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REVIEW ON HERBAL PLANTS AND THEIR ACTIVE CONSTITUENTS IN TREATMENT OF ALZHEIMER'S DISEASE.

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ABSTRACT :-

The most frequent kind of dementia is Alzheimer's disease, a neurological disorder. that progresses over time and affects over 10 million individuals worldwide. It was first published in 1906 by Alois Alzheimer, who wrote on a patient he had seen in 1901. A neurological disease that is complex, progressive, and Alzheimer's is characterized by changes in personality, memory loss, and a decrease in mental abilities.

A number of medical systems, most notably the Unani system, have employed medicinal plants, which have proven to be effective in treating and managing memory problems. The neuroprotective properties of these herbs are then explained by the bioactive components. Alkaloids, polyphones, terpenoids, and flavonoids are among the compounds being investigated for their potential to reduce oxidative stress, reduce neuroinflammation, and alter important molecular pathways connected to the pathophysiology of Alzheimer's disease. Clinical experiments have confirmed the efficacy of most herbs and plants, and their chemical evaluation has also been completed. Still, the fundamental workings of acts are not fully understood. Herbal and medicinal plant remedies are becoming more popular as complementary and alternative therapies.The role of bioactive components in neurodegenerative herbs and their significance for loss of memory connected to Alzheimer's and Before Alzheimer's is reviewed in-depth in this article based on a systematic review of recent research.

The paper covers the probable mechanisms of action for these herbal ingredients' therapeutic benefits, such as antioxidant activity, anti-inflammatory characteristics, cholinesterase inhibition, and neurotransmitter system regulation.

Keywords:- *Alzheimer's disease, dementia, neurological disease, herb*

INTRODUCTION:-

Alois Alzheimer, a German doctor who documented the first instance of "presenile dementia," is honoured by the name of the illness[2].The neurodegenerative disease known as Alzheimer's disease is clinically characterised by abnormally altered behaviour, diminished cognitive function, and memory issues that get worse with time. Approximately 80% of dementia diagnoses are caused by Alzheimer's disease. There has been irreversible damage to the brain's neurons involved in thinking, learning, and remembering. The symptoms are apparent[1]. As the illness worsens, it begins to damage neurons in other areas of the brain, impairing one's ability to perform daily tasks like eating, walking, and sitting up straight. Furthermore, the cortical connection between the subcortical nuclei and frontal, temporal, and parietal cortices is gone, as is the cholinergic basal nucleus.

BRAIN ANATOMY:-

Microtubules are a component of the internal support structure seen in healthy neurons. These microtubules function as tracks, carrying chemicals and nutrients from the cell's body to the terminals of the axon before returning again. The microtubules are stabilised when a certain type of protein called tau attaches to them.Tau undergoes chemical alteration in Alzheimer'sdisease . It starts to couple with other tau threads and they entangle with one another[4].

The microtubules break down as a result, causing the transport system of the neuron to collapse (see the figure below). The development of these neurological tangles (NFTs) may lead to cell death eventually after causing communication problems amongst neurons.Apart from NFTs, other anatomic pathologies associated with Alzheimer's disease are macroscopic cerebrocortical atrophy and microscopic senile plaques (SPs; sometimes called beta-amyloid plaques) (refer to the image below). The first areas of atrophy and tangle deposition are the medial temporal lobe and the hippocampal region. Early in Alzheimer's Disease , brain MRI shows this, which aids in the development of a clinical diagnosis.[3]

