

# **A REVIEW ON SESBANIA GRANDIFLORA ITS EFFECT ON THE TREATMENT OF DEMENTIA AND NEURO DISEASE AND OTHER DISEASES**

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## **Abstract**

*One of the most often used folk medicines is Sesbania grandiflora, better known as the Agati or Hummingbird tree. Anemia, bacterial infections, TB, and other illnesses can be treated with the plant's pharmacological properties. Agati's anticancer and hepatoprotective properties are attributable to the presence of phytochemical ingredients. Sesbania grandiflora's therapeutic characteristics are the topic of this article. Normal psychological functioning and behavioural patterns are disrupted by dementia. One to four percent of the world's population over the age of 65 is affected by dementia, which is a neurological disease. Dementia is caused by a number of different factors. Because dementia is more common in those who have cardiovascular and neurodegenerative conditions (such hypertension, hypercholesterolemia, diabetes and cerebral ischemia), these people are more likely to develop it. In addition to alcohol and tobacco use, these conditions are exacerbated. Alzheimer's dementia, vascular dementia, frontotemporal dementia, semantic dementia, and dementia with Lewy bodies are the most frequent kinds of dementia. As we get older, Alzheimer's and Lewy body dementias become more common. It is the second most frequent kind of dementia after Alzheimer's disease (AD), and it can be caused by long-term cardiovascular disease (CVD). Deterioration in semantic memory is a hallmark of semantic dementia (knowledge of objects, people, concepts and words). synuclein aggregation in Lewy body dementia (LBD) impairs neuronal growth and has a significant impact on the disease aetiology. Alzheimer's disease, Parkinson's disease, schizophrenia, and other neurodegenerative diseases all have a strong genetic component, as do frontotemporal dementia and Alzheimer's disease. An important part of this study is the discussion of the role of glutathione (GSH), SOD, GPx, and Catalase (Cat) during oxidative stress and the link between mitochondrial dysfunction and many disorders, including dementia. The purpose of this review is to examine the types, risk factors, and underlying mechanisms of dementia, as well as new therapy techniques, in order to maximise the chances of finding new and effective therapeutic strategies.*

**Keywords:** *Dementia, Alzheimer disease, Sesbania grandiflora, Antioxidant, Phytochemicals.*

## **Introduction**

When someone has dementia, their memory and cognitive abilities deteriorate over time. In the short term, the only therapy options for Alzheimer's disease are symptomatic usage of acetylcholine esterase inhibitors (AChEIs) and the nonselective N-methyl-D-aspartate receptor antagonist memantine [1]. A form of Alzheimer's disease, known as Alzheimer's dementia, is the most prevalent cause of memory loss in the elderly. Degeneration of specific brain regions, such as the frontal and temporal regions, is the hallmark of Alzheimer's disease (AD). CNS and peripheral autonomic and somatic nerve systems are thought to include the most essential neurotransmitter, acetylcholine (ACh) [2].

One of the world's smallest trees, *Sesbania grandiflora*, often known as the crimson wisteria or agate, is said to have originated in either India or South East Asia. An Asian native, it can be found growing in vegetable gardens and on dikes between rice paddies, along roadsides, and in backyards all over the continent [3-4]. The antioxidant activity of *Sesbania grandiflora* acetone and ethanol extracts was assessed by DPPH test, total Phenolic content, reducing power assay, and prevention of lipid oxidation in linoleic acid emulsion. Neuroprotective benefits in mice treated with celecoxib were found the cholinergic system was altered and that oxidative stress was blocked by inhibiting the AchE enzyme. Most *sesbania* species are soft, semi or somewhat woody, perennial nitrogen-fixing trees ranging in height from 1-4 metres. *Sesbania grandiflora* produces huge, up to 10cm-diameter red or white blooms [5].

Particularly during the first three- or four-years following planting, the plant's astounding growth rate stands out. Within three years, plantations in Australia and India had reached heights of 8 metres (24 feet). During the summer months, *sesbania* is grown as a cover crop and green manure. Soil organic matter is added during the *sesbania*-growing phase. Organic stuff is broken down by micro-organisms[6]. Gums, waxes, and resins, all of which are resistant to degradation, are used to bind soil particles into granules or aggregates. There are several advantages to having a well-aggregated soil in your garden. There are numerous uses for the tree, including foraging for food, firewood, papermaking, and landscape decoration. It also has the ability to reforest eroded land and grassy wastelands in the tropical regions. There is a problem with the quality of the wood. *Sesbania grandiflora* blossoms and young pods are both consumed as vegetables in Southeast Asia. The phytochemicals in *Sesbania grandiflora* are responsible for its antipyretic, anti-inflammatory, antioxidant, antibacterial, thrombolytic, and membrane-stabilizing activities. Researchers have discovered that *Sesbania grandiflora* has powerful hepatoprotective, cardioprotective, antiurolithialytic, and anxiolytic properties[7-9].

### **Taxonomy**

1. Kingdom: Plantae
2. Super division: Spermatophyta
3. Class: Magnoliposides
4. Order: Fabals
5. Family: Leguminosae
6. Genus: *Sesbania*
7. Species: *Sesbania grandiflora*

### **Biological description**

**Leaves:** The leaves of *Sesbania grandiflora* are deep green, pinnate, approximately 30cm long and mild tart in taste[10].

**Flowers:** The flowers are 7-9cm long, deep pink to red in colour. It taste acrid, bitter and astringent.

**Bark:** The bark of *Sesbania grandiflora* are lightly grey in colour, corky and deeply furrowed.

**Seed:** The seeds are oblong, brown or dark green coloured.

**Pod:** The pods are slender and straight, pale yellow coloured, 20-60cm long and contains 15- 50 seeds, each 8 mm in size.

