REVIEW PAPER

Passiflora as A Natural Remedy for Alzheimer's disease: Current Evidences

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ABSTRACT

Alzheimer's disease is a progressive, globally prevalent neurodegenerative disorder characterized by cognitive decline, memory impairment, and hallmark pathological features such as extracellular amyloid-beta plaques and intracellular neurofibrillary tangles composed of hyperphosphorylated tau protein. This review discusses the neuroprotective potential of Passiflora species has attracted growing scientific attention with a longstanding history of use for their sedative, anxiolytic, and anti-inflammatory properties. Preclinical studies have shown that extracts from Passiflora incarnata and Passiflora edulis possess multifaceted benefits in experimental models of Alzheimer's disease, including attenuation of amyloid-beta-induced neurotoxicity, inhibition of tau protein hyperphosphorylation, and enhanced cognitive performance. The bioactive constituents attributed to these effects primarily flavonoids, alkaloids, and phenolic acids are noted for their potent antioxidant and anti-inflammatory activities. The extensive traditional use of Passiflora, combined with its diverse pharmacological actions and favorable safety profile, positions it as a promising candidate for adjunctive therapy in Alzheimer's disease. Further investigation into Passiflora and its active compounds may provide valuable opportunities for the development of disease-modifying interventions for Alzheimer's and related neurodegenerative disorders.

Keywords: Alzheimer's Disease, Passiflora, Phytocompounds, Neuroinflammation, Neuroprotective.
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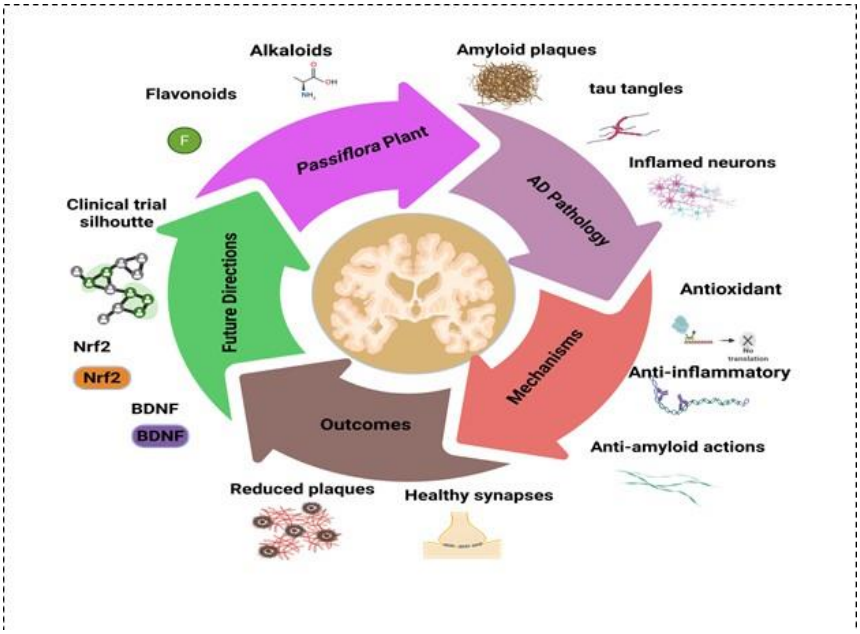
GRAPHICAL ABSTRACT:



1. INTRODUCTION

Alzheimer's Disease (AD) is a progressive neurodegenerative disorder that primarily affects cognitive functions, leading to impaired thinking and memory loss. This condition manifests in changes to personality, declines in speech ability, behavioral deterioration, reduced task performance, slowed thought processes, and abnormal gait[1]. AD is a major medical concern as it is the

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leading cause of dementia, predominantly affecting individuals over 55 years of age[2]. Globally, approximately 50 million people suffer from dementia, a figure expected to double every 20 years until 2050[3]. Several hypotheses explain AD's underlying causes. The cholinergic hypothesis notes a reduction in enzymes related to acetylcholine in the cerebral cortex, leading to cholinergic neuronal loss and cognitive decline[4]. Another theory involves tau protein abnormalities; over-phosphorylation of tau causes neurofibrillary tangles that disrupt brain structure and synaptic function, promoting neurodegeneration[5]. Herbal medicines, longstanding in traditional systems like Ayurveda, contain phytochemicals such as polyphenols, flavonoids, sterols, triterpenes, and alkaloids, many of which have demonstrated neuroprotective effects. Flavonoid-rich compounds, in particular, have shown promise in improving cognitive deficits and slowing AD progression[6]. Among botanicals, Passiflora species are emerging as candidates for natural AD remedies due to their multi-targeted effects including anti-amyloid, anti-tau, antioxidant, and anti-inflammatory activities, although human clinical trials remain limited, highlighting the need to translate preclinical findings into clinical validation. Advances in extract standardization, bioavailability enhancement such as nanoformulations and combination therapies with conventional drugs or other botanicals could unlock its potential. Future studies must prioritize rigorous clinical trials, biomarker-driven approaches, and personalized medicine to assess disease-modifying effects[7]. Figure 1 shows the various parts of Passiflora.

