EFFECT OF HEBAL COMPOUNDS IN THE ALZHEIMER'S DISEASE

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ABSTRACT:

Alzheimer's disease [AD] continues to be a major worldwide wellbeing concern that calls for creative therapeutic strategies. The possibility for herbal therapy to work in tandem with traditional medications to treat AD is examined in this review. We examine the molecular processes of important herbal components and how they interact with common medications. To illustrate the advantages and drawbacks of integrated AD therapy, case studies, clinical trials, comparative analyses, and historical viewpoints are examined. The study also highlights current trends, safety issues, and potential avenues for future research regarding the utilization of herbal medication for AD.

Keywords: Alzheimer's disease [AD], Neurodegenerative Disorders, Herbal Therapy, Integrated therapy.

INTRODUCTION

Alzheimer's disease (AD), the most common form of dementia, is characterized by a gradual decline in cognitive function, primarily due to the accumulation of amyloid-beta plaques and neurofibrillary tangles in the hippocampal region of the brain (Alzheimer's Association, 2024; Querfurth & LaFerla, 2010). Currently, approximately 5 million middle-aged and older adults in the United States are living with AD, and this number is projected to rise to 7.7 million by 2030 as the population ages (Hebert *et al*., 2013). While some early-onset forms of the disease are linked to specific genetic mutations—such as those in the APP, PSEN1, and PSEN2 genes—most cases occur after the age of 60 and are considered late-onset. In these cases, genetic factors like the APOE ε4 allele contribute to risk, although they do not guarantee disease development. It is estimated that genetic factors play a definite role in 10% to 15% of AD cases (Gatz *et al*., 2006). Currently, available treatments for Alzheimer's disease (AD) primarily offer symptomatic relief, with no curative therapies yet available. Cholinesterase inhibitors (e.g., donepezil, rivastigmine) and NMDA receptor antagonists (e.g., memantine) may temporarily improve or stabilize symptoms, but they do not halt disease progression (Cummings *et al*., 2019). Despite extensive research, efforts to discover a definitive cure have largely been unsuccessful. The underlying pathology of AD involves progressive neuronal loss in the cerebral cortex, subcortical regions, and particularly in the hippocampus, which plays a critical role in memory and learning (Braak & Braak, 1991; Querfurth & LaFerla, 2010). Alzheimer's disease (AD) typically presents initially with subtle mood disturbances, short-term memory loss, and difficulty in acquiring new information. Early symptoms often include forgetting names or recent events, misplacing items, and language difficulties such as word-finding problems (Alzheimer's Association, 2024). As the disease progresses, individuals may exhibit behavioral and psychological symptoms such as irritability, agitation, and aggression (Cummings *et al*., 2015). In the advanced stages, patients experience disorientation regarding time, place, and identity, along with a complete loss of bladder and bowel control. Ultimately, they become entirely dependent on caregivers, often requiring institutional care in specialized facilities (Prince *et al*., 2016). Although no cure currently exists, studies suggest that even modest delays in disease onset or progression—through medical or lifestyle interventions—could significantly reduce the global burden of AD over the next five decades (Brookmeyer *et al*., 2007).

