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ROLE OF HERBAL DRUGS IN THE PREVENTION AND TREATMENT OF ALZHEIMER'S DISEASE

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ABSTRACT

Alzheimer's Disease (AD) ailment is a neurological issue wherein the death of brain cells causes memory misfortune and psychological decay. Restorative plants are assuming a huge job in the administration of AD and memory shortage. The significant conventional helpful techniques are Ayurvedic, Homeopathy, Unani and Siddha frameworks of medication. Customary arrangement of medication is essentially preventive, defensive, nutritive and therapeutic. Consequently, customary medications are protected and innocuous which treat the patients with less or no reactions. Various logical looks into have been done on therapeutic uses of herbs. Herbs have calming and cancer prevention agent exercises that might be utilized in the treatment of AD. Alzheimer's patients have an acetylcholine inadequacy. Calming herbs may decrease irritation of the mind tissue in the treatment of Alzheimer's disease such as Ginkgo biloba, Salvia officinalis, Rosmarinus officinalis, Melissa officinalis, Glycyrrhiza glabra, Galanthus nivalis, Huperzia serrate, Commiphora whighitii, Panax ginseng, Acoras calamus, Withania somnifera, Tinospora cordifolia, Nardostachys jatamansi etc. Acetylcholine is a synapse that assumes a key job in subjective capacity and thinking. The minds of those with mellow to-direct Alzheimer's sickness, a dynamic kind of dementia, have anomalous low acetylcholine focuses. This implies any aggravate that improves the cholinergic framework in the mind might be helpful in rewarding Alzheimer's infection and comparable cerebrum glitches. The herbs that hinder Acetylcholinesterase (AchE) contain normal COX-2 inhibitors, additionally revealed as restorative herbs, for AD sign.

KEYWORDS: Alzheimer's disease, Dementia, cognitive function, β amyloid degradation, Acetylcholinesterase inhibitors.

1. INTRODUCTION

Alzheimer's disease is defined as the degenerative disease of the brain resulting in progressive memory loss, impaired thinking, deterioration, and changes in personality and mood. It includes deterioration of language, comprehension, memory, and thinking and learning capability. The term Alzheimer was first coined by a German physician, Alois Alzheimer, in 1915. The WHO mentioned Alzheimer's disease as the most common cause of dementia; however, not all dementia is a result of Alzheimer. Alzheimer's is becoming a growing burden and the leading cause of disability among older people, and there is no cure for it. It is set to be the biggest killer among the growing elderly population.[1]

Alzheimer's disease worsens over time. It is a progressive disease, where dementia symptoms gradually worsen over a number of years. In its early stages, memory loss is mild, but with late-stage Alzheimer's disease, individuals lose the ability to carry on a conversation and respond to their environment. Those with Alzheimer's disease live an average of eight years after their symptoms become noticeable to others, but survival can range from 4 to 20 years, depending on age and other health conditions.[26]

Alzheimer's disease typically begins with mild forgetfulness in the elderly. Early on, before memory problems interfere with day-to-day functioning, a diagnosis of mild cognitive impairment (MCI) is often made. As years go by, deficits become more severe and patients are forced to curtail their usual activities. Deficits in other cognitive domains become increasingly apparent, including executive dysfunction, anomia and other language problems, visuospatial dysfunction and ultimately, global cognitive impairment.[2]

Alzheimer's disease is the most common form of dementia in the elderly. It is clinically characterised by impairment of cognitive functions and changes in behaviour and personality. Alzheimer's disease is associated with progressive and irreversible loss of neurons, particularly in the cortex and hippocampus, extracellular senile plaques containing aggregated Aβ and neurofibrillary tangles composed of the hyperphosphorylated form of the microtubular protein tau.[46]

Alzheimer's disease, the most prevalent form of dementia, afflicts approximately 10% of the population over age 65. The cardinal features of Alzheimer's disease are progressive loss of memory and disordered cognitive function. Alterations in behaviour and a decline language function can also be observed in the early stages of Alzheimer's disease. The impairment in cognitive abilities occur gradually, with a loss of short-term memory generally preceding loss of distant memory. In the advanced stages, the individual may not recognize spouse or children, and the levels of arousal and alertness are severely impaired. Other signs of Alzheimer's disease include reduced verbal frequency, naming deficits, and impairment of speech exemplified by failure to arrange words in proper order (dysphasia). Ultimately, with progression in disease, motor function is impaired and the patient may fall into a vegetative state. Death is usually associated with complications of immobility (e.g. pneumonia or pulmonary embolism).[45]

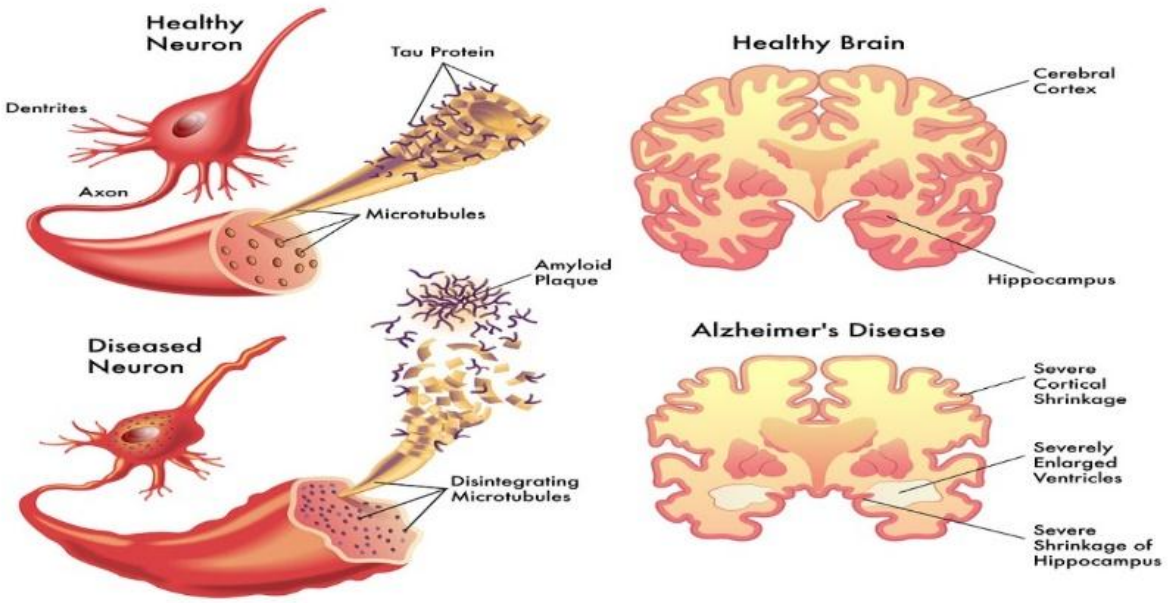


Fig. no. 1: Comparison between normal and AD brain.

