects in animal models, including hypotensive and renoprotective effects in rats with impaired kidneys (Abdel-Zaher et al., 2017). This is due to increased eNOS expression and NO production, which lowers blood pressure (Eisvand et al., 2020).

2.7. Anti-inflammatory effect

Researchers have found that ginkgo extract reduces inflammation in both humans and animals, with ginkgetin demonstrating greater inhibitory effects than isoginkgetin (Hill, 2024). Traditional Chinese medicine has used *G. biloba* flavonoids to treat coughs, asthma, and lung disorders (Tabassum et al., 2022). The strongest compounds in GBEs, bilobetin and isoginkgetin, have been found to be anti-inflammatory. They do this by increasing NO inhibition ratios and decreasing the levels of TNF-α, IL-6, PGE2, and cyclooxygenase 2 mRNA. This suggests that new anti-inflammatory drugs might be possible (Li et al., 2019).

2.8. Anti-lipidemic effect

Dyslipidemia, defined by elevated triglycerides, diminished HDL cholesterol, and heightened LDL cholesterol, is associated with obesity and insulin resistance (Tabassum et al., 2022). In aortic tissue, *G. biloba* has been observed to reduce MDA levels while elevating glutathione (GSH) levels (Huang et al., 2018). *G. biloba* therapy markedly decreases cholesterol, triglycerides, and HDL-C levels in male rabbits while elevating HDL-C levels (Tabassum et al., 2022).

2.9. Anti-obesity effects

Administration of Ginkgolide B has been shown to aid in weight reduction, possibly via activating the insulin signaling pathway (Tabassum et al., 2022). The Ginkgolide B components ginkgetin, isoginkgetin, bilobetin, and sciadopitysin have moderate to strong inhibitory effects on pancreatic lipase (PL), perhaps positioning them as lead compounds for the development of bioflavonoid-type PL inhibitors (Liu et al., 2018). Ginkgolide B and C have been investigated in a model of obesity induced by a high-fat diet, revealing their impact on hepatic steatosis, lipid accumulation, and lipolysis (Luo et al., 2017).

2.10. Anti-platelet activity

Platelet-activating factor (PAF) is a signaling molecule that facilitates the immunological response to infection and neuronal injury. It stimulates the PAF receptor (PAFR) to initiate inflammatory proteins. A type of ginkgolide called ginkgolide B lowers the expression of CD40L and normal T cells by platelets activated by thrombin and collagen (Tabassum et al., 2022). Like ginkgolides, bilobalide has health benefits, such as anti-inflammatory properties and lowering the inflammation and pain caused by low oxygen levels (Huang et al., 2014).

2.11. Antioxidants

The health claims for ginkgo may come from its high flavonoid and terpenoid content, but its exact effects are still not clear (Hill, 20224). Antioxidants, like ginkgo products, help keep you healthy by stopping diseases linked to oxidative stress (Martínez-Solís et al., 2019; de Souza et al., 2020; Šamec et al., 2022). Amentoflavone is a strong antioxidant that showed a lot of promise in food models and *in vitro* experiments. It was excellent at getting rid of DPPH, ABTS, superoxide, and hydroxyl radicals (Šamec et al., 2022).

2.12. Anti-viral activity

Biflavonoids have been investigated for more than two decades as prospective anti-viral medicines, demonstrating inhibitory effects against many viruses (Menezes & Diederich, 2021; Šamec et al., 2022). Amentoflavone has garnered attention during the coronavirus pandemic for its antiviral properties against SARS-CoV-2 (Singh, 2021; Hossain et al., 2021). Ginkgetin, extracted from ginkgo leaves, exhibits antiviral effects by blocking sialidase, a crucial enzyme in the influenza virus's life cycle (Šamec et al., 2022). A combined *in vitro* and *in silico* investigation investigated the anti-SARS-CoV-2 effects of biflavonoids including sciadopitysin, ginkgetin, isoginkgetin, amentoflavone, and bilobetin (Šamec et al., 2022). The evaluated drugs had significant anti-SARS-CoV-2 3CLpro activity, with sciadopitysin identified as the most effective inhibitor (Šamec et al., 2022). The mechanisms of inhibition have been validated via kinetic investigations and molecular docking simulations (Xiong et al., 2021).

2.13. Anxiety

Ginkgo leaf extract may alleviate anxiety symptoms in generalized anxiety disorder patients, but Xanax users should avoid it due to potential drug effectiveness reduction (Nordqvist, 2023). Animal studies indicate that the antioxidant content of ginkgo could potentially alleviate anxiety symptoms, although conclusive findings are still pending (Hill, 2024). Ginkgo leaf extract may

improve mood and antidepressant activity, reduce corticosteroid synthesis, and prevent neuron degeneration and memory enhancement in generalised anxiety disorder (GAD) patients. Medications such as GBE and *G. biloba* products treat GAD, a common mental illness (Singh et al., 2017). Research has shown that GBE can enhance emotional function and stabilize mood in cognitively impaired patients, while extract of *G. biloba* 761 (EGb 761) alleviates anxiety symptoms in individuals experiencing mental deterioration (Woelk et al., 2007; Montes et al., 2015).

