PHARMA RESEARCH BULLETIN
Open Access Journal (ISSN: 2582-676X)

Review article
Volume 5, Issue 1, 2026, 26-40

Ginkgo biloba in Neurodegenerative Disease

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Received: 09 October 2025; Accepted: 29 December 2025; Published: 19 January 2026

Abstract: Neurodegenerative diseases (NDDs) are characterized by progressive neuronal loss resulting from disrupted proteostasis, altered energy metabolism, chronic inflammation, synaptic dysfunction, and pathological protein aggregation. These disorders share common features such as gliosis, neuronal atrophy, and intracellular protein inclusions, although they differ in the specific neuronal populations affected and the proteins involved. Hallmark pathological features include amyloid plaques, neurofibrillary tangles, and extensive cortical atrophy, particularly in the temporal and parietal regions. Among herbal therapeutics, *Ginkgo biloba* has emerged as a widely used medicinal plant with potential benefits in multiple neurodegenerative conditions, including Alzheimer's disease, Parkinson's disease, Huntington's disease, multiple sclerosis, and ataxia. Its neuroprotective effects are primarily attributed to antioxidant, anti-inflammatory, vasoactive, and anti-apoptotic properties. Standardized *Ginkgo biloba* leaf extract contains flavonoid glycosides and terpenoids, which act as the principal bioactive constituents responsible for free radical scavenging, protection against hypoxia-induced neuronal damage, and inhibition of amyloid-β–mediated neurotoxicity. Owing to these properties, *Ginkgo biloba* extract is commonly used as a dietary supplement to support cognitive function and mitigate age-related memory decline.

Keywords: *Ginkgo biloba*, Neuroprotective, Anti-dementia, Antipsychotic, Anti-inflammatory, Antineoplastic, Vasoactive, Anti-platelet activity.

1. Introduction

Neurodegenerative diseases are not a single disorder but a group of major brain-related conditions, including Alzheimer's disease, Huntington's disease, Parkinson's disease, ataxia, and others. These disorders are progressive in nature, meaning that neurons in the brain and other peripheral organs undergo gradual and irreversible damage. Current therapeutic approaches for the management of neurodegenerative diseases are often associated with significant side effects. To overcome these limitations, the use of herbal or natural approaches has emerged as a promising alternative. Over the past few decades, the global use of natural products and medicinal plants has increased substantially. Herbs play a multifaceted role in medicine due to their broad spectrum of therapeutic properties. Medicinal plants contain phytochemicals or secondary metabolites, which are bioactive compounds responsible for their pharmacological effects. *Ginkgo biloba* is one of the most well-known medicinal plants because of its wide range of healing properties and its cultivation across different regions of the world. Ginkgo is commonly referred to as a "living fossil," as it is among the oldest surviving plant species. Today, it is one of the most widely used medicinal herbs, offering numerous health benefits [1]. *Ginkgo biloba* is a gymnosperm tree species indigenous to East Asia and is also known as the maidenhair tree. It is commonly referred to as ginkgo or gingko. The name "Ginkgo" originates from a Japanese word, while "biloba" refers to its characteristic two-lobed leaves [2]. *Ginkgo biloba* typically grows to a height of 20–30 meters, although truly ancient specimens may reach 40–50 meters. The development of the main branches largely depends on light availability. Trunk diameter varies with age, ranging from 50 cm to 1 m in most trees, while exceptionally old individuals may attain diameters of 3–5 m. The lifespan of *Ginkgo biloba* is remarkably long, extending up to 1,000–2,000 years [3].

The leaves of *Ginkgo biloba* are dark green when young and turn golden or light yellow at maturity. The foliar epidermis exhibits distinctive anatomical features, with stomata present only on the lower leaf surface, making the leaves hypostomatic [4]. Female ginkgo trees produce oval to rounded, fleshy fruits measuring approximately 2.5–3.5 × 1.6–2.2 cm, similar in size to a small jujube. The fruits are green when immature and turn yellow upon ripening. The mature seed measures 20–30 × 16–24 mm and consists of a thick seed coat enclosing an embryo embedded within the tissue of the female gametophyte. This seed, commonly referred to as the Ginkgo "nut," measures 19–30 × 11–14 mm when the fleshy outer layer is removed [3].

1.1 Geographical Distribution

This species of the genus *Ginkgo biloba* grows successfully under a wide range of climatic conditions, substrates, and environmental settings, tolerating considerable variation in water availability and temperature, as shown in **Table 1**. The only exception includes the wild and semi-wild populations dating back approximately 300 years, which are found in China [5]. This remarkable adaptability enables *Ginkgo biloba* to be cultivated in nearly all regions of the world [6]. Except for Antarctica, ginkgo is planted worldwide, spanning a latitudinal range of more than 103°. The northernmost distribution of *Ginkgo biloba* in the Northern Hemisphere extends to 60°03′N in Europe. However, more than 99% of the remaining ginkgo trees worldwide are concentrated in Eastern Asia, particularly in Japan, China, and Korea. *Ginkgo biloba* was first introduced to Europe around 1730 in the Botanic Garden of Utrecht, the Netherlands, from where it subsequently spread to other parts of the continent. The species also exhibits a broad elevational range, growing naturally at altitudes between 300 and 1,250 meters above sea level [7].

Table 1: Geographical distribution.