Figure 1. Various parts of Passiflora (a) Diverse and vibrant flowers of Passiflora species (b) The leaves, which are often utilized in herbal remedies for their calming and sedative properties (c) The fruits commonly referred to as passion fruits (d) The seeds valued for oil content and potential health benefits

2. ALZHEIMER'S DISEASE

Nervous system disorders significantly impact global health, affecting over one billion people according to the World Health Organization (WHO)[8]. These disorders span diseases of both the central and peripheral nervous systems, including Parkinson's disease, epilepsy, schizophrenia, AD, dementias, neuroinfections, brain tumors, traumatic injuries, stroke, and migraine[9]. Estimates predict that by 2030, more than 65.7 million people worldwide will be living with AD[10]. The disease is linked to multiple risk factors, such as aging, genetic predisposition, traumatic brain injury, infections, cardiovascular issues, lifestyle diseases like obesity, diabetes, hypertension, and environmental exposures to heavy metals. Its pathological hallmarks include the extracellular buildup of amyloid-beta (Aβ) plaques and intracellular tau tangles, which are associated with neuroinflammation, mitochondrial malfunction, loss of synapses, and neuronal death[11]. Plants have long been used in traditional medicine, with secondary metabolites like alkaloids, saponins, flavonoids, terpenes, and notably phenolic compounds being valued for their health

benefits[12]. Flavonoids, with strong antioxidant capabilities, are abundant in many fruits, vegetables, grains, flowers, tea, and wine, and serve to neutralize reactive oxygen species (ROS), offering substantial neuroprotective effects. Clinical research highlights their ability to mitigate oxidative damage, which is heightened in AD[13].

3. MEDICINAL USE OF PASSIFLORA

The Passiflora plant, a member of the Passifloraceae family and often called passion fruit, is widely found in tropical regions across the globe. It is traditionally used in herbal medicine to help alleviate anxiety, nervousness, and neuralgia[14]. Commonly referred to as passionflowers or passion vines, these plants are largely climbing vines, though some are shrubs or herbaceous, with the majority belonging to the family Passifloraceae[15]. Although their greatest diversity is in the Americas, Passiflora species are rare in Asia, Australia, and tropical Africa, but certain species, such as *Passiflora caerulea*, have naturalized beyond their native range. The genus is valued for its rich phytochemistry, producing alkaloids such as notably beta-carboline harmala alkaloids like harmine and harmaline, phenolics, glycosyl flavonoids, cyanogenic compounds, and monoterpenoids compounds that are especially concentrated in the leaves and roots[16]. Traditional medicine has employed various Passiflora species to treat conditions such as anxiety, opioid withdrawal, insomnia, attention deficit hyperactivity disorder. Scientific studies have substantiated several pharmacological properties, including anxiolytic, spasmolytic, hypnotic, sedative, narcotic, and anodyne effects, and extracts have shown promise in managing adjustment disorders and anxious mood. Passionflowers, particularly *Passiflora incarnata*, are recognized for their high flavonoid content including quercetin, vitexin, and isovitexin, indole alkaloids like harman, harmine, harmaline, and phenolic compounds, which collectively contribute to strong antioxidant activity[17]. This antioxidant capacity, primarily mediated by flavonoids, is thought to protect against oxidative stress, a key factor in neurodegenerative diseases such as AD and Parkinson's (PD). Harmine and harmaline alkaloids, in particular, have shown anti-parkinsonian effects, likely due to their ability to counteract oxidative damage in the substantia nigra and basal ganglia regions especially vulnerable in PD[22]. Overall, Passiflora species represent a valuable source of bioactive compounds with a broad spectrum of medicinal potential, but further clinical research is essential to fully understand their safety, efficacy, and therapeutic applications in modern medicine[23].

Table 1 shows medicinal uses of *Passiflora* species.

