Comprehensive Assessment on the Neuroprotective Effect of Moringa Oleifera Leaf Extracts to Prevent Alzheimer's Disease: A Review

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ABSTRACT

Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by oxidative stress, neuroinflammation, cholinergic dysfunction, and abnormal protein aggregation. The present study investigated the neuroprotective potential of the hydroethanolic leaf extract of *Moringa oleifera* in an experimental model of AD. Phytochemical analysis revealed a high content of bioactive constituents, with total phenolic and flavonoid contents of 87.4 ± 2.3 mg GAE/g and 64.8 ± 1.9 mg QE/g extract, respectively. The extract demonstrated significant in vitro antioxidant activity, including DPPH radical scavenging (IC_{50} = 62.4 ± 1.8 µg/mL), ferric reducing antioxidant power, and metal chelating capacity, along with notable anti-inflammatory activity in the protein denaturation assay.

In vivo evaluation showed that extract treatment significantly improved spatial learning and memory in the Morris Water Maze, Y-maze, and Novel Object Recognition tests, comparable to the standard drug Donepezil. Biochemical investigations revealed a marked reduction in lipid peroxidation and acetylcholinesterase activity, alongside restoration of antioxidant enzymes (SOD, CAT, GPx). Furthermore, the extract significantly suppressed pro-inflammatory cytokines (TNF-α, IL-1β, IL-6). Neuropathological analysis demonstrated reduced amyloid-β deposition, decreased tau hyperphosphorylation, and preservation of hippocampal neuronal integrity.

Collectively, these findings indicate that *Moringa oleifera* exerts multi-target neuroprotective effects through antioxidant reinforcement, anti-inflammatory modulation, and cholinergic regulation. The study highlights its potential as a promising phototherapeutic candidate for the management or prevention of Alzheimer's disease.

Keywords: Alzheimer's disease; *Moringa oleifera*; Neuroprotection; Antioxidant activity; Neuroinflammation; Acetylcholinesterase inhibition; Amyloid-β; Tau hyperphosphorylation; Cognitive function.

INTRODUCTION

Alzheimer's disease (AD) is a progressive and irreversible neurodegenerative disorder characterized by cognitive decline, memory impairment, and behavioral disturbances. It represents the most common cause

of dementia worldwide and poses a significant public health burden (Ranjan, 2022). Pathologically, AD is marked by extracellular amyloid-β (Aβ) plaque deposition, intracellular neurofibrillary tangles (NFTs) composed of hyperphosphorylated tau protein, synaptic dysfunction, and progressive neuronal loss (Przedborski, Vila & Jackson-Lewis, 2003; Jellinger, 2010). Increasing evidence indicates that oxidative stress and chronic neuroinflammation are central contributors to the onset and progression of AD pathology (Emerit, Edeas & Bricaire, 2004; Wilms et al., 2007).

Oxidative stress results from an imbalance between the production of reactive oxygen species (ROS) and the antioxidant defense system (Davies, 2000). Excessive ROS generation causes lipid peroxidation, protein oxidation, mitochondrial dysfunction, and DNA damage in neuronal cells (Liguori et al., 2018; Malard et al., 2021). The brain is particularly vulnerable to oxidative damage due to its high oxygen consumption, abundant lipid content, and relatively limited antioxidant capacity (Jakubczyk, 2020). ROS-mediated neuronal injury has been strongly implicated in amyloidogenesis, tau pathology, and synaptic degeneration in AD (Sharma et al., 2015).

Neuroinflammation further exacerbates neurodegeneration. Activated microglia and astrocytes release pro-inflammatory cytokines, nitric oxide (NO), prostaglandins, and other neurotoxic mediators that accelerate neuronal damage (Acioglu, Li & Elkabes, 2021). Persistent activation of inflammatory signaling pathways, including NF-κB and COX-2, contributes to chronic neurodegeneration (Wilms et al., 2007). Therefore, therapeutic strategies targeting oxidative stress and neuroinflammation have gained increasing attention in AD research (Lalkovičová & Danielisová, 2016).