Country	Region
China	Zhejiang Province, Guangxi, Guizhou, Sichuan Province, etc.
Japan	Tsukuba, Ibaraki, Okayama, Tokyo, Fukuoka
Korea	Seoul, Incheon
Netherland	Utrecht
Austria	Vienna University
France	Montpellier
Germany	Hannover
Italy	Padua
North America	Pennsylvania
India	Uttarakhand

1.2 Historical Use and Traditional Knowledge

Among living tree species, *Ginkgo biloba* is considered the oldest surviving species. Fossil records indicate that ginkgo species first appeared during the Permian Period, approximately 286–248 million years ago. *Ginkgo biloba* is the sole extant representative of the family Ginkgoaceae. Its long-term survival is attributed to its extraordinary adaptability to diverse environmental conditions, which also contributes to its high resistance to diseases. In addition, the preservation of ginkgo trees within sacred temple grounds, where they were carefully maintained by Buddhist monks, has played a significant role in their continued existence. The medicinal use of ginkgo was first documented approximately 5,000 years ago in China, where it was primarily used as a remedy for asthma [8]. Around 2,000 years ago, the Chinese Materia Medica Shen Nong Ben Cao Jing recorded Ginkgo biloba as a medicinal herb, although its use at that time was limited mainly to the seeds. Subsequently, the leaves of *Ginkgo biloba* were incorporated into Traditional Chinese Medicine for the treatment of heart and lung disorders [9].

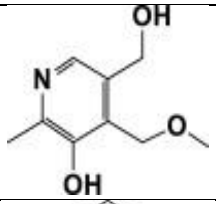
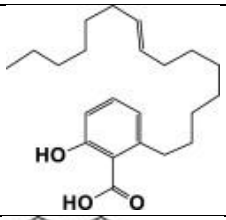
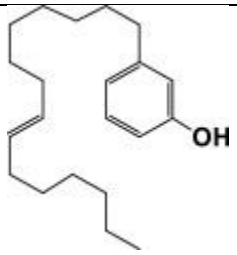
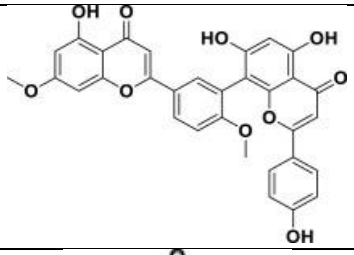
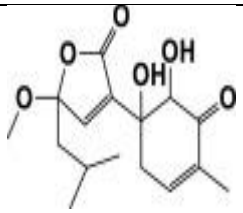
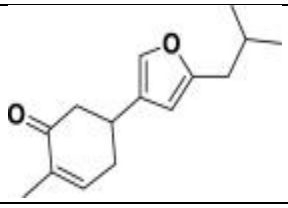
2. Phytochemistry

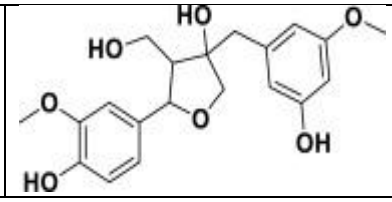
2.1 Phytochemical Constituents

As reported previously, the major bioactive constituents of *Ginkgo biloba* include bioflavonoids, terpenoids, flavonoids, polyphenols, organic acids, and several other compounds, as summarized in **Table 2**. Among these bioactive components, the most important constituents are ginkgolides and bilobalide. The ginkgolides

comprise several derivatives, namely ginkgolides A, B, C, J, and M, while bilobalide is a unique sesquiterpene lactone. These stereoisomeric forms share a similar molecular framework but differ in the number and spatial arrangement of hydroxyl functional groups [10]. Bilobalide and ginkgolides A, B, and C are considered the principal pharmacologically active terpenoids present in *Ginkgo biloba*. Standardized leaf extracts of *Ginkgo biloba* typically contain approximately 24% flavonoid glycosides, 6% terpenoids (primarily terpene lactones), and 5–10% organic acids. Flavonoids in ginkgo leaves are present mainly in the form of glycosides. Consequently, standardized ginkgo leaf extracts are commonly formulated to contain about 24% flavonoids and 6% terpene lactones. In addition to these major constituents, ginkgo leaves contain smaller amounts of alkylphenols, such as ginkgolic acids, as well as biflavonoids. Another notable compound is ginkgotoxin, which is structurally related to vitamin B_6. The active constituents identified in *Ginkgo biloba* extracts include catechins, flavones, ascorbic acid, flavone glycosides, lactones, sesquiterpenes, diterpene lactones, ginkgolides, iron-based superoxide dismutase, and p-hydroxybenzoic acid [11]. Among the flavonoids, the major compounds are quercetin, rutin, and quercetin-3-β-D-glucoside, while minor flavonoids include kaempferol, isorhamnetin, and quercetin derivatives [12].

Table 2: Phytoconstituents of *Ginkgo biloba*.

Compound	Structure	Plant part used	References
Ginkgotoxin		Seed	[13]
Ginkgoic acid		Seed	[14]
Ginkgol		Fruit	[15]
Ginkgetin		Leaves	[16]
Bilobanol		Leaves	[17]
Bilobanone		Leaves	[18]

Ginkgool		Roots	[19]

3. General Medicinal Use of *Ginkgo biloba*

Ginkgo biloba, often referred to as a "living fossil," has been used as a medicinal herb for human health for more than 2,000 years. The leaves of ginkgo are commonly used in medicinal teas, while its seeds have long been recognized for their therapeutic benefits in Chinese herbal medicine. *Ginkgo biloba* has been employed for thousands of years in Traditional Chinese Medicine to treat a wide range of disorders, including bronchitis, asthma, tuberculosis, cognitive impairment, and gastrointestinal discomfort. Modern scientific studies have demonstrated its efficacy as a dietary supplement and as a memory-enhancing agent [20]. *Ginkgo biloba* has been used therapeutically or prophylactically for various neurological conditions, such as Parkinson's disease, multiple sclerosis, Alzheimer's disease, Huntington's disease, ataxia, and frontotemporal dementia. Owing to its antioxidant, neuroprotective, anti-inflammatory, and immunomodulatory properties, ginkgo has also shown promising potential as a therapeutic agent for cardiovascular system disorders [21]. Ginkgo extracts have been reported to inhibit blood clot formation, strengthen capillary walls, enhance peripheral blood circulation, and exhibit neuroprotective and wound-healing properties. Additionally, they possess anti-asthmatic effects and protect brain cells against hypoxic conditions [22]

