



Herbal Wisdom for Alzheimer's Disease: A Comprehensive Review

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Abstract

Alzheimer's Disease (AD) is a progressive disorder that leads to the degeneration of nerve cells, marked by a decline in cognitive abilities, including memory, reasoning, and behaviour. It stands as the primary cause of dementia in the elderly, leading to a gradual erosion of autonomy. Despite considerable research efforts, a definitive cure for AD remains out of reach, with existing treatments mainly focused on alleviating symptoms. The intricate nature of AD, which involves multiple pathological mechanisms, indicates that drugs targeting a single pathway might be inadequate. Herbal remedies, renowned for their diverse and multifunctional properties, present a promising alternative. This review examines the potential of herbal remedies to act as effective pharmaceuticals and nutraceuticals in treating and preventing AD. By addressing various aspects of AD concurrently, these natural therapies offer a new and hopeful strategy for managing this debilitating condition.

Keywords: Alzheimer's, Nutraceuticals, Remedies, Disease

1. Introduction

The most prevalent type of dementia is AD, accounting for 60–80% of all occurrences¹. Dr. Alois Alzheimer, the German psychiatrist first diagnosed this disease in the early 1900s, Alzheimer's has since become synonymous with memory loss, cognitive deterioration, and the profound impact it has on individuals and their loved ones. As the leading cause of dementia, Alzheimer's weaves a web of complexities that extend far beyond memory lapses. The disease's prevalence doubles every 5 years after 60 years of age². For 85 and older, estimates of the prevalence have been as high as 30-47%^{1,2}.

Alzheimer's disease is not just a neurological challenge; it's a human challenge that requires a multidisciplinary approach, an unwavering commitment to research, and a compassionate perspective that acknowledges the humanity of those affected with varied cognitive, non-cognitive and physical symptoms (Table 1). According to Dr. Alois, Amyloid plaques and Neurofibrillary Tangles (NFTs) are the key pathological features in the autopsied brains of people with AD, Amyloid plaques are deposits of

β -amyloid found outside brain cells and in cerebral blood vessels, a condition called Cerebral Amyloid Angiopathy (CAA) (Figure 1). On the other hand, NFTs, primarily consisting of twisted filaments containing hyperphosphorylated tau proteins, contribute to the loss of neurons and synapses³.

2. Etiology

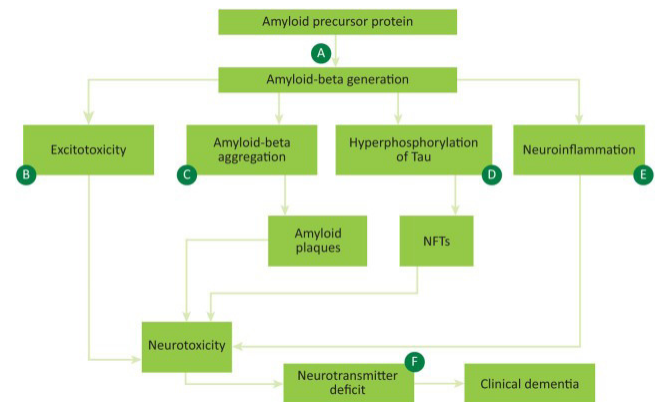


Figure 1. Etiology of Alzheimer's disease with therapeutic targets⁴.

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3. Clinical Presentation

Table 1. Clinical presentation of Alzheimer's disease⁵⁻⁷

Alzheimer's Symptoms	
Cognitive non-cognitive Functional	
Memory loss	Delusion inability to take care of self.
Language Disorder	Hallucination
Circumlocution	Depression
Anomia	Uncooperativeness
Perceptual problem motor hyperactivity	
Apraxia	
Repetitive Mannerism	
Confused State	
Executive dysfunctionality	
Diagnosis	
Neurological Examination	
Mental status examination (MMSE scale test, Mini cog test)	
Rule out Vitamin B12 and folate deficiency test.	
EEG, CT or MRI scans	

4. Medications and Their Limitations

4.1 Cholinesterase Inhibitors (ChEIs)

Donepezil, Galantamine, and Rivastigmine are the cornerstones of treatment for mild-to-moderate AD symptoms⁸. Managing treatment is a significant issue in AD, with non-adherence to therapy frequently standing in the way of successful therapy⁹.