2.14. Asthma and COPD symptoms

Research indicates that ginkgo may alleviate symptoms of asthma and chronic obstructive pulmonary disease (COPD) owing to its anti-inflammatory properties (Tao et al., 2019; Hill, 2024). Researchers found that using ginkgo extract along with glucocorticosteroid medicine reduced the amount of inflammatory chemicals in saliva compared to using standard treatment alone (Tang et al., 2007; Hill, 2024).

2.15. Blood circulation and heart health

Ginkgo seeds have long been used in traditional Chinese medicine to enhance energy channels in organ systems such as the kidneys, liver, brain, and lungs. Heart disease patients experience a 12% rise in circulating nitric oxide (Hill, 2024). Researchers have found that *G. biloba* and its isolated compound can benefit cardiovascular problems such as cardiotoxicity, arrhythmia, and heart failure (Akaberi et al., 2023). However, a double-blind trial found it did not reduce total mortality or cardiovascular disease-related death rates (Akaberi et al., 2023).

2.16. Cardiovascular disease

Wang et al. (2022) proposed that biflavonoids might contribute to the treatment of cerebrovascular illness. Ginkgetin greatly slowed down the production of lipids caused by oleic acid and lowered levels of total cholesterol and triglycerides. This suggests that it may be a natural way to treat atherosclerosis (Šamec et al., 2022). Dell'Agli et al. (2006) looked into how ginkgo biflavonoids could lower cAMP phosphodiesterase activity and help blood vessels relax. Amentoflavone, the most extensively researched biflavonoid from ginkgo, has demonstrated potential in safeguarding cardiovascular health (Šamec et al., 2022). Ginkgo leaf extract, which is high in catecholamines and antioxidants, can help prevent heart disease and improve blood flow, especially before heart surgery, by lowering lipid peroxidation and tissue necrosis (Mahadevan & Park, 2008).

2.17. Endocrine system

The endocrine system primarily regulates blood sugar levels (insulin), governs the differentiation, growth, and functionality of reproductive organs (testosterone and estradiiol), and facilitates body growth and energy metabolism (growth hormone and thyroid hormone). It is possible that ginkgo polysaccharides, isolated chemicals, and extracts from *G. biloba* could help treat endocrine disorders, especially type 2 diabetes mellitus, by increasing insulin production, protecting pancreatic β -cells, and acting as antioxidants (Akaberi et al., 2023).

2.18. Gastrointestinal system

G. biloba formulations and substances have demonstrated efficacy in addressing gastrointestinal disorders such as colitis, peptic ulcer, gastric ulcer, and inflammatory bowel disease (Akaberi et al., 2023). They possess hepatoprotective properties against hepatotoxicity and damage.

2.19. Glaucoma

G. biloba extract is easy to get and has many biological effects that could make it a useful treatment for glaucoma. These effects include improving both central and peripheral blood flow, reducing serum viscosity, relaxing vasospasm, acting as an antioxidant, stopping platelet activating factor, preventing apoptosis, and reducing excitotoxicity (Ritch, 2000). People with glaucoma and macular degeneration demonstrated improved eyesight after ingesting 120 mg of ginkgo daily for 8 weeks (Nordqvist, 2023).

2.20. Headaches and migraine

Research on ginkgo's efficacy in treating headaches is scarce; nevertheless, its anti-inflammatory and antioxidant qualities may be beneficial for stress-induced headaches or migraines resulting from diminished blood flow or constricted blood vessels (Hill, 2024). Nonetheless, excessive vasodilation may prove ineffective in alleviating migraine headaches (Hill, 2024).

2.21. Hepatoprotective effects

The antioxidant activity of *G. biloba* is thought to contribute to its hepatoprotective effects, which encompass the restoration of SOD, GPX, and CAT activities, enhancement of glutathione levels, and diminution of lipid peroxidation and hydroperoxide concentrations in the liver (Ganesan et al., 2018). *G. biloba* exhibits hepatoprotective properties against carbon tetrachloride-induced hepatic oxidative damage and has demonstrated the ability to inhibit liver fibrosis in rats (Shenoy et al., 2001; Zhou et al., 2010).

2.22. Immunity system and cancer

Various models have demonstrated the cytotoxic, anti-tumor, and anti-cancer properties of *G. biloba* extracts (Akaberi et al., 2023). They can help many types of cancer by blocking the ERK/NF- kappa B signaling pathway and metastasis in stomach cancer, encouraging cell death, and controlling GST-Pi expression in liver cancer (Akaberi et al., 2023). *In vitro* studies have shown that ginkgo leaves can stop cell growth and fight cancer. This might be because they contain flavonoids (Ahmed et al., 2017; Silva et al., 2019; Silka et al., 2022). The biflavonoids ginkgetin and amentoflavone from ginkgo have been studied the most. They stop the growth of cancer cells by stopping the cell cycle, starting apoptosis, speeding up autophagy, and targeting signaling pathways that aren't working properly (Adnan et al., 2020). Ginkgo leaf extract also has antioxidant, antiangiogenic, and gene expression effects, improving cellular tolerance to oxidative stress and reducing angiogenesis (Sagar et al., 2006). *G. biloba* exocarp extracts (GBEE) can treat hepatocellular carcinoma and Lewis lung cancer (Han et al., 2016).

