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Evaluation of Anti Alzheimer Potential of Medicinal Plants

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Abstract
Alzheimer's disease (AD) is characterized by severe memory loss that affects one's ability to operate in social and professional contexts. More than 20 million individuals worldwide are affected by it, making it the most prevalent type of dementia. An elusive memory loss, corresponding functional deterioration, and behavioral abnormalities are hallmarks of AD. AD is the most common cause of disability in the elderly and patients may survive for more than ten years after receiving their diagnosis. From its lowest level at ages 65 to 70 to rates that may approach 6 percent for those over the age of 85, the incidence of AD ranges from 1 to 4 percent of the population per year. Over a hundred novel products are currently undergoing clinical trials thanks to ayurvedic medicinal plants, which have shown to be the most fruitful source of leads or medication development. Indeed, the use of several Ayurvedic medicinal plants and their ingredients for treating.

Keywords: Alzheimer's disease, medicinal plants, anti-Alzheimer activity, neuroprotection, acetylcholinesterase inhibition, phytochemicals, antioxidant activity, cognitive function, memory enhancement, neurodegenerative disorders.

Aim & Objective:

Aim :

provide safer, multi-targeted, and more affordable alternatives to synthetic drugs.

Objcetive :

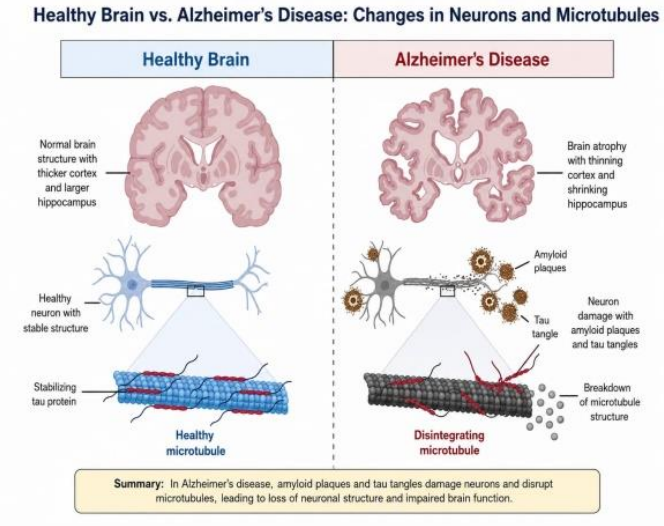
Inhibition of Amyloid-Beta (Aβ) Aggregation: A major hallmark of AD is the formation of amyloid plaques. Compounds in plants like Turmeric (Curcumin) and Gotu Kola aim to prevent these proteins from clumping together and disrupting brain cell communication.

Mitigation of Oxidative Stress: AD is characterized by excessive free radicals that damage neurons. Herbal antioxidants from Ginkgo biloba and Bacopa monnieri help neutralize these molecules and protect the brain's delicate fatty structures.

Anti-Inflammatory Action: Chronic neuroinflammation worsens brain damage. Bioactive compounds like withanolides in Ashwagandha inhibit pro-inflammatory pathways (e.g., NF-

Introduction:

Alzheimer's disease (AD) is a condition marked by a progressive decline in cognitive ability and is brought on by plaque buildup in the hippocampal region of the brain. More than 5 million Americans have this condition, which is the most prevalent type of dementia in middle-aged and older persons; by 2030, it is projected that this number will rise to 7.7 million. Most cases of the disease develop after the age of 60, although some early-onset varieties are associated with a particular genetic flaw. Genetic factors undoubtedly play a part in 10% to 15% of cases, even though the etiology is unknown. The efforts to develop a cure for AD have been incredibly unsuccessful thus far, and the treatments that are now used to treat the illness only effectively treat its symptoms. A loss of neurons in the hippocampus, cortex, and subcortical regions is the underlying etiology. Short-term memory loss, difficulty learning new material, mood swings, trouble remembering words, forgetting names, and misplacing things are all early symptoms of AD. Patients with AD also frequently display aggression, irritation, and irritability. In severe situations, individuals lose all memory, sense of time and place, and become entirely incontinent. Patients eventually need all-encompassing care as they become completely dependent on others. The patient must be placed in a nursing home with 24-hour nursing care because of their complete reliance on others. AD thus poses a significant challenge for patient management.



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Explanation:

This diagram compares a normal healthy brain with a brain affected by Alzheimer's disease. In Alzheimer's disease, the brain shrinks (brain atrophy), and harmful structures called amyloid plaques and tau tangles damage neurons. These changes cause the breakdown of microtubules, leading to memory loss and impaired brain function.

Plan of Work :

1. Phase 1: Plant Selection & Extraction
   - Plant Selection: Select the plant based on ethnomedicinal use, traditional texts, or preliminary screening for memory enhancement and neuroprotection.
   - Preparation: Collect the relevant plant part, dry it, and grind it into a fine powder.

2. Phase 2: In Silico & In Vitro Evaluation (Screening)

In Silico (Computer-Aided): Identify bioactive compounds using databases (e.g., KNApSAcK). Perform molecular docking using tools like PyRx or SwissDock to see if phytoconstituents bind to Alzheimer's targets like Acetylcholinesterase (AChE) or Amyloid-beta.

In Vitro Enzyme Inhibition:

Anti-Cholinesterase: Test extracts against AChE and Butyrylcholinesterase (BChE) using standard Ellman's assay.

Anti-Amyloidogenic: Assess the extract's ability to inhibit Amyloid-beta or Tau protein aggregation (e.g., via Thioflavin T assays).

In Vitro Antioxidant Assays: Measure radical scavenging capacity using DPPH and ABTS assays, as oxidative stress is a key driver of Alzheimer's disease.

3. Phase 3: In Vivo Studies (Animal Models)

Animal Grouping: Use rodent models (mice or rats) divided into groups: Normal, Disease Control (e.g., induced by scopolamine, aluminum chloride, or injection), Standard Drug (e.g., Donepezil), and Extract-treated groups.

Behavioral Testing: Assess cognitive and memory functions using established mazes like the Morris Water Maze or Elevated Plus Maze.

4. Phase 4: Safety Assessment & Compound Isolation

Toxicity Testing: Perform acute and sub-acute toxicity studies according to OECD guidelines to determine the safe dosage range.

Compound Isolation: If the extract shows strong efficacy, use chromatographic techniques (e.g., Column chromatography, HPLC) to isolate and characterize the pure active molecules (e.g., via NMR or LC-MS).

