

Ginkgo biloba Herbal Plant Used for Treating Dementia and Alzheimer's Disease

Imanshu^{1*}, Mohita Thakur¹, Deepika Bhatia^{2*},

¹*School of Pharmacy, Desh Bhagat University, Mandi Gobindgarh, Punjab, India*

^{2*}*Associate Professor University Institute of Pharma Sciences, Chandigarh University Ghuruan, Mohali, Punjab, 140413, India*

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Abstract

Cognitive dementia is the most vulnerable cause of Alzheimer's disease around the world, through which there will be cognitive decline in neuronal signals that are generated by the generation of nerve impulses through the region of the brain to the cerebral cortex. This disease should affect the age group of 50-65 or above 65 years of age, but in some cases, this may affect adults with vascular dementia, where the person may be unable to learn and remember things, and physical and mental behavioral changes may be seen in these cases. In this review, we studied the Ginkgo biloba as an herbal plant drug which has been used for the treatment of cerebral and vascular dementia or Alzheimer's disease, which is used in the treatment of neurodegenerative disease or disorder. The herbal extract of Ginkgo biloba leaves that would be beneficial for memory boosters and improves the learning and remembering capability in an adult or affected person or patient. As usual, the herbal extract may help to improve the nerve conduction in between cerebral cortex, where the nerve conduction or generation of nerve impulses occurs throughout the whole body.

*Corresponding Author:

Dr. Deepika Bhatia (bhatia.deepika89@gmail.com)

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1. Introduction

Globally, Dementia is most leading cause of changes in physical and mental behavior of a person's condition, and by this Alzheimer's disease (AD) is the world's number one neurodegenerative disease, which is most probably caused by vascular dementia (VD) [1]. Worldwide, the number or percentage of the global population, 25-40 %, is being affected by this cognitive disease. There will be various type of dementia which affects the vascular dementia that cause some other neurodegenerative disease like Parkinson's disease where effective cause of dementia with Lewy bodies, or by dementia of fronto-temporal lobes present in the substantia nigra region of the brain, Alzheimer's disease where there will be deposition of amyloid protein, neurofibrillary tangles, and also there is a deposition of tau protein in the cerebral cortex in the region of brain, or Huntington's disease; in this disease there is progression in the brain

eventually by which brain cannot perform its functions properly though the causative effects is by signal defective genes on chromosome number 4 which is the one of the 23 human chromosome that carries a person's entire genetic code or coding system [2].

Alzheimer's disease is an irreversible, progressive neurodegenerative disease that slowly affects or destroys the memory and thinking skills, mental and physical behavior of an individual, eventually even the ability to perform or carry out their daily routine activities and the simplest tasks [3].

It is the most common cause of dementia.

Dementia is the loss of intellectual abilities, like thinking, remembering things, and reasoning. These are several activities that are severe enough to interfere with daily functioning.

