INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA):IJPS00]
Journal Homepage: https://www.ijpsjournal.com

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Review Article

Ginkgo Biloba Used As Neuroprotective Action In Vedas Technology

Kajal Gupta[1]*, Mansi Sharma[1], Ishu[2], Mukesh Choudhary[2], Aashutosh Sinwal[2], Akash Dinesh Shah[2], Aparna Ballavi Panda[2], Atharwa Deepak Amrutkar[3]

[1]Master of Pharmacy, School of Pharmaceutical Sciences, Jaipur National University, Jaipur, Rajasthan, India-302017
[2]School of Pharmaceutical Sciences, Jaipur National University, Jaipur, Rajasthan, India- 302017
[3]Jaipur National University, Institute for Medical Sciences and Research Centre, Jaipur, Rajasthan, India-302017

ARTICLE INFO

Received: 16 Sep 2024
Accepted: 19 Sep 2024
Published: 30 Sep 2024
Keywords:
Gingo Biloba, Neuroprotective effects, China, Alzheimer's disease, Parkinson's disease
DOI:
10.5281/zenodo.13863070

ABSTRACT

One of the world's oldest tree species is the Gingo biloba. Ginkgo trees have existed since the Permian Period, which lasted from 286 to 248 million years ago. The genus Ginkgo only has one living member Ginkgo biloba. Ginkgo biloba contains chemicals with medicinal potential due to their unusual structures. Along with linkedin and ginkgolides, these compounds also contain flavones, ginkgo ghrelins, and ginkgolide acids. Ginkgo flavone glycosides (ginkgetin, biotin, and sciadopitysin) and terpene lactones (ginkgolides and diterpenes) are the two primary components of Ginkgo biloba. Different elements have different quantities. Recent research has demonstrated that GBE inhibits Aβ-induced neurotoxicity by blocking many processes such as mitochondrial failure, ROS buildup, glucose absorption, AKT activation, JNK and ERK 1/2 pathways, and apoptosis—the benefits of G in preventive. Biloba extract inhibited the action of 6-hydroxydopamine, which stopped PC12 cells from dying in a Parkinson's disease model. According to several case reports, ginkgo usage is associated with bleeding episodes, including severe brain hemorrhage. Be careful when administering ginkgo to patients who are using anticoagulant or antiplatelet medication, have bleeding issues, or are using NSAIDs.

INTRODUCTION

Paleobotanists are familiar with the fossil records of the Ginkgoaceae family of plants. Members of this family first appeared 300 million years ago, during the Permian period, and peaked 200 million years ago, during the Jurassic. Currently, only Ginkgo biloba L. remains. In this group, you'll find

***Corresponding Author:** Kajal Gupta
Address: *Master of Pharmacy, School of Pharmaceutical Sciences, Jaipur National University, Jaipur, Rajasthan, India-302017*
Email ✉: issingh1022@gmail.com
Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

