



Review Article

HERBAL REMEDIES ON ALZHEIMER DISEASE: A REVIEW

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ABSTRACT

Alzheimer's disease (AD) is related to cognitive impairment, dementia observed generally in aged population. It gradually worsens memory power of the patient for AD. There are many categories of Anti-Alzheimer's drugs available for management of AD in the market for example rivastigmine, Galantamine, donepezil, due to lack of patient compliance successful outcomes were not observed. Apart from this including Nutraceuticals for example vit B complex, vit c, vit d, zinc, in diet daily routine, Aromatherapy, modifications in the regular schedule, practicing yoga regularly relaxes mind and body from tensions, blood circulation, detoxification of organs due to rhythmic breathings and reduce frequency of incidence of headache are proven to show best results by relieving stress according to patient information. At present herbal medicine for example brahmi, green tea, cognium, medhabati, has turn out to be best choice for the management of AD because of its availability, very economic, good patient compliance, ease of formulation and lower deleterious side effects. Novel techniques ayurveda can be used for the development of herbal medicine. This review totally discusses about the herbal medicine used in occurrence of AD, its Pathophysiology, different stages in the disorder, various selective therapeutic targets for AD, available Anti AD herbal drugs such as Curcumin, Withaniasomnifera, Bhrami, Ginkgo biloba, guggul, ginseng, herbs with essential oils, volatile oils, source and cultivation of the herbs, mechanism of action of the Phytochemicals in the herb responsible for treating AD.

Key words: Alzheimer's disease [AD], Nutraceuticals, Herbal medicine, novel techniques, ayurveda, gongkobiloba, bhrami

INTRODUCTION

Alzheimer's is a neurodegenerative disorder caused due to cognitive impairment. the first patient found in 1906. Alzheimer's disease International (ADI) is the international federation of Alzheimer associations

around the world, in official relations with the World Health Organization believes that the key to winning the fight against alzhimers herbal medicine is used. World Alzheimer's Month, celebrated each September, with World Alzheimer's Day on September 21, is an opportunity to raise global awareness about Alzheimer's and its impact on families and the important work of our members throughout the world. Alzheimer's & Related Disorders Society of India in Kerala is the Indian association that compiles all the issues related to AD. Numerous strategies, drugs, herbal medicines and various drug delivery systems exist for AD but they don't assure permanent cure for it,usage of herbal medicine along with a suitable drug delivery system as a remedy for AD is the best choice when compared to All.

Impulse transmission, with World Alzheimer's Day on September 21, is an opportunity to raise global awareness about Alzheimer and its impact on families and the important work of our members throughout the world. Alzheimer's & Related Disorders Society of India in Kerala is the Indian association that compiles all the issues related to AD. Numerous strategies, drugs, herbal medicines and various drug delivery systems exist for AD but they don't assure permanent cure for it, usage of herbal medicine along with a suitable drug delivery system as a remedy for AD is the best choice when compared to Allopathic medicine as they overcome the unwanted side effect and improves patients compliance.^[1,2,3]

Alzheimer's is a neurodegenerative disease that is irreversible and branded by cognitive and memory decline. It is currently estimated that AD which is the commonest form of Alzheimer's accounts for three-quarters of all cases.AD is also the 4th leading cause of death in elderly patients that are 64 years of age and older. The key pathological marks of AD are considered to be senile plaques and neurofibrillary tangles.

Increasing evidence also suggests that A β peptides play a vital role in AD pathogenesis. There is currently no therapies for modifying AD. Simultaneous cholinergic and glutamatergic significance in the genesis of AD has been demonstrated.

Individuals with AD have lower concentrations and functions of Ach [Acetylcholine], which important for cognitive performance. The cholinergic theory of AD is supported by these abnormalities, such as depletion of cholinergic neurons and reduced Achactivity. Misfolded protein builds up in the aged brain, causing oxidative stress-induced damage, as well as metabolic loss and synapse malfunction. Large concentrations of DNA oxidation products such 8-hydroxydeoxyguanosine in mitochondria and nuclei indicate oxidative injury in AD. While senile plaques consist of amyloid fibrils with A β peptides, NFTs contain bundles of the paired helical filament of microtubule-associated protein tau. A β is a 40 or 42 amino acid peptide derivative from amyloid precursor protein (APP), a transmembrane protein, by sequential cleavages of β -secretase (BACE 1) and γ -secretase (A β 42 being more hydrophobic, self-aggregating, and containing more amino acids than the 40). Several mechanisms have been described to explain AD pathology and treatment is usually based on the diverse proposed pathological mechanisms. Some of the proposed mechanisms of AD include the Tau hypothesis, amyloid cascade hypothesis, excitotoxicity, cholinergic hypothesis, and others. The amyloid cascade hypothesis dates back to 1992 when it was postulated that the A β peptide accumulation and deposition in the brain parenchyma plays an important role in understanding AD pathogenesis. Unlike in normal people where A β is cleaved from APP, released into the cell exterior, and degraded; in aging patients and pathological conditions, A β peptides may accumulate due to the decreased metabolic activity to degrade A β . Hence an increased level of A β 42 induces the formation of amyloid fibril and its accumulation leads to the development of senile plaques and the induction of tau which ultimately causes neurotoxicity, neurodegeneration, and neuronal cell death. The mutation of APP, Presenilin1, and 2 genes (PSEN1& PSEN2), responsible for the alteration of proteolytic cleavage of APP increasing the ratio of longer self-aggregating A β peptides, which was discovered in families with early-onset AD, as well as a considerable portion of Down's syndrome patients