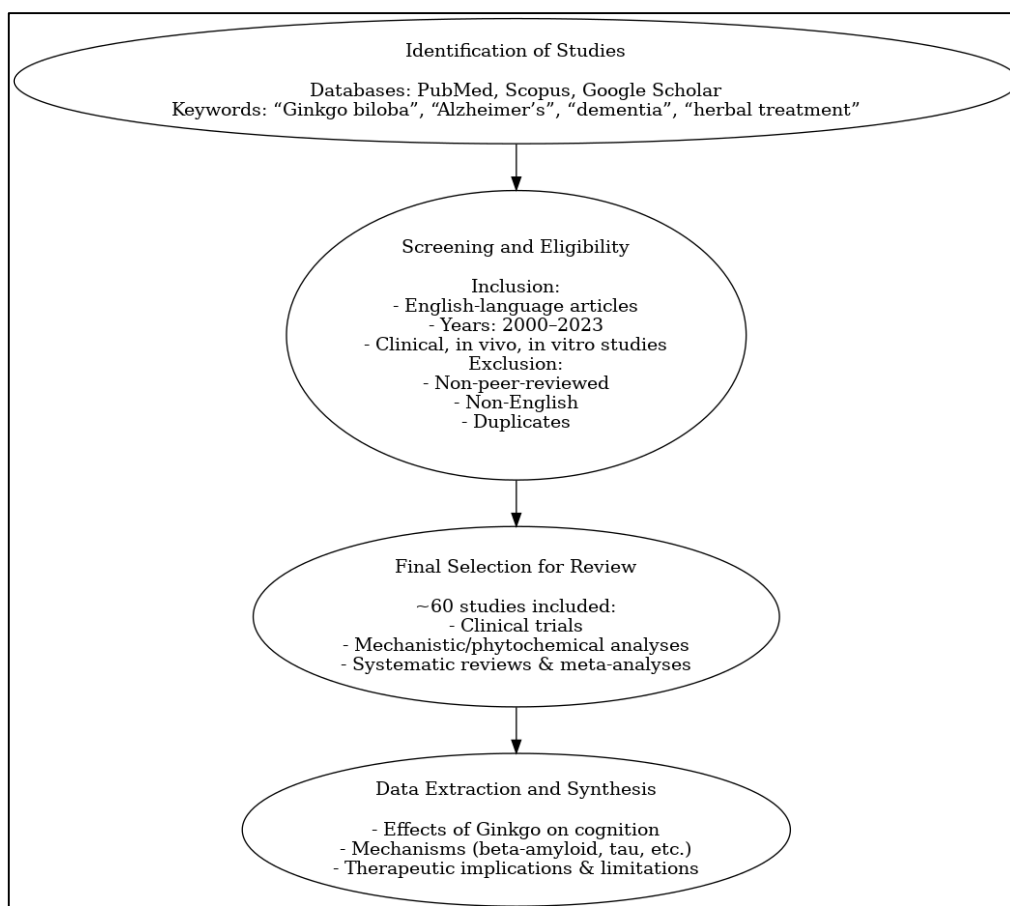
Alzheimer's disease was first examined by the German physician in 1906, and the name of the

disease was coined by Dr. Alois Alzheimer as Alzheimer's. He recognized that there is a collection of brain cell abnormalities as a disease.

One of the patients of Dr. Alois died within a few years after suffering from severe memory problems, difficulties understanding things, lots of confusion, and some behavioral changes in his patient. After the death of his patient, while he wants to know about the facts behind the death of his patient, so thereafter he is

performing a brain autopsy. The doctor observed that there was a dense accumulation of neuritic plaques surrounding the nerve cells of the cortex region in the brain [4].

He also catches up with the signs of twisted bands of neurofibrillary fibers tangles inside the nerve cell. But nowadays this neurodegenerative brain disorder is denoted by his name, and during the autopsy, he found that these plaques and tangles have a definite diagnosis or characteristics of Alzheimer's disease (AD) [5].



Epidemiology

Although Alzheimer's disease (AD) is diagnosed in adults too in an age group, it is much more common in older age groups of about 75 years or older than 80 years. And somehow, 80 percent of the elderly population affected with Alzheimer's disease (AD) globally is age 65 and older.

Moreover, Alzheimer's disease (AD) is highly correlated with aging, and women have a longer life expectancy as compared to men because they account for women's over 2/3rd of the elderly population with this disease [6].

There must be a loss of memory, physical or mental behavior, which was the first outcome of this disease (AD). After the progression of Alzheimer's, several other changes could be seen in an individual, like as cognitive impairment such including remembering things, learning

new things, etc., language is disrupted.

In structural changes, there will be a progressive loss of connection between the neurons (synapses) and in neurons themselves, in an early stage of this condition. Later on, the brain gets shrunken through the cerebral cortex, which appears shriveled, and the fluid-filled ventricles get expanded [7].

In microscopic changes, there could be a hallmark of Alzheimer's disease (AD) that is visible only under the microscope. There is deposition of beta amyloid plaques between the neurons, and microtubules are associated the tau protein aggregation in between the neurofibrillary tangles inside the neurons, significantly affecting the structure will get

persist by this factor and after that the neurons may die by the progression of this amyloid protein and tau fibrillary tangles [8].

