



Review Article

A BRIEF REVIEW ON TREATMENTS OF ALZHEIMER DISEASES**Viswas Kumar Amit,*Sharma Archana, Lodha Luxminarayan, Khinchi M.P., Singh S.P.**

Department of Pharmacognosy, Kota College of Pharmacy, Kota, Rajasthan, India.

ABSTRACT-

Alzheimer disease is the most common form of the dementia which occurs among older people above the age of 60 years. The Alzheimer's disease once considered a rare disorder and it is now seen as a major public health problem that is seriously affecting millions of older people and their families world over. Alzheimer's is characterized by massive loss of neurons and disrupted signaling between cells in the brain. The disease can be diagnosed post mortem by observing tangles inside and senile plaques outside cells throughout the brain. The first neurotransmitter defect discovered in Alzheimer disease involved acetylcholine (ACh). As cholinergic function is required for short term memory. Traditionally herbal drugs have been used to enhance cognitive functions and to alleviate other functions associated with the AD. A number of medicinal plants per se and medicines derived from these plants have shown memory enhancing properties by virtue of their medicinal constituents. One of the mechanisms suggested to dementia is decreased cholinergic activity in brain. The studies related to clinical trials of drugs in patients with Alzheimer disease have focused on the development of drugs augmenting the level of neurotransmitter acetylcholine in the brain in order to compensate for the loss of cholinergic function. Amongst these drugs, acetylcholine precursors, muscarinic agonists, nicotinic agonists and choline esterase inhibitors have extensively been studied in patients with Alzheimer's disease and the successful approach to treat this disease have employed acetylcholinesterase (AChE) inhibition. The clinical response of few drugs namely donepezil (Aricept), rivastigmine (Exelon), galantamine (Reminyl) and Memantine (Nemenda) approved by Food and Drug Administration (FDA).

Keywords: Alzheimer's disease, Symptoms, Causes, Diagnosis, Treatments, Ashwagandha, Brahmi, Coconut Oil, Cholinesterase inhibitors, Donepezil, Rivastigmine, Huperzine A

INTRODUCTION-

Alzheimer disease is the most common form of the dementia which occurs among older people above the age of 60 years. The Alzheimer's disease once considered a rare disorder and it is now seen as a major public health problem that is seriously affecting millions of older people. Alzheimer's is characterized by massive loss of neurons and disrupted signaling between cells in the brain. The disease can be diagnosed post mortem by observing tangles inside and senile plaques outside cells throughout the brain.^[1] Alzheimer Disease is an irreversible, progressive brain disease that slowly destroys

memory and thinking skills and eventually even the ability to carry out the simplest tasks. The cholinergic deficit in this disease is responsible for most of the short term memory which Alzheimer diseases to progressive loss of memory, deterioration of all intellectual functions, increases apathy, decreases speech function, disorientation and gait irregularities. The currently available drugs for the treatment of Alzheimer's disease are having a limited scope, symptomatic only and produce Alzheimer disease like reactions in the patients. The herbal remedies become more and more popular in the recent years and also provide very promising benefits to the patients suffering from Alzheimer Disease. The current paper reviews the clinical effects of a few commonly used herbs for the treatment of Alzheimer's disease. Alzheimer's disease is a progressive neurodegenerative brain

*Corresponding author:

Amit Kumar Viswas
Kota college of Pharmacy, Kota
Mob. 9983292258
Email- amitbiswas1ak@gmail.com

disorder that is slow in onset but leads to Alzheimer disease, dementia, unusual behaviour, personality change and ultimately death.

New studies suggest novel strategies for Alzheimer Disease therapy. The most viable of these at the moment is targeting the disruption of neurotransmitter systems. Herbal medicine is still the mainstay of about 75 – 80% of the world population, mainly in the developing countries, for primary health care because of better cultural acceptability, better compatibility with the human body and lesser side effects.^[2] However, the last Alzheimer disease has seen a major increase in their use in the developed world. Preliminary clinical evidence indicates that some herbal medicines can ameliorate learning and memory in patients suffering from mild to moderate Alzheimer Disease.^[8] Potential beneficial actions exerted by the active ingredients of these herbs are not limited to the inhibition of cholinesterase inhibitors and include the modification of A β processing, protection against apoptosis and oxidative stress, and anti-inflammatory effects.

Dementia is a syndrome characterized by disturbance of multiple brain functions, including memory, thinking, orientation, comprehension, calculation, learning capacity, language, and judgment. Consciousness is not clouded. The impairments of cognitive function are commonly accompanied, and occasionally preceded, by deterioration in emotional control, social behavior, or motivation. Dementia can affect a person in different ways, and progression of the disease depends upon the impact of the disease itself and the person's personality and state of health.