2.23. Immunomodulatory effects

G. biloba polysaccharides (GBPS) are good immune modulators that can boost immune and anticancer responses (Tabassum et al., 2022). GBPS-2 and GBPS-3 improve the activity of NO, TNF-α, IL-1, and IL-6 and make macrophages better at phagocytosis (Ren et al., 2019). This makes them possible as immune-boosting supplements. A study found that eating *G. biloba* (GB) can lower the harmful effects of diazinon and oxidative stress (Tabassum et al., 2022). However, eating a lot of GB may weaken immune system (Tabassum et al., 2022). *G. biloba* exocarp polysaccharides (GBEP) affect both cellular and humoral immunity. This suggests that they could be used as a medicine to stop diseases from happening and boost immunity when taken in the right amounts (Parsad et al., 2003; Xu et al., 2008).

2.24. Metabolomics disease

People use ginkgo leaf extracts to treat metabolic disorders like hyperlipidemia, but the definition of their bioactive constituents is still lacking (Liu et al., 2018). Liu et al. (2018) looked at how ginkgetin, bilobetin, and sciadopitysin can stop pancreatic lipase from working. Pancreatic lipase is an important enzyme for controlling fat absorption.

2.25. Memory enhancement, dementia, and Alzheimer's

Researchers have found that *G. biloba* extract, EGb 761, is clinically effective in treating Alzheimer's dementia and improving cognitive function (Mix & Crews, 2002; Nordqvist, 2023; Hill, 2024). It promotes healthy blood circulation and protects the brain from neuronal damage. While some studies show a reduction in cognitive decline in dementia patients, others fail to replicate this (Hill, 2024). Researchers have found that ginkgo leaf extract can stop the production of amyloid beta peptide (A β), the buildup of reactive oxygen species (ROS), and the death of neurons. These are all things that are known to contribute to Alzheimer's disease (Yao et al. 2004). It also improves cerebral blood flow, life span, and memory complaints (Yang et al., 2005). However, its effectiveness in humans remains uncertain.

2.26. Muscular and skeletal system

G. biloba extracts have antioxidant and anti-apoptotic effects, potentially mitigating osteoporosis. Research indicates that *G. biloba* extract can elevate bcl-2 expression and diminish bax expression in osteoblasts while enhancing mineral content in osteoporosis-induced rats (Akaberi et al., 2023). These chemicals may also mitigate osteoarthritis.

2.27. Neuroprotective effects

G. biloba seeds have been shown to prevent neurodegenerative disorders by improving cerebral blood supply and blood circulation (Wang & Zhang, 2019). Studies have shown that GBE can improve various ailments, such as Alzheimer's disease and brain ischemia (Zuo et al., 2017). Ginkgo, a plant known for its biflavonoids, has potential for treating neurodegenerative diseases (Barbalho et al., 2022). According to Kang et al. (2005), ginkgetin, amentoflavone, and ginkgetin protect neurons the most against cytotoxic insults caused by oxidative stress and amyloid-β. Amentoflavone has therapeutic potential in treating Alzheimer's, Parkinson's, depression, and aging (Varshney et al. 2021) but shows poor brain permeability in mice *in vivo* (Colovic et al., 2008).

2.28. Premenstrual syndrome (PMS)

Ginkgo may help treat premenstrual syndrome symptoms, with a 23% reduction in symptoms (Hill, 2024). Further research is needed to understand the cause-and-effect relationship.

2.29. Renal system

G. biloba extracts may help protect the kidneys in a number of different ways, including stopping the harmful effects of carbon tetrachloride, stopping TiO₂ from hurting renal cells, lowering inflammation, and increasing antioxidant activity (Akaberi et al., 2023). These extracts are also good for diabetic nephropathy, improving renal ischemia-reperfusion injury, chronic kidney disease, and hypertension-induced renal injury (Akaberi et al., 2023).

2.30. Respiratory system

According to Akaberi et al. (2023), *G. biloba* extracts, flavonoids, and ginkgolides may help people who have breathing problems by stopping leukocyte elastase activity, reducing inflammation, stopping pulmonary fibrosis, and keeping the balance of M1/M2 macrophages. EGb761 also prevents acute lung injury by decreasing NF-kB activation pathways (Akaberi et al., 2023). Ginkgolide M and B can reduce inflammatory cell aggregation and improve lung damage (Wu et al., 2016). One protein, EGb 761, which is involved in problems with blood clotting, can lower swelling in the lungs and control the activity of leukocyte elastase (Tao et al., 2019).

