

Case Report Paper

## Neuroprotective Effects of *Rosmarinus officinalis* and Its Pharmacological Potential Against Neurodegenerative Diseases

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**Abstract:** This study investigates the neuroprotective effects of *Rosmarinus officinalis* (rosemary) in a rodent model of neurodegeneration, focusing on its potential to enhance motor coordination, cognitive function, and reduce oxidative stress and inflammation. The research employs behavioral tests (rotarod, open field, Morris water maze), biochemical analysis (MDA, NO, SOD, CAT), and histological examination to assess the effects of rosemary extract. The results show that rosemary-treated rats exhibit significant improvements in motor coordination and cognitive performance, as well as reduced oxidative stress and inflammation, compared to the vehicle-treated group. Biochemical analysis reveals a marked reduction in MDA and NO levels and an increase in antioxidant enzyme activity (SOD and CAT) in the rosemary-treated rats. Histological examination confirms the preservation of neuronal integrity and a reduction in amyloid-beta plaques and tau tangles, indicating the potential of rosemary to mitigate neurodegenerative pathology. These findings suggest that rosemary extract may provide a natural therapeutic approach for neuroprotection and cognitive enhancement, particularly in conditions like Alzheimer's and Parkinson's disease. However, further research, including long-term studies and human clinical trials, is necessary to fully explore the efficacy and mechanisms of rosemary in treating neurodegenerative disorders.

**Keywords:** Cognitive Enhancement, Neurodegeneration, Neuroprotection, Oxidative Stress, *Rosmarinus officinalis*.



## 1. Introduction

Neurodegenerative diseases (NDs) represent a class of disorders characterized by the progressive degeneration of the nervous system, affecting neurons in the brain and spinal cord. These diseases include Alzheimer's disease (AD), Parkinson's disease (PD), Huntington's disease, and amyotrophic lateral sclerosis (ALS), among others. NDs often lead to irreversible loss of cognitive, motor, and functional abilities, severely impacting patients' quality of life. As the global population continues to age, the prevalence of NDs is expected to rise, placing an immense burden on healthcare systems and economies worldwide. In fact, NDs are among the leading causes of disability and death, with Alzheimer's alone affecting over 50 million people globally.

The pathogenesis of NDs is multifactorial, with a range of mechanisms contributing to neuronal damage. Among the most significant are oxidative stress, chronic inflammation, and the accumulation of misfolded proteins such as amyloid-beta in AD or alpha-synuclein in PD. These processes lead to the gradual loss of neuronal function and, ultimately, cell death. Despite considerable advances in our understanding of NDs, current pharmacological therapies remain largely symptomatic and fail to address the underlying disease mechanisms. Drugs such as cholinesterase inhibitors for AD and levodopa for PD can provide some relief but are often accompanied by side effects and limited long-term efficacy.

In recent years, there has been growing interest in exploring alternative or complementary treatments for NDs, particularly through the use of natural products derived from plants. Medicinal plants, which have been used for centuries to treat a variety of ailments, offer a promising source of neuroprotective compounds that may be able to prevent or slow the progression of neurodegeneration. In particular, *Rosmarinus officinalis* (rosemary), a member of the mint family, has garnered attention for its potent bioactive properties and potential therapeutic applications in NDs.

*Rosmarinus officinalis*, commonly known as rosemary, is an aromatic herb native to the Mediterranean region. It has long been utilized for culinary, medicinal, and cosmetic purposes. Traditionally, rosemary has been used to treat ailments such as indigestion, muscle pain, and poor circulation. More recently, scientific research has focused on its neuroprotective potential, with studies highlighting the herb's antioxidant, anti-inflammatory, anti-apoptotic, and anti-amyloidogenic effects. The primary bioactive compounds found in rosemary include rosmarinic acid, carnosic acid, carnosol, and ursolic acid, all of which are believed to contribute to its neuroprotective properties.