4. Pharmacological Properties of *Ginkgo biloba*

Ginkgo biloba is currently recognized as a prominent phytotherapeutic agent with a wide range of therapeutic applications. In the traditional Chinese medical system, the nuts and leaves of *Ginkgo biloba* have been used for thousands of years in the treatment of respiratory disorders, particularly bronchitis and asthma [23]. Historically, ginkgo nuts have been utilized for the management of respiratory conditions such as asthma and chest pain, as well as for bladder irritation and the treatment of alcoholism. In contrast, the leaves of the plant are primarily responsible for many of its therapeutic effects, including the management of cardiovascular disorders and skin infections.

Moreover, *Ginkgo biloba* has been extensively studied for its potential role in the management of neurological and vascular disorders. Current research suggests its usefulness in alleviating symptoms associated with Alzheimer's disease, cerebrovascular accidents (stroke), epilepsy, and peripheral vascular disease [24]. Substantial evidence supports the diverse pharmacological activities of *Ginkgo biloba* extracts (GBE), including the reduction of cardiovascular disease risk, inhibition of ischemia-induced oxidative damage, improvement of cerebral and hepatic blood flow, hepatoprotective effects, and antiplatelet activity. The potential anticancer properties of GBE have also been investigated; however, this area remains only partially established. Notably, for most therapeutic indications, studies indicate that whole *Ginkgo biloba* fruit extracts demonstrate greater efficacy than isolated individual constituents, highlighting the importance of synergistic interactions among its bioactive compounds [25].

4.1 Antioxidant Effect

During tissue growth and aging, processes such as lipid peroxidation, oxidative protein damage, DNA oxidative stress, and other oxidative insults frequently occur. These alterations can lead to abnormalities in neurological function, sensory organs, and the cardiovascular system, thereby contributing significantly to the development of degenerative diseases. Reports indicate that diseased tissues exhibit increased levels of oxidatively damaged lipids, proteins, and DNA, accompanied by reduced endogenous antioxidant defenses. Because *Ginkgo biloba* contains multiple and structurally diverse antioxidant constituents, evaluating the contribution of each antioxidant component is particularly challenging. Nevertheless, the antioxidant activity of *Ginkgo biloba* has been demonstrated to be effective against a broad spectrum of free radical–generating species, including hydroxyl radicals, superoxide anions, oxyferryl species, peroxyl radicals, and nitric oxide (NO) [26]. This antioxidant potential is largely attributed to its rich composition of terpenes, flavonoids, and

bioflavonoids. Overall, *Ginkgo biloba* exhibits potent antioxidant activity against free radicals associated with aging, thereby providing protective effects for the brain, retina, and cardiovascular system [27].

4.2 Anti-Inflammatory Effect

Inflammation is a complex biochemical process that leads to the disruption of tissue homeostasis. Both acute and chronic inflammation can be triggered by various stimuli, including chemical, mechanical, and physical factors. *Ginkgo biloba* contains flavonoids that act as anti-inflammatory polyphenolic compounds, a property that has been well established in earlier studies [28]. Among the major bioactive constituents of *Ginkgo biloba*, the principal biflavones—particularly ginkgetin—have demonstrated strong binding affinity toward leukocyte elastase, suggesting a potential mechanism for their anti-inflammatory action. Furthermore, biflavones have been shown to significantly reduce inflammatory cell infiltration and pro-inflammatory cytokine levels in lung tissue extracts of treated mice [29].

4.3 Hepatoprotective Effects

The hepatoprotective activity of *Ginkgo biloba* has been largely attributed to its antioxidant properties. These effects are presumed to result from the restoration of key antioxidant enzymes, including superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase, along with an increase in glutathione (GSH) levels and a reduction in lipid peroxides and hydroperoxides in hepatic tissue. *Ginkgo biloba* extract (GBE) has been shown to exert significant hepatoprotective effects against carbon tetrachloride (CCl_4)-induced hepatic oxidative damage. The underlying mechanism of action of *Ginkgo biloba* appears to involve an initial reduction in hepatic lipid peroxidation, followed by modulation and inhibition of enzymes associated with glutathione metabolism. Experimental studies have further demonstrated that the hepatoprotective and antioxidant properties of GBE effectively protect rat livers against fibrosis and oxidative injury [30].

4.4 Antiaging Effect

Increased wrinkling and a dry, dull appearance of the skin are characteristic indicators of the aging process, which is associated with collagen degradation and impaired desquamation [31]. Leaf extracts of *Ginkgo biloba*, including ethanol extracts prepared in aqueous solutions, have demonstrated notable skin-protective activity [32]. Treatment with EGb 761 has been shown to prevent freezing-induced damage and to reduce reperfusion injury by decreasing tissue lipid peroxidation, thereby indicating its potential anti-aging effects. Furthermore, total lactones of ginkgo (TLG) have exhibited significant anti-aging activity by reducing lipid peroxidation, nitric oxide (NO) levels, and neuronal apoptosis in aging mouse models [33].