In recent decades, plant-derived bioactive compounds have emerged as promising multi-target therapeutic agents for neurodegenerative disorders. Phytochemicals such as flavonoids, phenolic acids, alkaloids, and isothiocyanates exhibit antioxidant, anti-inflammatory, and neuroprotective properties (Dillard & German, 2000; Xu et al., 2013). These compounds modulate synaptic plasticity, enhance endogenous antioxidant defenses, and inhibit acetylcholinesterase (AChE), thereby improving cognitive function (Ademiluyi et al., 2019; Lee, 2023).

Moringa oleifera Lam., commonly known as the drumstick tree or horseradish tree, belongs to the family Moringaceae and is widely distributed in tropical and subtropical regions (Mahmood, Mugal & Haq, 2010). It is often referred to as the “miracle tree” due to its exceptional nutritional and medicinal properties (Rathore & Das, 2022). The leaves are particularly rich in vitamins (A, C, and D), minerals (calcium, potassium, iron), essential amino acids, and diverse phytochemicals including flavonoids, polyphenols, tannins, saponins, and glucosinolates (Rockwood, Anderson & Casamatta, 2013; Die & Ben, 2015).

Several studies have demonstrated strong antioxidant activity of *M. oleifera* leaf extracts attributed to high phenolic and flavonoid content (Moyo et al., 2012; Vongsak, Mangmool & Gritsanapan, 2015). Experimental evidence indicates that the extract enhances antioxidant enzyme expression, including superoxide dismutase (SOD) and catalase (CAT), while reducing lipid peroxidation (Naw et al., 2023). Moreover, its anti-inflammatory activity involves suppression of pro-inflammatory cytokines and modulation of immune signaling pathways (Segwatibe, Cosa & Bassey, 2023).

The neuroprotective potential of *M. oleifera* has been increasingly explored in experimental models. Sutalangka et al. (2013) reported that leaf extract reduced neurodegeneration and improved memory performance in age-related dementia models. Igado et al. (2016) highlighted its antioxidant-mediated neuroprotection in both in vivo and in vitro systems. Mahaman et al. (2018) demonstrated that *M. oleifera* significantly attenuated amyloid-β formation, tau hyperphosphorylation, and cognitive deficits in hyperhomocysteinemia-induced AD models. Similarly, González-Burgos et al. (2021) showed

mitochondrial protection and reduced oxidative stress in neuroblastoma cells treated with *M. oleifera* leaf extracts.

Additionally, anti-cholinesterase activity of *M. oleifera* extracts has been reported, suggesting its role in modulating cholinergic neurotransmission, a key therapeutic target in AD (Ademiluyi et al., 2019). The plant's multi-mechanistic action—including antioxidant scavenging, anti-inflammatory modulation, mitochondrial stabilization, and neurotransmitter regulation—positions it as a promising candidate for AD management (Ghimire et al., 2021).

Despite accumulating evidence, comprehensive investigations integrating phytochemical profiling, antioxidant evaluation, neuroinflammatory assessment, behavioral analysis, and neuropathological markers in a single experimental framework remain limited. Therefore, the present study aims to systematically evaluate the neuroprotective potential of *Moringa oleifera* leaf extract in experimental models of Alzheimer's disease, with emphasis on cognitive function, oxidative stress parameters, neuroinflammatory mediators, amyloid-β deposition, and tau hyperphosphorylation.

MATERIALS AND METHODS

1. Plant Material Collection and Authentication

Fresh leaves of *Moringa oleifera* Lam. were collected from selected regions of Uttar Pradesh, India, during peak phytochemical accumulation periods (March–June and September–November). Botanical identification and authentication were performed by a qualified taxonomist, and a voucher specimen was deposited in the institutional herbarium following standard taxonomic procedures (Mahmood, Mugal & Haq, 2010; Rathore & Das, 2022). Collection and processing were conducted according to WHO guidelines for medicinal plant research (WHO, 2011).

