



Herbal Drugs Used In Treatment Of Alzheimer's Disease

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ABSTRACT

A chronic neurodegenerative condition called memory loss disease causes β -amyloid plaque & neurofibrillary knot to form inside the brain of those who have it. Loss, depression, neuroinflammation, and other neurotransmitter dysregulation are further characteristics. The possibility that natural chemicals are alternative treatment for Alzheimer's disease has been studied. Brain-protective, anti-allergic, anti-amyloidogenic, and antibacterial substances are abundant in the Indian ayurvedic approach's traditional botanicals & formulas. By enhancing Reviving the nervous system and mental recall function, by means of neurogenesis they enhance quality of life. Modern research in conjunction with a wealth of traditional herbal plant knowledge (such as sankhpushpi,) may offer novel functional leads for the development of Alzheimer's medications. This article reviews the numerous clinical and experimental studies that support the use of Ayurveda, an ancient Indian herbal treatment system, to treat alzheimer disease and improve cognitive performance. This article offers a contemporary viewpoint in the plants used for traditional Indian medicine's significance in treating AD and possible mechanisms of action.. This study's primary goal is to present a comprehensive analysis of readily available and efficient herbal medications for the in order to treat AD.

KEYWORDS : Alzheimer's disease illness plaques, Ayurvedic neuroinflammation, and neurofibrillary tangles.

INTRODUCTION :

A majority common illness linked to old age is memory loss, affects about 24 millions people around the world. Patients double every 20 years due to the aging of the global population. These numbers could be significantly decreased during the next fifty years by therapeutic approaches that can delay the Alzheimer's disease's beginning or limit its course. A major global health concern, Alzheimer's disease mostly affects the elderly. According to research, 47 million individuals had dementia in 2015; By twenty-fifth that This fig is expected to reach to increase to 131 million (1). Dietary practices are one lifestyle element that has a significant effect on the illness chances. Several studies have connected bioactive compounds in a range of food sources to the illness's potential prevention (2). Numerous studies indicate that most important lifestyle variables that can decrease risk of AD is eating a healthy diet. Neuroprotection from balanced nutrition raises the possibility that bioactive substances may affect the main harmful mechanisms in Alzheimer's disease (3,4,5) Cognitive decline & formation of elderly plaques (EP) have been the distinguishing clinical-pathological indications of AD. There are numerous potential strategies to reduce growth of dementia & controlling its action are provided by herbal therapy. The manufacturing and distribution of drugs made from medicinal plants has accelerated, and it appears that their scientific and economic importance in the healthcare industry is growing(6) . There are now only FDA-approved treatment options for AD, such as partial NMDA receptor antagonists (memantine), (most recently)(7). Plant compounds having anti-neurodegenerative or neuroprotective qualities are among the many herbs that have been found to contain beneficial neurochemical components(8). These herbs' anti-inflammatory and anti-amyloidogenic qualities increase brain function. *Withania somnifera*, *Ginkgo biloba*, and *Curcuma longa* (turmeric) (ashwagandha), *Shankhpushpi* (*Convolvulus pluricaulis*), also *Tinospora cordifolia* (giloy). Scientists have extensively researched the nootropic qualities of several well-known medicinal herbs (9).

