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Review On Herbal Therapy for Alzheimer's Disease

Authors: - 1. Ashutosh.V. Mahalley* 2. Abhishek. M. Naik 3. Yashkumar. R. Dhole, 4. Dr. Swati P. Deshmukh.

Shraddha Institute of Pharmacy Kondala zambre washim-444505.

3. Assistant Professor Department of Pharmacology, Shraddha Institute of Pharmacy Kondala zambre, Washim-444505.

4. Professor Department of pharmacology shraddha institute of pharmacy, kondala zambre, Washim-444505.

Abstract

Alzheimer's complaint (announcement) is related to cognitive impairment, madness observed generally in aged population due to neurodegeneration in an ongoing manner. It gradationally worsens memory power of the case. The hallmark opinion features include conformation of senile pillars and Neurofibrillary be fuddlements (NFT'S). Too little vacuity of Acetyl choline (ACh) a neurotransmitter in the cerebral region due to metabolism by an enzyme Acetyl choline esterase before showing its action and neural death are the primary reasons for announcement. There are numerous orders of Anti-Alzheimer's medicines available for operation of announcement in the request but due to lack of patient compliance successful issues weren't observed. piecemeal from this including Nutraceuticals in diet diurnal routine, Aromatherapy, variations in the regular schedule, rehearsing yoga regularly relaxes mind and body from pressures, wakefulness, blood rotation, detoxification of organs due to metrical breathings and reduce frequency of prevalence of headache are proven to show stylish results by relieving stress according to check. At present herbal drug has turn out to be stylish choice for the operation of announcement because of its vacuity, veritably profitable, good case compliance, ease of expression and lower injurious side goods. new ways can be used for the development of herbal drug. This review completely discuses about the circumstance of announcement, its Pathophysiology, different stages in the complaint, colorful picky remedial targets for announcement, available Anti AD herbal medicines similar as Curcumin, Withania somnifera, Bhrami, Ginkgo biloba, guggul, ginseng, sauces with essential canvases,

unpredictable canvases, source and civilization of the sauces, medium of action of the Phytochemicals in the condiment responsible for treating announcement.

Keywords: Alzheimer's Disease, Dementia, Treatments, Herbal Medicine, Cognitive Impairment

Introduction:

Alzheimer's Brain Disease that Causes Memory loss of other cognitive impairment. It's the Most common Adults Couse of dementia in older, adults. The Disease is named after pr. Alois Alzheimer in 1906 using Criteria of progressive memory loss, disorientation & pathological markers (sasenile plaques, & neurofibrillary tangles.) Alois Alzheimer's noticed a presence of amyloid plaques & a massive loss of neurons while examining the brain of his first patient that suffered from memory loss & change of personality before dying & described the condition as a serious Disease of the cerebral cortex [1]. These plaques & tangles in the brain are Still Considered Some of the main features of Alzheimer's Disease. Another feature is the loss. of Connections between nerve cells (neurons) in the Brain. Neurons transmit messages between different parts of the brain from the Brain to Muscle e organs in the Body Many other Complex brain changes are thought to play a role in Alzheimer's too. This Damage initially takes place in parts. of the Brain involved in memory, including the entorhinal cortex & Hippocampus. It later affects areas in the cerebral cortex, such as those responsible for language, reasoning social behavior. Eventually, many other areas of the brain are damaged [2]. Progressive loss of cognitive function can be Caused by cerebral disorder like Alzheimer Disease. or others factors such as intoxication, infection, abnormality in the pulmonary & circulatory system which cause a reduction in the oxygen supply to the brain, nutritional Deficiency, vitamin B12 Deficiency, tumors. Others [3]. Alzheimer's Disease is the most prevalent chronic neurodegenerative disease with 5.7 million people living with the disease in the USA alone & this is projected to increase to 13.8 million people by 2050. Globally, The Number of people currently suffering with dementia is estimated to be 50 million of which 30-35 million have Alzheimer's Disease. The risk of Developing the disease is influenced by Both Genetic and environment factors, however the biggest risk factor by far is age the older you are more likely you are to develop the disease but it is not an inevitable part of ageing. for instance, about one in 50 people aged Between 65 to 69 have dementia and this figure rise to one in five for those aged between 85 to 89. Given the Global increase in life expectancy, this represents a huge societal and economic challenge in the impact extending to those living with the AD, along with their caregivers and family [4 ,5].