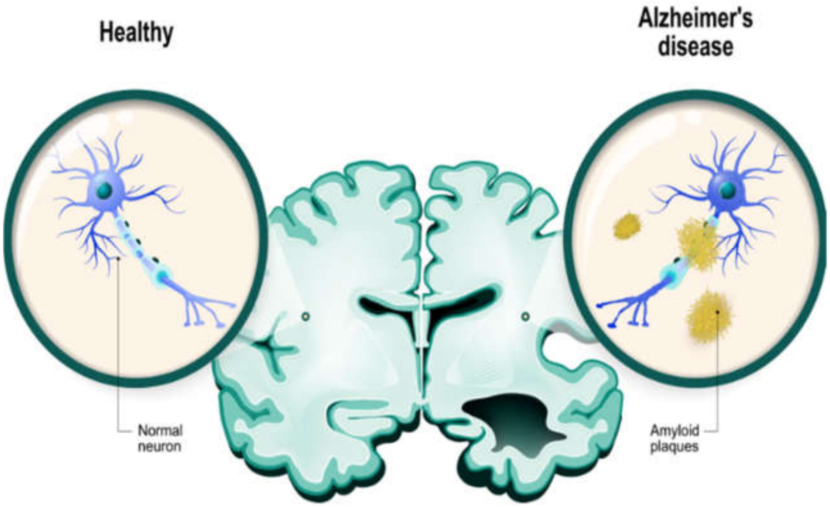


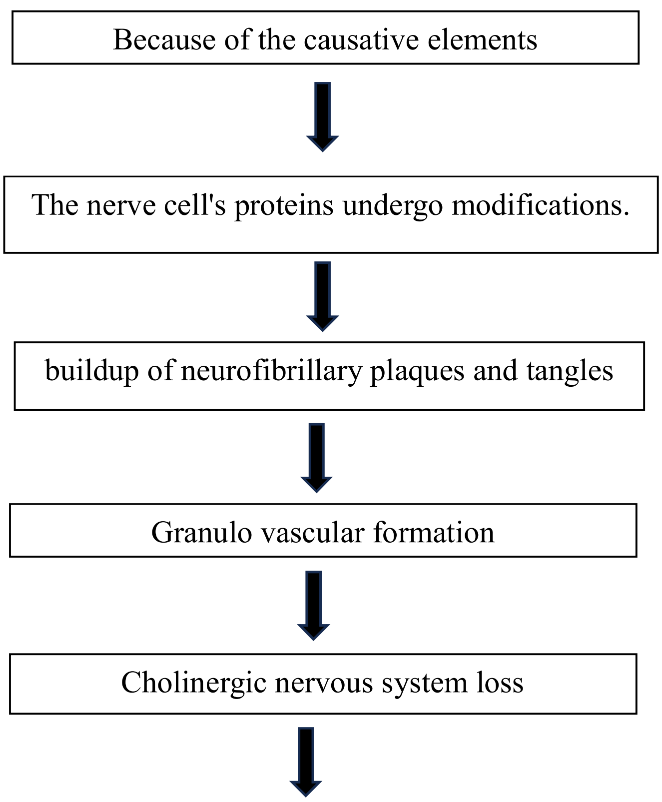
Fig.1 Image of Healthy brain and Alzheimer's brain

Several stages involved in Alzheimer's illness:

S.NO.	STAGES	REFERENCE
1.	Mild cognitive impairment	(Petersen *et al*., 2001).
2.	Moderate Alzheimer's illness	(Alzheimer's Association, 2024).
3.	Severe Alzheimer's illness	(McKhann *et al*., 2011).
4.	Very Extreme Alzheimer's illness	(Reisberg *et al*., 1982).

Pathophysiology of Alzheimer's Disease:

Alzheimer's disease (AD) is neuropathologically characterised by the buildup of β-amyloid (Aβ) plaques in the extracellular space and the creation of neurofibrillary tangles (NFTs) formed of hyperphosphorylated tau protein within neurones (Querfurth & LaFerla, 2010, Selkoe & Hardy, 2016). According to De Strooper and Karran (2016), the accumulation of Aβ leads to neurodegenerative processes such as synaptic dysfunction, neuronal death, and eventually dementia. Despite the important role of amyloid pathology, pharmaceutical efforts to target Aβ have not shown significant therapeutic improvements, especially in symptomatic persons.According to Morris *et al*. (2014) and Jack *et al*. (2018), there is a weak correlation between amyloid burden and cognitive impairment in later stages of Alzheimer's disease. This suggests that while Aβ may trigger the disease process, it is not solely responsible for symptom progression.



