

Review

Phytotherapy in Neurodegenerative Diseases: Mechanisms, Clinical Evidence, and Integrative Perspectives.

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Abstract

Background: Global population ageing is leading to a significant increase in the incidence of neurodegenerative diseases, such as dementia, with Alzheimer's disease being the most prevalent form. Conventional pharmacological treatments have limitations, highlighting the need to explore complementary therapeutic approaches.

Objective: To analyse the scientific evidence on the possible effects and mechanisms of action of medicinal plants in the context of dementia.

Methods: Review of the scientific literature on medicinal plants with potential application in dementia, including *Ginkgo biloba*, *Bacopa monnieri*, *Huperzia serrata*, *Rhodiola rosea*, and *Curcuma longa*. **Results:** The medicinal plants analysed demonstrate therapeutic potential through various mechanisms of action, including antioxidant, anti-inflammatory, and neuroprotective properties. The synergy between plant compounds is of great importance for treatment.

Conclusion: Herbal medicine emerges as a promising complementary therapeutic strategy in the prevention and treatment of dementia, offering vast potential through the synergy of its compounds. Continuous and rigorous research is essential to understand the full therapeutic potential of medicinal plants and integrate them safely and effectively into health care.

Keywords: Neurodegenerative Diseases; Dementia; Alzheimer's Disease; Medicinal Plants; Herbal Medicine.

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1. Introduction

The increase in longevity observed globally over recent decades has led to a substantial growth in the elderly population. According to United Nations projections ¹, it is estimated that by 2050, the number of people aged 60 years or older will reach 2.1 billion worldwide. This phenomenon of population ageing brings with it an increased incidence of neurodegenerative diseases, with dementia being the most common condition.

Dementia is a term used to describe a set of symptoms affecting the brain and its cognitive function, such as memory, language, reasoning, and judgment. It is not a specific disease but a collection of symptoms that can originate from various diseases and conditions ^{2,3}.

According to the World Health Organization, in 2021, dementia already affected an impressive 57 million people worldwide, with more than 60% residing in low- and middle-income countries. Each year, approximately 10 million new cases are registered, highlighting the rapid progression of this condition.

Currently, dementia is the seventh leading cause of death globally and one of the major causes of disability and dependency among older adults.

The economic impact of dementia is also significant. In 2019, dementia was estimated to cost the global economy USD 1.3 trillion. About 50% of these costs are attributable to care provided by informal caregivers—such as family members and close friends—who dedicate, on average, 5 hours daily to the care and supervision of affected individuals. It is important to note that women are disproportionately affected by dementia, both directly and indirectly. Women have a higher number of disability-adjusted life years and higher mortality due to dementia. Additionally, they provide 70% of care hours to people living with this condition, highlighting their crucial and often overburdened role in supporting those affected ⁴.

Among dementias, Alzheimer's disease is the most prevalent, accounting for more than 60% of cases ⁵⁻⁷. Alzheimer's disease is a chronic neurodegenerative disorder affecting the central nervous system, characterised by progressive cognitive decline. Its impact extends far beyond the affected individual, resulting in a significant burden for families and public health ⁸⁻¹⁰.

Parkinson's disease is the second most prevalent type of dementia ¹¹, characterised by the degeneration of dopaminergic neurons, leading to changes affecting movement, mental health, sleep, pain perception, and other aspects of health and quality of life. Common symptoms include tremors, intense and painful muscle contractions, speech difficulties, and disturbances in smell and taste ^{12,13}.

According to Aarsland *et al.* ¹⁴, approximately 30% of patients with Parkinson's have cognitive impairment, and up to 75% develop impairment after 10 years of the disease. It is important to note that Parkinson's and Alzheimer's diseases, being distinct types of dementias, present respective cognitive impairments with different developmental patterns. In Parkinson's disease, this impairment arises from the involvement of Lewy bodies ^{14,15}, while in Alzheimer's disease, it appears to be caused by the accumulation of beta-amyloid plaques and tau protein tangles ¹⁶.

For both Alzheimer's and Parkinson's diseases, conventional pharmacological treatments, although available, have limitations in terms of efficacy and side effects ^{8,17-21}.