Table 1. **Medicinal uses of *Passiflora* species**

Species	Traditional Use	Bioactive Compounds	Pharmacological Effects	Clinical Evidence / Side Effects
P. incarnata	Anxiety, insomnia, nervousness	Flavonoids (vitexin, isovitexin), alkaloids (harman)	Sedative, anxiolytic, anticonvulsant	Clinical trials support anxiolytic effects; rare dizziness
P. edulis	Digestive disorders, hypertension	Anthocyanins, polyphenols, carotenoids	Antioxidant, antihypertensive	Limited human studies; generally recognized as safe (GRAS)
P. foetida	Anti-inflammatory, wound healing	Passifloricin, luteolin, quercetin	Anti-inflammatory, antimicrobial	Traditional use; no major side effects reported
P. caerulea	Sedation, pain relief	Harmala alkaloids, glycosides	Analgesic, muscle relaxant	Animal studies only; potential drowsiness
P. quadrangularis	Asthma, diarrhea, hemorrhoids	Cyanogenic glycosides, saponins	Antispasmodic, bronchodilator	Limited safety data; avoid excess cyanide exposure
P. ligularis	Antioxidant, cardiovascular health	Vitamin C, phenolic acids	Cardioprotective, vasodilator	No clinical trials; low toxicity
P. alata	Cough, bronchitis, anxiety	Flavonoids, maltol	Expectorant, anxiolytic	Traditional use in Brazil; mild GI upset
P. laurifolia	Diuretic, anti-arthritic	Tannins, leucocyanidin	Diuretic, anti-inflammatory	Anecdotal evidence; avoid in kidney disease
P. maliformis	Fever, headaches	Passicol, edulilic acid	Antipyretic, analgesic	No modern studies; traditional use in Caribbean

P. nitida	Neuroprotection, antioxidant	Chrysin, apigenin	Neuroprotective, anti-amyloid	Preclinical studies (STZ-induced AD models)

Figure 2 shows (a) the causes of AD such as plaques, inflammation, mitochondrial dysfunction, and neuronal damage and (b) mechanism of flavonoids from Passiflora protect the brain by reducing inflammation, oxidative stress, apoptosis, and Aβ aggregation.

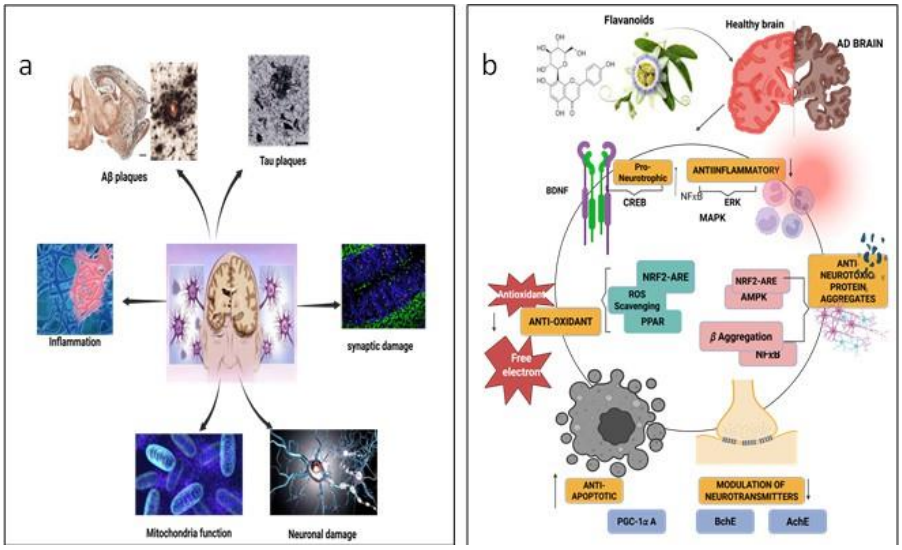

Figure 2. (a) Causes of AD and (b) Mechanism of flavonoids from Passiflora to protect the brain by reducing inflammation, oxidative stress, apoptosis, and β-amyloid aggregation

The selective vulnerability of certain neuronal populations such as dopaminergic neurons in the substantia nigra pars compacta in Parkinson's disease, whose degeneration leads to classic motor and non-motor symptoms and is associated with alpha-synuclein aggregation and genetic mutations, the fast-fatigable motor neurons in ALS that degenerate due to metabolic stress underscores the complexity of neurodegenerative disease pathogenesis[24]. These findings collectively emphasize the importance of selective neuronal vulnerability in such disorders and highlight the potential value of compounds like GA in counteracting oxidative stress, neuroinflammation, and apoptosis key pathways implicated in neurodegeneration.

