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Review on Introduction of Alzheimer's disease and herbal agent to treatment Alzheimer's diseases

Author - Mr. Mayurbalasaheb Waghule
Guided by - Prof. Khade Poonam.
Principle - Dr. MeghaSalve Mam
Department of bachelor of pharmacy
ShivajiraoPawar college of pharmacy Pachegaon. Ahmadnagar 413725

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ABSTRACT-
In short, Alzheimer's disease (AD) is a disease in which brain cells die. It is the most common cause of dementia and is characterized by a loss of mental ability and independence in everyday activities. Hypotheses were put forward: Cholinergic and amyloid are the two main causes of the disease. AD is considered a complex disease. In addition, the disease is influenced by many risk factors, including advanced age, genetics, head trauma, vascular disease, infections and environmental variables. Currently, only two types of drugs are approved for the treatment of Alzheimer's disease, namely cholinesterase enzyme inhibitors and N-methyl-d-aspartate (NMDA) antagonists. These medications are only effective in treating the symptoms of AD; They do not treat the underlying cause of the disease.
Current treatments have huge side effects, are inadequate, have poor patient compliance, and are expensive. Therefore, there is an urgent need for viable alternative treatments for Alzheimer's disease with minimal or no side effects. The current review indicates that herbal medicines have many advantages over the currently available synthetic drugs for the management of Alzheimer's disease, helping patients recover better and faster from neurodegenerative disorders.
Medicinal plants can improve the quality of life of patients with Alzheimer's disease.
Keyword- Alzheimer's disease, herbal medicine, neurogenerative , herbal drug treatment.

I. INTRODUCTION –

Alzheimer's disease (AD) is a severe neurodegenerative disease that represents a serious health problem. By 2050, the number of people affected is expected to reach 152 million. The disease Is characterized by progressive loss of memory and cognitive functions in People. Currently, the diagnosis of AD is based on clinical symptoms and cognitive tests, which are subjective and, in Cases, inaccurate.(1)

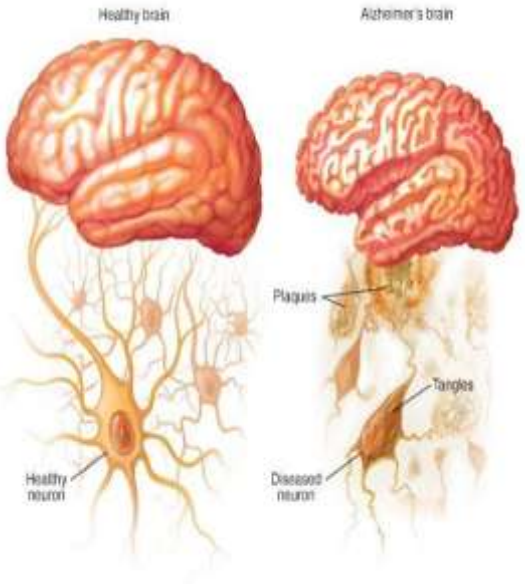

Figure 2.differance between healthy brain and Alzheimer's brain (9)

The main feature of this disease is difficulty in managing everyday household activities and cognitive and emotional disorders in the elderly. Treating Alzheimer's disease is a clinical challenge. With the development of cholinesterase inhibitors and the N-methyl-D-aspartate antagonist (memantine), good prospects for controlling AD symptoms have emerged. Treatment decisions must be based on clinical studies and take into account the pathophysiology and epidemiology of the disease. (2)

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The main objectives of these clinical trials are to reduce behavioral and psychological symptoms of dementia (BPSD) and improve cognitive function and functional activity status, thereby reducing impairments in instrumental activities of daily living (IADL) and increasing institutionalization rates (nursing homes). Be lowered Positioning).Unfortunately, only a limited number of studies have addressed this topic and follow-up periods have been less than two years. Despite the lack of sufficient therapeutic efficacy in mild and moderate AD, these drugs are still considered as first-line treatment for AD (3). Cost-effectiveness studies suggest that memantine (4,5) and idonepezil (6) are beneficial in reducing hospitalization and/or cognitive impairment in patients with AD. More recently, two of Clinical trials showed no improvement in cognitive deficits (7,8) or a reduction in institutionalization (8).

Modern therapies have enormous side effects, are inadequate, rarely follow patient recommendations and are expensive. There is therefore an urgent need to develop possible alternative treatments for Alzheimer's disease with little or no side effects as Ayurveda, traditional Chinese rituals, meditation and exercise have been proven effective since ancient times.

