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REVIEW ON HERBAL DRUG TREATMENT FOR ALZHEIMER DISEASE

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Abstract: Alzheimer's disease is a common progressive neurodegenerative ailment reported in many victims characterized by memory loss, language deficits, depression, personality and behavioral impairments along with dementia. Present day therapies have enormous adverse effects, insufficient, low patient compliance and costly. So, there is an urgent need for possible alternative treatments for Alzheimer's disease with minimal or no side effects. Present review state that herbal medication have many advantages over the currently available synthetic medications for management of Alzheimer's disease for better and fast recovery of patient from neurodegenerative disorders. Medicinal plants can boost life quality of patients with Alzheimer's disease.

Index terms- Alzheimer's disease, herbal medicine, neurogenerative, herbal drug treatment.

1. INTRODUCTION

Alzheimer's disease is the most common cause of dementia. The word dementia describes a set of symptoms that can include memory loss and difficulties with thinking, problem-solving or language. These symptoms occur when the brain is damaged by certain diseases, including Alzheimer's disease. A German psychiatrist in 1906, Dr. Alois Alzheimer first identified brain of a woman who lost her life due to some unusual symptoms such as loss of memory, unpredictable behavior, cognitive impairment later he concluded that the death was due the presence of neuritic plaques and neuro fibrillary tangles and named the disease as Alzheimer's Disease[1,2]. Alzheimer's disease (AD) is a common progressive neurodegenerative ailment reported in many victims characterized by memory loss, language deficits, depression, personality and behavioral impairments along with dementia[3].

Present day therapies have enormous adverse effects, insufficient, low patient compliance and costly. So, there is an urgent need for possible alternative treatments for AD with minimal or no side effects, since from ancient times Ayurveda, traditional Chinese rituals, meditation, and exercise have been shown to be efficient. Traditional medicines are being rediscovered for the treatment of AD including

antioxidants, anti-inflammatory, antiapoptotic, neurotrophic and anti-amyloid drugs. Herbal treatment for AD has more advantages when compared to currently existing drug therapies with more safety and efficacy. Herbal medicines also improve the patients' quality of life as they can be consumed as Nutraceuticals and even any slight increase in dose may not cause a problem when consumed. Active constituents of plants, herbs and their extracts may lead to the discovery of medicines successfully which can be successfully used for the treatment of AD. It is generally believed that research on natural product chemistry has a large number of new possibilities in the treatment of AD. Various herbal medicinal plants are reviewed in this Article which has shown significant results in treatment of different neurogenerative disorders like Alzheimer's Disease.

1. Ashwagandha:

Synonyms: Ashwagandha, Indian ginseng, Winter cherry.

Biological Source: *Withania somnifera* is a small shrub belonging to family Solanaceae.

Chemical constituents: *W.somnifera* contains withanoloides somniferine, pseudo-withanine, tropine, somniferinine, withaferins, sitoindoside7 and 8, and anferine, Withanine, pseudo-tropine, 3-agloyloxytropene, somnine, choline, and are some of the other chemical compounds.

Role in Alzheimer's Disease: The roots suppress nuclear factor (NF-B), and regulates the expression of genes involved in oxidative stress and inflammatory mediators and thereby producing anti-oxidative and anti-inflammatory effect by preventing A β development. [4].



Figure No.1: Morphological Diagram of *Withania somnifera*

2. Bramhi:

Synonyms: Indian pennywort, water hyssop, waterhyssop, thyme-leaved gratiola and herb of grace.

Biological Source: *Bacopa monnieri* belongs to family- Scrophulariaceae.

Chemical Constituents: *Bacopa* contains many alkaloids, such as Brahmine and Herpestine, Hersaponin, saponins, monnierin that are responsible for the medicinal value. Other active constituents include betulic acid, Stigmastanol, numerous bacosides, and bacopasaponins.

Role in Alzheimer's Disease: The bacosides improve kinase activity, neuronal synthesis, and restore synaptic activity. These neuronal repair actions are valuable in AD management. In hippocampus it enhances protein kinase activity that may contribute to its nootropic activity which means an improvement in cognitive functioning. It also comprises of flavonoid glycosides (Myricetin, kaempferol, quercetin), Terpenes and ginkgolides which inhibit AchE activity. Traditionally, Ayurvedic medical system has been using it for anxiety relief, as a tonic for the brain to enhance learning and memory development, and prevention of epilepsy[5].

