**Project on**

**A Review on indigenous plants and their phytochemicals used for the prevention and treatment of Alzheimer's disease (AD)**

[In the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy]

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# APPROVAL

This project paper, A review on indigenous plants and their phytochemicals used for the prevention and treatment of Alzheimer's disease (AD) submitted to the Department of Pharmacy, Faculty of Allied Health Sciences, Daffodil International University, has been accepted as satisfactory for the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy and approved as to its style and contents.


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……………………………                    Internal Examiner 1


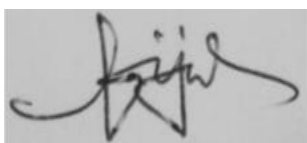…………………………….                    Internal Examiner 2


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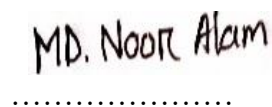
# DECLARATION

I hereby declare that this project reports A review on indigenous plants and their phytochemicals used for the prevention and treatment of Alzheimer's disease (AD), is done by me under the supervision of Farhana Israt Jahan Assistant Professor Department of Pharmacy Faculty of Allied Health Sciences Daffodil International University, I also declare that neither this project nor any part thereof has been submitted elsewhere for the award of Bachelor or any degree.

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Finally, I would like to express my gratitude towards my parents and other family members for their kind cooperation and encouragement which helped me in completion of this project.

# DEDICATION

*My Parents*

*The persons who always encourage me in every sphere of my life.*

## Abstract

As a devastating neurological ailment, Alzheimer's disease (AD) requires significant research on appropriate treatment alternatives. The effects of plant extracts on the reduction of AD symptoms have been thoroughly investigated. An important measure of naturally occurring substances and plant extracts with the ability to inhibit the enzyme AChE have been found as a result of the fact that naturally-occurring molecules from plants are thought to be a potential source of novel inhibitors, which, in accordance with the cholinergic hypothesis raises the brain's acetylcholine levels, which enhances cholinergic function. functions in Alzheimer's patients and reduces the symptoms of this neurological condition. Presented here highlights of around 35 studies in all, representing the most significant report papers between 2006 and 2022. plant-derived substances, plant extracts, and essential oils were discovered to cause AChE inhibition in the first semester. These impacts are brought on by plant extracts from a few different species, including Ginkgo Biloba, Corydalis (Papaveraceae), Stephania venosa (Menispermaceae), Catharanthus roseus (Apocynaceae), Ervatamia hainanensis (Apocynaceae) stems, Curcuma longa, Bacopa monnieri etc. There are many bioactive plants in our country which can cure Alzheimer's disease by proper using this plant compound. So we should do more research on these bioactive plants.

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# Chapter one
# Introduction

# A Review on indigenous plants and their phytochemicals used for the prevention and treatment of Alzheimer's disease (AD)

## 1. Introduction

Alzheimer's disease (AD) is a neurological condition that worsens over time and is linked to memory loss. and a cognitive impairment. It is distinguished by little to no Patients with AD have acetylcholine in their brains. Consequently, the cholinergic theory, acetylcholinesterase suppression (AChE), an enzyme that facilitates the breakdown of acetylcholine, boosts the brain's acetylcholine levels, resulting in enhancing cholinergic processes in people with AD. Additionally, despite the fact that it is well agreed upon that AChE Indicators of AD can be lessened with antagonists (AChEi), but they neither stop nor stop the spread of the disease. the majority of medications AD therapy options at the moment include AChEi:n Galantamine (1), tacrine (2), donepezil (3), and rivastigmine (4), each of which has a minimal impact and some form of consequence [1]. Rivastigmine (3), a natural AChEi alkaloid that served as the basis for the lead chemical, received US-FDA approval in 2000. The US-FDA recognized galantamine (4), a natural alkaloid that was initially discovered in Galanthus spp., in 2001. In China, Huperzine A (5), an alkaloid found in Huperzia spp., is used to treat the symptoms of AD and is marketed as a nutritional supplement for memory support. This alkaloid has undergone extensive research, with encouraging findings emerging from investigations on its potency, tolerability, and safety, as well as from assessments of animals' intellectual function. Considering the relationship between regulators 3, 4, and 5 AChEi are crucial to using natural items therapeutic approach for the treatment of AD, numerous studies Several teams have concentrated their research on naturally occurring plant-derived chemicals as potential sources of either novel or AChEi that works better. These investigations produced the finding of several significant secondary metabolites as well as plant extracts, which are both distinguished by the capacity to prevent AChE. Conversely, the reality that a sizeably substantial number of research papers have reported in this area over the past few generations may plainly be seen due to the advancement of colorimetric techniques, which enabling the quick and simple filtering of many samples. The most commonly used technique for measuring anti-AChE inhibition effect and detecting AChEi, even in complicated combinations, is Ellman's [2–6]. Over the past few years, a variety of studies on the recently found AChEi

