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REVIEW ARTICLE **OPEN ACCESS**

Treatment of Alzheimer's diseases in various system of medicine: In practice - an overview

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ABSTRACT
Alzheimer's disease (AD) is one of the fourth leading causes of death in developed nations after heart disease, cancer, and stroke. Alzheimer's disease is characterized by impairment of learning and memory capacity (Cognition) caused by neurodegeneration and formation of amyloid beta tangles in the brain. No cure for Alzheimer's exists and the drugs currently available to treat the disease have limited effectiveness. It is believed that therapeutic intervention that could postpone the onset or progression of Alzheimer's disease would dramatically reduce the number of cases in the future. Currently available treatments with different system of medicines are not a 100% cure the disease, whereas all are symptomatic relief. There is high demand to develop treatment, which target the molecular level to change the progression of the disease conditions; remove or inhibit the further formation of beta amyloid fragments in the central nervous system. This review summarizes the information of stable solution for AD treatment through biological and cellular activities. Clinical applications of various systems of the medicine in practice to provide sufficient baseline information, that could be used in treatment campaigns and patient improvement process, thereby providing new functional leads from different path for the treatment Alzheimer's disease.
Key Words: *AD-Alzheimer's Disease, Aβ - Amyloid beta, Ach – Acetyl Choline, AChE- Acetyl Choline Esterase; ChEI – Choline Esterase Inhibitors.*

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INTRODUCTION

Ecological humiliation, increased industrialization, changes in life style and excessive use of pesticides, herbicides, fertilizer and other toxic chemicals in the production of food materials are serious threatening to human beings and posing health hazards. These toxic chemicals are producing neurotoxins which cause neurodegenerative disorders by affecting the transmission of the neurotransmitters in between the neurons. Alzheimer's disease (AD) is the most common disease among the different kind of neurodegenerative disorders. It's a common form of the dementia which generally occurs at the age of 60 years. Alzheimer's disease is an irreversible, progressive brain disorder that slowly abolishes the memory, intellectual skills and eventually decreases the ability to carry out the simplest tasks. The World Health Organization (WHO) declared that 5% of men and 6% of woman of those who above the age of 60 years are affected with Alzheimer's type dementia worldwide. WHO, reported that currently 5 million people affected in USA and 35.6 million people living worldwide in future will be further increased with dementia 7.7 million in USA and 65.7 and 115.4 million dementia in the year of 2030 and 2050 worldwide respectively. The principal pathogenesis of AD is known as loss of neurons in the hippocampus, cortex, and subcortical structures. Presently available curative agents for Alzheimer's disease have been disappointing and the drugs which currently available to treat the AD is address only its symptoms and with limited effectiveness. Recently many researcher looking for better drug from various system of medicinal practice like allopathic, siddha, Ayurveda, Homeopathy etc., Siddha and Ayurveda are similar way of treatment with natural source of drug substance. It shows good response in control of AD related symptoms with minimal side effects. (1-5)

MODERN MEDICINE FOR THE TREATMENT OF ALZHEIMER'S DISEASES

Abundant proof produced by researcher that an inter-relation between the cholinergic neurotransmitter system with cognitive performance and memory function. Acetyl cholinesterase (AChE) succeeded in being a reliable therapeutic target for Alzheimer's indicative progress. Pharmacologic approaches have been focused on neurotransmitters alterations which associated with AD diseases conditions to manipulate and provide normal life. The available treatment strategies are characterized as symptomatic or neuroprotective. In clinical trials the pharmacologic treatment is produced similar output in symptomatic and neuroprotective effects, the key difference in neuroprotective therapy is cumulative benefits will continue, after discontinuation of the treatment. At present practicable pharmacologic therapies, including cholinesterase inhibitors (ChEIs) and N-methyl-D-aspartate (NMDA) receptor antagonists are considered symptomatic treatments based on their ability to slow the clinical progression of cognitive, behavioral, and functional domains (6-10).