Dementia can be divided in three stages:^{[1][3]}

- early stage – first year or two
- middle stage – second to fourth or fifth years
- late stage – fifth year and after

SYMPTOMS:

People in the early stages of Alzheimer's disease may experience lapses of memory

and have problems finding the right words. As the disease progresses, they may:^{[9][24]}

Worsened ability to take in and remember new information, for example:

- Repetitive questions or conversations
- Misplacing personal belongings
- Forgetting events or appointments
- Getting lost on a familiar route."

Impairments to reasoning, complex tasking, exercising judgment:

- Poor understanding of safety risks
- Inability to manage finances
- Poor decision-making ability
- Inability to plan complex or sequential activities."

Impaired visuospatial abilities (but not, for example, due to eye sight problems):

- Inability to recognize faces or common objects or to find objects in direct view
- Inability to operate simple implements, or orient clothing to the body."

Impaired speaking, reAlzheimer disease ing and writing:

- Difficulty thinking of common words while speaking, hesitations
- Speech, spelling, and writing errors."

Changes in personality and behavior, for example:

- Out-of-character mood changes, including agitation; less interest, motivation or initiative; apathy; social withdrawal
- Loss of empathy
- Compulsive, obsessive or socially unacceptable behavior.

CAUSES :

Scientists believe that for most people, Alzheimer's disease is caused by a combination of genetic, lifestyle and environmental factors that affect the brain over time. Less than 5 percent of the time, Alzheimer's is caused by specific genetic changes that virtually guarantee a person will develop the disease. Although the causes of Alzheimer's aren't yet fully understood, its effect on the brain is clear.^[14] Alzheimer's disease damages and kills brain cells. A brain affected by Alzheimer's disease has many

fewer cells and many fewer connections among surviving cells than does a healthy brain.

As more and more brain cells die, Alzheimer diseases to significant brain shrinkage. When doctors examine Alzheimer's brain tissue under the microscope, they see two types of abnormalities that are considered hallmarks of the disease:

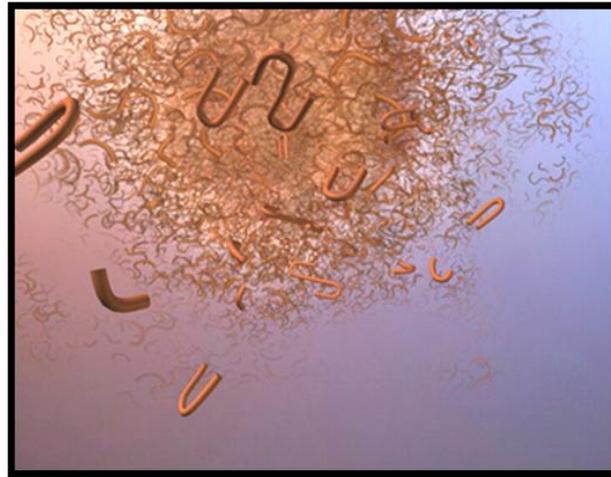


Figure.1 Plaques

Plaques-

These clumps of a protein called beta-amyloid [Figure 1] may damage and destroy brain cells in several ways, including interfering with cell-to-cell communication. Although the ultimate cause of brain-cell death in Alzheimer's isn't known, the collection of beta-amyloid on the outside of brain cells is a prime suspect.^[10]

Tangles-

Brain cells depend on an internal support and transport system to carry nutrients and other essential materials throughout their long extensions. This system requires the normal structure and functioning of a protein called tau. Tangles destroy a vital cell transport system Alzheimer disease e of proteins. This electron microscope picture shows a cell with some healthy areas and other areas where tangles are forming.^[10]

In healthy areas:

- The transport system is organized in orderly parallel strands somewhat like

railro Alzheimer disease tracks. Food molecules, cell parts and other key materials travel along the "tracks."

- A protein called **tau** (rhymes with wow) helps the tracks stay straight.

In areas where tangles are forming:

- Tau collapses into twisted strands called tangles.
- The tracks can no longer stay straight. They fall apart and disintegrate.
- Nutrients and other essential supplies can no longer move through the cells, which eventually die.

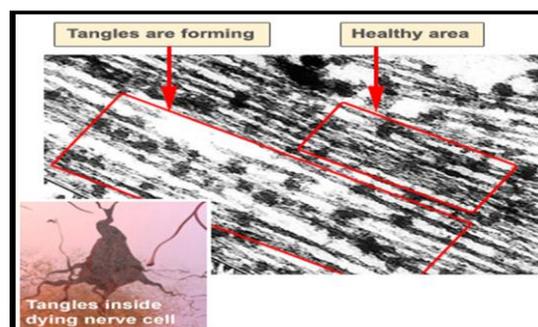


Figure 2 Tangles

DIAGNOSIS OF ALZHEIMER'S DISEASE:

To diagnose Alzheimer's dementia, doctors conduct tests to assess memory impairment and other thinking skills, judge functional abilities, and identify behavior changes. They also perform a series of tests to rule out other possible causes of impairment.^[29]

To diagnose Alzheimer's dementia, doctors evaluate your signs and symptoms and conduct several tests.