derived from plants, fungi, and marine creatures have also been published [7–10]. The bulk of these AChEi, notably indole, isoquinoline, quinolizidine, piperidine, and steroidal alkaloids, are classified as alkaloids. On the contrary extreme, a number of strong and non-alkaloidal AChEi have been isolated from terpenoids, flavonoids, and other phenolic chemicals found in nature. Remarkably, despite the fact that there is a wealth of literature on the investigation of AChEi derived from plants, this topic continues to be a focus of research as evidenced by the rising number of publications submitted each year. As a result, the goal of this study is to give a thorough assessment of the literature, especially that published between 2006 and 2012 (first semester) on chemicals derived from plants, plant extracts, and essential oils that have been shown to inhibit AChE. It is advised that readers check the aforementioned reviews if they are interested in prior findings as well as Only those studies presenting quantitative results (IC50 and/or percentage of inhibition at a specific concentration) have been included for the sake of conciseness and to concentrate our emphasis on the most pertinent findings. The present review did not include extracts or essential oils with IC50 > 0.5 mg/ml since they were deemed to be only mildly active. Except for a few, only molecules with IC50 50 M have been taken into account. Additionally, results on AChE inhibition included in the systematic study, unless otherwise noted, pertain to in vitro tests using AChE from electric eel. Synthetic/semisynthetic AChEi or natural AChEi of fungal, marine, or microbial origin.

## 1.1 Microglia Induced Neuro-inflammation in Alzheimer's Disease

Microglial cells, which make up around 15% of the total number of cells in the brain, are widely distributed throughout the central nervous system (CNS) of the body. As the indigenous macrophages, they are essential for immune defense and CNS homeostasis maintenance. [14] Microglia are activated and scavenge thru out the entire brain when pathogenic infiltration, tissue injury, and matrix proteins are present. DAM typically displays a distinctive two aspects methodology as AD developments; it starts with an initial TREM2-independent excitation that includes changes in the microglia markers and genetic algorithms (ga with AD [20] and is then decided to follow by a supplemental TREM2-dependent excitation that is characterized by the representation of high levels of lipid metabolism and phagocytic gene petitions. [21] Its most important feature associated with

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AD is withering, namely the aging of the microglia, which is a critical factor in the onset of AD. Age-related changes in the phenotype and functioning of microglia include increased expression of pro-inflammatory cytokines such as interleukin-1beta (IL-1), tumor proliferation factor-alpha (TNF-), and IL-6, among others. Dystrophic microglia are also present in aging and AD brains. [22] Recent research has demonstrated a tight relationship between immunological aging, neuro-inflammation, and AD. Inflammasome activation has been directly connected to time of life functional decline, and microglial-induced neuro-inflammation has been proven to be a significant driver of AD progression. [23]
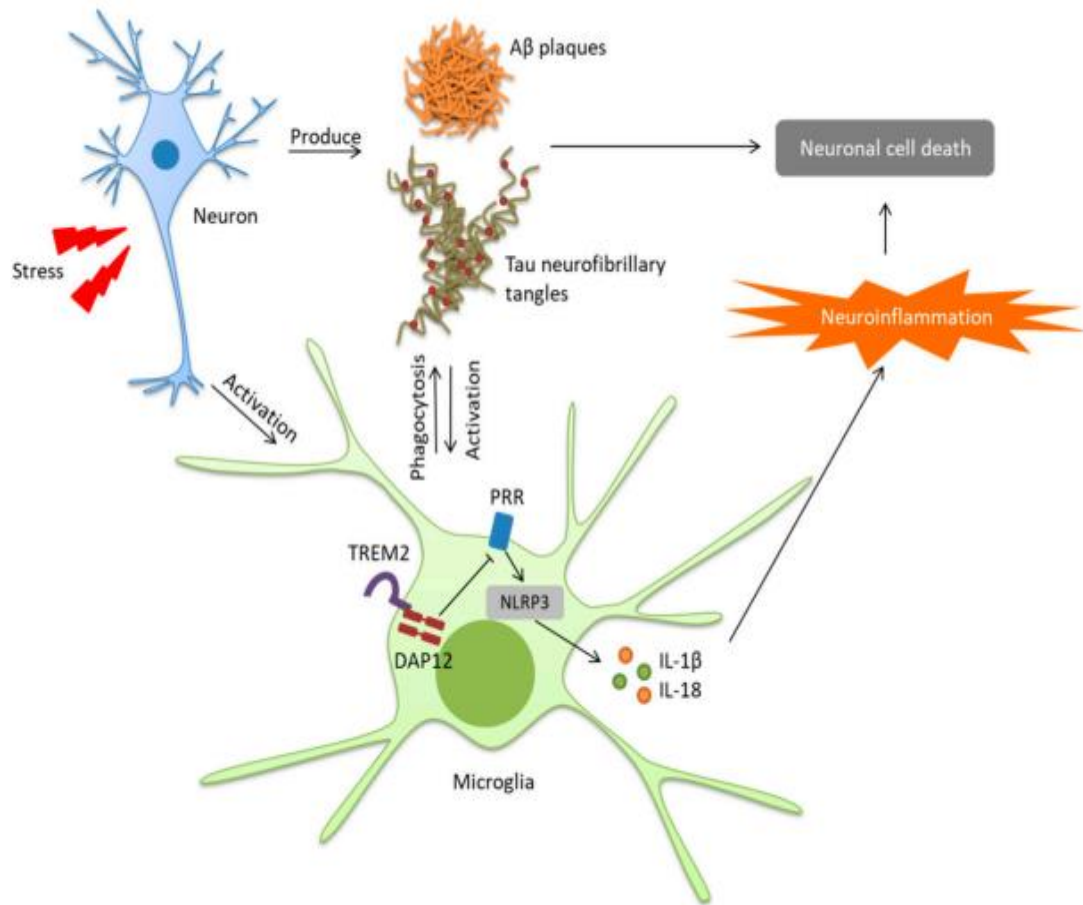


