Neurotherapeutic Potential Of *Moringa Oleifera* Leaves: A Review Of Preclinical Evidence From Rodent And *Drosophila Melanogaster* Ischemia Models

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Abstract. Ischemic stroke remains a leading cause of long-term disability globally, with locomotor deficits, gait asymmetry, and balance dysfunction posing significant challenges to functional recovery. Existing treatment strategies offer limited functional recovery, creating a need for complementary neurotherapeutic options. *Moringa oleifera* leaves are rich in bioactive compounds, such as flavonoids, polyphenols, and isothiocyanates, and have multifaceted neurotherapeutic properties. Preclinical studies in rodent and *Drosophila melanogaster* models show mechanisms through which *Moringa oleifera* leaves exert neuroprotective, anti-inflammatory, antioxidant, and neuroplasticity-inducing effects. Moringa oleifera leaves have been shown to reduce infarct volume, improve neurobehavior, and modify acetylcholinesterase activity, all of which enhance motor recovery in the existing literature. Despite promising findings, most studies are limited by small sample sizes, reliance on pretreatment models, and a lack of human trials and standardised protocols. Critically, the absence of human clinical trials restricts immediate translational application. This review aims to guide future research to prioritise well-designed controlled studies to establish the efficacy, safety, and optimal dosing of *Moringa oleifera* leaves for neurotherapeutic potential in ischemic stroke patients.

Keywords: Antioxidant Mechanisms; Ischemic Stroke; Locomotor Rehabilitation; *Moringa oleifera*; Neuroplasticity; Neuroprotection.

INTRODUCTION

Stroke is the second most prevalent cause of death and disability globally, which makes it a vital concern [1]. A rupture of a cerebral artery can lead to an ischemic or haemorrhagic stroke, which impacts blood flow to the brain area and leads to neuronal impairment and death, and loss of function [2]. Cerebral hypoperfusion leads to a series of events known as cerebral ischemia [3]. The brain suffers from a lack of oxygen and nutrients, resulting in increased oxidative stress, mitochondrial dysfunction, neuroinflammation, blood-brain barrier (BBB) leakage, and ultimately cell death and necrosis [4]. Ischemic stroke commonly causes hemiparesis, or one-sided weakness, which affects up to 80% of survivors [5]. The impairment reduces voluntary use of the paretic limb and disrupts motor coordination; as a result, spasticity develops, producing abnormal synergies and non-smooth movements. Hemiparesis directly affects gait, and patients present with decreased muscle strength, impaired limb progression, and compensatory mechanisms (hip hiking or circumduction) [6]. In addition to weakness, the majority of patients also develop impaired balance through loss of trunk control and proprioception, leading to a high risk of falls (70% of survivors fall in the first post-stroke year) [7].

More than half of stroke survivors experience gait impairment, one of the most incapacitating aftereffects of the stroke [8]. Gait dysfunction is characterised by a very slow walking speed (frequently <0.4 m/s in the subacute phase vs. ~1.2 m/s for healthy adults), limited endurance, and significant asymmetry between limbs in both step length and timing [9]. Only ~1/3 of stroke survivors reach the 0.8 m/s threshold required for safe community walking [10]. These impairments persist into the chronic phase and significantly increase independence and participation in community roles. Together, hemiparesis, gait asymmetry, and balance impairment represent the cornerstone of locomotor deficits seen after ischemic stroke and highlight the importance of early and intensive task-specific rehabilitation to enable walking and reduce the risk of long-term disability.

Native to northwestern India's sub-Himalayan region, the moringa tree (*Moringa oleifera Lam*.) is now cultivated extensively as a medicinal plant in Africa, the Middle East, Southeast Asia, and South America [11]. It is in the *Kingdom Plantae, Division Magnoliophyta, Class Magnoliopsida, Order Brassicales, Family Moringaceae, Genus Moringa, and Species M. oleifera* [12]. *Moringa* is known by other names such as horseradish tree, drumstick tree, mulangay, mlonge, benzolive, sajna, kelor, saijihan, or marango, to name a few. It has been and continues to be greatly valued in the tropics and subtropics for its use in the kitchen and for health purposes [13].

The health benefits of consuming moringa leaves can last for months without refrigeration, whether in fresh, roasted, or dried form. The moringa tree is called "the miracle tree" for good reason; many of its medicinal claims have recently been confirmed through research [14]. In addition to bioactive molecules, the leaves also contain a balanced profile of essential amino acids and are an important source of vitamins A and C. These compounds give *Moringa* significant antibacterial, anti-inflammatory, anticancer and antioxidant effects [15]. Numerous types of chemicals, including ascorbic acid, flavonoids, phenolics, and carotenoids, are responsible for the antioxidant actions. To protect cells from oxidation, antioxidant activity is crucial [16]. The plant's leaves are utilitarian, as they are high in protein, have a balanced overall amino acid profile, and contain major amino acids [17].