4.5 Antilipidemic Effect

The hallmark features of dyslipidemia include elevated total cholesterol, increased levels of low-density lipoprotein (LDL) cholesterol, and reduced levels of high-density lipoprotein (HDL) cholesterol. *Ginkgo biloba* extract has been shown to significantly reduce plasma total cholesterol and triglyceride levels while markedly increasing HDL cholesterol levels compared with control groups. Additionally, ginkgo extract was found to increase glutathione (GSH) levels and decrease malondialdehyde (MDA) concentrations in aortic tissue in a dose-dependent manner, indicating its antioxidant and lipid-modulating effects [34].

5. Specific Relevance to Neurodegenerative Disease

Ginkgo biloba extract (GBE) has been used therapeutically for a variety of clinical conditions, with varying degrees of success. Conditions commonly addressed include, but are not limited to, peripheral vascular diseases, Alzheimer's disease, Parkinson's disease, age-related neurodegenerative dementias, and neurosensory disorders such as tinnitus [35]. *Ginkgo biloba* has been reported to offer neuroprotective effects against brain damage and may also enhance the efficacy of antidepressant therapies. The herb has been shown to alleviate mental fatigue and impaired concentration, effects that are partly attributed to improved cerebral blood flow. Further research has demonstrated that GBE modulates multiple neurotransmitter systems within the central nervous system. Notably, GBE exhibits mild antidepressant and anxiolytic effects, which are believed to result from the reversible inhibition of monoamine oxidase (MAO) A and B enzymes [36].

6. Clinical Evidence for Neuroprotective Effect

Standardized *Ginkgo biloba* leaf extract is widely used as a therapeutic agent for the management of dementia and memory impairment, including Alzheimer's disease. Several clinical trials have reported improvements in cognitive performance in patients with Alzheimer's disease as well as in elderly individuals, as summarized in **Table 3** [37]. The use of *Ginkgo biloba* extract (GBE) for the treatment and prevention of Alzheimer's disease, peripheral vascular disorders, Parkinson's disease, age-related neurodegenerative dementias, and neurosensory conditions such as tinnitus has been explored, with varying degrees of clinical success [38]. In addition, GBE has been employed in the management of a wide range of cardiovascular and neurological conditions, including peripheral occlusive arterial disease (POAD), thrombosis, myocardial ischemia, depression, multi-infarct dementia, and cerebral insufficiency characterized by memory impairment, reduced attention, anxiety, and disorientation. Further studies have also investigated the potential benefits of GBE in conditions such as traumatic brain injury, hypertension, stroke, and antidepressant-induced sexual dysfunction [39].

Table 3: Clinical Studies Carried Out for *Ginkgo biloba* for neuroprotective effect.

Sr.no	Study	Finding	References
1	Age-related effects of *Ginkgo biloba*	EGb 761, an extract from *Ginkgo biloba*, has demonstrated effectiveness in treating dementia and moderate cognitive impairment and may have neuroprotective benefits.	[40]
2	The effectiveness and safety of standardized *Ginkgo biloba* extract in the management of vascular cognitive impairment	In patients with vascular cognitive impairment, *Ginkgo biloba* at doses of 120 mg and 60 mg significantly improved the Clinical Global Impression score compared to placebo. On other neuropsychological tests, though, the effects were minimal.	[41]
3	Role of Medicinal Plants in Neurodegenerative Diseases	*Ginkgo biloba* been studied for its neuroprotective and antioxidant effects in neurodegenerative diseases. Nanotechnology-based delivery of these natural compounds is a promising approach	[42]
4	Examining the *Ginkgo biloba* Research Timeline Over the Past 50 Years	Because of its anti-inflammatory, antioxidant, and neuroprotective qualities, *Ginkgo biloba* has demonstrated therapeutic promise in a variety of chronic conditions, including neurological diseases.	[43]
5	*Ginkgo biloba* extract has antioxidant and neuroprotective properties that help prevent AD and other neurological disorders.	The extract from *Ginkgo biloba* regulates vascular flow and inhibits platelet-activating factors, which both improve neurological and cognitive performance. Against Alzheimer's disease and other neurological illnesses, it demonstrates neuroprotective and antioxidant benefits.	[44]
6	Extract from *Ginkgo biloba* in Parkinson's Disease	The *Ginkgo biloba* effect is examined to determine how copper in the brain relates to the protective effect of EGb761 against the MP neurotoxin.	[45]
7	Alzheimer's disease treatment implications of *Ginkgo biloba* in neuroprotection	The brain degenerates, and *Ginkgo biloba* is downregulated. Moreover, EGb761-treated hippocampus synaptosomes showed an increase in choline uptake. Acetylcholine is an important neurotransmitter involved in memory and learning processes, and choline is a precursor in its manufacture. AD has been closely linked to the loss of basal forebrain cholinergic neurons.	[46]
8.	Effect of *Ginkgo biloba* extract on neuropsychiatric symptoms of dementia	The neuropsychiatric inventory score improved in patients taking EGb 761 but did not change in those receiving a placebo. Treatment with EGb at a once-daily dose of 240 mg was safe, effective and improved	[47]

		the well-being of their caregivers.	
9.	*Ginkgo biloba* effects on cognitive function	Treatment with ginkgo 120mg twice a day did not improve cognitive performance in persons with multiple sclerosis.	[48]
10.	Effect of *Ginkgo biloba* on cognitive function in acute ischemic stroke	The study found that *Ginkgo biloba* may have protective effects that have been seen in ischemic stroke.	[49]

6.1 Summary of Clinical Trial

Indeed, available research demonstrates that EGb is remarkably effective in improving mental health and cognitive function in patients with Alzheimer's disease or vascular dementia. Based on current evidence and comparative studies, it is suggested that EGb, when administered at a recommended dose of 240 mg/day for a duration exceeding 24 weeks, can produce significant improvements in cognitive performance in patients with mild dementia [50].