Figure 1: Microglia induced neuroinflammation in Alzheimer's disease. [24]

## 1.2 Diagnosing Alzheimer's dementia

In order to diagnose Alzheimer's dementia, your primary care physician, a physician with instruction in having to treat developmental disorders (a neurologist), or a physician with training in treating older adults (a geriatrician), will review your symptoms, [57] medical history, medication information, and have a conversation with someone who is well familiarized with you, such as a close friend or family member. [58] Your doctor will also perform a physical examination and many tests on you. When you see the doctor, they will evaluate: [59] Regardless of whether your cognitive or memory capabilities are impaired, or whether your character or conduct change, the severity of your memory loss or mental changes How your intellectual problems affect your incapacity to carry out daily tasks. the cause of your discomfort Your doctor might advise comprehensive memory tests or other scientific or brain imaging examinations. [60-63]
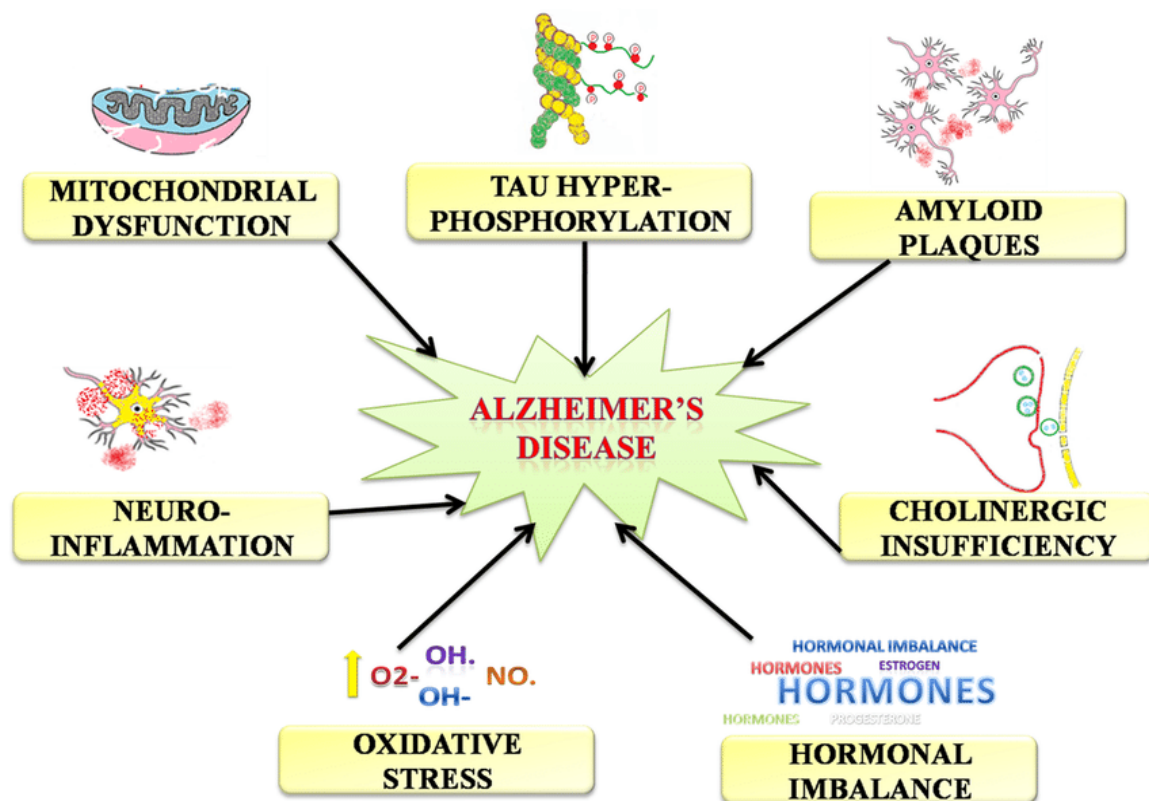


Figure 2: Causes of Alzheimer's disease [64]