Mechanistic Insights into Moringa oleifera's Neurotherapeutic Potential. Moringa oleifera demonstrates several neurotherapeutic effects that qualify it as a potential therapy following stroke rehabilitation [16]. The bioactive constituents of *Moringa* have multiple mechanisms of action that affect oxidative stress, inflammation, and neuronal repair [18]. We can broadly classify these effects into three actions: neuroprotection, neuroplasticity, and preservation of muscle function.

The neuroprotective role of Moringa oleifera's leaves. Neuroprotection is the most critical activity in the prevention of significant adverse outcomes of neurological injury related to stroke, traumatic brain injury, and neurodegenerative diseases [19]. Neuroprotection encompasses mechanisms to prevent or mitigate neuronal damage, such as inhibiting necroptosis, oxidative stress, and neuroinflammation [20]. Because drug therapies for ischemic strokes (e.g. tissue plasminogen activator (tPA)) have narrow time windows for effective intervention and significant deleterious side effects, natural neuroprotective agents are being sought out [21]. Phytochemicals from medicinal herbs hold a special

place in knowledge because of their ability to promote neuroplasticity through neurogenesis, synaptogenesis, and angiogenesis, thereby restoring brain function after a lesion [22]. One group of phytochemicals, the leaves of *Moringa oleifera*, has potential as a neuroprotective agent due to its diverse and safe phytochemical profile.

Moringa oleifera leaves contain flavonoids, polyphenols, alkaloids, and tannins that exhibit powerful antioxidant capacity [23]. These bioactive compounds scavenge free radicals and help regulate redox homeostasis and oxidative stress, which are primary contributors to neuronal injury in ischemic stroke [24]. Extracts of *Moringa* leaves via solvents (i.e., methanol, ethanol, and acetone) resulted in notable radical scavenging activity, increased antioxidant enzyme activities (i.e., superoxide dismutase (SOD) and catalase (CAT)), and lower lipid peroxidation [25]. Similar reports of moringa supplementation indicate modulation of genes involved in endogenous antioxidant defence mechanisms, thereby protecting neurons from oxidative damage [24]. The antioxidant function of *Moringa oleifera* contributes to the maintenance of synaptic structure and synaptic plasticity, both of which are pivotal for the recovery of motor and cognitive functions [26].

In addition to its antioxidant properties, *Moringa oleifera* also has significant anti-inflammatory activity. Neuroinflammation, driven primarily by overactive microglia and excessive cytokine release, is an essential event in secondary neuronal injury after ischemia [27]. Phytochemicals from *Moringa* leaves, e.g., moringin, astragalin, and isoquercitrin, have been shown to inhibit pro-inflammatory mediators, including nitric oxide, TNF-α, IL-1β, IL-6, COX-2, and NF-κB, and to stimulate anti-inflammatory cytokines, e.g., IL-10 [28]. *Moringa* extracts have also shown comparable, and sometimes superior, anti-inflammatory activity to standard anti-inflammatory drugs, with the added advantage of inducing survival molecular mechanisms (e.g., Nrf2) in in vitro and in vivo models [29]. *Moringa* induces a healthy neuronal environment by inhibiting neuroinflammation, thereby enhancing the potential for neuroplastic repair and resilience. Through its antioxidant and anti-inflammatory properties, as shown in Figure 1, *Moringa oleifera* leaves preserve synaptic integrity, reverse oxidative and inflammatory neuronal damage, and facilitate BDNF-mediated neuroplasticity [26].

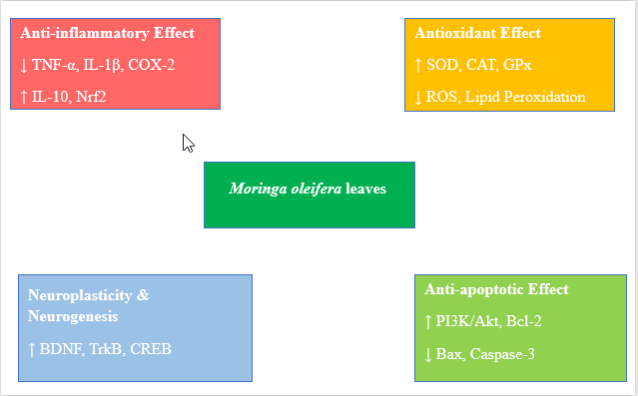

Figure 1 – Neuroprotective mechanisms of *Moringa oleifera* through antioxidant, anti-inflammatory, anti-apoptotic, and neuroplasticity pathways