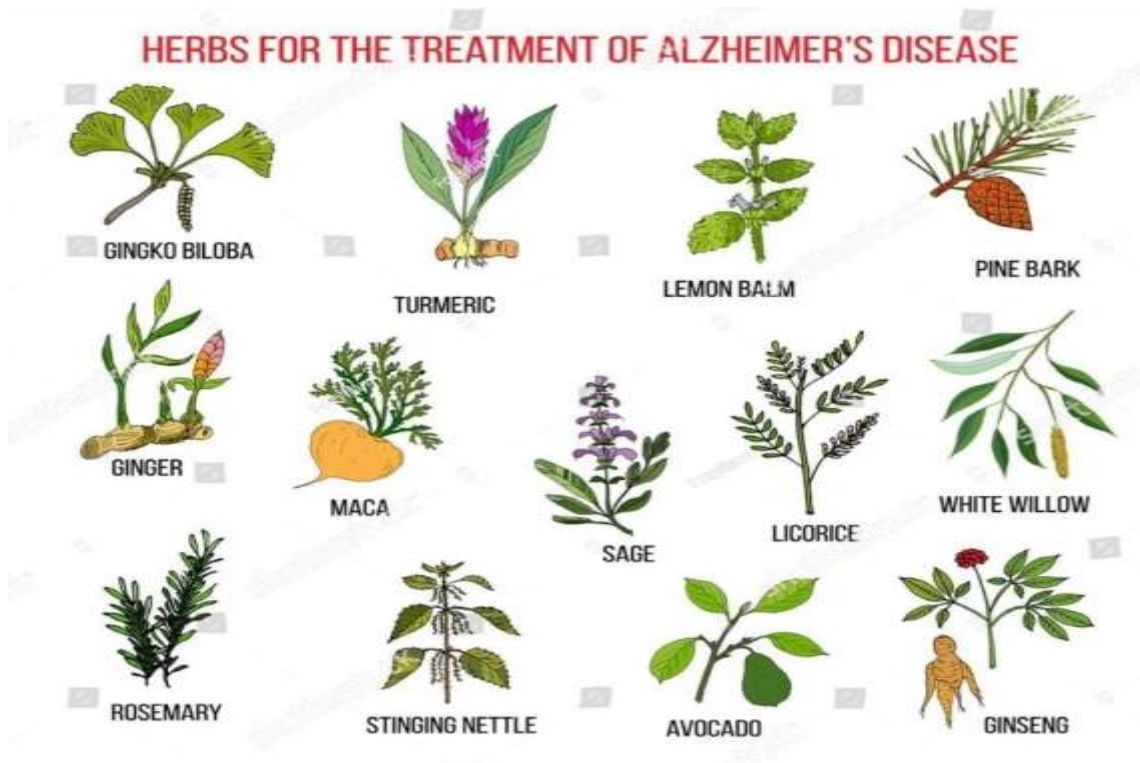


Fig No.1: Using Herbs to Treat Alzheimer's Disease The cause

CAUSES :

Alzheimer's diseases are marked by slow and steady damage to the brain caused by the death of nerve cells over time. Growing older is primary cause, and age is the most significant element. The rate of memory loss about 2 times for every 5 years of age increase starting at age 65. Cardiovascular diseases (CVD) are responsible for AD. They increase stroke-induced dementia, and memory loss (10). Obesity increases the risk of type II diabetes because it impairs glucose tolerance. Cognitive performance may be hampered by neuroinflammation and beta-amyloid (A-beta) accumulation brought on by chronic hyperglycemia (11). Smoking, brain injury due to trauma, depression, myocardial and cerebrovascular illness, the APOE e4 genotype, are possible risk factors for AD. One is 10% to 30% more likely to get AD if they have a first degree relative who has the condition. A person's risk is three times higher than that of the general population if they have two or more siblings who have late-onset AD (12).

TYPES OF ALZHEIMER'S DISEASES

• Alzheimer's disease with an early onset (EOAD):

This kind usually manifests between the ages of 30 and 60, before the age of 65 (13).

Alzheimer's disease with a late onset (LOAD):

the most common type of the illness, which typically manifests after age 65. It accounts for roughly 90–95% of instances and is impacted by aging, exposure to the environment, and the existence of the APOE 4 gene variation (14).

Alzheimer's disease that runs in families is called as familial FAD.

Each child has a fifty percent likelihood of inheriting the genetic (15). The most usual type of memory loss illness, particularly in patients with a late beginning, is sporadic (16).

Phases of Alzheimer's disease:

- **First phase:**

During the "forgetfulness phase," people typically have trouble remembering current affairs & tendency to lose track of when object are located (17).