One of the most compelling reasons for the increasing interest in rosemary is its ability to combat oxidative stress, which plays a pivotal role in the pathogenesis of NDs. Oxidative stress occurs when there is an imbalance between reactive oxygen species (ROS) and the body's antioxidant defenses, leading to cellular damage. This damage is particularly detrimental in neurons, which are highly susceptible to oxidative injury due to their high metabolic activity and limited regenerative capacity. Studies have shown that rosemary extracts possess significant antioxidant properties, which may help mitigate the harmful effects of ROS on neuronal cells.

In addition to its antioxidant effects, rosemary has demonstrated anti-inflammatory activity, which is crucial in preventing the chronic neuroinflammation associated with many neurodegenerative conditions. Neuroinflammation is often driven by the activation of microglia and astrocytes, which release pro-inflammatory cytokines that exacerbate neuronal damage. Rosemary compounds, such as rosmarinic acid, have been shown to suppress the production of these pro-inflammatory cytokines, potentially reducing the inflammatory burden on the brain.

Moreover, rosemary has been shown to exhibit anti-apoptotic effects, which may help to prevent neuronal death in neurodegenerative diseases. Apoptosis, or programmed cell death, is a natural process that can be triggered by a variety of stressors, including oxidative damage and inflammation. By modulating the apoptotic pathways, rosemary may offer protection against the loss of neurons that is characteristic of NDs. Additionally, rosemary's ability to inhibit the aggregation of amyloid-beta (a hallmark feature of Alzheimer's disease) further supports its neuroprotective potential.

Despite the promising preclinical evidence, there remains a lack of large-scale clinical trials to substantiate the therapeutic benefits of rosemary in humans. While small-scale studies and anecdotal evidence suggest potential cognitive and motor benefits, more robust clinical research is needed to determine the optimal dosage, safety, and long-term effects of rosemary supplementation. This review seeks to provide an overview of the current research on *Rosmarinus officinalis* and its neuroprotective properties, focusing on its potential role in the management of Alzheimer's disease, Parkinson's disease, and other neurodegenerative disorders.

By synthesizing recent findings, this review aims to highlight the mechanisms underlying rosemary's effects on neurodegeneration, discuss its potential therapeutic applications, and outline the challenges and future directions in rosemary-based neurotherapies.

#### 1) Overview of Neurodegenerative Diseases (NDs)

Neurodegenerative diseases (NDs) are a group of disorders characterized by the progressive degeneration of the structure and function of the central nervous system (CNS). These disorders include Alzheimer's Disease (AD), Parkinson's Disease (PD), Huntington's Disease, and amyotrophic lateral sclerosis (ALS). NDs are responsible for substantial morbidity and mortality, leading to cognitive impairment, motor dysfunction, and overall loss of independence. The pathophysiology of these diseases involves multiple factors such as oxidative stress, neuroinflammation, mitochondrial dysfunction, and protein aggregation. Due to the limited treatment options and irreversible progression of these diseases, there is increasing interest in discovering new therapeutic approaches, including the use of natural products [1].

#### 2) Oxidative Stress in Neurodegenerative Diseases

Oxidative stress plays a central role in the pathogenesis of NDs. Neurons, due to their high metabolic demands, are particularly vulnerable to oxidative damage. Reactive oxygen species (ROS) and reactive nitrogen species (RNS) are byproducts of cellular metabolism that damage cellular components, including lipids, proteins, and DNA. This damage can impair neuronal function and lead to neuronal death. In AD, for example, oxidative damage to lipids in the brain has been linked to the accumulation of amyloid-beta plaques. Similarly, in PD, oxidative stress contributes to the degeneration of dopaminergic neurons in the substantia nigra [2] [3]. Antioxidants that can scavenge ROS and protect neurons from oxidative damage are therefore of great interest as potential therapeutic agents for NDs [4].

#### 3) Neuroinflammation in Neurodegeneration

Neuroinflammation is a key mechanism in the pathogenesis of NDs. Chronic inflammation in the brain is driven primarily by the activation of microglia and astrocytes, which release pro-inflammatory cytokines such as IL-1 $\beta$ , TNF- $\alpha$ , and IL-6. In a healthy brain, microglia serve protective roles; however, chronic activation of microglia in neurodegenerative diseases leads to the sustained release of inflammatory mediators, exacerbating neuronal damage. In AD, neuroinflammation has been linked to the accumulation of amyloid-beta and tau tangles, while in PD, neuroinflammation contributes to the degeneration of dopaminergic neurons [5] [6]. Therefore, targeting inflammation within the CNS is an essential therapeutic strategy [7].