Thus, the importance of exploring complementary therapeutic approaches is highlighted, aiming to improve the quality of life of patients with or at risk of developing dementia, providing more comprehensive care ²²⁻²⁵.

Naturopathy is a traditional medicine system recognised by the World Health Organization, based on two central philosophies: holism and vitalism ²⁶. Holism argues that health should be viewed as an integral whole, meaning the "whole" individual is greater than the sum of its constituent parts. Vitalism refers to the belief in the body's innate capacity to heal itself.

Originating in Europe, naturopathy has a global presence, being practised in over 108 countries—equivalent to 40% of all nations and covering all WHO regions ²⁷.

Since ancient times, plants have been the basis for treating various diseases, long before modern medicine. It is estimated that, in the past, a large proportion of the global population depended on herbal remedies ²⁸. This millennial practice persists in various regions worldwide, including East Asia, South Asia, the Middle East, and Southeast Asia, where herbal medicine remains a popular therapeutic option due to accessibility, cultural acceptance, and perceived efficacy ²⁹⁻³¹.

The use of plant-derived natural products has been associated with a range of health benefits, including improving metabolic status and treating related disorders ³², acting as an adjuvant in cancer therapy ^{33,34}, modulating cardiovascular risk factors ^{35,36}, alleviating mental disorders ³⁷, treating gastrointestinal diseases, promoting wound healing, and combating viral infections ³⁸.

The persistence and breadth of medicinal plant use highlight their importance as a complementary and valuable therapeutic approach, with the potential to promote health and well-being across diverse populations.

Thus, the objective of this study is to contextualise the pathogenesis of dementia and analyse the scientific evidence of naturopathic approaches focusing on medicinal plants, as well as their possible effects and mechanisms in dementia.

2. The Pathogenesis of Dementia and the Naturopathic Approach

Consciousness is a physiological state of human brain function that allows it to receive and interpret signals from the environment. These signals are encoded within the brain's functional structure, and their permanent memories are used to plan and execute behaviours necessary for survival ³⁹. Learning and memory, which form the foundation of human consciousness, are continuous processes lasting a lifetime, and their effectiveness depends, in turn, on the efficiency of numerous physiological processes occurring at cellular, tissue, and systemic levels. Disruption of any physiological cycle ultimately leads, in the short or long term, to impaired learning and memory and to the disintegration of human consciousness, collectively referred to as dementia ³⁹.

According to Blaszczyk ³⁹, the primary underlying factor in brain ageing and dementia, including Alzheimer's disease, is a loss of control over glucose metabolism, resulting in an energy imbalance in the brain. The author suggests three key contributing factors: the loss of the brain's ability to detect blood glucose levels, reduced somatomedin C activity, and sleep disturbances.

Compensatory mechanisms, such as type 2 diabetes and hypertension, are seen as factors that exacerbate the problem ⁴⁰. The resulting inability of the brain and muscles to utilise glucose leads to hypoactivity, systematic reduction of unused neuronal networks (including crucial structures such as cortical pyramidal neurons and cerebral pyramidal tracts), and ultimately the development of dementia ⁴¹⁻⁴³. The energy crisis also affects emotional regulation and, together with chronic stress and sleep disturbances (which impair waste clearance and glymphatic neurogenesis), culminates in microglial deficiency and uncontrolled neurodegeneration ⁴⁴⁻⁴⁶.

Despite the irreversible loss of dead neurons, Blaszczyk ³⁹ suggests that early intervention focused on enhancing cognitive metabolism with essential energy nutrients such as nicotinamide adenine dinucleotide (NAD), somatomedin C, vitamin D, and phosphate, combined with a low-fat diet and physical activity, may slow or even reverse the neurodegenerative cascade. This approach aims to improve the function and maintenance of cognitive networks into older age, offering a window of opportunity to treat or slow dementia before it reaches a point of no return ⁴⁷.

Additionally, potential benefits of supplementing vitamin B3 precursors (such as nicotinamide riboside chloride) to support neuronal viability and slow cortical neuron ageing have been highlighted ⁴⁸. Moreover, phosphate/calcium (Ca/P) homeostasis for cerebral energy metabolism appears to be important ⁴⁹. Thus, restoring this balance, potentially through vitamin D supplementation ⁵⁰, may improve energy metabolism and alleviate chronic fatigue, providing a potential treatment or prevention pathway for individuals with neurodegenerative diseases.

