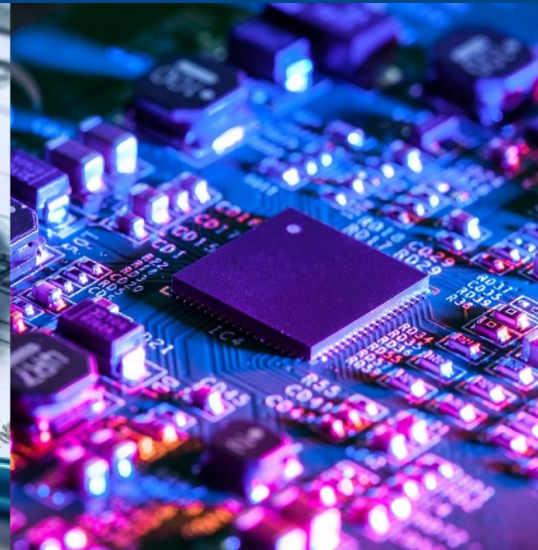
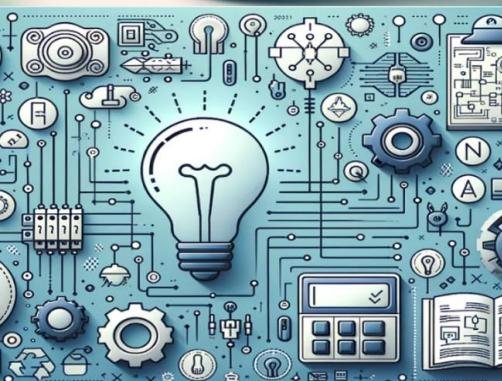




# International Journal of Multidisciplinary Research in Science, Engineering and Technology

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## International Journal of Multidisciplinary Research in Science, Engineering and Technology (IJMRSET)

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# Formulation and Evaluation of Herbal Powder for the Treatment of Dementia

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**ABSTRACT:** Alzheimer's disease, its pathophysiology, current treatment options, and potential therapeutic strategies, including the use of neuroprotective herbs. The discussion covers various hypotheses related to Alzheimer's disease, such as the amyloid cascade hypothesis, tau hypothesis, cholinergic hypothesis, excitotoxicity, and neuroinflammation. Several herbs are highlighted for their potential in managing Alzheimer's disease, including: Ashwagandha (*Withania somnifera*): An Indian medicinal plant with antioxidant, anti-inflammatory, and neuroprotective properties. Curcuma longa (Turmeric): A spice with anti-inflammatory, antioxidant, and neuroprotective effects, which may help in reducing amyloid- $\beta$  and tau protein accumulation. Ginkgo biloba: An ancient tree species with neuroprotective properties, which may improve cognitive function and memory. Sage (*Salvia officinalis*): A herb with cholinesterase inhibitory activity, antioxidant, and anti-inflammatory properties, which may benefit patients with Alzheimer's disease. Ginseng: A traditional herbal medicine with cognitive-enhancing properties, which may improve memory and cognitive function. Gotu Kola (*Centella asiatica*): A plant with neuroprotective and cognitive-enhancing properties, which may help in reducing amyloid- $\beta$  accumulation and improving memory. Lemon balm (*Melissa officinalis*): A herb with anticholinesterase activity, antioxidant properties, and potential benefits in managing Alzheimer's disease symptoms. These herbs have been studied for their potential therapeutic effects on Alzheimer's disease, and some have shown promise in preclinical and clinical trials. However, more research is needed to fully understand their efficacy and safety in managing this complex condition.

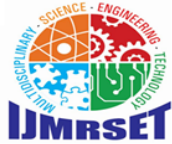
**KEYWORDS:** Ashwagandha, Ginseng, Ginkgo biloba, Gotu.kola, Lemon.balm, Sage, Curcuma longa, Herbal Powder for the treatment of Dementia

## I. INTRODUCTION

Dementia can be defined as a syndrome characterized by a cluster symptoms and signs many fasted by difficulties in memory ,disturbances in language and other cognitive functions, changes in behaviors, and impairment in activities of daily living. Alzheimer disease(AD)which named after the German psychiatrist Alois Alzheimer, who first described this disorder more than one century ago, is the most common cause of dementia, accounting for up to 75 % of all dementia cases, Alzheimer disease is a progressive.neurodegenerative.disorder. Dementia is caused by many different diseases or injuries that directly and indirectly damage the brain. Alzheimer disease is the most common form and may contribute to 60–70% of cases. Other forms include vascular dementia, dementia with Lewy bodies (abnormal deposits of protein inside nerve cells), and a group of diseases that contribute to frontotemporal dementia. degeneration.of.the.frontal.lobe.of.the.brain). Currently more than 55 million people have dementia worldwide, over 60% of whom live in low-and middle-income countries. Every year,there are nearly 10 million new cases. Dementia results from a variety of diseases and injuries that affect the brain. Alzheimer disease is the most common form of dementia and may contribute to 60–70% of cases. Dementia is currently the seventh leading cause of death and one of the major causes of disability and dependency among older people globally.Neurodegenerative pathways implicated in Alzheimer disease.Several overlapping mechanism have been proposed to explain future treatment are based on modification of these pathways.