an actual species. This once-common Chinese plant made it through the catastrophic extinctions of the Paleogene and Cretaceous periods and the Pleistocene glaciation. The beauty and therapeutic value of ginkgo have contributed to its global diffusion. One of the world's oldest tree species is the Gingo biloba. Ginkgo trees have existed since the Permian Period, which lasted from 286 to 248 million years ago. The genus Ginkgo only has one living member, Ginkgo biloba. Cityscapes around the United States soon began to feature the ginkgo tree, which Frank Lloyd Wright had a fondness for. Legend has it that Buddhist monks protected the holy grounds' trees. The plant's remarkable adaptability and resilience to diseases contribute to its longevity. [1] Around five thousand years ago, ginkgo was used medicinally in China, mostly for asthma treatment. It has several advantages because of its exceptional adaptability to the environment, complete absence of pests and diseases, and high resistance to air pollution. The species' high rate of survival, as well as its highly reproducible resistance and stress sensitivity genes, make it ideal for use in urban greenery schemes. It has become standard practice to plant it in college campuses, parks, and gardens across the world. In many different countries, these trees serve as sources of spiritual and creative inspiration for people. Ancient temples in East Asia, deserted cities, and riverbanks all contain artifacts from bygone eras. The ginkgo tree, which is revered as China's national tree, represents tranquility and hope in traditional Chinese belief systems. [2] Among the many herbal remedies included in the Chinese Pharmacopeia, ginkgo biloba leaves stand out. Several diseases, including cardiovascular and cerebrovascular issues, are treated with formulations derived from these. It was proven to be useful in reducing heart problems in the 1960s. In the United States and Europe, ginkgo biloba leaf extract is the most consumed herbal supplement, making it one of the world's best-selling herbal treatments. Its medicinal uses include free radical scavenging, oxidative stress reduction, brain damage mitigation, and platelet aggregation inhibition. On top of all those benefits, it fights against cancer, inflammation, and the signs of aging. Studies in humans have shown that it can effectively cure several neurological illnesses, including Alzheimer's disease and other forms of cognitive impairment. [3]

PHYTOCONSTITUENTS OF PLANT

Ginkgo biloba contains chemicals with medicinal potential due to their unusual structures. Along with linkedin and ginkgolides, these compounds also contain flavones, ginkgo ghrelins, and ginkgolide acids. The flavonoids and terpenoids comprise the bulk of the sixty bioactive components found in ginkgo extract. These two components typically make up around a quarter of the extract and six percent of the total. Sitosterols, organic acids, polysaccharides, tannins, proanthocyanidins, and carotenoids are among its many other components.[4]

Terpenoids

A group of small-molecule organic molecules called plant secondary metabolites are produced by plants that engage in secondary metabolic activities. The function of these compounds in information transmission and stress tolerance in plants is species-specific; they are stored in specific organs or tissues of plants. Only bilobalides (sesquiterpenes) and ginkgolides (diterpenes) contain t-butyl [C17(CH3)3] among the terpenoids found in ginkgo. These compounds are found in nature and have functional groups that can be used for the prevention and treatment of cardiac and neurological issues. The endosperm and embryo of ginkgo seeds contain the most terpenes, whereas the seeds themselves are abundant in ginkgolides and bilobalides.[5]

Alkylphenols and Alkylphenolic Acids

Cardanols, α-hydroxycardanols, cardans, urushiols, and urushiol are the five distinct forms

of alkylphenols found in Ginkgo biloba leaves. Another group of acids that includes ginkgolic acids is the alkylphenolic acids. Among the many harmful poisons present in ginkgo biloba are these compounds. Due to its poisonous, mutagenic, and sensitizing properties, ginkgolic acid has a unique position in this context. On the other hand, research has demonstrated that they can have positive pharmacological effects on humans; for instance, ginkgolide acid C17:1 has demonstrated some anticancer benefits.[6]

Flavonoids

Natural bioactive compounds known as flavonoids have far-reaching effects on human health. The chemical class that includes the leaves of Ginkgo biloba includes isoflavonoids, flavones, proanthocyanidins, and flavonol glycosides. Having said that, quercetin, kaempferol, and isorhamnetin are the most common multiform glycosides. Ginkgo leaf extract mostly contains flavonoids. Extracts from ginkgo leaves include 110 flavonoids, spread over 7 different groups. A total of 52 flavonol glycosides and 7 flavonols make up the first group. The aglycones of flavonol glycosides include isorhamnetin, quercetin, and kaempferol. Along with syringes and myricetin, the aglycon group also contains lari citrin, patulin, and myricetin 3′, 4′-dimethyl ether. Fifteen flavones and fourteen flavone glycosides make up category two. Flavanones and their glycosides made up the third class, isoflavones and their glycosides made up the fourth class, and flavan-3-ole formed the fifth class. Thirteen bioflavonoids made up class six, while nine ginkgolides made up class seven.[7]