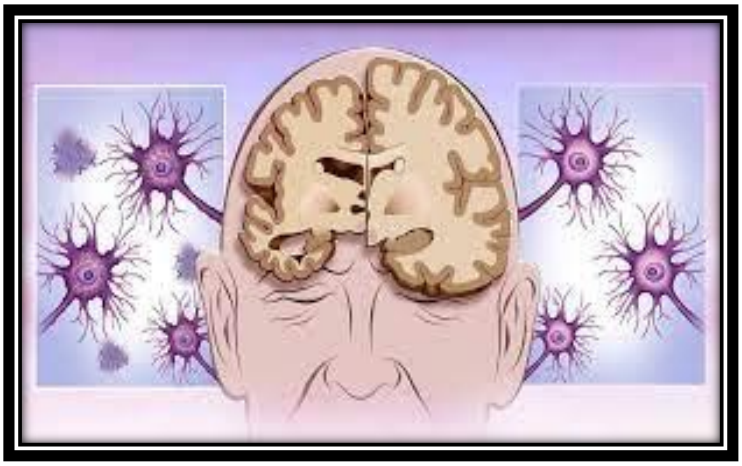

Fig no.1 : Difference between normal brain and Alzheimer's disease [6].

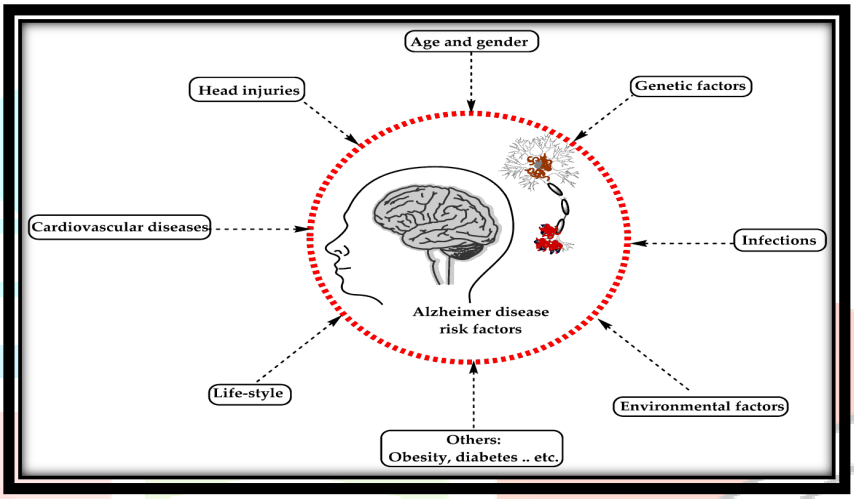

Fig no.2: Causes of Alzheimer's disease [7].

The clinical phases of Alzheimer's Disease can be classified into four phases.[8]

1.Pre-clinical or Presymptomatic stages: This stage is characterized by mild memory loss & early pathological changes in cortes and Hippocampus, with no functional impairment in the daily activity's absence of clinical sign and symptoms.

2.**The Mild or early stage of AD**: Where several symptoms start to appears in patient, such as a trouble in the daily life of the patient with a loss of Concentration & memory, disorientation of place and time, a change in the mood, a development of depression.

3. **Moderate AD stage**: In which the disease spread to cerebral cortex areas that results in an increased memory loss with trouble recognizing family & friend, a loss of impulse control difficulty in madding, writing and speaking.