RESULTS AND DISCUSSION

Role of Moringa oleifera in neuroplasticity modulation. Compounds ranging from the flavonoids quercetin and kaempferol, the most globally relevant phytochemicals in moringa leaves, have been repeatedly demonstrated to reverse oxidative and inflammatory stress that inhibits Brain-Derived Neurotrophic Factor (BDNF) signalling [30]. In various rodent and cell models, moringa extracts increased BDNF/TrkB–CREB signalling, preserved synaptic proteins (such as PSD-95, synapsin-1, synaptophysin), and improved behavioural parameters of learning and memory, all of which are mechanistic processes closely related to synaptogenesis and neuronal viability [31]. For example, a controlled comparison of leaf extract and seed oil showed that pretreatment significantly improved memory and induced TrkB/CREB signalling (including a larger signal observed with seed oil) [32]. Other work has also shown that *Moringa* restores PSD-95/synapse function after a neurotoxic challenge and, overall, supports its profile as a neuroprotective, anti-inflammatory agent relevant to plasticity [31]. There is also much converging evidence from the nutrition–neuroscience literature showing that flavonoids can enhance BDNF and/or the resilience of synaptic function [33].

Following a stroke, several lines of evidence suggest that activity-dependent synaptogenesis and BDNF signalling within motor networks may play essential roles in recovery. That enhanced post-stroke recovery is associated with elevated BDNF levels [34]. In Preclinical ischemia models, using moringa leaves has shown decreased oxidative stress, modulation of apoptosis (↓Bax/caspase-3), improved histology, and enhanced neurobe-

havioral outcomes; all conditions that facilitate BDNF-mediated synaptic remodelling and neuronal survival [35]. First-level studies of cerebral protection in global ischemia /reperfusion models (including studies of leaves or flowers) are consistent with the mechanisms of plasticity described above [35]. While no direct human stroke trials assessing the use of moringa leaves to examine BDNF or measures of synaptogenesis have been conducted, these data collectively provide a basis for considering *Moringa* as a suitable adjunct to rehabilitation, aimed at improving BDNF signalling, synaptic integrity, and neuronal survival in the post-ischemic brain.

Muscle function preservation offered by Moringa oleifera. In addition to its antioxidant activity, supplementation with Moringa oleifera leaves also inhibits skeletal muscle atrophy by regulating atrophic markers and muscle cell protein balance [36]. Histological results show that moringa leaves prevented the decline in the cross-sectional area of muscle fibres (indicative of disuse atrophy) and improved muscle coordination when coupled with exercise [37]. Part of its protective effects stemmed from its ability to maintain mitochondrial ATP production, which is required for muscle contraction and endurance [38]. Moreover, *Moringa* leaves increase the glutathione redox ratio (GSH/GSSG) by stimulating the activity of major antioxidant enzymes (e.g., catalase, superoxide dismutase, glutathione peroxidase, and glutathione transferase), which help maintain muscle cell homeostasis and protect against oxidative damage, as typically observed in conditions like post-stroke [39].

Moringa acts as a dual regulator; it increases mitochondrial energy output (suitable for endurance and recovery) while simultaneously strengthening antioxidant defences, so that the extra ROS don't cause harm [40]. This is achieved through Nrf2-mediated induction of several enzymes, including γ-glutamyl cysteine ligase (γ-GCL), which is essential for glutathione synthesis, and glutathione reductase (GR), which is vital for glutathione recycling, to maintain a stable GSH ratio, even with high ROS production [41]. Heme oxygenase-1 (HO-1) may also protect mitochondrial function by generating cytoprotective molecules, such as carbon monoxide [42]. Bioactive components of moringa leaves (e.g., glucosinolates, flavonoids, phenolic acids) activate the Nrf2-activator response element (ARE) pathway, which results in increases in the phase II antioxidant enzymes to restore redox homeostasis [43]. Quercetin, the most abundant flavonoid in moringa leaves, induces mitochondrial biogenesis [44]. The therapeutic effects of moringa leaves are not limited to antioxidant activity, but also include preconditioning skeletal muscle to improve endurance, toughness, and recovery from periods of disuse or disuse-induced atrophy associated with stroke.

Preclinical evidence on the therapeutic effects of Moringa oleifera leaves on locomotor function after ischemic stroke. Studies using *Drosophila* melanogaster have documented the therapeutic efficacy of *Moringa oleifera* leaf extract on locomotor behaviour, as demonstrated in climbing and activity tests. *Moringa oleifera* leaves extract treatment improved survival, delayed age-related decline, and improved negative geotaxis performance, which is representative of fly locomotor behaviour [45]. The benefits of *Moringa oleifera* leaf extract are achieved through molecular mechanisms that include modulation of antioxidant defence mechanisms, regulation of growth factors, and regulation of apoptotic events. *Moringa oleifera* leaf extract's bioactive compounds reduced oxidative stress, improved glutathione homeostasis, and ultimately protected neuronal and muscular functions required for functional movement. Histology also showed that *Moringa oleifera* leaf extract-fed flies exhibited fewer and better-organised muscles than controls, supporting protective effects against locomotor decline [45].