Risk Factors

Genetics: About 1% of cases of Alzheimer's disease are caused by mutations in the genes APP, PSEN1, or PSEN2, which affect Amyloid- β processing. Certain mutations in APOE and TREM2 can enhance the risk of developing the more common sporadic form of the condition.

Sex: The overall incidence of Alzheimer's disease in women is up to twice that of men. This was the difference which can't be described by women's somehow hormones and lifestyle might be playing a vital role as a part of this.

Lifestyle: Here is a raft of the probably adaptable risk factor for Alzheimer's disease has been determined. They should also include some other diseases or factors as follows as diabetes, obesity, depression, smoking, and low educational attainment.

A Global Problem

In the year 2015, around 55 million people worldwide suffered from dementia or Alzheimer's disease. When there is increase the growth of population growth and ages and the number of patients or people are expecting to surpass 160 million people in the upcoming 2050 [9].

The incidence of Alzheimer's disease is in the range from 1% at the age of 65-70 approximately, to 4% over the age of 85. And all the numbers of this disease could be increased per year would be double from the previous or last amendments. The estimates of prevalence of Alzheimer's disease range from lowest figure of 3% of the population at 65-years to the highest report was estimated near about 47% of 85%-year-old people [10].

And the death rate by affecting this Alzheimer's disease must be highly increasing approx. 10% per year worldwide. Recently, there is an estimation of about the affected population was 40 years for men's and 55 years for women's have fallen under this widely and un-curable disease. However, the median of survival for this disease were initially diagnosed.

Symptoms

The onset of action and manifestations of Alzheimer's disease is usually very slow and gradually increasing the progression of amyloid

protein, tau tangles, in the brain, and seldom occurring at the age of 65 [11].

It occurs in the following three stages:

- **Stage 1:** In this stage a person can forget the things, poor insight, mild difficulties with finding words, personality changes, difficulties to doing calculations, misplacing and loss the things from surroundings, continuous repetition of same statement at a time and a minor degree of disorientation.
- **Stage 2:** This stage the ability of thinking and memory get worse, inappropriate using more word at same time, loss of basic self-thinking and caring activities, could not recognize the distant family and friends, a persons have difficulty to communicating things, wanders off, and become mentally and physically capability to do work and recognize the things getting trouble and may experience of hallucinations become occur.
- **Stage 3:** This is the last stage where bedridden, incontinent, uncomprehending and individual get mute, there will be several severe changes in loss of ability to hold the conversion, trouble in movement, eating, or disability to control bladder and bowel and lack of ability to do recent activities.

Other signs can be seen as:

- Family history: in this a scientist believes that the genes play an essential role for the progression of this Alzheimer's disease (AD).
- Social engagements
- Quality of sleep taken by individual
- Daily healthy diet
- Physical and mental stimulation of a person, and
- Vascular health also.

Mechanism of Alzheimer's disease

Beta-amyloid Opinion

It shows that there will be rise in the production of aggregation growth of beta amyloid fibers which leads to the senile plaques, or cause neurotoxicity and other clinically significant of Alzheimer's.

Although several drugs which is being evolve for Alzheimer's disease at targeting site of beta amyloid for Amyloidosis by obstructing and diminishing the production of amylogenic A β peptides, or by decomposition of A β oligomers and other A β protein clusters in the cerebral cortex of brain [12].