Centrally active Choline esterase inhibitors (ChEIs), which targeting acetyl choline esterase alone or affecting both AChE and butryl choline esterase, were the first class of drugs approved by the US Food and Drug Administration (FDA) for the treatment of Alzheimer's disease. The following therapeutic drugs are known choline esterase inhibitors include Donepezil hydrochloride (Donepezil), Galantamine hydrochloride (Galantamine), Rivastigmine tartrate (Rivastigmine), and Tacrine hydrochloride (Tacrine). The benefit of Galantamine is also acts as an allosteric nicotinic receptor modulator, which has been shown to stimulate the presynaptic release of Ach and other neurotransmitters. Because of their more promising therapeutic profiles, greater convenience and absence of hepatotoxicity, the second-generation ChEI agents (*i.e.,* donepezil, galantamine, and rivastigmine) largely have supplanted the first approved drug in this class, tacrine. Currently, memantine hydrochloride (memantine) is the only available drug for targeting cognitive symptoms via a putative glutamatergic mechanism (11-14).

Effectiveness of allopathic drugs in the treatment of Alzheimer's Diseases: (15-19)

Generic Name	Brand Name	Treatment Dose	Reported Adverse events	Effects on daily living	Comments/ special notes
Donepezil	Aricept	5 – 10 mg / day	Risk of muscle cramps and insomnia, Nausea, Insomnia, weight loss, Myasthenia and syncope	Very small effect	It may more effective at 10 mg/day than 5 mg/day
Galantamine	Razadyne	8 or 12 mg, b.i.d.	Nausea, vomiting, dizziness, tremor, abdominal pain, syncope	Very small effect	Act an allosteric modulator at presynaptic level to stimulate the presynaptic nicotinic receptors. The effective dose range between 16-24 mg/day
Memantine	Namenda	5 mg / day	Infrequent but can include headache, dizziness, confusion, somnolence, and infrequent Hallucinations.	Very small effect	Significant improvement is low as compared to Choline esterase inhibitors and it may have effects when long term treatment.
Rivastigmine	Exelon	3, 4.5 and / or 6 mg b.i.d.	Somnolence, vomiting, Nausea, anorexia, sweating, fatigue, asthenia, weight loss and sometime severe esophageal rupture	Very small effect	The transdermal formulation of Rivastigmine is better tolerated than oral and it avoid first pass hepatic metabolism
Tacrine	Cognex	Data not reported	Risk of liver toxicity	Data not reported	Rare use / not in use in current practice

Siddha & Ayurveda drugs for the treatment of Alzheimer's diseases

Indigenous practice of traditional medicines in Tamil Nadu, India knowingly Siddha & Ayurveda is used for various ailments from several millennium. Alzheimer's disease have become more popular in the recent years and the patients with Dementia may faster the brain's degeneration due Alzheimer's disease. The traditional treatments with siddha and Ayurvedha drugs, has drawn the attention of the scientific community. Many herbals from Siddha & Ayurveda treatments have been researched and the benefits of herbal treatments for Alzheimer's and Dementia have been very promising improvement. The uses of some medicinal herbs have been touted to beyond the modern allopathic drug treatment. So many natural compounds are no wonders the medicinal herbs may hold the key to cure this devastating disease. In addition, these herbs are inexpensive and can be easily obtained. Clinical research is being conducted around the world to test the efficacy of herbal medicines vis-a-vis prescription medicines in treating Alzheimer's or dementia patients. The results of herbal products are very promising and highly effective as prescription drugs but also with minimal side effects. Herbal supplements also used as substitute for pharmaceutical drugs or can be used in conjunction with the latter. In the present review, attempts have been made to present state of art of studies made on the role of few herbal medicines in the treatment and management of Alzheimer's disease (20-23).

List of drugs used in the treatment of Alzheimer's disease in Siddha & Ayurveda

Plant Name	Siddha & Ayurveda Name /Common Name	Indication & Medicinal Uses	References
Acorus calamus	Vasambu/Bach	Improve Memory Functions	24-27
Albizzia julibrissin	Cilavakai/Mimosa, Persian Silk Tree	Antidepressant	28-29
Albizzia lebbeck	Indian Siris	Nootropic, Anxiolytic	30-32
Anemarrhena asphodeloides	Zhi Mu	Learning and Memory	33
Amazonian herbal	Marapuama	Nootropic	34
Artemisia absinthium	Macipattiri/Absinth, Green ginger	Improve memory & for the restoration of declining mental function.	35
Bacopa monnieri	Vallarai / Brahmi	Improve Memory	36-38
Centella asiatica	Mandookaparni	Improve Memory Functions	39-43
Celastrus Paniculatus	Malkangni	Improve Memory Functions	44-47
Clitoria ternatea	Butterfly Pea Memory enhancer,	Nootropic, Antistress, anxiolytic	48-50
Commiphora whighitii	Guggul	Learning and Memory	51-52
Cornus officinalis	Dogwood fruit	Anti-amnesic	53
Eclipta alba	Bhringraj	sedative, muscle-relaxant, anxiolytic, Nootropic and anti-stress	54-55
Evolvulus alsinoides	Shankhpushpi	Improve Memory Functions	21
Foeniculum vulgare	Bari Saunf	Improve Strengthening Effects, Improvement in certain psychomotor functions, Mental health	24-25
Ficus religiosa	Peepal Tree	Anti-amnesic	24-25
Glycyrrhiza glabra	Mulethi	Learning and Memory	56-57
Hypericum perforatum	St. Johnswort Nootropic,	Antiamnestic effects	58
Leontopodium alpinum	Edelweiss	Memory Enhancer	59
Panax ginseng	Ginseng, five fingers	Enhancing physical performance, Improved fasting blood glucose levels, Elevated mood.	60-63