showing an early manifestation of AD, further supports the amyloid cascade hypothesis. In spite of the numerous pieces of evidence supporting the amyloid cascade hypothesis, it has been constantly shown that A β accumulation and subsequent deposition do not relate to neuronal loss or cognitive decline. In addition, many patients display amyloid plaque burden without symptoms of memory impairment indicating that the theory may not be entirely as proposed. Tau is a protein associated with the microtubule that enhances the polymerization and stabilization of microtubules in the cell cytoskeleton. In the tau hypothesis, it is poised that hyperphosphorylation of tau causes it to dislodge from microtubules and aggregate into paired helical filaments (PHFs) and NFTs and that tau tangle pathology occurs before A β plaque formation. Hence the main cause of neurodegeneration in AD is tau phosphorylation and aggregation. The cholinergic hypothesis was postulated due to the recognition of the role of acetylcholine in memory and learning as cholinergic deficits were demonstrated in AD patients' brains. Some other hypothesis describes the role of vascular burden while others propose a role for Apo epsilon 4 (APo ϵ 4) allele of the apolipoprotein (apo) gene coding for a protein involved in the metabolism of cholesterol and lipid transport. Most of the AD drug research has been directed towards identifying molecules that target one or more of the existing postulated mechanisms of AD pathogenesis.^[4,5,6,7]

HISTORY OF ALZHEIMERS DISEASE

In 1906 Dr. Alois Alzheimer upon his scrutiny identified brain of a woman who lost her life due to some unusual symptoms such as loss of memory, unpredictable behavior, cognitive impairment he then conclude the death was due the presence of neuritic plaques and neuro fibrillary tangles and named the disease as ALZHEIMERS DISEASE. It has been developed into a predominant neurodegenerative disease in the elderly population. A component of healthy nerve cells, Amyloid precursor protein derivative β Amyloid protein deteriorates and lead to the formation of Neuritic plaques, they are also called as senile, dendritic or amyloid plaques. Nerve cells along with various other components it consists of twisted protein fibers positioned within nerve cells. These fibers consist of a protein, called tau, which normally occurs in neurons. When incorrectly processed, tau molecules clump together to form Neuro fibrillary tangles. This disease may be in some wainter related to brain infection, plaque formation being one or the other excessive in older individuals or abnormal in some other way in persons who ultimately develop Alzheimer disease.^[8,9,]

Warning signs for AD are:

- Memory loss that affects day-to-day abilities. Difficulty performing familiar tasks
- Problems with language
- Disorientation in time and space.
- Problems with abstract thinking.
- Misplacing things
- Changes in mood and behaviour.
- Loss of initiative In general, population think these signs are part of usual aging, it's not true. Upon observation of these symptoms or changes in capabilities or behavior, they must consult a doctor. Reasons for These changes include depression, drug interactions or an infection. On diagnosis of Alzheimer's disease in early stage it is possible to get proper treatment.^[11,12]

VARIOUS THERAPEUTIC TARGETS TO TREAT AD: ^[11,12,13]

▯ Targeting Amyloid beta protein (Anti-Amyloid approach)

▯ Targeting Amyloid transport.

▯ Modulation of Secretase enzyme

▯ Targeting amyloid clearance

▯ Amyloid based vaccination therapy

▯ Targeting Tau protein

▯Neurgenesis

Anti inflammatory

- Increases Anti oxidant capacity of body
- Lowers the risk of heart diseases
- Prevents cancer
- Preventing and treating AD
- Delays aging and fights age related chronic diseases

Withania somnifera Solanaceae.