4. MECHANISMS OF NEUROPROTECTION

Experimental evidence converges on the assertion that Passiflora exerts multi-modal pharmacological effects relevant to AD. These include antioxidative, anti-inflammatory, neuroprotective, and memory-enhancing actions, largely attributable to its high content of flavonoids, alkaloids, and other polyphenolic compounds[25]. The pharmacological profile of Passiflora species reveals a wide spectrum of bioactivities highly relevant to AD pathology, mediated by diverse phytochemicals targeting multiple pathogenic mechanisms involved in neurodegeneration[26]. This multifaceted mode of action spans cholinesterase inhibition, antioxidant defense, anti-inflammatory modulation, and direct interference with Aβ and tau protein pathology, alongside enhancing neurogenesis, mitochondrial function, and synaptic plasticity. One important mechanism is cholinesterase inhibition, where Passiflora compounds such as harmane, harmaline, and vitexin effectively block acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE), thereby increasing acetylcholine availability in synapses. These alkaloids demonstrated IC50 values comparable to the standard AD drug galantamine in in vitro AChE assays, highlighting Passiflora's potential to improve cognitive function by enhancing cholinergic neurotransmission-an approach central to current AD treatments[27].

5. CONCLUSION

The pharmacokinetics of Passiflora's bioactive compounds such as flavonoids, triterpenoids, and alkaloids remain poorly characterized, with uncertainties around their absorption, metabolism, bioavailability, and ability to cross the blood-brain barrier; innovative formulations like nanoparticle encapsulation might enhance delivery, but such solutions are still experimental. Issues related to standardization and quality control pose further challenges, as the therapeutic consistency of Passiflora extracts varies by cultivation, extraction, and composition, and optimal dosing protocols are undefined; the risk of herb-drug interactions is also yet to be systematically addressed, a significant consideration for elderly AD patients on multiple medications. Although preclinical data support Passiflora's antioxidant, anti-inflammatory, and anti-amyloid properties, the exact molecular pathways and holistic impact in the full spectrum of AD pathology particularly on synaptic dysfunction and neurodegeneration are not fully understood, and biomarker-driven, personalized approaches common in modern AD drug development are lacking in Passiflora research. Passiflora's diverse pharmacological profile including antioxidant, anti-inflammatory, and

cholinesterase-inhibitory actions suggests that it could be valuable in combination therapies with conventional drugs or other neuroprotective botanicals to target multiple aspects of AD and also alleviate non-cognitive symptoms like agitation and sleep disturbances. Future research should prioritize genetic and molecular investigations, standardized extract quantification, pharmacokinetic studies, and large-scale randomized controlled trials to establish efficacy, safety, and optimal formulation; focusing on personalized medicine and prevention cohorts may maximize benefits.

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Conflicts of Interest
Nil

Authors’ Contributions
Conceptualization, Drafting the article, Data curation, Data collection, Manuscript – writing, Avula Madhu Bindhu (AMB); Validation, Manuscript - review and editing, Lakshman Kumar Dogiparthi (LKD). All authors have read and agreed to the published version of the manuscript**.**