Passiflora actinia	Passion flower	Anxiolytic	64
Polygala tenuifolia	Chinese Senaga	cognition-enhancing activity	65-68
Prunus amygdalus	Badam	Nerve Tonics	69
Ptychopetalum olacoides	Muira puama	Improve memory	70
Pueraria tuberosa	Indian Kudzu	Nootropic activity	71
Rubia cordifolia	Indian Madder	Antihyperglycemic, Antistress and Nootropic activity	72
Tabernaemontana divaricata	Crape jasmine	Preventing forgetfulness and Improving the memory	73
Thespesia populnea	Indian Tulip Tree	Alzheimer's disease	74
Vitis vinifera	Grape seed	Nootropic, Adaptogenic	75- 77
Withania somnifera	Ashwagandha	Improve Memory Functions	78-79

Homeopathy system of medicine for the treatment of Alzheimer's diseases

Homeopathy is known as a branch of medical sciences & therapeutics, practiced worldwide, which believes in treating the patient who disease and not merely diseased parts of the patients. The traditional objectives of the homeopathy treatment are to find the simillimum or the therapy that covers the most prominent features of the case. Homeopathy can slow the progression of the disease and ease symptoms, as shown by the Heel studies. There is no single remedy effective for the treatment of all patients. However, several remedies are often associated with this disease.

This holistic approach goes in a long way in the management of various chronic and deep-seated diseases, including Alzheimer's. The homeopathic medicines are formulated from natural substances and the therapeutic values exhibited through stimulating the body's own healing power. The efficacy of multi-drug formulations of homeopathic medicines is proved by effects on both relieving symptoms of Alzheimer's disease and influencing the reduction of the formation of amyloid plaques in the brains (80-81).

The role of homeopathic medicine for various diseases is 'probably do not talk of the 'cure' in real sense, but more of 'control' and 'relief''.

Alzheimer's disease is a condition approach to dementia care, which distinguishes the personal history, character; behavior and individuality of the person have a positive impact on the alzheimers's disease progression. Homeopathy system of medicines offers positive treatment if not cure, where homeopathy system of medicine had a major role on reduction of disease conditions.

List of Homeopathic medicines used in the treatment of Alzheimer's disease as known as Baryta Carb, Natrum Sulf, Nux Vomica, Alumina, Mercurius, Ignatia, Calcarea Carb, Lycopodium, Staphisagria, Chamomilla, Terentula and Conium (80-83).

CONCLUSION

The treatment strategies of Alzheimer's disease and its management for patients with chronic conditions will have to include a variety of interventions directed at multiple targets. The current treatment with modern medicines approved by USFDA and other regulatory authorities are not significant improvement in the treatment and cure of the diseases as well as produce numerous side effects which affect normal day to day life. Moreover, these drugs are symptomatic and do not alter the progression of the underlying disease. This warrants for the exploration of better therapeutics with least side effects for the treatment and management of the disease. Medicinal herbs are abundantly available throughout the world can help in the development of effective therapeutics for the disease.

The aim of this review is to 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. This review gives sum herbal drug details from which scientists can get lead to work extensively to find out the technique and will further establish the authenticity to carry out advance research work in this field to find out the new molecule for future prevention and treatment of Alzheimer's & memory deficient CNS disorders. The available drugs for Alzheimer's disease strategies are everlasting. Since the

researches are need more anxiously for finding a definitive and permanent solution, which is still an unidentified decision that can be put forward.

CONFLICT OF INTEREST

We declared that we don't have any conflict of interest.

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