## 1.3 Pathogenesis of Alzheimer's disease

AD's pathogenesis has so far remained mostly unknown. The much more prevalent form of AD, late onset sporadic AD, is caused by the environment and genetic predisposition. To comprehend the illness mechanism and create a medicine that would treat the sickness, numerous investigations have been conducted. Amyloid protein and aberrant tau protein, or both of them, are the two primary components that cause AD to occur. The excess supply of -amyloid proteins (A) and hyperphosphorylated Tau protein, which can result in dementia and the loss of synaptic connections and neurons in the cerebral cortex and hippocampus, are hallmarks of AD [2]. In AD patients, the buildup of beta-amyloid protein and neurofibrillary tangles has been seen. Neurofibrillary tangles and oxidizing are caused by the excess production and buildup of A, as well as lipid peroxidation, inflammation, cell feature disruption, and mortality [3]. The hyper phosphorylation of the tau protein causes tangles to accumulate in the hippocampus, which eventually results in cell death [4]. It has been shown that a variety of biochemical alterations within cells, including oxidative stress, inflammation, metabolism issues, disruption of Ca2+ homeostasis, and the buildup of unfolded/misfolded proteins, cause neuronal cell death in AD patients [5]. Oxidative damage and the inflammatory process are the two pathways that contribute to AD, and both of them have received extensive research in the research.
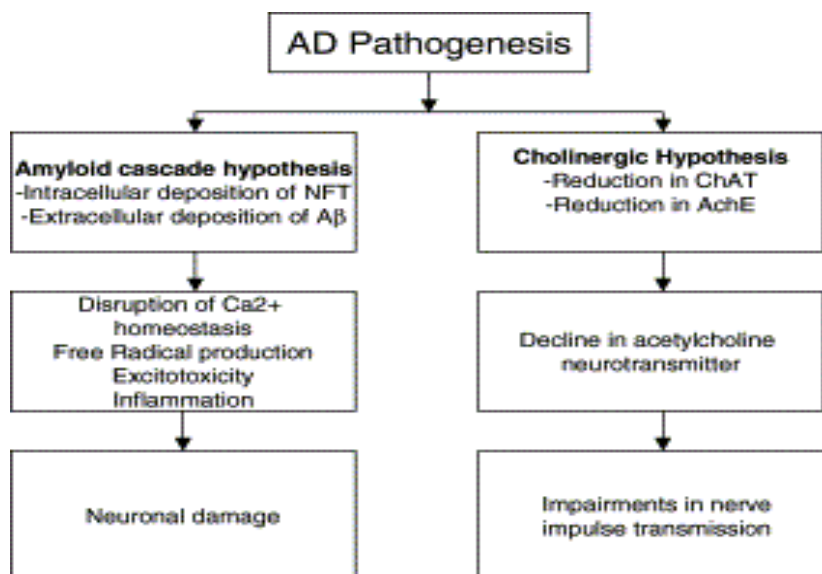


Figure 3: Pathogenesis of Alzheimer's disease [24]

# *Chapter two*
# *Purpose of the study*

## 2.1 Purpose of the study

➢ Therapy for Alzheimer's disease (AD) that can halt or delay the illness's course are desperately needed. With the median population age increasing, the financial and psychological toll that Alzheimer's disease has on patients, their families, and society as a whole will only get worse.

➢ There are many bioactive herbs that, when used properly, can treat Alzheimer's disease. A promising pharmacological approach will be evaluated in this study through short-term clinical studies. If the study is successful, the information gathered could improve Alzheimer's treatment almost immediately.

➢ The main objective of this investigation to find out plant which have pharmacological efficacy for management of Alzheimer's disease and also to find out bioactive compounds which have efficacy for inhibiting Acetylcholine.

# *Chapter three*
# *Materials & Methodology*

## 3.1 Materials and Procedures

A framework of research methodologies, as well as methods for gathering and analyzing data, is provided by a methodological review. This chapter discusses the techniques used in the investigation. Key phrases including " Alzheimer's disease" " plant used as Alzheimer's disease prevention," " compound used as Alzheimer's disease treatments" and "diagnostic" were searched for utilizing web-based search engines, academic bibliographic databases, PubMed, Research Gate, and Medline. It gives an account of the learning environment.

## 3.2 Research Methodology

This is a summary of prior studies on different plant extract trials as an Alzheimer's disease treatment. Searched many review paper on about this topic around 35 research paper (2006-2022) was downloaded. Then gained more knowledge about those paper & finally summarized those paper.

## 3.3 Inclusion Criteria

Studies on all type of indigenous plant candidates in clinical trials for Alzheimer's ailment.

## 3.4 Exclusion Criteria

Plants which are not indigenous to Bangladesh and also their bioactive compound.

## 3.5 Data Collection Procedure

Information regarding Alzheimer's collected by immediately reading previous research articles, while the remaining part came from scouring the internet for pertinent data. Numerous plant's activity regarding the disease was documented.

**3.6 Method of data analysis**

All of the information gathered was systematically arranged from earlier study reports.

# *Chapter four*
# *Results & Discussion*

**A Review on indigenous plants and their phytochemicals used for the prevention and treatment of Alzheimer's disease (AD)**

## 4.1 Medicinal Plants used for Alzheimer's disease

Several investigations reported that medicinal plants are utilized in the Alzheimer's disease treatment which includes following plants:

### 4.1.1 Corydalis (Papaveraceae)

Folk medicine practitioners who manage memory impairment utilizing Corydalis (Papaveraceae) have discovered benzylisoquinoline alkaloids with anti-AChE action [25]. The isoquinoline alkaloids stylopine (22), epiberberine (23), pseudo dehydrocorydaline (24), pseudocopsitine (25), and pseudoberberine were isolated from the ethanolic extract of the C. turtschaninovii tuber, which had earlier been discovered to suppress AChE. (26). The IC50 values for each of these alkaloids were 15.8, 6.5, 8.4, 4.3, and 4.5 M in the study using mouse brain cortex as a source of AChE enzyme, respectively [26]. Additionally, the two most active alkaloids, 25 and 26, were discovered to have anti-amnesic properties [17, 18]. The highest AChE suppression was seen in alkaloids from Corydalis species possessing benzylisoquinoline skeletons, aromatic methylenedioxy groups, and quaternary nitrogen atoms [7, 17, 18]. Six protoberberine alkaloids 23, 27, and 31 were discovered in Coptis chinensis rhizomes, which are commonly used during Chinese medicine to treat a variety of illnesses. The alkaloids found in Coptidis rhizomes were found to have cognitive-improving and neuroprotective consequences, and an assessment of their antiAChE interaction revealed that their IC50 samples ranged from 0.44 to 0.80 M for berberine (27), palmatine (28), jateorrhizine (29), coptisine (30), and groenlandicine (31), while they were marginally greater for epiberberine (23) (IC50 = [28].