Carboxylic Acids

There are a lot of physiologically active organic acids found in plants. Carboxylic acids make up around 13% of ginkgo biloba extract. The following acids are included in this group: quinic acid, chlorogenic acid, ascorbic acid, gallic acid, sinapinic acid, ferulic acid, vanillic acid, coffee acid, six-hydroxybenzoic acid, p-coumaric acid, and p-hydroxybenzoic acid. On top of that, ginkgo biloba leaves contain phenolic acids that are either glycosidic or bound together chemically. The dominant component of ginkgo leaves, quinic acid, accounts for 2.26 g/100 g of dry weight. The 2.24 grams of shikimic acid contained in 100 grams of dry weight is also rather little. Malic acid came in last with a concentration of 0.58 g/100 g dw.[8]

Polysaccharides

Ginkgo contains several bioactive components, including polysaccharides. A combination of purification techniques, such as gel filtration and ion exchange chromatography, with extraction methods including enzymatic extraction, hot water extraction, and ultrasound-assisted extraction allows for the isolation of pure polysaccharides from ginkgo. [9] A wide variety of structurally varied polysaccharides, largely classified by the content of monosaccharides, were prevalent in sarcotesta, seeds, and leaves. On the other hand, the majority of them include varying mole proportions of rhamnose (Rha), galactose (Gal), mannose (Man), xylose (Xyl), arabinose (Ara), glucose (Glu), and fucose (Fuc). Mannose (Man) is abundant in ginkgo seeds, while galactose (Ga) and glucose (Glu) are more abundant in the sarcotesta than in the leaves. An interesting discovery is that Ginkgo biloba polysaccharides have molecular weights between 1.0 kDa to 5679 kDa. Ginkgo polysaccharides have several advantageous medical uses, but they are especially useful for preventing cancer, inflammation, hepatitis, depression, immune system suppression, and alopecia due to their high antioxidant content.[10]

Lignins

The highest concentration of lignin is found in the covers of ginkgo seeds. Up to 40% of them could consist of these substances. There are twenty-four different lignans and isomers that this plant has

created so far. Lignins are a secondary metabolite of lignocellulosic biomass, which limits their widespread application despite their intriguing physicochemical features and strong biological activity. Lignin mostly consists of the phenylpropane units p-hydroxyphenyl (H), guaiacyl (G), and syringyl (S). The lignocellulose cell walls are protected from environmental challenges and phytopathogens because they thicken and strengthen them. Lignin is therefore a macromolecule that has bioactive properties.[11]

Proanthocyanidins

Active and functional polyphenolic substances are known as proanthocyanidins. Their composition consists of flavan-3,4-alcohol polymers and polyhydroxy flavan-3-alcohol oligomers connected by one C4-C8 or C4-C6 bond (type B) or an extra C2-O-C7 or C2-O-C5 link (type A). (-)-epicatechins and (+)-catechins are two compounds that fall under this category. In ginkgo leaves, you may find proanthocyanidins in a concentration of 4-12%; standardized extracts contain just 7% of these compounds. Free radical scavenging and antioxidant activity can be exhibited by proanthocyanidins and flavan-3-oils; nevertheless, the exact composition of these molecules is an area of active investigation. Along with alleviating the symptoms of ischemia-reperfusion damage, they also exhibit anti-inflammatory, antihypertensive, anti-atherosclerotic, anti-aggregating, immunomodulatory, and antibacterial activities.[12]

Polyprenols

An isoprene unit (containing a hydroxyl group) terminates polyprenols, which contain two varieties of betulaprenol and twelve to twenty cis-isoprene units. Polyphenols are mostly found in plants' photosynthetic organs as a mixture of homologs that are structurally and chemically similar to dolichols. The lipids contained in Ginkgo biloba leaves contain unsaturated polyisoprenoid alcohols called polyprenols. Polyprene acetate is the most common type they use in that region. The polyprenols found in ginkgo leaves are beneficial chemicals that have a variety of uses, including hepatoprotective, antimicrobial, antiviral, and immunomodulatory effects.[13]