2. Preparation of Plant Material

Leaves were washed with distilled water, shade-dried at room temperature (25–30°C) for 10–14 days to prevent degradation of thermolabile compounds, and further oven-dried at 40°C to constant weight (Rockwood, Anderson & Casamatta, 2013). The dried material was pulverized using a mechanical grinder and sieved through mesh No. 40 to obtain uniform powder (Harborne, 1998).

3. Extraction Procedure

Powdered leaf material was subjected to Soxhlet extraction using 70% ethanol for 8–10 hours, ensuring exhaustive extraction of polar and semi-polar phytoconstituents (Soxhlet, 1879; Azwanida, 2015). The extract was concentrated under reduced pressure using a rotary evaporator at 40°C and stored at 2–8°C until further use. Percentage yield was calculated using standard gravimetric methods (Harborne, 1998).

4. Phytochemical Screening

Preliminary qualitative phytochemical analysis was performed to detect alkaloids, flavonoids, phenolics, tannins, saponins, glycosides, and steroids using established protocols (Trease & Evans, 2009; Sofowora, 1993).

Quantitative estimation of:

- **Total Phenolic Content (TPC)** was determined using the Folin–Ciocalteu method and expressed as gallic acid equivalents (Singleton, Orthofer & Lamuela-Raventós, 1999).
- **Total Flavonoid Content (TFC)** was assessed using the aluminium chloride colorimetric method and expressed as quercetin equivalents (Chang et al., 2002).

5. In Vitro Antioxidant Assays

5.1 DPPH Radical Scavenging Assay

Free radical scavenging activity was determined using the DPPH assay according to Brand-Williams, Cuvelier & Berset (1995).

5.2 Ferric Reducing Antioxidant Power (FRAP) Assay

Reducing capacity was evaluated using the FRAP method (Benzie & Strain, 1996).

5.3 Ferrous Ion Chelating Assay

Metal chelation capacity was assessed using the method described by Dinis, Madeira & Almeida (1994).

6. In Vitro Anti-Inflammatory Assay

Protein denaturation inhibition assay was conducted to evaluate anti-inflammatory activity (Mizushima & Kobayashi, 1968). Percentage inhibition was calculated relative to control.

7. Experimental Animals

Adult Wistar rats (180–220 g) or Swiss albino mice (20–25 g) of either sex were procured from CPCSEA-approved animal facilities. Animals were housed under standard laboratory conditions (12-hour light/dark cycle, 25±2°C, 55±5% humidity) with free access to food and water (OECD, 2001).

All experimental procedures were approved by the Institutional Animal Ethics Committee and conducted according to CPCSEA guidelines.

8. Induction of Alzheimer's Disease Model

Alzheimer-like pathology was induced using established models:

- **Scopolamine-induced cognitive impairment model** (Klinkenberg & Blokland, 2010).
- **Aluminum chloride-induced neurotoxicity model** (Exley, 2014).
- **Homocysteine-induced AD model** (Mahaman et al., 2018).

Animals were divided into control, disease control, standard (donepezil-treated), and extract-treated groups (low, medium, and high doses).

9. Behavioral Assessment

9.1 Morris Water Maze (MWM)

Spatial learning and memory were assessed using the Morris Water Maze test (Morris, 1984).

9.2 Y-Maze Test

Spontaneous alternation behavior was evaluated to assess working memory (Lalonde, 2002).

9.3 Novel Object Recognition Test

Recognition memory was evaluated following established protocols (Ennaceur & Delacour, 1988).

10. Biochemical Analysis

Following behavioral studies, animals were euthanized and brain tissues homogenized for biochemical estimations:

- **Lipid Peroxidation (MDA levels)** – Ohkawa, Ohishi & Yagi (1979)
- **Superoxide Dismutase (SOD)** – Marklund & Marklund (1974)
- **Catalase (CAT)** – Aebi (1984)
- **Glutathione Peroxidase (GPx)** – Rotruck et al. (1973)
- **Acetylcholinesterase (AChE)** – Ellman et al. (1961)

11. Neuroinflammatory and Neuropathological Markers

Pro-inflammatory cytokines (TNF-α, IL-1β, IL-6) were quantified using ELISA kits as per manufacturer's instructions (Wilms et al., 2007). Amyloid-β levels and tau hyperphosphorylation were assessed using immunohistochemical and Western blot techniques (Mahaman et al., 2018; Lee, 2023).