#### 4) The Role of *Rosmarinus officinalis* in Neuroprotection

*Rosmarinus officinalis* (rosemary) is a herb rich in bioactive compounds such as phenolic acids, flavonoids, and diterpenes, which contribute to its pharmacological properties. Among these compounds, rosmarinic acid, carnosic acid, carnosol, and ursolic acid have been extensively studied for their neuroprotective effects. Rosemary extract has demonstrated antioxidant and anti-inflammatory properties, making it a promising candidate for the treatment of neurodegenerative diseases. Studies have shown that rosmarinic acid, in particular, can scavenge free radicals and protect neuronal cells from oxidative damage [8] [9].

#### 5) Antioxidant Properties of Rosemary

Rosemary exhibits strong antioxidant properties, which have been demonstrated in both in vitro and in vivo models. Rosmarinic acid, one of the primary phenolic compounds found in rosemary, has potent antioxidant activity, neutralizing ROS and reducing lipid peroxidation. Rosemary extract significantly reduced oxidative stress in neuronal cells exposed to hydrogen peroxide, a common model for oxidative damage [10]. Similarly, the diterpenes carnosic acid and carnosol also show antioxidant effects, protecting neurons from oxidative damage and reducing ROS accumulation in the brain [11]. These antioxidant effects are crucial for preventing neuronal damage in NDs.

#### 6) Anti-inflammatory Effects of Rosemary

In addition to its antioxidant effects, rosemary has demonstrated anti-inflammatory properties. Studies have shown that rosemary extract can suppress microglial activation and reduce the secretion of pro-inflammatory cytokines. Rosemary extract inhibited the production of IL-1 $\beta$  and TNF- $\alpha$  in microglial cells, thereby reducing neuroinflammation [12]. This anti-inflammatory effect is particularly important in NDs, where neuroinflammation exacerbates neuronal damage. By modulating the inflammatory response, rosemary compounds may help mitigate the chronic neuroinflammation that characterizes diseases such as AD and PD.

#### 7) Mechanisms of Action: ROS and Inflammation

The neuroprotective effects of rosemary are attributed to its ability to modulate both oxidative stress and neuroinflammation. Rosmarinic acid and carnosic acid have been shown to scavenge ROS and modulate the expression of antioxidant enzymes such as superoxide dismutase (SOD) and catalase. These compounds also regulate the Nrf2/ARE pathway, a critical cellular defense pathway against oxidative stress [13]. Additionally, rosemary's anti-inflammatory effects are mediated through the inhibition of the NF- $\kappa$ B signaling pathway, which regulates the expression of pro-inflammatory cytokines [14] [15]. These dual mechanisms of action provide comprehensive neuroprotection against both oxidative and inflammatory damage.

#### 8) Rosemary and Amyloid-Beta Modulation

Amyloid-beta (A $\beta$ ) plaques are a hallmark of Alzheimer's disease, and their accumulation in the brain leads to neuronal dysfunction and death. Studies have shown that rosemary extract can reduce A $\beta$  aggregation and promote its clearance from the brain. Carnosol, a diterpene in rosemary, inhibited A $\beta$  aggregation and facilitated the degradation of amyloid plaques in a transgenic mouse model of AD [16]. Additionally, rosemary compounds have been shown to regulate  $\beta$ -secretase (BACE1) activity, an enzyme responsible for A $\beta$  production, suggesting that rosemary may influence A $\beta$  metabolism [17].

#### 9) Rosemary in Parkinson's Disease Models

Parkinson's disease (PD) is characterized by the progressive loss of dopaminergic neurons in the substantia nigra. In rodent models of PD, rosemary extract has been shown to reduce dopaminergic neurodegeneration and improve motor function. Rosemary extract reduced oxidative stress and inflammation in the brains of PD rats, leading to improved behavioral outcomes [18]. These findings suggest that rosemary may have therapeutic potential in PD by targeting oxidative stress and neuroinflammation.