4. Severe AD stages: which involves the spread of the disease to the entire cortex area with a severe accumulation of neurite plaques & neurofibrillary tangles resulting in a progressive functional cognitive impairment where the patients Cannot recognize their family at all and may become bedridden with difficulties in swallowing & urination eventually leading to the patient's death due to their complications.

Anti- Alzheimer's agent

Rivastigmine: It is a parasympathomimetic or cholinergic agent for the treatment of mild to moderate dementia of the Alzheimer's type. It is a cholinesterase inhibitor that inhibits both butyrylcholinesterase and acetylcholinesterase. It is a carbamate derivative that is structurally related to physostigmine, but not to donepezil and tacrine.

Mechanism of action: It inhibits the enzymes acetylcholinesterase (ACHE) and butyrylcholinesterase (BuChE), which are present both in the central nervous system (CNS) and peripherally. Central cholinergic neurons are important for regulation of memory, thus in the CNS the boost of acetylcholine caused by AChE blockade contributes to improved cognitive functioning, in particular, rivastigmine appears to be somewhat selective for AChE in the cortex and hippocampus-two regions important for memory-over other areas of the brain. Rivastigmine's blockade of BuChE in glia may also contribute to enhanced acetylcholine levels.

Adverse effects: Rivastigmine have received thorough study as it has been on the market for some time. The main adverse effects associated with the use of rivastigmine are gastrointestinal. The primary symptoms are nausea and vomiting. These acute effects primarily occur during the initial dose escalation phase of therapy with upward dose titration of the drug to achieve a therapeutic dose. These events can be minimized using a slow titration schedule and taking the medication with food if prescribing an oral formulation. In a study done to analyze the safety and tolerability of cholinesterase inhibitors used to treat Alzheimer dementia, researchers found rivastigmine to be the drug to have the highest rate of gastrointestinal side effect.

Pharmacokinetic: It is well absorbed orally, with a bioavailability of about 40% in the 3-mg dose Pharmacokinetics is linear up to 3 mg BID, but nonlinear at higher doses. Eliminationism through the urine. Peak plasma concentrations are about one hour, with peak cerebrospinal fluid concentrations at 1.4-3.8 hours.

Uses: It is a parasympathomimetic and a reversible cholinesterase inhibitor. It is used in the treatment Alzheimer's disease that is associated with memory loss and cognitive deficits is a deficiency of acetylcholine as a result of selective loss of cholinergic neurons in the cerebral cortex, nucleus basalis, and hippocampus.

Dose: The oral doses of rivastigmine should be titrated with a 3 mg per day increment every 2 to 4 weeks. The initial initial dose of 1.5 mg twice daily is recommended followed by an increase by 1.5 mg/dose after four weeks.

Brand Name: Exelon Capsule, Rivasmine Capsule, Rivamer Capsule.

TACRINE: It is centrally active cholinesterase inhibitor that has been used to counter the effects of muscle relaxants, as a respiratory stimulant, and in the treatment of Alzheimer's disease and other central nervous system disorders.

Mechanism of action: The mechanism of tacrine is not fully known, but it is proposed that the drug is an anticholinesterase agent which reversibly binds with and inactivates cholinesterase's. This inhibits the hydrolysis of acetylcholine released from functioning cholinergic neurons, thus leading to an accumulation of acetylcholine at cholinergic synapses. The result is a prolonged effect of acetylcholine.

Use: It is used to treatment the mild to moderate dementia of the Alzheimer's type.

MEMANTINE: It is an amantadine derivative with low to moderate-affinity for NMDA receptors. It is a noncompetitive NMDA receptor antagonist that binds preferentially to NMDA receptor-operated cation channels. It blocks the effects of excessive levels of glutamate that may lead to neuronal dysfunction.