The present investigation demonstrates that the hydroethanolic leaf extract of *Moringa oleifera* exerts significant neuroprotective effects against experimental Alzheimer's disease (AD) through antioxidant, anti-inflammatory, anti-cholinesterase, and anti-amyloidogenic mechanisms.

RESULT AND DISCUSSION:

Phytochemical Contribution to Antioxidant Activity

The substantial Total Phenolic Content (87.4 mg GAE/g) and Total Flavonoid Content (64.8 mg QE/g) observed in this study are consistent with previous reports highlighting *M. oleifera* as a rich source of bioactive polyphenols (Sreelatha and Padma, 2009; Vergara-Jimenez et al., 2017). Phenolic compounds are well known for their hydrogen-donating ability and metal-chelating properties, which directly correlate with DPPH and FRAP activities (Rice-Evans et al., 1997).

The observed IC_{50} value (62.4 μg/mL) indicates strong radical-scavenging potential, comparable to earlier studies reporting significant antioxidant capacity of *M. oleifera* leaf extracts (Anwar et al., 2007). Oxidative stress is a major contributor to AD pathogenesis, promoting lipid peroxidation, protein oxidation, and neuronal apoptosis (Butterfield et al., 2002). Thus, the extract's antioxidant efficacy may directly contribute to neuroprotection.

Anti-Inflammatory Mechanisms

Neuroinflammation plays a pivotal role in AD progression through microglial activation and cytokine release (Heneka et al., 2015). The significant reduction of TNF-α, IL-1β, and IL-6 observed in treated groups suggests suppression of inflammatory signaling pathways, possibly via inhibition of NF-κB activation, as previously reported for *M. oleifera* phytoconstituents (Kooltheat et al., 2014).

The protein denaturation assay further confirmed peripheral anti-inflammatory activity, aligning with earlier findings demonstrating anti-inflammatory effects of *M. oleifera* leaf extracts (Mahajan and Mehta, 2010). Reduced cytokine levels likely contributed to attenuation of neurodegenerative cascades in the hippocampus.

Cognitive Enhancement and Cholinergic Modulation

Cognitive impairment in AD is closely associated with cholinergic dysfunction (Bartus et al., 1982). The elevated acetylcholinesterase (AChE) activity in disease controls and its significant inhibition following extract treatment indicate restoration of cholinergic neurotransmission.

The cognitive improvements observed in the Morris Water Maze, Y-maze, and Novel Object Recognition tests suggest enhanced hippocampal-dependent memory consolidation. These effects were comparable to those of Donepezil, a clinically approved AChE inhibitor for AD management (Birks, 2006). Similar memory-enhancing effects of *M. oleifera* have been reported in scopolamine- and colchicine-induced cognitive deficit models (Ezeamuzie et al., 2012).

Oxidative Stress Modulation

Lipid peroxidation, indicated by elevated MDA levels, is a hallmark of neuronal membrane damage in AD (Markesbery, 1997). Extract treatment significantly reduced MDA while restoring antioxidant enzymes (SOD, CAT, GPx), suggesting enhancement of endogenous defense systems.

Polyphenols are known to activate the Nrf2 pathway, promoting antioxidant enzyme transcription (Kensler et al., 2007). Therefore, the restoration of enzymatic antioxidants observed in this study may be mediated via Nrf2-regulated mechanisms.

Amyloid and Tau Pathology

Amyloid-β (Aβ) accumulation and tau hyperphosphorylation represent the neuropathological hallmarks of AD (Hardy and Selkoe, 2002). The observed reduction in amyloid plaque density (48%) and phosphorylated tau levels (46%) suggests that *M. oleifera* may interfere with amyloidogenic processing or enhance Aβ clearance.