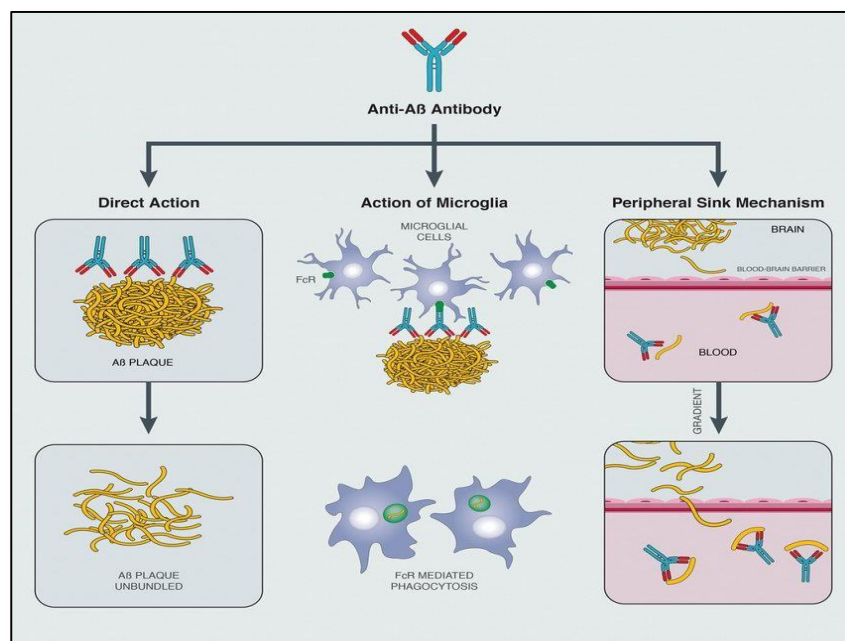


Fig 1. Depiction of the beta-amyloid cascade hypothesis of AD, through which there should be accumulation of Aβ, which imitates the progression of Alzheimer's disease.

Tau Opinion
Neurofibrillary tangles

A healthy neuron can provide internal strength, which is partially made by the structural cells known as

microtubules.

These microtubules go ahead to tracks, guiding molecules to provide nutrients from the body of the cell down to the ends of the axons and return. There is a unique protein, tau helps to make these microtubules in stable conditions [26].

But in Alzheimer's disease (AD), this Tau can be converted chemically and being to couple with other threads or fibers of tau neurofibrillary tangles, and they become tangled or bind together.

After that, when this binding is done by tau tangles, the microtubules disintegrate, collapsing into the neurons or neuronal transport system in the cortex of the brain.

Thus, as a result, there is a malfunction in the communication between the neurons, and after several intervals of time, the cell or neurons die due to the progression of these neurofibrillary tangles inside the brain's cortex region [13].

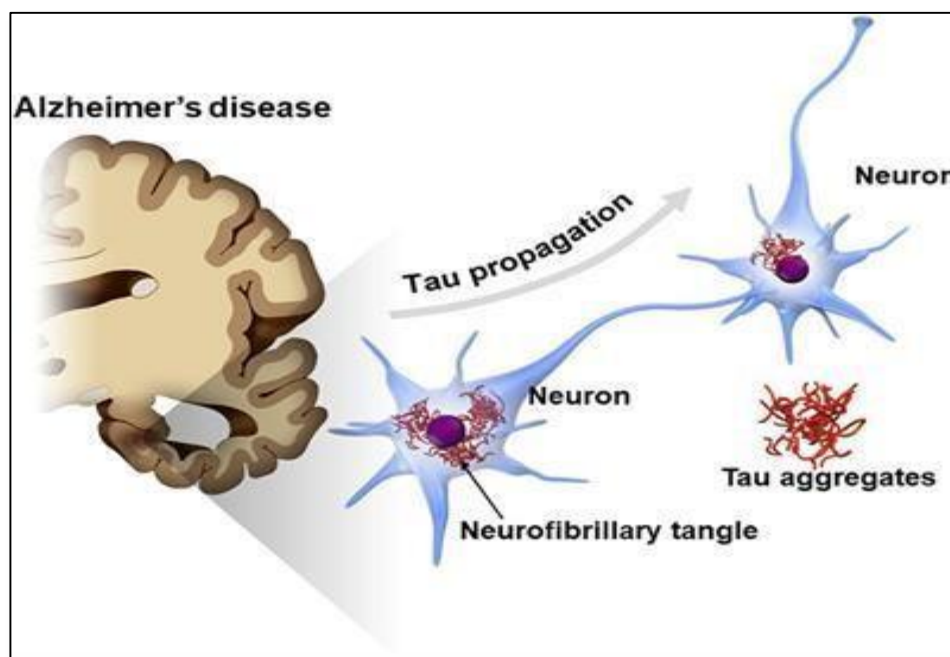


Fig 2. Pathology of AD in the brain by the deposition of neurofibrillary tangles (NFTs), which disrupt the neural network in a

stereotypical framework.