- **Second recognized phase:**

referred to as the "confusional phase." Memory loss is accompanied by a decrease in generalized intellectual ability and an increasingly short attention span. Disorientation, trouble finding words, and other speech abnormalities may be observed (18).

- **Third phase:**

"dementia phases" are defined by a person's behavior that seems erratic and occasionally strange, as well as a lack of purpose. As persons in this stage have additional declines in their memory capacity, their ability to calculate (dyscalculia), and their language skills are severely impacted and eventually destroyed, it is necessary to continuously monitor their remaining intellectual and self-care capacities. Self-care activities including clothing, grooming, using the restroom, and feeding require ongoing support. Additionally, there is a progressive physical waste that will require assistance with walking. There may be a period of one or two years of nearly vegetative life before death (19).

PATHOPHYSIOLOGY OF ALZHEIMER'S :

There are subsequent dilatation of ventricles and generalized atrophy of the cerebral cortex. There are more deposits in the temporal cortex, hippocampus, and Meyernet's nucleus basalis. These individuals have cognitive difficulties because of the pathological alterations that cause neuronal death and decreased neurotransmitter levels, particularly acetylcholine. Since the fundamental pathological origin of Alzheimer's disease is still unclear. Given what is now known, numerous theories on the pathophysiology of AD are proposed (20).

RISK FACTORS:

Age:

Approximately 5% of adults aged 65 to 74 suffer from Alzheimer's disease. Individuals in excess of 85 are fifty per cent more vulnerable (21).

Genetics:

There is no proof that sporadic Alzheimer's disease is inherited genetically. It is believed that this gene produces the protein that moves cholesterol through blood vessels. ApoE4 is one gene variant that has been shown to raise the risk of developing the condition more than others. However, the ApoE2 variation prevents the sickness (22).

Cases that appear prior to the age of 60 may be caused by chromosome mutation. If a person has one inherited chromosomal mutation, their chance of developing memory loss is 50% (23).

Education :

The prevalent causes, people with less education seem to be more vulnerable. It is thought that as education levels increase, the brain forms more synaptic connections, albeit the exact cause of this association is unknown. This enables patients to create a “synaptic reserve (24).