4.2 Challenges Associated with Adherence to ChEIs

4.2.1 Gastrointestinal AEs

Nausea, vomiting, and diarrhoea are common. They result from muscarinic receptor activation in the gut, partly unaffected by anticholinergic meds, possibly linked to central autonomic factors, and can lead to weight loss¹⁰.

4.2.2 Cardiovascular AEs

Including bradycardia¹⁰, QT interval prolongation with wandering atrial pacemaker and torsades de pointes¹¹, and vertigo.

4.2.3 Neuromuscular AEs

Overstimulation of nicotinic receptors can lead to muscle weakness and cramps, with rare instances of

muscle weakness associated with a specific AChEI, methionate, potentially causing respiratory distress.

4.2.4 Uncommon Adverse Events (AEs)

AChEIs can also cause dyspepsia, seizures, tremors, urinary obstruction, exacerbation of chronic obstructive pulmonary disease, and dyspepsia. They should be kept an eye out for even though they are uncommon⁸.

4.3 Memantine

It is an NMDA receptor of glutamate antagonist. According to a few reports, people with autism may experience difficulties starting to speak or stutter when taking memantine¹². Few studies also suggest that it also has some effect on agitation, hallucinations and delusions¹³.

4.4 Ashwagandha (*Withania somnifera*)

It is classified as a "Rasayana", indicating its rejuvenating qualities, and is recognized for its antioxidant, free radical-fighting, and immune-enhancing abilities¹⁴.

Ashwagandha root contains various compounds like alkaloids, withanolides, sitoindosides, and flavonoids. Slows down the progression by inhibiting the activation of nuclear factor B, decreasing the production of A β peptides, preventing cell death or apoptosis, restoring normal functioning of synapses and boosting antioxidants by enhancing Nrf2 movement to the nucleus for increased antioxidant enzyme expression at the molecular level¹⁵.

Ashwagandha root extracts support nerve cell growth, protect against damage from A β in neurons, and offer neuroprotection in neurodegenerative diseases. They reduce inflammation, prevent cell death, and decrease anxiety. *Ashwagandha* can enter the brain and potentially reduce brain inflammation, showing promise for Alzheimer's. Its alkaloid content calms the central nervous system, enhances memory, and has the potential for reducing Alzheimer's-related deficits in animal models. In conclusion, *Ashwagandha's* varied benefits, especially its neuroprotection and memory enhancement, make it a promising herbal remedy for Alzheimer's¹⁶.

4.5 Turmeric (*Curcuma longa*)

Turmeric, a spice originating from South and Southeast Asia, is historically used in traditional medicine. Curcuminoids, the active compound found in turmeric,

exhibit anti-inflammatory, antioxidant, and potential anti-cancer properties. Studies have shown that curcuminoids can inhibit the aggregation of amyloid- β -protein, reduce inflammation induced by A β , and affect enzymes involved in the progression of AD¹⁷.

It has anti-inflammatory effects by inhibiting the Egr-1 protein, reducing chemotaxis, and suppressing enzymes like COX-1, COX-2, and COX-3¹⁸. Curcuminoids are potent antioxidants that protect against free radical damage and offer potential benefits in neurodegenerative disorders like Alzheimer's, Huntington's, and Parkinson's diseases. Studies in animals have shown that curcumin can reduce damage from cerebral ischemia, lipid peroxidation, and amyloid levels in Alzheimer's models. Its anti-inflammatory, antioxidant, and anti-amyloid properties make curcumin a promising treatment for Alzheimer's disease^{16,19}.

4.6 *Shankhpushpi (Convolvulus pluricaulis)*

Convolvulus pluricaulis extracts have been found to enhance memory and learning abilities in a recent study. The plant contains various compounds like triterpenoids, flavonoids, alkaloids (*Shankhapushpine*), glycosides, anthocyanins, and steroids, which have pharmacological effects such as improving memory and acting as nootropics. These components help alleviate different types of stress, including traumatic, chemical, and psychological stressors²⁰.