### 4.1.2 Stephania venosa (Menispermaceae)

It was discovered that the Thai medicinal herb Stephania venosa (Menispermaceae) had a high level of AChE inhibitory action in the brain. To discover AChEi, the ethanolic extract of S. venosa was submitted to bioassay-guided fractionated (which have more efficacious for AD) [29]. Stepharanine (34), cyclanoline (35), and N-methyl stepholidine (36) were found to be the preceding reasonably healthy quaternary protoberberine alkaloids, with IC50 values of 14.10, 9.23, and 31.30 M, correspondingly. Similar fractionation techniques were used to determine the substances that inhibited AChE in Chelidonium majus (Papaveraceae) [30]. Eight-hydroxy dihydrochelerythrine (37), eight-hydroxydihydrosanguinarine (38), and berberine were shown to be the three active components (27). Compounds 37 and 38 were discovered to significantly induce anti-AChE activity with an IC50 = 0.61 and 1.37 M, respectively. [31]

### 4.1.3 Magnolia x soulangiana (Magnoliaceae)

The alkaloid-rich extract taken from Magnolia x soulangiana (Magnoliaceae) was used to isolate taspine (39). Although its selective inhibition is equivalent to that of tacrine (IC50 = 0.22 M), this alkaloid was shown to have a dose-dependent and persistent inhibitory action on AChE (IC50 = 0.33 M). It was also found to be more potent than galanthamine (IC50 = 3.2 M). Comparable findings were made when using human AChE in the in vitro experiment (IC50 = 0.54 M). Compound 39, which functions as a specific AChEi, was found to be ineffective towards BChE. (for Alzheimer's disease). [32]

### 4.1.4 Catharanthus roseus (Apocynaceae)

The plant Catharanthus roseus (Apocynaceae) is well well-known for producing vincristine and vinblastine, two alkaloids that are valued for their ability to fight cancer. Several additional substances with biological C. roseus is another species of interest. For instance, the When the plant's roots were isolated and the alkaloid serpentine (40), IC50 = 0.775 M), was discovered to be a powerful in vitro AChEi. comparable to physostigmine, which has an IC50 value of 6.45 M also which have ability to management AD [33].

### 4.1.5 Ervatamia hainanensis (Apocynaceae) stems

Traditional Chinese medicine plant Ervatamia hainanensis (Apocynaceae) stems were used for the biomarker fractionation that produced numerous monoterpenoid indole alkaloids, a number of which have significant AChE antagonistic effects [34]. For instance, it was discovered that coronaridine (41) and voacangine (42) each had an IC50 of 8.6 and 4.4 M, respectively, with the only difference between them being the methoxy group linked to the aromatic ring. The above values are comparable to galanthamine's (3.2 M) value. The presence of a hydroxyl group on the aromatic ring in 10-hydroxycoronaridine (43) caused a decrease in AChE inhibition (IC50 = 29 M), on the other hand. Coronaridine (41) and voacangine (42)—both indole alkaloids—were found in the stalks of Tabernaemontana australis (Apocynaceae), had been brain protective action (which help alzheimers patients). [35]

### 4.1.6 T. divaricata

**T. divaricata** of intriguing illustration of novel properties with strong AChE inhibition effect. Four bisindole alkaloids, were discovered to be produced by the crude alkaloid extract taken from the root of T. divaricata. [36] With an IC50 of 0.227 M for 19,20-dihydrotabernamine (44) and 0.071 M for 19,20-dihydroervahanine A (45), accordingly, the investigation of AChE inhibition demonstrated that both compounds are significantly higher active than galanthamine (IC50 = 0.594 M). Because compound 45 showed greater inhibition than compound 44, it is likely that the addition of a carbomethoxy group at C16' improves enzymatic inhibitory. [37]

### 4.1.7 Withania somnifera

Solanaceae is the family to which Withania somnifera originates. It had stabilizing impacts on stress and prevented memory loss (500 mg/d). In a prior investigation, Withania somnifera's cholinergic action was noted. Because it can raise the level of acetylcholine in the brain, withania somnifera has memory-improving and cognitive processing properties. [38] In human neuroblastoma cells, withania somnifera has been shown to have time- and amount of the drug neurotic expansion action. Strengthens dendritic and axon regrowth with withania somnifera. According to a molecular modeling research, withanamides A and C bind to A and prevent the production of fibrils. [39]