2. Pathophysiology

The pathological features of Alzheimer's disease include the presence of β-amyloid plaques, tau enriched neurofibrillary tangles, neuronal loss and alterations in many neurotransmitter systems. Affected brain regions include the entorhinal cortex; hippocampus; amygdala; association cortices of the frontal, temporal and parietal lobes; and subcortical nuclei that project to these regions. Characteristically, the brains of Alzheimer's disease patients contain two distinct types of insoluble material that are hallmarks of the brain lesions associated with

the disorder: extracellular neuritic plaques containing β-amyloid and intracellular tau enriched neurofibrillary tangles. As with Lewy bodies in Parkinson's disease, it is unclear whether the tangles and plaques are casual or by products of degenerative processes. However, considerable evidences suggested that alterations in Aβ processing may be necessary components of cell destruction. One theory of the pathogenesis of Alzheimer's disease proposes that increased production or decreased secretion of the Aβ peptides leads to accumulation of these peptides. A second theory proposes that an abnormal tau protein causes the formation of intracellular neurofibrillary tangles. Tau proteins are important in the maintenance of cytoskeleton function and axonal transport of proteins. Another theory is that Aβ accumulation is a precipitating factor that is followed by the development of the tau enriched tangles in the dying neurons.

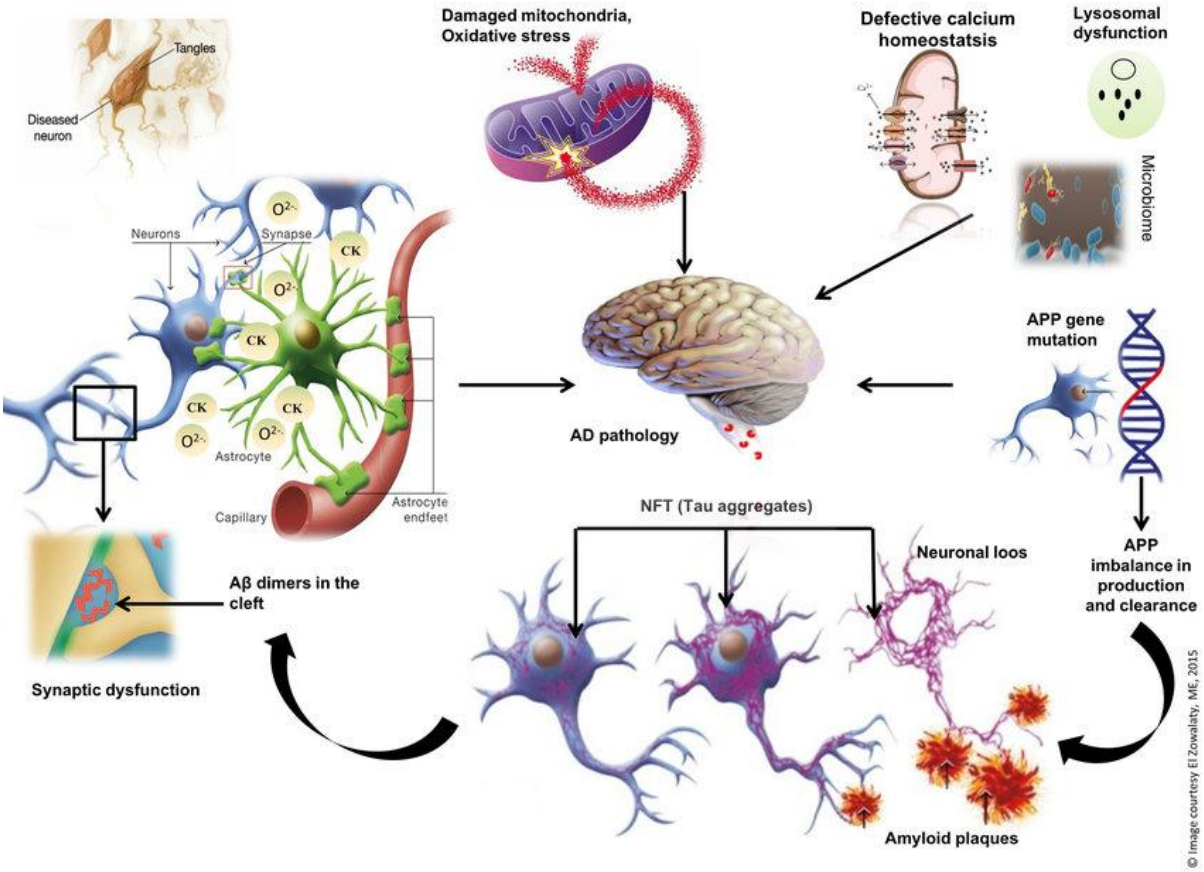


Fig No. 2: Pathophysiology of Alzheimer's disease.