7. Pathophysiology of Neurodegenerative Disease

The pathophysiology of neurodegenerative diseases is illustrated in **Figure 1** [51].

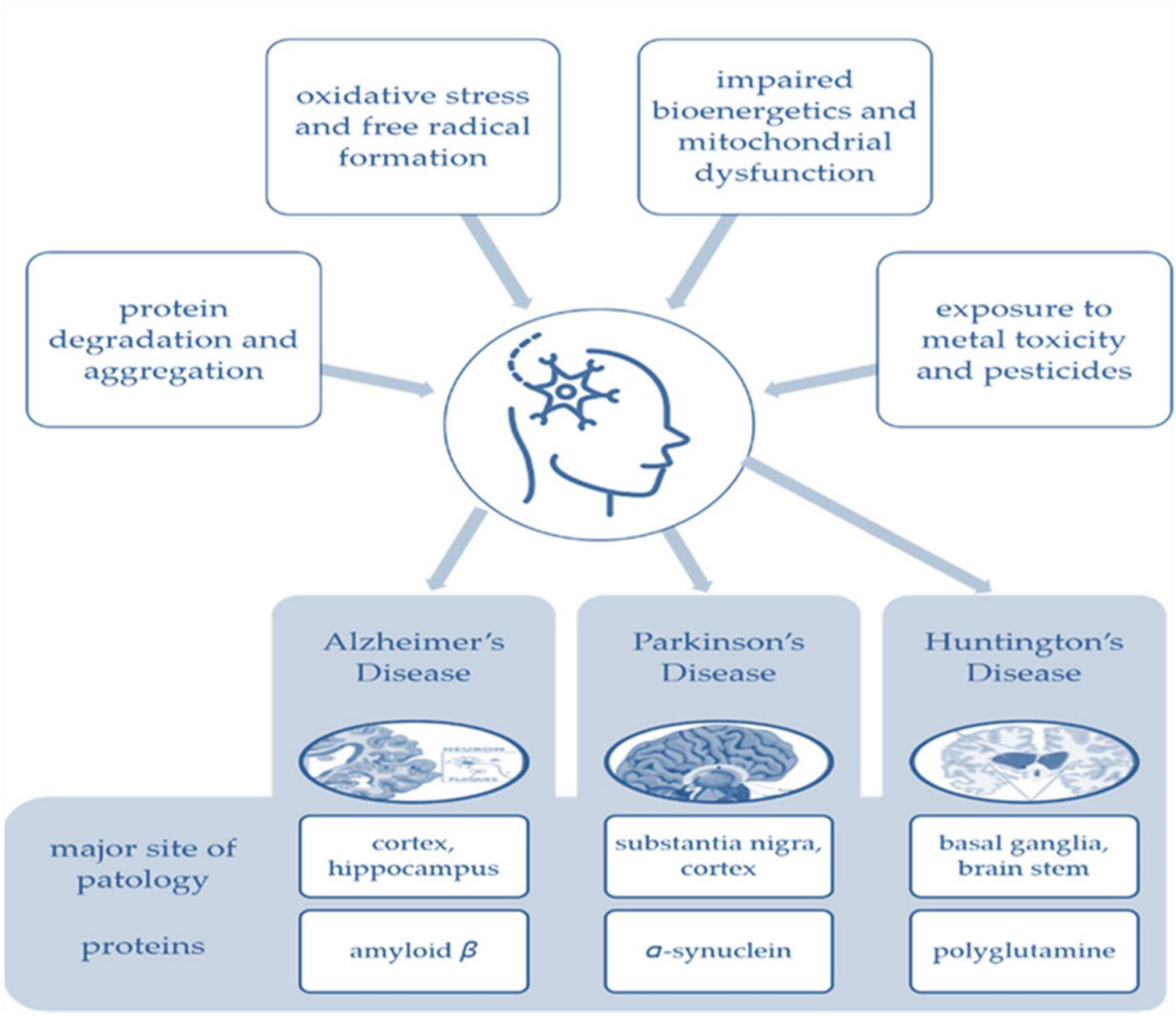


Figure 1: Neurodegenerative disease major site of pathology and proteins.

7.1 Parkinson's disease

Parkinson's disease (PD) is the second most common chronic neurodegenerative disorder, primarily caused by the loss of dopaminergic neurons and their projections in the substantia nigra. This neuronal degeneration

weakens the activity of the nigrostriatal pathway, leading to motor dysfunctions such as tremors, rigidity, bradykinesia, and impaired balance [52]. The neuroprotective effects of *Ginkgo biloba* have been demonstrated in various PD models. In a mouse model treated with 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), continuous administration of EGb761 mitigated MPTP-induced reductions in dopaminergic nerve terminals. Additionally, direct injection of MPTP into rat brains induces dopaminergic neurotoxicity, which can be prevented not only by EGb761 administration but also through prior treatment to block MPTP-induced neuronal damage [53]. EGb761 has also been shown to reduce levodopa-induced neurotoxicity in the 6-hydroxydopamine (6-OHDA) model of Parkinson's disease. Furthermore, paraquat, an insecticide linked to PD development, triggers PC12 cell death, which can be inhibited by EGb761. The main bioactive components of EGb761, illustrated in **Figure 2**, exert neuroprotective effects by reducing lipid peroxidation, suppressing oxidative stress, and preventing MPTP-induced neurodegeneration in the nigrostriatal pathway [54].