MECHANISM OF ACTION OF GINKGO BILOBA

Ginkgo flavone glycosides (ginkgetin, biotin, and sciadopitysin) and terpene lactones (ginkgolides and diterpenes) are the two primary components of Ginkgo biloba. Different components have different quantities. Standardized Ginkgo biloba (EGb) 761 extract has been used in most ginkgo effect investigations. Animal studies have shown that ginkgo biloba extract influences several different areas of the brain and networks involving neurotransmitters. Additionally, EGb761 has modest inhibitory effects on anticholinesterase and improves cholinergic transmission in the brain. It seems that ginkgo extract can be used to reverse the reversible suppression of rat brain monoamine oxidase's serotonin and dopamine absorption. In rats, this prevents stress-induced corticosterone hypersecretion and decreases the amount of adrenal peripheral benzodiazepine receptors.[14]

Research on the potential neuroprotective properties of ginkgo biloba extract is extensive. Long-term administration of EGb761 to middle-aged rats seems to enhance their short-term memory, perhaps as a result of a decrease in free radical generation in the prefrontal cortex. It also prevents age-related hippocampal degeneration in mice. Ginkgo biloba extract also prevents neuronal death and oxidative stress, which are symptoms of Alzheimer's disease and brain ischemia, respectively. Free radical scavenging is how it does this.[15] There have been a lot of positive results from research looking at ginkgo's effects on the cardiovascular system. In addition to its effects on blood vessel dilation and metabolic regulation,

ginkgo also helps keep cell membranes in place. When administered to the vascular endothelium, ginkgo biloba extract promotes the release of endogenous relaxing factors such as prostacyclin and endothelium-derived relaxing factors. Additionally, it can control nitric oxide synthesis and exert vasorelaxation qualities under inflammatory situations that damage tissues, such as ischemia. Another class of compounds that can block platelet-activating factor activity include terpene lactones. The fibrin-breaking abilities of ginkgo extract are further highlighted.[16]

NEUROPROTECTIVE EFFECTS OF GINKGO BILOBA

Anxieties, amyloid-β, glutamate, nitric oxide, cyanide, and 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine [MPTP] were among the chemicals that cultured neurons were shown to be protected from in controlled experiments. The neuroprotective effect of GBE has been validated by research employing in vitro and in vivo models. Additionally, EGb761 reduced neuronal damage in in vivo investigations whether administered orally (per os) or intraperitoneally (i.p.) at dosages ranging from 10 to 100 mg/kg. Hypoxia, heat stress, subchronic cold stress, amphetamine-induced behavioral sensitization, focal cerebral ischemia, temporary middle cerebral artery occlusion (MCAO), and gerbils and rats have all shown this.[17] Another model of amyotrophic lateral sclerosis, a transgenic mouse, has also shown this. The neuroprotective effects of EGb 761 have been associated with ginkgolides (1-100 μM in vitro or 50-100 mg/kg in vivo), bilobalide (25-100 μM in vitro or 10 mg/kg in vivo), and on occasion even the flavonoid fraction (25-100 μg/ml in vitro or 40-100 mg/kg in vivo). Not only can EGb 761 scavenge free radicals, but it also modulates the transcription of many genes involved in oxidative stress control. Because this is a hallmark of neurodegenerative illnesses like Alzheimer's and Parkinson's, it suggests that EGB 761 can protect neurons from oxidative damage by increasing cellular tolerance to oxidative stress.[18]