Ashwagandha

- To treat cancer
- AsImmunostimulants
- Increases libido and sexual function
- As free radical and anti oxidant
- For anxiety and depression.^[11,12]

STAGES OF ALZHIEMERS DISEASE

(1) Mild AD

- Person may function independently in the early stage.
- They can do their social activities.
- Person may feel as if they are suffering from memory lapses, such as disremembering commonly used words or the location of ordinary objects.
- Common difficulties faced by them are Problems coming up with the right word or name, be unable to remember material that one has just read, Misplacing a valuable object.^[13,14,15]

(2) Moderate AD

- Greater care is needed to the patient as the disease progresses.
- It is classically the longest stage and can last for many years.
- Individuals may have greater difficulty performing tasks
- Confusing words, getting frustrated or angry, or acting in unexpected ways.

(3)Severe AD

- Individuals lose the ability to respond to their environment, to carry on a conversation and, eventually, to control movement, communicating pain becomes difficult, memory and cognitive skills continue to get worse, substantial personality changes may take place and performing.[11,12,13,]

Symptoms include

- Forgetfulness of events or about one's own personal history
- Feeling moody or withdrawn, especially in socially or mentally challenging situations
- Confusion about where they are or what day it is.[11,12,13]

Medicinal plants used in the treatment of AD:

Present day therapies are insufficient and have enormous adverse effects. So there is an urgent need for possible alternative treatments for AD with minimal or no side effects. Various medicinal plants are suggested to enhance the memory and treat AD. Herbal therapy for AD has more advantages when compared to currently existing drug therapies with unavoidable side effects. It can also improve the patients' quality of life as they can be consumed as Nutraceuticals and even any slight increase in dose may not be a problem when consumed. In order to deliver these herbal formulations a proper route of administration must be selected so that they reach the site and show the.[31,32]

AD over the years has remained the most form of dementia, creating a global concern especially in elderly people. It is a neurodegenerative disorder that truncates a patient's social and occupational life. A major challenge is an increase in the number of people living with an undeserving health condition. Despite the high medical attention to Alzheimer's patients, the efforts to reverse the neurological disorder seem abortive. Although these drugs also exact their side effect complicating the patient's health conditions. The treatment of Alzheimer's disease is through regulation of neurotransmitters enzymes such as cholinesterase inhibitors or NMDA receptors through synthetic drugs which has not given perfect therapeutic solution.[34,35]

Herbal Medicine is currently in the front line as an alternative measure to ameliorating Alzheimer's neurological disorder. Some herbs have the ability to improve brain functions as a result of the naturally dawned phytochemicals. These plants with antioxidants (flavonoids, beta-carotene, vitamin C, and vitamin E) can help reduce the pathophysiology of neurodegenerative symptoms through countering of oxidative stress that is scientifically linked to one of the accelerators of Alzheimer disorder. Different herbs used are shown in. Since ancient times, traditional medicine has been practiced all over the world. These natural therapies including herbs and medicinal plants have been described to be useful for the treatment of AD, dementia, amnesia, and other diseases. Herbal medicines originated in the ancient cultures of the Egyptians, Indians, and Chinese. Due to the significant effect on the use of herbs, medicinal plants, and their biologically active chemicals, to treat disease and improve health without remarkable side effects, there is a renewed scientific interest in the uses of medicinal plants to treat AD. Although numerous herbal medicines have been effective experimentally, only a few have been clinically tested. Various secondary metabolites from plants have also been commercialized and utilized.[34,35]

Some of the medicinal plants which have been investigated and reported to be utilized in AD treatment include Ginkgo biloba, Centella Asiatica, Withania somnifera, Savia officinalis, Tinosporacordifolia, Lepidummeyenii, Curcuma long, Glycyrrhizaglabra, Magnolia Officinalis, Convolvulus pluricaulis and others.[36,37] Increase neurotrophic factor secretion and improves mitochondrial dysfunction. Molecular enzyme study revealed that ginsenosides found in ginseng possess high AChE inhibitory activities which are an effective mechanism of reducing AD symptoms. Gintonin, a bioactive glycoprotein reduces the

formation of $A\beta$, improves learning and memory capacity through the activation of phosphatidic acid receptors involved in hemolysis. It also ameliorates AD symptoms through the stimulation of autophagy, anti-inflammatory mechanism, anti-apoptosis, and oxidative stress regulation which proved through extensive in vitro and in vivo studies. The role of gintonin in the management of AD has been scientifically proven many years ago, it regulates the G protein-coupled lysophosphatidic acid receptors thereby affecting the cholinergic system, neurotrophic factors leading to reduction in the level of plaque formation. Research has shown that mice administered with gintonin had improved memory impairment through the reduction in $A\beta$ plaque deposition and the release of $sA\beta PP\alpha$ in the body.^[37,38]