Studies carried out in animal models of ischemic stroke (middle cerebral artery occlusion) provide experimental evidence that *Moringa oleifera* leaf extracts improve locomotor function [35]. Mice and rats treated with *Moringa* derivatives showed superior average performance in neurobehavioral tests of motor coordination and balance (rotarod, grid-walking, and grip strength) compared with untreated ischemic groups [46]. The functional improvements observed will have a molecular basis: it has been reported that *Moringa* treatment increases the expression of neurotrophic and growth factors that promote neuronal survival and synaptic plasticity, while also inhibiting apoptotic signalling pathways [24]. Specifically, the regulatory differences in downstream signalling included the downregulation of apoptotic signalling molecules, such as caspase-3, and pro-apoptotic proteins, along with the upregulation of Bcl-2 and several additional

anti-apoptotic proteins [47]. When the researchers examined the results histologically, they found that *Moringa* effectively reduced infarct volume, preserved cortical and striatal neurons, prevented neuroinflammation, and thereby improved locomotor performance [48].

In preclinical studies utilising rodent models of middle cerebral artery occlusion-induced ischemic stroke, *Moringa oleifera* leaf extracts have been shown to exhibit therapeutic and neuroprotective effects [49]. *Moringa oleifera* leaf extracts in treatment groups improved neurological scores, and treated groups exhibited reduced stroke deficits and improved overall motor performance compared to the untreated stroke groups [35]. These were also correlated with increased cortical and striatal neuronal sparing, a smaller infarct area, and reduced neuroinflammation, indicating genuine cerebral protection. Nevertheless, although global neurological scores were consistently better, more subtle locomotor evaluations, such as rotarod, ladder climbing, or grip strength, were not widely used in these studies [35]. Furthermore, it is worth noting that most of these studies implemented pretreatment with *Moringa* before stroke induction, used small sample sizes, and utilised juvenile male rats, thereby limiting the translational relevance of the findings [46]. Therefore, while there is compelling evidence that *Moringa oleifera* leaves may reduce oxidative stress and protect neural tissue, tightly controlled studies with larger sample sizes and standardised behavioural tests are warranted.

Across a variety of animal models, there is evidence that *Moringa oleifera* can improve locomotor impairments, in part by modulating cholinergic signalling via effects on acetylcholinesterase (AChE) [50]. Acetylcholinesterase, an enzyme whose primary function is to terminate Acetylcholine (ACh) by breaking down the neurotransmitter [51]. In various rodents, administration of Moringa oleifera leaves consistently reduced AChE activity. When *Moringa oleifera* leaves are applied, brain AChE activity decreases in disease or stress models, which corresponds to improved performance on behavioural measures such as reduced anxiety, hyperactivity, and enhanced exploration in open-field tasks, often with concurrent antioxidant and anti-inflammatory effects [52]. Mechanistically, decreasing AChE would increase synaptic ACh, presumably enhancing circuits responsible for motor initiation and coordination, as reported in original studies and reviews included in the summary of Moringa oleifera leaves' effects on rats' cholinergic tone and behaviours [31].

Researchers also reported concomitant effects in *Drosophila melanogaster*: *Moringa oleifera* leaves improved negative geotaxis (climbing) and other locomotor responses following toxicant exposure [45]. *Moringa oleifera* leaves were found to be responsible for sustaining antiretrovirals regimens-induced locomotor function impairments, and also reduced the locomotor impairments caused by exposure to paraquat in flies (as in rodent data connecting *Moringa oleifera* leaves and functional locomotion when AChE activity is inhibited, as with parasitic and insectivorous fishes) [53]. Both models suggest a similar mechanism by which *Moringa oleifera* leaves isothiocyanates and phenolics diminish the effect of AchE on direct inhibition of acetylcholine (or secondary inhibition through antioxidative mechanisms), enhanced stabilisation of acetylcholine signalling, and downstream consequences for motor behaviour [54].

Histological and molecular investigations show that the pharmaceutical efficacy of *Moringa* leaves was related to their array of phytochemicals containing anti-inflammatory and antioxidant activities, such as flavonoids, phenolic acids, and isothiocyanates [55]. The phytochemicals regulated the body's endogenous antioxidant defence mechanisms by modulating antioxidant enzymes bilaterally, including superoxide dismutase, catalase, and glutathione peroxidase, and by reducing markers of lipid peroxidation (malondialdehyde) [40]. Histology-plasma showed less oedema, less microglial activation, and, overall, less tissue degeneration in brains treated with *Moringa* leaf extracts. The extracts also modulated neurotransmitter control, including restoring balance to the damaged serotonin and catecholamine systems altered by ischemia [20].

Future perspectives and emerging trends. Future research on *Moringa oleifera* leaves and locomotor rehabilitation offers opportunities to achieve greater rigour, moving beyond preclinical findings into translational research. With that rigour comes a recent emphasis on standardised dosing and pharmacokinetic assessment regimes that improve reproducibility and comparability between studies. Findings to date are primarily based on young adult male mice and fruit flies, with uncertain generalizability. Expanding re-

search to include various species models, both male and female, and across age differences will only add translational and clinical value.