HERBAL PLANT USEFUL IN THE THERAPEUTIC PREVENTATION OF ALZHEIMER'S ILLNESS

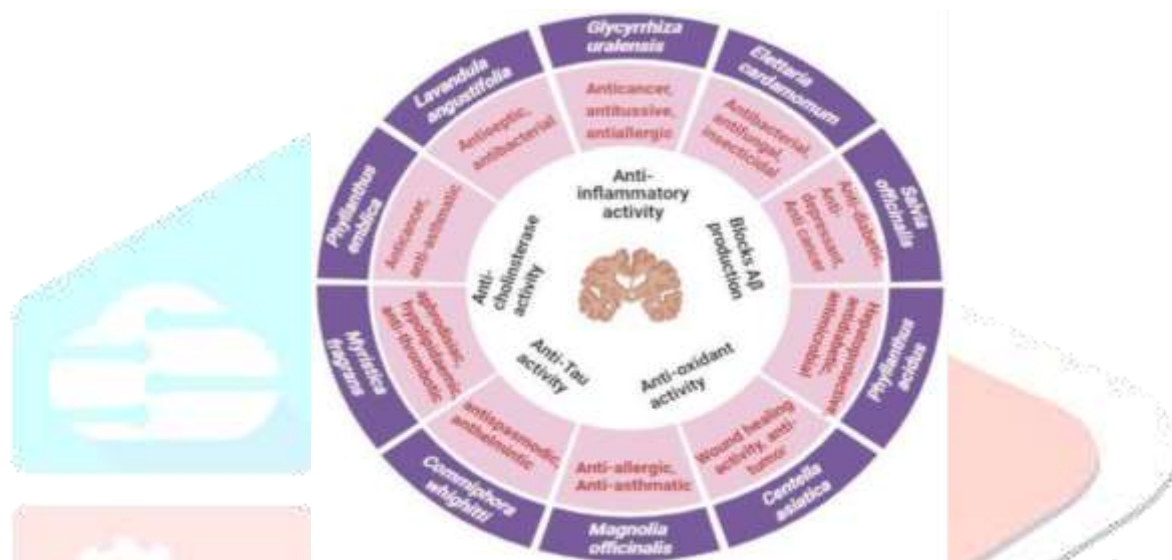


Fig No. 2: Various biological and herbal actions against AD

Turmeric, or *Curcuma longa*, is a spice of life

Turmeric, a perennial rhizome that is a member of the Zingiberaceae family, is especially referred to as “Indian Saffron” in Eu-rope. The two most significant active components of the turmeric plant are turmeric hydrophobic and hydrophilic curcuminoids like curcumin, as illustrated in fig. (25).

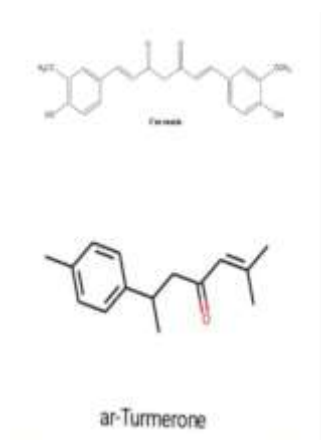


Fig 3 a) ar-Turmerone and (b) curcumin's chemical structures that are phytochemically active.

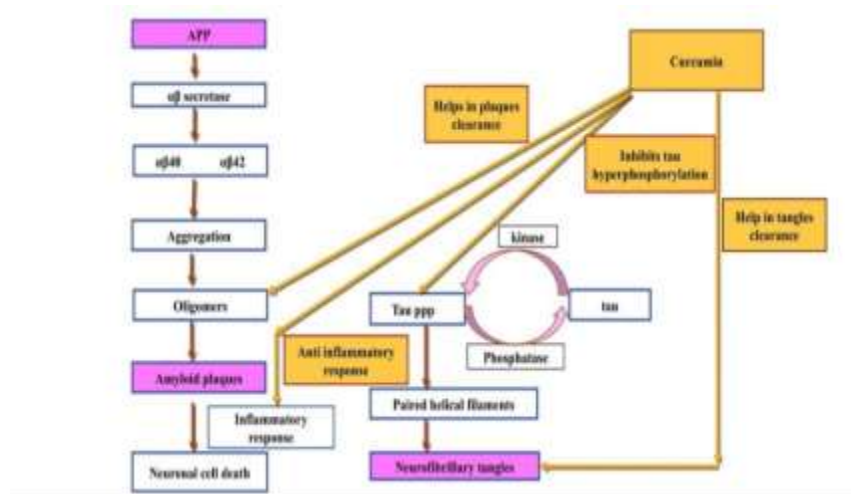


Fig No. 4: The several ways that curcumin offers neuroprotection against Alzheimer's disease are depicted in this flowchart.

Although turmeric is regarded as a popular cooking spice, it has anti-fungal, and anti-amyloid properties, antioxidant, and therapeutic qualities (26,27). Nonetheless, its therapeutic qualities have been used in the Ayurvedic, Siddha, and Unani medical systems since the Vedic era (28,29). Using the Alzheimer transgenic APPSw mouse model (Tg2576), another in-vivo study showed that a dose of 160 ppm curcumin significantly reduced the expression of the pro-inflammatory cytokine IL-1 β and the astrocytic inflammatory marker GFAP (30). A low dose of curcumin reduces the oligomerization tendency for A β production (31). CUR-PBCN showed sustained-release capabilities by releasing 75% of the medication gradually over the course of 24 hours. The different ways that curcumin can function as a multitarget medication are detailed in Fig. 4 (32).

The two histological markers of Alzheimer's disease, hyperphosphorylated tau and A β , are inhibited by the active drugs in terms of their development and neurotoxicity.