Important Medicinal Plants with Anti-Alzheimer Activity

1. Bacopa monnieri (Brahmi):
   - Contains **bacosides**
   - Enhances memory and learning
   - Exhibits antioxidant and neuroprotective effects

2. Withania somnifera (Ashwagandha):
   - Active compounds: **withanolides**
   - Reduces amyloid plaque formation
   - Improves neuronal regeneration

3. Curcuma longa (Turmeric):

- Active compound: **curcumin**
- Strong antioxidant and anti-inflammatory activity
- Inhibits amyloid aggregation

4. Ginkgo biloba:

- Contains **ginkgolides and bilobalide**
- Improves cerebral blood flow
- Enhances cognitive function

5. Centella asiatica (Gotu kola):

- Contains **asiaticosides**
- Promotes neuronal growth and memory enhancement

6. Panax ginseng:

- Active compounds: **ginsenosides**
- Neuroprotective and anti-inflammatory effects

Medicinal Plants with Anti-Alzheimer Potential :

Several medicinal plants have demonstrated significant cognitive-enhancing and neuroprotective effects:

1. **Curcuma longa (Turmeric/Haldi):**

- **Active Component:** Curcumin (polyphenol).
- **Mechanism:** Potent anti-inflammatory and antioxidant, reduces amyloid plaques by inhibiting -amyloid aggregation, and crosses the blood-brain barrier.
- **Activity:** Curcumin treatment reduces plaque burden by ~40% and improves cognitive function in AD mouse models.

2. Bacopa monnieri (Brahmi):

- **Active Component:** Bacosides A and B (triterpenoid saponins).
- **Mechanism:** Inhibits acetylcholinesterase (AChE), acts as an antioxidant, and restores cholinergic neuron density.
- **Activity:** Prevents neurotoxicity induced by aluminum chloride and improves cognitive retention in aged rats.

3. Withania somnifera (Ashwagandha):

- **Active Component:** Withanolides and withanamides.
- **Mechanism:** Reduces neuroinflammation by modulating cortisol, enhances dendritic arborization (neurite growth), and reduces amyloid toxicity.
- **Activity:** Improves executive function and memory in humans with mild cognitive impairment.

4. Centella asiatica (Gotu Kola/Mandukparni):
- **Active Component:** Asiatic acid, asiaticoside.
- **Mechanism:** Reduces A 1-40/1-42 levels and increases dendritic arborization in the hippocampus.

5. Celastrus paniculatus (Jyotishmati):
- **Active Component:** Sesquiterpenes.
- **Mechanism:** Acts as a neuroprotective and memory enhancer by elevating cholinergic activity.

Literature Review :

1. Pathophysiological Targets for Medicinal Plants in AD:

To scientifically evaluate the anti-Alzheimer potential of a medicinal plant, researchers screen extracts and isolated pure compounds against a specific matrix of established cellular and molecular targets:

The Cholinergic Pathway

The historic cholinergic hypothesis states that a substantial decline in acetylcholine (ACh) levels—driven by the selective loss of cholinergic neurons in the basal forebrain and hippocampus—correlates directly with cognitive deficits. Medicinal plants are heavily screened for their ability to bind to the acyl-binding pocket and choline-binding site of the acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) enzymes, thereby blocking ACh breakdown and enhancing neuro-transmission.

Oxidative Stress & Mitochondrial Dysfunction:

The brain consumes a disproportionate amount of oxygen, making it highly susceptible to reactive oxygen species (ROS). Toxic $\text{A}\beta$ oligomers target mitochondria, damaging mitochondrial DNA (mtDNA), disrupting the electron transport chain (ETC), and exhausting cellular ATP production. Natural antioxidants neutralize free radicals and upregulate endogenous cellular defenses.

Neuroinflammation:

Aggregated proteins activate microglial cells and astrocytes through key cellular pathways. This chronic activation triggers a massive release of pro-inflammatory cytokines—including tumor necrosis factor-alpha ($\text{TNF}-\alpha$), interleukin-1 beta ($\text{IL}-1\beta$), and interleukin-6 ($\text{IL}-6$)—which accelerates neuronal death. Medicinal herbs are evaluated for their ability to calm this neuroinflammatory cycle.

2. Profile of Key Medicinal Plants & Lead Compounds:

Thousands of plants have been ethnopharmacologically linked to cognitive enhancement. Below are the most heavily researched medicinal plants whose multi-targeted anti-Alzheimer properties have been systematically validated in vitro, in vivo, or through clinical trials.

Bacopa monnieri (Brahmi)

Long classified as a premier Medhya Rasayana (nootropic rejuvenator) in Ayurvedic tradition, Bacopa monnieri targets multiple facets of AD pathology simultaneously.

Primary Bioactive Compounds:
Triterpenoid saponins known as *Bacosides* (specifically Bacoside A, composed of Bacoside A_3, Bacopasaponin C, and Bacopaside II).

Mechanisms of Action:

Aggregation Inhibition:
Bacoside A physically blocks the self-assembly of $\text{A}\beta_{1-42}$ monomers and prevents their toxic binding interaction with neuronal membranes.

Neuroprotection:
Hexane and ethanolic extracts significantly reduce glutamate-induced excitotoxicity, protecting neurons from endoplasmic reticulum (ER) and oxidative stress.

Cognitive Enhancement:
In vivo models (such as Morris water maze tests) demonstrate that oral administration improves escape latency and reverses scopolamine-induced amnesia. It also dampens microglial activation by suppressing $\text{TNF}-\alpha$ and interleukins.

Withania somnifera (Ashwagandha):

Commonly referred to as Indian Ginseng, the roots of this Solanaceae family plant possess powerful adaptogenic and neuroprotective properties.

Primary Bioactive Compounds:
Steroidal lactones termed *Withanolides* (such as Withaferin A and Withanolide D) alongside specialized *Withanamides* (A and C).

Mechanisms of Action:

Fibril Inhibition:
Molecular docking and in vitro modeling show that Withanamides A and C bind directly to the hydrophobic core of $\text{A}\beta$ peptides, arresting fibril synthesis before plaques can mature.

Synaptic Regeneration:
It stimulates neurite outgrowth, promoting substantial dendritic and axonal regeneration in damaged cortical and hippocampal networks.

Cholinergic Support:
It reverses memory deficits by elevating free acetylcholine concentrations in the neocortex and hippocampus.

Curcuma longa (Turmeric) :
Epidemiological studies historically revealed a significantly lower prevalence of AD in regions with high dietary intake of turmeric, prompting deep scientific investigation into its active compound.

Primary Bioactive Compound:
Curcumin (a hydrophobic polyphenol).

Mechanisms of Action:
Plaque Clearance:
Curcumin directly crosses the blood-brain barrier (BBB), binds directly to amyloid plaques, and actively assists in dissolving existing aggregates while lowering overall plaque burden by over 40%.

Anti-Inflammatory Command:
It heavily suppresses pro-inflammatory transcription factors, preventing astrocytes and microglia from initiating downstream chronic neuroinflammation.

Metabolic Modification:
Curcumin aids in lowering intracellular cholesterol esters, which are known to facilitate amyloid accumulation.