3. Gotu kola:

Synonyms: Kodavan, Indian pennywort and Asiatic pennywort

Biological Source: *Centella asiatica* belonging to family Apiaceae.

Chemical Constituents: It contains various chemical constituents such as Pentacyclic triterpinoids, Centellose, Centelloside, Madecassoside and Asiaticoside derivatives which include Asiatic acid and Asiaticaside.

Role of *Centella asiatica* in Alzheimer's Disease: *C. asiatica* decreases free radical concentrations and inhibit β -Amyloid cell death. Water extract of this plant has the ability to reduce Oxidative stress, prevents shrinkage of neuronal process. Extract of this plant protects DNA against damage. This plant is essential for brain and nerve cells.

4. Turmeric:

Synonyms: Turmeric.

Biological Name: Rhizomes of *Curcuma longa* are used which belongs to family Zingiberaceae

Chemical Constituents: Major Chemical constituents of turmeric are Curcuminoids, which include curcumin, bisdemethoxycurcumin and demethoxycurcumin. zingiberene, curcumol, Alpha- and beta-tumerone, artumerone, curlone, are some of the other chemical constituents found in the turmeric plant [59].



Figure No. 2: Morphological Diagram of *Curcuma longa*

Role in Alzheimer's Disease: Curcumin has anti-inflammatory properties by inhibiting the development of astrocyte, microglia, TNF- α and IL-1. It also limits microglial development, lower the level of cholesterol, prevent brain dysregulation and inhibit acetylcholinesterase. By using above mechanism *C. longa* limits AD progression[4].

5. Shankpushpi:

Synonyms: Shankpushpi

Biological Source: *Convolvulus pluricaulis* is a brain tonic which belongs to family Convolvulaceae.



Figure No. 3: Morphological Diagram of *Convolvulus pluricaulis*

Chemical Constituents: Commonly found chemical in *Convolvulus pluricaulis* are Glycosides, flavonoids, Coumarines, Alkaloids other constituents include Sitosterol, Tetracosane, Hydroxy cinnamic acid along with glucose.

Role in Alzheimer's Disease: The tau protein in tauopathy is greatly reduced by Shankpushpi extracts, it also increases antioxidant enzyme activity and reduces oxidative-stress mediated by tau protein. It calms the nerves by regulating stress hormones, Adrenaline and cortisol. It calms the nerves by regulating stress hormones, Adrenaline and cortisol [6,7].

6. Liquorice:

Synonyms: licorice(U.S.) or Liquorice(U.K.)

Biological Source: Glycyrrhiza glabra belongs to family Fabaceae.

Chemical Constituents: Linalool oxide, geraniol, benzoic acid, terpinen, tetramethyl pyrazine, propionic acid, ethyl linolenate, butanediol, feuferaldehyde, methyl ethyl ketone, furfuryl formate, trimethylpyrazine, glycyrrhizin, tannin, and glycyrrhizic acid are some of the important chemical constituents of liquorice.

Role in Alzheimer's Disease: Recent experimental report suggests that the *G. glabra* will be the source of potential drug for Alzheimer and other neurodegenerative disorders. Another report on rat has shown that. The memory enhancing effect of aqueous extract root of *G. glabra* is seen at 150mg/kg orally administered orally [8,9].



Figure No. 4: Morphological Diagram of Glycyrrhiza glabra

7. Giloy:

Synonyms: Giloy, Guduchi

Biological Sources: Tinospora is the herbaceous plant belonging to family Menispermaceae which possesses memory enhancing properties.



Figure No.5: Morphological Diagram of Tinospora cordifolia

Chemical Constituents: Phytochemicals alkaloids, steroids, diterpenoid lactones, aliphatic, and glycosides have been isolated from the different parts of the plant body, including root, stem, and whole plant.

Role in Alzheimer's Disease: It enhances cognitive function by immune-stimulation and increasing acetylcholine synthesis, this choline supplementation increases cognitive function. Pharmacological activity of this plant includes anti-inflammatory, anti-oxidant and anti-stress properties. Aqueous extract of *T. cordifolia* roots showed logical memory enhancement and verbal learning [10,11]

8. Drumstick Tree:

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

Biological Name: *M. oleifera* is a medicinal herb belonging to Moringaceae family.

Chemical Constituents: It contains vitamin A and C, tannins, isothiocyanates, alkaloids and saponins and polyphenols i.e, flavonoids, chlorogenic acid, glucosinolates, and phenolic acids are the main chemical constituents in *M. oleifera*.