Withania somnifera (Ashwagandha)

A common “adaptogen,” aphrodisiac, and nervine tonic in Ayurveda, ashwagandha aids the body in managing stress (33). The root of the nightshade (Solanaceae) plant ashwagandha is the portion most frequently used. According to some theories, its rasayana (rejuvenative) properties include antioxidants, radical scavenging, and systemic immune support (34).



Fig No. 5: Withaferin A's molecular makeup. Withania somnifera produces this lactone, which has painkiller properties.

Within memory loss, neurons die as a result of $A\beta$ plaques. Withanamides found in WS stop this death of neurons (35,36). According to research, the primary periphery impacts of both withanolides and the presence of withanosides on amyloidosis load have a major influence on the form that is soluble of LRP in plasma (sLRP) and liver lipid receptor-associated protein (LRP). In treating familial AD, WS may be useful since AD results in amyloid deposits being inadequately cleared from the brain, which leads the family variants of the illness to manifest earlier (37).

Ginkgo biloba:

The maidenhair tree, often known as ginkgo biloba, has been utilized as a traditional cure for many generations. The well-defined compound EGb 761 is produced by extracting the leaves of Ginkgo biloba. As shown in Fig 6 ginkgo biloba extracts contain strong phytochemical substances that prevent amyloidogenesis and $A\beta$ aggregation (38, 39, 40).

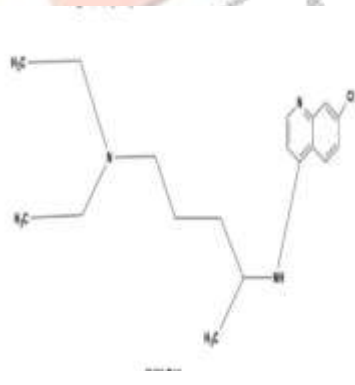


Fig.No. 6: The Egb761 extract of ginkgo biloba's bioactive chemical structure.

In a big research, 41 patients aged 65 and older received one daily dose of an antioxidant mixture of vitamin C, while 622 people served as controls.

Tinospora cordifolia (Giloy)

In Ayurvedic medicine, The Menispermaceae family includes TC, often known as the Giloy. is used as a rejuvenator or adap-togen. Among its many additional qualities are , immunomodulatory, and

antioxidant. Studies on both humans and animals have lately revealed *Tinospora cordifolia*'s purported antistress properties(41, 42,43).A recent study found that *T. cordifolia* leaf extract had painkiller qualities. The tinosporaside that is seen in Fig. 6 (44).

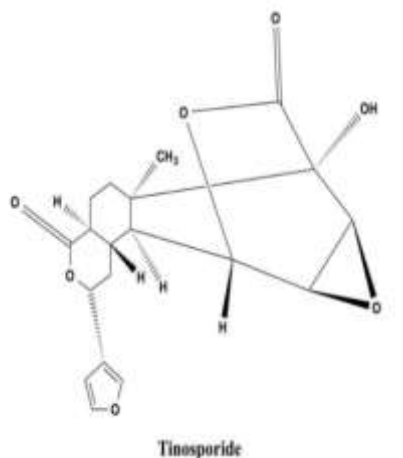


Fig. No. 7: Tinosporide's chemical makeup after being isolated from *T. cordifolia* stems.

Since different antioxidant substances cause the formation of free radicals, research has been done to date to examine their potential for protection against oxidative stress and neuroinflammation(45). Choline supplementation, which strengthens the immune system and increases the manufacturing of the neurotransmitters which is necessary for recall and comprehension,, is partially responsible for its impact on cognitive function. Guduchi roots results in significant improvements in logical memory and verbal learning.(46).This highlights the plant's historical significance in conventional medical techniques as well as its potential as a useful tool for memory enhancement(47)

Convolvulus pluricaulis (Shankpushpi):