Alzheimer:

Alzheimer disease (AD) was officially listed as the sixth leading cause of death in the united states in 2019 and is the fifth leading cause of death among Americans aged 65 and older. It has Impacted the lives of the elderly around the world, it is now more important than ever to develop an effective treatment not only to slow the progression of this disease but also to creat a.preventive.approach. Alzheimer's disease (AD) is the most common type of dementia, accounting for 60% to 80% of all cases. It is estimated that this debilitating neurodegenerative disorder currently affects 50 million patients worldwide and indirectly impacts the lives of tens of millions who deal with many years of



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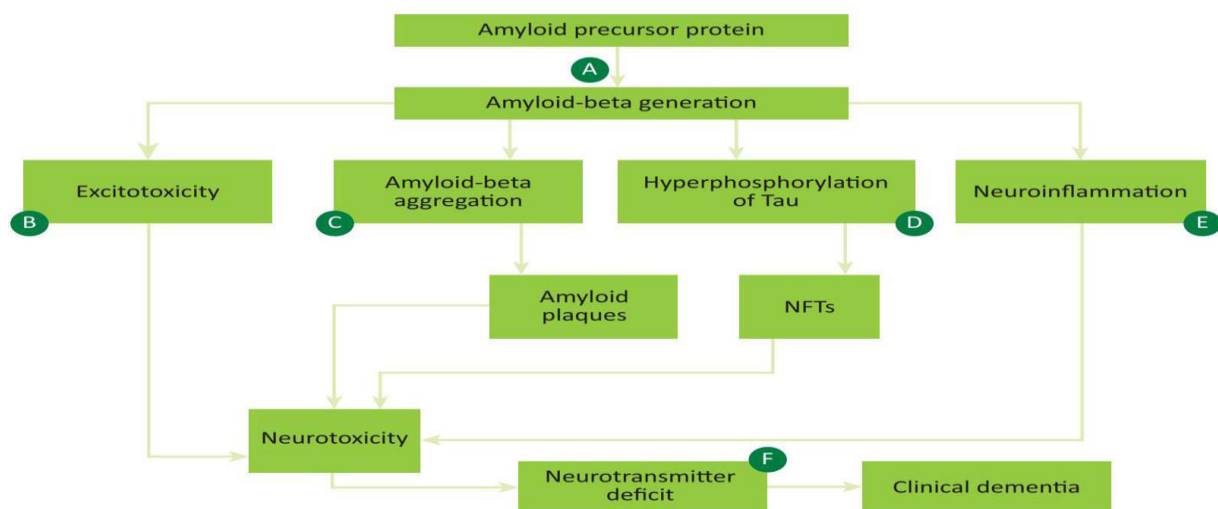
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cognitive decline in their loved ones. A small percentage of all AD cases are linked to dominant genetic mutations in three genes codifying for APP (amyloid precursor protein), PSEN1 (presenilin 1), and PSEN2 (presenilin 2) and are typically associated with early-onset forms of the disease in which clinical symptoms appear before the age of 65. The majority of the patients exhibit late-onset Alzheimer's disease (LOAD), which appears later in life and is sporadic in nature. Although in these cases the disease is not hereditary and shows no single genetic cause, current evidence supports the existence of a number of genetic risk factors, among which the presence of the E4 allele in the ApoE (apolipoprotein E) gene occurring in about 16% of the population--is the most significant.

Lifestyle behaviors such as poor diet and reduced physical activity, as well as environmental and metabolic risk factors including diabetes, cerebrovascular disease, head injury, and stress, are typically linked with an increased risk for the disease. The deposition of amyloid $\beta$  (AB) in the brain parenchyma and the cerebral vasculature, together with the presence of intraneuronal neurofibrillary tangles and the gradual loss of synapses, are central neuropathological hallmarks of AD, although, to this day, it remains unclear what primarily triggers and drives the progression of the disease. In spite of the more than 100 years that have passed since the discovery of the disease, the complex molecular mechanisms leading to the pathophysiology of AD have still not been fully elucidated. Among the different multifactorial pathways affected by the disease, vascular abnormalities, mitochondrial detrimental changes, oxidative stress, reduced brain glucose utilization, and neuroinflammation are currently being considered as important players in the initiation and/or progression of the disease.



(Fig1.Plaque.formation.in.brain)



(Figure.No.2.Causes.of.dementia)



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### Amyloid.cascade.hypothesis:

The amyloid hypothesis of AD began to gain traction in the 1990s, and centres on abnormal processing of the amyloid precursor protein (APP), leading to production of amyloid beta (AB). secretase enzymes cleave APP and aberrancy of this process, specifically mutation in gamma and beta secretase, can lead to the abnormal production of AB. Amyloid beta can then trigger a cascade leading to synaptic damage and neuron loss, and ultimately to the pathological hallmarks of AD: amyloid plaques and neurofibrillary tangles (NFTs) composed of hyperphosphorylated tau protein, with resulting neurodegeneration.

### Tau.hypothesis:

Tau is a protein expressed in neurons that normally functions in the stabilization of microtubules in the cell cytoskeleton.