2.31. Sexual dysfunction

By boosting blood circulation to the affected areas, the herb ginkgo, known for raising blood nitric oxide levels, may help reduce the symptoms of sexual dysfunction (Mashhadi et al., 2021). Research indicates that ginkgo may be less effective than antidepressant medicines or SSRIs. Ginkgo and treatment were successful in enhancing sexual desire and satisfaction but not in addressing sexual dysfunction (Meston et al., 2008).

2.32. Tinnitus, geriatric, and psychiatric disorders

Ginkgo leaf extract has been proposed as a potential remedy for tinnitus (Rejali et al., 2004), a prevalent auditory condition (Drew & Davies, 2001), and has demonstrated efficacy against senile macular degeneration (Diamond et al., 2000), vertigo (Issing et al., 2005), and schizophrenia (Atmaca et al., 2005), with clinical trials indicating beneficial effects on antioxidant enzyme levels.

2.33. Vision and eye health

There is little research on how ginkgo affects vision and eye health. While ginkgo supplements may increase blood flow to the eyes, they do not necessarily improve vision (Kang and Lin, 2018; Hill, 2024). More research is needed to determine if ginkgo can improve vision capacity or slow the progression of degenerative eye disease (Evans, 1996; Hill, 2024).

4. Conclusion and Future Perspectives

Research on the plant *G. biloba* has shown promising results in treating numerous symptoms and disorders. Nonetheless, potential drug interactions and adverse effects are under investigation in clinical trials. The utilization of varied procedures and research techniques complicates the assessment of efficacy and inter-study comparisons. Subsequent research should establish

more sensitive and systematic outcome measures, validate interrater and intrarater reliability, and corroborate patient descriptions and diagnoses. Some of the ways that *G. biloba* might be used as a medicine are to protect DNA from oxidative damage, stop mitochondrial reactive oxygen species and apoptosis, and control the membrane potential of mitochondria. Comprehending these characteristics enables clinicians and researchers to make informed decisions that enhance patient experiences, safety, and analysis.

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References

- Abdel-Zaher, A.O., Farghaly, H.S., El-Refaiy, A.E. & Abd-Eldayem, A.M. (2017). Protective effect of the standardized extract of ginkgo biloba (EGb761) against hypertension with hypercholesterolemia-induced renal injury in rats: Insights in the underlying mechanisms. Biomedicine & Pharmacotherapy, 95, 944-955.
- Adnan, M., Rasul, A., Hussain, G., Shah, M.A., Zahoor, M.K., Anwar, H.... & Selamoglu, Z. (2020). Ginkgetin: A natural biflavone with versatile pharmacological activities. Food and Chemical Toxicology, 145, 111642.
- Ahmed, H.H., Shousha, W.G., El-Mezayen, H.A., El-Toumy, S.A., Sayed, A.H. & Ramadan, A.R. (2017). Biochemical and molecular evidences for the antitumor potential of *Ginkgo biloba* leaves extract in rodents. Acta Biochimica Polonica, 64(1), 25-33.
- Aizawa, T., Kuwabara, M., Kubo, S., Aoki, S., Azuma, R., Kiyosawa, T. (2019). Protective effect of extract of Ginkgo biloba 761 against frostbite injury in rats. and Reconstructive Surgery, 143, 1657-1664.
- Akaberi, M., Baharara, H., Amiri, M.S., Moghadam, A.T., Sahebkar, A. & Emami, S.A. (2023). Ginkgo biloba: An update review on pharmacological, ethnobotanical, and phytochemical studies. Pharmacological Research-Modern Chinese Medicine, 100331.
- Atef, F., Abdelkawy, M.A., Eltanany, B.M., Pont, L., Fayez, A.M., Abdelhameed, M.F.... & Otify, A.M. (2025). A comprehensive investigation of *Clerodendrum infortunatum* Linn. using LC-QTOF-MS/MS metabolomics as a promising anti-alzheimer candidate. Scientific Reports, 15(1), 859.
- Atmaca, M., Tezcan, E., Kuloglu, M., Ustundag, B. & Kirtas, O. (2005). The effect of extract of *Ginkgo biloba* addition to olanzapine on therapeutic effect and antioxidant enzyme levels in patients with schizophrenia. Psychiatry and Clinical Neurosciences, 59(6), 652-656.
- Barbalho, S.M., Direito, R., Laurindo, L.F., Marton, L.T., Guiguer, E.L., Goulart, R.D.A.... & Araújo, A.C. (2022). *Ginkgo biloba* in the aging process: A narrative review. Antioxidants, 11(3), 525.
- Chillemi, S. & Chillemi, M. (2011). The Complete Herbal Guide: A Natural Approach to Healing the Body. Lulu Inc., North Carolina.
- Colovic, M., Fracasso, C. & Caccia, S. (2008). Brain-to-plasma distribution ratio of the biflavone amentoflavone in the mouse. Drug Metabolism Letters, 2(2), 90-94.
- Dai, C.X., Hu, C.C., Shang, Y.S. & Xie, J. (2018). Role of *Ginkgo biloba* extract as an adjunctive treatment of elderly patients with depression and on the expression of serum S100B. Medicine, 97(39), e12421.
- de Souza, G.A., de Marqui, S.V., Matias, J.N., Guiguer, E.L. & Barbalho, S.M. (2020). Effects of *Ginkgo biloba* on diseases related to oxidative stress. Planta medica, 86(06), 376-386.
- Dell'Agli, M., Galli, G.V. & Bosisio, E. (2006). Inhibition of cGMP-phosphodiesterase-5 by biflavones of Ginkgo biloba. Planta medica, 72(05), 468-470.