The plant's capacity to prevent lipid buildup and protein damage further highlighted its neuroprotective qualities. Administration of *C. pluricaulis* extract also lessened alterations in endogenous antioxidant enzyme levels associated with AI administration, compared to the usual AD treatment with rivastigmine²¹.

4.7 *Ginkgo (Ginkgo biloba)*

Ginkgo biloba is highly preferred for its therapeutic potential in Alzheimer's. It contains bilobalide which acts as a neuroprotective compound that fights free radicals and improves cognitive function and memory. Its flavonoids are linked to memory support.

In Europe, *G. biloba* extract is widely used for various forms of dementia, rich in terpenoids and flavonol glycosides, and beneficial for age-related memory disorders in Europe and Asia. Notably, a nanosized extract shows promise by

increasing acetylcholine release in the brain, improving absorption²².

Preclinical studies indicate its potential to reduce oxygen radicals, lower inflammation, and influence processes like corticosteroid production and glucose utilization²³.

4.8 *Jyotishmati (Celastrus paniculatus)*

It holds great potential in safeguarding neuronal cells from various forms of damage. Its strong antioxidant properties effectively shield against toxicities induced by substances like hydrogen peroxide and glutamine. Moreover, it enhances memory performance by boosting cholinergic activity. The aqueous extract of *Jyotishmati* is well-known for its antioxidant and cognition-enhancing qualities²⁴. Particularly, Extracts are notable for their ability to protect neuronal cells from toxicity caused by hydrogen peroxide, primarily due to their antioxidant effect and free radical scavenging capabilities. It accomplishes this by shielding neuronal cells from H₂O₂-induced damage through its antioxidant activity and the activation of its proteins. Additionally, its extracts protect neuronal cells from toxicity caused by glutamate by regulating its receptor activities²³.

4.9 *Liquorice (Glycyrrhiza glabra)*

It includes flavonoids, saponins, isoflavonoids, coumarins, and stilbenoids, all are utilized in AD²⁵. In dementia, Scopolamine, and liquorice have been proven to enhance memory. It has been demonstrated that liquorice enhances memory in mice. A 1-month-old albino rat's memory and learning capacity were observed to increase after six weeks of oral *G. glabra* plant extract feeding, according to another study. Additionally, research revealed that the extract of glycyrrhiza significantly decreased A β aggregation and radical-scavenging activities²⁶.

4.10 *Nutmeg (Myristica fragrans)*

It is used to treat leukaemia, body aches, vomiting, tachycardia, dizziness, mental difficulties, and memory issues. Its qualities include antibacterial, antioxidant, and depressive. For three days, mice of different ages received three different oral doses 5, 10 and 20 mg/kg p.o of nutmeg N-hexane extract. This drug was found to be effective at 5 mg/kg in reversing

learning and memory deficits caused by scopolamine and diazepam and also works best in reversing memory loss and treating AD^{23,27}.

4.11 Guduchi (*Tinospora cordifolia*)

Belongs to the Menispermaceae family and helps both healthy and memory-impaired animals remember things better. By boosting acetylcholine production and immune system stimulation, choline supplements enhance cognitive function. *T. cordifolia* synergistically complements many herbal preparations, making it a valuable component in polyherbal formulations. Importantly, *T. cordifolia* is an extraordinary herbal medicine in managing conditions such as depression, AD, and attention deficit hyperactivity disorder as it has shown no serious toxicity. In *Ayurveda*, it is referred to as a memory and learning enhancer. The application of the guduchi root aqueous extract enhanced logical memory and verbal learning²⁸.

4.12 Brahmi (*Bacopa monnieri*)

Brahmi is recognized for its distinctive features like multiple branches, oblong leaves, and purple flowers. It is rich in saponins and triterpenoid bacosaponins. *Brahmi* is often combined with other herbs to address memory issues, including those associated with Alzheimer's disease. Scientific research supports its memory-enhancing, adaptogenic, neuroprotective, and antibacterial properties. *Brahmi* and its bioactive compounds have neuroprotective characteristics, which involve reducing reactive oxygen species, decreasing neuroinflammation, inhibiting the aggregation of Amyloid- β , and enhancing cognitive and learning abilities²⁹. Animal studies have shown promise in reducing cholinergic degeneration and enhancing cognitive abilities in Alzheimer's-like conditions^{23,30}.