Ginkgo biloba (Maidenhair Tree):
Standardized extracts of Ginkgo biloba (such as EGb 761) are widely utilized in European pharmaceutical frameworks to slow cognitive decline.

Primary Bioactive Compounds:
Flavonoid glycosides and terpene lactones (*Ginkgolides* and *Bilobalide*).

Mechanisms of Action:
It functions primarily by enhancing cerebral blood flow, optimizing mitochondrial ATP production, scavenging ROS, and protecting hippocampal neurons from $\text{A}\beta$-mediated toxicity.

Previous studies show:

- Bacopa monnieri contains bacosides that improve synaptic activity
- Demonstrates antioxidant properties
- Enhances cognitive performance in clinical studies
- Inhibits acetylcholinesterase enzyme

Based on a review of scientific literature, Bacopa monnieri (often known as Brahmi) is a recognized nootropic herb with a strong profile for cognitive enhancement and neuroprotection. Its pharmacological activities are primarily attributed to a mixture of triterpenoid saponins known as **bacosides**.

Here is a summary of the findings based on previous studies:

1. Bacosides and Synaptic Activity Improvement :

- **Mechanism:** Bacosides promote the repair of damaged neurons by upregulating neuronal synthesis, kinase activity, and promoting dendritic arborization (growth of nerve branches) in the brain.
- **Synaptic Restoration:** They aid in the restoration of synaptic activity, leading to enhanced nerve impulse transmission, particularly in the hippocampus, which is vital for memory formation.

2. Antioxidant and Neuroprotective Properties :

- **Free Radical Scavenging:** Bacopa monnieri demonstrates significant antioxidant capabilities by scavenging free radicals (reactive oxygen species - ROS) and reducing lipid peroxidation, which protects brain cells from damage.
- **Enzyme Modulation:** Studies show it increases endogenous antioxidant enzyme activity, such as superoxide dismutase (SOD) and catalase, reducing oxidative stress-induced neurodegeneration.
- **Neuroprotection:** The herb has demonstrated the ability to reduce -amyloid deposits, a hallmark of Alzheimer’s disease.

3. Cognitive Performance in Clinical Studies :

- **Memory and Attention:** Clinical trials, particularly using standardized extracts (e.g., CDRI-08), have demonstrated improvements in verbal learning, delayed word recall, memory acquisition, and attention in both healthy individuals and those with cognitive decline.
- **Anxiolytic Effect:** It is often described as a "calming cognitive enhancer," showing efficacy in reducing anxiety.
- **Long-term Efficacy:** Cognitive improvements are usually observed after 12 weeks of consistent supplementation, suggesting it works better for chronic rather than acute cognitive enhancement.

4. Acetylcholinesterase (AChE) Enzyme Inhibition :

- **Cholinergic Modulation:** Bacopa monnieri acts as a natural inhibitor of acetylcholinesterase, the enzyme responsible for breaking down acetylcholine.
- **Alzheimer's Potential:** By inhibiting this enzyme, it increases the levels of acetylcholine in the brain, improving cholinergic function and offering a potential natural alternative in managing neurodegenerative diseases like Alzheimer's.

5.Core Pathological Targets of Medicinal Plants:

- **Anti-Amyloidogenic Activity**: Compounds like curcumin (from Turmeric) and ginsenosides (from Ginseng) help prevent the formation of amyloid-beta (Aβ) plaques and may even aid in their clearance.
- **Cholinesterase Inhibition**: Plants such as *Huperzia serrata* and *Bacopa monnieri* act similarly to standard AD drugs (like donepezil) by inhibiting acetylcholinesterase, thereby increasing acetylcholine levels to improve memory and learning.

6. Pathogenesis and Pharmacotherapeutic Targets of AD:

- **Amyloid-Beta (Aβ) Accumulation**: The abnormal clipping of amyloid precursor protein leads to extracellular Aβ peptide deposition, forming cytotoxic **senile plaques** that choke neuronal connections.
- **Tau Hyperphosphorylation**: Hyperphosphorylated tau proteins detach from microtubules, collapsing the neuron's internal transport system into intracellular **neurofibrillary tangles**.
- **Cholinergic Dysfunction**: Severe loss of cholinergic neurons in the basal forebrain causes a sharp decline in the neurotransmitter **acetylcholine (ACh)**, destroying memory and learning capacity.
- **Oxidative Stress & Neuroinflammation**: Microglial overactivation releases pro-inflammatory cytokines (e.g., IL-1β, TNF-α) and reactive oxygen species (ROS), causing severe, widespread **lipid peroxidation** in lipid-rich brain tissues.

7. **Comparative Analysis of High-Priority Medicinal Plants:**

The following table summarizes the most heavily researched traditional medicinal herbs utilized in ethnopharmacological systems like Ayurveda and Traditional Chinese Medicine (TCM):

8. Detailed Phytochemical Breakdown and Preclinical Evidence :

***Bacopa monnieri* (Brahmi)**

- **Chemical Profile**: Dominated by triterpenoid saponins known as **bacosides**, alongside bacopasides and alkaloids like brahmine.
- **Scientific Insights**: In vivo testing shows that *Bacopa* reverses scopolamine-induced amnesia and protects neurons from aluminum-induced toxicity. It upregulates endogenous antioxidant enzymes—Superoxide Dismutase (SOD) and Glutathione (GSH)—while reducing cortical Aβ levels.
- **Clinical Trials**: Human double-blind trials demonstrate that 300–450 mg daily for 12 weeks significantly upgrades information processing speed, verbal learning, and delayed recall in elderly subjects without clinical signs of dementia.

***Curcuma longa* (Turmeric):**

- **Chemical Profile**: Enriched with hydrophobic polyphenols called **curcuminoids** (curcumin, demethoxycurcumin, bisdemethoxycurcumin).

- **Scientific Insights**: Curcumin easily crosses the blood-brain barrier due to its lipophilic structure. It recognizes the secondary structure of Aβ aggregates, inserting itself to promote the mechanical disassembly of preformed amyloid plaques. Furthermore, it downregulates the expression of presenilin-1 (PS1) and GSK-3β, limiting further Aβ generation.