### **Ecology**

As a result, *Sesbania grandiflora* thrives in hot, humid conditions. Saline and alkaline soils can support its growth. It is able to endure water logging[11].

### **Phytochemistry**

There are alkaloids, flavonoids, glycosides, steroids, proteins, carbohydrates, terpenoids, anthraquinone and saponins in *Sesbania grandiflora*, which constitute the plant's phytochemical elements[12].

### **Nutritive value of *Sesbania grandifolia***

Water, carbohydrates, proteins and lipids, as well as minerals (Iron, calcium, sodium and potassium) and vitamins (thiamine, riboflavin, niacin, ascorbic acid and beta-carotene) are found in *Sesbania grandiflora* leaves, flower, bark and seeds (Arginine, histidine, isoleucine, leucine, lysine and methionine). Medical carpin and sativan are present in the roots, in addition to isoflavonids. Agati seeds contain the active chemicals leucocyanidin and cyaniding[13-14].

### **Medicinal plants**

In Ayurveda, the entire plant and its derivatives are utilised to treat a wide range of illnesses and infections[15-17].

**Leaves :** For migraine, sinusitis, rheumatic disease, arthritis, gout, and wound healing, fresh leaves are utilised. To cure oral and throat infections, leaves can be used as a tonic or paste.

**Flowers:** Constipation, insomnia, and headaches can all be relieved by the floral juice of *Sesbania grandiflora*.

**Bark :** There are many uses for bark in the treatment of gonorrhoea, small pox, malaria and eruptive fever.

**Root:** The roots of red flowered variety *Sesbania grandiflora* is used to treat rheumatism.

**Seed :** The oil of *Sesbania grandiflora* seed has anthelmintic activity.

## **Dementia**

Memory, reasoning, direction, understanding, calculation, learning capacity, language, and judgement are only few of the higher cortical functions that are impeded when a person is suffering from dementia according to the WHO's International Classification of Diseases (ICD 10, 1992). Alzheimer's disease, Parkinson's disease, multiple sclerosis, and other neurodegenerative disorders all fall under the umbrella term "dementia." Other disorders, such as a lack of cerebral blood flow, mitochondrial malfunction, and oxidative damage all contribute to dementia. It is a clinical syndrome that arises when an individual's mental and cognitive faculties diminish over time, resulting in significant memory loss[18]. Dementia is frequently caused by metabolic diseases, energy management dysregulation, AIDS, immuneactivated macrophages, or systemic infections. Dementia can also be caused by environmental causes like as poisons in the misuse substances or air pollution. Genetic mutations and gene polymorphisms are also linked to dementia. The following are the most common kinds of dementia:

### **Types of Dementia**

#### **Parkinson's disease with dementia (PD)**

The existence of subcortical lesions has been found to be one of the primary causes of Parkinson's disease (PD). It's a form of dementia that develops after Parkinson's disease has already progressed. Difficulty remembering and slowing of thinking processes are hallmarks of this dementia, which is also accompanied by other psychotic symptoms such as hallucinations. Among the hallucinations were crisp, colourful, and rarely fragmented images of family and friends. Donepezil, a synthetic medicine that improved cognition and hallucinatory symptoms, was used as a treatment for dementia, but it didn't address the disease's core cause. Rivastigmine, a dual cholinesterase inhibitor, was also used. Rivastigmine was proven to be an effective treatment for the extrapyramidal symptoms[19].

#### **Lewy body dementia (LBD)**

For example, Lewy bodies might be spherical, triangular, or even irregular in shape. Truncated versions were discovered next to the nucleus. Neurofilament proteins such as ubiquitin, -synuclein, and related enzymes are found in a dense inner core and an outside section that is abnormally condensed and phosphorylated. Patients with LBD were more likely to experience visual, olfactory, and auditory hallucinations[20]. Hallucinations elicited an array of emotions, from terror to amusement. Patients exhibited hypophonic speech, stooped posture, and stumbling stride. Clozapine, Chlormethiazole, and lorazepam were among the synthetic antipsychotics used in treatment. There were also certain neuroleptics, such as Thioridazine and Sulpiride.

## **Vascular dementia ( VaD)**

This type of dementia occurs when an underlying vascular condition such as a cardiac stroke, atherosclerosis, or cardiac arrest causes many brain tissue lesions, such as haemorrhage infarctions, sclerosis of the hippocampus, and white matter lesions in the brain. As a result of these alterations, dementia develops. Motor delay, sad mood, low motivational energy, anxiety, strange ideas, and physical irregularities are all indications of this condition. It is also possible that a cerebral vascular injury can result in corticospinal and extrapyramidal side effects, such as muscle weakness and slowness, which can contribute to the postponing of behavioural patterns and decision-making abilities. Donepezil, a drug used to treat Alzheimer's disease, improved patients' cognition, but it was shown to have numerous negative effects. There was a significant improvement in executive functioning, verbal fluency, and behavioural patterns with the use of rivastigmine. Memantine had a moderate effect on cognition, but it also had less adverse effects in patients[21].

## **Huntington's disease with dementia (HD)**

Huntington's disease is a kind of hereditary dementia caused by mutations in the Huntington gene. symptoms of the disease are made up of many impairments, such as mental and physical impairments.

**Movement disorders :** Involuntary as well as voluntary disorders are included in this category. Continuous and jerky movements make up this style. Dysphagia, muscle rigidity, and postural abnormalities are all symptoms of Parkinson's disease[22].

**Cognitive disorders :** Aphasia, agnosia, and problems with cognitive speed and flexibility are all too common in people. Patients have a difficult time recalling their past experiences and memories. As a result, visual and judgmental impairments were expected to occur.

**Psychotic disorders :** Depression, irritability, and apathy are the three most prevalent symptoms of depression. Feelings of worthlessness, self-blame, changes in sleep patterns, changes in food, worry, loss of energy, and hopelessness are among the most common symptoms.