4.13 Drumstick Tree (*Moringa oleifera*)

Antioxidant Vitamins C and E found in its leaf extract help Alzheimer's patients think more clearly. This plant has nootropic qualities and helps relieve stress in Alzheimer's patients. Monoamines, which are involved in memory, are impacted. The study by Gangul and Guha, published in the IJMR 2008, suggests that *M. oleifera* may be beneficial for AD based on its observed protective effects in a rat model. The

study found alterations in neurotransmitters and EEG patterns in rats modelling AD. It modifies the levels of norepinephrine, dopamine, and serotonin, which lessens the severity of colchicine-induced AD³¹.

4.14 Amla (*Embllica officinalis*)

It is crucial in treating AD and memory loss by enhancing and reversing memory impairments³².

One research study tested the memory-enhancing effects of a combination of piracetam, amla (*E. officinalis*), and turmeric on rats exposed to aluminium-induced cognitive impairment. Rats received aluminium chloride for six weeks and were given amla, curcumin (from turmeric), and piracetam for the same duration. Memory was assessed on days 21 and 42. The combination of amla, curcumin, and piracetam reduced oxidative stress and improved memory, suggesting a potential treatment for memory loss due to their antioxidant and memory-enhancing properties³³.

4.15 Guggulu (*Commiphora*)

Many plant species, including *C. mukul*, *C. myrrha*, *C. kua* and *C. wightii bhandari*, release *guggulu*, an oleogum resin. It has an earthy or pale-yellow colour, a sharp, astringent taste, and a sweet aroma. It is composed of a mixture of 25–40% alcohol-soluble resins, 30–65% water-soluble gum, and about 8% volatile oils, solutes, mucilage, and sugar. Heerabomyrrhols, commiphorinic acid, and commiphoric acids are examples of excipients that dissolve in alcohol. The primary chemical components known as boswellic acids, specifically 3-O-acetyl-11-keto- β -boswellic acid, exhibit neuroprotective properties and as a strong anti-inflammatory in AD³⁴. Additionally, it has nonphenolic aromatic acids, ferulic acid, and phenols, all of which are beneficial for AD³⁵ and strong antioxidants³⁶.

4.16 Ginseng (*Panax ginseng*)

The root of *P. ginseng* has been used traditionally to treat ageing-related conditions and improve overall health. There are only two clinical trials conducted on using it to treat AD. These studies found that consuming 4.5 gm of *P. ginseng* per day over twelve weeks significantly improved cognitive function in people with AD, according to tests like the Mini-Mental State

Examination (MMSE) and the Alzheimer's Disease Assessment Scale (ADAS). The effects were temporary though; they disappeared when the treatment was discontinued. Another study involving higher doses of Korean Red Ginseng (9 gm per day) for twelve weeks resulted in improvements in the Clinical Dementia Rating and Alzheimer's Disease Assessment Scale - Cognitive Subscale (ADAS-Cog) score³⁷.

4.17 Chinese Club Moss (*Huperzine A*)

It is a natural cholinesterase inhibitor. It is derived from Chinese herb *Huperzia serrata*. Evidence suggests that it may function comparably to currently used inhibitors in terms of symptomatic efficacy. Furthermore, It may be helpful as an AD disease-modifying treatment due to its antioxidant and neuroprotective qualities³⁸. It improves cognitive function in dementia patients by selectively inhibiting acetylcholinesterase activity, which increases acetylcholine levels in the brain³⁹.

4.18 Snowdrop (*Galanthus nivalis*)

The primary chemical component found in *Galanthus nivalis*, a member of the Liliaceae family, is Galantamine. Contrary to common misconceptions, Galantamine is classified as an isoquinoline alkaloid. Clinical studies have primarily focused on assessing the effectiveness of Galantamine in treating mild to moderate AD and various forms of memory

impairment. This medication works as a selective and competitive inhibitor of acetylcholinesterase, a crucial enzyme. It is theorized that this action may alleviate some of the symptoms associated with AD. Furthermore, this drug has been demonstrated to allosterically modulate nicotine acetylcholine receptors on cholinergic neurons, thereby increasing the release of acetylcholine. This mechanism can be beneficial in the treatment of AD⁴⁰.