Mechanism of action: It is a noncompetitive low-affinity N-methyl-D-aspartate (NMDA)receptor antagonist that binds to the magnesium site when the channel is open. (1) If amyloid's synaptic effects lead to a steady (tonic) leak of glutamate and result in excessive calcium influx in postsynaptic neurons, this could cause memory problems and, in the long term, accumulation of free radicals and thus destruction of neurons. (2) It blocks the downstream effects of tonic glutamate release by "plugging" the NMDA long channel and thus may improve memory and prevent neurodegeneration. (3) Because memantine has low affinity, when there is a phasic burst of glutamate and depolarization occurs, this is enough to remove memantine from the ion channel and thus allow normal neurotransmission. It also has o antagonist properties and weak 5HT, antagonist properties, but it is not clear what these contribute to the actions of this agent in Alzheimer's disease. Since its mechanism of action in Alzheimer's disease is so different from cholinesterase inhibition, memantine is usually given concomitantly with a cholinesterase inhibitor to exploit the potential of both of these approaches and to get additive results in patients. Pharmacokinetic: It is well absorbed orally with a bioavailability of approximately 100%. Peak plasma concentrations are reached in 3-7 hours. Food has no effect on absorption. The volume of distribution is 9 to 11 L/kg and proteins binding 45%. It is excreted predominantly in the urine, unchanged [8].

Brand name: Axure 5-20 mg tablet.

Use: it is used to treat memory loss.

Side effect: Bloating or swelling of the face, arms, hands, lower legs, or feet, Headache, nervousness, pounding in the ears, rapid weight gain, slow or fast heartbeat, tingling of the hands or feet, unusual weight gain or loss.

Medicinal plant used in the treatment of Alzheimer's disease:

Present day curatives are inadequate and have enormous adverse goods. So, there's a critical need for possible indispensable treatments for announcement with minimum or no side goods. colorful medicinal shops are suggested to enhance the memory and treat announcement. Herbal remedy for announcement has further advantages when compared to presently being medicine curatives with necessary side goods. it can also ameliorate the cases' quality of life as they can be consumed as Nutraceuticals and indeed any slight increase in cure may not be a problem when consumed. In order to deliver these herbal phrasings a proper route of administration must be named so that they reach the point and show the remedial action.

Phytochemical screening and mechanism of action:

Phytochemicals are the chemical molecules contained in plants not usually processed for pharmacological purposes. Phytochemicals influence the function of various receptors for both excitatory and inhibitory neurotransmitters in the brain and thus can maintain or alter the chemical balance of the brain.

1.Curcuma longa:

Fig.no.3: Curcuma Longa

It's generally called as turmeric used in Asia for thousands of times in Ayurveda, Siddha, Unani, traditional Chinese drug. The world's largest patron, consumer and exporter of turmeric is India. It's an imperishable herbaceous factory. The turmeric greasepaint contains 60- 70 carbohydrates, 6- 13 water, 6- 8 proteins, 3- 7 essential canvases, 2- 7 salutary fiber, 1- 6 curcuminoids. It has been proven that curcumin operation is useful in the treatment of announcement and madness it also has the capability to drop the conformation of Amyloid pillars and detainments declination of neurons as these both are hallmark of announcement the overall memory of announcement cases is bettered Curcuminoids are proven to have strong antioxidant action demonstrated by the inhibition of the conformation and propagation of free revolutionaries. It decreases the low- viscosity lipoprotein oxidation and the free revolutionaries that beget the deterioration of neurons, not only in announcement but also in other neuron degenerative diseases similar as Huntington's and Parkinson's complaint. The situations of beta- Amyloid in announcement mice that were given low boluses of curcumin were dropped by around 40 in comparison to those that weren't treated with curcumin. In addition, low boluses of curcumin also caused a 43 drop in the so- called "shrine burden" that these beta- Amyloid have on the smarts of announcement mice.

Unexpectedly low boluses of curcumin given over longer period were actually more effective than high boluses in combating the neurodegenerative process of announcement, at advanced attention, curcumin binds to Amyloid beta and block its tone assembly [9,10].