Changes in the Alzheimer's-affected

Brain

The disease is affecting the cerebral cortex and leads to memory loss and several changes in other coherent emerging approaches come forward. The clinical manifestations of Alzheimer's disease (AD) were conventionally made during these stages [26].

Significance of mild Alzheimer's disease (AD)

- Loss of memory, physically and mentally unstable, confused about their surroundings or a familiar place (impaired thinking perception).
- It takes a long time to perform a daily routine task
- Shivering hands to accomplish paying bills and holding things such as money, a coffee cup, and certain difficult-to-grab food items.
- Involuntary judgments that may lead to wrong thoughts
- Loss of sensation and psychological imbalance
- Behavioral and personality changes may be seen
- They may feel stressed and depressed or in an anxious state

These are all the significant signs and manifestations of dementia and the neurodegenerative disease of Alzheimer's, with early and late progression of the cognitive decline in certain activities [14].

Moderated Alzheimer

Further, Alzheimer's disease (AD) has spread to the region of the brain in the cerebral cortex, which helps to control sensory perceptions such as thinking, reasoning, consciousness, and language [16].

The significant manifestation is as follows:

- Enhance the risk of memory deprivation
- Attention span is condensed
- Complications in acknowledging the family, friends, and society
- Troubling in language, like reading and writing issues with numbers and letters
- Difficult to organize thoughts
- A person may suffer from anxiety, restlessness, agitation, sometimes delusions and hallucinations, or paranoia may occur.

Severe Alzheimer's

This was the last, as we called, the final stage of Alzheimer's disease (AD), where the amyloid plaque and neurofibrillary tangles are extensively aggregated all over the brain, and the

region of the brain has been shrunk continuously [17].

In this, there may be other significant causes that may occur, such as.

- Continuous decline the body weight
- Skin infections and seizures may produce
- Difficulty in swallowing food and liquid nutrients
- Insufficiency in controlling bladder and bowel movements
- A person has built the ability to groan, moan, and grunt

Diagnosis

There will be no diagnostic test to identify the source of progression of Alzheimer's disease (AD), but somehow, we can just imagine the physical behavior and body language of a person to determine that it will be affected by this neurodegenerative disease. Also, we can imagine the technology outlines the perception of Alzheimer's plaques and neurofibrillary tangles that have an extra significant and accurate [18].

- **Medical Opinion-** There must be any past injury or serious surgery, or any current persistent circumstances to recognize the actual signs of Alzheimer's disease (AD) symptoms.
- **Medication Opinion-** In some situations there will be irregular or OTC (over the counter) using or medication have to be taken by a person through which after some laps of time there would be an allergies or any adverse effects of that medication which the individual has taken and the list of medication that has to be mention in their current list of the drug and dose was also the significant cause of Alzheimer's disease (AD) [19].

Plan of Treatment or Herbal Plant Approach for Treating Alzheimer's Disease (AD)

The Ginkgo biloba plant is used for the treatment of AD. There will be some basic pharmacology of this **herbal plant**:

Common name: Maidenhair tree (Ginkgo biloba)

Type: Tree

Native Range: Southern China

Bloom time: April

Description Bloom: Green

Water: Medium

Suggested Use: Street Tree

Flower: Insignificant

Tolerant: Deer, Clay Soil, Air Pollution



Fig 3. Leaves and Fruits of Ginkgo biloba



Fig 4 Seeds of Ginkgo biloba

Physical description

The shape of the tree is pyramidal, has a columnar, sparingly branched trunk which is about 30m tall (100 ft) and 2.5m in diameter (8 ft). The color of the bark is grayish, and corky texture. Wood is light-colored, soft, and weak, and has little economic value. The leaves are lathery, which is up to 8 cm long (3 inches) and sometimes twice as broad [21].