Looking ahead, the priority action is significant, randomised, properly controlled clinical trials that test the therapeutic efficacy of *Moringa oleifera* leaves directly with patients with stroke. These trials do need to focus on functional motor recovery but should also assess neuroprotection, infarct volume reduction, and protection of previously injured neurons, as shown in preclinical studies. As the field of stroke recovery and rehabilitation advances, *Moringa oleifera* leaves have the potential not only to serve as a nutritional dietary supplement but also as a promising adjunct neurorehabilitation therapy, combining additional therapeutic options from traditional herbal medicine with rehabilitation techniques underpinned by neuroscience.

CONCLUSIONS

Moringa oleifera leaves show considerable preclinical promise for locomotor recovery after ischemic stroke through mechanisms involving antioxidant, anti-inflammatory, and neuroprotective pathways. While these data show promise for potential changes in motion, systematic, translational, and clinical research is needed to validate their therapeutic effects on stroke rehabilitation in humans.

Conflict of interest

The authors declare that they have no conflict of interest.

REFERENCES

1. Katan, M., & Luft, A. (2018). Global burden of stroke. *Seminars in Neurology, 38*(02), 208–211. doi: 10.1055/s-0038-1649503

2. Hu, X., De Silva, T. M., Chen, J., & Faraci, F. M. (2017). Cerebral vascular disease and neurovascular injury in ischemic stroke. *Circulation Research, 120*(3), 449–471. doi: 10.1161/circresaha.116.308427

3. Dong, S., Maniar, S., Manole, M. D., & Sun, D. (2017). Cerebral hypoperfusion and other shared brain pathologies in ischemic stroke and Alzheimer's disease. *Translational Stroke Research, 9*(3), 238–250. doi: 10.1007/s12975-017-0570-2

4. Kim, S., Jung, U. J., & Kim, S. R. (2024). Role of oxidative stress in blood–brain barrier disruption and neurodegenerative diseases. *Antioxidants, 13*(12), 1462. doi: 10.3390/antiox13121462

5. Ali, J.S., Ramadan, R. M. E., & Aboushady, R. M. N. (2020). *Stroke rehabilitation strategies to enhance activities of daily living.* Lap Lambert Academic Publishing

6. Nesi, B., Taviani, A., D'Auria, L., Bardelli, R., Zuccarello, G., Platano, D., Benedetti, M. G., & Benvenuti, F. (2023). The Relationship between Gait Velocity and Walking Pattern in Hemiplegic Patients. *Applied Sciences, 13*(2), 934. doi: 10.3390/app13020934

7. Shahid, J., Kashif, A., & Shahid, M. K. (2023). A Comprehensive Review of Physical Therapy Interventions for Stroke Rehabilitation: Impairment-Based Approaches and Functional Goals. *Brain Sciences, 13*(5), 717. doi: 10.3390/brainsci13050717

8. McKenna, C., Chen, P., & Barrett, A. M. (2016). Stroke: Impact on Life and Daily Function. In *New York: Springer* (pp. 87–115). doi: 10.1007/978-0-387-98188-8_5

9. Alharbi, S. (2019). *Gait Asymmetry and the Risk of Knee Osteoarthritis in Post-Stroke Individuals.* (Thesis; University of Salford)

10. Grau-Pellicer, M., Chamarro-Lusar, A., Medina-Casanovas, J., & Ferrer, B. S. (2019). Walking speed as a predictor of community mobility and quality of life after stroke. *Topics in Stroke Rehabilitation, 26*(5), 349–358. doi: 10.1080/10749357.2019.1605751

11. He, S., Yang, J., Wei, J., Wu, J., Zheng, Y., Zhang, Y., & Peng, X. (2021). Genetic diversity of eleven Moringa oleifera Lam. germplasm introduced to Yunnan, southwest China and their backgrounds during worldwide cultivation. *Genetic Resources and Crop Evolution, 68*(8), 3345–3356. doi: 10.1007/s10722-021-01192-7

12. Madrigales-Reátiga, L. F., Gutiérrez-Dorado, R., Perales-Sánchez, J. X. K., & Reyes-Moreno, C. (2021). The Moringa Genus. In *book: Biological and Pharmacological Properties of the Genus Moringa* (pp. 1–20). doi: 10.1201/9781003108863-1

13. Narina, S. S., Catanzaro, C., & Gilani, A. H. (2019). Moringa and Tamarind: Potential Drought-Tolerant Perennial Crops. In M. Pessarakli, *Handbook of Plant and Crop Stress*, (4th Ed), (pp. 813-831). CRC Press