Herbal treatment of AD offers greater benefits than currently existing pharmacological therapies and provides greater safety and effectiveness. Medicinal plants also improve the quality of life of patients as they can be used as nutraceuticals and even a slight increase in dosage does not pose a problem when consumed. The active ingredients of plants, herbs and their extracts could lead to the discovery of medicines that can be successfully used in the treatment of AD. It is widely accepted that research into the chemistry of natural products opens up many new possibilities in the treatment of atopic dermatitis. (10)

Treatment –

There is no cure for AD, but there are many therapeutic options that can regulate disease progression and improve patients' quality of life. Maintaining good cardiovascular fitness (11), continuing mental activity (12), and consuming plant-based foods (13) can help improve cognitive function and reduce the risk of heart disease. Alzheimer's disease is vital. . a greater Influence on the development of the disease (17). From a pharmacological perspective, AD symptoms can be alleviated by administration of two classes of approved drugs: acetylcholinesterase inhibitors, which inhibit the enzymatic breakdown of acetylcholine (14), and acetylcholine receptor antagonists. N-Methyl-D-Aspartate (NMDA), which prevent glutamate. Binding to NMDA receptors to prevent cell death after excessive neuronal activation (15). Approved AchE inhibitors include donepezil, galantamine and rivastigmine, while the only approved NMDA-Receptor antagonist is memantine.

However, these drugs cannot treat or prevent Alzheimer's disease; Therefore, there is growing interest in discovering disease-modifying therapies that inhibit or slow the pathophysiological development of Alzheimer's disease (16).

This article discusses various medicinal plants that have shown significant results in treating various neurogenerative diseases such as Alzheimer's disease.

1. Lavender

Synonyms: Garden lavender, English lavender, Lavender angustifolia

Biological source: Lavandulaangustifolia is a flowering plant in the mint family (Lamiaceae).

Chemical components: Common secondary plant substances are carotenoids, phenolic acids and ascorbic acid. These are factors responsible for the powerful inhibitory and antioxidant effects of AChE, which are useful in the treatment of AD.

Figure 2. Lavender (20)

Role in Alzheimer's disease: The effect of the aqueous extract of Lavandulaangustifolia Mill was studied on AD rats. There were Promising results where learning deficits in AD rats were reversed by lavender extract The results demonstrated the promising therapeutic potential of L. angustifolia to improve and treat Alzheimer's disease. Lavender extract has a positive effect on the plasticity of

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synaptic transmission , thus improving impaired memory in animals suffering from Alzheimer's disease. These results suggest a possible therapeutic role of lavender in the treatment of Alzheimer's disease [18,19].Lavender is primarily used as an aromatic essential oil for relaxation. In a single-blind, randomized, controlled trial of women, 80 women who bathed in lavender oil daily experienced improved mood, less aggression, and a more positive attitude (24).

Likewise, according to a randomized double-blind study, The combination of lavender (60 drops of lavandula tincture per day) and imipramine (100 mg per day) was more effective in treating depression than either drug alone. Control test.The results of this study suggest that taking moderate amounts of lavender may help reduce the number of tricyclic antidepressants needed to treat depression, resulting in fewer side effects (25).

2. Ashwagandha

Synonyms: Ashwagandha, Indian Ginseng, Winter Cherry.

Biological source: Withaniasomnifera is a small shrub from the solanaceae family.

Chemical Components: W.somnifera contains Withanoloidessomniferin, pseudo-withanin, tropine, somniferin, withaferin, Sitoindoside 7 and 8 as well as anferin, withanin, pseudotropin, 3-agloyloxytropane, somnin, choline and some of the other Chemical compounds.

Figure 3.Ashwagandha(21)

Role in Alzheimer's disease –

Roots suppress nuclear factor (NF-B) and regulate the expression of genes involved in mediators of oxidative stress and inflammation, thereby inducing antioxidant and anti-inflammatory effects by preventing the development of Aβ.(22).The total alkaloid extract of ashwagandha root has shown a calming effect on the central nervous system (CNS). In several mammal species, suggesting that this plant can be used for relaxation. A recent double-blind, randomized, placebo-controlled study of ashwagandha's effects on stress found that it reduced stress symptoms, difficulty concentrating, and reversed forgetfulness in a dose-dependent manner, with 500 mg per day being most effective (23).

3.Guava-

Synonyms: Apple guava, Lemmon guava, Common guava.

Biological Source: Psidiumguajava is an evergreen shrub

Family -Myrtaceae.

Chemical composition: Main phytoconstituent of P. guajava is Linoleic acid. Other chemicals found in this plant aretheflavonol Morin, morin-3-O-arabinoside, quercetin and quercetin-3-O-arabinoside.

Figure 4.Guava(27)

Role in Alzheimer's Disease:

Guava leaf extract was examined for its antioxidant properties in the linoleic acid system using the thiocyanate method . A free radical scavenging test was conducted, the results of which showed that guava leaves had significant antioxidant activity that could be effective in the treatment of AD. (26).