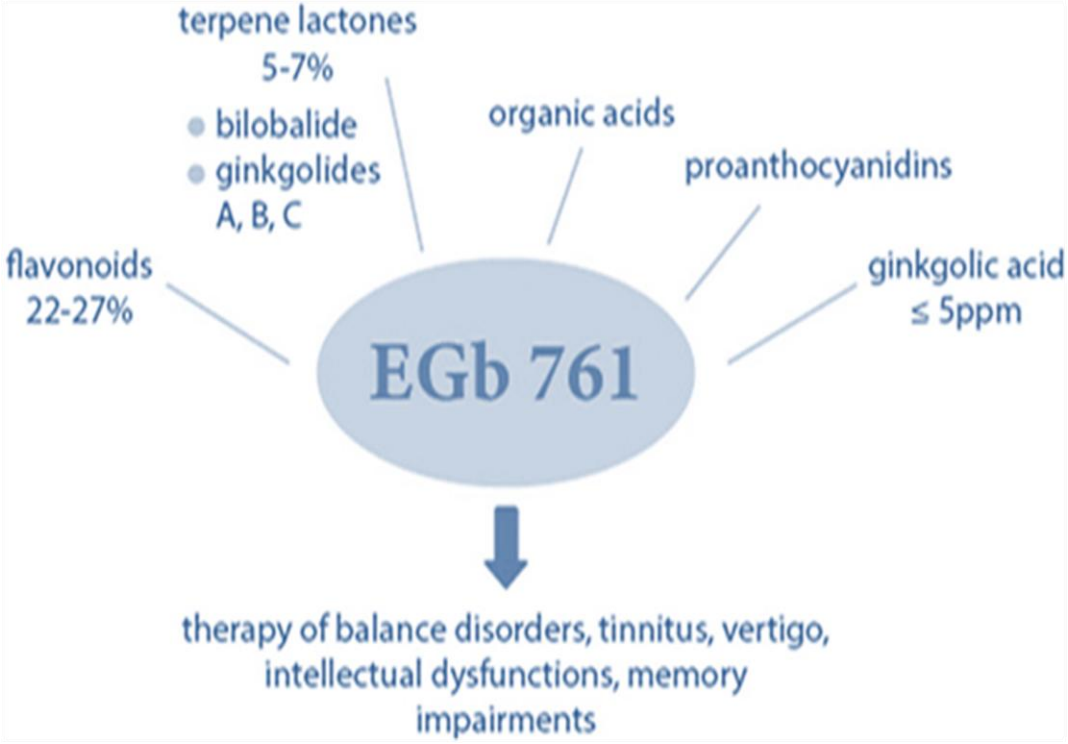


Figure 2: Main components of EGb 761.

7.2 Alzheimer's Disease

Alzheimer's disease (AD) is a prevalent cause of dementia and often leads to social isolation. It is a progressive neurological disorder commonly associated with aging. AD is characterized by gradual cognitive decline, memory loss, and the formation of amyloid plaques and neurofibrillary tangles in the brain [55]. Plaques arise from abnormal processing of the amyloid-β protein, while tangles result from hyperphosphorylation of the tau protein. Risk factors for AD include age, genetic predisposition, comorbid health conditions, and educational level, among others. In advanced stages, patients may experience muscle rigidity, slowed motor function, and eventually become bedridden, requiring continuous care [56]. The active constituents of *Ginkgo biloba* leaves improve blood circulation, strengthen capillary walls, prevent blood clot formation, and protect neurons from hypoxic damage. Leaf extracts are widely used to alleviate memory loss, concentration difficulties, and to safeguard against neurodegenerative disorders such as Parkinson's and Alzheimer's disease [57]. Numerous studies have demonstrated the benefits of *Ginkgo biloba* for AD, including enhancement of memory, mitigation of dementia associated with reduced cerebral blood flow, and improvement of cognitive function through its antioxidant and neuroprotective properties. GBE exerts these effects by modulating cerebral blood flow, thereby reducing mental fatigue and enhancing concentration. Its flavonoid and terpenoid constituents are primarily responsible for its antioxidant, anti-inflammatory, and neuroprotective activities. Overall, *Ginkgo biloba* enhances neurological function and cognition by improving blood flow and protecting the brain from ischemic damage, as illustrated in **Figure 3** [58].