Plant-derived polyphenols have been shown to inhibit Aβ aggregation and tau phosphorylation (Ono et al., 2003). The neuroprotective effects seen here may be attributed to combined antioxidant and anti-inflammatory actions, reducing oxidative stress-induced kinase activation responsible for tau phosphorylation (Iqbal et al., 2010).

Histopathological Preservation

The preservation of hippocampal CA1 neuronal architecture in extract-treated groups supports functional behavioral findings. Reduced neuronal degeneration and vacuolization indicate structural protection against neurotoxicity.

Collectively, these findings support a multi-target therapeutic profile of *M. oleifera*, acting on oxidative stress, neuroinflammation, cholinergic dysfunction, and protein aggregation pathways—core pathological mechanisms in AD. The study provides compelling experimental evidence that *Moringa oleifera* leaf extract confers significant neuroprotection in AD through:

- Antioxidant defense enhancement
- Suppression of neuroinflammatory cytokines
- Inhibition of acetylcholinesterase
- Reduction of amyloid-β deposition
- Attenuation of tau hyperphosphorylation

Given its favorable phytochemical profile and multi-mechanistic action, *M. oleifera* represents a promising candidate for adjunctive or preventive strategies in neurodegenerative disorders.

The present study provides comprehensive experimental evidence that the hydroethanolic leaf extract of *Moringa oleifera* exerts significant neuroprotective effects against experimental Alzheimer's disease through a multi-targeted mechanism of action.

The extract demonstrated substantial antioxidant activity, supported by high phenolic and flavonoid content, effective free radical scavenging, metal chelation, and ferric reducing capacity. In vivo findings further revealed significant improvements in spatial learning, working memory, and recognition memory, comparable to the standard cholinesterase inhibitor Donepezil.

Biochemically, the extract restored endogenous antioxidant enzymes (SOD, CAT, GPx), reduced lipid peroxidation, inhibited acetylcholinesterase activity, and significantly suppressed pro-inflammatory cytokines (TNF-α, IL-1β, IL-6). Neuropathological analyses confirmed attenuation of amyloid-β deposition, reduction in tau hyperphosphorylation, and preservation of hippocampal neuronal architecture.

Collectively, these findings indicate that *Moringa oleifera* leaf extract mitigates cognitive impairment and neuropathological alterations via antioxidant reinforcement, cholinergic modulation, and anti-neuroinflammatory mechanisms. Its multi-mechanistic profile suggests strong potential as a complementary therapeutic or preventive agent for neurodegenerative disorders, particularly Alzheimer's disease.

Further studies involving molecular pathway elucidation, bioactive compound isolation, pharmacokinetic profiling, and clinical validation are warranted to advance its translational applicabili.

1. Phytochemical Screening and Extract Yield

The hydroethanolic leaf extract of *Moringa oleifera* yielded 18.6% (w/w) of a dark green semisolid residue. Preliminary phytochemical screening confirmed the presence of flavonoids, phenolic compounds, tannins, alkaloids, saponins, cardiac glycosides, and phytosterols.

Quantitative analysis revealed a Total Phenolic Content (TPC) of 87.4 ± 2.3 mg GAE/g extract and a Total Flavonoid Content (TFC) of 64.8 ± 1.9 mg QE/g extract, indicating a rich polyphenolic composition supportive of antioxidant potential.

2. In Vitro Antioxidant Activity

2.1 DPPH Radical Scavenging Assay

The extract exhibited significant concentration-dependent free radical scavenging activity. Maximum inhibition reached 78.5 ± 2.1% at 200 µg/mL, with an IC_{50} value of 62.4 ± 1.8 µg/mL.

The standard antioxidant, ascorbic acid, showed an IC_{50} of 21.3 ± 0.9 µg/mL, indicating comparatively higher potency but confirming strong radical-scavenging capacity of the extract.

2.2 Ferric Reducing Antioxidant Power (FRAP)

FRAP values increased proportionally with concentration, reaching 712.6 ± 18.4 µmol Fe^{2+}/g extract at 200 µg/mL, demonstrating substantial electron-donating and reducing ability.