REFERENCES

1. Kamalakannan K, Seetharaman S, Sockalingam A, VijayaRani KR, Subramanian K. Phytoflavonoids-A Future Perspective for the Therapeutic Potential of Alzheimer’s Disease. Pharmacognosy Research. 2025;17(3).
2. Acero N, Ortega T, Villagrasa V, Leon G, Muñoz-Mingarro D, Castillo E, Martínez-Solís I. Phytotherapeutic alternatives for neurodegenerative dementias: Scientific review, discussion and therapeutic proposal. Phytotherapy Research. 2023;37(3):1176-1211.
3. Mahajan K, Sharma S, Gautam RK, Goyal R, Mishra DK, Singla RK. Insights on therapeutic approaches of natural anti-Alzheimer's agents in the management of Alzheimer's disease: A future perspective. Journal of Alzheimer’s Disease. 2024;102(4):897-923.
4. Echeverry González SM, Santos AM, Júnior CCS, Saravanan S, Castellanos L, Serafini MR, Aragon M. Natural therapies: a systematic review of the medicinal applications of Passiflora ligularis. Phytochemistry Reviews. 2025;1-16.
5. Dhawan K, Dhawan S, Sharma A. Passiflora: a review update. Journal of Ethnopharmacology. 2004;94(1):1-23.
6. Garmidolova A, Halkoglu-Hristova P, Georgiev V. Exploring the multifunctionality of Passiflora caerulea L.: From traditional remedies to modern applications. Applied Sciences. 2025;15(6):3251.
7. Piccirillo S, Preziuso A, Serfilippi T, Cerqueni G, Terenzi V, Lariccia V, Magi S. Unveiling the Potential Neuroprotective Effect of Bioactive Compounds from Plants with Sedative and Mood-Modulating Properties: Innovative Approaches for the Prevention of Alzheimer's and Parkinson's Diseases. Current Neuropharmacology. 2025;23(10):1169-1183.
8. McGrowder DA, Miller F, Vaz K, Nwokocha C, Wilson-Clarke C, Anderson-Cross M, Alexander-Lindo R. Cerebrospinal fluid biomarkers of Alzheimer’s disease: current evidence and future perspectives. Brain Sciences. 2021;11(2):215.
9. Van Marum RJ. Current and future therapy in Alzheimer’s disease. Fundamental & Clinical Pharmacology. 2008;22(3):265-274.
10. Shen L, Ji HF. Associations between gut microbiota and Alzheimer’s disease: current evidences and future therapeutic and diagnostic perspectives. Journal of Alzheimer’s Disease. 2019;68(1):25-31.
11. Bhardwaj D, Mitra C, Narasimhulu CA, Riad A, Doomra M, Parthasarathy S. Alzheimer's disease—current status and future directions. Journal of Medicinal Food. 2017;20(12):1141-1151.
12. Bhardwaj D, Mitra C, Narasimhulu CA, Riad A, Doomra M, Parthasarathy S. Alzheimer's disease-current status and future directions. Journal of Medicinal Food. 2017;20(12):1141-1151.
13. Teixeira JP, de Castro AA, Soares FV, da Cunha EF, Ramalho TC. Future therapeutic perspectives into the Alzheimer’s disease targeting the oxidative stress hypothesis. Molecules. 2019;24(23):4410.
14. perspectives. Journal of Alzheimer’s Disease. 2016;50(4):927-945.
15. Meldolesi J. Alzheimer’s disease: Key developments support promising perspectives for therapy. Pharmacological Research. 2019;146:104316.
16. Hampel H, Prvulovic D, Teipel S, et al. The future of Alzheimer's disease: the next 10 years. Progress in Neurobiology. 2011;95(4):718-728.
17. Ubhi K, Masliah E. Alzheimer's disease: recent advances and future perspectives. Journal of Alzheimer’s Disease. 2012;33(s1):S185-S194.
18. Guest FL. Early detection and treatment of patients with Alzheimer’s disease: future perspectives. Reviews on Biomarker Studies in Psychiatric and Neurodegenerative Disorders. 2019:295-317.
19. Mangialasche F, Kivipelto M, Solomon A, Fratiglioni L. Dementia prevention: current epidemiological

evidence and future perspective. Alzheimer's Research & Therapy. 2012;4(1):6.

20. Hampel H, Lista S, Teipel SJ, et al. Perspective on future role of biological markers in clinical therapy trials of Alzheimer's disease: a long-range point of view beyond 2020. Biochemical Pharmacology. 2014;88(4):426-449.
21. Chopra K, Misra S, Kuhad A. Current perspectives on pharmacotherapy of Alzheimer's disease. Expert Opinion on Pharmacotherapy. 2011;12(3):335-350.
22. Chauhan S, Pandit NK, Mohanty A, Meena SS. Resource recovery of bioactive compounds from food waste and their diverse industrial applications. Biomass Conversion and Biorefinery. 2023:1-21.
23. Iweala EJ, Adurosakin OE, Innocent U, et al. Anti-aging potential of bioactive phytoconstituents found in edible medicinal plants: a review. Sci. 2024;6(2):36.
24. Okoro NO, Odiba AS, Osadebe PO, Omeje EO, Liao G, Fang WW, Wang B. Bioactive phytochemicals with anti-aging and lifespan extending potentials in Caenorhabditis elegans. Molecules. 2021;26(23):7323.
25. Chen SQ, Wang ZS, Ma YX, Zhang W, Lu JL, Liang YR, Zheng XQ. Neuroprotective effects and mechanisms of tea bioactive components in neurodegenerative diseases. Molecules. 2018;23(3):512.
26. Gonçalves S, Mansinhos I, Romano A. Neuroprotective compounds from plant sources and their modes of action: an update. In: Plant-Derived Bioactives: Chemistry and Mode of Action. Singapore: Springer Singapore; 2020:417-440.
27. Wise PM, Dubal DB, Wilson ME, Rau SW, Böttner M. Minireview: neuroprotective effects of estrogen—new insights into mechanisms of action. Endocrinology. 2001;142(3):969-973.