- Diamond, B.J., Shiflett, S.C., Feiwel, N., Matheis, R.J., Noskin, O., Richards, J.A. & Schoenberger, N.E. (2000). *Ginkgo biloba* extract: mechanisms and clinical indications. Archives of physical medicine and rehabilitation, 81(5), 668-678.
- Dincel, D., Aydemir, G.G., Altınbaşak, O., Altınbaşak, B.B. & Mayda, P.Y. (2023). A review of medicinal properties of *Ginkgo biloba* L. Journal of Kocaeli Health and Technology University, 1(1), 1-19.
- Drew, S. & Davies, E. (2001). Effectiveness of *Ginkgo biloba* in treating tinnitus: double blind, placebo controlled trial. BMJ, 322(7278), 73.
- Eisvand, F., Razavi, B.M. & Hosseinzadeh, H. (2020). The effects of *Ginkgo biloba* on metabolic syndrome: A review. Phytotherapy Research, 34(8), 1798-1811.
- Evans, J. R., & Cochrane Eyes and Vision Group. (1996). Ginkgo biloba extract for age-related macular degeneration. Cochrane Database of Systematic Reviews, 2013(1).
- Ganesan, K., Jayachandran, M. & Xu, B. (2018). A critical review on hepatoprotective effects of bioactive food components. Critical Reviews in Food Science and Nutrition, 58(7), 1165-1229.
- Han, D., Cao, C., Su, Y., Wang, J., Sun, J., Chen, H. & Xu, A. (2016). *Ginkgo biloba* exocarp extracts inhibits angiogenesis and its effects on Wnt/β-catenin-VEGF signaling pathway in Lewis lung cancer. Journal of Ethnopharmacology, 192, 406-412.
- Hill, A. (2024).12 Possible benefits of *Ginkgo biloba*, plus side effects and dosage. Reviewed by Jared Meacham. https://www.healthline.com/nutrition/ginkgo-biloba-benefits#antioxidants
- Hossain, R., Islam, M.T., Ray, P., Jain, D., Saikat, A.S.M., Nahar, L.... & Calina, D. (2021). Amentoflavone, new hope against SARS-CoV-2: an outlook through its scientific records and an in silico study. Pharmacognosy Research, 13(3).
- Huang, P., Zhang, L., Chai, C., Qian, X. C., Li, W., Li, J.S.... & Cai, B.C. (2014). Effects of food and gender on the pharmacokinetics of ginkgolides A, B, C and bilobalide in rats after oral dosing with ginkgo terpene lactones extract. Journal of Pharmaceutical and Biomedical Analysis, 100, 138-144.
- Huang, W.C., Chen, Y.L., Liu, H.C., Wu, S.J. & Liou, C.J. (2018). Ginkgolide C reduced oleic acid-induced lipid accumulation in HepG2 cells. Saudi pharmaceutical journal, 26(8), 1178-1184.
- Hwang, J.H., Choi, H., Woo, E.R. & Lee, D.G. (2013). Antibacterial effect of amentoflavone and its synergistic effect with antibiotics. Journal of Microbiology and Biotechnology, 23(7), 953-958.
- Isah, T. (2015). Rethinking Ginkgo biloba L.: Medicinal uses and conservation. Pharmacognosy Reviews, 9(18), 140-148.
- Issing, W., Klein, P. & Weiser, M. (2005). The homeopathic preparation Vertigoheel® versus Ginkgo biloba in the treatment of vertigo in an elderly population: A double-blinded, randomized, controlled clinical trial. Journal of Alternative & Complementary Medicine, 11(1), 155-160.
- Kang, S.S., Lee, J.Y., Choi, Y.K., Song, S.S., Kim, J.S., Jeon, S.J., Han, Y.N., Son, K.H. & Han, B.H. (2005). Neuroprotective effects of naturally occurring biflavonoids. Bioorganic & Medicinal Chemistry Letters, 15, 3588-3591.
- Kang, J. M. & Lin, S. (2018). Ginkgo biloba and its potential role in glaucoma. Current Opinion in Ophthalmology, 29(2), 116-120.
- Krauze-Baranowska, M. & Wiwart, M. (2003). Antifungal activity of biflavones from *Taxus baccata* and *Ginkgo biloba*. Zeitschrift für Naturforschung C, 58(1-2), 65-69.
- Kushwaha, S.K., Sharma, C.S., Singh, H.P., Ankalgi, A., Ranawat, M.S. & Mehtab, R. (2014). *Ginkgo biloba* a source of bioactive natural products: a review. Indo American Journal of Pharmaceutical Research, 4(12), 5622-9.
- Li, M., Li, B., Hou, Y., Tian, Y., Chen, L., Liu, S.... & Dong, J. (2019). Anti-inflammatory effects of chemical components from Ginkgo biloba L. male flowers on lipopolysaccharide-stimulated RAW264. 7 macrophages. Phytotherapy Research, 33(4), 989-997.
- Li, Y., Zhu, X., Wang, K., Zhu, L., Murray, M. & Zhou, F. (2022). The potential of Ginkgo biloba in the treatment of human diseases and the relationship to Nrf2–mediated antioxidant protection. Journal of Pharmacy and Pharmacology, 74(12), 1689-1699.
- Liang, Z.H., Jia, Y.B., Wang, M.L., Li, Z.R., Li, M., Yun, Y.L. & Zhu, R.X. (2019). Efficacy of *Ginkgo biloba* extract as augmentation of venlafaxine in treating post-stroke depression. Neuropsychiatric Disease and Treatment, 2551-2557.
- Liu, P.K., Weng, Z.M., Ge, G.B., Li, H.L., Ding, L.L., Dai, Z.R. ... & Hou, J. (2018). Biflavones from *Ginkgo biloba* as novel pancreatic lipase inhibitors: Inhibition potentials and mechanism. International Journal of Biological Macromolecules, 118, 2216-2223.