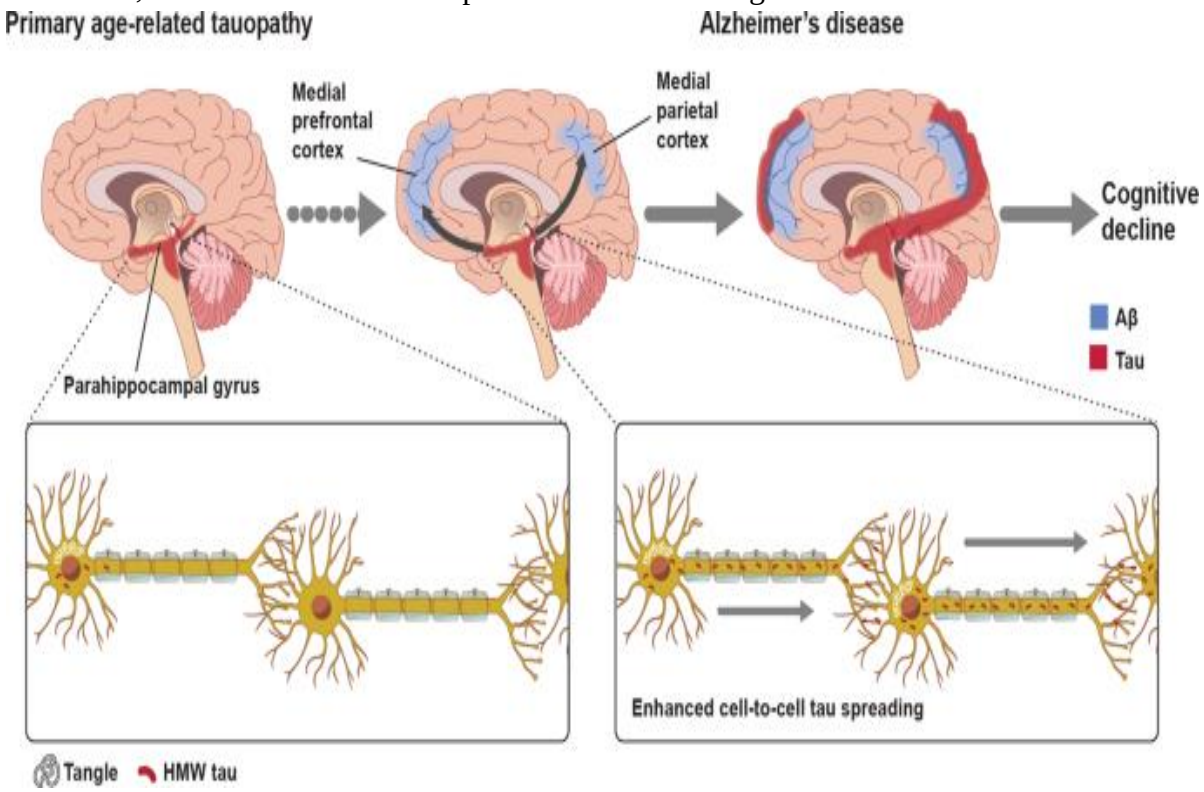
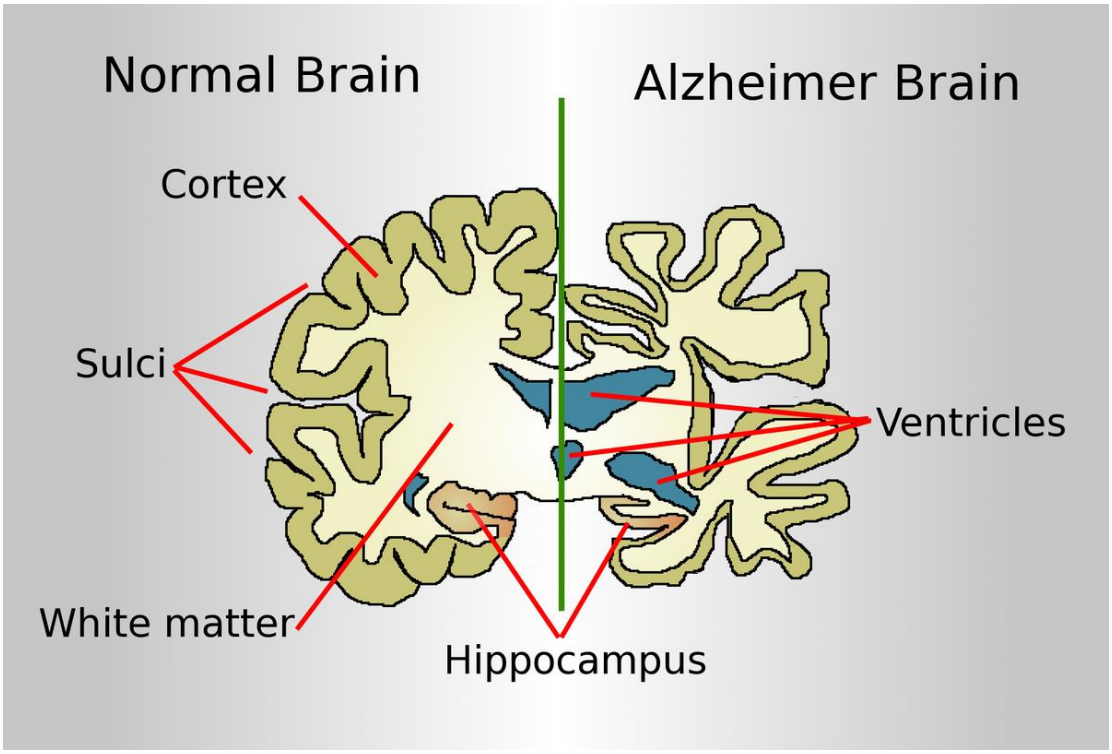