4.19 Periwinkle (*Vinca minor*)

Vinpocetine is linked to several different mechanisms of action, including enhanced cerebral metabolism, increased brain uptake of glucose and oxygen, and enhanced hypoxic resistance⁴¹. It has been suggested that obstructing voltage-gated sodium channels, regulating the release of neurotransmitters, and enhancing the effects of adenosine in cytotoxic hypoxia have neuroprotective effects⁴². Several actions of vinpocetine may be advantageous in AD, according to reports. Intracerebroventricular streptozotocin-induced oxidative stress and cognitive dysfunction can be lessened by vinpocetine⁴³.

5. Herbal Treatment

Following are the available Herbal Treatment options for AD (Table 2).

Table 2. Phytoconstituents and its structure⁴⁴⁻⁵⁹

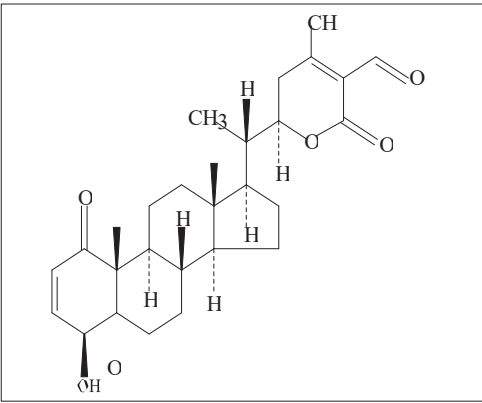
Biological Source	Family	Phytoconstituents	Molecular structure
<i>Withania somnifera</i>	Solanaceae	Withanolides	

Table 2. Continued...

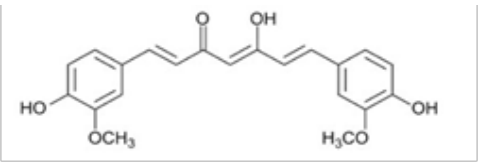
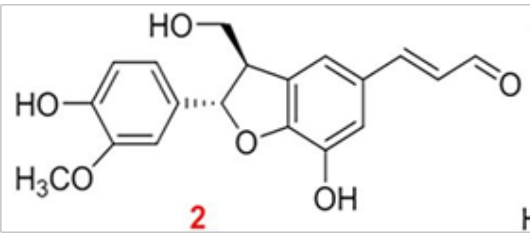
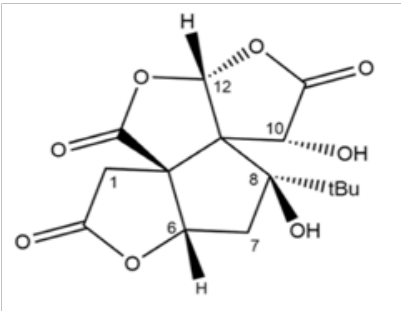
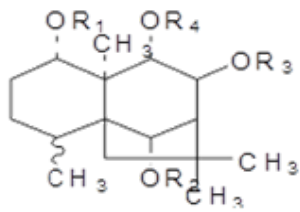
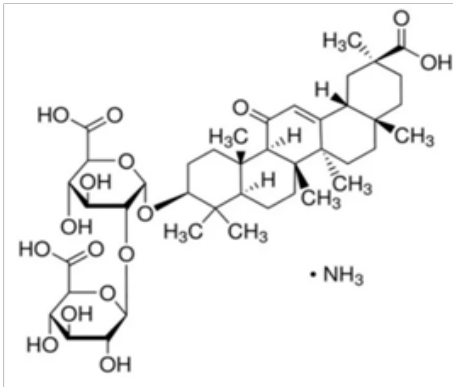
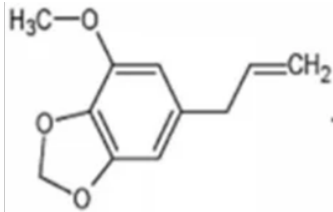
Biological Source	Family	Phytoconstituents	Molecular structure
<i>Curcuma longa</i>	Zingiberaceae	Curcumin	
<i>Convolvulus pluricaulis</i>	Convolvulus pluricaulis	Phenylpropanoids, Alkaloids, Flavonoids, Glycosides.	
<i>Ginkgo biloba</i>	Ginkgoaceae	Bilobalide and Ginkgolide	
<i>Celastrus paniculatus</i>	Celastraceae	Celapanin and Celapanigin	
<i>Glycyrrhiza glabra</i>	Fabaceae	Glycyrrhizin	
<i>Myristica fragrans</i>	Myristicaceae	Myristicin	