### 4.1.8 Curcuma longa

A member of the Zingiberaceae family is curcuma longa. Because of the consumption of turmeric, AD incidence is low in Southeast Asian nations. Its anti-inflammatory properties are linked to a reduced risk of AD. [40] The buildup of plaque in the brain is decreased by curcumin. Oxidative stress and amyloid pathology are reduced by turmeric. In one study, when animals with AD received low dosages of curcumin vs a control medication, the A level was lowered by up to 40%. Low doses of curcumin resulted in a 43% reduction in the amount of A plaques in the mice with AD's brains. [41] According to a prior study, low dosages of curcumin given over a lengthy period of time are more successful at treating AD than greater doses of the drug. [42]

### 4.1.9 Convolvulus pluricaulis

Convolvulus pluricaulis is a member of the Convolvulaceae family. It is employed as a recollection booster. Convolvulus pluricaulis aqueous and ethyl acetate extract has been linked to improved memory and learning, according to a prior study. [43] Additional study found that a variety of bioactive molecules, including steroids, anthocyanins, flavonol glycosides, and triterpenoids, are responsible for the nootropic and memory-improving effects. Convolvulus pluricaulis has been bred to reduce anxiety by controlling the body's production of the stress chemicals cortisol and adrenaline. [44] Convolvulus pluricaulis ethanolic extract and its aqueous and ethyl acetate fractions dramatically increased rats' capacity for learning and memorization. Convolvulus pluricaulis administration raised the acetylcholinesterase activity in the CA1 and CA3 hippocampus areas linked to recollection.[45]

### 4.1.10 Centella asiatica

The Apiaceae family includes Centella asiatica. It appears to contain saponins, asiaticosides, madecassoside, madasiatic acid, brahmoside, brahminoside, siatic acid, thankuniside, glycoside, triterpine, thankunic acid, vellarin, asiaticosides, thankuniside, and isothankuniside. [46] It also contains tannins, ascorbic acid, centoic acid, centellic acid, and centoic acid. The herb Centella asiatica is used to treat epilepsy, rheumatoid arthritis, psychological issue, and unhappiness. [47] It has diuretic, anti-convulsant, anti-spasmodic,

tonic, stimulant, emmenagogue, antioxidant, and spermatogenic properties (Heidari et al., 2007). The reactive response to stress was decreased and the A pathology was reversed by Centella asiatica. reported that Wistar rats treated with fresh leaf extract from Centella asiatica (Linn) had improved learning performance and declarative memory. [48] For this investigation, adult rats that were 2.5 months old were chosen. Outcomes were contrasted with those of control subjects that were similar in age. The dose of 6 mL of extract significantly improved spatial learning. Passive avoidance tests showed that the administration of Centella asiatica extract improved memory recall. [49] According to these findings, Centella asiatica improves adult rats' capacity for learning and memory retention. Centella asiatica's effectiveness in AD was observed by Veerendra and Gupta in 2003. It has been noted to have cognitive boosting properties and antioxidant effects. Rats were given aqueous extract of Centella asiatica (100, 200, and 300 mg/kg) for 21 days to treat cognitive impairment and oxidative stress brought on by the drug streptozotocin (STZ). On days 1 and 3, male Wistar rats received bilateral intracerebroventricular injections of STZ at a dose of 3 mg/kg. [50]

### 4.1.11 Celastrus paniculatus

Celastrus paniculatus is a member of the Celastraceae family. Its antioxidant action protected brain cells from harm caused by hydrogen peroxide. Administration of Celastrus paniculatus inhibits glutamine-induced toxicity's damaging effects on neuronal cells. The potential of Celastrus paniculatus to enhance brain health is due to the neurotransmitter acetylcholine that it enhances.[51] Celastrus paniculatus aqueous extract possesses anti-oxidant and brain-improving qualities. Because of their antioxidant and free radical scavenging properties, Celastrus paniculatus extracts could protect brain cells from hydrogen peroxide-induced damage. [52]

### 4.1.12 Nardostachys jatamansi

Nardostachys jatamansi is a member of the Caprifoliaceae family. It includes the sesquiterpene valeranone, which is used to relieve stress. [53] In a study, Nardostachys jatamansi improved learning and memory in old and young mice and restored amnesia caused by scopolamine and diazepam. Additionally, Nardostachys jatamansi cured

amnesia brought on by maturing. Nardostachys jatamansi has been shown to be effective in preventing stress-related memory loss. [54]

### 4.1.13 Bacopa monnieri

In herbal medicine, bacopa monnieri is frequently employed as a cardiotonic, diuretic, and nerve tonic as well as a remedy for rheumatism and asthma. It also applies to sleeplessness and epilepsy [49]. Saponins and triterpenoids are the primary chemical components of B. monnieri. These substances have been identified from B. monnieri, including bacopasides III, IV, and V, bacosides A and B, bacosaponins A and B, and bacosaponins C. It's also been claimed that B. monnieri contains several saponin glycosides, including jujubogenin bisdesmosides, bacopasaponins D, E, and F. In addition, several substances with antioxidant properties, also as alkaloids, sterols, betulic acid, polyphenols, and sulfhydryl, have been discovered in B. monnieri. B. monnieri has been used in conventional medicine to enhance cognition and memory [51]. The benefits of B. monnieri extracts on neuropharmacology and their nootropic properties have been the subject of numerous investigations [52]. B. monnieri increases protein kinase activity in the hippocampus, which has a nootropic effect [53]. Rats administered B. monnieri extract displayed reduced cholinergic degradation and an improvement in intelligence in an animal Alzheimer model [54]. According to another investigation, B. monnieri enhanced ACh levels while inhibiting AChE activity [55]. Additionally, B. monnieri preparations shielded neuronal cells from the harm done by -amyloids. B. monnieri may also lessen intracellular oxidative stress because neuronal chronic treatment with the extract showed lower ROS levels. According to a clinical research with AD patients, the polyherbal composition comprising B. monnieri extract significantly reduced the degree of inflammation and oxidative stress while also improving cognitive functioning [57]. To even further evaluate B. monnieri's possible neuroprotective activity towards AD, however, in-depth studies are required.