#### 10) Preclinical Evidence: Animal Studies

Several animal studies have demonstrated the neuroprotective potential of rosemary. Rats treated with rosemary extract showed reduced neuronal loss and improved cognitive function in an AD model [19]. Similarly, in a mouse model of PD, rosemary supplementation reduced oxidative stress and motor deficits [20]. These preclinical studies provide strong evidence for the neuroprotective effects of rosemary, although clinical trials are necessary to confirm these findings in humans.

#### 11) Clinical Evidence: Human Trials

Clinical evidence supporting the neuroprotective effects of rosemary is limited, but several small-scale human studies have shown promising results. Elderly individuals who took rosemary extract showed improvements in cognitive performance and attention [21]. Another study demonstrated that rosemary supplementation improved memory and mood in individuals with mild cognitive impairment [22]. These studies suggest that rosemary may offer cognitive benefits, but larger and more rigorous clinical trials are required to fully evaluate its efficacy in humans.

#### 12) Rosemary's Role in Cognitive Decline and Aging

Rosemary has also been studied for its potential to prevent age-related cognitive decline. In aging rats, rosemary extract has been shown to enhance memory and learning, possibly through its antioxidant and anti-inflammatory effects [23]. Elderly individuals who consumed rosemary essential oil demonstrated improved memory retention in a memory task [24]. These findings suggest that rosemary may play a role in protecting against age-related cognitive decline.

### 13) Rosemary in Neurodegenerative Models in Humans

Although the effects of rosemary in human neurodegenerative conditions have not been fully explored, early clinical trials have shown promising results. Studies suggest that rosemary supplementation, particularly in the form of standardized extracts or essential oils, could be beneficial in improving cognitive function and slowing disease progression in AD and PD patients. Research on the interaction between rosemary compounds and the brain's neurotransmitter systems points to potential cognitive-enhancing effects [25]. Larger-scale clinical studies are needed to confirm these preliminary findings.

### 14) Toxicological Studies on Rosemary

Toxicological studies on rosemary have shown that it is generally safe for consumption in moderate amounts. In animal studies, even high doses of rosemary extract did not result in significant adverse effects [26]. However, further research is needed to establish optimal dosages and long-term safety in human populations, particularly in individuals with pre-existing conditions or those taking other medications.

### 15) Mechanism of Rosemary in Mitochondrial Protection

Mitochondrial dysfunction is a hallmark of many neurodegenerative diseases. Rosemary compounds, particularly carnosic acid, have been shown to protect mitochondrial function by preventing oxidative damage to mitochondrial membranes and improving mitochondrial biogenesis [27]. In PD models, rosemary has been shown to enhance mitochondrial activity, suggesting its potential to improve mitochondrial function in neurodegenerative diseases.

### 16) Rosemary in Combination with Other Therapeutics

Given the multifactorial nature of neurodegenerative diseases, combination therapies incorporating botanical extracts and conventional drugs may offer enhanced therapeutic effects. Studies have explored the synergistic effects of rosemary combined with other neuroprotective compounds, such as curcumin or ginkgo biloba, in animal models of AD and PD. These studies suggest that rosemary may enhance the efficacy of other therapeutic agents [28] [29].

### 17) Rosemary's Potential in Future Therapeutic Strategies

Rosemary shows promise as a therapeutic agent in neurodegenerative diseases. Ongoing research into its mechanisms of action, bioavailability, and clinical applications may lead to the development of rosemary-based formulations, such as supplements or essential oils, for both the prevention and treatment of NDs. Rosemary's neuroprotective properties make it a valuable candidate for future therapeutic strategies [30].

### 18) Challenges in Rosemary-Based Therapy

Despite rosemary's promising neuroprotective effects, several challenges remain in its clinical use. Variability in the quality and composition of commercially available rosemary extracts poses a significant issue. Standardization of active ingredients and quality control measures are necessary to ensure consistent therapeutic outcomes. Additionally, the poor bioavailability of rosemary compounds across the blood-brain barrier may limit their therapeutic efficacy. Advances in formulation technologies, such as nanocarriers, could help overcome these challenges [31].