Table 2. Continued...

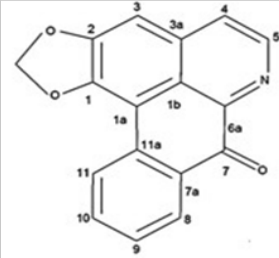
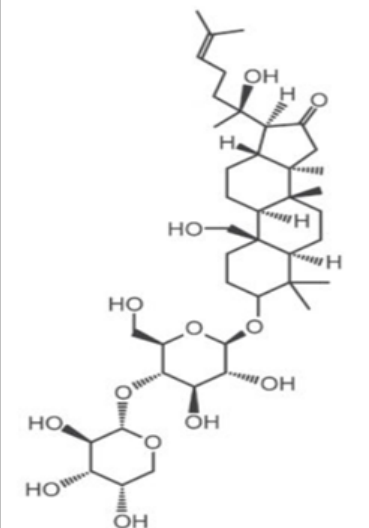
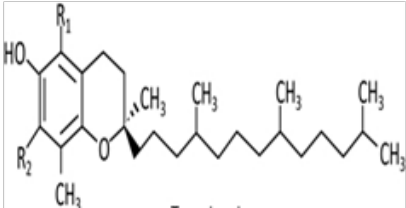
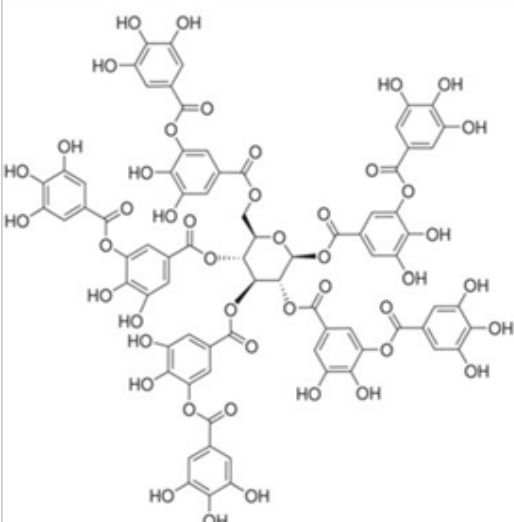
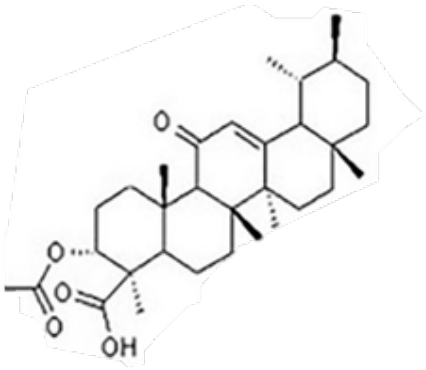
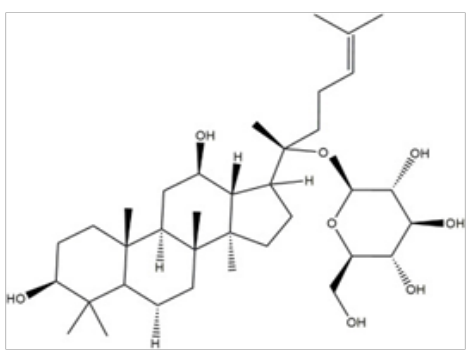
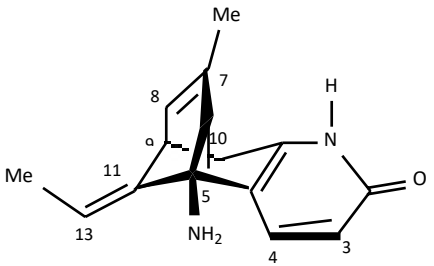
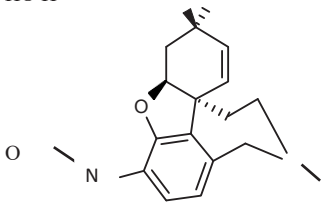
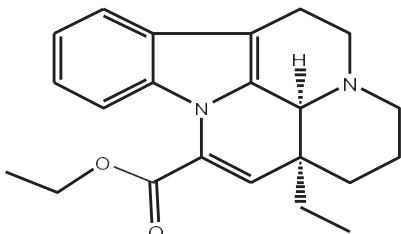
Biological Source	Family	Phytoconstituents	Molecular structure
<i>Tinospora cordifolia</i>	Menispermaceae	Choline, Tinosporin, Isocolumbin, Palmatine	
<i>Bacopa monnieri</i>	Scrophulariaceae	Brahmine, Nicotine, Herpestine, Bacosides A and B	
<i>Moringa oleifera</i>	Moringaceae	Antioxidant Vitamins C and E	
<i>Emblica officinalis</i>	Euphorbiaceae	Amino Acids, Tannins, Phenols and Alkaloids	