Hyperphosphorylation causes it to accumulate into these NFT masses inside nerve cell bodies. These tangles then aberrantly interact with cellular proteins, preventing them from executing their normal functions. Hyperphosphorylation occurs downstream of AB, with research suggesting that accumulation of AB may initiate this process. Additionally, there is evidence that toxic tau can enhance AB production via a feedback loop mechanism.

### Cholinergic.hypothesis:

An initial breakthrough in Alzheimer disease came in the 1970s with the demonstration of a cholinergic deficit in the enzyme cholinesterase. This along with the recognition of the role of acetylcholine in memory and learning, led to the cholinergic hypothesis of AD and stimulated attempts to therapeutically increase cholinergic activity. Cholinergic depletion is a late feature of the neurodegenerative cascade, potentiating cholinergic transmission.

### Excitotoxicity:

Excitotoxicity defined as overexposure to the neurotransmitter glutamate, or overstimulation of its N-methyl-D-aspartate (NMDA) receptor, plays an important role in the progressive neuronal loss of cholinergic neurons is affected by this process, resulting in excessive influx of calcium into cells.

### Neuroinflammation:

Neuroinflammation an inflammatory response in the CNS characterized by accumulation of glial cells, appears to be a central event in AD pathophysiology. The brain was traditionally considered an 'immune-privileged organ, isolated from the immune system by factors such as the blood-brain barrier and apparent inability of brain immune cells to mount an innate immune response, but opinion on this has subsequently shifted dramatically. In the 1990s, seminal epidemiological evidence suggested that anti-inflammatory drugs may have a protective effect in AD and neuroinflammatory cascades are now considered an important target for treatment in Alzheimer disease, and both amyloid plaques and NFTs may act as drivers for this immune response. Unfortunately, meta-analysis have demonstrated no benefit of non-steroidal anti-inflammatory drugs, aspirin or steroids over placebo in patients with already symptomatic AD, some evidence suggests that naproxen may have a role in prevention of AD in healthy older people. It may be that the therapeutic window for such treatment occurs early in the disease process and as such by the time symptoms emerge, this opportunity has been lost.

### Neuroprotective.herbs.for.the.management.of.Alzheimer.disease:

While herbs and herbal remedies have a long history of traditional use and appear to be safe and effective they have unfortunately received little scientific attention. Numerous plants and their constituents are recommended in traditional practices of medicine to enhance cognitive function and to alleviate other symptoms of AD, including poor cognition, memory loss, and depression. A single herb or a mixture of herbs is normally recommended depending upon the complexity of the condition. The rationale is that the bioactive principles present in the herb not only act synergistically but may also modulate the activity of other constituents from the same plant or other plant species. This approach has been in Ayurveda, traditional Chinese medicine (TCM), and native Americans system of medicine, where a single herb or a combination of two or more herbs is commonly prescribed for any specific disease. In this manuscript, we review a subset of herbs useful for AD based on their properties, functional characteristics, and mechanistic action. The rationale for memory related disorders including AD, the identification of phytochemicals from these plants sources for their potential in Alzheimer disease therapy, determination of the neuropharmacological activities of these herbs.



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### Ashwagandha.(Withania.Somnifera):

Ayurveda a popular Indian system of medicine has a well developed line of action for managing and treating brain associated disorders. A list of about 450 ayurvedic medicinal plant, 56 popular plants, or their active metabolites is available for neurological disorders in ayurvedic prescription. One of the traditional, well known Indian medicinal plants is withania somnifera which is marketed as a common ingredient in several ayurvedic formulation for the treatment of neurological disorders. withania somnifera properly known as ashwagandha in Sanskrit has been used extensively in herbal medicine since its introduction in 600 BC; it is an evergreen woody shrub of the solanaceae family and has been given several names with different meanings, such as 'Indian winter cherry' or 'Indian ginseng' in english 'punir' or 'Asgandha' in hindi and 'asgand' in urdu. The species name 'somnifera' means 'sleep inducer' in latin, due to its amazing anti-stress properties, while the popular name 'Ashwagandha' comes from 'ashwa' (horse) and 'gandha' (smell), as the root have a characteristic 'wet horse' smell. In ayurvedic literature, it is classified as a rejuvenating agent, since it promotes both physical and mental health, revitalizes the body in an incapacitated state and maintains longevity. W.somnifera is a potentially useful for many neurological disorder such as epilepsy, Alzheimer disease, Parkinson disease cerebral ischemia and tardive dyskinesia. In addition to its neurological effects, W.somnifera possesses several other pharmacological properties, such as anti inflammatory, anti diabetic, cardioprotective, anti hepatitis, anti osteoporotic, and anti neoplastic activities. Several investigations have demonstrated that neuronal cells are vulnerable to oxidative damage due to their high poly unsaturated fatty acid content in membranes and the brain elevated oxygen consumption. Higher concentration of reactive oxygen species and lipid peroxidation are associated with oxidative stress, disrupting the balance between pro-oxidant and anti-oxidant levels and leading to eventual neuronal loss. Withania somnifera extract and its active constituents as shown in the rest of this article, have been demonstrated to possess anti oxidant enzymes, amyloid beta clearance, calcium influx, neurite outgrowth, lipid peroxidation, and inflammation, and similar debilitating processes that are involved in Alzheimer.