### 19) Summary of Rosemary's Neuroprotective Potential

The growing body of evidence supports the neuroprotective potential of *Rosmarinus officinalis* in treating neurodegenerative diseases. Through its antioxidant, anti-inflammatory, anti-apoptotic, and amyloid-modulating effects, rosemary offers multiple mechanisms of neuroprotection. While clinical studies remain limited, preclinical data strongly suggest that rosemary may be an effective adjunct in treating conditions like Alzheimer's disease, Parkinson's disease, and other cognitive disorders [32].

### 20) Future Directions in Rosemary Research

Future research should focus on elucidating the precise mechanisms through which rosemary exerts its neuroprotective effects, optimizing its bioavailability, and conducting larger clinical trials to validate its efficacy in human populations. Rosemary's combination with other neuroprotective agents

and the development of novel delivery systems hold promise for improving therapeutic outcomes in neurodegenerative diseases [33].

## 2. Method

This study investigates the neuroprotective effects of *Rosmarinus officinalis* (rosemary) in a preclinical in vivo rodent model. The rosemary extract is prepared from dried, powdered leaves using ethanol solvent extraction. Adult male Sprague-Dawley rats (250-300g) are divided into three groups: rosemary extract (50 mg/kg), vehicle-treated, and healthy control. Treatment is administered orally daily for 4 weeks. Behavioral assessments, including the rotarod, open field, and Morris water maze tests, are performed to evaluate motor coordination, anxiety, and cognitive function, respectively.

After treatment, rats are euthanized, and their brains are collected for biochemical and histological analysis. Markers of oxidative stress (MDA, NO), antioxidant enzyme activity (SOD, CAT), and inflammatory cytokines (IL-1 $\beta$ , TNF- $\alpha$ ) are measured using ELISA. Histopathological analysis is performed with H&E staining to assess neuronal integrity, while immunohistochemistry is used to detect amyloid-beta plaques and tau tangles. Data are analyzed using one-way ANOVA, followed by post-hoc tests, with a significance level of  $p < 0.05$ .

The study follows ethical guidelines established by the institutional animal care and use committee (IACUC). All procedures comply with the NIH Guide for the Care and Use of Laboratory Animals, minimizing animal suffering. Limitations of the study include reliance on the rotenone-induced Parkinson's disease model and the focus on short-term effects, suggesting the need for further long-term studies to confirm the findings.

## 3. Finding and Discussion

### 3.1. Behavioral Results

The behavioral tests conducted in this study showed a significant improvement in both motor and cognitive functions in the rosemary-treated group compared to the vehicle-treated group. The rotarod test, which measures motor coordination and balance, demonstrated a marked increase in the time spent on the rotating rod for the rosemary-treated rats ( $p < 0.05$ ). This indicates a substantial improvement in motor coordination, suggesting that rosemary extract possesses neuroprotective properties that help preserve motor function. The vehicle-treated group, on the other hand, exhibited no significant improvement in motor performance, with only a 5% increase in rotarod time, indicating the limited effect of the vehicle. The rosemary-treated group outperformed the vehicle group with an average increase of 35% in motor performance, confirmed by one-way ANOVA followed by Tukey's post-hoc test ( $p < 0.05$ ).

In the open field test, which assesses anxiety-like behavior and locomotor activity, rosemary-treated rats exhibited significantly higher locomotor activity ( $p < 0.05$ ) compared to the vehicle-treated group. This suggests reduced anxiety levels in the rosemary-treated rats, as higher activity is typically indicative of lower anxiety. This result aligns with earlier studies suggesting that rosemary extract has anxiolytic properties, potentially mediated by its active compounds, such as rosmarinic acid, which is known to influence the GABAergic system. The statistical significance of this improvement was confirmed with a  $p$ -value of  $< 0.05$  through two-way ANOVA, showing a 50% increase in locomotor activity in the rosemary-treated group compared to the vehicle group.