3. Types of alzheimer's disease

1. Mild ad

Symptoms in this stage including getting lost, trouble handling money and paying bills, repeating questions, taking longer than before to complete daily routine tasks, poor judgement, losing things or misplacing them in odd places, mood and personality changes.[49]

2. Moderate ad

In moderate AD damage occurs in areas of the brain that control languages, reasoning, sensory processing and conscious thought. Problems may include increased memory loss and confusion, difficulty in recognizing family and friends, inability to learn new things, difficulty in carrying out tasks that involve multiple steps, problems coping with new situations, and psychiatric symptoms such as hallucinations, delusions and paranoia.[49]

3. Severe ad

People with severe AD cannot communicate and are completely dependent on others for their care. Near the end, the person with AD may be in bed most or all of the time. They may have inability to recognize oneself or family and communicate. Other symptoms include weight loss, seizures, skin infections, difficulty in swallowing, groaning, grunting, increased sleeping, lack of control of bowel and bladder.[49]

The most frequent cause of death of people with AD is aspiration pneumonia. This type of pneumonia develops when a person cannot swallow properly and takes food or liquids in to the lungs instead of air. During the final stages of the disease, most patients require constant supervision and help performing basic self-care tasks such as bathing and feeding.[48]

The hallmark pathological features of AD are extracellular amyloid plaques and intracellular neurofibrillary tangles, compared with neuronal and synaptic loss, vascular amyloidosis, astrocytosis and microgliosis. Most of these changes occur in a stereotypical regional distribution, with medial temporal structures involved in memory affected earliest and most severely.

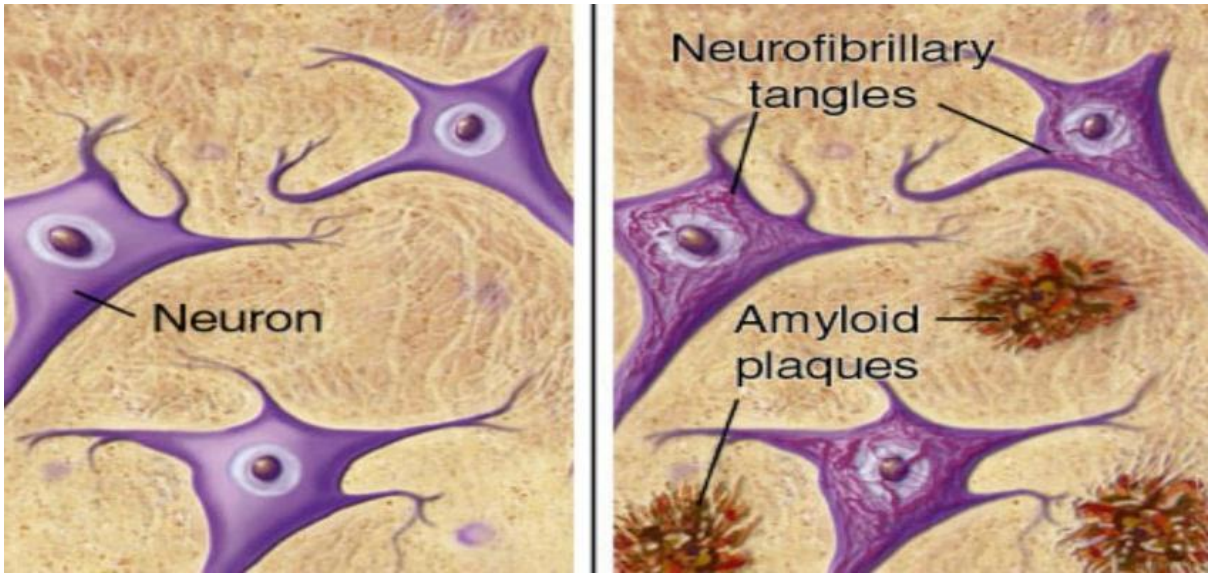


Fig. no. 3: Diagramatic representation of neurofibrillary tangles and Amyloid plaques.

4. Causes

1. **Age related changes in the brain:** One of the great mysteries of Alzheimer's disease is why it largely strikes older adults. Research on how the brain changes normally with age is shedding light on this question. For e.g. scientists are learning how age-related changes in the brain may harm neurons and contribute to Alzheimer's disease.[3]

2. **Genetics:** The most researchers learn about Alzheimer's diseases, the more the realize that genes play an important role in development. Early onset Alzheimer's is a rare form of the disease. It occurs in people age 30 to 60 and represents less than 5% of all people who have Alzheimer's disease. Most cases of early onset Alzheimer are familial Alzheimer's disease, cause by changes in one of three known genes inherited from the parent. Most people with Alzheimer's disease have late onset Alzheimer's, which usually develops after age 60.[3]

3. **Environmental/lifestyle factors:** Research also suggests that a host of factors beyond basic genetics may play a role in the development and course of Alzheimer's disease. There is a great deal of interest, for e.g., in association between cognitive decline and vascular and metabolic conditions such as heart disease, stroke, high BP, diabetes and obesity. Understanding these relationships and testing them in clinical trials will help us understand whether reducing risk factors for these conditions may help you Alzheimer's as well.[3]

4. **Plaques:** These clumps of protein called as β-amyloid may damage and destroy brain cells in several ways, including interfering with cell to cell communication. Although the

ultimate cause of brain cell death in Alzheimer's isn't known, the collection of β-amyloid on the outside of brain cells is a prime suspect.[3]

5. Tangles: Brain cells depend on an internal support and transport system to carry nutrients and other essential materials throughout their long extensions. This system requires the normal structure and functioning of protein called tau. In Alzheimer's, threads of tau protein twist into abnormal tangles inside brain cells, leading to failure of the transport system. This failure is also strongly implicated in the decline and death of brain cells.[3]