2.Withania somnifera:

Fig.no.4: Withania Somnifera

This factory is generally called as Ashwagandha or Indian ginseng; it contains different types of chemical element similar as alkaloids, steroidal lactones, saponins. Recently has been used as medicinal factory in Ayurveda as it possesses multiple uses. The bioactive element and the shops excerpt are used in treatment and forestallment of colorful conditions similar as Arthritis, incompetence, amnesia, cancer and neurodegenerative diseases. It has capability to revitalize jitters, bone gist and reproductive system property. Ashwagandha can ameliorate cognitive geste in rats subordinated to oxidative damage that occurs in announcement and can reverse accumulation of β- Amyloid peptides (Aβ) intertwined in the complaint. Researches stated that Withania somnifera produces its salutary goods by reducing oxidative damage, enhancing poisonous Aβ concurrence and can devaluate neurodegeneration. The medium of action of Withania somnifera in humans isn't clear. Beast studies have shown that the Sitoindosides VII- X and Withaferina A (glycowithanolides) are the active phytophenols, responsible for the medium of increased cortical Muscarnic acetylcholine capacity, with amodulation of cholinergic neurotransmission. These studies indicate the use of Withania somnifera can beget significant changes in neurological birth functions. Molecular modeling studies showed that Withanamides- A, C Uniquely bind to active half of beta- amyloid and help fibril conformation. Waterless excerpt increases the cholinergic exertion, whereas Methanol excerpt causes neuritis outgrowth in cure and time dependent anner in mortal neuroblastoma cells. Experimenters hypothecate that it can be applied clinically in forestallment, and conceivably repair, of central nervous system disease [11].

3.Bacopa monnieri:

Fig.no.5: Bacopa monnieri

Bacopamonniera (Bhrami) in the Ayurveda system of Indian Herbal Medicine has been used for centuries. Traditionally, Ayurvedic medical system has been using it for anxiety relief, as a alcohol for the brain to enhance literacy and memory development, and forestallment of epilepsy. Aging leads to colorful degenerative changes in the body, and the volume and quality of these changes depend on upon the deconstruction and physiology of the towel. The factors that contribute to these changes are oxidative damage to the DNA and hormonal insufficiency. Normal stress response requires accompanied functioning of colorful hormones and neurotransmitters. Bacopa contains numerous alkaloids, similar Asbrahmine and Herpestine, saponins, d-mannitol, Hersaponin and monnierin that are responsible for the medicinal value. Other active ingredients include betulic acid, Stigmastarol, beta sitosterol, multitudinous bacosides, and bacopasaponins. The bacosides enhance kinase exertion, neuronal conflation, and restore synaptic exertion. These neuronal form conducts are precious in announcement operation. In hippocampus it enhances protein kinase exertion that may contribute to its nootropic exertion which means an enhancement in cognitive functioning. Bhrami excerpts have shown protection of neurons from beta- Amyloid convinced cell death by suppressing cellular acetyl cholinesterase exertion. It has also reversed conduct similar as reduction of acetyl choline, reduction in Choline acetyl Transferases, drop in Muscarinic cholinergic receptor list in anterior cortex and hippocampus [12].

4. Commiphorawightii:

Fig.no.6: Commiphorawightii

It is generally called as guggul set up in northern Africa to central Asia, this shop grows abundantly in thirsty and semi-arid climates and tolerates poor soil. Effectively used in Unani and ayurvedic drug. Goo guggul excerpt contains colorful phytochemicals similar as Diterpenoids, triterpenoids, steroids, long chain aliphatic tetrols, carbohydrates, unpredictable can vasesy, lignans, and Amino acids. It has significant defensive effect against the Streptozotocin- convinced memory deficiency model of madness and the effect can be attributed to its cholesterol lowering anti-oxidant and anti-acetylcholinesterase exertion these compliances suggest Guggu lipid as an implicit Anti-dementia medicine. It acts on impairment in literacy and memory and dropped acetylcholinesterase situations in hippocampus [13].