EFFECT OF GBE AGAINST Aβ AGGREGATION

Aβ plaques build up and become a hallmark of Alzheimer's disease. In recent times, scientists have extensively debated GBE's capacity to protect neurons against Aβ-induced neurotoxicity. An abundance of recent research has demonstrated that GBE inhibits Aβ-induced neurotoxicity by blocking many processes such as mitochondrial failure, ROS buildup, glucose absorption, AKT activation, JNK and ERK 1/2 pathways, and apoptosis. Supposedly, GBE reduces free cholesterol levels in the blood, which in turn prevents the brain from producing Aβ. The amounts of free and intracellular cholesterol are believed to impact amyloidogenesis and AβPP processing, making this an important finding. Given these results, more research is required to determine which active ingredients have anti-amyloidogenic properties. Furthermore, GBE can hinder the formation of Aβ oligomers. The main cause of Aβ neurotoxicity and a potential way for its release from clearance by proteolytic cleavage is the β-sheet form of Aβ oligomers, which is widely recognized. Therefore, a key technique for reducing Aβ toxicity might be to prevent the development of the β-sheet structure in Aβ oligomers. The interaction between Aϋ and other transition metal ions, such as copper, iron, and zinc, can also impact its oligomerization, along with Aϋ itself. It is also possible that the production of Aβ fibrils is inhibited by GBE's iron chelating capabilities. Since GBE has several modes of action, it is reasonable to assume that it is a powerful tool in the fight against AD.[16,18]

In controlled laboratory settings, transthyretin has been demonstrated to inhibit Aβ aggregation through the entanglement of Aβ monomers. Additionally, GBE prevents Aβ fibril production

by increasing transthyretin gene expression. Also, research has shown that flavonoid compounds, bilobalide, and ginkgolide J all inhibit Aβ aggregation. In addition, GBE helps maintain the ROS/RNS balance in cells by regulating mitochondrial oxidative phosphorylation (OXPHOS) in reaction to oxidative stress caused by Aβ. Research indicates that GBE improves mitochondrial activity in reaction to damage caused by Aβ by adding positive impacts on cellular OXPHOS functionality. The results of GBE in preventing Aβ-induced toxicity are promising, but further research is needed to understand how exactly each component of GBE reduces AỤ-induced toxicity in AD.[19]

PARKINSON'S DISEASE

Tremors, stiffness, slowness of movement, trouble walking, issues with cognition and behavior, and more are symptoms of Parkinson's disease, another neurological disorder. The benefits of G in preventive. Biloba extract inhibited the action of 6-hydroxydopamine, which stopped PC12 cells from dying in a Parkinson's disease model. According to Bax, the extract prevented the activation of caspase-3 and Bcl-2. Therefore, it was clear that G. If you suffer from Parkinson's disease, you could find that ginkgo biloba extract works better than levodopa.[20]

COGNITIVE ABILITY

The cognitive mechanism known as working memory has a limited capacity to retain information. Both discriminative reasoning and spatial memory are tested on the Object-Location Memory test. G. During the hold part of the working memory task, Silberstein et al. (2011) found that middle-aged male volunteers who were otherwise healthy tested positive for Ginkgo biloba extract. According to the findings, an amplitude was found at the occipital and frontal sites, and the steady state visually evoked potential (SSVEP) latency was increased at the left temporal and left frontal sites.[21]

NEUROPLASTICITY, NEUROGENESIS, AND SYNAPTOGENESIS

The capacity of synapses to undergo structural adaptation in response to dysfunctions or functional demands imposed on impaired brain systems is known as neuroplasticity. By manipulating mitochondrial energy metabolism using nitrosative stress, serum deprivation, and complex inhibitors, Abder-Kadel et al. (2007) were able to reproduce mitochondrial defects associated with aging. When tested in vitro, EGB 761 improved mitochondrial functioning at concentrations as low as 0.01 mg/ml, according to ATP levels, mitochondrial membrane potential, and markers for mitochondrial function. That EGB 761 maintained its mitochondrial membrane potential was demonstrated by these experiments. In related research, Eckert et al. (2006) demonstrated that EGB 761 might potentially repair PC12 cells damaged by sodium nitroprusside, a nitric oxide donor.[22]