Synthetic medications such Amantadine, Levetiracetam and Tetrabenazine were employed in the treatment of the patient. Clinical investigations also examined the use of Coenzyme-Q10, Creatine, and Minocycline as neuroprotective agents. 11 Serotonin reuptake inhibitors were also found to be beneficial to HD sufferers. Mood stabilisers such as carbamazepine and valproate were expected to improve emotional stability and impulsivity.. To alleviate psychotic-related symptoms, antipsychotics were thought to be beneficial. In clinical trials, Donepezil, Rivastigmine, and Memantine were found to have inconclusive results[23].

## **Frontotemporal Dementia (FTD)**

Progressive atrophy in the frontal and/or temporal lobes is a characteristic feature of this form of dementia. In honour of the physician Arnold Pick, it is sometimes known as Pick's sickness. Affected proteins include phosphorylated tau, TDP-43/FUS, and trans active response DNA-binding protein-43 (TDP-43). There are two distinct forms of FTD:

1. Variation in how a person acts Disinhibition, apathy, and a change in personality are all symptoms of FTD. Poor financial decision making might stem from a lack of self-control. As a result, patients lose their ability to feel empathy for their loved ones. Reduced sensitivity to the emotional and other needs of others in the community. Different elements of this type include binge-eating, an increase in sweets or alcohol use, and weight gain[24].

2. People with Progressive Aphasia have problems with word comprehension, object naming, and language prediction.

Hyperreflexia, spasticity, weakness, muscular atrophy, and dysphagia are some of the most common motor symptoms.

The amount of synthetic drugs consumed was staggering. Fluoxetine, Fluvoxamine, Sertraline, and Paroxetine are commonly used as selective serotonin reuptake inhibitors to treat neuropsychiatric disorders. Taking antipsychotics such Olanzapine, Risperidone, and Aripiprazole improved cognitive capacities, delusions, agitation, neuropsychiatric symptoms, and general behaviour. Selegiline, Donepezil, and Rivastigmine are cholinergic medicines that have been shown to improve behaviour and cognition in animal tests. Rather than addressing the underlying problem, these man-made medications could merely mask the symptoms[25].

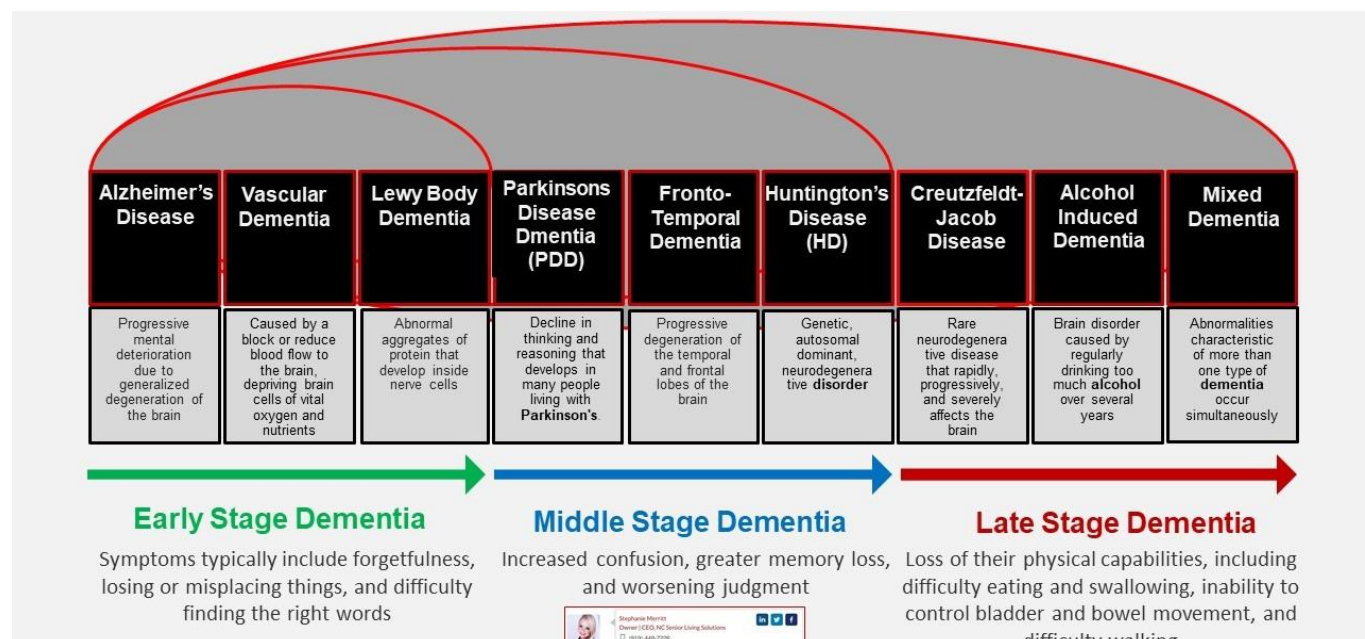
## **Creutzfeldt – Jakob dementia (CJD)**

Iatrogenic or spontaneous dementia is among the rarest kinds of Alzheimer's. An aberrant prion protein is the primary event that takes place. This type of dementia is thought to be caused by an aberrant prion protein that serves as a template for the host prion protein to fold improperly into a pathogenic shape. This is an autocatalytic process. Synthetic medications such as Quinacrine were used to test their efficacy in trials, but they were found to have no effect on the progression of Parkinson's disease. Flupirtine has been shown to protect the brain by increasing bcl-2 levels and restoring glutathione levels to normal. Patients with CJD showed a marked improvement in their cognitive abilities. While it was found to totally eradicate the aberrant prion protein strain in mice, pentosan polysulfate has yet to be tried in people. There is currently no cure for this type of dementia, despite the use of synthetic medications[26].