***Withania somnifera* (Ashwagandha) :**

- **Chemical Profile**: Features complex steroidal lactones categorized as **withanolides** (specifically Withanolide A and Withanone), alongside sitoindosides.
- **Scientific Insights**: Its metabolite, **sominone**, triggers the neurotrophic factor receptor RET, forcing direct axonal and dendritic regeneration and synaptic reconstruction in damaged cortical networks. Middle-aged APP/PS1 mouse models treated with Ashwagandha root extract demonstrated clear clearance of Aβ accumulations due to the systemic upregulation of low-density lipoprotein receptor-related protein (LRP) in the liver

9. Summary of Polypharmacological Mechanisms:

Reviewing the broad spectrum of botanical active constituents points to an overarching **polypharmacological network**:

- **AChE Inhibition**: Bioactives like Huperzine A and Asiatic acid block the acetylcholinesterase enzyme, structurally forcing higher acetylcholine concentrations into the synaptic cleft to keep neurotransmission active.
- **Anti-Amyloidogenic Effects**: Curcumin and withanamides target the Aβ(25–35) sequence motif, intercepting the self-assembly of monofilaments and preventing the subsequent activation of apoptotic cascades.
- **Nootropic Neurogenesis**: Leaf and root extracts provoke phosphorylation of **CREB** (cyclic AMP response element-binding protein) and elevate dendritic marker proteins (MAP2), which replaces damaged structural elements with fresh neural extensions.

10. Critical Clinical Gaps and Future Perspectives:

- **Standardization Deficits**: Natural extract compositions fluctuate drastically based on plant geography, harvest season, and extraction solvent parameters.
- **Pharmacokinetic Limitations**: Many active components, such as raw curcumin, display poor gastrointestinal absorption, fast metabolic degradation, and limited bioavailability at target sites in the brain.
- **Need for Scale**: More multi-center, long-term, randomized human clinical trials are necessary to verify therapeutic margins, evaluate drug-herb interactions, and formulate standardized delivery systems.

Mechanisms of Action :

- **Cholinesterase Inhibition:**
  Inhibiting AChE/BuChE enzymes increases acetylcholine (ACh) levels, which are deficient in AD patients.

- **Anti-Amyloidogenic Activity:**
  Plants like *Curcuma longa* and *Withania somnifera* prevent the formation and aggregation of -amyloid fibrils.

- **Antioxidant Activity:**
  Phytochemicals (phenols, flavonoids) neutralize free radicals, protecting neurons from oxidative stress-induced damage.

- **Neuroinflammation Reduction:**
  Modulating pathways like NF-B, medicinal plants inhibit the release of inflammatory cytokines (TNF-, IL-1).

Advantages of Medicinal Plants & Limitations & Challengesh :

Advantages of Medicinal Plants

- Multi-target therapeutic approach
- Lower toxicity compared to synthetic drugs
- Cost-effective and widely available
- Potential for long-term use

Limitations and Challenges

- Lack of large-scale clinical trials
- Variability in plant composition
- Poor bioavailability of some compounds (e.g., curcumin)
- Standardization issues

Herbal Medicine :

Simple herbal supplemental agents and therapeutic agents are included in the idea of HM in the conventional medical system. HMs can be made up of a single natural component, a fraction rich in a particular compound, a single medicinal plant, or a mixture of more than 10–20 different medicinal herbs. The World Health Organization (WHO) defined HM in 2005 as plant-derived products or preparations that have therapeutic or other advantages for human health and incorporate either raw or processed components from multiple plants. According to the National Institutes of Health, HM is a type of natural product that is a part of complementary and alternative medicine (CAM) and is typically sold as a prescription pill or dietary supplement with the purpose of enhancing human health. A conventional or orthodox drug, in contrast, is described as "a chemical substance utilized in the treatment, cure, prevention, or diagnosis of disease or used to otherwise increase physical or mental well-being". The general consensus is that HM contains many components made from a single plant extract or several different herbal medicines. In this essay, we examine how this term largely describes HM. CAM, a collection of non-conventional medical systems, includes the use of HM as one of its

components in the treatment of disorders. According to data from 2008, the HMs market is expected to exceed $60 billion annually. According to estimates, 25% of all current medications come directly or indirectly from plants, including 60% of anti-tumor and antibacterial medications. Nearly 65% of the world's nations have rules and regulations governing the use of HMs.

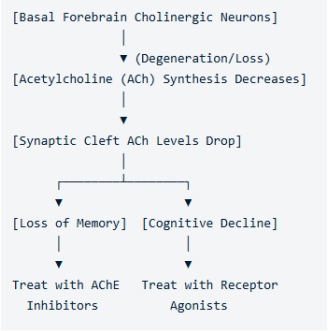
Pathophysiology of Alzheimer's disease :

Although these characteristics are not always present, neuroimaging of a patient with AD or another dementia may indicate atrophy of the brain, including enlarged ventricles and sulci and narrower gyri. The primary neuropathology factor behind AD symptoms is neuronal loss. Microscopically, senile plaques and neurofibrillary tangles are signs of Alzheimer's disease (NFTs). A protease cleavage result of the amyloid precursor protein, filamentous 3-amyloid, is seen in plaques, which are extracellular deposits. The aberrant rearrangement of microtubule-associated proteins, such as tau, causes NFTs to develop intracellularly. NFTs and senile plaques are both present to some extent in the brains of healthy elderly people despite being diagnostic of AD when seen in high quantities. When AD is in its early stages or in normal brains, f-amyloid plaques are diffuse and often benign deposits; however, as the disease progresses, the plaques take on a compact b-pleated shape and are subsequently linked to dystrophic neuritis. These advanced plaques are considered to be a more neurotoxic variety.

Cholinergic Hypothesis :

Acetylcholine was the first neurotransmitter to be found to be defective in AD (ACh). It was found that the short-term memory impairment in AD was largely caused by a cholinergic deficiency since cholinergic function is necessary for short-term memory function. In the cortex and hippocampus, regions of the brain important in cognition and memory, markers for cholinergic neurons such as choline acetyltransferase and acetylcholinesterase, enzymes responsible for the synthesis and breakdown of ACh, respectively, are diminished. Cholinergic neurons are primarily impacted in the nucleus basalis and the entorhinal cortex, where the earliest loss of neurons occurs. Up to 90% of the cholinergic neurons in the nucleus basalis of Mynert may go as the disease worsens.

Loss of cholinergic activity in these regions has been shown to be linked to reductions in learning ability and memory in animal studies. In the same way that dopaminergic impairments underlie Parkinson's disease and its clinical manifestations, it is believed that the resulting decrease in ACh-dependent neurotransmission causes the functional deficits in AD. Drugs that increase ACh levels in the brain have been the focus of clinical pharmacological trials in AD patients in an effort to make up for the loss of cholinergic function in the brain. ACh precursors, muscarinic agonists, nicotinic agonists, and



cholinesterase inhibitors have all been used as these medications. Cholinesterase inhibitors such as donepezil, rivastigmine, and galantamine are currently accessible and have been utilized in the best-developed and most successful methods to date. Most of these drugs' studies have been conducted on AD patients, with the majority of them concentrating on those with mild to moderate disease. The most recent AD medication shifts away from ACh enhancement and concentrates on a different receptor complex. Memantine had been used for many years in Europe before it was authorized for the US market in October 2003. Patients with moderate to severe illness stages are targeted by the marketing of memantine.