However, it is important to note that other causes may contribute to dementia development. For example, alcohol and drug use are associated with a higher risk of neurodegenerative diseases ^{51,52}. Alcohol can directly damage the brain as a neurotoxin ⁵² or indirectly through malnutrition, particularly thiamine (vitamin B1) deficiency ^{53,54}. Alcohol use disorder is common among older adults, and alcohol-related dementia is often underdiagnosed ⁵⁵. Identifying such substance use is therefore crucial for naturopathic professionals to advise and refer patients to specialised care.

On the other hand, Lewy's body dementia is characterised by abnormal deposits of the alpha-synuclein protein within neurons. These accumulations, known as Lewy bodies, impact various critical brain areas responsible for thinking, movement, behaviour, and mood. This form of dementia frequently presents with Parkinsonian symptoms such as tremor and muscle rigidity ^{56,57}.

Another example is vascular dementia, which develops due to disrupted blood flow in the brain caused by strokes, small cerebral infarcts, or small vessel disease ^{58,59}. This reduced blood supply causes localised brain damage in the affected areas, and symptoms may appear suddenly after a stroke or progress gradually with multiple small infarcts over time ⁶⁰.

Beyond supplementation, other techniques may be important in dementia management. Aromatherapy is a non-pharmacological intervention using plant essential oils for therapeutic purposes, administered via inhalation, ingestion, or topical application ⁶¹.

Empirical evidence suggests that plant essential oils (such as *Lavandula*) may be valuable in managing agitation and behavioural and psychological symptoms of dementia. They are believed to act on the neuro-limbic system and enhance neurotransmitter synthesis, potentially producing antidepressant, anxiolytic, and/or sedative effects ^{62,63}. Some essential oils also demonstrate in vitro anticholinesterase activity ^{64,65}, a mechanism particularly relevant in dementia treatment and management ⁶⁶. These are summarised in Table 1.

Table 1. Essential Oils with In Vitro Anticholinesterase Activity ^{64,65}.

Plant (Essential Oil)	In Vitro Anticholinesterase Activity
<i>Ocimum basilicum</i> (Basil)	IC ₅₀ 0.22 mg/mL
<i>Ocimum africanum</i> (African Basil / Small-leaf Basil)	IC ₅₀ 0.175 mg/mL
<i>Ocimum americanum</i> (White Basil / Field Basil)	IC ₅₀ 0.57 mg/mL
<i>Ocimum minimum</i> (Basil Herb)	IC ₅₀ 0.152 mg/mL
<i>Ocimum canum</i> (Sweet Basil / Field Basil)	IC ₅₀ 0.362 mg/mL
<i>Eucalyptus camaldulensis</i> (Red Eucalyptus)	IC ₅₀ 0.190 mg/mL

Additionally, a pilot randomised, placebo-controlled clinical trial investigated the efficacy and feasibility of topically applied individualised essential oil preparations to reduce agitation in people with dementia. Results showed promising effects, suggesting that a larger multicentre clinical trial is feasible and justified.

Dietary modifications have also proven important in this population. According to Davis *et al.* ⁶⁷, multiple preclinical studies confirm the benefits of ketosis—a metabolic state in which the body burns fat rather than carbohydrates for energy—on cognition and systemic inflammation. With renewed focus on neuroinflammation as a pathogenic factor in cognitive decline, and given the reduction in systemic inflammation observed with a ketogenic diet, this dietary approach may delay, improve, or prevent cognitive decline progression.

These authors also note that several small human studies have already shown cognitive benefits of ketogenic interventions in dementia cases. While larger controlled studies are needed to confirm these benefits, the ketogenic diet shows promise in delaying or mitigating cognitive decline symptoms.