## **Alzheimer's Dementia (AD)**

In AD, presynaptic cholinergic neurons are lost, which then progresses to the loss of cortical cholinergic neurons and eventually dementia. Amyloid  $\beta$ -protein (A complex) accumulation in

extracellular cortical plaques and neurofibrillary tangles formed of phosphorylated tau protein are the hallmarks of this type of dementia. Neurotransmitter imbalances are caused by these changes in hippocampus, cortex, and nucleus basalis. There are a variety of signs and symptoms associated with this sort of mental health problem. These include: confusion and disorientation; aggressiveness; paranoia; sleep difficulties; apathy; aphasia; depression; and incontinence of the urine system. Restrictive, dyskinetic, and Babinski-like symptoms were seen in the patients with extrapyramidal symptoms. To treat Alzheimer's disease, a variety of synthetic medicines were employed. Tacrine, donepezil, and rivastigmine were the most often used cholinesterase inhibitors. They also evaluated the muscarinic cholinergic agonists Xanomeline and Milameline for their ability to alleviate symptoms. A majority of these medications could only address the cognitive deficiencies that were discovered while conducting the testing trials. Rivastigmine, Donepezil, Memantine, and Galantamine are all FDA-approved medications for the treatment of most kinds of dementia. There is a pressing need to find new medications that could potentially treat dementia, as other synthetic drugs merely provide symptomatic relief to demented individuals[27-29]. It's possible that medicinal herbs can be of use in this area. Numerous phytoconstituents in medicinal plants demonstrate a wide range of activities. Dementia-related symptoms and progression can both be slowed or even reversed with the use of these herbs. Plants used to treat Alzheimer's disease reveal a variety of processes, including modulation of plaques, acetylcholinesterase, beta and gamma-secretase, glutathione, NMDA receptors, and cerebral blood flow. For dementia research, many different medicinal plants have been tested, and the majority have demonstrated promising biological effects.



**Fig 1 : Different types of Dementia**



## **Risk factors involved in the precipitation of Dementia :**

**Cerebral Ischemia :** A condition known as cerebral ischemia occurs when the brain's supply of oxygen and glucose is cut off [53]. Neuronal depolarization results in activation of glutamate receptors, which affects the ionic gradients of Na<sup>+</sup>, Ca<sup>++</sup>, Cl<sup>-</sup>, and K<sup>+</sup> in the brain as a result of energy failure. Peri-infarct depolarization occurs as glutamate levels rise in the extracellular space [54]. There is also cerebral edema as a result of water changes. The upregulation of enzyme systems such as lipases, proteases, and endonucleases occurs as a result of an increase in intracellular Ca<sup>++</sup>. Due to a multitude of metabolic mechanisms, free O<sub>2</sub> radicals are produced and apoptotic cell death ensues. Platelet and endothelium selectins, a range of molecules, platelet activating factor, tumour necrosis factor, and an assortment of interleukins [55] are among the inflammatory mediators induced by free radicals. Ca<sup>2+</sup> homeostasis in neurons is regulated by mitochondrial malfunction, which impacts normal neuronal activity. The opening of the mitochondrial transition pore is facilitated by elevated intracellular calcium levels in the mitochondrial matrix, which may eventually lead to cerebral ischemia[30].

**Hypertension :** Many diseases, such as Alzheimer's, stroke, atherosclerosis, myocardial infarction, and cardiovascular disease, are made worse by hypertension, which is presently defined as systolic blood pressure (SBP) over 140 mm Hg and diastolic blood pressure (DBP) over 90 mm Hg. The prevalence of hypertension in the general population is estimated to be 25 percent, with a 50 percent prevalence among those over the age of 70. The increased risk of AD and VaD is most closely connected with high blood pressure in midlife (about 30 years of age), although high blood pressure in later life does not appear to have the similar association with risk. The development of cognitive dysfunction and the risk of Vascular Degeneration (VaD) are closely linked when hypertension, or high blood pressure, occurs in middle age or later in life. Infarcts in the lacunae or cortex, leukoaraiosis, and eventually cognitive loss are considered to be caused by hypertension altering the vessels in the brain. An increase in the production of A $\beta$ , which can lead to neural malfunction, the loss of synapse and neuronal connections, as well as dementia. Hypotension is characterised by a DBP 70 mm Hg. The decline in blood pressure in old age [61] can also have negative effects on cognition, despite the fact that it has been found to be a substantial risk factor for AD and VaD when blood pressure is elevated. As a result of pathological alterations such as the development of A $\beta$  plaques, reduced artery pressure may lead to hypoxicischemic changes that could operate synergistically with existing pathology to aggravate the degree of dementia[31].

**Hypercholesterolemia :** The development of vascular cognitive impairment is also associated with a high cholesterol level. The NF- $\kappa$ B pathway is activated in hypercholesterolemia. NF-B is well-known for its functions in inflammation and immunological responses, as well as cell division and death. The phosphorylation of IB by IB kinase is one of the most important mechanisms for NF-B activation (IKK). Two catalytic and one regulatory subunits of IKK (IKK- and IKK-) are affected by an IB kinase (IKK). An important role for the NF-B family of transcription factors in promoting inflammation is played. The nuclear translocation of NF-B is

regulated by both conventional and non-conventional mechanisms. There are many stimuli that can activate NF-B, but the most common is RelA/p50, which is the primary effector of NF-B. RelB/p52 complexes are bound to DNA through the nf-b pathway after a delay in response to a restricted spectrum of stimuli. Many neurodegenerative illnesses, including Huntington's, Parkinson's, stroke, and Alzheimer's, have been linked to NF-B activation. It is also important to note that cholesterol has a crucial function in regulating the activity of enzymes involved in the creation of A protein and APP metabolism. Cleavage of APP occurs in the hydrophobic bilayer and is catalysed by the  $\alpha$ -secretase,  $\beta$ -secretase, and  $\gamma$ -secretase enzyme activities. Cholesterol levels alter  $\beta$ -secretase activity, resulting in lower levels of soluble APP and higher levels of neurotoxic A proteins[32].