Role in Alzheimer's Disease: Its antioxidant effect has been linked to improvements in learning and memory. *M. oleifera* reversed the effects of colchicine on NE, 5-HT, and DA levels in the brain. Other studies have also shown that *M. oleifera* prevent memory loss in laboratory models for dementia [4].



Figure No. 6: Morphological Diagram of *Moringa oleifera*

9. Ginseng:

Synonyms: Asian ginseng, Chinese ginseng, Korean ginseng

Biological Source: Roots of *Panax ginseng* Belongs to Family Araliaceae.



Figure No. 7: Morphological Diagram of *Panax ginseng*

Chemical Constituents: Phytoconstituents of this plant are polysaccharides, Ginsenosides, peptides, Polyacetylenic alcohols, fatty acids. It also contains saponins like Protopantrrol, Protopanaxadiaol and Oleanolic acid.

Role in Alzheimer's disease: *Panax Ginseng* has capability to enhance the psychomotor and cognitive performance and is beneficial to Alzheimer's Disease by improving the brain Cholinergic function, reducing the level of AD and repairing the damaged neuronal network [12].

10. Guggul:

Synonyms: Indian bdellium-tree, gugal, guggul, gugal, or mukul myrrh tree

Biological Sources: Commiphora wightii is a Flowering plant belonging to Family Burseraceae.



Figure No. 8: Morphological Diagram of Commiphora wightii.

Chemical Constituents: Gum guggul extract contains various important phytochemicals like Diterpenoids, triterpenoids, long chain aliphatic tetrols, volatile oils, steroids, carbohydrates, lignans, and Amino acids.

Role in Alzheimer's Disease: It has major protective effect against the Streptozotocin-induced memory deficit model of dementia and the effect can be credited to its cholesterol lowering anti-oxidant and anti-acetylcholinesterase activity these observations suggest Guggulipid as a potential Anti-dementia drug. It acts on decreased acetylcholinesterase levels in hippocampus and enhance memory and learning process [13].

11. Ginkgo:

Synonyms: Maidenhair tree, ginkgo, Ginkgo biloba

Biological Source: Ginkgo biloba is a large tree belonging to Family Ginkgoaceae.



Figure No. 9: Morphological Diagram of Ginkgo biloba

Chemical Constituents: Chemical constituents of G. biloba include ginkgolides, bilobalide, and ginkgetin and other terpenes.

Role in Alzheimer's Disease: Extract of G. biloba containing around 24% of flavonoids and 6% of terpene lactones shows action to treat depression and headache. These compounds possess remarkable anti-AChE and antioxidant properties that are useful against Alzheimer's Disease. Report suggests that methanolic extract of G. biloba gives anti-AChE and antioxidant properties when tested in vivo. There is strong evidence that standardized ginkgo extract shows several molecular and cellular neuroprotective mechanisms, which include anti-inflammatory effects and β -amyloid aggregate inhibition. G. biloba influences intellectual capacity in Alzheimer's disease animal model without altering histopathological consequences of β amyloid precursor protein overexpression [14,15].

12. Black Pepper:

Synonyms: pepper, common pepper, black pepper, white pepper, Madagascar pepper, Piper nigrum, true pepper, pepper vine

Biological Source: Piper nigrum is a flowering plant belonging to Family Piperaceae.



Figure No. 10: Morphological Diagram of Piper nigrum

Chemical Constituents: Main phytochemical present in Black pepper is piperine. Other phytochemicals present are amides, pyrrolidines, piperidine, beta-carotene, lauric-acid, palmitic acid, pepper phellandrene and trace amount of safrole.

Role in Alzheimer's Disease: It is wellknown medicinal plant for its anti-oxidant, anti-inflammatory and anti-hypertensive action. A recent reports have shown anti-oxidative stress and neurodegenerative activity of methanol extracts of Piper nigrum seeds in Alzheimer induced rat. The anxiolytic and antidepressant activity in Alzheimer rat model is shown by methanolic extract of Piper nigrum fruit according to recent report [16,17].

13. 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 which belongs to Family Lamiaceae.



Figure No. 11: Morphological Diagram of Salvia officinalis

Chemical Constituents: main Phytochemicals present are 1,8-cineole, α -pinene, viridiflorol camphor, α and β - thujone due to which anti-oxidant action is seen.

Role in Alzheimer's Disease: To the patients in mild to moderate stage of AD a fixed dose of 60 drops/kg extract is administered for a period of 4 months to a Patient having mild to moderate Alzheimer's Disease, results from the study declared that patients are free from agitation throughout their life time. The extract of this plant also protects brain from oxidative damage [18].