- Liu, Y., Liu, Y. & Zhang, W. (2020). Network pharmacology-based strategy to investigate the pharmacological mechanisms of *Ginkgo biloba* extract for aging. Evidence-Based Complement Alternative Medicine, 8508491, 1-10.
- Luo, L., Li, Y., Wang, D., Zhao, Y., Wang, Y., Li, F. ... & Huang, C. (2017). Ginkgolide B lowers body weight and ameliorates hepatic steatosis in high-fat diet-induced obese mice correlated with pregnane X receptor activation. RSC advances, 7(60), 37858-37866.
- Mahadevan, S. & Park, Y. (2008). Multifaceted therapeutic benefits of *Ginkgo biloba* L.: Chemistry, efficacy, safety, and uses. Journal of Food Science, 73(1), R14-R19.
- Martínez-Solís, I., Acero, N., Bosch-Morell, F., Castillo, E., González-Rosende, M. E., Muñoz-Mingarro, D.... & Villagrasa, V. (2019). Neuroprotective potential of *Ginkgo biloba* in retinal diseases. Planta Medica, 85(17), 1292-1303.
- Mashhadi, Z.N., Irani, M., Mask, M.K. & Methie, C. (2021). A systematic review of clinical trials on Ginkgo (*Ginkgo biloba*) effectiveness on sexual function and its safety. Avicenna Journal of Phytomedicine, 11(4), 324.
- Menezes, J.C. & Diederich, M.F. (2021). Bioactivity of natural biflavonoids in metabolism-related disease and cancer therapies. Pharmacological research, 167, 105525.
- Meston, C.M., Rellini, A.H. & Telch, M.J. (2008). Short-and long-term effects of *Ginkgo biloba* extract on sexual dysfunction in women. Archives of Sexual Behavior, 37, 530-547.
- Mix, J.A. & Crews Jr, W.D. (2002). A double-blind, placebo-controlled, randomized trial of *Ginkgo biloba* extract EGb 761® in a sample of cognitively intact older adults: neuropsychological findings. Human Psychopharmacology: Clinical and Experimental, 17(6), 267-277.
- Montes, P., Ruiz-Sanchez, E., Rojas, C. & Rojas, P. (2015). Ginkgo biloba extract 761: a review of basic studies and potential clinical use in psychiatric disorders. CNS & Neurological Disorders-Drug Targets (Formerly Current Drug Targets-CNS & Neurological Disorders), 14(1), 132-149.
- Nordqvist, J. (2023). Health benefits of *Gingko biloba*. Reviewed by Debra Rose Wilson. https://www.medicalnewstoday.com/articles/263105
- Nowak, A., Kojder, K., Zielonka-Brzezicka, J., Wróbel, J., Bosiacki, M., Fabiańska, M., Wróbel, M., Sołek-Pastuszka, J. & Klimowicz, A. (2021). The use of *Ginkgo biloba* L. as a neuroprotective agent in the Alzheimer's disease. Frontiers in Pharmacology, 12, 775034.
- Parsad, D., Pandhi, R. & Juneja, A. (2003). Effectiveness of oral *Ginkgo biloba* in treating limited, slowly spreading vitiligo. Clinical and Experimental Dermatology, 28(3), 285-287.
- Ražná, K., Sawinska, Z., Ivanišová, E., Vukovic, N., Terentjeva, M., Stričcík, M., Kowalczewski, P.Ł., Hlavačcková, L., Rovná, K., Žiarovská, J. et al. (2020). Properties of *Ginkgo biloba* L.: Antioxidant characterization, antimicrobial activities, and genomic MicroRNA based marker fingerprints. International Journal of Molecular Sciences, 21, 3087.
- Rejali, D., Sivakumar, A. & Balaji, N. (2004). Ginkgo biloba does not benefit patients with tinnitus: a randomized placebo-controlled double-blind trial and meta-analysis of randomized trials. Clinical Otolaryngology & Allied Sciences, 29(3), 226-231.
- Ren, Q., Chen, J., Ding, Y., Cheng, J., Yang, S., Ding, Z.... & Ding, Z. (2019). *In vitro* antioxidant and immunostimulating activities of polysaccharides from *Ginkgo biloba* leaves. International Journal of Biological Macromolecules, 124, 972-980.
- Ritch, R. (2000). Potential role for Ginkgo biloba extract in the treatment of glaucoma. Medical Hypotheses, 54(2), 221-235.
- Sagar, S.M., Yance, D. & Wong, R.K. (2006). Natural health products that inhibit angiogenesis: a potential source for investigational new agents to treat cancer—Part 1. Current Oncology, 13(1), 14.
- Sahoo, A.K., Dandapat, J., Dash, U.C. & Kanhar, S. (2018). Features and outcomes of drugs for combination therapy as multitargets strategy to combat Alzheimer's disease. Journal of Ethnopharmacology, 215, 42-73.
- Salam, S.A., George, C.S., Al-Abdulsalam, N.K., Abdel-Moneim, A.M. & Essawy, A.E. (2025). *Ginkgo biloba* attenuates complete Freund's adjuvant-induced inflammatory pain by suppressing the NF-κB-CXCL1/CXCR2 signaling cascade in the rat spinal cord. Redox Report, 30(1), 2447778.
- Samec, D., Karalija, E., Dahija, S. & Hassan, S.T. (2022). Biflavonoids: Important contributions to the health benefits of Ginkgo (Ginkgo biloba L.). Plants, 11(10), 1381.
- Shahrajabian, M.H., Sun, W. & Cheng, Q. (2022). *Ginkgo biloba*: A famous living fossil tree and an ancient herbal traditional Chinese medicine. Current Nutrition & Food Science, 18(3), 259-264.