Adherence to the MIND diet (Mediterranean-DASH Intervention for Neurodegenerative Delay) has also been associated with a lower risk of incident dementia in middle-aged and older adults, suggesting a potentially significant protective role for brain health ⁶⁸. Barnes *et al.* ⁶⁹ studied this diet among participants without cognitive impairment but with a family history of dementia and found that cognitive changes and brain MRI outcomes over three years did not differ significantly between those following the MIND diet and those following a control diet with mild caloric restriction. This finding suggests that

caloric restriction itself may contribute to cognitive benefits, potentially reducing observable differences compared to the MIND diet. Additionally, three years may not be a sufficient period to detect significant differences in cognitive decline progression among individuals starting with healthy cognitive function.

However, as noted by Samieri *et al.* ⁷⁰, a personalised nutrition approach focusing on optimal prescription for the most appropriate target population and relevant timeframe may significantly enhance dementia prevention efforts.

From a dementia management perspective, therapeutic massage itself can be an effective non-pharmacological strategy to improve behavioural and psychological symptoms in people living with dementia ⁷¹. Given its simplicity and potential benefits, naturopathic practitioners and family caregivers should be encouraged to apply massage to their patients and relatives. However, further research is needed to provide clearer recommendations regarding the frequency and types of massage that are most effective for this purpose.

According to Smith *et al.* ⁷², sensory-based interventions may provide multiple benefits for individuals with dementia and Alzheimer's disease residing in care facilities. Among these techniques, the authors highlight:

- Strong evidence: massage proved to be an effective intervention;
- Moderate evidence: multisensory activities based on occupational therapy and environment, such as light use, gardening, meal-related activities, music, Montessori, animal-assisted therapy, dance, and yoga, showed benefits;
- Inconclusive evidence: aromatherapy, art therapy, Snoezelen rooms, and interventions combining visual and auditory stimuli.

The use of specific medicinal plants is a vast and complex field. In this work, our aim is to further explore this area, as detailed in the following sections.

3. Medicinal Plants in Dementia Management

3.1. *Ginkgo Biloba*

Ginkgo biloba is an ancient plant and the only living species in the division Ginkgophyta. It is extremely resistant to disease ⁷³, can live for more than 1000 years, and reaches up to 40 meters in height. Originally native to China, *Ginkgo biloba* is now cultivated worldwide ⁷⁴.

For centuries, Traditional Chinese Medicine has used extracts of this plant to treat circulatory disorders, asthma, tinnitus, vertigo syndrome, and cognitive problems ⁷⁵. These applications are attributed to its vasodilatory, antioxidant, neuroprotective, and anti-inflammatory effects ⁷⁶⁻⁸².

Since 2000, *Ginkgo biloba* extract has been included in the Anatomical Therapeutic Chemical (ATC) Classification as an anti-dementia substance, alongside cholinesterase inhibitors and memantine (drugs used in the treatment of Alzheimer's disease) ⁸³. This recognition highlights why it is considered one of the most credible and widely used phytotherapies worldwide ^{84,85}.

Further reinforcing its relevance, the European Medicines Agency (EMA) approved the use of *Ginkgo biloba* for the improvement of "age-associated cognitive impairment and quality of life in mild dementia," based on what is termed "well-established use" across several European countries ⁸⁶. For example, in Germany, *Ginkgo biloba* extract (particularly the standardised extract EGb 761) is a well-established phytomedicine and widely prescribed for the treatment of cognitive impairment and mild-to-moderate dementia. The German S3-Leitlinie "Demenzen" ⁸⁷ guidelines acknowledge its efficacy in improving certain cognitive symptoms and quality of life in dementia patients.

Table 2. Representation and mechanisms of *Ginkgo biloba*.

Botanical drawing	Mechanisms of compounds
	Flavonoids and their metabolites may interact with neuronal receptors and modulate kinase signalling pathways, transcription factors, and gene and/or protein expression, which regulate memory and learning processes in the hippocampus ^{88,89}. They may also improve cerebrovascular blood flow and synaptic plasticity, both contributing to enhanced memory, learning, and cognitive functions ⁸⁸. Terpene lactones exhibit multiple biological activities, including peripheral vasoregulation, platelet-activating factor receptor antagonism, neuroprotective properties, and prevention of membrane damage caused by free radicals ⁹⁰. These effects may provide protection against learning and memory impairments.