Fig.no 1 Brain Anatomy.



- Difference between normal brain and Alzheimer's brain .

- **Table No.2 Difference between Alzheimer's and Dementia:-**

Alzheimer's disease	Dementia
Alzheimer's disease is the type of dementia that is most common .	Dementia is defined by difficulties with thinking, memory, speech, and language.
Duration- Average of 8 to 20 years	Duration- permanent damage that comes in stages.
Typical age is 65 years but can occur as early as 30.	Typical age between 65 years and older.

PHYSIOLOGY OF ALZHEIMER'S DISEASE:-

The development of tau tangles and beta-amyloid plaques in the brain causes neuronal damage and cognitive impairment, which is the hallmark of Alzheimer's disease. These anomalies cause inflammation and interfere with brain cell-to-brain transmission. Decreased neurotransmitter levels, including acetylcholine, also play a role in compromised signaling. Neurodegeneration primarily affects the hippocampus and cortex, critical for memory and cognition. Alzheimer's disease development is influenced by age, genetics, and environment. The significant cognitive impairment observed in advanced stages of the disease is a result of

synapse malfunction, neuronal death, and extensive brain atrophy that develop as the disease progresses.

PATHOPHYSIOLOGY OF ALZHEIMER'S DISEASE:-

Many factors, such as oxidative stress and mitochondrial dysfunction, cholinergic dysfunction, and toxicity, have been related to Alzheimer's disease.Twenty Patients experience inflammation and amyloid plaque production due to temporo-frontal brain shrinkage and neuronal death. The primary features of Alzheimer's Disease are an uneven cluster of protein fragments and a tangled bundle of fibres.The cortex of the brain and parenchyma afterward observe an increase in monocytes, macro and microglial cells.Entorhinal cortex, the hippocampus and brain regions suffer neuronal death as a result of Alzheimer's Disease . Furthermore,the cervical connection betweenThe cholinergic basal nucleus has disappeared, along with the subcortical nuclei and the frontal, temporal, and parietal cortices. A distinct pattern of accumulated tangles can be seen in theThe hippocampal cornu ammonis 1 region, cortical association area, trans-entorhinal cortex, and entorhinal cortex where the frontal, parietal, and temporal lobes converge.[5]

Causes of Alzheimer's disease:-

Lifestyle, environmental, and genetic factors are probably contributing factors, in addition to age-related alterations in the brain. The significance of any individual component in raising or reducing Alzheimer disease risk.[6]

Although the precise origin of the condition is unknown, age, heredity, and specific lifestyle factors may be involved. Alpha-amyloid plaque and tau tangles, two aberrant deposits of proteins in the brain, are linked to the advancement of Alzheimer's. To gain a deeper understanding of these aspects, study is ongoing.

SYMPTOMS OF ALZHEIMER'S DISEASE-

Early in the course of Alzheimer's disease, very modest symptoms including partial memory loss are present. They become worse with time and result in aberrant conduct. The symptomatic disease is being identified from a clinical, epidemiological, and pathological perspective.

Other symptoms:-

confusion
Personality changes
Language difficulties
Unexplained mood swings
Problem with attention

MECHANISM OF ALZHEIMER'S DISEASE:-

Molecular mechanism :

Complicated molecular pathways underlie Alzheimer's disease, which is essentially typified by aberrant protein aggregation buildup. Tau tangles and amyloid beta plaques are important participants. Tau protein clumps inside neurons, causing structural damage, whereas amyloid beta forms plaques outside neurons, impairing transmission. These anomalies lead to oxidative stress and inflammatory reactions, which accelerate

neurodegeneration. Susceptibility is influenced by genetic variables, particularly those linked to the presenilin and apolipoprotein E (APOE) genes. Understanding the precise order and interaction of events remains a challenge due to the complexity of Alzheimer's disease.