There is a long history of herbal medicine use to boost memory and cognitive functions and manage behavioral and psychological symptoms associated with dementia/VaD. Some of the most commonly used and studied herbs include Ginkgo biloba, Huperziaserrata, Curcuma longa, Panax ginseng, Panaxnotoginseng, Bacopamonnieri, Salvia miltiorrhiza, Crocus sativus, and Camellia sinensis. summarises the nomenclature, key bioactive compounds, and mechanisms of action of these herbs.^[39,40]

And decreases anxiety in patients with dementia and/or VaD. For example, a randomised, double blind, placebocontrolled trial of 216 participants with AD or vascular dementia showed a significant improvement in attention and memory function in the EGb761-treated group after 24- week treatment. In a more recent trial, 404 people with dementia (333 AD and/or mixed dementia and 71 VaD) were treated with 240 mg EGb 761 or placebo over 24 weeks. The results demonstrate that ginkgo treatment significantly improves cognitive function and neuropsychiatric symptoms. No difference was found between the AD and VaD groups. These effects have been confirmed by several metaanalyses, indicating that ginkgo treatment stabilises or slows decline in cognition, function, and behaviour . A recently published systematic review, in which nine relatively high quality clinical trials (six studies included participants with VaD or mixed dementia) were recruited, reported that EGb761 not only enhances scores of neurocognition but also improves activities of daily living in patients with AD and/o.^[41,42]

(1) Ginkgo biloba

This is a natural medicinal plant whose leave is used in the management of cognitive impairment in Alzheimer's patients the plant extracts contain flavone glycosides (24%), terpene lactones (6%). The flavone glycosides consist of quercetin, kaempferol, and isorhamnetin and terpene lactones consist of A, B, and C ginkgolides and bilobalide. This plant extract prevents $A\beta$ induced neurotoxicity by inhibiting neuronal apoptosis, ROS accumulation, glucose uptake, mitochondrial dysfunction, and activation of extracellular signal-regulated kinase (ERK) and c-JUN N-terminal kinase (JNK) pathways through the regulation of glutathione peroxidase, catalase, and SOD activity]. Scientific research results of Yang [proved that Ginkgo biboba has the potentials to improve cognitive function for the treatment of AD patients. The neuroprotective activity of Ginkgo biboba is believed to be through the activities of the flavonoids, terpenoids, and organic acid contained in the plant.^[38]



Fig.no.(1),ginkgo biloba.^[38,54]

Synonyme: ginkgo

Biological name: the maidenhair tree

Chemical composition: 2,4,6, trihydroxybenzoic acid

Pharmaceutical activity: antioxidant, neurotransmitter, antiplatelet

Uses: treat sickness, cerebral vascular, insufficient cognitive disorder, dementia, sexual dysfunction, vasodilator.

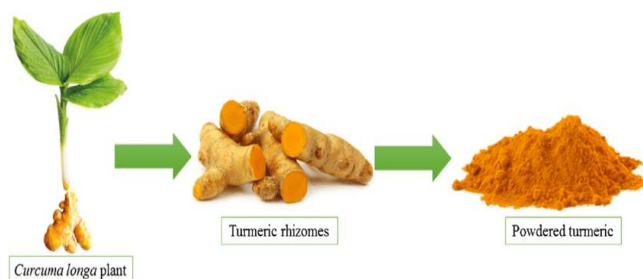
(2) Curcuma plants

Curcuma longa is of the family Zingiberaceae. It is used in the treatment of Alzheimer's patients because of its anti-amyloidogenic, antioxidant, and anti-inflammatory activities.

Studies using experimental rats reveal the potential of Curcuma longa plant extracts inhibiting the formation of fibrils and A β aggregation.

The experimental results also showed a reduction in oxidative stress and improvement in cognitive functions.

This could be due to the ability of the extract to inhibit nuclear factor kappa-light-chain-enhancer of activated B cells (NF- κ B) induced Inducible nitric oxide synthase (iNOS), COX.^[39]



Fig,no.(2),curcuma plants.^[39,55]

Synonyme: curcumasoloensisvaletton

Biological namea: hidden lilies

Chemical compositon: diferuloylmethane, demethoxycurcumin, bisdemethoxycurcomin.

Pharmacological activity: inflametry, antioxidant, antibacterial, expectorant, anticancer.

Uses: contain bioactive agent, natural antiinflametry compound, lower your risk of heart.

(3) GlycyrrhizauralensisFisch

GlycyrrhizauralensisFisch. (F. Fabaceae) is also acknowledged as Chinese Liquorice, and it holds effective EA. A 300% surge in EA over the minimum amount of energy expended by the body to maintain vital processes was observed with G. uralensis when plant extracts were screened.

In addition, GegenQinlian Decoction is used to cure diabetes mellitus and contains liquorice in it. Its function is that it lessens blood sugar and rises serum insulin concentrations in type II diabetic mice.