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4. Henna-

Synonyms: Hina tree, mignonette tree, Egyptian privet**Biological Source:** Lawsoniainermis is a flowering plant

Family- Lythraceae.

Chemical components - Pseudoephedrine, methylcarbamate, Phytol, Aspidofractinine-3-methanol, phenol, 2,6- bis(1,1-dimethylethyl)-4-methyl

Figure 5.Henna (28)

Role in Alzheimer's Disease-

Memory loss caused by oxidative neurodegeneration was successfully reversed by Lawsoniainermis. The exact mechanism of this reversal is unknown; However, the antioxidant potential is contained in the nootropic abilities of the plant (29).

5.Sage:

Synonyms: Common sage, culinary sage, Dalmatian sage, golden sage, kitchen sage, true sage, broadleaf sage.**Biological Source:** Salvia officinalis is an evergreen flowering shrub**Family -** Lamiaceae.

Chemical Constituents- 1,8cineole, α-pinene, vridiflorol camphor,

Figure 6.sage (30)

Role in Alzheimer's disease –

A constant dose of 60 drops/kg of extract is administered to patients with mild to moderate AD for 4-month periods to a patient with mild to moderate Alzheimer's disease. The test results showed that Patients did not experience shock throughout the entire period of use. The extract of this plant also protects the brain from oxidative damage (31).

6.Shankhpushpi (Convolvulus pluricaulis)

Botanical Name- Convolvulus Microphyllus

Family-Convolvulaceae

Chemical composition - Convoline, Convolamine

Figure 7.Shankhpushpi (Convolvulus pluricaulis) (32)

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Role in Alzheimer's disease –

Several species of Shankapushpi have been described, including Convolvulus pluricaulis (CP), Convolvulus microphyllus, Evolvulusalsinoides and Clitoriaternatea (CT). Shankhpushpi is a plant widely grown in India, where the entire plant is used in various recipes as a nervous system tonic and improves memory and cognitive functions [33, 34, 35].A variety of secondary metabolites have been isolated, including triterpenoids, flavonol glycosides, anthocyanins, and steroids, which may be responsible for the nootropic and memory-enhancing properties of Shankhpushpi, among other pharmacological activities (35-38).Shankhpushpi is believed to calm nerves by regulating the production of stress hormones, adrenaline and cortisol in the body [38]. It is also recommended for nervous disorders such as stress, anxiety, mental fatigue and insomnia [7, 41, 35].Ethanolic extracts of CP and ethyl acetate and its aqueous fractions significantly improved learning and memory in rats (59). The ethanolic extract of CP also had significant antioxidant activity when tested in vitro [33, 34, 39, 40].

A whole plant ethanol extract administered to cholesterol-fed gerbils significantly reduced serum cholesterol, LDL cholesterol, triglycerides and phospholipids [35].

7. Turmeric (Curcuma longa)

Synonyms: Curcuma domestica**Family** - Zingiberaceae.

Chemical composition - Curcumin, demethoxycurcumin and bisdemethoxycurcumin.

Figure 8. Turmeric (42)

Role in Alzheimer's Disease-

Curcumin has anti-inflammatory properties by inhibiting the development of astrocytes, microglia, TNF-α And IL-1. It also limits the development of microglia, lowers cholesterol levels, prevents brain dysregulation and inhibits acetylcholinesterase. Through the mechanism described above, C. longa limits the progression of AD(22).Turmeric has anti-inflammatory, antiseptic and antibacterial properties and has long been used in Indian medicine to treat various medical conditions. This versatile spice helps detoxify the liver, balance cholesterol levels, fight allergies, improve digestion, and strengthen the immune system (43). Epidemiological studies show a 4.4 times lower incidence of AD in Southeast Asian countries where turmeric is commonly used as a food seasoning (44).

Other studies suggest that turmeric's nonsteroidal anti-inflammatory properties are associated with a reduced risk of Alzheimer's disease (46). In fact, when curcumin was administered to older mice with advanced plaque deposits similar to those in Alzheimer's disease, curcumin reduced the amount of plaque deposits (45, 46,47,48).

It reduced oxidative damage and reversed amyloid pathology in AD transgenic mice (47,48).

8.Drumstick Tree:

Synonyms: Drumstick tree,horseradish tree, benoil tree or benzolive tree.