loss of intellect, function, and memory

Intracellular neurofibrillary tangles (NFTs) formed of hyperphosphorylated and improperly folded tau proteins—normally associated with microtubule stability—are a defining neuropathological feature of Alzheimer's disease (AD) (Braak & Braak, 1991; Wang & Mandelkow, 2016). These abnormal tau proteins lose their capacity to stabilise microtubules, resulting in cytoskeletal disintegration and decreased neuronal transport, which eventually contribute to neurodegeneration (Iqbal *et al.*, 2010). The failure of β-amyloid-targeted therapies to produce meaningful clinical outcomes has shifted the focus to tau-directed therapeutics (Congdon & Sigurdsson, 2018; Cummings *et al.*, 2021).However, even anti-tau methods have failed to provide meaningful disease-modifying effects in late-stage clinical trials, demonstrating that the pathophysiology of Alzheimer's disease is complex and poorly understood (He *et al.*, 2021).

This complication highlights the importance of taking into account additional pathophysiological contributors such as endoplasmic reticulum stress and the unfolded protein response, gut microbiota dysbiosis, metal ion dysregulation, excitotoxicity, impaired autophagy, chronic neuroinflammation, oxidative stress, lipid dysregulation, insulin resistance, and infectious agents (Heneka *et al.*, 2015; Butterfield and Halliwell, 2019). Given the limited success of monotherapies targeting amyloid or tau, there is a growing consensus that multifactorial treatment strategies targeting a broader range of disease mechanisms are required to meet the unmet need for safe and effective AD therapies (Cummings *et al.*, 2022; Hampel *et al.*, 2021).

HERBAL MEDICINE IN ALZHEIMER'S ILLNESS:

In traditional medical systems, herbal medicine (HM) includes both basic plant-based remedies and more complex formulations, which may include single medicinal plants, enriched extracts, isolated bioactive compounds, or polyherbal mixtures containing 10-20 or more plant ingredients (World Health Organisation [WHO], 2013). The World Health Organisation defines herbal medicines as "plant-derived materials or preparations with therapeutic or other human health benefits" that may comprise raw or processed components from one or more botanical sources (WHO, 2013). The National Centre for Complementary and Integrative Health (NCCIH) in the United States defines herbal medicine as a naturally derived product that is commonly marketed as a prescription drug or dietary supplement to promote health (National Institutes of Health [NIH], 2023).Conventional or orthodox medicine, on the other hand, is defined as the use of chemical substances to treat, prevent, or diagnose disease, as well as to improve physical or mental well-being (Bodeker & Ong, 2005).

Herbal medicine, a key component of CAM systems, has been used for ages to treat a variety of diseases. According to early 2000s reports, the worldwide herbal medicine business was rising at a rate of more than $60 billion per year (Ekor 2014). Currently, around 25% of modern medications are sourced from plant sources, with roughly 60% of antibacterial and anticancer treatments traced back to natural botanical components. Regulatory policies for HMs differ greatly between nations. Approximately 65% of countries have dedicated regulatory frameworks for herbal medicines (WHO, 2019).Herbal products are regulated as dietary supplements in the United States under the Dietary Supplement Health and Education Act (DSHEA) of 1994, with almost 20,000 items registered (FDA, 2023). The United States Food and Drug Administration (FDA) has designated approximately 250 herbs as "Generally Recognised As Safe (GRAS)" due to extensive traditional use (Bent, 2008).

In the United Kingdom, roughly 500 herbal medicines have been approved, whereas Germany recognises approximately 3,500 unique herbal formulations (Ekor 2014). In contrast, the Netherlands does not have a formal registration system for HMs. In Asia, regulatory frameworks are well established: China lists 657 HMs in its Pharmacopoeia, Korea lists 515 (via the Korean Herbal Pharmacopoeia), and India lists 1,242 under its Ayurvedic, Siddha, and Unani Pharmacopoeias. Japan uses a formal approval procedure rather than a registration system and has authorised at least 1,469 herbal medicines to far (WHO, 2019). Herbal medicines in these locations may be classified as functional foods, prescription pharmaceuticals, over-the-counter (OTC) drugs, dietary supplements, or self-medication items, depending on national rules.