14. Karmakar, S., Mondal, P. C., & Horijan, B. (2024). Chemistry and Significance of Moringa oleifera, a Miracle Tree Review. *Chron Aquat Sci, 10*(01), 19–36. doi: 10.61851/coas.v1i10.02

15. Natsir, H., Wahab, A. W., Budi, P., Dali, S., & Arif, A. R. (2019). Amino acid and mineral composition of moringa oleivera leaves extract and its bioactivity as an antioxidant. *Journal of Physics Conference Series, 1317*(1), 012030. doi: 10.1088/1742-6596/1317/1/012030

16. Ercan, K., Gecesefa, O. F., Taysi, M. E., Ali, O. A. A., & Taysi, S. (2020). Moringa oleifera: A review of its occurrence, pharmacological importance and oxidative stress. *Mini-Reviews in Medicinal Chemistry, 21*(3), 380–396. doi: 10.2174/1389557520999200728162453

17. Su, B., & Chen, X. (2020). Current Status and Potential of Moringa oleifera Leaf as an Alternative Protein Source for Animal Feeds. *Frontiers in Veterinary Science, 7*, 53. doi: 10.3389/fvets.2020.00053

18. Chiș, A., Noubissi, P. A., Pop, O., Mureșan, C. I., Tagne, M. a. F., Kamgang, R., Fodor, A., Sitar-Tăut, A., Cozma, A., Orășan, O. H., Hegheș, S. C., Vulturar, R., & Suharoschi, R. (2023). Bioactive Compounds in Moringa oleifera: Mechanisms of Action, Focus on Their Anti-Inflammatory Properties. *Plants, 13*(1), 20. doi: 10.3390/plants13010020

19. Jain, K. K. (2019). Neuroprotection in traumatic brain injury. In *Springer protocols handbooks* (pp. 281–336). doi: 10.1007/978-1-4939-9465-6_4

20. Karvandi, M. S., Hesari, F. S., Aref, A. R., & Mahdavi, M. (2023). The neuroprotective effects of targeting key factors of neuronal cell death in neurodegenerative diseases: The role of ER stress, oxidative stress, and neuroinflammation. *Frontiers in Cellular Neuroscience, 17*, 1105247. doi: 10.3389/fncel.2023.1105247

21. Peña, I. D., Knecht, T., & Borlongan, C. (2018). Combination therapy for ischemic stroke: Novel approaches to lengthen the therapeutic window of tissue plasminogen activator. *Brain Circulation, 4*(3), 99. doi: 10.4103/bc.bc_21_18

22. Kumar, G., & Khanum, F. (2012). Neuroprotective potential of phytochemicals. *Pharmacognosy Reviews/Bioinformatics Trends/Pharmacognosy Review, 6*(12), 81. doi: 10.4103/0973-7847.99898

23. Kurniawan, Y. S. (2021). A Comparative Study on Phytochemical Screening and Antioxidant Activity of Aqueous Extract from Various Parts of Moringa Oleifera. *Indonesian Journal of Natural Pigments, 3*(2), 43-47.

24. Goel, F. (2025). Exploring the therapeutic role of Moringa oleifera in neurodegeneration: antioxidant, anti-inflammatory, and neuroprotective mechanisms. *Inflammopharmacology, 33*(7), 3653–3669. doi: 10.1007/s10787-025-01794-y

25. Shahbaz, M., Naeem, H., Batool, M., Imran, M., Hussain, M., Mujtaba, A., Alsagaby, S. A., Abdulmonem, W. A., El-Ghorab, A. H., Ghoneim, M. M., Shaker, M. E., Abdelgawad, M. A., & Jbawi, E. A. (2024). Antioxidant, anticancer, and anti-inflammatory potential of Moringa seed and Moringa seed oil: A comprehensive approach. *Food Science & Nutrition, 12*(9), 6157–6173. doi: 10.1002/fsn3.4312

26. Worku, B., & Tolossa, N. (2024). A Review on the Neuroprotective Effect of Moringa oleifera. *Oxidative Medicine and Cellular Longevity, 2024*(1), 7694516. doi: 10.1155/2024/7694516

27. Jurcau, A., & Simion, A. (2021). Neuroinflammation in cerebral ischemia and Ischemia/Reperfusion injuries: From pathophysiology to therapeutic strategies. *International Journal of Molecular Sciences, 23*(1), 14. doi: 10.3390/ijms23010014

28. Azlan, U. K., Annuar, N. A. K., Mediani, A., Aizat, W. M., Damanhuri, H. A., Tong, X., Yanagisawa, D., Tooyama, I., Ngah, W. Z. W., Jantan, I., & Hamezah, H. S. (2023). An insight into the neuroprotective and anti-neuroinflammatory effects and mechanisms of Moringa oleifera. *Frontiers in Pharmacology, 13*, 1035220. doi: 10.3389/fphar.2022.1035220