### Curcuma.longa:

It has been estimated that up to 1.5 billion people worldwide are suffering from central nervous system (CNS) disorders. The most challenging of the CNS diseases are neurodegenerative diseases, attributed to age-related gradual decline in neurological function, often accompanied by neuronal death. It has been shown that several mechanisms such as protein aggregations, oxidative stress and neuroinflammation are involved in neuronal death and damage. Recently, the use of natural compounds such as curcumin have been proposed as an alternative and effective strategy in the treatment of neurodegenerative and neurological diseases. Curcumin is a hydrophobic polyphenol that is derived from the rhizomes of the Curcuma longa. It has been well documented that curcumin possesses a wide variety of important pharmacological activities including anticancer, antimicrobial, anti-inflammatory, anti-amyloid, antioxidant, and neuroprotective effects. Traditionally, turmeric has been used for several ailments and especially it is widely consumed for dietary and medicinal purposes in Southeast Asia, China, and India. It can also cross the blood-brain barrier (BBB) and due to its pleiotropic therapeutic effects, curcumin has been regarded as a potential therapeutic factor for a large number of nervous system diseases. In addition, curcumin has vast application in the treatment of many other diseases such as cancer, diabetes, cystic fibrosis, malaria, and hypertension. Due to the pleiotropic actions of curcumin on the nervous system, it could be regarded as a potent neuroprotective compound in the treatment of CNS-associated diseases. Beneficial effects of curcumin in neuro inflammatory diseases including Alzheimer's disease (AD).

### Ginkgo.biloba.

Origin and History of Ginkgo biloba :

Ginkgo biloba is the oldest living tree species in the world. The Ginkgo species dates all the way back to the Permian Period some 286 to 248 million years ago. Today, Ginkgo biloba is the only surviving member of the Ginkgo family. This survival is said to be owed to its extraordinary malleability, resistance to disease, and to Buddhist monks who cultivated and preserved the trees on sacred grounds. Ginkgo was a favorite of Frank Lloyd Wright and soon made its approach into city landscapes across the USA [30]. The documented medicinal uses of Ginkgo in China can be tracked back nearly 5000 years, mainly for asthma treatment.

### Sage.(Salvia.officinalis.)

The genus Salvia, commonly known as sage, is the largest member of Lamiaceae or mint family containing over 900 species throughout the world. The plants are mostly aromatic and perennial (Figures 1 and 3), with flowers in different colors. Many species of Salvia, including Salvia officinalis (common sage), are native to the Mediterranean region and some of the Salvia species have been used worldwide as flavoring spices as well as traditional herbal medicine.



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Sage tea has been traditionally used for the treatment of digestive and circulation disturbances, bronchitis, cough, asthma, angina, mouth and throat inflammations, depression, excessive sweating, skin diseases, and many other diseases. Salvia essential oils have been used in the treatment of a wide range of diseases like those of the nervous system, heart and blood circulation, respiratory system, digestive system, and metabolic and endocrine diseases. In addition, sage essential oil has been shown to have carminative, antispasmodic, antiseptic, and astringent properties.

### II.COMMON NAMES

*S. officinalis* has numerous common names. Some of the best known names include sage, common sage, garden sage, golden sage, kitchen sage, true sage, culinary sage, dalmatian sage, and broadleaf sage. Cultivated forms include purple sage and red sage. In Turkey, *S. officinalis* is widely known as *adaçayı*, meaning "island tea." In the Levant, it is called *maramia*.

### III. MEMORY

Amongst many herbal extracts, *Salvia* species are known for the beneficial effects on memory disorders, depression, and cerebral ischemia. *S. officinalis* (common sage), *Salvia lavandulaefolia* (Spanish sage), and *Salvia miltiorrhiza* (Chinese sage) have been used for centuries as restoratives of lost or declining mental functions such as in Alzheimer's disease. In AD, the enzyme acetyl cholinesterase (AChE) is responsible for degrading and inactivating acetylcholine, which is a neurotransmitter substance involved in the signal transferring between the synapses. AChE inhibitor drugs act by counteracting the acetylcholine deficit and enhancing the acetylcholine in the brain. Essential oil of *S. officinalis* has been shown to inhibit 46% of AChE activity at a concentration of 0.5 mg/ml. A study shows that *S. officinalis* improves the memory and cognition, and with increasing dosage, the mood gets elevated as well as alertness, calmness, and contentedness increase. A randomized, double-blind clinical study has shown that an ethanolic extract from common sage (*S. officinalis*) as well as Spanish sage (*S. lavandulaefolia*) is effective in the management of mild to moderate AD, and study on patients did not show any adverse effect on them on taking sage. Administration of *S. lavandulaefolia* (Spanish sage) has been reported to be effective in improving the speed of memory and mood. *Salvia* essential oil also has been reported to improve immediate word recall.

A number of studies have investigated the effects of the aromas of plant essential oils on cognition and mood. The aroma of *S. officinalis* produced significant enhancement effect in the quality of memory factor derived from Cognitive Drug Research (CDR) system. The findings suggest that the aromas of essential oils of *Salvia* species have some, but not all the effects found following the oral consumption of the herb.