Microsporangia (pollen forming) and female ovules are borne on separate trees. Pollen grains are carried to the female trees by the blowing wind. Megasporangiate (female) trees bear paired ovules, which, when fertilized, produce yellowish plum-like seeds about 2.5 cm long (1 inch) consisting of many inner nut-like portions which is surrounded by the fleshy covering outside [22].

Table 1. Indicate the features of the Ginkgo biloba plant

Common name of the plant	Part used	Biological source and species	Chemical constituents	References
Maidenhair tree	Seeds and Leaves	Ginkgo biloba Species: Ginkgoaceae	Terpenoids like as Ginkgolide, Bilobalide or Quercetin, Kaempferol, shikimic acid, ascorbic acid, Catechin	9, 10, and 12

Table 2. Indicating the basic characteristics of Ginkgo biloba

Microscopic Characters	Macroscopic Characters
Upper epidermis: Single layer of sub-rounded or sub-square cells, covered with thin but marked cuticles	General appearance: whole leaves, folded, fragmented, where some petioles. Fan-shaped (2-12 cm in width and 2-9.5 cm in length) from petioles to apical margin; the apex is sinuate, usually truncate or centrally cleft.
Collenchyma: the inner side of the upper and lower epidermis of the midrib, visible in mature and old leaves	Surface: Glabrous, with wrinkled appearance due to prominent dichotomous venation appearing parallel and extending from the lamina base to the apical margin
Palisade Tissue: it is just underneath the upper epidermis, elongated at right angles to the surface, which is irregular in appearance	Color: leaves are yellowish green to green, brown, often browner at apical edges, and usually the upper surface is darker. Petioles must be green to greenish brown.
Spongy Tissue: Cells of the mesophyll are smaller than the palisade cells and separated by a large intercellular space.	Odor and Taste: it should be slightly aromatic in odor and bitter in taste.
Vascular Bundles: It takes place at regular intervals along the width of the lamina: a cluster of calcium oxalate, collateral, with xylem dorsal, phloem ventral, surrounded by fibers.	
Cluster of Calcium Oxalate: Scattered amid parenchymatous cells	
Secretory Canals: Large and distinct, present in the mesophyll between vascular bundles	
Fiber Bundles: Walls slightly thickened, surrounded by vascular bundles.	
Lower Epidermis: Single layer of sub-rounded or sub-square cells, covered with a thin cuticle	

But some herbal plants cure or prevent the progression or aggregation of beta-amyloid protein and neurofibrillary tangles of tau protein of Alzheimer's disease, such as curcuma longa, Bacopa monniera, centella asiatica, ginkgo biloba, panax ginseng, nardostachys jatamansi, Rosmarinus officinalis, etc., various species of herbal plants that are used to treat and prevent Alzheimer's disease (AD) [24].

According to the herbal medication approach, a

herbal plant, ginkgo biloba, is utilized in the therapy for treating dementia and mild consequences of deterioration of neuronal fibers in the cerebral cortex of the brain. We avail

ourselves of the herbal extract of Ginkgo biloba that has been suggested to refine and boost the cognitive function and avert to reduce the accumulation of amyloid protein precursors and tau fibrillary tangles.

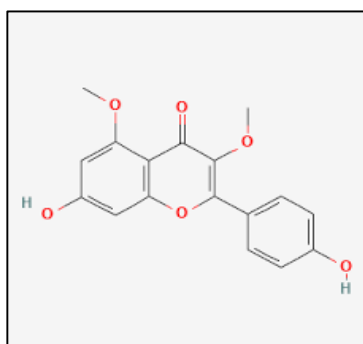
Ginkgo biloba juice or extract is extensively used for numerous neurodegenerative diseases like Parkinson's and Huntington's, mood disturbance, in several heart diseases, but it is also used for Alzheimer's disease. This herbal plant accommodates various organic properties like flavonoids, terpenes lactones, and ginkgolic acid [6, 16, 19].