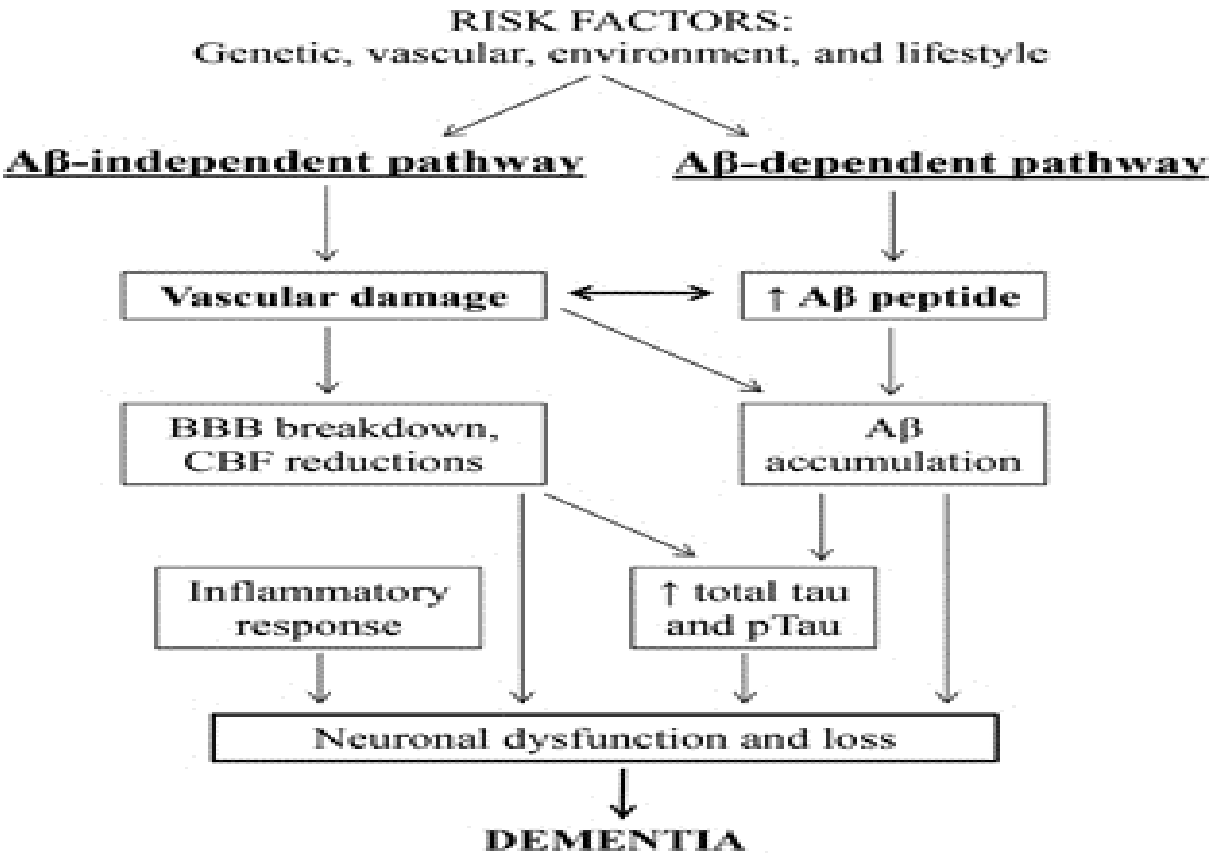


Fig No. 4: Flow chart for risk factors leading to dementia.

5. Symptoms

- **Symptoms commonly experienced during the early stages of Alzheimer's disease include**

- Mild forgetfulness – especially short-term memory loss
- Mood changes, including irritability and anxiety
- Difficulty processing new information and learning new things
- Loss of spontaneity and initiative
- Confusion about time and place

- Communication difficulties
- Decline in ability to perform routine tasks.

- **As Alzheimer's disease progresses the following symptoms may develop:**

- Increasing short-term memory loss and confusion
- Difficulty recognising family and friends
- Shorter attention span and feelings of restlessness
- Difficulty with reading, writing and numbers
- Possibly neglectful of hygiene
- Loss of appetite
- Personality changes (e.g.: aggression, significant mood swings)
- Requires increasing assistance with daily tasks.

- **Towards the later stages of the disease the following symptoms may be experienced:**

- Inability to understand or use speech
- Incontinence of urine / faeces
- Inability to recognise self or family
- Severe disorientation
- Increasing immobility and sleep time.

The changes brought about by Alzheimer's disease can be increasingly difficult for family members and friends as the person's condition deteriorates and they become unable to recognise loved ones.[23,24]

6. Diagnosis

There is a no single test to diagnose Alzheimer's disease. Diagnosis involves a full assessment of medical and psychiatric history to rule out other possible causes. Therefore, a variety of tests are required to obtain a conclusive diagnosis, which may include:

- A neurological and physical examination
- Blood and urine tests
- Brain scans
- Mental status assessment to determine the level of mental deterioration
- Caregiver interview to determine the level of dependency.

- Scans to check brain structure and function may be recommended. The different types of scans used may include CT scanning (computerised tomography), MRI (magnetic resonance imaging) and PET (positron emission tomography).

7. Treatment

As there is no known cure for Alzheimer's disease, treatment focuses on managing symptoms and supporting the person and their family. This may include:

- Treating medical conditions that may contribute to confusion or physical decline eg: lung disease or anaemia
- Encouraging stimulating activities in order to encourage the person to continue their normal activities as much as possible
- Providing memory aids and memory triggers such as calendars and written reminders
- Encouraging social interaction to help prevent feelings of loneliness and depression
- Contacting support groups that may be able to offer family/caregivers assistance
- Encouraging regular routine to reduce confusion
- Not smoking.[27]

- **Allopathy**

The drugs which are used are as follows:

a. **Cholinergic activators:** Tacrine, Rivastigmine, Donepezil, Galantamine.
b. **Glutamate (NMDA) antagonist:** Memantine.
c. **Miscellaneous cerebroactive drugs:** Piracetam, Pyritinol (Pyrithioxine), Dihydroergotoxine (Codergocrine), Piribedil, Gingko biloba.[33,34]

- **Herbal drugs**

The list of herbal drugs that are effective on Alzheimer's disease are, Ginkgo biloba, Salvia officinalis, Rosmarinus officinalis, Melissa officinalis, Glycyrrhiza glabra, Galanthus nivalis, Huperzia serrate, Commiphora whighitii, Panax ginseng, Acoras calamus, Withania somnifera, Tinospora cordifolia, Nardostachys jatamansi, ect.