Pharmacological and Herbal Treatment :

ACh synapse degradation inhibitors are the mainstay of AD treatment, even though no medication has been demonstrated to entirely preserve neurons. The only medications recognized by the Food and Drug Administration as effective for treating AD are acetylcholinesterase/cholinesterase inhibitors and memantine. Although research has been done on other pharmaceuticals, their use is still debatable. Examples include selegiline, vitamin E, estrogen, and anti-inflammatory medications. Ginkgo biloba is one of the many additional medications that have been tried in an effort to alter the course of AD or ameliorate its symptoms. Tacrine, a cholinesterase inhibitor, is infrequently used because it could be hazardous to the liver and requires frequent laboratory monitoring. However, donepezil, rivastigmine, and galantamine frequently cause cholinergic side effects as nausea, anorexia, vomiting, and diarrhea. They also have low frequencies of significant adverse events. Only approximately 200 years ago, herbal medicines dominated the major pharmacopoeias, and many of the synthetic pharmaceuticals used today had their roots in the plant life. When basic and clinical pharmacology became the dominant fields of medicine, herbal medicine experienced a sharp downturn. However, there is ongoing interest in herbal treatment for many illnesses, including psychiatric and neurological conditions. There are several causes for this problem: Patients see that herbal medicine is consistent with their philosophical values and views, they are dissatisfied with conventional treatment, they want control over their healthcare decisions. Numerous research and documentation suggest that herbal remedies have a special role in the treatment of AD. The study on several Ayurvedic medicinal herbs that have demonstrated potential in reversing AD pathology is compiled in the current review. The report provides sufficient baseline data that could be used in drug discovery campaigns and development processes, thereby supplying new functional leads for AD. It does this by summarizing information regarding the phytochemical, biological, and cellular activities as well as the clinical applications of these various plants. The different Ayurvedic nervine herbs that are suggested for AD and their effects on the brain are described here.

Ashwagandha (Withania somnifera)

As a nervine tonic, aphrodisiac, and "adaptogen," ashwagandha is widely used in Ayurveda to assist the body adapt to stress . The root of ashwagandha, which belongs to the nightshade (Solanaceae) family, is the component that is most frequently used. It is classified as a rasayana (rejuvenative) and is thought to have antioxidant, free radical scavenging, and immune system-supporting properties. Ashwagandha has a soothing impact in contrast to other adaptogens, which have a tendency to be stimulating, and may therefore be especially beneficial for persons with AD. This herb may be used to induce relaxation since a complete alkaloid extract of ashwagandha root had a soothing impact on the central nervous system (CNS) in various mammalian species. In a recent double-blind, randomized, placebo-controlled trial on Ashwagandha's effects on stress, it was discovered that the herb's potential to improve focus and reduce symptoms of forgetfulness depended on dose, with 500 mg/day being more helpful. There were no further negative consequences discovered. This herb's aqueous extracts have been shown to boost cholinergic activity, including acetylcholine content and cholineacetyl transferase activity in rats, which may help to explain some of the effects on cognition and memory. Additionally, new studies have revealed fascinating details about this herb's capacity to promote neurite development. In human neuroblastoma cells, treatment with the methanol extract of Ashwagandha resulted in dose- and time-dependent neurite outgrowth. Ashwagandha was discovered to significantly raise the levels of the dendritic markers MAP2 and PSD-95 in cells, indicating that it promotes the growth of dendrites. In a follow-up study to the one mentioned above, the same research team gave amyloid peptide to cultured rat cortical neurons. This caused axonal and dendritic shrinkage as well as the loss of pre and postsynaptic stimuli. Following treatment with an Ashwagandha methanol extract, both axons and dendrites significantly recovered.

Turmeric (Curcuma longa) :

Turmeric comes from the plant Curcuma longa, often known as Haldi, and is used in curries and other hot cuisines from India, Asia, and the Middle East. Similar to many other herbal treatments, curcumin was first consumed as a meal before people realized it had powerful medical properties. Since ancient times, it has been widely utilized in Ayurveda (Indian system of medicine) as a painkilling and anti-inflammatory substance to treat pain and inflammation in the muscles and skin. It has also demonstrated anti-cancer qualities. In Ayurvedic medicine, curcumin is revered as a "cleanser of the body," and now, science is uncovering an increasing number of diseases that can be treated by turmeric's active components. Curcuma longa is the scientific name, and the Zingiberaceae family includes the gingers. Because it is sterile and does not generate seeds, turmeric is a plant. The plant bears dull yellow flowers and can reach heights of 3 to 5 feet. The plant's underground rhizomes or roots are used to make food

and medicine. The rhizome is a thick, fleshy underground stem that is encircled by the bases of previous leaves. Turmeric is a recognizable bright yellow spice that is made from rhizomes that have been boiled, dried, and crushed.

Epidemiological studies of Alzheimer's disease and effect of curcumin :

Numerous studies and research findings suggest that AD is less common and prevalent in India. In India, the prevalence of AD among persons aged 70 to 79 is 4.4 times lower than it is in the United States. Researchers looked into the relationship between curry consumption and cognitive function in 1010 Asians between the ages of 60 and 93. According to the study, people who consume curry frequently (more than once a month) and sometimes (less than once a month) scored higher on the MMSE test of cognitive function than people who consume curry never or infrequently.

Mechanism of action of curcumin on Alzheimer's disease :

The method by which AD destroys nerve cells is thought to involve several characteristics, including metal toxicity, beta-amyloid plaque development, oxidative damage, and inflammation.

Curcumin on haemoxygenase pathway:

An effective inducer of hemoxygenase, a protein that offers effective cytoprotection against several types of oxidative stress, is the natural antioxidant curcumin. Curcumin stimulates hemoxygenase activity by encouraging the inactivation of the Nrf2-keap1 complex and enhanced binding to no-1ARE. An early rise in reduced glutathione was seen after astrocytes were incubated with curcumin at a concentration that encouraged hemoxygenase activity, and then a large rise in oxidized glutathione content. Glutathione is a vital component for antioxidant enzymes that defend the mitochondria from endogenous oxygen radicals and is a significant antioxidant in the aqueous phase. Its level represents the body's ability to scavenge free radicals. Lipid peroxidation and oxidative damage result from GSH depletion, which harms tissues.