This plant's extracts possibly will be beneficial to reduce the danger of AD in persons having a tendency to develop diabetes due to genetic hereditary as with diabetes there is a greater likelihood^[40]



Fig.no.(3),glycyrrhizauralensisfisch.^[40,56]

Synonyme: genus glycyrrhiza.

Biologicalname :chinesliquorice

Chemical composition: triterpene,glycoside,chalcones,flavanones.

Pharmacological activity: antiviral,antibacterial,inhibitcox2, and NO₂,

Uses: treat peptic ulcer,constipation,cough.

(4)SoporaflavescensAiton

SoporaflavescensAiton (Fabaceae) is also identified as Ku Shen. The use of methanol for the root extraction of *S. flavescens* stimulated a 400% upsurge of EA in a yeast ER action evaluation . Also, there happened to be a high EA (EC₅₀ estimates of 3.2 μ g/ml) with methanolic extract of the whole plant.

A similar analysis was performed to study the capability of both Prenylflavonoids and lavandulyl flavonoids gotten from the roots of *S. flavescens*, to oust 17 betaestradiol (E₂) from the ER of rat uterine.The outcomes displayed small binding affinities of prenylated flavonoids; But, the groups at position 8 improved their binding ability to the ER of rat uterine ER. Some compounds such as sophoflavescenol, a prenylatedflavonol segregated from *S. flavescens* have anti-AD activity Prenylatedflavonols from *S. flavescens* obstruct the invention of progressive glycation endproducts (AGE), in addition to BACE1 and the AChloweringcholinesterases (ChE).

There is also an activity-guided separation procedure that is allowed to classify compound sophoflavescenol holding high repressive actions against AGE, BACE1, and ChEs by isolating the active principles from *S. flavescens*. In addition, another investigation described non-competitive BACE1 repressive outcomes of lavandulyl flavanones from *S. flavescens*. Consistent with the inhibition of BACE1, the flavones cause a decrease of A β released by human embryonic kidne.,^[41]



Fig.no.(4)*Sophoraflavescens*Aiton,^[41,57]

Synoname:sophoraangustifoliasiebold

Biologicalname :sophoraflavescens

Chemical composition: mutrin,oxymetrin,lupeol.

Pharmacological activity:antitumor,antimicrobial,antipyretic,antiinflammatory.

Uses:treatfever,jaundice,asthama,ulcer,skin.

(4) Bacopamonneri:

Bacopamonneria (Bhrami) in the Ayurveda system of Indian Herbal Medicine has been used for centuries. Traditionally,Ayurvedic medical system has been using it for anxiety relief, as a tonic for the brain to enhance learning and memory development, and prevention of epilepsy. Aging leads to various degenerative changes in the body, and the quantity and quality of these changes depend on upon the anatomy and physiology of the tissue. The factors that contribute to these changes are oxidative damage to the DNA and hormonal deficiency. Normal stress response requires synchronized functioning of various hormones and neurotransmitters. Bacopa contains many alkaloids, such Asbrahmine and Herpestine,saponins,d-mannitol, Hersaponin and monnierin that are responsible for the medicinal value. Other active constituents include betulinic acid, Stigmastanol, beta-sitosterol, numerous bacosides, and bacopasaponins. The bacosides enhance kinase activity, neuronal synthesis, and restore synaptic activity. These neuronal repair actions are valuable in AD management. In hippocampus it enhances protein kinase activity that may contribute to its nootropic activity which means an improvement in cognitive functioning. Bhrami extracts have show protection of neurons from beta- Amyloid induced cell death by suppressing cellular acetyl cholinesterase activity. It has also reversed actions such as depletion of acetyl choline, reduction in Choline acetyl Transferases, decrease in Muscarinic cholinergic receptor binding in frontal cortex and hippocampus.^[42]



Fig.no.(5),Bacopamonneri ^[42,58]

Synoname:waterhyssop

Biological name :bacopamonneri

Chemical composition:alkaloids,brahmine,nicotine,herpestine,bucosideAand B saponinsAand B,C ,triterpenoid.

Pharmacological activiy:memoryinhance,anxiolytic,antidepresion,analgesic,

Uses: ayurvedicmedicine,increase brain chemical,thinking,lerning,andmeomory,usedalzhimers.