Biological Name : M. oleifera is a medicinal herb

Family: Moringaceae

Chemical Composition : vitamin A and C, tannins, isothiocyanates, alkaloids and saponins and polyphenols i.e, flavonoids, Chlorogenic acid, glucosinolates, and phenolic acids

Figure 9.drumstick tree(49)

Role in Alzheimer's disease –

Its antioxidant effects have been linked to improving learning and memory. M. oleifera

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reversed the effect of colchicine on NE, 5-HT, and DA levels in the brain. Other studies have also shown that M. oleifera prevented memory loss in Laboratory models of dementia (22).

9. Brahmi (Bacopamonnieri)

Synonyms: water hyssop, waterhyssop, brahmi, thyme-leafed gratiola

Family- Scrophulariaceae

Chemical composition – hersaponin, apigenin, D-mannitol, monnierasides I-III, plantainoside B and cucurbitacin; the alkaloids brahmine, herpestine and nicotine (50).

Figure 10. Brahmi (Bacopamonnieri) (51)

Role in Alzheimer's disease –

BM may act by reducing divalent metals, removing reactive oxygen species, reducing lipid peroxide formation, and inhibiting lipoxygenase activity (52). Traditionally, bone marrow is used to improve memory and cognitive function (53).BM extracts have been extensively studied for their neuropharmacological and nootropic effect. In the hippocampus, BM increases protein kinase activity, which may contribute to its nootropic effects (54). BM also inhibited cholinergic degeneration and showed cognitive-enhancing effects in a rat model of Alzheimer's disease (55).

BM extracts protect neurons from amyloid-beta-induced cell death by suppressing cellular acetylcholinesterase activity. Furthermore, neurons treated with BM extract expressed lower levels of reactive oxygen species, suggesting that Brahmi reduced intracellular oxidative stress (56).MB-enriched phytochemicals were evaluated for safety and short-term tolerability in healthy adult volunteers. A detailed study of clinical, hematological, biochemical and electrocardiographic parameters revealed no adverse effects in any of the volunteers who received a single capsule containing the fortified herb orally for 30 days (300 mg in the first 15 days and 450 mg in the next 15 Days) (57)..Based on the above: After a study and other clinical trials conducted to determine the effectiveness of BM in the treatment of memory and attention disorders, BM has now been introduced in the Indian market for the treatment of memory and attention disorders . These clinical studies of Bacopa serve as a model for other herbs to determine their effective dosage range, time to reach therapeutic levels, and their effects over extended periods of administration.

10.Gotu kola

Synonyms: Kodavan, Indian pennywort and Asiatic pennywort

Biological Source: Contellaasiatica**Family :** Apiaceae.

Chemical composition -Pentacyclictriterpinoids, Centellose, Centelloside, Madecassoside and Asiaticoside derivatives which include Asiatic acid and Asiaticaside.

Figure 11. Gotu kola (58)

Role in Alzheimer's disease –

C.asiatica reduces the concentration of free radicals and inhibits the death of β-amyloid cells. The aqueous extract of this plant has the ability to reduce oxidative stress and prevent the contraction of neuronal processes. The extract of this plant protects DNA from damage. This plant is important for the brain and nerve cells. In

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Ayurvedic medicine, gotu kola is one of the important herbs that rejuvenates nerve and brain cells and is said to increase intelligence, longevity, and memory (59). Asiaticoside derivatives, including asiatic acid and asiaticosides, have been shown to reduce hydrogen peroxide-induced cell death, reduce free radical concentrations, and inhibit amyloid beta cell death in vitro, suggesting a possible role for gotu kola in treatment and prevention from AD can be concluded. And beta-amyloid toxicity [60].

II. CONCLUSION –

Many people who use herbal medicines find that alternative health solutions are more compatible with their values, beliefs and philosophical approach to health and life. It also seems likely that many people feel that herbal medicines give them the strength to undergo treatment without consulting a doctor (it is precisely this approach that could account for the growing popularity of patient-initiated diagnostic procedures, such as whole-body diagnostics , underlie).The risk is that many people believe that herbal remedies do not cause toxin problems or, in fact, side effects. Furthermore, they ignore the numerous possible connections between herbal medicine and randomly identified drugs. The Ayurvedic system of medicine has gained popularity in recent years in terms of nutritional and treatment options. The initial development of Ayurvedic herbal supplements included only anecdotal or epidemiological information (or both), without any understanding of how they work. The Ayurvedic medicine industry has come a long way, from the days when it was not considered necessary to test Ayurvedic preparations before use, to numerous double-blind, randomized, controlled trials and the introduction of best manufacturing practice guidelines for the Industry . In order to provide a "proof" of concept, a more scientifically based and high quality approach was chosen. And "operating mode".The allopathic and Ayurvedic medical systems are based on independent principles. Allopathic medicines are prescribed on a symptomatic basis while Ayurvedic medicines are prescribed based on the balance of the three energies (Vata, Pita and Kapha) required for maintaining good health.

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