Beta-Amyloid plaques:

The presence of beta-amyloid plaques is the most obvious sign of AD. These plaques are essentially a collection of beta amyloid fibrils, which are tiny fibres. A proactive therapeutic approach for the treatment of AD would be the suppression of A-beta generation, prevention of A-beta fibril formation, and destabilization of pre-formed A-beta because the deposition of beta amyloid protein is a constant pathological hallmark of brains affected by AD. In compared to AD mice who did not get curcumin treatment, those that received low dosages of the herb saw a 40% reduction in beta-amyloid levels. Low doses of curcumin also resulted in a 43% reduction in the "plaque burden" that these beta-amyloid deposits had on AD mice's brains. Surprisingly, low dosages of curcumin administered over a longer period of time were actually more efficient than large doses at halting the neurodegenerative process associated with AD. Curcumin binds to amyloid beta and prevents its self-assembly at greater concentrations. Two aromatic end groups are among the key chemical characteristics of amyloid beta, and any changes to these groups have a significant impact on the protein's function. Curcumin crosses

the blood brain barrier and attaches to plaques because of its lipophilic nature. Curcumin destabilizes the A-beta polymer and was a more effective inhibitor of A-beta 40 aggregation. Curcumin inhibits aggregation and disaggregates to generate fibrillar A-beta 40 in in vitro tests. A Japanese study found that curcumin destabilizes the fA-beta (1-40) and fA-beta (1-42) as well as their extension utilizing fluorescence spectroscopic examination with thioflavin T and electron microscopic analyses. Isoxazoles and pyrazoles produced from curcumin bind to the amyloid beta peptide (Abeta) and prevent the metabolism of amyloid precursor protein (APP). Multi-photon microscopy showed that curcumin penetrates the blood-brain barrier and shrinks the senile plaques after being administered to APPswe/PS1dE9 mice for seven days. Another study found that curcumin increased the removal of amyloid-beta from the brains of AD patients through phagocytosis. The chemical characteristics of curcumin that have been clinically examined and its varied effects on AD point to the possibility of doing additional research and developing more effective medications based on curcumin for treating AD.

Brahmi (Bacopa monnieri)

The bitter-tasting creeper plant brahmi, also known as bacopa, is typically used in Ayurvedic medicine as a nerve tonic, diuretic, and cardiotonic as well as a treatment for epilepsy, insomnia, asthma, and rheumatism. Saponins and triterpenoid bacosapo nins, such as bacopasides III to V, bacosides A and B, and bacosaponins A, B, and C, are the main components of Bacopa monnieri (BM). The jujubogenin bisdesmosides bacopasaponins D, E, and F are additional saponin glycosides. Alkaloids, plant sterols, betulic acid, polyphenols, and sulfhydryl compounds are other components with antioxidant action. The reduction of divalent metals, scavenging of reactive oxygen species, reduction of lipid peroxide production, and inhibition of lipoxygenase activity could all be effects of BM. Traditionally, BM was utilized to enhance cognition and memory. The neuropharmacological effects and nootropic properties of BM extracts have been thoroughly studied. In order to assess the short-term safety and tolerability of an increased phytochemical composition of BM in healthy adult volunteers. Clinical, hematological, biochemical, and electrocardiographic parameters were carefully examined, but none of the volunteers who took a single capsule containing the enriched herb orally for 30 days (300 mg for the first 15 days and 450 mg for the following 15 days) experienced any negative side effects. The BM has now been offered in the Indian market for the treatment of memory and attention deficit disorders based on the aforementioned study and additional clinical studies conducted to establish the efficacy of BM in memory and attention disorders. These clinical investigations with Bacopa serve as a guide for future research with additional herbs to determine their dose ranges that are beneficial, how long it takes to reach therapeutic levels, and how they affect the body over a longer period of time.

Gotu Kola (Centella asiatica)

Gotu kola is one of the key revitalizing herbs for nerve and brain cells in the Ayurvedic school of medicine and is thought to be able to increase intellect, lifespan, and memory. There may be a role for gotu kola in the treatment and prevention of AD and beta-amyloid toxicity. Asiaticoside derivatives, such as asiatic acid and asiaticoside, have been shown to decrease hydrogen peroxide-induced cell death, decrease free radical oncentrations, and inhibit beta-amyloid cell death in vitro. In the brains of PSAPP (APP/ Sw x PS1M146L) mice, gotu kola extracts restored beta-amyloid pathology and altered the oxidative stress response.

Jyotishmati (Celastrus paniculatus)

Jyotishmati is a prized medicinal plant that has long been utilized in Ayurveda to enhance memory, focus, and cognitive function because of its beneficial effects on the brain. The aqueous extracts of CP seeds are antioxidant and cognitively stimulating. In part because of their antioxidant qualities and capacity to stimulate antioxidant enzymes, CP extracts rescued neuronal cells from H2O2-induced damage. By modifying glutamate receptor function, CP extracts also provided protection for neuronal cells from glutamate-induced damage. Additionally, the CP extracts shielded neuronal cells because of their capacity to stimulate the antioxidant enzyme catalase, reduce lipid peroxidation, and scavenge free radicals. Additionally, CP seed aqueous extracts contain dose-dependent cholinergic action, which enhances memory function.

Jatamansi (Nardostachys jatamansi)

Jatamansi is safe and has balancing effects, much like its relative valerian in Western culture. The plant has a long history of therapeutic usage and enjoys great respect in the Ayurvedic medical system. The plant's rhizomes and roots have been the subject of chemical research because they are useful as medicines. Numerous sesquiterpenes and coumarins are present in them. One of the main ingredients of the root essential oil is the calming sesquiterpene valeranone, which is also present in valerian. Spirojatamol, nardostachysin, jatamols A and B, and calarenol are examples of further terpenoids. The main coumarin is jatamansi. Nardostachys jatamansi (NJ) extracts significantly reduced all of the symptoms of chronic fatigue syndrome (CFS) in rats, according to studies on the plant's function in the central nervous system. NJ extracts decreased CFS-induced elevations in lipid peroxidation, nitrite, and superoxide dismutase levels as well as low catalase levels. The information shows that NJ has strong antioxidant properties. Similar to this, an alcoholic extract of this plant was given to young and old mice, and it dramatically enhanced learning and memory while also reversing the amnesia brought on by scopolamine and diazepam. Additionally, it corrected mice's naturally occurring aging-induced amnesia, indicating that the substances in this plant may be helpful in regaining memory in older people as well as in those suffering from age-related dementia.

Materials and Methods :

1. Reagents and Chemicals Used

The measurements of the activities were carried out using a 96-well microplate reader (PerkinElmer Multimode Plate Reader EnSpire) at the National Center for Biotechnology Research. The chemical products and reagents used were: Folin–Ciocalteu reagent (FCR), 1,1-diphenyl-2-picrylhydrazyl (DPPH), butylated hydroxylanisole (BHA), butylated hydroxyltoluene (BHT), quercetin, α-Tocopherol, ascorbic acid, neocuproine, 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonicacid)-diammoniumsalt(ABTS), trichloroacetic acid (TCA), potassium ferricyanide (C6N6FeK3), phenanthroline, silver nitrate (AgNO3), trisodium citrate (Na3C6H5O7), acetylcholinesterase from electric eel (AChE, Type-VI-S, EC 3.1.1.7, 827.84 U/mg, Sigma), butyrlcholinesterase from horse serum (BChE, EC 3.1.1.8, 7.8 U/mg, Sigma), acetylthiocholine iodide, S-Butyrylthiocholine iodide, 5,5′-Dithiobis(2-nitrobenzoic) acid (DTNB), and galantamine, which were obtained from Sigma-Aldrich; and sodium carbonate, aluminum nitrate (Al(NO3)3, 9H2O), iron (III) chloride (FeCl3), sodium bicarbonate (NaHCO3), copper (II) chloride (CuCl2), potassium persulfate (K2S2O8), and potassium acetate (CH3CO2K), which were obtained from Biochem Chemopharma. All other chemicals and solvents were of analytical grade.