A systematic review by Yuan *et al.* ⁹¹ aimed to analyse the scientific evidence regarding the efficacy of *Ginkgo biloba* extract in dementia treatment. According to the authors, the results of the meta-analyses reviewed suggest that the extract has potentially beneficial effects compared with placebo on cognitive performance, activities of daily living, and global clinical impression in dementia treatment, at doses above 200 mg/day (generally 240 mg/day) administered for at least 22 weeks. A favourable safety profile for human consumption was also reported.

For dementia treatment, the authors further concluded that the available evidence consistently indicates that dosages below 200 mg/day and treatment durations shorter than 22 weeks may not be adequate to produce clinically relevant effects.

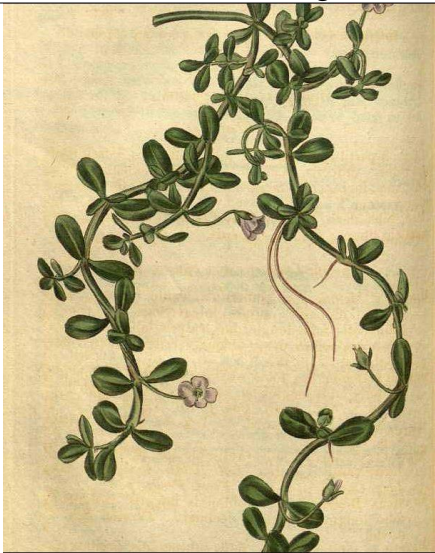
3.2. *Bacopa Monnieri*

Bacopa monnieri, also known as Brahmi ⁹², is a perennial plant of the *Scrophulariaceae* family, traditionally used in *Ayurvedic* medicine as a neural tonic to enhance intelligence and memory, improve brain function, and promote longevity ^{93,94}.

Research has demonstrated that this plant possesses significant antioxidant and neuroprotective properties, positioning it as a potentially valuable candidate in the management of Alzheimer’s disease ⁹². Additionally, *Bacopa monnieri* has been reported to exhibit sedative, antimicrobial, anti-inflammatory, calcium antagonist, anticonvulsant, anti-ageing, cognition-enhancing, antinociceptive, broncho-vasodilatory, anticancer, hepatoprotective, antiallergic, antidepressant, antihypercholesterolemic, antiemetic, and anti-ulcer activities ⁹⁵⁻¹⁰⁸.

In a randomised controlled clinical trial, Delfan *et al.* ¹¹⁰ evaluated the effects of *Bacopa monnieri* on cognitive performance and sleep quality in individuals with mild cognitive impairment. The results demonstrated a significantly greater effect compared to the placebo control group, particularly in overall cognitive performance after two months, verbal fluency after two months, and attention after the first month of intervention. However, the plant did not show significant effects on sleep quality after two months compared to placebo. The prescribed dose of *Bacopa monnieri* extract was 160 mg/day.

Table 1. Representation and mechanisms of *Bacopa monnieri*.

Botanical drawing	Mechanisms of compounds
	Recent studies have identified novel saponins, bacopasides I–XII, which may help elucidate the plant’s anti-dementia mechanisms ¹⁰⁹. According to the study by Le <i>et al.</i> ⁹³, it attenuates OBX-induced cognitive dysfunction through mechanisms involving the upregulation of synaptic plasticity-related signalling and BDNF transcription, as well as protection of cholinergic systems against OBX-induced neuronal damage.

In another phase 2 clinical trial, ¹¹¹, the effects of *Bacopa monnieri* were compared with those of donepezil in patients with Alzheimer’s disease. Donepezil is a drug specifically developed for the treatment of Alzheimer’s disease. It acts as a cholinesterase inhibitor, preventing the breakdown of acetylcholine, a neurotransmitter essential for memory and learning. By increasing acetylcholine availability in the brain, donepezil helps improve neuronal communication, thereby alleviating some cognitive symptoms of Alzheimer’s disease ^{112,113}. Overall, the study results indicated that a daily dose of 300 mg of *Bacopa monnieri* over 12 months was as effective as donepezil treatment over the same period. Moreover, *Bacopa monnieri* demonstrated some superiority in memory function testing after 12 months. Based on these promising results, the authors recommend conducting a multicentre phase 3 randomised clinical trial.