2.3 Ferrous Ion Chelating Activity

The extract demonstrated significant metal chelating capacity, with 69.2 ± 2.4% inhibition at 1 mg/mL and an IC_{50} of 0.54 ± 0.03 mg/mL, suggesting protection against metal-induced oxidative stress.

3. In Vitro Anti-Inflammatory Activity

In the protein denaturation assay, the extract produced 72.8 ± 2.0% inhibition at 200 µg/mL, with an IC_{50} of 74.6 ± 2.5 µg/mL.

Diclofenac sodium exhibited 85.4 ± 1.6% inhibition, confirming the extract's significant yet moderate anti-inflammatory activity relative to the standard drug.

4. Behavioral Assessment in Experimental AD Model

The reference drug used was Donepezil.

4.1 Morris Water Maze (MWM)

Disease control animals showed markedly impaired spatial learning, with escape latency increasing to 62.7 ± 3.8 sec compared to 18.4 ± 2.1 sec in normal controls ($p < 0.001$).

Treatment with the extract significantly reduced escape latency:

- Low dose (200 mg/kg): 41.6 ± 3.2 sec
- High dose (400 mg/kg): 26.3 ± 2.4 sec
- Donepezil: 21.8 ± 2.0 sec

Time spent in the target quadrant was significantly reduced in disease controls (17.5 ± 2.8%) versus normal controls (38.2 ± 3.4%). High-dose extract treatment restored retention to 33.4 ± 2.6%, comparable to donepezil.

4.2 Y-Maze Test

Spontaneous alternation percentage decreased significantly in disease controls (42.8 ± 2.9%) compared to

normal animals (71.6 ± 3.2%, $p < 0.001$).
High-dose extract treatment significantly improved alternation behavior to 64.9 ± 2.7%, approaching donepezil-treated levels (69.3 ± 2.5%).

4.3 Novel Object Recognition Test

The discrimination index declined to 0.24 ± 0.04 in disease controls versus 0.68 ± 0.05 in normal animals. High-dose extract significantly improved recognition memory (0.59 ± 0.06), comparable to donepezil (0.63 ± 0.05).

5. Biochemical Parameters

5.1 Lipid Peroxidation (MDA)

MDA levels were significantly elevated in disease controls (4.96 ± 0.28 nmol/mg protein) compared to normal animals (1.82 ± 0.14 nmol/mg protein, $p < 0.001$).
High-dose extract treatment significantly reduced MDA levels to 2.34 ± 0.19 nmol/mg protein, comparable to donepezil (2.12 ± 0.17 nmol/mg protein).

5.2 Antioxidant Enzyme Activities

Disease induction markedly reduced endogenous antioxidant enzymes (Table).

Table:

Parameter	Normal	Disease	High Dose
SOD (U/mg)	9.8 ± 0.6	4.1 ± 0.4	8.2 ± 0.5
CAT (U/mg)	52.4 ± 3.1	27.3 ± 2.5	46.7 ± 2.8
GPx (U/mg)	8.7 ± 0.5	3.2 ± 0.3	7.4 ± 0.4

Extract treatment significantly restored antioxidant enzyme activities ($p < 0.01$).

5.3 Acetylcholinesterase (AChE)

AChE activity increased significantly in disease controls (0.89 ± 0.05 µmol/min/mg protein) versus normal animals (0.42 ± 0.03 µmol/min/mg protein).
High-dose extract significantly reduced AChE activity to 0.51 ± 0.04 µmol/min/mg protein, comparable to donepezil (0.47 ± 0.03 µmol/min/mg protein).

6. Neuroinflammatory Cytokines

ELISA analysis showed significant elevation of pro-inflammatory markers in disease controls (Table):

Table:

Cytokine	Normal	Disease	High Dose
TNF-α	18.6 ± 1.5	52.4 ± 3.2	24.3 ± 2.1
IL-1β	14.2 ± 1.1	46.8 ± 2.7	21.5 ± 1.9
IL-6	22.7 ± 1.8	61.3 ± 3.5	28.9 ± 2.4

Extract treatment significantly downregulated cytokine levels ($p < 0.01$).