(5)Withaniasomnifera

This plant is commonly called as Ashwagandha or Indian ginseng; it contains different types of chemical constituents such as alkaloids, steroidal lactones, saponins. Anciently it has been used as medicinal plant in Ayurveda as it possesmultiple uses. The bioactive component and the plants extract are used in treatment and prevention of various diseases such as Arthritis, impotence, amnesia, cancer and neurodegenerative disorders. It has capability to revitalize nerves, bone marrow and reproductive system property. Ashwagandha can improve cognitive behavior in rats subjected to oxidative damage that occurs in AD and can reverse accumulation of β -Amyloid peptides ($A\beta$) implicated in the disease. Researches stated that Withaniasomnifera produces its beneficial effects by reducing oxidative damage, enhancing toxic $A\beta$ clearance and can attenuate neurodegeneration. The mechanism of action of Withaniasomnifera in humans is not clear. Animal studies have shown that the Sitoindosides VII-X and WithaferinA A (glycowithanolides) are the active phytophenols, responsible for the mechanism of increased cortical Muscarnic acetylcholine capacity, with a modulation of cholinergic neurotransmission. These studies indicate the use of Withaniasomnifera can cause significant changes in neurological baseline functions. Molecular modeling studies showed that Withanamides-A, C Uniquely bind to active moiety of beta-amyloid and prevent fibril formation. Aqueous extract increases the cholinergic activity, whereas Methanol extract causes neuritis outgrowth in dose and time dependent manner in human neuroblastoma cells. Researchers postulate that it can be applied clinically in prevention, and possibly repair, of central nervous system disorders.^[43]



Fig.no.(6),Withaniasomnifera ^[43,59]

Synoname: ashwagandha

Biological name :withaniasomenifera

Chemical composition: withanolide D and withanolideA, antitumor,glycoside(20,30)

Pharmacological activity: antimicrobial, antitumor,cardio protective, antidiabetic,

Uses: treat insominia,boost nutrition ,treat inflammation,

(6)Magnolia officinalis

It is commonly called as Houpa magnolia they Are distributed widely in mountains and valleys of china at higher altitudes.The whole bark contains phytochemicals such as Magnolol, Honokiol, Two Polyphenolic compounds. This plant shows peroxisome-proliferator activated receptor gamma agonistic activity (PPAR Gamma) and acts as GABA modulator. It is potentially used as Anti-oxidant, Anti-inflammatory, Anti-microbial properties. Oral pretreatment of two extract products of Magnolia officinalis (10 mg/Kg/Day in ethanol) into drinking water for 3 months ameliorated memorial dysfunction and

prevented Amyloid beta accumulation in the brain. The extracts also showed a decrease in amyloid precursor proteins and its products. Hence it is effective in treatment and prevention of AD through memory Enhancement antiamyloidogenic effects through down regulation of - Secretase activity and the extent of neuroprotective efficacy depends on area where it is cultivated and methods followed during manufacturing.^[44]



Fig.no.(7),Magnolia officinalis.^[44,60]

Synonyme: magnolia hypoleuca

Biological name :magnolia officinalis.

Chemical composition: ligans,neoligans, alkaloids,phenylethanoid,glycoside.

Pharmacological activity:antimalarial,dietry supplement,cosmetics,anticancer,anti depression, antioxidant,

Uses: its used in anxiety, asthma, depression, gastrointestinal disorder,headache,

(7) Commiphorawightii

It is commonly called as guggul found in northern Africa to central Asia, this plants grows abundantly in arid and semiarid climates and tolerates poor soil. Effectively used in Unani and ayurvedic medicine. Gum guggul extract contains various phytochemicals such as Diterpenoids, triterpenoids, steroids, long chain aliphatic tetrols, carbohydrates, volatile oils, lignans, and Amino acids. It has significant protective effect against the Streptozotocininduced memory deficit model of dementia and the effect can be attributed to its cholesterol lowering anti-oxidant and anti-acetylcholinesterase activity these observations suggest Guggulipid as a potential Anti-dementia drug. It acts on impairment in learning and memory and decreased acetylcholinesterase levels in hippocampus.^[45]



Fig.no.(8),Commiphorawightii^[45,61]

Synonyme:Indian bdellium tree

Biological name:commiphorawightii

Chemical composition:steroids,aliphatic ester,carbohydrate,inorganic ion.

Pharmacological activity:antioxidant,anticancer,antiinflammation,

Uses: its used as herbal medicine,its used in inflammation,and cancer.

(8)Rosmarinus officinalis

This plant is commonly called as rosemary native to North Africa and Spain used as culinary condiment and also in perfume preparations. It is a good source of Vitamin B-6,iron, calcium. Monoterpenes (pinene, camphene, myrcene, limonene), Monoterpenols (borneol) are the chemical constituents. Essential oil extracted from this plant contain 1, 8-Cineole hence used in Aromatherapy, it stimulates body and brain, Improves cognitive performance in terms of speed and accuracy. Researchers have revealed that certain Phytochemicals in the herb put a stop to the degradation of acetylcholine, an important brain chemical needed for normal neurotransmission. A shortage of this chemical is normally seen in Alzheimer's patients.^[46]



Fig.no.(9),, Rosmarinus officinalis.^[46,62]

Synonym: rosmarinus officinalis,

Biological name: rosemary.