- Shahverdian, A. & Jafari, M. (2025). Dietary Supplement Safety in Older Adults: A Review of Published Case Reports. The Senior Care Pharmacist, 40(1), 32-49.
- Shen, X., Niu, X., Li, G., Deng, X. & Wang, J. (2018). Amentoflavone ameliorates Streptococcus suis-induced infection in vitro and in vivo. Applied and Environmental Microbiology, 84(24), e01804-18.
- Shenoy, K.A., Somayaji, S.N. & Bairy, K.L. (2001). Hepatoprotective effects of *Ginkgo biloba* against carbon tetrachloride induced hepatic injury in rats. 260-266.
- Singh, S.K., Barreto, G. E., Aliev, G. & Echeverria, V. (2017). *Ginkgo biloba* as an alternative medicine in the treatment of anxiety in dementia and other psychiatric disorders. Current Drug Metabolism, 18(2), 112-119.
- Singh, S.K., Srivastav, S., Castellani, R.J., Plascencia-Villa, G. & Perry, G. (2019). Neuroprotective and antioxidant effect of *Ginkgo biloba* extract against AD and other neurological disorders. Neurotherapeutics, 16(3), 666-674.
- Singh, A.V. (2021). Potential of amentoflavone with antiviral properties in COVID-19 treatment. Asian Biomedicine, 15(4), 153-159.
- Silva, A.M., Silva, S.C., Soares, J.P., Martins-Gomes, C., Teixeira, J.P., Leal, F. & Gaivão, I. (2019). *Ginkgo biloba* L. leaf extract protects HepG2 cells against paraquat-induced oxidative DNA damage. Plants, 8(12), 556.
- Slika, H., Mansour, H., Wehbe, N., Nasser, S.A., Iratni, R., Nasrallah, G.... & Eid, A.H. (2022). Therapeutic potential of flavonoids in cancer: ROS-mediated mechanisms. Biomedicine & Pharmacotherapy, 146, 112442.
- Sultan, S., Jahangir, A., Gussak, I.B., Kostis, J.B., JamilTajik, A. & Jahangir, A. (2018). Interactions between supplements and medications. latrogenicity: causes and consequences of iatrogenesis in cardiovascular medicine, 370-389.
- Tabassum, N.E., Das, R., Lami, M.S. et al. (2022). Ginkgo biloba: A treasure of functional phytochemicals with multimedicinal applications. Hindawi Evidence-Based Complementary and Alternative Medicine, 8288818, 1-30.
- Tang, Y., Xu, Y., Xiong, S., Ni, W., Chen, S., Gao, B.... & Du, C. (2007). The effect of *Ginkgo biloba* extract on the expression of PKCα in the inflammatory cells and the level of IL-5 in induced sputum of asthmatic patients. Journal of Huazhong University of Science and Technology, 27, 375-380.
- Tao, Z., Jin, W., Ao, M., Zhai, S., Xu, H. & Yu, L. (2019). Evaluation of the anti-inflammatory properties of the active constituents in *Ginkgo biloba* for the treatment of pulmonary diseases. Food & Function, 10(4), 2209-2220.
- Trabert, M. & Seifert, R. (2024). Critical analysis of ginkgo preparations: comparison of approved drugs and dietary supplements marketed in Germany. Naunyn-Schmiedeberg's Archives of Pharmacology, 397(1), 451-461.
- Vaghef-Mehrabany, E., Maleki, V., Behrooz, M., Ranjbar, F. & Ebrahimi-Mameghani, M. (2020). Can psychobiotics "mood" ify gut? An update systematic review of randomized controlled trials in healthy and clinical subjects, on anti-depressant effects of probiotics, prebiotics, and synbiotics. Clinical Nutrition, 39(5), 1395-1410.
- Varshney, M., Kumar, B., Rana, V.S. & Sethiya, N.K. (2023). An overview on therapeutic and medicinal potential of poly-hydroxy flavone viz. Heptamethoxyflavone, Kaempferitrin, Vitexin and Amentoflavone for management of Alzheimer's and Parkinson's diseases: A critical analysis on mechanistic insight. Critical Reviews in Food Science and Nutrition, 63(16), 2749-2772.
- Wang, Y., Wang, R., Wang, Y., Peng, R., Wu, Y. & Yuan, Y. (2015). *Ginkgo biloba* extract mitigates liver fibrosis and apoptosis by regulating p38 MAPK, NF-kB/lkBa, and Bcl-2/Bax signaling. Drug Design, Development and Therapy, 6303-6317.
- Wang, H.Y. & Zhang, Y.Q. (2019). The main active constituents and detoxification process of *Ginkgo biloba* seeds and their potential use in functional health foods. Journal of Food Composition and Analysis, 83, 103247.
- Wang, T., Bai, S., Wang, W., Chen, Z., Chen, J., Liang, Z., ... & Xie, P. (2020). Diterpene ginkgolides exert an antidepressant effect through the NT3-TrkA and Ras-MAPK pathways. Drug Design, Development and Therapy, 1279-1294.
- Wang, L.T., Huang, H., Chang, Y.H., Wang, Y.Q., Wang, J.D., Cai, Z.H.... & Fu, Y.J. (2022). Biflavonoids from *Ginkgo biloba* leaves as a novel anti-atherosclerotic candidate: Inhibition potency and mechanistic analysis. Phytomedicine, 102, 154053.
- Woelk, H., Arnoldt, K.H., Kieser, M. & Hoerr, R. (2007). Ginkgo biloba special extract EGb 761® in generalized anxiety disorder and adjustment disorder with anxious mood: A randomized, double-blind, placebo-controlled trial. Journal of psychiatric research, 41(6), 472-480.
- Wu, F., Shi, W., Zhou, G., Yao, H., Xu, C., Xiao, W.... & Wu, X. (2016). Ginkgolide B functions as a determinant constituent of Ginkgolides in alleviating lipopolysaccharide-induced lung injury. Biomedicine & Pharmacotherapy, 81, 71-78.