29. Manjunath, S. H., Nataraj, P., Swamy, V. H., Sugur, K., Dey, S. K., Ranganathan, V., Daniel, S., Leihang, Z., Sharon, V., Chandrashekharappa, S., Sajeev, N., Venkatareddy, V. G., Chuturgoon, A., Kuppusamy, G., Madhunapantula, S. V., & Thimmulappa, R. K. (2023). Development of Moringa oleifera as functional food targeting NRF2 signalling: antioxidant and anti-inflammatory activity in experimental model systems. *Food & Function, 14*(10), 4734–4751. doi: 10.1039/d3fo00572k

30. Ganjewala, D., Srivastava, G., Bansal, H., & Srivastava, N. (2024). Status Review of Emerging Neuroprotective Potential of Moringa oleifera and Desmodium Gangeticum. In J. Akhtar, M. Sarwat, & F. Bashir. *Medicinal Plants for the Management of Neurodegenerative Diseases,* 150-168. CRC Press

31. Mahaman, Y. A. R., Feng, J., Huang, F., Salissou, M. T. M., Wang, J., Liu, R., Zhang, B., Li, H., Zhu, F., & Wang, X. (2022). Moringa oleifera alleviates AB burden and improves synaptic plasticity and cognitive impairments in APP/PS1 mice. *Nutrients, 14*(20), 4284. doi: 10.3390/nu14204284

32. Arozal, W., Purwoningsih, E., Lee, H. J., Barinda, A. J., & Munim, A. (2022). Effects of Moringa oleifera in Two Independent Formulations and as a Neuroprotective Agent Against Scopolamine-Induced Memory Impairment in Mice. *Frontiers in Nutrition, 9*, 799127. doi: 10.3389/fnut.2022.799127

33. Amidfar, M., Garcez, M. L., Askari, G., Bagherniya, M., Khorvash, F., Golpour-Hamedani, S., & De Oliveira, J. (2023). Role of BDNF signalling in the Neuroprotective and Memory-enhancing Effects of flavonoids in Alzheimer's Disease. *CNS & Neurological Disorders - Drug Targets, 23*(8), 984–995. doi: 10.2174/1871527323666230912090856

34. Ikbal, M., Akbar, M., Amran, M. Y., Ladju, R. B., Hammado, N., & Wuysang, A. D. (2025). Serum brain-derived neurotrophic factor and vascular endothelial growth factor levels as biomarkers of cognitive function in acute ischemic stroke. *Acta Biomed, 96*(1), 16650.

35. Kirisattayakul, W., Wattanathorn, J., Tong-Un, T., Muchimapura, S., Wannanon, P., & Jittiwat, J. (2013). Cerebroprotective Effect of Moringa oleifera against Focal Ischemic Stroke Induced by Middle Cerebral Artery Occlusion. *Oxidative Medicine and Cellular Longevity, 2013*, 1–10. doi: 10.1155/2013/951415

36. Bewaji, C. O., & Lambe, M. O. (2017). Protective role of Moringa oleifera leaf-based diet on protein-energy malnutrition-induced skeletal muscle degeneration. *International Journal of Scientific Reports, 3*(2), 54. doi: 10.18203/issn.2454-2156.intjscirep20170358

37. Barodia, K., Cheruku, S. P., Kanwal, A., Menon, A., Rajeevan, R., Rukade, A., Shenoy, R. U. K., Prabhu, C., Sharma, V., Divya, K., Sumalatha, S., Nayak, Y., & Kumar, N. (2021). Effect of Moringa oleifera leaf extract on exercise and dexamethasone-induced functional impairment in skeletal muscles. *Journal of Ayurveda and Integrative Medicine, 13*(1), 100503. doi: 10.1016/j.jaim.2021.07.019

38. Ray, H., Patriasih, R., Sulastri, A., & Lesmana, R. (2020). The Potential of Moringa Oleifera in Mitochondrial Biogenesis Through Increased Total Oxphos Unit Expression. *Journal of Engineering Science and Technology, 15*(6), 4214-4222.

39. Duranti, G., Maldini, M., Crognale, D., Horner, K., Dimauro, I., Sabatini, S., & Ceci, R. (2021). Moringa oleifera Leaf Extract Upregulates Nrf2/HO-1 Expression and Ameliorates Redox Status in C2C12 Skeletal Muscle Cells. *Molecules, 26*(16), 5041. doi: 10.3390/molecules26165041

40. Camilleri, E., & Blundell, R. (2024). A comprehensive review of the phytochemicals, health benefits, pharmacological safety and medicinal prospects of Moringa oleifera. *Heliyon, 10*(6), e27807. doi: 10.1016/j.heliyon.2024.e27807

41. Saki, M., De Villiers, H., Ntsapi, C., & Tiloke, C. (2023). The Hepatoprotective Effects of Moringa oleifera against Antiretroviral-Induced Cytotoxicity in HepG2 Cells: A Review. *Plants, 12*(18), 3235. doi: 10.3390/plants12183235