3.3. *Huperzia Serrata*

Huperzia serrata, a plant belonging to the family of clubmosses, has been used in Traditional Chinese Medicine for more than 1,000 years in the treatment of a variety of conditions, including contusions, sprains, swellings, schizophrenia, and, more recently, myasthenia gravis and organophosphate poisoning ¹¹⁴⁻¹¹⁶.

Huperzine A, the principal bioactive compound isolated from *Huperzia serrata* in the 1980s, acts as a selective acetylcholinesterase inhibitor ¹¹⁷.

Ohba *et al.* ¹²⁰ demonstrated that *Huperzia serrata* and its constituent compounds may exert beneficial effects by mitigating oxidative stress and inhibiting acetylcholinesterase activity, ultimately leading to improved cognitive performance.

Supporting these findings, Ghassab-Abdollahi *et al.* ¹²¹ conducted a systematic review and concluded that, although further studies are warranted, current evidence suggests a beneficial effect of Huperzine A on cognitive function and daily living activities in patients with Alzheimer’s disease.

However, using a *Huperzia serrata* extract, Callizot *et al.* ¹¹⁹ reported that its neuroprotective activity relies on a precise synergy between three main constituents: Huperzine A and the phenolic acids caffeic and ferulic acid. According to their findings, the latter two enhance the neuroprotective activity mediated by Huperzine A, but not its acetylcholinesterase inhibitory properties, which are associated with adverse side effects.

These results highlight the importance of the synergy among multiple plant constituents as opposed to the isolated use of individual components.

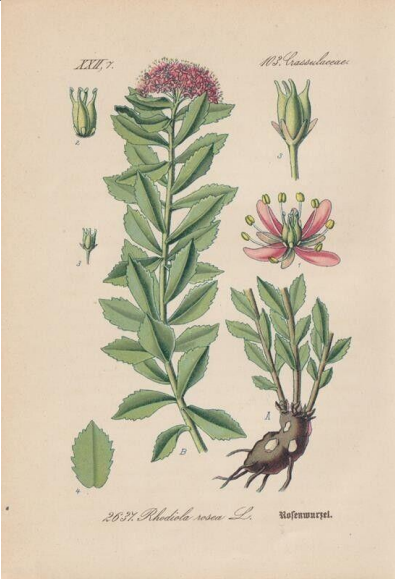
Table 4. Representation and mechanisms of *Huperzia serrata*.

Botanical drawing	Mechanisms of compounds
	Huperzine A, as a selective acetylcholinesterase inhibitor ¹¹⁷, prevents the breakdown of acetylcholine in the brain, thereby increasing its availability, which may enhance neuronal communication and prevent cognitive dysfunction ¹¹⁸. It's caffeic acid, in combination with ferulic acid, that contributes to neutralising reactive oxygen species, protecting cells from oxidative stress ¹¹⁹.

3.4. *Rhodiola Rosea*

Rhodiola rosea is a perennial plant belonging to the *Crassulaceae* family, with its principal bioactive compounds being rosavins (including rosin, rosavin, and rosarin) and salidroside ¹²²⁻¹²⁴. *Rhodiola* root preparations are widely used in traditional medical practices and are recognised for their multiple health benefits ¹²⁴, with animal studies reporting specific effects on lifespan extension ¹²⁵.

Table 5. Representation and mechanisms of *Rhodiola rosea*.

Botanical drawing	Mechanisms of compounds
	Rosarin and salidroside inhibit nitric oxide production in the inflammatory response, leading to a dose-dependent reduction of TNF-α (tumour necrosis factor alpha), IL-1β (interleukin-1 beta), and IL-6 (interleukin-6), observed in the kidney and prefrontal cortex of the brain ¹²⁶. These findings suggest that the plant's constituents can cross the blood-brain barrier and act in the brain, suppressing central nervous system inflammation ¹²⁷. An extract standardised to 2.7% w/w rosavin and 1% w/w salidroside, at a concentration of 20 μg/ml, was shown to neutralise the neuroinflammatory effect of corticotropin-releasing hormone (CRH) through inhibition of nuclear translocation of nuclear factor kappa B (NF-κB). This mechanism involves the modulation of mitogen-activated protein kinase kinase 2 (MKK2), extracellular signal-regulated kinases 1/2 (ERK1/2), and c-Jun N-terminal kinase (JNK), resulting in decreased expression of heat shock protein 70 (HSP70) ¹²⁸.