The antioxidant and anti-inflammatory properties of the *S. officinalis* or *S. lavandulaefolia* may offer a long-term protection in the pathogenesis of dementia. Also, the mood-enhancing properties of the herb may have applications in the treatment of advanced dementia, in which disturbed mood and agitation feature as a major problem. There is no report of negative side effects associated with *S. officinalis* or *S. lavandulaefolia* despite many years of usage. The cytoprotective effect of sage against A $\beta$  (amyloid beta plaques) toxicity in neuronal cells has also been proven by the data presented in a study which provides the pharmacological basis for the traditional use of sage in the treatment of AD. Rosmarinic acid as a component of sage has shown neuroprotective, antioxidative, and antiapoptotic effects against A $\beta$  toxicity, and this could contribute, at least in part, to the neuroprotective effect of sage. Therefore, it is possible that rosmarinic acid, the very low toxic natural compound, could be used as a therapeutic agent in the treatment of Alzheimer's disease.

#### Clinical Studies on *Salvia* Species against AD.

*Salvia officinalis* L. Preclinical and clinical studies have so far indicated that the extracts and essential oils of *Salvia officinalis* L., which have been used in European folk medicine for memory enhancement, have been favorable for acute memory and attention in healthy young and old participants.

Researchers have largely agreed that the observed effects for the *Salvia* species have resulted from their cholinesterase inhibitory effect. In this context, Akhondzadeh et al. clinically tested

*Salvia officinalis*, which has been used in European folk medicine for centuries, in Alzheimer's patients that were diagnosed using the National Institute of Neurological and Communicative Disorders and Stroke and Alzheimer's Disease and Related Disorders Association (NINCDS/ADRDA) criteria. The stage of the disease in the patients was established through



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ough the ognitive subscale scores of the Alzheimer's Disease Assessment Scale (ADAScog) and Clinical Dementia Rating Scale (CDR); based on this, the authors suggested that *S. officinalis* could potentially provide an option for AD therapy based on its in vitro cholinergic binding properties with modulation of mood and its ernhancing effect on cognitive p performance in humans. For instance, a randomized study was conducted by comparing the placebo group in thre centers in Tehran (Iran) over a period of four months. Te authors evaluated the efficacy and safety of a hydroalcoholic (45%) e xtract of *S. officinalis* cultivated in Iran at a fixed dose (60 drops/day) in patients with mild to moderate AD, whose age s ranged between 65 and 80 years (average of 71 years). The study revealed that the efficacy of *S. officinalis* extract in t he treatment of mild to moderate A was remarkable. The authors also noted that *S. officinalis* extract may reduce the ag itation of patients. Only six patients were recorded to have simple side effects such as vomiting and dizziness. Although it was found to be effective in patients with mild to moderate types of AD, the limitations of the study were concluded as a small number of patients and short followup time. On the other hand, no information was available on the phytoc hemical content of the extract, which is quite indispensable for assessing the pharmacological effect as well as the ratio nal dosing and quality control of herbal medicines (phytotherapeutics). In another doubleblind, placebocontrolled, and c rossover study using ethanol extract (53%) prepared from the dried sage leaves of *S. officinalis*, 30 healthy participants (average age: 24.4 years; 17 males and 13 females) attended the laboratory on 3 separate days (7 days apart as the wash out period) and were administered with doses of 300 and 600 mg of the extract in opaque capsules each time in balance d mode. Daily mood was assessed 1h before and 4h after.

### Ginseng

Ginseng is a traditional herbal medicine used for prevention and treatment of various diseases as a tonic. Recent scientif ic cohort studies on life prolongation with ginseng consumption support this record, as those who consumed ginseng fo r more than 5 years had reduced mortality and cognitive decline compared to those who did not. Clinical studies have al so shown that acute or longterm intake of ginseng total extract improves acute working memory performance or cogniti ve function in healthy individuals and those with subjective memory impairment (SMI), mild cognitive impairment (M CI), or early Alzheimer's disease (AD) dementia who are taking AD medication(s). Ginseng contains various compone nts ranging from classical ginsenosides and polysaccharides to more recently described intonin. However, it is unclear which ginseng component(s) might be the main candidate that contribute to memory or cognitive improvements or prev ent cognitive decline in older in dividuals. This review describes recent clinical contributors to ginseng components in c linical tests and in troduces emerging evidence that ginseng components could be novel candidates for cognitive impro vement in older individuals, as ginseng components improve SMI cognition and exhibits addon effects when co admini stered with early AD dementia drugs. The mechanism behind the beneficial effects of ginseng compo nents and how it i mproves cognition are presented. Additionally, this review shows how ginseng components can contribute to SMI, MC I, or early AD dementia when used as a supplementary food and/or medicine, and proposes a novel combination therap y of current AD medicines with ginseng component(s).