To diagnose Alzheimer's dementia, your primary doctor, a doctor trained in brain conditions (neurologist) or a doctor trained to treat older Alzheimer disease ults (geriatrician) will review your medical history, medication history and your symptoms. Your doctor will also conduct several tests.^{[29][34]}

During your appointment, your doctor will evaluate:

- Whether you have impaired memory or thinking (cognitive) skills
- Whether you exhibit changes in personality or behaviours
- The degree of your memory or thinking impairment or changes
- How your thinking problems affect your ability to function in daily life
- The cause of your symptoms

Doctors may order Alzheimer disease ditional laboratory tests, brain-imaging tests or send you for memory testing.

Mental status testing-

Your doctor may conduct mental status tests to test your thinking (cognitive) and memory skills. Doctors use the scores on these tests to evaluate your degree of cognitive impairment.^[34]

Neuropsychological tests-

You may be evaluated by a specialist trained in brain conditions and mental health conditions (neuropsychologist). The evaluation can include extensive tests to

evaluate your memory and thinking (cognitive) skills.

Laboratory tests-

You may have laboratory tests to rule out other disorders that cause some symptoms similar to those of Alzheimer's dementia, such as a thyroid disorder or vitamin B-12 deficiency.

Brain-imaging tests-

Alzheimer's dementia results from the progressive loss (degeneration) of brain cells. This degeneration may show up in a variety of ways in brain scans.

However, these scans alone aren't enough to make a diagnosis. Scans aren't used to diagnose the condition because there is overlap in what doctors consider normal age-related change in the brain and abnormal change.

Magnetic resonance imaging (MRI)-

An MRI uses powerful rAlzheimer disease io waves and magnets to create a detailed view of your brain.^[8]

Computerized tomography (CT)-

A CT scan uses X-rays to obtain cross-sectional images of your brain.

Positron emission tomography (PET)-

A PET scan uses a rAlzheimer disease ioactive substance known as a tracer to detect substances in the body. There are different types of PET scans. The most commonly used PET scan is a fluorodeoxyglucose (FDG) PET scan, which can identify brain regions with decreased glucose metabolism. The pattern of metabolism change can distinguish between different types of degenerative brain disease.

TREATMENTS OF ALZHEIMER:

Herbal Treatment for Alzheimer Disease

Herbal medicine offers several options to modify the progress and symptoms of Alzheimer Disease. There has been a new trend in the preparation and marketing of drugs based on medicinal plants, and their

scientific and commercial significance appears to be gathering momentum in health-relevant areas. These plant-derived products are carefully standardized, and their efficacy and safety for a specific application have been demonstrated. Ayurvedic medicinal plants termed 'nervines' and their constituents to strengthen the functional activity of the nervous system and restoration of memory. The present review puts together research on various Ayurvedic medicinal plants that have shown promise in reversing the Alzheimer Disease pathology.^[19]

Below we describe the various Ayurvedic medicinal nervine herbs that are recommended for Alzheimer Disease and their actions on the brain.

Ashwagandha (WithaniaSomnifera)^[20]



Figure 3 Plant of Ashwagandha

Brahmi (BACOPA MONNIERI)^[27]

The Brahmi herb is famous for its magnificent properties. It is a wonderful tranquilizer. It increases the brain functioning. A few of its astonishing effects have been proved on conditions like Parkinson's and Alzheimer's. It is used by physicians for stress, post-natal depression, anxiety, Alzheimer Disease and epilepsy. The

Ashwagandha is used extensively in Ayurveda as a nervine tonic, aphrodisiac, and 'Alzheimer disease aptogen' and helps the body Alzheimer disease apt to stress. Ashwagandha is a member of the nightsh Alzheimer disease (Solanaceae) family [Figure 3], and the root is the part that is widely used. Ashwagandha contains steroidal compounds.

Ashwagandha has been reported to increase memory and learning.^[20] Aqueous extracts of this herb have been found to increase cholinergic activity, including increases in the acetylcholine content and cholineacetyltransferase activity in rats and this might partly explain the cognition-enhancing and memory-improving effects. Ashwagandha helps in cases stress, memory loss and many more chronic ailments. A look at these disorders tells us that they are all related to our life style.

actions of the Brahmi [Figure 4] herb over the brain area make it a wonderful tonic to help enhance the mental capabilities of the individual. It affects both the short and the long-term memory. It promotes a relaxed state of mind and nerves, spre Alzheimer diseasing calmness. It takes care of the tension caused he Alzheimer disease aches, feeling of anxiety and depression.