ADULT NEUROGENESIS

New insights into neurogenesis in certain adult brain regions have revolutionized neurology studies, especially those focusing on neurodegeneration. In 2009, Tchantchou et al. investigated EGB761-related neurogenesis. The only components of EGB 761 that showed a dose-dependent increase in cell proliferation in the hippocampus neurons of the AD mice model were quercetin and bilobalide. Researchers found that the extract's bilobalide and quercetin boosted CREB (cyclic-AMP response element binding protein) phosphorylation in these cells. In addition, it improved neurogenesis and synaptogenesis in mice by increasing levels of bilobalide, quercetin, brain-derived neurotrophic factors, and pCREB. This study's results suggest that increased neurogenesis and synaptogenesis could be due to a shared final signaling pathway driven by CREB phosphorylation. Because it

protects the mitochondria from oxidative stress, EGB761 is a major neuroprotective drug.[23]

ANTI-INFLAMMATORY EFFECT

Ameisoflavone, bilobalide, ginkgolides (A or B), and water-soluble polysaccharides were some of the constituents included in the commercial formulations and laboratory extracts studied for their anti-inflammatory activities. Every single study has shown that it effectively postpones the onset of inflammation. Reductions in interferon, prostaglandin E2, tumor necrosis factor-alpha, nitric oxide, interleukin-1, interleukin-4, interleukin-6, interleukin-12, and interleukin-1β are usually observed in inflammatory tissues. In addition, the MAPK and NF-κB signaling pathways underwent alterations due to a decrease in the translocation of the nuclear protein NF-κB. The activation of heme oxygenase and amphibian protein kinase is another improvement.[21,22]

ANTITUMOR ACTIVITY

The administration of various medications to specific tumor cell lines formed the basis of the tissue culture approach used to study anticancer activity. Extensive studies have been conducted on the usage of ginkgo extracts or chosen ingredients; nevertheless, a review of articles published mostly between 2015 and 2022 indicates that further research is needed. While it is common practice to examine the effects of a single chemical on no more than two or three tumor cell lines, researchers have examined the extract and seven other ginkgo compounds on at least 22 cancer cell lines. Several studies have shown that chemicals found in fresh male flowers, bilobol in fruit, ginkgolide B polysaccharides in leaves, and other plant-derived components can suppress the development of cancer cells at key phases of their proliferation. Some of its derivatives are biotin, isoginkgetin, amentoflavone, and sciadopitysin.[24]

ANTIOXIDANT ACTIVITY

We looked at the antioxidant activity of ginkgo seed fermented supernatant, organic acid-rich leaf extracts made in different solvents, ginkgolide, procyanidins, flavones, polysaccharides and monomers, and ginkgolide as a whole. The results of this research cannot be compared since they all used various methodologies, such as DPPH, ABTS, scavenging hydroxyl radicals, or superoxide anion approaches. Nevertheless, every study showed that the substrates under study had antioxidant activity, and this activity was frequently graded as quite high. While the exact timing of this movement is dependent on the season, it is most apparent when the leaves are plucked in the autumn. The EGb761 extracts that are both made in a lab and sold in stores are highly effective. Extracts with 40% and 70% alcohol by weight perform better than those with 96% alcohol by weight in the second scenario. The most potent antioxidants were procyanidins and flavones, two extracts found in ginkgo leaves.[25]

ANTI-MICROBIAL ACTIVITY

Research into ginkgo's antibacterial properties has been ongoing for some time. To begin, we looked at how well various plant extracts (from fruits, leaves, and roots) and their specific components (from ginkgo or free phenolic acids, for example) worked against the small set of bacterial species. Staphylococcus aureus and Escherichia coli were the microbes most frequently tested. More study on anti-bacterial action was prompted by the results of these experiments, which revealed that the activity of particular bacterial taxa was repressed. Amentofavone, ginkgetin, polyprenol, ginkgolic acid C15:1 monomer, and leaf extracts from different solvents (methanol, chloroform, water, and ethanol) have all been the subject of recent research. The microbial community now includes a far broader range of species, including gram-positive and gram-negative bacteria, intestinal microflora specific to the animals under study, and harmful fungi in humans.[26]