**Diabetes :** Diabetes mellitus (DM) is a global health issue that is on the rise at an alarming rate. Metabolic disorders including diabetes mellitus (DM) have been linked to deterioration in mental abilities among the elderly. The pancreatic cells of Type 1 DM are unable to produce insulin, resulting in a deficiency in insulin synthesis. Insulin resistance is a hallmark of type 2 diabetes. Oxidative stress and the accumulation of glycation end products can lead to functional or cellular impairments in the brain as a result of high blood sugar. In the absence of an enzyme, reducing sugars and free amino groups of proteins, nucleic acids, and lipids react to create sugar-derived AGEs. Individuals with diabetes are more likely to develop them because of the greater availability of glucose in their bloodstreams. This results in decreased flexibility of arteries due to aberrant interactions of changed extracellular matrix proteins with other matrix proteins and integrins. Additionally, AGE precursors modify plasma proteins to form ligands that attach to endothelial cell AGE receptors[33]. Neurodegenerative illnesses are linked to the activation of a transcription factor known as NF $\kappa$ B when the AGE receptor is bound to it. Changing mitochondrial dynamics or mitochondrial malfunction in organs such the pancreas, liver, skeletal muscle, and white adipose tissue can lead to insulin resistance, obesity, and diabetes. Neuronal function, survival, and development are all dependent on the proper functioning of mitochondria in the brain.

**Oxidative stress :** Oxidative stress occurs when the body's antioxidant systems are overwhelmed by oxidation. Due to the damage caused by oxygen free radicals, oxidative stress is harmful to the body. Apoptosis, viral multiplication, and inflammatory reactions are all affected by oxidative stress. Biomarkers of oxidative stress include gene transcription factors such as NF-B and AP-1, which undergo an oxidation and reduction cycle. It is vital to sustain normal physiological functions at low levels, while large quantities of free radicals are harmful. Stabilizing these free radicals is done by giving them electrons from antioxidants. In dementia, the existence of reactive oxygen species (ROS) and an elevated level of lipid peroxidation, as well as a decrease in polyunsaturated fatty acids (PUFAs), are hallmarks of the disease. Inflammation, injury, and reduced cerebral blood flow have long been linked to dementia, and ROS have been shown to cause cell damage and death as a result. Mitochondria are thought to be the primary source of ROS. One of the most prevalent oxygen free radicals is superoxide anion

(O<sub>2</sub>•), which is formed when electrons in the mitochondrial respiratory chain transfer inefficiently[34]. The production of superoxide anion (O<sub>2</sub>•) is the result of complexes I and III leaking electrons onto molecular oxygen. The amount of electrons available on the mitochondrial respiratory chain affects the rate at which O<sub>2</sub>• is generated. Hyperoxia and hyperglycemia, such as diabetes, enhance the generation of superoxide anion (O<sub>2</sub>•). Superoxide anions (O<sub>2</sub>•) tend to accumulate in hypoxia because the final electron acceptor (O<sub>2</sub>) is absent from complex IV. Dismutases enzymes convert Superoxide anion (O<sub>2</sub>•) to hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) in order to remove it from the body (H<sub>2</sub>O<sub>2</sub>). A free radical, (O<sub>2</sub>•), is more dangerous than H<sub>2</sub>O<sub>2</sub> because it is more reactive.

**Tobacco smoking :** Around 1.3 billion people smoke cigarettes around the world, and that number is expected to rise to 1.7 billion by 2025. Individuals who smoke cigarettes for an extended period of time run the risk of developing cardiovascular diseases (CVS). Tobacco smoke can aggravate mitochondrial dysfunction and cause oxidative stress over time by generating reactive oxygen species (ROS). It is thought that the underlying mechanism in the pathophysiology related with tobacco consumption is chronic smoking's negative effects on complex IV and complex III activities in mitochondrial respiratory chain (MRC). The oxidative stress caused by mitochondrial malfunction in neurons may eventually contribute to dementia. Atherosclerosis and thrombosis are common side effects of smoking, and it also raises the likelihood of cognitive deterioration. An increased risk of ischemic stroke and, ultimately, dementia, can be attributed to smoking tobacco, which has been shown to cause atherosclerosis. To make matters worse, studies have shown evidence that nicotine can both reduce the neurotoxic effects of A and protect against dementia. Because of the presence of nicotine in cigarettes, nicotinic acetylcholine receptors are upregulated and activated, protecting cells against the cytotoxic effects of A[35].

**Alcohol consumption:** Consumption of alcoholic beverages is a major public health concern worldwide. There are both good and negative effects on disease pathology associated with alcohol consumption. Moderate alcohol consumption has been shown to be advantageous (under specific circumstances), while excessive consumption is harmful to one's health. Our body's physiology is affected differently by different drinking habits. Heavy drinking and alcoholism have a negative impact on memory function. In contrast, a new study has found that persons who give up drinking or consume more than 14 units a week are more likely to develop dementia. Neurodegenerative illnesses including cerebellar degeneration and alcoholic dementia may be triggered by long-term chronic alcohol consumption. Despite this, the underlying mechanisms of alcohol-induced neurotoxicity are still a mystery[36-37]. Activated microglial cells with high AGE-albumin levels may play a significant role in alcohol-induced neurodegeneration, according to one hypothesis. Ethanol promotes ROS formation and weakens cellular defensive mechanisms, making it more vulnerable to infection. The liver is the primary location of ethanol metabolism in the body, and these harmful effects of ethanol are most obvious there.