### 4.2: Bioactive compounds found to be effective against Alzheimer's Disease

There are many Bioactive compounds found to be effective against Alzheimer's Disease.
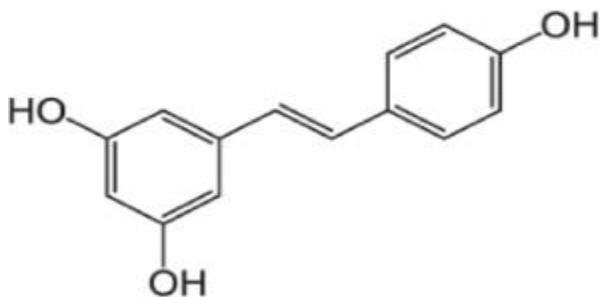
## 4.2.1 Resveratrol



Figure 4: Resveratrol

A polyphenolic substance that belongs to the stilbenes family, resveratrol is. Red wine, almonds, the skin of grapes and other fruits, and red wine all contain resveratrol [58]. Numerous research has demonstrated its anti-cancer, anti-inflammatory, antioxidant, and cardiovascular protection capabilities. They also revealed that it has neuroprotective effects and the ability to reduce blood glucose levels [59]. By scavenging Free radicals, elevating gluthatione levels, and enhancing endogenous antioxidants, resveratrol has a strong antioxidant effect [96]. By causing the non-amyloidogenic cleavage of APP and improving the clearance of -amyloid, resveratrol can also decrease the amount of -amyloids [60]. Additionally, neuronal cells' AChE activity was suppressed by resveratrol [61]. Resveratrol for AD was the subject of a randomized, double-blind, placebo-controlled experiment that demonstrated its safety, tolerability, and efficacy to lessen Alzheimer's vital signs.
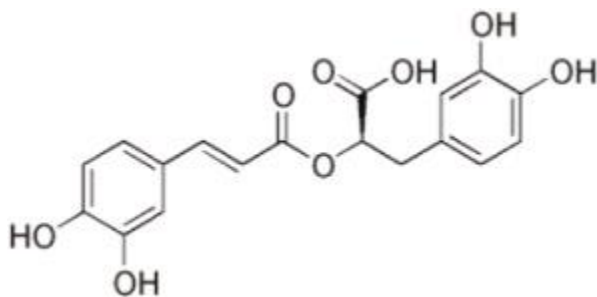
## 4.2.2 Rosmarinic acid



Figure 5: Rosmarinic acid

One sort of carboxylic acid found in several Lamiaceae species is rosmarinic acid. Numerous pharmacological properties of rosmarinic acid include neuroprotective, anticancer, antiviral, antibacterial, anti-inflammatory, and antioxidant properties [49]. The

ability of rosmarinic acid to decrease NF-B and TNF- production may be the strategy by which it dramatically reduces the risk of amyloid-induced memory loss [64]. The ability of rosmarinic acid to suppress ROS production, caspase-3 activation, and DNA fragmentation may provide an explanation for how it inhibits apoptotic pathways. By lowering lipid peroxidation and inflammatory processes, rosmarinic acid may also protect locomotor activity, short-term spatial memory, and biochemical abnormalities of brain tissue shown in a rat model of AD [113]. Investigations in clinical trials are required to support the effectiveness of rosmarinic acid versus AD.
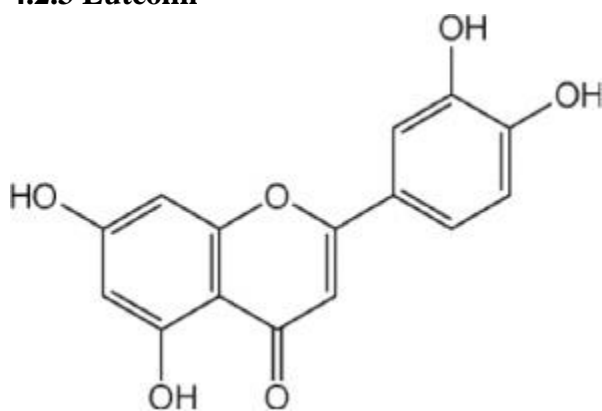
### 4.2.3 Luteolin