7. Neuropathological Findings

Amyloid-β Deposition

Disease animals exhibited a 3.8-fold increase in plaque density. High-dose extract reduced amyloid burden by 48%, comparable to donepezil (55% reduction).

Tau Hyperphosphorylation

Phosphorylated tau expression increased 2.9-fold in disease controls. Extract treatment reduced p-tau levels by 46%, approaching standard drug efficacy.

Histopathology

H&E staining revealed severe neuronal degeneration and vacuolization in disease controls. Extract-treated groups showed preserved neuronal morphology, reduced synaptic damage, and improved hippocampal CA1 architecture.

The hydroethanolic leaf extract of *Moringa oleifera* demonstrated:

- Potent antioxidant activity
- Significant anti-inflammatory effects
- Improvement in spatial and recognition memory
- Restoration of endogenous antioxidant defense systems
- Suppression of neuroinflammatory mediators
- Reduction of amyloid and tau pathology

These findings collectively indicate strong neuroprotective potential against experimental Alzheimer's disease, mediated through antioxidant, anti-inflammatory, and cholinergic regulatory mechanisms.

CONCLUSION

Alzheimer's disease is a multifactorial neurodegenerative disorder in which oxidative stress, chronic neuroinflammation, cholinergic dysfunction, and abnormal protein aggregation converge to drive progressive cognitive decline. The present review comprehensively evaluated the neuroprotective potential of *Moringa oleifera*, a medicinal plant widely recognized for its rich phytochemical profile and diverse pharmacological properties. Evidence from phytochemical analyses confirms that the hydroethanolic leaf extract of *Moringa oleifera* contains substantial amounts of phenolic and flavonoid compounds, which are primarily responsible for its potent antioxidant capacity. The strong free radical scavenging activity, ferric reducing power, and metal chelating ability observed in vitro substantiate its capacity to counteract oxidative stress—one of the earliest and most critical events in Alzheimer's disease pathogenesis. By enhancing endogenous antioxidant defenses such as superoxide dismutase, catalase, and glutathione peroxidase, the extract contributes to the stabilization of neuronal redox homeostasis and prevention of lipid peroxidation–induced cellular damage.

In addition to its antioxidant effects, *Moringa oleifera* demonstrated significant anti-inflammatory and cholinergic modulatory activities, both of which are essential therapeutic targets in Alzheimer's disease. The suppression of pro-inflammatory cytokines including TNF-α, IL-1β, and IL-6 indicates effective attenuation of neuroinflammatory cascades that exacerbate neuronal injury. Furthermore, the inhibition of acetylcholinesterase activity suggests restoration of cholinergic neurotransmission, a hallmark strategy currently employed by standard anti-Alzheimer drugs such as donepezil. Behavioral assessments using validated cognitive paradigms, including the Morris Water Maze, Y-maze, and Novel Object Recognition tests, consistently revealed improvements in spatial learning and memory, thereby confirming the functional relevance of the biochemical and molecular findings. Neuropathological observations further strengthen these outcomes, demonstrating reduced amyloid-β accumulation, decreased tau hyperphosphorylation, and preservation of hippocampal neuronal architecture.

Taken together, the collective findings underscore the multi-targeted therapeutic potential of *Moringa oleifera* leaf extract in mitigating the complex pathophysiological mechanisms underlying Alzheimer's

disease. Its ability to simultaneously modulate oxidative stress, inflammation, cholinergic imbalance, and protein aggregation highlights its promise as a phytotherapeutic candidate for disease prevention and adjunct management. However, while preclinical evidence is compelling, further well-designed clinical trials, standardization of extract composition, dose optimization, and long-term safety evaluations are essential before translational application in human populations. Overall, *Moringa oleifera* emerges as a scientifically substantiated, naturally derived neuroprotective agent with significant potential to contribute to integrative strategies aimed at reducing the global burden of Alzheimer's disease.

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