According to Indian practitioners, Shankpushpi can be made from *Canscora decomposed* Schult. (CD), *Evolvulus alsinoides* Linn.(EA), *Clitorea The ternatea* Linn(CT),and *Convulus pluricaulis* Choisy met hanolic extracts. As a nerve tonic, Shankpushpi has been used to improve cognitive function and memory (48). Increased mental agility, sleepiness, lower levels of anxiety, depression medicine, lowering stress, anti-cancer, are memory loss casing thinks. Network pharmacology investigations reveal that chemicals from *C. pluricaulis* can interact with a variety of signaling pathways, synapses, and proteins (49).This research points to a possible method by which Shankpushpi improves memory through its actions on the cholinergic system. The Shankpushpi pharmacological relevance is thus increased by the nootropic and memory-enhancing qualities of its metabolites. Further highlighting *Convolvulus pluricaulis*' potential as a memory-enhancing drug, numerous studies have consistently demonstrated that administering extracts from the plant can increase brain power in old rat (50).

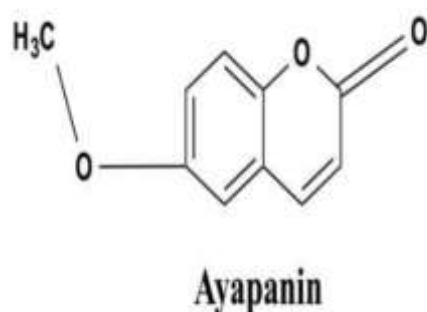


Fig.No. 8: The chemical makeup of Ayapanin that was separated from Shankhpushpi's sources. It enhances spatial memory impairment brought on by scopolamine.

Panax Ginseng

Inflammation, cancer, heart disease, and neurological disorders are just a few of the conditions that can be treated with PG, a popular traditional Chinese medicine that is a member of the Araliaceae family.[51] Furthermore, a recent study indicated that it may be able to treat AD and other central nervous system disorders because of its neuroprotective qualities. Phytochemicals such as saponins, phytosterol, sugars, carbohydrates, and amino acids are found in ginseng (52).



Fig. No. 9: panax ginseng with structure

Centella asiatica

Umbelliferae family, or Apiaceae plant *Centella asiatica* has applied as conventional drug. Numerous biological activity and therapeutic benefits have been found in both the entire plant and its extract, which comprises *C. asiatica* aqueous and ethanolic extracts (53). these contains triterpenoids, including Asiatic acid and Asiaticoside. It possesses potent antioxidant qualities that can reduce Fe^{3+} , are stimulate the antioxidant defenses in mind Additionally, it prevents DNA damage and lowers lipid peroxidation .



Fig.No. 10: Centella asiatica extract yielded Asiaticoside's bioactive chemical structure.

Cinnamon zeylanicum (Cinnamon)

Cinnamaldehyde and a flavonoid there are contain main ingredient like cinnamon. Catechin are epigallocatechin gallate (EGCG), which can penetrate the BBB and attack all three of the AD hallmarks—that is, the The main phenolic compounds that have been extracted from cinnamon thus far include those that inhibit A β accumulation, tau hyperphosphorylation, and plaque destruction .

In PC12 neuronal cells, cinnamon lowers the toxicity, formation, and synthesis of A β plaques. Similar inhibitory effects are seen in AD fly models (57).It also helps to reduce acetylcholinesterase activity and inhibit tau phosphorylation (54).



**Fig. No.11: the chemical structures of the phytochemically active compounds
(a) gallate of epigallocatechin and (b) the cinnamon-derived catechin.**

Conclusion

Because of its increasing prevalence, AD is a worldwide health issue. It results in neurodegeneration and cognitive impairment. Numerous data gathered from in vitro, clinical, and animal research suggests that the herbal plants examined in this study promote neurogenesis in addition to their many other therapeutic advantages. When contemporary technology and techniques are blended with traditional medicines that have a solid body of knowledge, the formulations are improved.It could be used in the creation of medications to treat AD and other neurodegenerative illnesses.

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