**Atherosclerosis** : As the artery wall thickens as a result of chronic inflammation, the coronary artery becomes clogged with cholesterol, macrophages, and smooth muscle cells (SMC) and eventually restricts blood flow. Atherosclerosis is considered to be the primary underlying pathological condition that may eventually lead to a number of cerebrovascular and cardiovascular diseases. Both the large and the medium-sized arteries are known to be affected by atherosclerosis, a heart condition. The circle of Willis is part of the cerebral circulation of the human brain[38]. Atherosclerosis, which worsens as people age, is more likely to affect the blood arteries in the circle of Willis. Thrombosis can occur when atherosclerotic plaques rupture. Embolization is a medical emergency caused by blood artery occlusion, which is caused by a thrombus. Cavotid artery embolism usually occurs in the extracerebral sections of vertebral artery. An atherosclerotic aneurysm is caused by damage to the cerebral vascular wall and infrequently ruptures, resulting in bleeding. As a result, vascular dysfunction in the brain plays a role in the development of stroke and vascular dementia. The aetiology of CVS diseases such as hypertension, cardiac hypertrophy, atherosclerosis, and other endothelial disorders is linked to the production of reactive oxygen species (ROS) as a result of mitochondrial malfunction. Beta cells in the pancreas are destroyed, LDL protein is oxidised, and endothelial cells become dysfunctional when mitochondrial reactive oxygen species are produced in excess. Plaque rupture may be facilitated by apoptosis in mitochondrial dynamics. Atherosclerotic lesions that develop over time as a result of subclinical bouts of plaque rupture are known as hemodynamically significant lesions. Infarctions and strokes can be caused by the rupture of flow-limiting plaques[39-40].

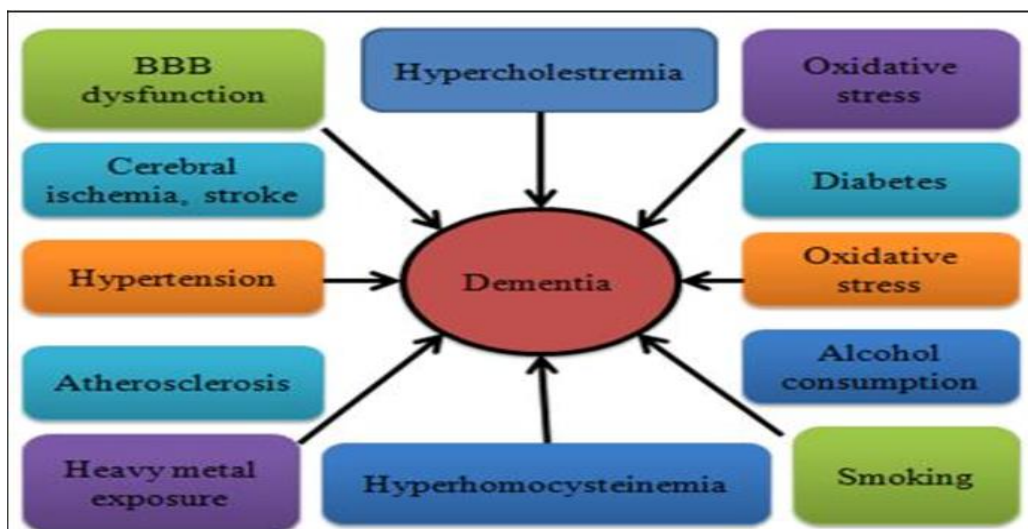
**Stroke** : Dementia and cognitive impairment are common after a stroke. Cerebrovascular illness and dementia have a close association. In most cases, a stroke is the trigger for the development of vascular dementia. However, the fundamental mechanisms of post-stroke cognitive impairment are still a mystery to researchers. After a stroke, those who are at high risk of cognitive impairment and dementia may be at greater risk of developing these conditions. One of the most prominent risk factors for VaD is a stroke, which can lead to an increase in  $\beta$ -amyloid formation and phosphorylation of tau protein[41]. As a result of the ischemia episode, APP expression rises in the extracellular spaces of the brain and astrocytes produce more amyloid precursor protein. White matter degeneration and cell death result from the interaction between amyloid and factors like apolipoproteins and inflammatory factors including apolipoproteins and presenilins. When it comes to apoptosis, neuronal death begins several hours after ischemic stroke and lasts for several days, apart from necrotic cell death.

**Blood Brain Barrier Dysfunction** : Another probable explanation for cognitive failure is that the blood-brain barrier has been damaged. The BBB is a critical regulator of the neuronal and glial cell environment and is found in all vertebrates. It restricts free diffusion of circulating chemicals, leukocytes, and red blood cells into the brain interstitial space. Endothelial-like, high-resistance tight junctions that connect brain capillary endothelial cells provide a barrier between the blood and the brain. Damage to the endothelial cells' tight connections leads in abnormal

angiogenesis, vascular regression, hypoperfusion of the central nervous system (CNS), and inflammatory responses; it can also have adverse effects on synaptic plasticity and neuronal survival. In fact, the number of endothelial mitochondria decreased, as did the number of microvascular fragments, the thickness of the basement membranes, and the width of the channels. The BBB's amyloid inflow and efflux are controlled by two major receptors[42-44].