1. **Curcuma longa**

- **Synonym:** Turmeric, Indian Saffron, Haldi
- **Biological source:** Turmeric consists of dried, as well as, fresh rhizomes of the plant known as Curcuma longa L. belonging to family Zingiberaceae.
- **Chemical constituents:** Turmeric contain about 5% of volatile oil, yellow colouring substance known as curcuminoids. The chief component of curcuminoids is known as curcumin (50-60%).
- **Mechanism of action:** It has been used in various types of treatments for dementia and traumatic brain injury. Curcumin also has a potential role in the prevention and treatment of AD. Curcumin as an antioxidant, anti-inflammatory and lipophilic action improves the cognitive functions in patients with AD. A growing body of evidence indicates that oxidative stress, free radicals, beta amyloid, cerebral deregulation caused by bio-metal toxicity and abnormal inflammatory reactions contribute to the key event in Alzheimer's disease pathology. Due to various effects of curcumin, such as decreased Beta-amyloid plaques, delayed degradation of neurons, metal-chelation, anti-inflammatory, antioxidant and decreased microglia formation, the overall memory in patients with AD has improved.[20]

2. Bacopa monniera

- **Synonym:** Brahmi, Bacopa
- **Biological source:** It consists of leaves and stems of the plant known as Bacopa monniera L. belonging to family Scrophulariaceae.
- **Chemical constituents:** Brahmi is found to contain an alkaloid brahmine, herpestine and the mixture of 3 other alkaloids. It contains saponins, namely bacoside A and B.
- **Mechanical of action:** B monnieri's bioactive components i.e., bacosides protect the brain against oxidative damage and age-related cognitive deterioration with several mechanisms of action. In addition, bacosides prevent Aß aggregation and formation of fibrils as well as protect neurons against Aβ-induced toxicity. Bacosides present in B monnieri are commonly nonpolar glycosides, which enable it to cross the blood-brain barrier (BBB) via simple lipid-mediated passive diffusion.[17]

3. Centella asiatica

- **Synonym:** Gotu kola, centella, mandukparni
- **Biological Source:** It is the herb of Centella asiatica, belonging to family Umbelliferae.
- **Chemical constituents:** It contains saponins in the form of **α**-amyrin derivatives i.e. triterpenoid called asiaticoside and madecassoside about 1%.
- **Mechanism of action:** In Alzheimer's disease, extracts of Centella asiatica decreased beta-amyloid levels and oxidative stress, prevented the shrinkage of neuronal processes and protected against beta-amyloid-associated toxicity and behavioural abnormalities. Centella asiatica treatment significantly improved memory performance, decreased markers of cell death, increased antioxidant defence, and reversed mitochondrial deficits. There are many components to Centella asiatica, of which Asiatic acid has been the most studied in preclinical models. Asiatic acid does cross the blood-brain-barrier and produces antioxidant and neuroprotective effects.[10]

4. Ginkgo biloba

- **Synonym:** Ginkgo
- **Biological source:** It consists of leaves obtained from plant Ginkgo biloba L., belonging to family Ginkgoaceae.
- **Chemical constituents:** G. biloba was chemically characterized in nutritional and bioactive components namely, fatty acids, sugars, organic acids, tocopherols, phenolics and flavonoids. Palmitic, α-linolenic and oleic acids were the main fatty acids found; fructose was the most abundant sugar; quinic acid was the most abundant organic acid and α-tocopherol was, by far, the most abundant vitamer.

- **Mechanism of action:** The mechanism of action of ginkgo is believed to be produced by its functions as a neuroprotective agent, an antioxidant, a free-radical scavenger, a membrane stabilizer, and an inhibitor of platelet-activating factor via the terpene ginkgolide B. Other pharmacologic effects include the following: endothelium relaxation mediated by inhibition of 3', 5'-cyclic GMP (guanosine monophosphate) phosphodiesterase; inhibition of age-related loss of muscarinergic cholinoceptors and α-adrenoceptors; and stimulation of choline uptake in the hippocampus. Ginkgo extract also has been shown to inhibit beta-amyloid deposition.[5]

5. Salvia officinalis

- **Synonym:** Sage
- **Biological source:** It is the herb of Salvia officinalis L., belonging to family Labiatae.
- **Chemical constituents:** A wide range of constituents include alkaloids, carbohydrate, fatty acids, glycosidic derivatives (e.g., cardiac glycosides, flavonoid glycosides, saponins), phenolic compounds (e.g., coumarins, flavonoids, tannins), poly acetylenes, steroids, terpenes/terpenoids (e.g., monoterpenoids, diterpenoids, triterpenoids, sesquiterpenoids), and waxes are found in S. officinalis.
- **Mechanism of action:** It is more commonly referred for Alzheimer's disease treatment. It has been reported to assist the brain in the fight against AD. Sage contains the antioxidants carnosic acid and rosmarinic acid. These compounds are thought to protect the brain from oxidative damage.[37]

6. Rosmarinus officinalis

- **Synonym:** Rosemary, Satapatrika
- **Biological source:** It is the herb of Rosmarinus officinalis belonging to family Labiatae.
- **Chemical constituents:** The major constituents of this essential oil include α-pinene, myrcene, 1,8-cineole, camphor, camphene, α-terpineol, borneol, apigenin, carvacrol, eugenol, oleanolic acid, thymol, and ursolic acid and 45% terpenes.
- **Mechanism of action:** Rosemary (Satapatrika) contains the following natural COX-2 inhibitors: Apigenin, carvacrol, eugenol, oleanolic acid, thymol, and ursolic acid. 'If a synthetic COX-2 inhibitor could prevent Alzheimer's disease, so could a natural COX-2 inhibitor,' according to Duke 2007. In addition, Rosemary contains nearly two dozen antioxidants and another dozen anti-inflammatory compounds. Some of the strongest antioxidant substances in the herb are carnosic acid and ferulic acid, which have even greater reported antioxidant activity than the widely common synthetic antioxidants butylated hydroxytoluene (BHT) and butylated hydroxy anisole (BHA).[6]