Chemical composition:1.8 cineol (38.5%)camphor(17.1%),alpha pinene(12.3%)camphene(6.00%).

Pharmacological activity: wound healing,rashes,headache,expectorant,diuretics,

Uses:improve brain function hair growth,relieve pain ease stress increase circulation

(9)Morinda citrifolia:

It is a tree that belongs to Coffee family widely cultivated across Asia, Australia, and each part of the tree has medicinal value. Earlier in Polynesian and traditional culture they were used as a Tonic and famine food, few regulatory agencies approved skincare products prepared from it, chemical constituents include Alkaloids, Lignans, Oligo and polysaccharides, flavanoids, additionally it's a plant with high nutrition value it contains carbohydrates, dietary fibers, vitamin A, B3, C, Iron, potassium. When animals are administered with Noni juice there was a marked difference in free radical scavenging activity, Anticancer, Anti-inflammatory, Oxidation of LDL, are being reported, Anti-oxidant value of the extract varies depending upon the age of part taken, it also inhibits the metabolism of Acetylcholine by interfering with the action of Acetylcholine esterase.^[47]



Fig.no.(10),*Morindacitrifolia*,^[47,63]

Synoname:Indian mulberry

Biological name: noni

Chemical composition: 5,7acacetine 7,0.beta D ,glycopyrrolate,ajmaline,isomers,alizarine,

Pharmacological activity,antifungal,antioxidant,antiarthemitic,anticancer.

Uses:used in fungal infection, and arthemia,used in cancer.

(10) Utricadioica:

It is a veterinary folk medicine and perennial herb generally grown as a woody plant and generally grown as a weed plant in agriculture. This herb has medicinal uses in combination and alone it is used to treat many disease or problems related to infertility, lactation, management of internal organs functioning. The chemical constituents of this are Lignans, isolecithins, Terpenes, proteins, vitamins, minerals, flavanoids, and tannins. Methanolic extract of this plant with a dose of 0.5g/kg for 30 days is used for the growth of ornamental fish and has immunosimulatory activity. Along with regular exercise and this plant extract there is chance of reduction in brain lesions in rats.^[48]



Fig.no.(11),*Morindacitrifolia*,^[48,64]

Synoname:stinging nettle

Biological name : common nettle

Chemical composition: phenolic compound,srerols,fattyacids,alkaloids,terpenoise,flavonoids,ligans,

Pharmacological activity: antiviral,antimicrobial,anti cancer, nephroprotective,

Uses: used in cardio vascular disorder mostly in hypertention,

(11) Salvia lavandulaefoliaVahl

*Salvia lavandulaefolia*Vahl. (Lamiaceae), similarly called Spanish Sage, originated from Spain in which free oxygen radical neutralizing action, estrogenic activity (EA), inflammation-reducing properties, and anti-butyryl and anti-acetyl-cholinesterase activities are gotten from its extract. The acetylcholinesterase

inhibitor (AChEI) action is acquired from their essential oil and some of its modified terpenes. The ethanolic extract of the herb (5 mg/ml) and the modified terpenes (0.1 M) alpha- and beta-pinene and 1,8- cineol are the major source for the antioxidant activity while their anti-inflammatory effect in vitro was exhibited by the ethanolic extracts (50 mg/ml) and alpha-pinene and geraniol (0.2 mM). A possible EA was demonstrated through the initiation of β -galactosidase action in yeast cells transmitting a promoter promoted by estrogenic compounds exhibited by the essential oil of Spanish sage (0.01 mg/ml) and its modified terpene component geraniol (0.1-2 mM) . This property is an indication of its usefulness in AD.^[49]



Fig.no.(12), *Salvia lavandulaefolia*Vahl.^[49,65]

Synonym:salvia approximate pau

Biological name: Spanish sage,

Chemical composition: camphor(30.8to37.2%) 1,8 cineole(21.7to25.7%) camphene (7.2to9.4%)alpha pinene (4.8to5.5%)

Pharmacological activity: sedative,antioxidant,potentialdementia,oxidative,

Uses: flavoring agent .used in medicinal purpose,cultivated essential oil,

(12)Ginseng Ginsen

Ginseng,is one of the plants used in managing AD . It is a popular herb used in China, Japan, and Korea for memory and energy-boosting. Ginseng or Chinese ginseng as it is commonly known contains phytochemicals such ginsenosides (saponins) a derivative of triterpenoid dammarane, 20(S)-protopanaxadiol that inhibits aggregation of amyloid-beta ($A\beta$) removes $A\beta$ from neurons, in(50)



Fig.no.(13),, Ginseng Ginsen.^[55,66]

Synonym:panax ginseng

Biological name : genus panax

Chemical composition: ginseng saponins, ginseng oils, carbohydrates,sugar,organicacid,amino acids,

Pharmacological activity: antioxidant,promoting immune future,CNSfuture,relevestrees.