- Xiong, Y., Zhu, G.H., Wang, H.N., Hu, Q., Chen, L.L., Guan, X.Q.... & Ge, G.B. (2021). Discovery of naturally occurring inhibitors against SARS-CoV-2 3CLpro from *Ginkgo biloba* leaves via large-scale screening. Fitoterapia, 152, 104909.
- Xu, A., Ren, L., Zheng, Y. & Chen, H. (2008). Immunomodulatory effect of *Ginkgo biloba* exocarp polysaccharides on immunosuppressive mice induced by cyclophosphamide. Chinese Journal of Pharmacology and Toxicology, 22(1), 69.
- Yang, Y.L., Su, Y.W., Ng, M.C., Chang, C.L. & Lu, K.T. (2005). Extract of *Ginkgo biloba* EGb 761 facilitates fear conditioning measured by fear-potentiated startle. Neuroscience Letters, 383(1-2), 145-150.
- Yang, Z., Cespedes-Acuña, C.L., Yang, Z., Abu Bakar, M.Z., Chan, K W. & Deng, X. (2025). Plant foods and their bioactives as dietary enhancers for colon cancer treatment with 5-fluorouracil. Food Reviews International, 1-50.
- Yao, Z. X., Han, Z., Drieu, K. & Papadopoulos, V. (2004). Ginkgo biloba extract (Egb 761) inhibits β-amyloid production by lowering free cholesterol levels. The Journal of Nutritional Biochemistry, 15(12), 749-756.
- Zhou, Z.Y., Tang, S.Q., Zhou, Y.M., Luo, H.S. & Liu, X. (2010). Antioxidant and hepatoprotective effects of extract of *Ginkgo biloba* in rats of non-alcoholic steatohepatitis. Saudi Medical Journal, 31(10), 1114-1118.
- Zuo, W., Yan, F., Zhang, B., Li, J. & Mei, D. (2017). Advances in the studies of *Ginkgo biloba* leaves extract on aging-related diseases. Aging and Disease, 8(6), 812.



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