7. Matricaria recutita

- **Synonym:** German chamomile
- **Biological source:** It is a plant of Matricaria recutita belonging to family Asteraceae.
- **Chemical constituents:** It contains a large group of therapeutically interesting and active compound classes. Sesquiterpenes, flavonoids, coumarins, and polyacetylenes are considered the most important constituents of the chamomile drug. The coumarins are represented in M. chamomilla by herniarin, umbelliferone, and other minor ones. (Z)- and (E)-2-β-d-glucopyranosyloxy-4-methoxycinnamic acid (GMCA), the glucoside precursor of herniarin, were described as native compounds in chamomile. Eleven bioactive phenolic compounds, such as herniarin and umbelliferone (coumarin), chlorogenic acid and caffeic acid (phenylpropanoids), apigenin, apigenin-7-O-glucoside, luteolin and luteolin-7-O-glucoside (flavones), quercetin and rutin (flavonols), and naringenin (flavanone) are found in chamomile extract.
- **Mechanism of action:** Oxidative stress plays a key role in pathophysiology of many neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease, Huntington's disease, and so on. The present study evaluated the neuroprotective effect of German chamomile against aluminium fluoride (AlF_4^-)-induced oxidative stress in rats. The German chamomile showed dose-dependent neuroprotective activity by significant decrease in lipid peroxidation (LPO) and increase in the superoxide dismutase (SOD), catalase (CAT), glutathione (GSH), and total thiol levels in extract-treated animals as compared with negative control group ($P < 0.001$). The histopathological studies also

revealed the potent neuroprotective action of German chamomile against oxidative brain damage.[11]

8. **Melissa officinalis**

9. **Synonym:** Lemon balm, mint
10. **Biological source:** It is the herb of Melissa officinalis belonging to family Lamiaceae.
11. **Chemical constituents:** The leaf of Melissa officinalis contains flavonoids (quercitrin, rhamnocitrin, luteolin), polyphenolic compounds (rosmarinic acid, caffeic acid, and protocatechuic acid), monoterpenoid aldehyde, monoterpene glycosides, triterpenes (ursolic and oleanolic acids), sesquiterpenes, tannins, and essential oils (citral). Thirty-three components were identified representing 89.30% of the total oil in the composition of the leaf. Six predominant components followed in the essential oils from Sefrou lemon balm were citronellal (14.40%), isogeraniol (6.40%), geraniol acetate (10.20%), nerol acetate (5.10%), caryophyllene (8.10%), and caryophyllene oxide (11.00%), representing 55.20% of the total oil.
12. **Mechanism of action:** Mechanisms of leaf extract action that are potentially relevant to cognitive function of rats after per os administration. Melissa officinalis is traditionally used in treating neurological disorders through its anti-AchE and antiagitation properties. Moreover, Melissa officinalis extract has nicotinic receptor activity and that it can displace nicotine from nicotinic receptors in homogenates of human cerebral cortex tissue and they suggested that these mechanisms can explain activity of MO extract in amnesia model.[38]

13. GLYCYRRHIZA GLABRA

- **Synonym:** Liquorice
- **Biological source:** It is obtained from dried, unpeeled roots and stolons of Glycyrrhiza glabra belonging to the family Leguminosae.
- **Chemical constituents:** Seven constituents, with antioxidant capacity were isolated from Glycyrrhiza glabra. The isolated compounds were identified as the isoflavones Hispaglabridin A, Hispaglabridin B, Glabridin, and 4′-O-Methylglabridin, the two chalcones, isoprenylchalcone derivative and Isoliquiritigenin, and the isoflavone, Formononetin.
- **Mechanism of action:** The neuroprotective effect from aqueous root extract of Glycyrrhiza glabra may be attributed to its antioxidant property by the virtue of which susceptible brain cells get exposed to less oxidative stress resulting in reduced brain damage and improved neuronal function. It exerts a protective effect against apoptotic neuronal cell death induced by Aβ fragments. Extract from the liquorice root is reported to treat or even prevent brain cell death in diseases like Alzheimer's and its associated symptoms.[41]

14. Galanthus nivalis

- **Synonym:** Snowdrop
- **Biological source:** It is the herbaceous plant of Galanthus nivalis L., belonging to family Amaryllidaceae.
- **Chemical constituents:** Snowdrops contain an active substance called galantamine (or galanthamine) which can be helpful in the treatment of Alzheimer's disease.
- **Mechanism of action:** Galantamine improves the function of nerve cells in the brain. It works by preventing the breakdown of a chemical called acetylcholine. People with dementia usually have lower levels of this chemical, which is important for the processes of memory, thinking, and reasoning.[12]

15. Huperzia serrata

- **Synonym:** Toothed clubmoss
- **Biological source:** It is plant of Huperzia serrata belonging to the family Lycopodiaceae.
- **Chemical consituents:** Huperzia serrata contains chemical constituents like huperzine A and lycodine.
- **Mechanism of action:** Huperzine A, reversibly and selectively inhibits AChE, crosses the blood–brain barrier (BBB) and prevents acetylcholine (ACh) breakdown. Huperzine A may ameliorate the memory deficits in rodents and monkeys via AChE inhibition.[15]

16. Commiphora whighitti

- **Synonym:** Guggul or Mukul
- **Biological source:** Oleo gum resin obtained from plant of Commiphora whighitii belonging to family Burseraceae.
- **Chemical constituents:** It contains guggulipid and guggulosterone.
- **Mechanism of action:** The guggulipid has been seen to be a potential cognitive enhancer for improvement of memory in scopolamine-induced memory deficits. Commiphora whighitti acts on impairment in learning and memory and decreased choline acetyl transferase levels in hippocampus. However, Commiphora whighitti shows maximum effects on memory functions and the potential for dementia disorder.[42]

17. Panax ginseng

- **Synonym:** Ninjin, Panax, Pannag, Chinese ginseng, ginseng root
- **Biological source:** It is dried roots of various panax species like Panax ginseng and Panax japonica belonging to family Araliaceae.
- **Chemical constituents:** Several saponin glycosides belonging to triterpenoid group, ginsenoside, chikusetsusaponin, panaxoside. More than 13 ginsenosides have been identified. Ginsenosides consists of aglycone dammarol whereas panaxosides have oleanolic acid as aglycone. It also contains large amount of starch, gum, some resin and a very small amount of volatile oil.
- **Mechanism of action:** Panax Ginseng contains saponins protopanaxadiol, protopantriol, and oleanolic acid saponins that are reported to have memory-enhancing action for the learning impairment induced by scopolamine. Ginseng is able to enhance the

psychomotor and cognitive performance and can benefit AD by improving the brain cholinergic function, reducing the level of AD, and repairing the damaged neuronal networks.[40]