Some herbal compounds used:

Brahmi

Bacopa monnieri (BM), commonly known as Brahmi, is a well-regarded herb in Ayurvedic medicine traditionally used as a diuretic, cardiotonic, and nerve tonic, and for managing ailments such as rheumatism, asthma, insomnia, and epilepsy (Singh & Dhawan, 1997; Russo & Borrelli, 2005). It is a creeping plant that thrives in damp, swampy environments and is known for its bitter flavour. Phytochemical analyses have revealed that BM is rich in saponins and triterpenoid compounds, primarily bacosides A and B, along with bacopasaponins A–C and bacopasides III–V (Deepak & Amit, 2004). Additionally, it contains saponin glycosides like bisdesmosides of jujubogenin (e.g., bacopasaponins D–F), and other bioactive compounds, including polyphenols, betulic acid, alkaloids, plant sterols, and sulfhydryl-containing antioxidants (Aguiar & Borowski, 2013).

These bioactive elements contribute to BM's antioxidant action by scavenging reactive oxygen species (ROS), preventing lipid peroxidation, decreasing lipoxygenase activity, and chelating divalent metal ions (Bhattacharya *et al*., 2000). BM has historically been used to improve memory and cognition, and modern research confirms its neuropharmacological and nootropic properties (Calabrese *et al*., 2008; Stough *et al*., 2001). Its cognitive-enhancing effects may be due to an increase in hippocampal protein kinase activity (Roodenrys *et al*., 2002).

BM has shown strong neuroprotective benefits in animal models of Alzheimer's disease, including the preservation of cholinergic neurones (Uabundit *et al*., 2010). In rats, BM extract corrected cognitive impairments caused by intracerebroventricular colchicine and ibotenic acid lesions while increasing choline acetyltransferase activity, muscarinic receptor binding, and acetylcholine levels in the frontal cortex and hippocampus (Shinomol & Muralidhara, 2011). Furthermore, BM extract protected neuronal cells from β-amyloid-induced toxicity by inhibiting acetylcholinesterase activity and lowering intracellular oxidative stress, resulting in decreased ROS production (Kumar *et al*., 2016).

A clinical safety research examining oral administration of BM in healthy volunteers—beginning with 300 mg/day for 15 days, followed by 450 mg/day for another 15 days—discovered no significant adverse effects across clinical, haematological, biochemical, and ECG parameters (Dev *et al*., 2009). Numerous clinical investigations have proven BM's efficacy in boosting memory, attention, and cognitive function, resulting in widespread use in the Indian herbal product market (Stough *et al*., 2001; Morgan & Stevens, 2010; Raghav *et al*., 2006). These findings provide a solid foundation for future research into the optimal dose, duration of action, and long-term efficacy of herbal nootropics such as BM (Pase *et al*., 2012).

Ashwagandha

Ashwagandha (Withania somnifera) has traditionally been used in Ayurveda as an aphrodisiac, nervine tonic, and adaptogen to combat stress and promote rejuvenation (Majeed *et al*., 2023; NIH, Mallinson, P. A. C., Joshi, M., *et al* 2025). It is derived mostly from the root of a Solanaceae-family plant known as rasayana, and has been linked to antioxidant, anti-free radical, and immune-boosting characteristics (Panda, 2024).
Unlike other adaptogens, which are stimulatory, Ashwagandha has a relaxing impact on the central nervous system, which might help Alzheimer's sufferers (Mikulska, 2023). A double-blind, randomised, placebo-controlled trial found that a standardised root extract (2.5 % withanolides, 500 mg/day) improved stress, concentration, sleep, and memory with no negative effects (Majeed *et al*., 2023).