NEURAL MECHANISM :

One of the brain regions impacted by Alzheimer's Disease is the locus coeruleus, the reticular structure, the hippocampus, the substance nigra, the cortex, the brain's hypo, the brain area known as the claustrum, and certain regions of the cerebral cortex.The location of neurotransmitter, neuromodulator, and neuropeptide expression determines which types of neurons are impacted.Neuron loss and brain shrinkage are the outcomes of the degenerative process. Pathobiology of disease also impacts cells that are not neurons; degenerative processes occur in the choroid plexus, blood vessels, astrocytes, microglia, and oligodendroglia. According to transgenic mice models of Alzheimer's Disease , structural alterations that can affect brain function, such as neurite degeneration and spine loss, are often associated with amyloid plaques.There is a clear correlation between Alzheimer's Disease cognitive impairments and synaptic loss. The early-stage synaptic dysfunction is probably reflected morphologically in synapse loss.In comparison to age-matched control brain tissues,Early structural studies of postmortem brains revealed that those with Alzheimer's Disease had fewer spines of dendritic cells and a reduced number of between the hippocampal and cerebral cortical synapses. Declining mental state was directly correlated with greater loss of dendritic spine[9]

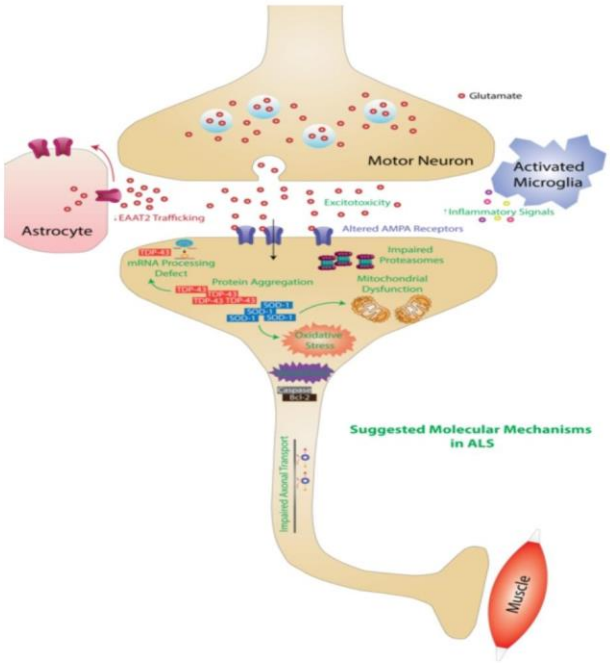


Fig.no 2 Neural mechanism of Alzheimer's disease.

A place for natural herbs in Alzheimer's disease treatment.

An individual's social and professional life is severely limited by this neurodegenerative illness.The growing population of persons with unworthy medical conditions is a significant challenge. Despite the fact that Alzheimer's patients receive a lot of medical attention, attempts to treat the neurological condition appear to be ineffective. Even yet, these medications also exact their complications making the patient's medical circumstances worse.

By controlling neurotransmitter enzymes, Alzheimer's disease is caused.such as synthetic N-methyl-D-aspartate receptors or cholinesterase inhibitors medications that haven't provided a flawless treatment solution[8].

Traditional medicine has been used all around the world since ancient times. Alzheimer's disease , dementia, and other conditions have been reported to respond well to these natural remedies, which include herbs and medicinal plants.Disorders such as amnesia. Herbal remedies were first used in the ancient Egyptian, Indian, and Chinese cultures.Some herbs naturally occurring phytochemicals have the power to enhance brain function[7]. Herbal remedies are very safe, affordable, and have potential efficacy.They may also have synergistic interaction between other drugs. Herbal remedies are useful for treating a wide range of illnesses, but they are particularly useful for mental and neurological conditions if patients are dissatisfied with their present course of therapy and want to make decisions about their care that align with their values and beliefs.These antioxidant-rich plants (beta-carotene, vitamin C, vitamin E, and flavonoids) can counteract oxidative stress, which has been scientifically related to being one of the factors that accelerates the development of neurodegenerative symptoms in neuropsychiatric patients[10].