2. Raw Material Extraction

The aerial parts of M. piperita were collected in 2020 from the Mila region (northeast Algeria). The plant was authenticated by Mr. Mohamed Kaabeche, a botanist at Ferhat Abbas University, Setif. A sample specimen was deposited in the herbarium (MEP 55/04/20) (Tables S1–S3). According to the British Pharmacopoeia, the essential oil was hydro-distilled for 3 h with a Clevenger apparatus before being stored at 4 °C until use. The aerial parts (60 g) of the plant were divided into three parts in equal weight (20 g) and separately extracted by maceration with 200 mL of solvents (chloroform, hexane, and petroleum ether). The extraction was performed three times with renewal of the solvent. The contents

were then filtered through Whatman filter paper no.1. The filtrate was evaporated at 40 °C by a rotary evaporator and kept in a refrigerator at 4 °C until use.

3. GC-MS Analysis

Agilent GC-MS using an HP-5MS column was employed with a temperature programmed at 60 °C in isothermal conditions, and helium gas was used at a 0.5 mL/min rate flow. The MS parameters were: electron energy, 70 eV; ionization, 2 A; temperature, 280 °C; resolution, 1000 scan time, 5 s. The following temperature program was applied: 40 °C to 150 °C, for 8 min and 5 min, respectively, and at a rate of 5 °C/min to 260 °C for 15 min. Compounds were identified by comparing the mass spectra with the spectral libraries NIST and Wiley.

4. Colorimetric Total Phenolic and Flavonoid Content

- **Colorimetric Total Phenolic (CTP)**
  The total phenolic content was determined by the Folin–Ciocalteu method with slight modification and the results were expressed in µg of gallic acid per mg of extract.
- **Colorimetric Total Flavonoid (CTF)**
  The total flavonoids were determined using the aluminum nitrate method and the results were expressed in µg of quercetin per mg of extract.

5. Colorimetric Antioxidant Capacity

In plants, antioxidants can be found in many different groups and forms, including carotenoids, phenolic compounds, benzoic acid derivatives, flavonoids, and coumarins. For the measurement of antioxidant content and total antioxidant capacity, various spectrophotometric techniques are used to provide a thorough profile of the antioxidant content and capacity of the tested samples. In this study, the antioxidant capacity of the essential oil and the nonpolar extracts was assessed using six different methods including DPPH•, reducing power, phenanthroline, silver nanoparticle, ABTS•+, and CUPRAC, compared with five standards: BHA, BHT, ascorbic acid, quercetin, and α-tocopherol.

6. Colorimetric DPPH Assay

The DPPH assay was evaluated according to the method of and BHA, ascorbic acid, quercetin, α-tocopherol, and BHT were used as positive standards for comparison of the obtained results.

7. Colorimetric Reducing Power Assay

The antioxidant capacity of the essential oils and the nonpolar extracts was evaluated using the potassium ferricyanide method and BHA, ascorbic acid, quercetin, α-tocopherol, and BHT were used as positive standards for comparison of the obtained results.

8. Colorimetric Phenanthroline Assay

The activity was determined by the phenanthroline method of and the results were given as A0.50 (µg/mL). BHA, ascorbic acid, quercetin, α-tocopherol, and BHT were used as positive standards for the comparison of the obtained results.

9. Colorimetric Silver Nanoparticle Assay

The silver nanoparticle activity was evaluated according to the method described by and the results were given as A0.50 (µg/mL). BHA, ascorbic acid, quercetin, α-tocopherol, and BHT were used as positive standards for the comparison of the obtained results.

Colorimetric ABTS Assay

The ABTS•+ activity was evaluated by the method in and the results were given as IC50. BHA, ascorbic acid, quercetin, α-tocopherol, and BHT were used as positive standards for the comparison of the obtained results.

10. **Colorimetric Cupric-Reducing Antioxidant Capacity (CUPRAC)**

The cupric-reducing antioxidant capacity was measured by the method of and the results were given as A0.50 (µg/mL). BHA, ascorbic acid, quercetin, α-tocopherol, and BHT were used as positive standards for the comparison of the obtained results.

11. Colorimetric Cholinesterase Inhibition Activity

The Ellman method was used to estimate the inhibitory potential of the studied samples and galantamine was used as a positive standard for the comparison of the obtained results.

12. Statistical Analysis

All estimated parameters were subjected to one-way analyses of variance (ANOVA), with the various tested extracts and essential oils serving as fixed factors. This was conducted in triplicate. An analysis of the differences in means between each treatment was carried out using the Tukey's multiple range test whenever the ANOVA test was statistically significant ($p < 0.05$).

13. Molecular Docking

A molecular docking study was conducted using GOLD version . Before running the docking experiments, potential ligands were built and prepared with the Maestro version 11.3 of Schrodinger's LigPrep module . For each ligand, several structures (up to 32) with various tautomers, protonation states at pH = 7.4 ± 1, and enantiomers were generated. All of these conformations were minimized and compiled as mol2 files. The crystal structures of AChE (4M0E) and BChE (2XQF) were downloaded from the Protein Data Bank (http://www.rcsb.org/ accessed on 20 April 2022) . For each enzyme, the residues within a radius of 6 Å around the co-crystal ligand were considered active sites. This selection was refined by adding every residue beyond 6 Å considered important for the continuity of the cavity . Then, all hydrogen atoms were added. Thereafter, the protonated states were defined and the side-chain orientation of the active site's residues was controlled using Schrödinger's protein preparation wizard. Finally, the intramolecular energy was lowered, and a mol2 file was saved. Enzyme ligand interactions were visualized using Maestro software version .

The co-crystallized ligand of each enzyme was removed and redocked in the active site using GOLD in which the target atoms are fixed, and the ligands are flexible. After successful redocking of the co-crystallized ligand (RMSD value < 1 Å), the same docking parameters were used for M. piperita major compounds .

Evaluation Process:

1. Absorbance Measurement:

- The intensity of the yellow color is measured at **412 nm**.
- **Higher Absorbance:** Means higher enzyme activity (the extract did not inhibit the enzyme well).
- **Lower Absorbance:** Means the extract successfully blocked the enzyme from breaking down the substrate.