Figure 6: Luteolin

Many medicinal plants, including those in the Magnoliophyta, Pteridophyta, Bryophyta, and Pinophyta families, contain the flavonoid composite luteolin [60]. Variety of biological consequences of luteolin, including anti-inflammatory, antioxidant, anticancer, antimicrobial, and neuroprotective effects, have been demonstrated [61]. The antioxidant activity of luteolin and its capacity to control the tau phosphatase/kinase system may help to explain its ability to lessen the hyperphosphorylation of the tau protein that zinc causes [116]. Additionally, luteolin has been shown to reduce the expression of the amyloid precursor protein and the production of -amyloids [62]. By reducing internalized ROS production, enhancing the antioxidant endogenous system, including boosting SOD, CAT, and GPx functions, and activating the NRF2 pathways, luteolin can also decrease mortality. Additional study found that luteolin enhanced memory and cognition in a streptozotocin-

induced AD rat model [63]. Considering these investigations, further evidence from clinical trials are required to verify the benefits of luteolin in preventing AD.
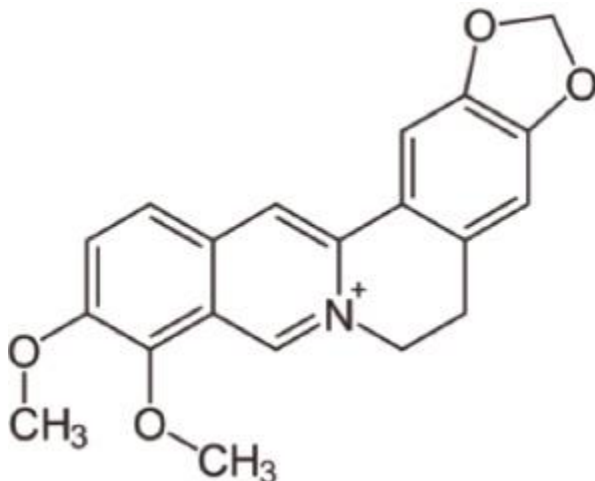
### 4.2.4 Berberine



Figure 7: Berberine

Isolated from the plant Coptis chinensis, berberine is a kind of isoquinoline alkaloids and a quaternary ammonium salt. Berberine has a wide range of biological effects, including cholesterol-lowering, AChE suppression, antioxidant action, and monoamine oxidase suppression [38]. Learning and spatial memory were greatly improved in berberine-fed Tg mice at a dose of 100 mg/kg orally [29]. The expressions of IL-6 and COX-2 brought on by -amyloid were considerably lowered in BV2 microglia cells treated with berberine [90]. Berberine also significantly decreased NF-B expression by blocking the PI3K/protein kinase B and MAPK pathways [28]. According to a study conducted, berberine can dramatically improve cognitive deficits, lower levels of A and APP, lessen the buildup of A in the hippocampus, and limit the growth of AChE activity.
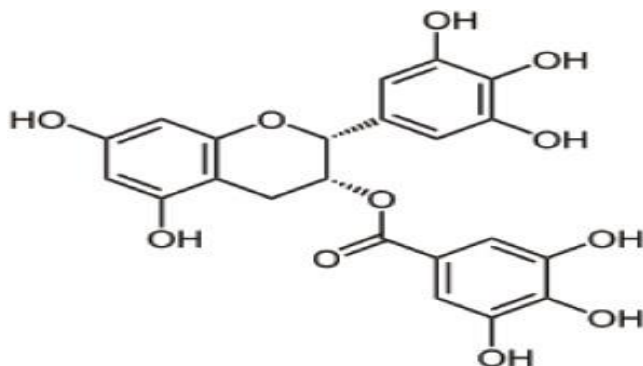
### 4.2.5 Epigallocatechin-3-gallate



Figure 8: Epigallocatechin-3-gallate

A catechin of the flavonoid group called epigallocatechin-3-gallate is discovered in Camellia sinensis. Numerous research has examined the impact of epigallocatechin-3-gallate on a wide range of disorders, including cancer, cardiovascular, and neurological diseases [82]. Epigallocatechin-3-gallate possesses powerful antioxidant activity. In mice with overexpressing dementia, epigallocatechin-3-gallate has been found to boost glutathione peroxidase activity, reduce AChE activity, and prevent the production of NO metabolites and ROS [46]. In mutation PS2 Alzheimer mice, epigallocatechin-3-gallate also improved learning and memory and reduced -secretase enzymatic activities. Epigallocatechin-3-gallate also reduced amyloid precursor protein production, inhibited beta-site APP cleaving enzyme 1 activity, and decreased -amyloid buildup to protect against LPS-induced memory problems and apoptosis. Additionally, it has been demonstrated to inhibit the expression of inflammation-related molecules like soluble intracellular adhesion, molecule-1 macrophage colony-stimulating factor, interleukin 1, IL-6, overexpression nitric oxide synthase (iNOS), and COX-2 as well as to prevent astrocyte initiation in neuronal cell.. In senescence-accelerated P8 mice, epigallocatechin-3-gallate has also been found to decrease A deposition and increase neprilysin enzyme production, which is the percentage enzyme for A's destruction.

# Chapter five
# Conclusion

**5.1 Conclusion**

For a few generations, there have been numerous studies to battle this terrible neurological condition. The manifestations of AD cannot be effectively reversed by any significant treatment or plant extract, despite the fact that a few medications are currently available for the management of AD and that several plants and their extracts are widely used in animal research and AD patients. There are numerous beneficial medicinal herbs that can be used to alleviate AD and lessen dementia. It has been demonstrated that the primary chemical constituents, such as flavonoids and alkaloids, have potent anti-AD actions. Therefore, it's essential to thoroughly research medicinal plants and discover fresh active AD components.

# *Chapter six*
# *Reference*

**Reference**

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