14. Henna

Synonyms: Hina tree, mignonette tree, Egyptian privet

Biological Source: Lawsonia inermis is a flowering plant belonging to Family Lythraceae.

Chemical Constituents: Primarily found phytochemicals in Lawsonia inermis are pseudoephedrine, methylcarbamate, Phytol, aspidofractinine-3- methanol, phenol, 2,6- bis(1,1-dimethylethyl)-4- methyl.



Figure No. 12: Morphological Diagram of Lawsonia inermis

Role in Alzheimer's Disease: Memory loss due to oxidative neurodegeneration was effectively reversed by Lawsonia inermis. The exact mechanism of this reversal is not known; however, the antioxidant potential is recounted for the nootropic ability of the plant [19].

15. Senna:

Synonyms: Sicklepod seeds, American Sicklepod, Chinese Sicklepod, Arsenic weed, Wild senna and foetid cassia

Biological Source: Cassia obtusifolia is a perennial and tropical plant belonging to Family Fabaceae.

Chemical Constituents: Some of the important phytoconstituents found in *C. obtusifolia* are 1–2% anthraquinones, 5–7% fats, 14–19% protein, and 66–99% carbohydrates

Role in Alzheimer's Disease: *C. obtusifolia* diminishes oxidative stress and Calcium dysregulation in primary hippocampal cultures and thus reduces chances of Alzheimer's Disease [20].



Figure No.13: Morphological Diagram of Cassia obtusifolia

16. Guava:

Synonyms: Apple guava, Lemmon guava, Common guava.

Biological Source: *Psidium guajava* is an evergreen shrub belonging to Family Myrtaceae.



Figure No. 14: Morphological Diagram of *Psidium guajava*

Chemical Constituents: Main phytoconstituent of *P. guajava* is Linoleic acid. Other chemicals found in this plant are the flavonol morin, morin-3-O-arabinoside, quercetin and quercetin-3-O-arabinoside.

Role in Alzheimer's Disease: The leaf extract of guava was evaluated for antioxidant properties in a linoleic acid system by the use of thiocyanate method. A radical scavenging assay was performed and results showed that guava leaves have significant antioxidant activity that can be effective in the management of AD[21].

17. Lemmon Balm:

Synonyms: Balm mint, sweet balm, bee balm, balm mint

Biological Source: *Melissa officinalis* is a herb of a mint family belonging to family Lamiaceae.

Chemical Constituents: Some of the important chemical constituents are Eugenol, Citronellal, Tannis, Citral A and B, Terpenes, Traces of Harmine, Rosemaric acid. The leaves contain monoterpenes and phenol carboxylic acid.

Role in Alzheimer's Disease: The Monoterpenes and phenol carboxylic acid in leaves shows weak anti-acetyl cholinesterase activity and Anti-oxidant, Anti-Amyloid, Anti-apoptotic effects respectively[22].

18. Lavender

Synonyms: Garden lavender, English lavender, Narrow leaved lavender

Biological Source: *Lavandula angustifolia* is a flowering plant in the Family Lamiaceae

Chemical Constituents: Commonly seen phytochemicals are carotenoids, phenolic acids, and ascorbic acid. These are the agents responsible for strong AChE inhibitory activities as well as antioxidant activities that are useful in the management of AD.

Role in Alzheimer's Disease: The *Lavandula angustifolia* Mill aqueous extract was evaluated for its effect on the AD rats. Promising results were obtained where learning deficiency in AD rats were reversed by the lavender extract. The results established a promising therapeutic potential in *L. angustifolia* in disease improvement and treatment of AD. The lavender extract exhibited positive effects on the plasticity of synaptic transmission and thus improves impaired memory in the Alzheimeric animals. These results suggest a potential therapeutic role of lavender in the treatment of AD [23, 24].