**Hyperhomocysteinemia** : Homocysteine is one of the most common indicators of neurodegenerative conditions. Memory loss, cognitive impairment, and stroke can all be caused by a rise in Homocysteine levels in the brain. In patients with HHcy, neurodegeneration is more likely to occur. Homocysteine levels are linked to cardiovascular disease, stroke, and dementia. The activation of matrix metalloproteinase-9 (MMP-9) by homocysteine induces extracellular matrix remodelling, in part through promoting redox signalling and influencing intracellular calcium dynamics. They are the calcium-dependent cysteine proteases that are linked to mitochondrial dysfunction and oxidative damage. High homocysteine levels have previously been linked to abnormalities of the mitochondria. B vitamin shortage has been shown to improve the clinical outcomes of patients with severe hyperhomocysteinemia (HHcy), which is a sign of B vitamin deficiency[45].

**Heavy metal** : Arsenic's toxicity and worldwide presence in drinking water and groundwater raise health concerns. High dosages of arsenic have been shown to have both neurodevelopmental and cognitive effects on the brain. In the hippocampus and other memory-related structures, arsenic exposure has been found to cause morphological and neurochemical abnormalities, as well as predicted learning and memory losses. Toxic metalloid As (As) is widespread in the environment, and chronic exposure to it through contaminated drinking water has become an issue of public health worldwide. Neurotoxin arsenic has long been known to damage memory and cognition. Synaptic plasticity is influenced by changes in the NMDA receptor complex as well as postsynaptic signalling proteins, which have been linked to arsenic-induced neurotoxicity, as well as learning and memory impairment[46]. Additionally, arsenic exposure has been linked to changes in the brain's ability to learn and remember, as seen by the disruption of neurotransmitters (norepinephrine, serotonin and dopamine). Arsenic exposure has been shown to alter neural synapses, which can impair spatial memory, according to some experts. Ca<sup>2+</sup>/calmodulin-dependent protein kinase IV, a key regulator of long-term depression (LTD) and learning and memory deficits, is downregulated in arsenic-exposed rats. Autophagy has also been shown to be induced by arsenic during the development of its harmful effects on the brain. Cell and tissue damage in the brain are caused by an imbalance in the cytoprotective autophagy, which in turn causes a decrease in the ability to learn and remember.



**Fig 2 : Different risk factors associated with the Dementia**

### **Traditional uses of *Sesbania grandiflora***

A vitiated vata and arthralgia can be alleviated by the root bark of the red-flowered type. Tonic, anthelmintic, febrifuge, astringent, cooling, bitter, and tonic are all properties of the bark. Scabies are treated externally using the crushed bark. Taking the bark's juice can help with dyspepsia, diarrhoea, and gastric pain. Slightly toxic sap nine-like substance is found in the leaves, which are pungently acerbic, sweetly aperitif, tonic and diuretic. Nasal catarrh, nyctalopia, and Cephalalgia were treated with the leaf juices. Leaves can be chewed to help with stomatalgia and mouth and throat disinfection[47]. Aromatic and medicinal properties include antipyretic and anti-inflammatory properties. It is used to treat nyctalopia and intermittent fevers with the juice of the blossoms. Sweet, bitter, astringent, cooling, bitter, tonic, laxative and febrifuge; treat scabies, dyspepsia, gastralgia, nyctalopia, anaemia, emaciation and vitiated states of tridosa;. anti-cancer activity, antioxidant activity, cardioprotective effect and antiuricolytic activity have been found in the ethanolextract of leaves and flowers. Leaf juice has antiuricolytic and hepatoprotective activity. Leaf extract has wound-healing and anti-ulcer activity, bark has anti-inflammatory and antibacterial properties. Seedoils and flowers have anthelmintic activity. Bark has anti-inflammation and anti-cancer properties[48].

### **Current therapeutic approaches in the treatment of Dementia :**

**Nuclear factor Kappa B- receptors antagonists :** Inflammation is regulated by the nuclear factor kappa-B (NF- $\kappa$ B) family of transcription factors. As NF- $\kappa$ B promotes inflammation, adhesion, and oxidation, it is hypothesised to contribute to cardiovascular disease and endothelial dysfunction. NF- $\kappa$ B has also been linked to amyloid beta-42-induced neuronal cell death and memory loss. The activation of NF- $\kappa$ B, which results in the overexpression of genes for pro-inflammatory enzymes, occurs in aging-induced dementia. VaD experiments have shown that NF- $\kappa$ B inhibition has a positive effect[49].

**NADPH oxidase inhibitor** : Enzyme complex NADPH oxidase, which is involved in microbial activation and ROS generation, is a multi-subunit enzyme. Multiprotein electron transport system creates huge amounts of superoxide from molecular oxygen by the reduction of oxygen molecule. NADPH oxidase is a key player in the production of reactive oxygen species (ROS) as well as host defence and signal transduction pathways. Several oxidative stress conditions, including high blood pressure, are associated with the superoxide-producing enzyme NADPH. In Alzheimer's disease brains, this enzyme is highly active[50]. Excessive production of ROS in the brains of APP mice is attributed to NADPH activity, and the inhibition of NADPH activity by either pharmacological inhibitors or NADPH oxidase complex assembly blocked ROS production and cerebrovascular dysfunction induced by A and ageing, according to the findings. ROS created in cerebrovascular cells by the enzyme NADPH oxidase may raise the risk of cellular malfunction, cellular death, and dementia, according to a study published in the journal Neurology. In STZ-induced diabetes in rats, the NADPH oxidase inhibitor 4hydroxy-3methoxyacetophenone (HMAP) significantly reduced endothelial dysfunction, cognitive impairment, and metabolic abnormalities[51].

**HMG-Co A Reductase inhibitors** : HMG-Co A reductase inhibitors, such as statins, are often prescribed to treat cardiovascular disease. A common application of statins is to lower serum cholesterol levels, which lowers the risk of coronary heart disease death. Statins may have neuroprotective and antioxidant properties, according to previous studies. Statins have been shown to aid animal learning and memory. By a variety of mechanisms, statins have been proven to reduce the incidence of ischemic stroke and related memory loss. Statins have also been shown to have a positive impact on LMethionine-induced VAD[52].