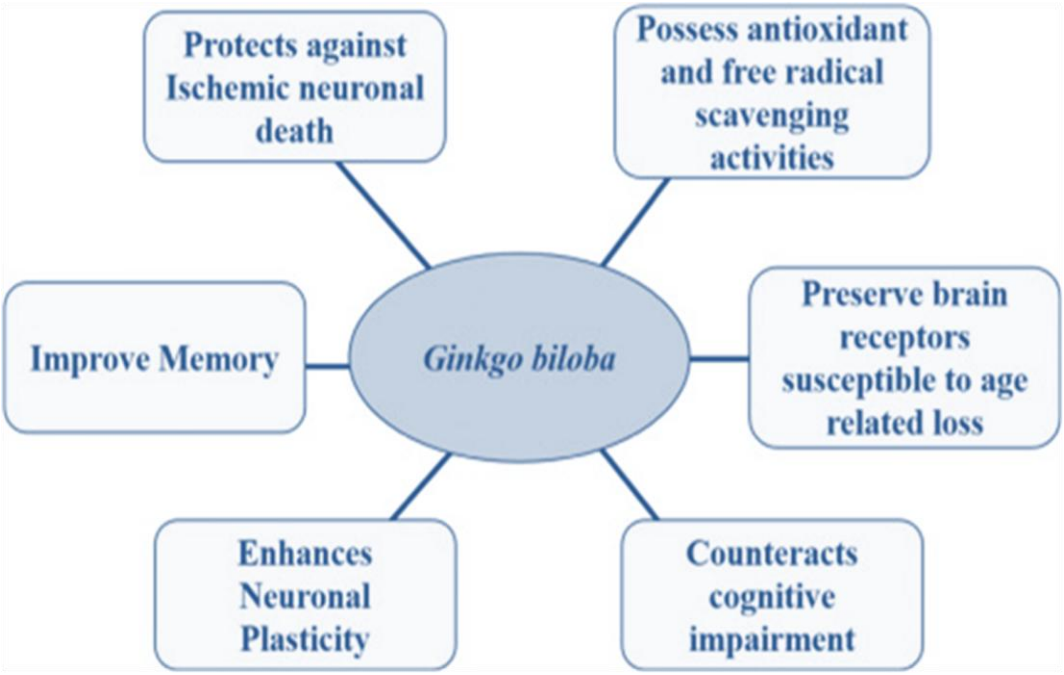


Figure 3: GBE has an array of activities relevant to neurological functions.

7.3 Huntington's disease

Huntington's disease, also known as Huntington's chorea, was first described by George Huntington from Ohio. It is an inherited genetic neurological disorder characterized by a range of symptoms, including muscle spasms, involuntary movements (chorea), mood disturbances, cognitive decline, and weight loss [59]. The structural and functional differences between a healthy brain and the brain affected by Huntington's disease are illustrated in **Figure 4** [60].

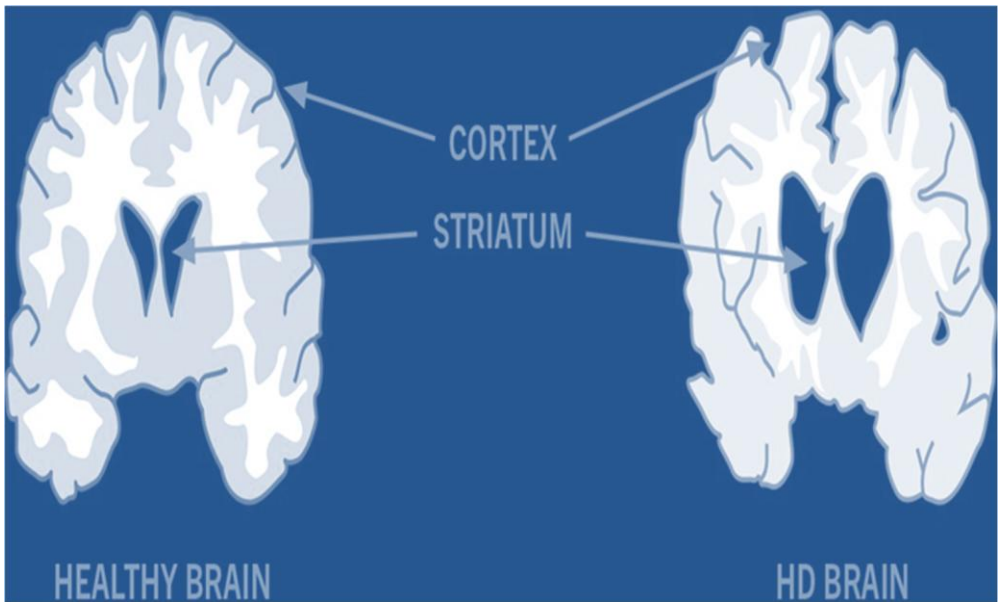


Figure 4: Difference between a Healthy brain and a Huntington's disease brain.

One specific standardized extract, EGb 761, has been shown to exert neuroprotective effects in Huntington's disease by modulating the expression of key proteins in the brain. In addition, owing to its potent antioxidant properties and its ability to enhance cerebral blood flow, EGb 761 has attracted considerable interest for its potential therapeutic effects in various neurodegenerative disorders [61]. The possible effects and underlying mechanisms of EGb 761 in Huntington's disease include:

7.3.1 Antioxidant Activity

Ginkgo biloba contains flavonoids and terpenoids, both of which exhibit potent antioxidant properties. These compounds may help mitigate oxidative stress, a key factor implicated in the pathogenesis of Huntington's disease.

7.3.2 Neuroprotection

Several studies suggest that *Ginkgo biloba* may exert neuroprotective effects capable of slowing the progression of neuronal damage. Such effects could be particularly beneficial in disorders like Huntington's disease, where neuronal loss is a central pathological feature.

7.3.3 Improvement of Cognitive Function

Several studies have demonstrated that *Ginkgo biloba* may enhance cognitive function in disorders such as Alzheimer's disease. Although Huntington's disease differs in pathology, these cognitive benefits could still be relevant for addressing the cognitive decline observed in HD patients [62].

7.4 Ataxia

Ataxia is a neurological disorder characterised by a loss of control over body movements, which can arise from genetic factors, acquired conditions, or specific episodes. Ataxias comprise a group of diverse genetic neurodegenerative disorders that occur when the cerebellum—which is responsible for coordination—fails to function properly or has impaired communication with other regions of the central nervous system [63]. Clinical features of ataxia include pyramidal syndrome, motor impairments, seizures, peripheral neuropathy, and cognitive deficits. Common symptoms are clumsiness, dysarthria (difficulty speaking), involuntary eye movements, impaired depth perception, and instability during standing or walking [64]. Ataxias are classified into two major types: hereditary ataxia and sporadic ataxia. *Ginkgo biloba* is a widely recognized herbal supplement, commonly used for circulatory and cognitive support. Although its effects specifically on ataxia are not well documented, some studies suggest that *Ginkgo biloba* possesses neuroprotective properties that may benefit ataxia-related conditions. By enhancing cerebral blood flow and promoting mental agility, it could potentially exert indirect therapeutic effects in ataxia. However, clinical evidence directly linking *Ginkgo biloba* to ataxia treatment remains limited [65]. Various proposed mechanisms for managing ataxia through *Ginkgo biloba* are outlined below:

7.4.1 Neuroprotective Effects

Ginkgo biloba has been reported to possess potent anti-inflammatory and antioxidant properties. These effects may help protect brain tissues in cases of ataxia that arise from oxidative stress or neurodegenerative processes.