PROTECTION OF OTHER ORGANS

The sensory organs are protected by EGb extract and ginkgo leaf capsules, according to the research. Patients with type 2 diabetes will find this particularly beneficial since it aids in the renewal and improvement of the retina's blood vessels, which in turn prevents or slows down the degeneration of these vessels—a major cause of visual problems. Additionally, ginkgo leaf extract's chemical constituents shield the auditory nerve from the cancer chemotherapy drug cisplatin's deleterious effects. Atherosclerotic lesions are less likely to form and blood vessels are protected by ginkgolide B, an ingredient in ginkgo leaves.[27]

ADVERSE EFFECT OF GINKGO BILOBA

It has been reported that ginkgo biloba is often safe and well-tolerated. There is a 240 mg daily limit for ginkgo extract. A few examples of mild side effects are allergic skin responses, diarrhea, gastrointestinal problems, palpitations, and headaches. According to several case reports, ginkgo usage is associated with bleeding episodes, including severe brain hemorrhage. Though a systematic review and meta-analysis looked for the effects of ginkgo on platelet aggregation, activated partial thromboplastin time, and prothrombin time, none were found.[20]

CONTRAINDICATIONS

Be careful when administering ginkgo to patients who are using anticoagulant or antiplatelet medication, have bleeding issues, or are using NSAIDs. The elderly patient experienced spontaneous bleeding from the iris into the anterior chamber of the eye while taking aspirin and ginkgo biloba, according to a case study. The combination of warfarin and ginkgo, according to a 2015 research conducted in a sizable Veterans Administration sample, increased the risk of bleeding episodes.[27] Few studies have examined the potential side effects of ginkgo during surgical procedures. It is recommended that doctors avoid taking ginkgo at least 36 hours before surgery, according to one research. Nursing mothers, expecting moms, and new borns should not take ginkgo due to a lack of data about its safety and effectiveness in these groups. It is important for clinicians to exercise caution when administering ginkgo biloba to patients with epilepsy or a history of seizures since ginkgo's toxin, which is mostly contained in the seeds but can also be found in the leaves, can reduce the threshold for seizures.[28]

CONCLUSION

In conclusion, Ginkgo biloba stands not only as a testament to nature's resilience but also as a vital contributor to human health and cultural heritage. Its longevity and adaptability remind us of the enduring bond between humanity and the natural world. The extensive medicinal properties of ginkgo, rooted in a profound history of traditional medicine, highlight its significance in modern therapeutic practices. As we continue to explore its wide-ranging effects, particularly in supporting cognitive health and cardiovascular well-being, it is crucial to approach its use with informed caution, recognizing potential risks associated with its active compounds. Moving forward, let us advocate for further research to unveil the depths of Ginkgo biloba's capabilities while fostering respect for the natural resources that enrich our lives. By bridging ancient wisdom with contemporary science, we can enhance our understanding of this remarkable tree, promoting sustainable practices that ensure its preservation for future generations. Embracing the lessons of Ginkgo biloba may inspire a holistic approach to health that honors the intricate interplay of nature and medicine, ultimately guiding us toward a healthier, more sustainable future.

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HOW TO CITE: Kajal Gupta , Mansi Sharma , Ishu , Mukesh Choudhary , Aashutosh Sinwal , Akash Dinesh Shah , Aparna Ballavi Panda , Atharwa Deepak Amrutkar, Ginkgo Biloba Used As Neuroprotective Action In Vedas Technology, Int. J. of Pharm. Sci., 2024, Vol 2, Issue 9, 1577-1586. https://doi.org/10.5281/zenodo.13863070