Ashwagandha contains ergostane-type steroidal lactones such as withanolides A-Y, withaferin A, and withanone, as well as alkaloids such as anaferine, tropine, cuscohygrine, and ashwagandhine, phytosterols, and amino acids such as tryptophan (Wikipedia, Withania somnifera; Mikulska, 2023).

Withanamides are powerful antioxidants that preserve neurones by neutralising beta amyloids. Molecular modelling indicates that withanamides A and C bind to Aβ (25-35) and prevent fibril formation (Rao, 2012; NIH/MedicalNewsToday, 2023).

Ashwagandha has been shown in preclinical models to improve cognitive function, with aqueous preparations increasing acetylcholine levels and choline acetyltransferase activity in rat brains. Methanol extracts stimulated neurite outgrowth and dendritic markers including PSD 95 and MAP2 in cultured neuroblastoma cells, and they repaired amyloid-induced dendritic and synaptic damage in rats, restoring memory function (Kurapati *et al*., 2013; Mikulska, 2023). Additionally, root extract reduced β-amyloid toxicity in human brain cell lines and improved plaque pathology and behaviour in transgenic Alzheimer's mice (Kurapati *et al*., 2013; Mikulska, 2023). However, clinical data on long-term safety and neurotherapeutic efficacy are limited, and systematic toxicity studies are still needed (Wikipedia, Withania somnifera; Panda, 2024).

Juglans regia

Walnuts include healthful lipids, important vitamins, α-tocopherol, and polyphenolic chemicals, including ellagic acid (Chauhan & Chauhan, 2020; Poulose, 2014). Walnut extract inhibits Aβ fibrillation and defibrillates preformed fibrils in vitro (Chauhan & Chauhan, 2020; Muthaiyah *et al*., 2011). Walnut phenolic acids have been shown to lower ROS levels, inhibit DNA breakage, and preserve cell membranes, resulting in reduced Aβ-induced cytotoxicity (Muthaiyah *et al*., 2011; Bhat *et al*., 2022).

According to evidence from both human and transgenic mouse studies, a walnut-rich diet boosts antioxidant defences, lowers oxidative stress (e.g., lipid peroxidation and protein oxidation), and slows cognitive decline in ageing and Alzheimer's models (Chauhan & Chauhan, 2020; Pandareesh *et al*., 2018). Regular walnut consumption may lower the risk of Alzheimer's disease by targeting numerous pathways, including Aβ aggregation, oxidative damage, neuroinflammation, and neural resilience (Pandareesh *et al*., 2018; Tan *et al*., 2022).

Emblica officinalis

In an animal model of scopolamine-induced amnesia, Emblica officinalis (amla) fruit hydroalcoholic extract injected intraperitoneally at 150, 300, 450, and 600 mg/kg effectively corrected memory impairment. This action was followed by normalisation of glutathione (GSH), malondialdehyde (MDA), and acetylcholinesterase (AChE) activity in brain tissue (Golechha *et al*. 2012). In a second research, tannoid-rich fractions of E. officinalis (50-200 mg/kg orally for 60 days) improved aluminium chloride-induced Alzheimer's disease in rats. The therapy lowered AChE activity, decreased amyloid precursor and Aβ1-42 expression, and enhanced spatial learning and memory (Thenmozhi *et al*., 2016). Each of these research emphasises E. officinalis's potential as a therapeutic agent in Alzheimer's disease, displaying antioxidant, anti-amyloidogenic, and cholinergic regulatory properties (Husain *et al*., 2019).

Drug / Family, Phytoconstituents, Mechanism of action, Application, Enzymatic assay/ target organism/ cell line of herbal compounds.

1. *Bacopa monnieri/ Scrophulariaceae.*

Bacoside A, bacoside, betulinic acid, D mannitol, stigmastanol, b sitosterol, stigmasterol.

Showed cognition-enhancing effect in a rat model of Alzheimer's and also inhibited cholinergic degeneration inhibition.