42. Cheng, Y., & Rong, J. (2017). Therapeutic Potential of Heme Oxygenase-1/carbon Monoxide System Against Ischemia-Reperfusion Injury. *Current Pharmaceutical Design, 23*(26), 3884–3898. doi: 10.2174/1381612823666170413122439

43. Ndlovu, S. S., Chuturgoon, A. A., & Ghazi, T. (2023). Moringa oleifera Lam Leaf Extract Stimulates NRF2 and Attenuates ARV-Induced Toxicity in Human Liver Cells (HepG2). *Plants, 12*(7), 1541. doi: 10.3390/plants12071541

44. Patintingan, C. G., Louisa, M., Juniantito, V., Arozal, W., Hanifah, S., Wanandi, S. I., & Thandavarayan, R. (2023). Moringa oleifera Leaves Extract Ameliorates Doxorubicin-Induced Cardiotoxicity via Its Mitochondrial Biogenesis Modulatory Activity in Rats. *Journal of Experimental Pharmacology, 15*, 307–319. doi: 10.2147/jep.s413256

45. Iorjiim, W. M., Omale, S., Bagu, G. D., Gyang, S. S., & Alemika, E. T. (2020). Moringa oleifera Leaf Extract Promotes Antioxidant, Survival, Fecundity, and Locomotor Activities in Drosophila melanogaster. *European Journal of Medicinal Plants,* 30–42. doi: 10.9734/ejmp/2020/v31i1530322

46. Cuschieri, A., Camilleri, E., & Blundell, R. (2023). Cerebroprotective effects of Moringa oleifera derivatives extracts against MCAO ischemic stroke: A systematic review and meta-analysis. *Heliyon, 9*(6), e16622. doi: 10.1016/j.heliyon.2023.e16622

47. Mustafa, M., Ahmad, R., Tantry, I. Q., Ahmad, W., Siddiqui, S., Alam, M., Abbas, K., Moinuddin, N., Hassan, M. I., Habib, S., & Islam, S. (2024). Apoptosis: a comprehensive overview of signalling pathways, morphological changes, and physiological significance and therapeutic implications. *Cells, 13*(22), 1838. doi: 10.3390/cells13221838

48. Khan, M. F., Yadav, S., & Banerjee, S. (2021). Review article on the Effects of Moringa on the central nervous system. *Journal of Young Pharmacists, 13*(4), 315–319. doi: 10.5530/jyp.2021.13.83

49. Li, L., Wang, L., & Zhang, L. (2024). Therapeutic Potential of Natural Compounds from Herbs and Nutraceuticals in Alleviating Neurological Disorders: Targeting the Wnt Signalling Pathway. *Journal of Agricultural and Food Chemistry, 72*(5), 2411–2433. doi: 10.1021/acs.jafc.3c07536

50. Onasanwo, S. A., Adamaigbo, V. O., Adebayo, O. G., & Eleazer, S. E. (2021). Moringa oleifera-supplemented diet protects against cortico-hippocampal neuronal degeneration in scopolamine-induced spatial memory deficit in mice: role of oxidative-inflammatory and cholinergic neurotransmission pathways. *Metabolic Brain Disease, 36*(8), 2445–2460. doi: 10.1007/s11011-021-00855-9

51. Trang, A., & Khandhar, P. B. (2025). *Physiology, Acetylcholinesterase*. StatPearls. StatPearls Publishing

52. Adebayo, O. G., Wopara, I., Aduema, W., Ebo, O. T., & Umoren, E. B. (2021). Long-term consumption of Moringa oleifera-supplemented diet enhanced neurocognition, suppressed oxidative stress, acetylcholinesterase activity and neuronal degeneration in the rat's hippocampus. *Drug Metabolism and Personalised Therapy, 36*(3), 223–231. doi: 10.1515/dmpt-2020-0189

53. Adefegha, S. A., Ogunsuyi, O. B., Aro, O. P., & Oboh, G. (2025). Effect of paraquat-induced toxicity and the therapeutic potentials of Moringa oleifera and Moringa stenopetala leaf alkaloid extracts. *Pharmacological Research - Reports, 4*, 100049. doi: 10.1016/j.prerep.2025.100049

54. Tumer, T. B., Rojas-Silva, P., Poulev, A., Raskin, I., & Waterman, C. (2015). Direct and Indirect Antioxidant Activity of Polyphenol- and Isothiocyanate-Enriched Fractions from Moringa oleifera. Journal of Agricultural and Food Chemistry, 63(5), 1505–1513. doi: 10.1021/jf505014n

55. Darekar, S., Patil, A., Bathe, S., & Doke, R. (2023). Moringa oleifera: A comprehensive review on pharmacology, phytochemistry, and clinical applications. *International Journal of Pharmaceutical Chemistry and Analysis, 10*(4), 243–252. doi: 10.18231/j.ijpca.2023.041