Ginseng (*Panax ginseng* Meyer) root has been traditionally used as a tonic in China, Japan, and Korea for over 2000 ye ars. The traditional tonic effects of ginseng extract include energizing the body, clearing brain and mood elevation, and finally brain health and longevity. Currently, ginseng is used as a functional food or alternative and/or a complementary medicine for health worldwide. There are several ginseng components, which are responsible for tonic such as ginseno sides, ginseng polysaccharides and gintonin. Accumulating evidences show that ginseng components exhibit beneficial e ffects against cognitive impairments. On the other hand, dementia is a brain disease including AD, in which normal cog nitive functions are maintained during the growth period, but cognitive dysfunctions with accompanying personality ch anges occur in old age. Besides cognitive decline, other common symptoms of AD include apathy (reduced interest in o thers), emotional changes (e.g., becoming easily angered), behavioral changes (e.g., repeating questions, leaving the ho use unconditionally), difficulties with language fluency, and weak will. But dementia does not affect the patient's consci ousness. AD dementia has various causes. Recent studies have identified that it is caused by a decrease in the ability to r emove neurotoxic waste products [e.g., Bamyloid ( $A\beta$ ) and tau protein] that accumulate in the brain with aging. If the waste product called  $A\beta$  is efficiently removed from the brain, there is no problem. Otherwise,  $A\beta$  molecules form aggr egates and become waterinsoluble  $A\beta$  polymers. Thus,  $A\beta$  polymers can lead to AD through brain inflammation and ox idative stresses. As these  $A\beta$  polymers spread to other brain areas, they cause toxicity to neurons, resulting in the death of nerve cells around Bamyloid plaques, which are large  $A\beta$  polymer aggregates. In addition, Bamyloid plaques induce d neuron deaths, observed in most patients with AD dementia, are closely asso ciated with the brain acetylcholine defi ciency. Bamyloid ( $A\beta$ ) and tau protein also induce glutamatemediated excitatory neurotoxicity via NMDA receptor overa ctivation, which results in neurodegeneration.



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### Goto.kola.(*Centella.asiatica*)

The accumulation of Bamyloid (A $\beta$ ) is a hallmark of Alzheimer's disease and is known to result in neurotoxicity both in vivo and in vitro. We previously demonstrated that treatment with the water extract of *Centella asiatica* (CAW) improves learning and memory deficits in Tg2576 mice, an animal model of A $\beta$  accumulation. However the active compounds in CAW remain unknown.

Here we used two in vitro models of A $\beta$  toxicity to confirm this neuroprotective effect, and identify several active constituents of the CAW extract. CAW reduced (A $\beta$ )induced cell death and attenuated A $\beta$ \_induced changes in tau expression and phosphorylation in both the MC65 and SHSY5Y neuroblastoma cell lines. We confirmed and quantified the presence of several mono and dicaffeoylquinic acids (CQAs) in CAW using chromatographic separation coupled to mass spectrometry and ultraviolet spectroscopy. Multiple dicaffeoylquinic acids showed efficacy in protecting MC65 cells against A $\beta$ \_induced cytotoxicity. Isochlorogenic acid A and 1,5 dicaffeoylquinic acid were found to be the most abundant CQAs in CAW, and the most active in protecting MC65 cells from A $\beta$ \_induced cell death. Both compounds showed neuroprotective activity in MC65 and SHSY5Y cells at concentrations comparable to their levels in CAW. Each compound not only mitigated A $\beta$ \_induced cell death, but was able to attenuate A $\beta$ \_induced alterations in tau expression and phosphorylation in both cell lines, as seen with CAW. These data suggest that CQAs are active neuroprotective components in CAW, and therefore are important markers for future studies on CAW standardization, bioavailability and dosing.

*Centella asiatica* (L.) Urban, (Apiaceae), known in the United States as Gotu Kola, is an edible plant that has been used for centuries in the Indian medical system of Ayurveda to boost memory, improve cognitive function and reverse cognitive impairments. Extracts of *Centella asiatica* have been shown to be neuroprotective or neurotropic in a number of pre clinical models. A great deal of variability exists in the chemical composition, and consequently biological properties, of different *Centella asiatica* extracts. In addition to variability due to diverse growing conditions of the source *Centella asiatica* plant material, the method of extraction has a substantial effect on the types of chemical compounds present in an extract. We have previously demonstrated that the chemical profile of an ethanol extract from *Centella asiatica* is quite different from that of a water extract of the same batch of plant material. In rodents, extracts of *Centella asiatica* have attenuated neurobehavioral and neurochemical effects of stroke, accelerated nerve regeneration, protected against oxidative neurotoxicity and showed anti-inflammatory and antioxidant effects. In addition to these effects, the cognitive enhancing action of water extracts of *Centella asiatica* has also been demonstrated in multiple animal models and in limited human studies. An extract of *Centella asiatica* was also shown to decrease A $\beta$  plaque burden in a transgenic mouse model of AD, however the extraction method was not described making it difficult to speculate which compounds may be responsible for that effect.

*Centella asiatica* (C. asiatica), also known as Indian Pennywort, is a member of the plant family Apiaceae. It is well known as an enhancer of cognitive functions. Several studies have demonstrated CA's effect on antidepressant, anticonvulsant, neuroprotection, and anti-inflammation. In vitro and in vivo studies showed that C. asiatica effectively improves memory impairment in AD models. C. asiaticaextracted with water attenuated the behavioral deficit in AD mouse models. Prolonged treatment of C. asiaticasignificantly alters Nicotinamide, glycerophospholipid, and purine metabolism associated with AD. C. asiatica's antioxidative property was explored in attenuating AD symptoms and normal aging. C. asiaticatreatment lowered the lipid peroxidation, ROS levels, rescued mitochondrial dysfunction. A randomized control study using C. asiatica on healthy elderly population showed improvement in age-related cognitive deficit and mood. Similarly, another study showed improvement in MCI, depression, insomnia, and loss of appetite the results are yet to be analyzed ved as a nutritional supplement for AD prevention.