Calculation of Percentage Inhibition:

The formula used is typically:

% Inhibition = [(Control Absorbance - Sample Absorbance) / Control Absorbance] × 100

Determination of IC_{50}:

Researchers test multiple concentrations to find the **IC_{50} value**—the concentration of the extract required to inhibit 50% of the enzyme activity. A **lower IC_{50}** indicates a more potent extract.

Antioxidant Activity:

Since oxidative stress plays a key role in Alzheimer's disease, antioxidant activity is evaluated using:

DPPH Radical Scavenging Assay:

- DPPH solution is mixed with plant extract.
- Incubated in dark for 30 minutes.
- Absorbance measured at 517 nm.

Hydrogen Peroxide Scavenging Assay:

- Measures the ability of extract to scavenge H_2O_2.

Reducing Power Assay:

- Indicates electron-donating capacity of the extract.

2. DPPH Radical Scavenging Assay:

This is the most common "screening" tool due to its stability and ease of use.

- **Mechanism:** DPPH (2,2-diphenyl-1-picrylhydrazyl) is a stable free radical with a deep violet color. When an antioxidant donor provides an electron, the DPPH is reduced and turns yellow.

The Process:

- Mix DPPH solution with varying concentrations of your plant extract.
- **Incubate:** 30 minutes in the dark (DPPH is light-sensitive).
- **Measurement:** Use a spectrophotometer at **517 nm**.

- **Result:** A decrease in absorbance indicates higher scavenging activity. This is usually expressed as an **IC_{50} value** (the concentration required to inhibit 50% of the DPPH radicals).

3. Hydrogen Peroxide (H_2O_2) Scavenging Assay :

H_2O_2 is not a free radical itself, but it can cross biological membranes and generate the highly toxic hydroxyl radical (•OH) inside cells.

- **Mechanism:** This assay measures the disappearance of H_2O_2 when incubated with the extract.
- **The Process:**
- H_2O_2 solution is prepared in a phosphate buffer.
- Extract is added and incubated (usually 10 minutes).
- **Measurement:** Absorbance is typically read at **230 nm**.
- **Significance:** In Alzheimer's, H_2O_2 contributes to the formation of amyloid plaques. High scavenging activity here suggests the extract could protect against plaque-induced oxidative damage.

4. Reducing Power Assay :

This assay measures the "antioxidant potential" by looking at the extract's ability to donate electrons to convert oxidized species into stable forms.

- **Mechanism:** It measures the transformation of **Ferric (Fe^{3+})** to **Ferrous (Fe^{2+})**.
- **The Process:**
- Extract is mixed with potassium ferricyanide and trichloroacetic acid.
- Added ferric chloride () reacts with the mixture.
- **Measurement:** Absorbance is measured at **700 nm**.

- **Result:** Unlike the other two tests, a **higher absorbance** indicates a stronger reducing power (more "Prussian blue" color formation).

RESULTS:

The present study evaluated the anti-Alzheimer potential of the selected medicinal plant extract using various in vitro assays and (if applicable) in vivo models. The results obtained are summarized below:

1. Phytochemical Screening

Preliminary phytochemical analysis of the plant extract revealed the presence of:

- Alkaloids
- Flavonoids
- Phenolic compounds
- Tannins
- Saponins

Phytochemical	Typical Biological Activity	Common Qualitative Test
Alkaloids	Pain relief (analgesic), antimicrobial, and central nervous system effects.	**Mayer's Test**: Creamy white precipitate. **Wagner's Test**: Reddish-brown precipitate.
Flavonoids	Potent antioxidants, anti-cancer, and anti-inflammatory agents.	**Alkaline Reagent Test**: Intense yellow color that turns colorless with acid.
Phenolic Compounds	Major antioxidants; protect cells from oxidative stress.	**Ferric Chloride Test**: Deep blue or green coloration.
Tannins	Astringent (wound healing) and antimicrobial properties.	**Lead Acetate Test**: Bulky white or yellow precipitate.
Saponins	Natural detergents; antifungal and cholesterol-lowering potential.	**Foam Test**: Persistent "honeycomb" froth after vigorous shaking.

Discussion:

Evaluation of Anti-Alzheimer Potential of a Medicinal Plant

Alzheimer's disease is a progressive neurodegenerative disorder that mainly affects memory, thinking ability, learning capacity, and behavior. It is one of the leading causes of dementia in elderly people worldwide. The disease is characterized by degeneration of brain cells, formation of beta-amyloid plaques, neurofibrillary tangles, oxidative stress, inflammation, and reduction in neurotransmitters such as acetylcholine. Current synthetic drugs used for Alzheimer's disease provide only symptomatic relief and may produce side effects after long-term use. Therefore, medicinal plants have gained significant attention as safer and cost-effective alternatives for the management of Alzheimer's disease.

Medicinal plants contain several bioactive phytochemicals such as alkaloids, flavonoids, tannins, terpenoids, saponins, glycosides, and phenolic compounds that possess neuroprotective properties. These compounds may help in improving memory, reducing oxidative stress, inhibiting acetylcholinesterase enzyme activity, preventing neuronal damage, and protecting brain function. Due to these therapeutic effects, many researchers are evaluating medicinal plants for their anti-Alzheimer potential.

The evaluation of anti-Alzheimer activity of medicinal plants generally begins with collection and authentication of plant material followed by extraction using suitable solvents such as ethanol, methanol, or water. The prepared extracts are then subjected to phytochemical screening to identify active constituents responsible for therapeutic activity.

One of the major mechanisms involved in Alzheimer's disease is the deficiency of acetylcholine neurotransmitter in the brain. Therefore, inhibition of acetylcholinesterase enzyme is considered an important therapeutic target. Many medicinal plant extracts show acetylcholinesterase inhibitory activity, which may improve cognitive function and memory retention. In vitro studies are commonly performed to evaluate this enzyme inhibition property.

Conclusion:

The creation of AD treatment methods has advanced greatly. Anti-inflammatory, anti-amyloid, anti-oxidant, and pro-cholinergic medications are a few of these tactics. For a therapeutic approach to be used successfully in clinical trials, it is important to have a better understanding of both the harmful and helpful effects of the medications. FDA-approved medications are currently available to treat AD symptoms and temporarily ease dementia. Though they typically have negative side effects, these medications do not treat the disease by changing its pathophysiology. The creation of alternative therapy modalities for AD remains very important. Recently, herbal medications have undergone extensive testing in human studies as well as in animal and cell models of AD. Herbal medications have fewer hazardous side effects, are easily absorbed via the BBB, and have a variety of synergistic effects, such as increased cognitive and cholinergic functioning. As a result, herbal medicines seem to be a potential complementary therapy for AD patients. However, more investigation into each herb's pathophysiology and phenotypic behavior in carefully planned clinical trials is required in order to evaluate their negative effects in AD patients.

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