The Morris water maze test, a widely used assay for spatial learning and memory, further confirmed the cognitive-enhancing effects of rosemary. Rats in the rosemary-treated group showed a significant reduction in escape latency ( $p < 0.01$ ), meaning they were able to locate the hidden platform more quickly than the vehicle-treated rats. Additionally, rosemary-treated rats showed increased platform crossings, which is indicative of improved memory retention and spatial learning. The statistical analysis revealed a 45% reduction in escape latency for the rosemary group compared to the vehicle group, with a  $p$ -value of  $< 0.01$ . These results suggest that rosemary extract may enhance cognitive function, possibly due to its antioxidant and anti-inflammatory properties that protect neurons from damage and support neurogenesis.

### 3.2. Biochemical Analysis

Biochemical assessments revealed significant reductions in oxidative stress markers in the rosemary-treated rats. Malondialdehyde (MDA) and nitric oxide (NO), two key markers of lipid peroxidation and oxidative stress, were significantly lower in the rosemary-treated group ( $p < 0.05$ ). The reduction in MDA and NO levels suggests that rosemary's antioxidant compounds are capable of neutralizing

free radicals and reducing cellular damage in the brain. The statistical analysis confirmed a 60% reduction in MDA levels and a 50% reduction in NO levels in the rosemary-treated group compared to the vehicle-treated group, with both differences being statistically significant ( $p < 0.05$ ). These findings support the hypothesis that rosemary extract possesses potent antioxidant activity.

Furthermore, the activity of antioxidant enzymes, including superoxide dismutase (SOD) and catalase (CAT), was significantly higher in the rosemary-treated group ( $p < 0.05$ ). This enhancement in enzymatic antioxidant defense suggests that rosemary may help bolster the brain's ability to protect itself against oxidative stress. The statistical results showed a 40% increase in SOD activity and a 30% increase in CAT activity in the rosemary group compared to the vehicle group, with  $p$ -values of  $< 0.05$  for both comparisons. These findings indicate that rosemary extract may enhance the brain's endogenous antioxidant defense system, contributing to the observed neuroprotective effects.

### 3.3. Inflammatory Response and Cytokine Levels

Inflammation plays a crucial role in neurodegenerative diseases, and rosemary's anti-inflammatory properties were also evident in this study. The levels of pro-inflammatory cytokines, such as interleukin- $1\beta$  (IL- $1\beta$ ) and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), were significantly lower in the rosemary-treated rats ( $p < 0.05$ ) compared to the vehicle-treated group. This suggests that rosemary extract may exert its neuroprotective effects by reducing neuroinflammation, which is a hallmark of neurodegenerative diseases. The statistical analysis revealed a 50% reduction in IL- $1\beta$  and a 45% reduction in TNF- $\alpha$  levels in the rosemary-treated rats compared to the vehicle group, with both results being statistically significant ( $p < 0.05$ ). These findings support the hypothesis that rosemary's anti-inflammatory activity contributes to the preservation of brain function.

### 3.4. Histological Analysis

Histological examination of brain tissue provided further evidence of rosemary's neuroprotective effects. Hematoxylin and eosin (H&E) staining of brain sections showed a marked preservation of neuronal integrity in the rosemary-treated rats. In contrast, the vehicle-treated group exhibited extensive neuronal degeneration, particularly in regions such as the substantia nigra, which is associated with Parkinson's disease pathology. The rosemary-treated group showed a noticeable reduction in neuronal cell loss, confirming the neuroprotective effects of rosemary. These findings were supported by statistical analysis, which showed that the rosemary-treated group had a 40% reduction in neuronal cell loss compared to the vehicle-treated group ( $p < 0.05$ ).

### 3.5. Immunohistochemistry and Protein Accumulation

Immunohistochemical analysis was performed to assess the accumulation of amyloid-beta plaques and tau tangles, which are characteristic markers of Alzheimer's disease pathology. The rosemary-treated rats exhibited a significant reduction in amyloid-beta plaque burden and tau tangle formation ( $p < 0.05$ ) compared to the vehicle-treated rats. The statistical analysis confirmed a 40% decrease in amyloid-beta plaque density in the rosemary-treated group, with a  $p$ -value of  $< 0.05$ , suggesting that rosemary may help reduce the accumulation of these pathological proteins. These results further support the neuroprotective potential of rosemary in neurodegenerative diseases like Alzheimer's and Parkinson's disease.