7.4.2 Mixed Clinical Evidence

The therapeutic effects of *Ginkgo biloba* are notably variable. While some studies report significant symptom reduction in various neurological disorders, others find no substantial clinical benefit.

7.4.3 Improved Blood Flow

Studies have shown that *Ginkgo biloba* can enhance blood flow, particularly by improving cerebral microcirculation. Increased blood flow may facilitate the delivery of oxygen and essential nutrients to neurons, potentially supporting their function and thereby alleviating some of the symptoms associated with ataxia.

7.4.4 Anti-Inflammatory Effects

Ginkgo biloba is reported to possess anti-inflammatory properties, which may be beneficial for neurodegenerative disorders associated with chronic inflammation. These effects could potentially mitigate

the harmful impact of inflammation on neurons and, in doing so, help alleviate some of the symptoms observed in ataxia.

7.4.5 Modulation of the Neurotransmitter System

Ginkgo biloba extracts may influence several key neurotransmitter systems involved in mood regulation and motor coordination, including dopamine and serotonin pathways. Consequently, modulation of these systems by *Ginkgo biloba* could help reduce some of the symptoms associated with ataxia [66].

7.5 Multiple Sclerosis

Multiple sclerosis (MS) is a chronic demyelinating disease of the central nervous system (CNS) triggered by autoimmune attacks. The disease is characterized by varying degrees of axonal and myelin sheath damage. Common clinical manifestations include muscle rigidity and spasms (Calabresi et al., 2004; Koriem et al., 2016). The classification of multiple sclerosis is summarized in **Table 4** [67].

Table 4: Classification of Multiple Sclerosis.

Types	Clinical feature
Relapsing/Remitting Multiple Sclerosis (**RRMS**)	Relapses are followed by incomplete remissions. During relapses, symptoms can get more severe.
Secondary Progressive Multiple Sclerosis (**SPMS**)	Gradual progression of symptoms and disability over time following a period of RRMS
Primary Progressive Multiple Sclerosis (**PPMS**)	Gradual progression of symptoms from the initial presentation
Progressive Relapsing Multiple Sclerosis (**PRMS**)	Gradual symptoms progress over time, accompanied by acute attacks of undesired effects

Ginkgo biloba, commonly used in dietary supplements, has attracted research interest for its potential benefits in enhancing blood circulation, managing cognitive and mental disorders, and exerting anti-inflammatory effects. Studies have indicated that *Ginkgo biloba* may also have therapeutic potential in multiple sclerosis (MS), a chronic autoimmune disease of the central nervous system. The proposed mechanisms underlying the effects of *Ginkgo biloba* in MS are outlined below:

7.5.1 Cognitive Function

Some studies have reported that *Ginkgo biloba* supplementation can improve performance on cognitive tests in patients with multiple sclerosis (MS).

7.5.2 Fatigue

Fatigue is a common and often disabling symptom in patients with multiple sclerosis (MS), significantly affecting daily functioning. Several studies suggest that *Ginkgo biloba* may help reduce MS-related fatigue. In clinical comparisons with a placebo, *Ginkgo biloba* supplementation was associated with a significant decrease in reported levels of tiredness.

7.5.3 Inflammation and Neuroprotection

Flavonoids and terpenoids present in *Ginkgo biloba* possess antioxidant properties and may also help reduce inflammation within the central nervous system, thereby providing potential neuroprotective benefits for patients with multiple sclerosis (MS) over the long term. However, it is important to note that direct clinical evidence supporting these effects in MS patients remains limited in the current literature.

8. Safety and Side Effects

Ginkgo biloba is generally considered safe when administered at appropriate doses. However, some adverse effects—often similar to those associated with anesthetics—have been reported, including headaches, dizziness, and skin allergies. Additionally, *Ginkgo biloba* may interact with other substances, particularly anticoagulants, potentially increasing the risk of bleeding [68].

9. Conclusion

Ginkgo biloba, a well-known herbal extract, has been extensively studied for its potential neuroprotective effects in neurodegenerative diseases, including Alzheimer's, Parkinson's, and Huntington's diseases. Its therapeutic potential is attributed to antioxidant activity, anti-inflammatory effects, and enhancement of cerebral blood flow. In Alzheimer's disease, *Ginkgo biloba* may improve cognitive function, slow disease progression, and reduce associated symptoms. In Parkinson's disease, it has been shown to alleviate motor dysfunction, enhance cognitive performance, and mitigate oxidative stress. Similarly, in Huntington's disease, *Ginkgo biloba* may reduce oxidative damage, support neuronal function, and slow disease progression. Looking forward, incorporating *Ginkgo biloba* into advanced drug delivery systems, such as nanotechnology-based formulations, may improve its bioavailability and therapeutic efficacy. Furthermore, investigating its synergistic interactions with other neuroprotective agents could lead to novel treatment strategies. Future research should focus on elucidating precise mechanisms, determining optimal dosages, and evaluating patient-specific responses to establish *Ginkgo biloba* as a reliable adjunct in the management of neurodegenerative disorders.

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How to cite this article: Chaudhary B, Sharma C, Lamba M. *Ginkgo biloba* in neurodegenerative disease. Pharm Res Bull. 2026;5(1):26-40.