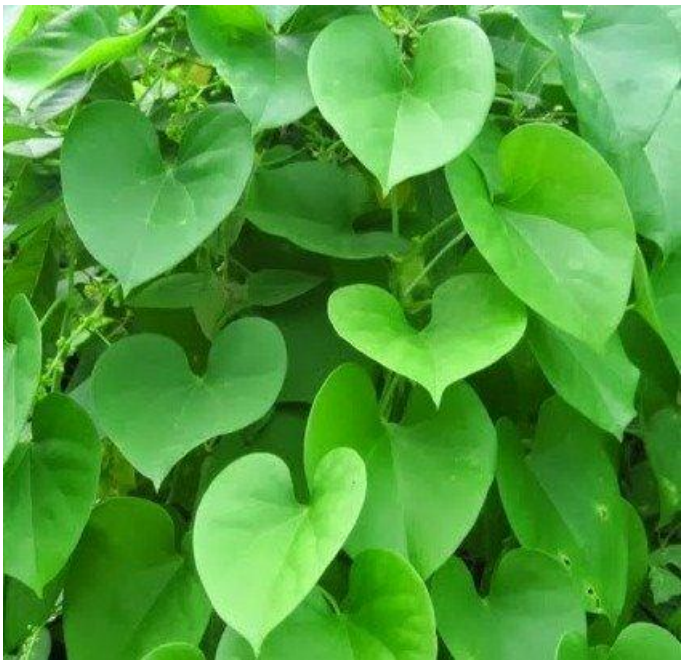
18. Acorus calamus

- **Synonym:** Sweet flag
- **Biological source:** Dried rhizomes of plant of Acoras calamus belonging to family Araceae.
- **Chemical constituents:** The plant has been extensively investigated and a number of chemical constituents from the rhizomes, leave and roots of the plant have previously reported which includes β- asarone, α- asarone, elemicine, cisisoelemicine, cis and trans isoeugenol and their methyl ethers, camphene, P- cymene, α- selinene, bgurjunene, β- cadinene, camphor, terpinen- 4- ol, aterpineol and a calacorene, acorone, acrenone, acoragermacrone, 2- deca -4,7 dienol, shyobunones, linalool and preisocalamendiol are also present.
- **Mechanism of action:** Acorus Calamus possesses a beneficial memory enhancing property for memory impairment, learning performance, and behaviour modification. Acorus Calamus inhibits the acetylcholinesterase (AChE). Acorus Calamus contains a majority of α-and β-asarone. In the Ayurveda medicine system, Acorus Calamus has been used for the treatment of memory loss and its related symptoms.[13]

19. Withania somnifera

- **Synonym:** Ashwagandha
- **Biological source:** It is dried roots of Withania somnifera belonging to family Solanaceae.
- **Chemical constituents:** Chemical constituents of Withania somnifera (WS) include alkaloids (isopelletierine, anaferine, cuseohygrine, anahygrine, etc.), steroidal lactones (withanolides, withaferins) and saponins. Sitoindosides and acylsterylglucosides in Ashwagandha are anti-stress agents. Active principles of Ashwagandha, for instance the sitoindosides and Withaferin-A, have been shown to have significant anti-stress activity against acute models of experimental stress.
- **Mechanism of action:** It is used for various kinds of disease processes and especially as a nervine tonic. It has a Cognition Promoting Effect and was useful in children with memory deficit and in old age people loss of memory. It was also found useful in neurodegenerative diseases such as Parkinson's, Huntington's and Alzheimer's diseases. It has GABA mimetic effect and was shown to promote formation of dendrites.[19]

20. TINOSPORA CORDIFOLIA



- **Synonym:** Heart-leaved moonseed, Giloe
- **Biological source:** It consists of aerial parts of Tinospora cordifolia belonging to family Menispermiaceae.
- **Chemical constituents**: The major phytoconstituent in Tinospora cordifolia includes tinosporine, tinosporide, tinosporaside, cordifolide, cordifol, heptacosanol, tinosporidine.
- **Mechanism of action:** Tinospora cordifolia possesses a memory improving effect in animals with memory deficits. The mechanism by which Tinospora cordifolia improves memory is the synthesis of acetylcholine and immunostimulation. Administration of Tinospora cordifolia increases the cognitive function in patients with AD.[43]

21. Magnolia officinalis

- **Synonym:** Magnolia
- **Biological source:** Bark and stems obtained from plant Magnolia officinalis belonging to family Magnoliaceae.
- **Chemical constituents:** Chemical investigations of the cortex of M. officinalis led to the isolation of several major phenolic compounds, notably the neolignan derivatives magnolol (5, 5'-diallyl-2,2'-dihydroxybiphenyl) and honokiol (5,3'-diallyl-2,4'-dihydroxybiphenyl).
- **Mechanism of action:** Magnolia officinalis, have the ability to enhance the choline acetyltransferase effects and inhibit the acetylcholine cleavage and have also been shown to release acetylcholine from the hippocampus. Both compounds exhibited in vivo antioxidant effects. Magnolol showed in vitro neuroprotective activity. The compound also exhibited anti-inflammatory effect in vivo and in vitro. Honokiol exhibits anti-inflammatory activity by inhibiting reactive oxygen species synthesis. As an anti-inflammatory and antioxidant agent, Magnolia officinalis plays an important role in the management of AD and memory deficits.

22. Collinsonia canadensis

- **Synonym:** Horsebalm
- **Biological source:** It is herb of Collinsonia canadensis belonging to family Lamiaceae.
- **Chemical constituents:** The chief chemical constituents of horsebalm are carvacol and thymol which are used for AD.