Although several herbal remedies have shown promise in experiments, only few have undergone clinical testing . Additionally,Many secondary metabolites found in plants have been used and made into products. Some of the therapeutic herbs that include Ginkgo biloba, Centella Asiatica, Withania somnifera, Salvia officinalis, and others that reportedly help treat Alzheimer's disease and have been researched. Some species include Glycyrrhiza glabra, Convolvulus pluricaulis, Magnolia Officinalis, Curcuma longa, Phy Dum Meyenii, Cordifolia Tinospora, and others.

A large assortment of herbs used for Herbs and medicinal plants are examples of natural therapies that have been connected to Alzheimer's disease (AD) treatment, dementia, amnesia, and others.

The benefits of whole medicinal plant extracts on Alzheimer’s disease have been the subject of numerous studies, which have also sought to isolate and pinpoint the active ingredients.There are numerous substances, such as lignans, flavonoids, and tannins, Alkaloids, sterols, polyphenols, and triterpenes have all shown a number of advantageous pharmacological actions, including as anti-cholinesterase, anti-inflammatory, anti-amyloidogenic, and antioxidant. Some substances, like old extract from garlic, ginkgo, melatonin, curcumin, and resveratrol.[11,12,13]

Table No.1 Summary of plants and its Constituents.

Sr no.	Botanical name	Family	Local name	Parts used	Active ingredient
1	Ginkgo biloba	Ginkgoaceae	Ginkgo	Dried green leaves	Fresh plant extract
2	Curcuma longa	zingiberaceae	Haldi, turmeric	Rhizomes	Curcuminoic
3	Salvia officinalis	Labiatae	Sage leaf	Leaves	Essential oils
4	Tinospora cordifolia	menispermaceae	Guduchi, giloy	The Stem	Terpenoid
5	Melisa officinalis	Labiatae	Lemon balm	The leaves	Tannin, eugenol
6	Glycyrrhiza glabra	Fabaceae	Liquorice	Root and Rhizomes	Glycyrrhizin
7	Centella asiatica	Apiaceae	Gotu kola	The whole plant	Triterpenes, saponies
8	Convolvulus pluricaulis	Convolvulaceae	Shankhpushpi	Leaves, flowers,stem, root	alkaloids, flavanoids
9	Withania somnifera	Solanaceae	Ashwagandha	Leaves, flowers,stem, root	steroidal lactones, alkaloids
10	Panax notoginseng	Araliaceae	Korean ginseng	Root	Ginsenoside
11	Emblica officinalis	Phyllanthaceae	Indian gooseberry	Fruit	ellagic acid, apigenin, chebulinic acid, quercetin, gallic acid
12	Murraya koenigii	Rutaceae	Curry Leaf Tree	Leaves and root	carbazole alkaloid
13	Uncaria tomentosa	Rubiaceae	cat's claw	Root and bark	indole alkaloids, glycosides
14	Crocus sativus	Iridaceae	saffron crocus	Stigmas	Carotenoids

15	Cassia obtusifolia	Leguminosae	wild senna	Dried and roasted leaves	Obtusifolium
17	Bacopa monnieri	Scrophulariaceae	Brahmi	The leaf	Steroids, triterpenes
18	Acorus calamus	Acoraceae	Vacha	Rhizomes	2,4,5-trimethoxy-1-propenylbenzene
19	Catharanthus roseus	Apocynaceae	Sadabahar	Leaves	vinblastine, vindoline
20	Hericium erinaceus	Hericiaceae	lion's mane mushroom	Fruit	polysaccharides, erinacines,

1.Ginkgo biloba:-

This plant has natural therapeutic properties, and The leaves are used to treat cognitive impairment in Alzheimer's patients. Flavone glycosides account for 24% of the plant extracts, whereas terpene lactones make up 6%. Isorhamnetin, kaempferol, and quercetin are among the flavone glycosides. The terpene lactones are made up of bilobalide, the three variables ginkgolides A, B, and C.By preventing neuronal apoptosis, reactive oxygen species buildup, glucose absorption, mitochondrial malfunction, and extracellular signal-regulated kinase activation, this plant extract guards against AΠ-induced neurotoxicity. via regulating the activity of SOD, catalase, and glutathione peroxidase.JNK) and the c-JUN N-terminal kinase (ERK) pathways[14].