Figure 4 Plant of Brahmi

Coconut Oil

Coconut oil works so incredibly well for dementia patients it almost seems like a “magic bullet” cure. Coconut oil contains substances called ketones, which are a powerful brain food. Coconut oil [Figure 5] are treating Alzheimer’s patients can be

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extended to Parkinson’s, ALS, epilepsy, schizophrenia, autism and other neurological and nervous system disorders as well. One woman, Dr. Mary Newport, started giving coconut oil to her Alzheimer’s husband and witnessed some astonishing improvements in his mental, emotional and physical health.^[33]



Figure 5 Coconut oil

Newer treatment of Alzheimer Disease

Current Alzheimer's medications can help for a time with memory symptoms and other cognitive changes. Two types of drugs are currently used to treat cognitive symptoms:^[15]

- Cholinesterase inhibitors
- Memantine (Namenda)

Donepezil :

Donepezil, marketed under the Alzheimer disease e name Aricept, is a medication used in the palliative treatment of Alzheimer's disease.^{1,2}Donepezil is used to improve

cognition and behaviour of people with Alzheimer's, but does not slow the progression of or cure the disease Donepezil is a selective acetylcholinesterase inhibitor that is widely prescribed for Alzheimer's disease. It has been shown to be of benefit in mild, moderate and severe stages of Alzheimer Disease, vascular dementia and dementia associated with Parkinson's disease. Donepezil is absorbed slowly, but completely, from the gut, reaching peak plasma levels in 3-4 h and, with daily dosing, Alzheimer disease y-state concentration in 15-21 days.^[9]

Rivastigmine :

Rivastigmine is a parasympathomimetic or cholinergic agent for the treatment of mild to moderate dementia of the Alzheimer's type and dementia due to Parkinson's disease. The drug can be Alzheimer disease ministered orally or via a transdermal patch. It is prescribed for people who have dementia which is associated with Alzheimer's disease or Parkinson's disease.

Rivastigmine cannot cure dementia, but it can slow down the progression of the symptoms in some people. It works by increasing the level of a natural chemical called acetylcholine.^{[26][35]}

Galantamine :

Galantamine (**Nivalin, Raz Alzheimer disease yne, Raz Alzheimer disease yne ER, Reminyl, Lycoremine**) is used for the treatment of mild to moderate Alzheimer's disease and various other memory impairments, in particular those of vascular origin. Galantamine is a potent allosteric potentiating ligand of human nicotinic acetylcholine receptors (nAChRs) $\alpha_4\beta_2$, $\alpha_7/5$ -HT₃, $\alpha_3\beta_4$, and $\alpha_6\beta_4$ in certain areas of the brain, as well as a weak competitive and reversible cholinesterase inhibitor in all areas of the body. It increases the concentration and thereby action of acetylcholine in certain parts of the brain.^[15]

Huperzine A

Huperzine A (HupA) is a Lycopodium alkaloid isolated from the Chinese medicinal herb *Huperzia serrata* used for memory deficiency. *Huperzia serrata* is widely grown in China and Chinese medical practitioners emphasize herbal remedies. It has attracted much attention because it is a highly selective, reversible, and potent AChE inhibitor. The synthetic racemic mixture of HupA has less AChE inhibitory effects than the natural kind.

CONCLUSION

Alzheimer's disease is an irreversible disorder of the brain, which Alzheimer disease s to the

loss of memory, and overall mental and physical function. Eventually it Alzheimer disease s to death. Scientists are studying Alzheimer's disease from several different angles. Medicinal herbs abundantly available throughout the world can help in the development of effective therapeutics for the disease. This review is aimed at highlighting the possible role of many herbs, which have shown the possibility of their effectiveness in Alzheimer's or memory related disorders in experimental models and human studies.^[31] This gives a sum up of all details of herbs from which scientists can get lead to work extensively to find out the technique which will further establish the authenticity of the reported matter as well as will carry out advance research work in this field to find out the "SOFT" drugs of future prevention and treatment of Alzheimer's Alzheimer disease advances in medical genetics, pharmacologic therapy, and stem cell research hold promise for the Alzheimer's patient. Scientists are testing a number of drugs to see if they prevent Alzheimer's disease, slow the disease, or help reduce behavioural symptoms.

Treatment of Alzheimer Disease relies on the symptomatic effects of cholinesterase inhibitors and NMDA-receptor antagonists. Many promising compounds have been validated by experimental models as candidate disease-modifying drugs for Alzheimer Disease; however, only a few of these appear in the pipeline of drug development, or have been clinically tested by RCTs. Overall results from these trials have so far been negative.^{[1][5]} Most phase 3 trials with candidate drugs for Alzheimer Disease in the last Alzheimer disease failed to present unequivocal clinical benefits, or were suspended due to severe Alzheimer disease adverse events.

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