Table 2. Continued...

Biological Source	Family	Phytoconstituents	Molecular structure
<i>Commiphora</i>	Burseraceae	Boswellic Acid	
<i>Panax ginseng Plant</i>	Araliaceae	Ginsenoside Compound K	
<i>Huperzia serrata</i>	Huperziaceae	Huperzine A	
<i>Galanthus nivalis</i>	Amaryllidaceae	Galantamine	HO H 
<i>Periwinkle-Vinca minor</i>	Apocynaceae	Vinpocetine	

6. Integration of Herbal Remedies and Traditional Medicine

Integrating herbal remedies with traditional medical interventions offers a comprehensive approach to managing Alzheimer's disease. Herbal remedies may enhance the effects of pharmaceutical drugs, potentially improving overall patient outcomes. This integration allows for a holistic treatment plan that addresses multiple facets of the disease, including cognitive decline, behavioural symptoms, and overall quality of life.

6.1 Customized Care

It may be possible to achieve better outcomes by designing treatment regimens based on each patient's unique requirements and sensitivity levels. This customisation is made possible by integrative medicine, which blends traditional and herbal treatments.

6.2 Lower Drug Doses

Combining herbal remedies with conventional treatments may allow for reduced medication dosages while maintaining therapeutic efficacy. This approach can help minimize the side effects commonly associated with higher doses of pharmaceutical drugs⁶⁰.

7. Safety and Precautions

It's important to use herbal remedies carefully even though they may have some benefits. Think about the following safety measures:

- Ensure the quality of the herbs you use.
- Observe any possible allergies.
- Monitor for any adverse effects.
- Follow recommended dosages.
- Seeking advice from a healthcare provider is essential before implementing any herbal remedy into an Alzheimer's treatment regimen. A trained healthcare professional can advise people on the safest and most suitable herbal supplement options, as herbal supplements may interact with medications or other medical conditions.

8. Conclusion

In conclusion, while no known cure for AD exists, exploring alternative therapies such as herbal remedies

offers hope for improving the quality of life for those affected. Herbs like Sage, *G. biloba*, Curcumin, Huperzine-A, and various *Ayurvedic* herbs have shown promise in enhancing cognitive health and managing symptoms.

8.1 Future Aspect

Further research is essential to fully understand the benefits, establish standardized dosages, and identify potential side effects of these herbal remedies. Continued study could lead to more effective and personalized treatment approaches, combining herbal and traditional medicine for better patient outcomes.

8.2 Limitations

The use of herbal remedies has limitations, including variability in product quality, potential interactions with conventional medications, and the need for more regulatory oversight. These factors must be considered to ensure safe and effective use in Alzheimer's treatment.

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