The extract of ginkgo biloba must build up or boost or exhibit the ability to enhance the level of neurotransmitter levels, increase the

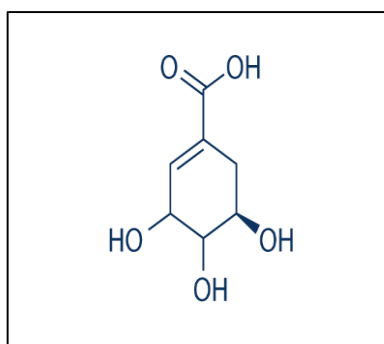
microcirculation, improve the blood flow in the cellular blood components, and provide the neuro-protective sheath to the cells and nerve fibers in the axonal region of the cerebral cortex region [18, 25].

Herbs of Ginkgo biloba are best for Alzheimer's disease (AD) and its correlated signs and symptoms. The herb shows therapeutic benefits in preventing Alzheimer's. The primary bioactive constituents of ginkgo include flavanol glycosides such as quercetin and Kaempferol, terpenoids like ginkgolide and Bilobalide, as well as several other constituents, including ascorbic acid, catechin, 6-hydroxykinurenic acid, protocatechuic acid, and shikimic acid [26].

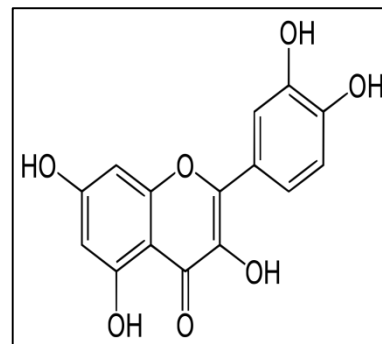
Structural Representation of Active and Phytochemicals Present in Ginkgo biloba



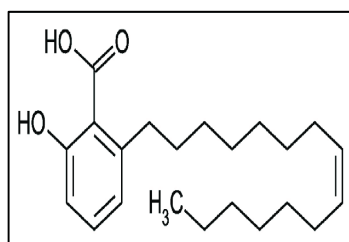
Kaempferol,



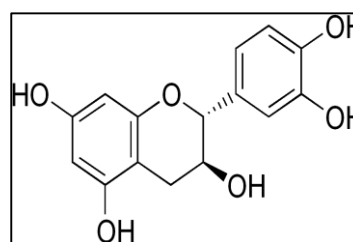
Shikimic acid



Quercetin



Ginkgolic acid



Catechin

The chief active constituent of ginkgo biloba is ginkgolides and its antioxidants that provide neuroprotective and cholinergic activities, which help in the conduction of nerve impulses and provide nerve transmission in Alzheimer's disease. It can increase blood circulation and produce direct action as a Vaso-relaxing agent. Though it should also decrease the BP (blood pressure) and obstruct the platelet accumulation [15].

Ginkgo biloba is beneficial in protecting against the A, β protein to get oxidative damage, where the hydrogen peroxide is lost by itself, also averts the oxidation of lipids, and binds to react oxygen species. The herbal extract increases the capability of nerve transmission for a memory

booster if it is preferred in the early stage of Alzheimer's disease (AD) [13].

Perhaps it is the best herbal plant or extract that can elevate brain health, and that's why it is beneficial for those patients suffering from mild to moderate dementia and Alzheimer's Disease (AD). It also helps to reduce the symptoms of anxiety by raising the level of glucose and utilizing that uptake level of glucose, which can produce ATP (adenosine triphosphate) should also increase and reduce the manifestations of anxiety [8, 19].

Leaf extract of ginkgo biloba is widely preferred in age-related memory disturbance in Asian as well as European countries. This helps to decrease the cognitive decline or reduce the

progression of neuritic plaques, and tau fibrillary tangles by which the person may lose their mental and physical stability, behavior, thinking, and remembering familiar things to their surroundings [13, 27].