Uses: improving health, immune system, stress, improve thinking, diabetes, erectile dysfunction.

(13) *Moringaolifera*

Moringaolifera with the family name, *Moringaceae* is locally used in the management of AD. This could be due to its vast bioactive components. *Moringaolifera* is highly rich in phytochemicals such as flavonoids, alkaloids, saponins, tannins, and isothiocyanates. These phytochemicals reduce the level of lipid peroxides by increasing the production of catalase and SOD thereby leading to improved cognition in the brain. It also enhances the stabilization of monoamines level and causes a decrease in the generation of tau hyperphosphorylation in hyperhomocysteinemia in experimental rats.^[51]



Fig.no.(14),, *Moringaolifera*.^[51,67]

Synonym: drum stick tree

Biological name : *moringaolifera*

Chemical composition: crude protein, crude oil, fiber, alkaloids, saponins, tannins, flavonoids.

Pharmacological activity: anticancer, antifungal, antioxidant

Uses : anemia, cancer, inflammation.

(14) *Phyllanthusacidus*

This plant is of the family *Phyllanthaceae*. The plant extract is used in the management of AD patient because it decreases lipid peroxidation, AChE activity and increases the level of brain antioxidant enzymes which improves cognitive functions, as well as cause reduction in oxidative stress (Uddin, Mamun, Hossain, MS Ashaduzzaman, et al. 2016). The result of *Phyllanthusamarus* and *Cynodondactylonmethanoic* extract in AD model, revealed that both extract synergically increased the level of catalase, nicotinamide adenine dinucleotide (NAD) + hydrogen (H) (NADH) dehydrogenase, and superoxide dismutase activity when compared to the controlled animal group, showing that the combination of these two extracts may serve as a new approach in treating AD patients (Alagan et al. 2019). Also, the ethanolic extract of *PhyllanthusEmblica* ripe and unripe fruits exhibited a significant effect on an AD mice model by improving the learning, memory, and antioxidant potential as well as decreasing AChE activity.^[52]



Fig.no.(15), *Phyllanthusacidus*,^[52,68]

Synonym: averrhoecida

Biological name: Phyllanthus acidus

Chemical composition: t-muurolol, caninol, cadinene and murolene

Pharmacological activity: vivo hepatoprotective and hypoglycemic, in vitro antioxidant, glucosidase inhibitory, inflammatory and antimicrobial activity

Uses: to treat a wide spectrum of diseases such as inflammatory rheumatism disorder hepatic diseases and diabetes

(15) Elettariacardamomum

Elettariacardamomum, likewise named Cardamom, is employed in India as menstrual disorders therapy. The Ginkgo Biloba and E. cardamomum seed extracts indicated the effect of both EA and anti-EA when an investigation was tested out to determine the Estrogenic activity of EA of E. cardamomum, Plantago ovata seeds, and Ginkgo biloba. It was remarkable to note that an alternative investigation presented that those treated a few weeks before and after birth with the extracts of E. cardamomum completely influenced learning and memory in mice, which suggests that it might similarly be of use in AD. Family of monocotyledonous flowering plants with 1600 species. Plants in the Zingiberaceae family are also known as pseudostems.^[54]



Fig.no. (16), Elettariacardamomum.^[53,69]

Synonym: green or true cardamom

Biological name: true cardamom

Chemical composition: essential oil (CEO) are 1,8-cineole, alpha-terpinyl acetate, sabinene, and beta-linalool,

Pharmacological activity: anti-inflammatory, analgesic, antioxidant, and antimicrobial effect,

Uses: asthma, nausea, diarrhea, cardiac, digestion, kidney problem

Conclusion

AD is the most prevalent neurodegenerative disease over the entire globe with no effective drugs or therapy to treat the disease. It appeals for the exploration of new chemical entities where medicinal plants can play a pivotal role being the rich source of pharmacological activity and vast diversity. The secondary metabolites of plants including alkaloids, flavonoids, and phenolic acids play a key role in improving regeneration and/or inhibition of neurodegeneration. Various natural remedies and individual plant parts have shown significant potential in the treatment and management of Alzheimer's disease. Medicinal plants of the same taxonomic origin share some common pharmacological properties. This review will provide us basis for further exploration and information of anti-Alzheimer's disease drugs by screening unexplored species from the already reported effective families.

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