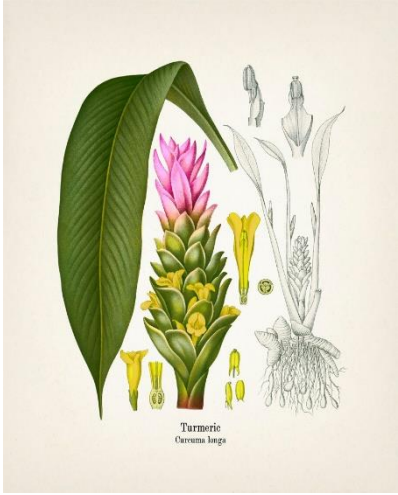
According to Nabavi *et al.* ¹²⁷, *Rhodiola rosea* demonstrates general neuroprotective properties, with scientific evidence supporting its role in combating oxidative stress and neuroinflammation, enhancing mitogen-activated protein kinase (MAPK) signalling pathways, improving the regulation of mitochondrial antioxidant enzymes, and reducing excitotoxicity.

3.5. *Curcuma Longa*

Predominant in South Asia, particularly in India, turmeric was initially cultivated as a dye and later incorporated as a cosmetic and as an aromatic and auspicious food ingredient. It is believed to be a hybrid selection and vegetative propagation of wild turmeric (*Curcuma aromatica*), native to India, Sri Lanka, the Eastern Himalayas, and other closely related species ¹²⁹.

Turmeric has a long history of medicinal use. Owing to its ability to modulate multiple molecular targets—such as transcription factors, enzymes, and cytokines—curcumin has demonstrated therapeutic potential for a wide range of diseases, including cancer, arthritis, diabetes, and Alzheimer’s disease ¹³⁰.

Table 6. Representation and mechanisms of *Curcuma longa*.

Botanical drawing	Mechanisms of compounds
	Curcumin has a unique molecular structure and multifaceted actions. It demonstrates anti-inflammatory, antioxidant, and neuroprotective properties ¹³¹, the ability to disaggregate tau filaments and activity against amyloid aggregation (plaques), one of the main pathological hallmarks of Alzheimer’s disease ¹³². Co-administration of curcumin with piperine significantly increases curcumin bioavailability. Studies have shown a 154% increase in rats and a remarkable 2000% increase in humans ¹³³⁻¹³⁵.

According to Brondino *et al.* ¹³⁶, there is currently insufficient evidence to recommend the use of *Curcuma longa* as a treatment for dementia. However, some studies suggest possible positive effects, reporting improvements in memory and attention ^{137,138}.

Kuszewski *et al.* ¹³⁹ emphasised the need for mechanistic studies at the level of endothelial brain function, possibly combining other bioactive nutrients to potentiate its anti-inflammatory effects and improve endothelial vasodilatory function.

Indeed, curcumin exhibits low bioavailability due to its hydrophobic nature, poor intestinal absorption, rapid metabolism, and systemic elimination ¹⁴⁰. Furthermore, curcumin glucuronidation, which renders the molecule conjugated, prevents it from crossing the blood–brain barrier (BBB) and exerting effects on the brain ¹⁴¹⁻¹⁴³.

However, piperine (*Piper nigrum*), a glucuronidation inhibitor, can enhance curcumin absorption, suggesting that glucuronidation is a major factor in its poor bioavailability ¹⁴⁴.

Thus, recent studies support the combined use of piperine and curcumin for various conditions ¹⁴⁵. Although further research is required in this specific area, curcumin–piperine supplementation may offer potential neuroprotective effects through its anti-inflammatory and antioxidant actions, as well as by improving vascular function ¹⁴⁶. Moreover, Ahmad *et al.* ¹⁴⁷ confirmed that the co-administration of curcumin and piperine increases curcumin bioavailability. In their *in vivo* study assessing the synergistic effects of curcumin and piperine in Alzheimer’s disease, a nanoformulation produced significant benefits, with positive outcomes in learning and memory.