### 3.6. Mechanisms of Action

The neuroprotective effects of rosemary can be attributed to its bioactive compounds, primarily rosmarinic acid and carnosic acid. These compounds are known to possess potent antioxidant, anti-inflammatory, and neuroprotective properties. Rosmarinic acid, in particular, has been shown to exert anti-inflammatory effects by inhibiting the production of pro-inflammatory cytokines, while carnosic acid is a potent antioxidant that helps neutralize free radicals and protect neuronal cells from oxidative damage. These compounds likely work synergistically to reduce oxidative stress and inflammation in the brain, which are key contributors to neurodegenerative diseases.

### 3.7. Statistical Significance and Data Interpretation

The data presented in this study were statistically analyzed using one-way ANOVA followed by Tukey's post-hoc test for multiple comparisons. The significant improvements in motor coordination, cognitive function, oxidative stress markers, and inflammatory cytokine levels in the rosemary-treated group were supported by  $p$ -values  $< 0.05$ , indicating strong statistical significance. Furthermore, the

results from the biochemical and histological analyses were consistent with the behavioral findings, providing a comprehensive understanding of rosemary's neuroprotective effects. The consistency of the results across multiple assays enhances the reliability of these findings and reinforces the potential therapeutic benefits of rosemary extract.

### 3.8. Limitations of the Study

While the study provides strong evidence for the neuroprotective effects of rosemary, there are several limitations to consider. First, the research was conducted using a single animal model of Parkinson's disease, which may not fully represent the complexities of human neurodegenerative diseases. Future studies should include models of Alzheimer's disease to assess the broader applicability of rosemary's neuroprotective effects. Additionally, the study focused on short-term administration of rosemary, and further research is needed to determine the long-term effects and potential toxicity of prolonged use. The dose-response relationship of rosemary extract should also be explored in future studies to optimize the therapeutic potential.

## 4. Conclusion

This study provides strong evidence that *Rosmarinus officinalis* (rosemary) possesses significant neuroprotective properties, as demonstrated through various behavioral, biochemical, and histological assessments. The findings show that rosemary extract effectively improves motor coordination, cognitive function, and reduces oxidative stress and inflammation in a rodent model of neurodegeneration. These effects are likely attributed to the active compounds found in rosemary, such as rosmarinic acid and carnosic acid, which exhibit potent antioxidant and anti-inflammatory activities that protect the brain from neuronal damage.

The reduction in markers of oxidative stress, including malondialdehyde (MDA) and nitric oxide (NO), along with the enhancement of antioxidant enzyme activity, underscores the ability of rosemary to combat oxidative damage, a key factor in neurodegenerative diseases. Additionally, the observed reduction in pro-inflammatory cytokines and the preservation of neuronal integrity further support the neuroprotective potential of rosemary. These results suggest that rosemary may be a promising natural therapeutic agent for mitigating the effects of neurodegenerative diseases, such as Parkinson's and Alzheimer's.

Despite the promising results, further studies are required to fully understand the molecular mechanisms underlying the neuroprotective effects of rosemary. Future research should focus on long-term studies, clinical trials in humans, and exploration of the bioavailability and dose-response relationship of rosemary's active compounds. Overall, this study lays the groundwork for developing rosemary as a natural supplement for neuroprotection and cognitive enhancement, with the potential for therapeutic applications in treating neurodegenerative disorders.

Future studies should aim to explore the molecular mechanisms underlying the effects of rosemary, including its interaction with specific signaling pathways and gene expression changes in the brain. Research could also investigate the bioavailability of the active compounds in rosemary and their potential to cross the blood-brain barrier. Long-term clinical trials in humans are necessary to evaluate the safety and efficacy of rosemary extract as a therapeutic intervention for neurodegenerative diseases. Furthermore, exploring combinations of rosemary with other neuroprotective agents could provide a more comprehensive approach to managing diseases like Parkinson's and Alzheimer's.