Although ginkgo herbs can increase the systemic blood flow which the deformability in RBCs should be enhanced, and reduce the accumulation of RBCs, and antagonize the PAF receptors (Platelet activation factor). Extract of ginkgo increases the proliferation of neural stem cells in the region of sub-ventricular and dentate gyrus in the cerebral cortex, through which the extract speeds up the recovery of memory and other cognitive functions that are declined with Alzheimer's disease (AD) [18, 22].

Moreover, all of these capabilities and significant features must be examined in young adults, where ginkgo is used as herbal medicinal plant, that show the improvement in the learning, thinking power and able to sharpen the memory of remembering working memory and some other executive functions which helps to intact the person with socioeconomic environment [26].

Other Pharmacological Plan of Treatment

Medications that are utilized for dementia and cerebral issues in Alzheimer's Disease

The signs of an insight enhancer are as per the following:

Alzheimer's Disease or various infrastructures, Gentle psychological hindrance and long-winded memory slip

Intellectually hinder kids, learning abandonment, a lack of ability to concentrate consistently, turmoil, or behavioral conditions. Spin-off of head injury or cerebrum medical procedure

Medications utilized for the treatment of Alzheimer's Disease

Cholinergic Activators

- Rivastigmine
- Donepezil
- Galantamine
- Tacrine

Glutamate Antagonists (NMDA)

- Memantine
- Various Drugs
- Piracetam
- Dihydroergotoxine
- Pyritinol
- Citicoline
- Piribedil

Singular medication

Rivastigmine

Carbamate subordinate of physostigmine, which

hinders or chaps both acetylcholine-esterase and butyrylcholine-esterase

Rivastigmine is incredibly lipid soluble and enters the cerebrum or crosses the blood-brain barrier (BBB). Plasma $t_{1/2}$ of Rivastigmine is around 2 hours

In a few clinical assessments, the standard is a 3.8-point improvement in the Alzheimer's Disease Assessment Scale. Rivastigmine is indicated in moderate or ongoing instances of Alzheimer's Disease

Transdermal patches are likewise accessible for the endorsed patient portion to achieve sufficient release of Rivastigmine as 9.5 mg or 13.3 mg every 24 hours

Donepezil

It might have Cerebro-specific and reversible effects of ACE maker, quantifiable improvement in a few psychological aspects too. Also, the exercises of everyday living score in Alzheimer's Disease.

It is advantageous to hoist the degree of Ach in the cortex, like in enduring neuron projection from the basal forebrain to the cerebral cortex or hippocampus.

$T_{1/2}$ of Donepezil is drawn out, it is considered once every day at bedtime. It enjoys a particular upper hand over Rivastigmine and Galantamine.

Galantamine

Normal alkaloids specifically barricade of cerebral acetylcholine-esterase and have some immediate activity at the nicotinic receptor. The unfriendly impact of Galantamine is queasiness, regurgitation, stomach pain, and extreme sleepiness.

Memantine

Memantine is all around consumed endured against Ach treat in Alzheimer's Disease and has some incidental effects, like migraine, discombobulation, and stoppage. Memantine is utilized for other kinds of dementia.

Pyritinol (Pyrithioxine)

System of activity: Pyritinol assists with expanding the choline uptake into neurons and furthermore increases the degree of acetylcholine. It is an effective precursor of dopamine, which is one of the synapse disposition sponsors in the brain.

It is utilized in construction and memory servers. There is some other utilization of the drug in natural mental conditions.

Piribedil

This dopaminergic agonist assists with working on memory, constriction, and tinnitus in old age

due to cerebral circulatory deficiency. It has additionally been accounted for in Parkinsonism

Citicoline

This is secured from choline and cytidine, which

Conclusion

Ginkgo biloba shows potential as a supportive herbal treatment for dementia and Alzheimer's disease due to its neuroprotective, antioxidant, and memory-enhancing properties. It may help reduce amyloid plaques, tau tangles, and

include the union of lecithin. Citicoline needs to treat cerebral capacity by increasing blood flow in the cerebrum or increment cerebral metabolism.

improve brain function. However, it is not a cure, and results vary across studies. When used alongside conventional medications, it may improve patient outcomes. More standardized clinical research is needed to confirm its safety and effectiveness.

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