Boosting memory and treating Alzheimer's is potential use.

Rat model of AD.

(Jayaprakasam B., Padmanabhan K., et al (2010)

2. *Withania somnifera*/Solanaceae

Withanolides, dehydrowithanolide R, withasomniferin A, withasomidienone, withasomniferols A to C, withaferin A, and withanine. (Sancheti S., Sancheti S., Um B.-H et al (2010)

Neuronal cell death started by amyloid plaques is blocked. (Chang C. L. and Lin C. S(2012)

Alzheimer's disease

Rat neuronal cells (PC-12) (Matsuda H., Murakami T et al (2001)

3. *Myristica fragrans*

Terpenes, flavonoids

Antioxidant, memory enhancement, ache inhibitor

(Zhang, C. R., Jayashree, E., et al (2015).

4. *Melissa officinalis*

Flavonoids

Anticholinesterase activity

Bhat, B. A., Almilaibary, A., et al(2022).

Plant, utilized part, bioactive phytochemicals, and biological activities

Myristica fragrans, also known as nutmeg, is a medicinal plant prized for its numerous therapeutic properties. Terpenes and flavonoids are abundant in extracts from its seeds, fruits, and leaves, contributing to their antioxidant, cognitive-enhancing, and analgesic properties. Notably, nutmeg has been demonstrated to improve memory skills and suppress acetylcholinesterase (AChE) activity, indicating its potential for treating neurodegenerative disorders such as Alzheimer's disease (Kurian, G. A., *et al*. 2007).
Juglans regia, also known as walnut, is a nutrient-dense plant whose fruits and leaves have been traditionally used for medicinal purposes. Walnuts, which are high in flavonoids, ellagic acid, and polyphenols, have powerful antioxidant qualities that help neutralize free radicals and decrease oxidative stress, all of which contribute to Alzheimer's disease (AD) pathology.

These bioactive chemicals also have neuroprotective properties by reducing inflammation and oxidative damage, which may postpone the onset of age-related neurodegenerative illnesses such as Alzheimer's disease. (Poulose, S.M., *et al*. 2014).

Clitoria ternatea, also known as butterfly pea, is a member of the Fabaceae (legume) family and contains a variety of bioactive chemicals, including alkaloids, phenolic compounds, phytosterols, tannins, flavonoids, and saponins. These constituents contribute to the plant's neuroprotective properties through a variety of pharmacological activities. Notably, butterfly pea inhibits cholinesterase, making it a good option for Alzheimer's disease treatment. It also has anti-inflammatory, antibacterial, and anxiolytic (anxiety-reducing) qualities, which support its traditional and therapeutic uses in cognitive and neurological problems. (Mukherjee, P.K. *et al* 2007)

Melissa officinalis, sometimes known as lemon balm, is a medicinal plant whose leaves have long been used to promote relaxation and cognitive function. The plant contains several bioactive phytochemicals, including flavonoids, caffeic acid, rosmarinic acid, and substances found in essential oils. These ingredients contribute to its acetylcholinesterase (AChE) inhibitory action, which may aid in improving cholinergic transmission, which is frequently reduced in Alzheimer's disease (AD). Additionally, its phenolic components have high antioxidant effects, providing neuroprotection by countering oxidative stress, which is a major factor to AD development.

Emblica officinalis, also known as Amla or Indian gooseberry, has long been prized in traditional medicine due to its powerful health benefits. This plant's fruit has a high concentration of flavonoids, gallic acid, ellagic acid, and vitamin C, all of which contribute to its antioxidant and medicinal properties. In the setting of Alzheimer's disease (AD), methanolic extracts of E. officinalis have shown cholinesterase inhibitory activities, implying a role in improving cholinergic function, which is frequently damaged in AD. In particular, ellagic acid, a crucial bioactive ingredient, has been demonstrated to inhibit acetylcholinesterase (AChE), laying the groundwork for the development of innovative therapeutics targeting the cholinergic system in AD. (A. Kumar & V. K. Parihar, 2011).