5.Magnolia officinalis:

Fig.no.7: Magnolia officinalis

It's generally called as Houpa magnolia they're distributed extensively in mountains and denes of demitasse at advanced mound. The whole dinghy contains phytochemicals similar as Magnolol, Honokiol, Two Polyphenolic composites. This factory shows peroxisome- proliferator actuated receptor gamma militant exertion (PPAR Gamma) and acts as GABA modulator. It's potentially used as Anti-oxidant, Anti-inflammatory, Anti-microbial parcels. Oral pre-treatment of two excerpt products of Magnolia officinalis (10 mg/ Kg/ Day in ethanol) into drinking water for 3 months perfected honorary dysfunction and averted Amyloid beta accumulation in the brain. The excerpts also showed a drop in amyloid precursor proteins and its products. Hence, it's effective in treatment and forestallment of announcement through memory improvement anti-amyloidogenic goods through down regulation of- Secretase exertion and the extent of neuro defensive efficacity depends on area where it's cultivated and styles followed during manufacturing [14].

6.Centella asiatica:

Fig.no.9: Centella asiatica

It's an imperishable flowering factory native to Asia used asculinary vegetable Cognitive enhancer and medicinal condiment. It contains colorful chemical ingredients similar as Pentacyclic triterpinoids, Centellose, Centelloside, Madecassoside and Asiaticoside derivations which include Asiatic acid and Asiaticaside they've shown to reduce Hydrogen peroxide convinced cell death, decreases free radical attention and inhibit β- Amyloid cell death. Water excerpt of this factory has shown mitigation of Aβ- convinced cell death and also it has downgraded Aβ- convinced alternations in Tau expression and phosphorylation in celllines (according to Gray nora.et.al,). It has the capability to reduce Oxidative stress, prevents loss of neuronal process (according to a check by Alzheimer's Drug Discovery Foundation). Excerpts of this factory reduces lipid peroxidation and protects DNA against damage (according to DhanasekaranM. et. al,). This factory is essential for brain and whim-whams cells and it’s able of enhancing intellect and longevity [15].

7.Rosmarinus officinalis:

Fig.no.11: Rosmarinus officinalis

This factory is generally called as rosemary native to North Africa and Spain used as culinary seasoning and also in incense medications. It's a good source of Vitamin B- 6, iron, calcium. Monoterpenes (pinene, camphene, myrcene, limonine), Monoterpenols (broneol) are the chemical ingredients. Essential oil painting uprooted from this factory contain1, 8- Cineole hence used in Aromatherapy, it stimulated body and brain, Improves cognitive performance in terms of speed and delicacy. Experimenters have revealed that certain Phytochemicals in the condiment put a stop to the declination of acetylcholine, an important brain chemical needed for normal neurotransmission. A deficit of this chemical is typically seen in Alzheimer’s cases [21-25].

8.Grape seeds extracts:

Fig.no.12. Grape seeds extracts

It's an evanescent woody unfolding factory in North east countries it's extensively cultivated. Consumed a table grape or converted into wine, jam, jelly, excerpts, seed canvases, raisins. Fruits from these shops are of different colors which include green, pink, orange, unheroic, dark purple, black. Variations of grandiloquent color in red wine are due to the volume of Anthocyanins and others polyphenolic colors. Grape polyphenols may heighten cognition and guard your pate by maintaining vascular health and function also they play important part in signaling neurotransmitters and reducing your threat of parlous oxidation, both linked to a lower threat of cognitive decline as a part of a factory- grounded diet [26-35].

Conclusion:

Due to poor patient compliance towards drugs and their lethal side effects upon choric usage, at present there was a paradigm shift of patient choice of medication towards herbal which made a revolution this due to many advantages over the medications it has less adverse effects and they target the site easily upon slight modification its physicochemical properties, in spite of all these herbal therapies is economical to all classes of population. Even on any slight overdose of medicine will not be a problem. Out of all these advantageous aspects herbal medicine became a best choice of medication for management AD along with this regular meditation and yoga add more benefits for better and fast recovery of patient from AD.

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