### IV. LEMON.BALM.(*Melissa.officinalis*)

*Melissa officinalis* (M. officinalis, lemon balm) is a medicinal plant from the Lamiaceae family. In Iran, this plant has been used as a folk medicine for numerous years. Medicinal preparations of this herb were used for treatment of indigestion, anemia, palpitations and mood disorders. M. officinalis impacts nervous disorders including reductions in excitability, anxiety and stress, and sleep disturbances. The total extract of M. officinalis and its different fractions have anticholinesterase activity. M. officinalis extract displays potent antioxidant activity and plant extracts can protect cells against oxidative damage induced by different pro-oxidant agents which eventually leads to lipid peroxidation. Administration of M. officinalis extract in AD patients can improve disease symptoms. The extract has been shown to alleviate scopolamine-induced amnesia in rats as an animal model of AD. However, the mechanism and constituents involved in these neuroprotective properties are not well known. In our previous study, we have reported that the acidic



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fraction of *M. officinalis* extract was more protective of PC12 cells against A $\beta$ -induced toxicity compared to the total extract. It has been postulated that *M. officinalis* extract contains compounds with affinity for the nicotinic receptor. Several studies reported the role of the nicotinic receptor in A $\beta$ -induced toxicity and nicotine attenuated A $\beta$ -induced toxicity in cultured neuron. In the current study we intended to investigate the neuroprotective effect of the acidic fraction of *M. officinalis* extract against A $\beta$ -induced oxidative stress and apoptosis in cultured cerebellar granule neurons (CGN). In addition, the role of the nicotinic receptor was investigated.

### V. METHOD

#### Collection of Material

All the ingredient are collected from local market and purchases from online

**Preformulation :-** Preformulation is the stage of development during which the physico chemical properties of the drug substance are characterized and established.



Figure no. 4.3.1 Angle of repose



Figure no. 4.3.2 Bulk & Tapped density



Figure no. 4.3.3 Moisture content



Figure no. 4.3.4 Solubility test

#### Flow property of powder :-

The flow of powder is a complex phenomenon that is sensitive to properties of the powder itself and external factors such as humidity. Within the powder many parameters affect flow properties. The main influencing factors are particle size and particle shape and width of particle size distribution.

**Bulk density:-** Bulk density measurement carried out by using flat round measuring cylinder with a volume of 50 ml. The measuring cylinder was half filled the 5 gm of powder and reading was observed to the nearest millimeter.

**Bulk density = w/v<sub>0</sub>**



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**Tapped density:-** After 50 ml and 100 tapsthe corresponding reading was observed to the nearest milliliters. The taped volume was recorded when the difference between the two volume was smaller than 1 ml.

**Tapped density:** After 50 tapping =W/V1  
After 100 tapping =W/V2

**Angle of repose :-** It was determined by fixed funnel method on to a bottom graph paper. The funnel was fixed on a height and moved according to the height of the conical heap in order to keep a constant distance between the top of the heap and funnel. The angle of repose was determined by measuring the height of cone of powder with the help of the formula.

$$\text{Tan (A)} = \text{height/base}$$

**Hausner's ratio :-** Flow property was defined according to the hausner ratio =(Tapped density)(Bulk density) Flow of powder was measured using a stander funnel. In a dry funnel,whose bottom opening has been blocked,the sample was introduced without compacting. After removing the blockage from the bottom opening of the funnel,the time taken for the entire sample to flow out through the funnel was measured.

$$\text{Hausner ratio} = (\text{Tapped density} / \text{Bulk density})$$



Figure no. 4.4.2.1 Extraction



Figure no. 4.4.2.2 Extaction



Figure no 4.4.2.3 Test



Figure no.4.4.2.4 Test & Maceration

### Phytochemical Screening of Drugs

Phyto chemical screening is identification of different classes of phyto constituents present in various parts of a plant. Phyto chemical are the chemicals that are present naturally in plant

#### Test for Alkaloids

**Mayer's test:** 5 gm of Ashwagandha powder was dissolved in 20 ml of ethanol. Then the mixture was treated with few drops of wagner's reagent yellow ppt obtained.

**Wagner's test:** 5gm of Turmeric powder was dissolved in 15 ml of methanol. then extract was treated with few drops of wagner's reagent brownish red ppt obtained.



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### Flavonoids test:

**Alkaline reagent test:** 10 gm of lemon balm powder was dissolved in 20 ml of ethanol and 80 ml water added then heated 45 min. filtered the extract and treated few drops of NaOH solution yellow colour ppt obtained.

**Sulphuric acid test:** 2gm of Ginkgo biloba powder was dissolved in 20 ml of ethanol stand for 24 hours. then extract was treated 2ml of sulphuric acid red colour show.

**Zinc hydro chloride test:** 5 gm of Ginseng powder was dissolved in 20 ml of ethanol stand for 2 days. Then extract was treated mixture of zinc dust & conc. HCl deep red to magenta colour obtained.