BENEFITS OF COMBINING BRAHMI AND ASHWAGANDHA

While Bacopa monnieri (Brahmi) and Withania somnifera (Ashwagandha) each have unique neuroprotective and memory-enhancing properties, data increasingly shows that their combination usage gives greater cognitive support than either herb alone. Preclinical studies show that combining these two herbs improves learning and memory by reducing oxidative stress and increasing acetylcholine levels—effects similar to standard cognitive enhancers like piracetam in animal models. (Tancreda G, Ravera S *et al.*, 2025).

A clinical trial using the BacoZen™ herbal blend (a combination of Ashwagandha and Brahmi) showed significant reductions in perceived stress, lower cortisol, improved mood and sleep, and enhanced memory test scores—all without adverse effects. (Gregory, J.; *et al*. 2024). Another randomised placebo-controlled research using a sustained-release Ashwagandha formulation found increases in memory, attention, and emotional well-being after 90 days. (Gopukumar K *et al*. 2021). These herbs have complimentary benefits: Brahmi aids memory consolidation and synaptic transmission, whilst Ashwagandha reduces stress and increases neurogenesis. When administered together, they provide both immediate symptom alleviation and food for brain regeneration, which improves cognitive recovery more efficiently than either herb alone.

CURRENT CHALLENGES AND LIMITATIONS IN THE ADMINISTRATION OF HERBS

One of the most difficult obstacles in treating neurological illnesses such as Alzheimer's disease is breaking through the blood-brain barrier (BBB), which restricts the admission of therapeutic medicines into the CNS. (Liu S., Jin X., Ge Y., *et al*. 2025). While herbal treatments are frequently delivered orally, their ability to cross the BBB via systemic circulation is questionable, prompting researchers to investigate other delivery methods. Intranasal administration (INA) is a well-studied, non-invasive technique for bypassing the BBB and delivering compounds directly to the CNS via the olfactory and trigeminal nerve pathways. (Jeong, SH; Jang, JH; *et al*., 2023). Nanoemulsions, lipid nanoparticles, and in-situ gels have demonstrated effective brain targeting with minimal systemic exposure. (Jain Koo, Chaemin Lim, *et al*. 2024).

Preclinical investigations, particularly those focussing on Alzheimer's therapy, have found enhanced memory and cognitive function in transgenic mice models after INA of herbal medicines and nanoparticles. However, clinical translation is still restricted, with few human trials assessing intranasal herbal treatments. (Taléns-Visconti R *et al*. 2023). Traditional medicine also employs topical massage with medicinal oils applied to the scalp and forehead to provide herbal treatments. Moderate-pressure massage has been shown to improve cerebral blood flow, vagal tone, and cortisol levels, lowering stress and promoting neurological resilience. Following such a massage, functional MRI data show increased blood flow to brain regions involved in emotional and cognitive regulation. (Field T, 2014.)According to recent study, endothelial cells that line the brain's capillaries play an important role in delivering tiny, lipophilic compounds, such as those contained in therapeutic oils, from the scalp to the frontal and prefrontal areas of the brain. These capillary endothelial cells, which constitute the blood-brain barrier (BBB), include transporter proteins and diffusion processes that may let bioactive herbal ingredients enter the central nervous system when given topically or transcranially. (Jeong, SH; Jang, JH; *et al*., 2023).

FUTURE DIRECTION

There is an urgent need for novel treatment approaches to preventing and treating Alzheimer's disease (AD). Although several promising disease-modifying and symptomatic therapies are currently in development, their successful translation into clinical practice remains uncertain. For complicated and chronic illnesses such as Alzheimer's disease, transitioning from a monotherapeutic paradigm to a more complete, individualised, and multitherapeutic strategy is becoming more helpful (Cummings *et al*., 2022; Nguyen *et al*., 2022).