Sr No.	Common Name	Scientific Name	Part Used	Chemical Constituents	Properties
1	Ashwagandha	<i>Withania somnifera</i> (F: Solanaceae)	Root extracts	Sitoinosides, withaferin	Antioxidant, adaptogenic, leukotriene signaling inhibitor
2	Bramhi	<i>Bacopa monnieri</i> (F: Scrophulariaceae)	Whole plant	Numerous bacosides, betulic acid, beta-sitosterol, bacopasaponins	Nerve tonic, Acetylcholinesterase inhibitor, anti-oxidant
3	Gotu kola	<i>Centella asiatica</i> (F: Apiaceae)	Whole plant	Centellose, Centelloside, Madecassoside and Asiaticoside derivatives	Reduce apoptosis and hippocampal A β Level, enhance memory
4	Turmeric	<i>Curcuma longa</i> L. (F: Zingiberaceae)	Rhizome extracts	Curcumins, flavonoids, phenols	Neuroprotective, anti-inflammatory, protein hyperphosphorylation inhibitor
5	Liquorice	<i>Glycyrrhiza glabra</i> (F: Fabaceae)	Root part	withanolides A to Y, withaferin A, and withanone	free radical scavenging activity, antioxidant activity
6	Shankpushpi	<i>Convolvulus pluricaulis choisy</i> (F: Convolvulaceae)	Leaf extracts	Ascorbic acid, flavonoids, rivastigmine, terpenoids, steroids	Antioxidant, muscarinic receptor stabilizer
7	Giloy	<i>Tinospora cordifolia</i> (F: Menispermaceae)	Roots	Steroids, Alkaloids, Polysaccharides, and Glycosides	Learning and memory enhancer, anti-oxidant
8	Drumstick Tree	<i>Moringa oleifera</i> (F: Moringaceae)	Fruit pod	vitamin A and C, alkaloids, tannins, saponins polyphenols i.e, flavonoids, chlorogenic acid and phenolic acids	Nootropic, Memory Enhancer Anti-inflammatory Anti-diabetic Anticancer
9	Ginseng	<i>Panax ginseng</i> (F: Araliaceae)	Root extract	Ginsenosides, gintonin	Neuroprotective
10	Guggul	<i>Commiphora wightii</i> (F: Burseraceae)	Gummy resin	Diterpenoids, triterpenoids, steroids, carbohydrates, volatile oils, lignans,	Anti-oxidant, anti-dementia, anti-cholinesterase activity

				and Amino acids.	
11	Ginkgo	Ginkgo biloba (F: Ginkgoaceae)	Leaf extracts	Terpenes, bilobalide, ginkgolide	Antioxidant, AChE inhibitor
12	Black Pepper	Piper nigrum (F: Piperaceae)	Methanolic extract of fruit	piperine, amide, piperidine, pyrrolidine and safrole	antioxidant, anti-inflammatory, anti-hypertension and anti-depressant activity
13	Sage	Salvia officinalis (F: Lamiaceae)	Arial part and leaf extracts	Carotenoids, rosmarinic acid, chlorogenic acid, Trolox	Antioxidant, AChE inhibitor, anticholinesterase activity
14	Heena	Lawsoniainermis L. (F: Lythraceae)	Leaf extract	Phytol, pseudoephedrine, aspidofractinine-3-methanol, phenol, 2,6-bis(1,1-dimethylethyl)-4-methyl, methylcarbamate	Antioxidant, nootropic potential
15	Senna	Cassia obtusifolia (F: Fabaceae)	Leaf seeds, fruits roots	Anthraquinone, fat, protein, carbohydrate.	Antioxidant,
16	Guava	Psidium guajava (F: Myrtaceae)	Leaf and fruit extract	Linoleic acid	Antioxidant, antidiabetic
17	Lemmon Balm	Melissa officinalis (F: Lamiaceae)	Leaf extract	Eugenol, Citronellal Tannis, Terpenes,	anti-ACEsterase Anti-oxidant, Anti-Amyloid, Anti-apoptotic
18	Lavender	Lavandula angustifolia (F: Lamiaceae)	Fresh flower extracts	carotenoids, phenolic acids, and ascorbic acid.	Memory Enhancement

Table 1: Taxonomic Distribution of Plants in Alzheimer's Disease

2. Conclusion:

Alzheimer is a complex disease-causing dementia, mental disability and death among humans. Current therapy can only relieve the symptoms of the disease and cannot prevent the progression. Due to poor patient compliance towards allopathic drugs and their lethal side effects upon choric usage, at present there was a great shift of patient choice of medication towards herbal. The secondary metabolites of plants including alkaloids, flavonoids, and phenolic acids play a key role in inhibiting neurodegeneration. Herbal medications have many advantages over the currently available synthetic medications as 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 cause any problem. Out of all these advantageous aspects herbal medicine became a best choice of medication for management of Alzheimer's disease along with this regular meditation and yoga add more benefits for better and fast recovery of patient from Alzheimer's disease. Medicinal plants can boost life quality of patients with Alzheimer's disease.

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