### Triterpenoid test:

**Libermann-burchard test:** 5 gm of sage powder dissolved in 50 ml of water then heated 45 min. extract was screened out then treated few drops of acetic anhydride and heated with sulphuric acid Green colour obtained.

**Salcowski test:** 5 gm of Gotu kola powder dissolved in 50 ml of water then heated 30 min extract was screened out then treated few drops of Sulphuric acid red colour show.

### Phenolic test:

**Feric chloride test:** 2ml extracted solution of sage react with FeCl<sub>3</sub> solution and added few drops of NaOH solution blue colour obtained.

### Preparation of Powder

Every herb selected with good quality by making sure its cleanliness. All leaf and root were collected from near by sources and grained with the help of grinding tool to get fine particles and the powder was sieved by the IS standard size of 90 micron then powder is dried and its ready to be utilized as a fine powder was collected and store in air tight container to keep away from moisture.

| Formula for preparation<br>According to European<br>Journal of Pharmaceuticals<br>& Medicine Research the<br>formulation has been divided<br>into 3 groups powder for the<br>treatment of Dementia. | Ingredient    | F1  | F2   | F3  |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------|-----|------|-----|
| S. NO                                                                                                                                                                                               |               |     |      |     |
| 1                                                                                                                                                                                                   | Ashwagandha   | 2gm | 3 gm | 4gm |
| 2                                                                                                                                                                                                   | Curcuma Longa | 2gm | 3 gm | 4gm |
| 3                                                                                                                                                                                                   | Ginseng       | 2gm | 3 gm | 4gm |
| 4                                                                                                                                                                                                   | Ginkgo Biloba | 2gm | 3 gm | 4gm |



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|   |            |     |      |     |
|---|------------|-----|------|-----|
| 5 | Sage       | 2gm | 3 gm | 4gm |
| 6 | Lemon Balm | 2gm | 3 gm | 4gm |
| 7 | Gotu Kola  | 2gm | 3 gm | 4gm |

Table: Formula for Preparation

### VI. RESULT AND DISCUSSION

#### Result:

The active ingredient tested in this paper exhibit the consider able properties as mentioned below .

#### Organoleptic Properties:

| S.NO | Organoleptic Properties | Observation       |
|------|-------------------------|-------------------|
| 1    | State                   | Solid fine powder |
| 2    | Color                   | Yellowish black   |
| 3    | Odor                    | Mint flavoure     |
| 4    | Texture                 | Amorphous nature  |

Table: Organoleptic properties of API

#### Solubility

As per the method following result obtain

| S.NO | Solvent     | Observation      |
|------|-------------|------------------|
| 1    | Water       | Soluble          |
| 2    | Ethanol     | Soluble          |
| 3    | Chloroforme | Slightly Soluble |
| 4    | Methanol    | Soluble          |

Table: Solibility Test

#### Flow Property:

As per the method given 4.4.1 following result obtain.

- The Bulk density of the preparation was 0.6 g/ml.
- Tapped density of preparation after 100 tapping =0.75 g/ml.

#### Angle of Repose :

As per the method the method given 4.4.1 the following result obtaine that angle of repose 19.29 which is fair (aid not needed).

#### Hausner' s Ratio :

As per the method given result obtains that Hausner's ratio of the API was 1.25 g/m

#### Carr's Index :

As per the method given result obtain that carr's index is 20 .



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### VII. CONCLUSION

Alzheimer's disease (AD) is a progressive, irreversible, and debilitating neurodegenerative disorder that affects millions of people worldwide. The disease is characterized by cognitive decline, memory loss, and behavioral changes, ultimately leading to complete dependence on caregivers.

1. Immunotherapies: Targeting A $\beta$  and tau proteins with antibodies or vaccines.  
 2. Tau-targeting therapies: Modulating tau protein phosphorylation and aggregation.  
 3. Neuroprotection and neuroregeneration: Promoting neuronal survival and regeneration.  
 4. Personalized medicine: Tailoring treatments to individual patient needs genetic profiles and herbs and herbal remedies have a long history of traditional use and appear to be safe and effective they have unfortunately received little scientific attention. numerous plants and their constituents are recommended in traditional practices of medicine to enhance cognitive function and to alleviate other symptoms of AD. While conventional medications are available, many people explore herbal remedies to complement or alternative to traditional treatments. Here are some herbs that have been studied for their potential in Alzheimer's disease management:

1. Ginkgo biloba: Improves cognitive function, memory, and blood flow to the brain.
2. Panax ginseng: Improves cognitive function, memory, and reduces oxidative stress.
3. Curcuma longa (Turmeric): Reduces inflammation, oxidative stress, and improves cognitive function.
4. . Melissa officinalis (Lemon balm): Improves cognitive function, memory, and reduces stress and anxiety.
5. Salvia officinalis (Sage): Improves cognitive function, memory, and reduces oxidative stress.
6. Centella asiatica (Gotu kola): Improves cognitive function, memory, and reduces oxidative stress
7. 7.Ashwagandha (Withania somnifera): Neuroprotection and neuroregeneration: Ashwagandha may promote neuronal survival and regeneration, potentially slowing disease progression.

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