- **Mechanism of action:** Horsebalm (Monarda) has been reported to prevent the breakdown of acetylcholine. Normally our body's protective blood-brain barrier helps prevent harmful substances in the blood from reaching the tissues of the brain. However, it can also prevent helpful medicines from reaching the brain. The horsebalm compounds seem to cross that great divide. Horsebalm is even used as a herbal shampoo by adding a few drops to your normal herbal shampoo.[1]

23. Bertholettia excelsa

- **Synonym:** Brazil nut
- **Biological source:** It contains seeds which are obtained from plant Bertholettia exelsa belonging to family Lecythidaceae.
- **Chemical constituents:** Bertholettia exelsa contain lecithin in high concentration.
- **Mechanism of action:** It has a high concentration of lecithin, which contains choline. Choline is a building block for acetylcholine. These building blocks enhance the concentration of acetylcholine in AD patients.[21]

24. Urtica dioica

- **Synonym:** Common nettle, stinging nettle
- **Biological source:** Roots, stems and leaves of herb obtained from Urtica dioica belonging to family Urticaceae.
- **Chemical constituents:** The major chemical constituents of Urtica dioica are flavonoids, tannins, volatile compounds and fatty acids, polysaccharides, isolectins, sterols, terpenes, protein, Vitamins and minerals**.**
- **Mechanism of action:** It contains biologically active compounds that reduce inflammation. It contains the mineral boron that is reported to enhance the levels of oestrogen, which is a hormone in the body, which can be beneficial in short-term memory. Stinging nettle has also been shown to elevate the mood in some Alzheimer's patients.[14]

25. Lepidium meyenii

- **Synonym:** Peruvian ginseng
- **Biological source:** It is an edible herbaceous biennial plant of Lepidium meyenii Walp., belonging to family Brassicaceae.
- **Chemical constituents:** Eighteen compounds were isolated from L. meyenii, including 7 alkaloids and 4 fatty acids and 7 other compounds. They were characterized as (3-hydroxybenzyl) carbamic acid, phenylmethanamine, N-benzyl formamide, N-benzyl acetamide, pyridin-4-ylmethanamine, n-(4-methoxybenzyl) aniline, uracil, succinic acid, decanedioic acid, n-hexa- decanoic acid methyl ester, heptanoic acid, solerole, pyromucic

acid methyl ester, 5-hydroxymethyl-2-furancar- boxadehyde, 5-(methoxymethyl)-1H-pyrrole-2-carbaldehyde, 1,7-dihydroxy-2,3, 4-trimethoxyxanthone, 1,7-di- hydroxy-3,4-dimethoxy-xanthone, (+)-pinoresinol.

- **Mechanism of action:** Lepidium meyenii exhibited memory enhancing activity in patients with AD. It enhances memory by increasing level of acetylcholine. It improves experimental memory impairment induced by ovariectomy, due in part to its acetylcholinesterase inhibitory and antioxidant effects. Results showed that Lepidium meyenii can enhance memory retention and learning abilities in AD patient and this activity might be related, at least in part, to its ability to decrease lipid peroxidation and acetylcholinesterase in AD patient.[47]

26. Nardostachys jatamansi

- **Synonym:** Spikenard
- **Biological source:** It is a flowering plant of Nardostachys jatamansi belonging to family Caprifoliaceae.
- **Chemical constituents:** Nardostachys jatamansi consist of following constituents but the main active constituents in the plant material are sesquiterpenes and coumarins. Jatamansone or valeranone is the principal sesquiterpene.
- **Mechanism of action:** It contains sesquiterpene valeranone that has been used for treatment of stress. In a study, Nardostachys jatamansi exhibited memory retention and learning enhancing abilities in aged and young mice and reversed scopolamine and diazepam induced amnesia. Nardostachys jatamansi also reversed aging induced amnesia

reported efficacy of Nardostachys jatamansi in the prevention of stress induced memory deficit.[50]

27. Celastrus paniculatus

- **Synonym:** Intellect tree
- **Biological source:** Obtained from dried ripe seeds of Celastrus paniculatus belonging to family Celastraceae.
- **Chemical constituents:** Triterpenoids like Pristimerin are present in Celastrus paniculatus plant11. Steroid alcohols such as β-amyrin and β-sitosterol are present in Celastrus paniculatus.
- **Mechanism of action:** It prevented neuronal cell damage against hydrogen peroxide toxicity due to its antioxidant activity. Administration of Celastrus paniculatus prevents neuronal cell damage caused by glutamine induced toxicity. Celastrus paniculatus increases cholinergic activity that contributes its ability to improving memory performance. Aqueous extract of Celastrus paniculatus has antioxidant and cognition enhancing properties. Celastrus paniculatus extracts protected neuronal cells against hydrogen peroxide induced toxicity in part by virtue of their antioxidant and free radical scavenging activities. C. paniculatus seed extract and its organic fractions possesses antioxidant and moderate anticholinesterase activity.[39]

28. Convolvulus pluricaulis

- **Synonym:** Shankhpushpi
- **Biological source:** Shankhpushpi consists of the whole aerial parts of Convolvulus pluricaulis belonging to family Convolvulus.
- **Chemical constituents:** It contains alkaloids, shankhpushpine, volatile oil, kaempferol, beta sitosterol, convolvul ursolic acid, cycloconvolvul ursolic acid.
- **Mechanism of action:** Convolvulus pluricaulis increases memory functions and learning abilities. Convolvulus pluricaulis has been reported to calm the nerves by regulating the stress hormones synthesis (cortisol and adrenaline) in the body. The ethanolic extract of Convolvulus pluricaulis and its aqueous and ethyl acetate fractions significantly improved memory retention and learning abilities in rats.[35]

8. CONCLUSION

Herbs play a promising role in the early treatment of Alzheimer's and other conditions involving poor memory and dementia. The use of herbal medicines in the treatment of AD should be compared with the pharmacological treatment currently in use. One of the chief benefits is that they have a low toxicity compared to pharmaceutical agents. Herbal medicines are fundamentally preventive, protective, nutritive and curative. They are more effective than allopathic medicines and also, they have less side effects than them. In addition, the herbal drug's potential value for prevention and treatment of AD only results from symptomatic changes and short treatment periods (< 6 months). In this way herbal drugs prove more efficient than the ones in current use.

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