4. Reflexões finais

Based on the studies analysed in this work, it is evident that the exploration of complementary therapeutic approaches, such as phytotherapy, is necessary to improve the quality of life of patients with neurodegenerative diseases.

Medicinal plants present a vast therapeutic potential due to their diversity of bioactive compounds and mechanisms of action, and scientific research continues to reveal their benefits, with both clinical and mechanistic studies deepening the understanding of their effects.

It can be concluded that the synergy among plant compounds is of great importance in treatment, as the complexity of phytotherapeutic formulas and their study becomes evident.

However, more long-term randomised clinical trials are needed to confirm the results and determine the therapeutic potential of medicinal plants in the prevention and treatment of neurodegenerative diseases.

It is crucial to emphasise that, in the clinical context, the efficacy of medicinal plants may vary considerably among individuals, influenced by various factors, including the quality and dosage of the supplements used. Therefore, although the dosages of some plants explored in this work are presented, it is clear that further research is needed to standardise the optimal doses of these herbal approaches.

Additionally, the potential interactions between medicinal plants and prescribed medications require careful evaluation by healthcare professionals. In this regard, it is also important to develop greater awareness of the ideal timing for the administration of phytotherapeutics, since their role may vary depending on the stage of the disease.

Overall, according to the evidence discussed in this study, in early stages, the intervention with medicinal plants may have a preventive or supportive role, focusing on cellular protection or the alleviation of mild symptoms. Conversely, in advanced stages, the capacity for intervention is more limited, and the focus may shift toward the management of behavioural symptoms or improving quality of life rather than attempting to reverse the course of the disease.

In light of all this, the importance of a personalised approach and constant dialogue among healthcare providers is emphasised, in order to ensure greater complementarity between conventional and non-conventional therapies. Only within an integrative health model is it possible to maximise health and well-being in patients with dementia.

5. Conclusões

The growing prevalence of neurodegenerative diseases, driven by global population ageing, demands the exploration of innovative and complementary therapeutic approaches. In this context, phytotherapy emerges as a promising field, with a wide range of medicinal plants showing therapeutic potential through multiple mechanisms of action. The synergy between the various bioactive compounds present in plants, as evidenced in studies on *Ginkgo biloba*, *Bacopa monnieri*, *Huperzia serrata*, *Rhodiola rosea*, and *Curcuma longa*, suggests that phytotherapy may offer significant benefits in the prevention and treatment of conditions such as Alzheimer's and Parkinson's disease.

The action of *Ginkgo biloba* lies primarily in the optimisation of microcirculation and antioxidant protection, which translates into improved cerebral metabolism and preservation of cognitive function in the early stages of dementia. Its extract, therefore, proves to be a valuable supportive intervention, provided that its dosage and duration are properly adjusted to maximise effects.

With respect to *Bacopa monnieri*, it emerges as a promising neural tonic, acting on neuroprotection and memory enhancement. Its efficacy, in certain contexts, approaches that of conventional pharmacological analogues, positioning it as a phytotherapeutic alternative with a favourable safety profile, whose further investigation may expand its clinical application.

The therapeutic relevance of *Huperzia serrata* is intrinsically linked to its active compound, Huperzine A, which acts as an acetylcholinesterase inhibitor. Its efficacy in increasing acetylcholine levels in the brain is remarkable. The plant extract, containing Huperzine A and other synergistic compounds, offers a broader and potentially safer approach than the isolated drug.

The mechanism of action of *Rhodiola rosea* centres on the suppression of oxidative stress and neuroinflammation. The ability of its compounds to cross the blood–brain barrier and exert a modulatory effect on inflammatory cytokines suggests an important role in the prevention and management of brain degenerative processes.

Finally, *Curcuma longa*, despite its vast neuroprotective and anti-inflammatory potential, faces the challenge of poor bioavailability of its main compound, curcumin. Its therapeutic success in dementia depends on overcoming this obstacle, which has been addressed through formulations that enhance its systemic absorption.

In summary, phytotherapy represents a valuable complementary therapeutic strategy, with the potential to improve the quality of life of patients with neurodegenerative diseases. Ongoing and rigorous research is essential to fully understand the therapeutic potential of medicinal plants and to integrate them safely and effectively into integrative healthcare.

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