A recent clinical study using a precision medicine framework to manage cognitive decline in AD found consistent improvement among 100 participants, particularly by addressing metabolic dysfunctions that underpin many cases of early AD, mild cognitive impairment (MCI), and subjective cognitive impairment (SCI) (Bredesen *et al*., 2022).

Among the many treatments, medicinal plants have emerged as potent agents capable of affecting metabolic and neurological processes. These herbs can improve memory, promote neuronal health, and restore cognitive function through a variety of physiological methods. Indeed, medicinal plants have been identified as a significant source of pharmacological leads, with over 100 plant-derived molecules now undergoing clinical trials (Howes *et al*., 2020). These herbs are typically administered individually or in combination—such as in formulations like Triphala—and provide several benefits, including reduced non-specific toxicity, improved therapeutic efficacy, and a lower risk of drug resistance.

Herbal medications have a wide safety margin and have long been used therapeutically due to their diverse chemical profiles and capacity to interact with several biological targets at the same time (Wang *et al*., 2020). As a result, many practitioners and patients prefer whole-plant preparations or multi-herbal combinations over isolated phytochemicals or synthetic analogues. These combinations are known to have synergistic benefits, such as reversing medication resistance, modifying immunological responses, and reducing side effects (Ekor 2014).

This rising body of research demonstrates the efficacy of systems-based, personalised herbal solutions for Alzheimer's disease management. Both single-herb and polyherbal therapy show potential for treating Alzheimer's disease and its prodromal phases. To fully realise their potential, additional thorough study is required. This includes large-scale, multicenter clinical trials as well as in-depth molecular studies to determine the mechanisms of action. Addressing present limitations—such as poor trial design, limited sample numbers, and incorrect endpoints—will be crucial. Integrating conventional knowledge, combinatorial bioscience, and high-throughput screening methods can lead to the development of new plant-based treatment approaches for Alzheimer's disease.

CONCLUSION

Alzheimer's disease (AD) is a major worldwide health burden, with considerable medical, psychological, and economic repercussions (Prince *et al*., 2016). Current pharmacological therapies, such as cholinesterase inhibitors (e.g., donepezil) and NMDA receptor antagonists (e.g., memantine), only give symptomatic relief and do not slow or stop disease development (Cummings *et al*., 2022). As a result, there is increased interest in alternative and complementary treatments, notably herbal medications, because to their possible neuroprotective and disease-modifying effects (Howes *et al*., 2020).

Withania somnifera (ashwagandha) and Bacopa monnieri (brahmi) are two well-known herbs that have showed potential in reducing AD pathology. These botanicals have a variety of pharmacological properties, including antioxidant, anti-inflammatory, cholinergic enhancement, and amyloid-beta clearance effects, which all contribute to neuroprotection and cognitive improvement (Kumar *et al*., 2022; Tewari *et al*., 2021). Their bioactive phytochemicals may operate synergistically, providing more therapeutic effects than traditional single-target medicines or isolated substances (Aguiar & Borowski 2013).

Despite these hopeful findings, a number of barriers prevent herbal medicines from being integrated into standard Alzheimer's treatment. Low oral bioavailability, restricted blood-brain barrier (BBB) permeability, formulation standardisation, and long-term safety are all issues that require more exploration (Wang *et al*., 2020). Innovative delivery strategies, including as intranasal administration and nanoparticle-based formulations, are being investigated to increase CNS targeting and treatment effectiveness (Sharma *et al*. 2020).

To verify these techniques, well-designed, large-scale clinical studies are required to determine dose, effectiveness, and safety. In the future, combining herbal remedies with conventional treatments using evidence-based, personalised medicine strategies may improve AD treatment outcomes. Advances in pharmacokinetics, molecular pathway analysis, and multi-targeted interventions hold great promise for maximising the complementary benefits of herbal and conventional therapies.

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