Fig no.3 Ginkgo Biloba.

2.Curcuma longa:-

In both modern and Indian medical systems, curcumin, or turmeric, an ancient Indian herb used to make curry powder, has been thoroughly studied for its potential to treat a wide range of illnesses,such as gastric ulcers, arthritis, haemorrhoids, breast cancer, colon cancer, atherosclerosis, liver disorders, and cystic fibrosis.It's been applied to traumatic brain injury and dementia in a variety of ways.Curcumin may play a part in the management and prevention of Alzheimer's Disease. Alzheimer's patients benefit from curcumin's antioxidants, lipophilic, and anti-inflammatory properties, which enhance cognitive performance. An increasing amount of research points to the role of free radicals, beta amyloid, oxidative stress, aberrant inflammatory responses,The critical event involved Alzheimer's disease pathology and brain dysregulation caused by bio-metal poisoning.[15,27]

Fig. no 4 Curcuma longa

3.Salvia officinalis:-

Of all the genera in the Lamiaceae family, Salvia, or sage, is the largest. Numerous species that have historically been utilised as brain-boosting tonics are included in it. A wide range of active chemicals found in many Salvia species have been shown to support both neurodegenerative disease prevention and cognitive enhancement in vitro and in animal experiments.The molecular mechanisms linked to cognition can be influenced by salvia plants and their contents. These mechanisms include impacts regarding oxidative stress, inflammation, neurotrophins, amyloid-β, cholinergic activity, and anxiolytic/antidepressant behaviours[16].

Fig.no 5 Salvia officinalis.

4.Glycyrrhiza glabra :-

This Fabaceae family plant, which contains coumarins that the treatment of Alzheimer's disease involves the use of isoflavonoids, saponins, flavonoids, or stilbenoids. Together, these phytochemicals suppress cytotoxicity, reactive oxygen species production, and Glutathione activity. Glycyrrhiza experiment results glabra plant extract was given orally to an albino rat that was one month old for Memory and learning capacity improved after six weeks. And additionally,According to Tapia-Rojas's study, glycyrrhiza inflata extract, a Various glycyrrhiza species significantly reduced A□ aggregation and actions that scavenge radicals. It reduced the production of mitochondria and oxidative stress.This may be linked to licochalcone's activity. The plant extract contains liquiritigenin[22,26]

Fig.no 6 Glycyrrhiza glabra.

5.Centella asiatica:-

Gotu kola, or Centella asiatica, has been demonstrated in certain trials to have possible neuroprotective and cognitive-enhancing benefits. On its precise function in Alzheimer's disease, however, not much is known.

High antioxidant activity in Centella asiatica, a traditional medicinal herb, reduces the build-up of amyloid-β (Aβ) inside the neural system.Additionally, Alzheimer's disease's (AD) pathogenesis is initiated by oxidative stress caused by aggregated Aβ. The working memory loss brought on by Streptozotocin was alleviated by Centella asiatica .In a dose-dependent way, Centella asiatica may be able to stop the death of hippocampus neurons .Centella asiatica enhanced memory by reducing hippocampal neuronal death[18].

Fig.no 7 Centella asiatica.

6.Withania somnifera :-

India's Ayurvedic medication, Withania somnifera, also known by its common name, ashwagandha, A neurodegenerative disorder is a group of disorders that includes Alzheimer's disease . the steroidal chemicals found in ashwagandha, Among these are steroidal lactones of the ergostane type, amorphous with A–Y, dehydro withanolide R. Additional components comprise theTogether with alkaloids, phytosterols sitoindosides VII through XX and the hormone beta-s ,and elevated levels of iron [9,15]. It has been demonstrated that a subset of these substances, called withanamides, is able to scavenge free radicals generated during AD onset and development[19].

Fig.no 8 Withania somnifera.