**Angiotensin II blockers** : There are many roles for the RAS in the brain, and each one has a distinct function. There is evidence that angiotensin II (AT-II) in the brain contributes to cognitive loss and may be blocked by angiotensin receptor blockers (ARBs) in Alzheimer's disease in addition to its vasoactive effects[53]. Antioxidative stress and ischemic brain damage can be prevented by AT-II type 1 receptor blockers (ARBs), which have been shown to lessen the onset of stroke, stroke severity, the incidence of dementia as well as the progression of dementia.

**PPAR $\gamma$  Agonists** : There are three PPAR isoforms:, / and. Preserving the integrity of the endothelium barrier is one of the most important aspects of cardiovascular health. Neuronal death can be prevented by activating PPAR- receptors in the central nervous system, which reduces oxidative stress and inflammation[54]. Amyloid precursor protein degradation, beta-site enzyme 1 (BACE 1), and Wnt signalling can all be affected by the action of PPAR agonists. Furthermore, PPAR agonists have the capacity to alter a wide range of signalling molecules and pathways. A recent study found that PPAR- is linked to improved memory and cognitive performance in patients with Alzheimer's disease (AD).

**Androgens** : Some tissues, including the brain, are affected by testosterone, a gonadal sex hormone. These additional benefits include an increase in muscular mass, an increase in sexual desire and libido as well as a lowered chance of osteoporosis. The induction of neurogenesis by testosterone is also well-documented. During some key times of central nervous system (CNS) development, the presence or lack of this hormone determines the adult's morphological and behavioural characteristics. Mitogen-activated protein kinase (MAPK) signalling is involved in androgens' neuroprotective action in neurons[55]. MAPK activation in cultured hippocampus neurons can be triggered by testosterone and its metabolite dihydrotestosterone (DHT), which involves phosphorylation of ERK-1 and ERK-2. Neuroprotection against beta-amyloid damage can be mediated by pharmacological reduction of MAPK/ERK signalling. Proteolytic cleavage of Bcl-2-associated death promoter protein (Bcl-2) was found to be reliant on the phosphorylation of p90kDa ribosomal S6 kinase (Rsk) (BAD). androgen-induced phosphorylation of Rsk prevented and bad inhibited androgen neuroprotection. Since androgen shortage causes elevated blood glucose levels, total cholesterol, low-density lipoprotein (LDL), levels of pro-inflammatory cytokines and a thicker artery wall, it is known to degrade endothelial functioning[56] .

**Inducible Nitric oxide synthase (iNOS)** : In order to maintain the homeostatic conditions of the circulatory, immunological, and neurological systems, nitric oxide (NO) plays a critical function. Isoforms of the NO synthase (NOS) enzyme are found in three categories: neuronal, iNOS, and endothelium (eNOS). Brain nitric oxide (NO) is a key signalling and redox component in the brain, and iNOS plays a critical role in neuroinflammation by generating high levels of NO[57].

**HDAC ( Histone Deacetylase ) Inhibitors** : Nuclear and cytoplasmic proteins' lysine residues can be more easily acetylated through posttranslational means thanks to the use of HDAC inhibitors, which block the activity of histone deacetylases. This results in an increase in the expression of genes that defend against an ischemia insult when HDAC inhibition is used. TSA, sodium butyrate (SB), and vorinostatator suberanilohydroxamic acid have been shown to have neuroprotective properties in hypoxia-ischemia injury[58]. The blood levels of chemokine CXCL10, IL-1, and COX-2 in the ipsilateral hemisphere are prevented by HDACis, which demonstrate neuroprotection. As a part of the homeostasis of protein acetylation, HDACs play a critical role in the regulation of important cellular functions, such as the transcription of genes, which are controlled by HDACs. Chromatin-associated histone proteins serve an important role in the regulation of gene expression and other processes in cells, including neurons. In both in-vivo and in vitro models of brain diseases, HDAC inhibition has been shown to have neuroprotective effects[59-60].

## Conclusions

Many societies have used medicinal plants or ethnomedicine for centuries, and *Sesbania grandiflora* is one of those plants. Different components of plants are utilised as human food in Ayurveda for the treatment of microbiological infections and anaemia, laxatives,



hepatoprotective and cardioprotective agents, urinary stones prevention and treatment. All of the plant's parts can be employed as effective therapeutic agents, either alone or in conjunction with other medicinal herbs. The plant's pharmacological properties are enhanced by the presence of phytochemicals and phytonutrients. Dementia is a condition characterised by a significant decline in cognitive abilities to the point that it poses a significant risk to daily activities and employment. Dementia symptoms include a variety of impairments, including I changes in daily activities, abnormal behaviour, and a decline in cognitive abilities. While dementia most commonly strikes those over 65, it can strike anyone younger than 65, a condition known as early onset dementia. Numerous factors exist for why some people with cognitive abnormalities aren't diagnosed with dementia until much later on in the course of the disease. As a result, MCI is regarded to be at the highest risk for developing dementia, despite having significant cognitive deficits. Dementia can now be treated with a few number of medications. Even if existing drugs can alleviate symptoms, they cannot stop the progression of the disease. Alzheimer's disease progress can be prevented by disrupting the underlying illness pathogenesis mechanism. The development of more disease-modifying drugs with unique therapeutic methods is crucial if we are to find new treatments that target the underlying pathogenic pathways. Several novel therapeutic agents are briefly discussed in this review, including antagonists of nuclear factor kappa-B (NF- $\kappa$ B) receptors, inhibitors of NADPH oxidases, inhibitors of HMG-Co A reductases, angiotensin II blockers, agonists of PPAR receptors and androgen, as well as inhibitors of histone deacetylase (HDAC). These agents may provide new therapeutic strategies for further dementia-oriented research.

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