7. Panax Notoginseng:-

Neurodegenerative conditions such cerebral ischemia and Alzheimer's disease (AD) have been treated with panax notoginseng saponins (PNS). Even while there is growing evidence that Panax notoginseng saponins protects neurons, the essential chemicals and their functional targets are yet unknown. An in vitro model of Aβ-induced neuron injury was used to evaluate the possible functional components of Panax notoginseng saponins for the treatment of Alzheimer's Disease and their underlying molecular mechanisms. Potential mechanisms were hypothesised using a network pharmacology approach and confirmed by molecular biology techniques.[20]

Fig.no 9 Panax notoginseng.

8.Bacopa Monnieri:-

Under the ancient Ayurvedic medical system, It has been said that bacopa monnieri (Scrophulariaceae) improves memory. and intellect.There is additional proof that B. monnieri may be able to safely improve cognitive function in senior citizens through a double-blind, placebo-controlled, randomised research. Escape latency time in Morris, An Alzheimer'sdisease model in rats, showed neuroprotective impacts in recent in vivo investigations. An enhanced version of the water maze test and a decrease in neurons were reduced following treatment with B. monnieri[17].

Fig.no 10 Bacopa monnieri.

9.Murraya koenigii:-

Fig.no 11 Murraya koenigii.

10.Crocus sativus:-

The effects of extracts from the blue-purple blossom known as Crocus sativus or saffron,on memory and brain health are currently the subject of intensive research by numerous researchers. Middle Eastern countries are the native home of Crocus sativus.In individuals suffering from moderate Alzheimer's disease and mental disability (MCI), saffron may be able to enhance everyday activities and cognitive performance.Saffron's chemical composition varies based on the natural surroundings of the nation of origin, but it generally consists of approximately 63% sugars They consist of 10% moisture, 5% basic fibre, 5% nutrients, 5% fat, 12% protein, and traces of thiamine, riboflavin, and vitamins. among other substances[23].

Fig.no 12 Crocus sativus.

11.Convolvulus pluricaulis:-

The family Convolvulaceae includes Convolvulus pluricaulis. It functions as an agent to improve memory. A prior study demonstrated that Ethyl acetate and aqueous improve memory and learning capacities. Other research has identified a variety of secondary metabolites that have nootropic and memory-enhancing effects, including steroids, anthocyanins, flavonol glycosides, and triterpenoids.Convolvulus pluricaulis has been reported to reduce anxiety by controlling the production of stress hormones[24].

Fig.no 13 Convolvulus pluricaulis.

12.Cassia obtusifolia:-

Recently, it has been demonstrated that the ethanolic fraction of Cassia obtusifolia (Fabaceae) seeds can reduce memory in rats. The seeds have traditionally been utilised in conventional Eastern medicine . In mouse primary hippocampal cells, cassia obtusifolia in extract (COE) improved mitochondrial protection and decreased dysregulation of calcium.

COE did not have any impact on the mortality of cells caused by oligomeric Aβ incubation. It was discovered that the aglycone obtusifolia and glucose-obtusifolia, which were separated from the seeds of C. obtusfolia L., inhibited the activity of acetylcholinesterase in vivo as well as in vitro. Nonetheless, In a recent investigation found that individuals with chronic hepatitis B had hepatotoxicity linked to Cassia obtusifolia[25].

Fig.no 14 Cassia obtusifolia.

CONCLUSION:-

To cure Alzheimer's Disease and lessen dementia, numerous beneficial herbal remedies can be used. The principal chemical components—such as alkaloids and flavonoids—have been demonstrated to be quite effective in combating Alzheimer's Disease . Thorough examination of medicinal plants and the discovery of novel active ingredients to combat Alzheimer's Disease .

Numerous herbal plants have demonstrated potential neuroprotective effects, with active constituents showing promising results in preclinical studies. Compounds such as flavonoids, alkaloids, and terpenoids found in various plants exhibit anti-inflammatory, antioxidant, and anti-amyloid properties, which are particularly relevant to Alzheimer's disease pathology. These compounds may contribute to the modulation of neuroinflammation, reduction of oxidative stress, and interference with the aggregation of amyloid-beta plaques, hallmark features of Alzheimer's disease. Despite these promising findings, it is important to acknowledge the limitations and challenges associated with herbal treatments. The variability in the composition of herbal products, lack of standardisation formulations, and limited clinical evidence pose hurdles in establishing their efficacy and safety definitively. Additionally, the complex nature of Alzheimer's disease demands a comprehensive and multifaceted approach, possibly involving a combination of herbal remedies and conventional treatments.

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