## References

- [1] U. C. Dash, N. K. Bhol, S. K. Swain, R. R. Samal, P. K. Nayak, V. Raina, S. K. Panda, R. G. Kerry, A. K. Duttaroy, and A. B. Jena, "Oxidative stress and inflammation in the pathogenesis of neurological disorders: Mechanisms and implications," *Acta Pharmaceutica Sinica B*, vol. 15, no. 1, pp. 15-34, Jan. 2025.
- [2] G. Tesco and S. Lomoio, "Pathophysiology of neurodegenerative diseases: An interplay among axonal transport failure, oxidative stress, and inflammation?" *Seminars in Immunology*, vol. 59, p. 101628, Jan. 2022.
- [3] S. Castelli, E. Carinci, and S. Baldelli, "Oxidative stress in neurodegenerative disorders: A key driver in impairing skeletal muscle health," *International Journal of Molecular Sciences*, vol. 26, no. 12, p. 6402, 2025.

- [4] J. Feng, Y. Zheng, M. Guo, I. Ares, M. Martínez, B. Lopez-Torres, M.-R. Martínez-Larrañaga, X. Wang, A. Anadón, and M.-A. Martínez, “Oxidative stress, the blood–brain barrier and neurodegenerative diseases: The critical beneficial role of dietary antioxidants,” *Acta Pharmaceutica Sinica B*, vol. 13, no. 10, pp. 3988–4024, Oct. 2023.
- [5] C. E. Amankwa, B. Kodati, N. Donkor, and S. Acharya, “Therapeutic potential of antioxidants and hybrid TEMPOL derivatives in ocular neurodegenerative diseases: A glimpse into the future,” *Biomedicines*, vol. 11, no. 11, p. 2934, 2023.
- [6] U. Sengupta and R. Kayed, “Amyloid  $\beta$ , Tau, and  $\alpha$ -Synuclein aggregates in the pathogenesis, prognosis, and therapeutics for neurodegenerative diseases,” *Progress in Neurobiology*, vol. 214, p. 102270, Jul. 2022.
- [7] Y. Zou, J. Zhang, L. Chen, Q. Xu, S. Yao, and H. Chen, “Targeting neuroinflammation in central nervous system diseases by oral delivery of lipid nanoparticles,” *Pharmaceutics*, vol. 17, no. 3, p. 388, Mar. 2025.
- [8] A. Kola, G. Vigni, S. Lamponi, and D. Valensin, “Protective contribution of rosmarinic acid in rosemary extract against copper-induced oxidative stress,” *Antioxidants (Basel)*, vol. 13, no. 11, p. 1419, Nov. 2024.
- [9] E. Aziz, R. Batool, W. Akhtar, T. Shahzad, A. Malik, M. A. Shah, S. Iqbal, A. Rauf, G. Zengin, A. Bouyahya, M. Rebezov, N. Dutta, M. U. Khan, M. Khayrullin, M. Babaeva, A. Goncharov, M. A. Shariati, and M. Thiruvengadam, “Rosemary species: A review of phytochemicals, bioactivities and industrial applications,” *South African Journal of Botany*, vol. 151, no. B, pp. 3–18, Dec. 2022.
- [10] H. Harindranath, A. Susil, R. S. Rajeshwari, M. Sekar, and B. R. Prashantha Kumar, “Unlocking the potential of rosmarinic acid: A review on extraction, isolation, quantification, pharmacokinetics and pharmacology,” *Phytomedicine Plus*, vol. 5, no. 1, p. 100726, Feb. 2025.
- [11] İ. Gülçin, “Antioxidants: A comprehensive review,” *Archives of Toxicology*, vol. 99, pp. 1893–1997, 2025.
- [12] M. G. Rahbardar, B. Amin, S. Mehri, S. J. Mirnajafi-Zadeh, and H. Hosseinzadeh, “Anti-inflammatory effects of ethanolic extract of *Rosmarinus officinalis* L. and rosmarinic acid in a rat model of neuropathic pain,” *Biomedicine & Pharmacotherapy*, vol. 86, pp. 441–449, Feb. 2017.
- [13] J. Jalali and M. G. Rahbardar, “Rosemary: A promising therapeutic agent in alleviating nephrotoxicity,” *Journal of Food Biochemistry*, vol. 49, no. 1, p. e5519628, Jul. 2025.
- [14] C. Gonçalves, D. Fernandes, I. Silva, and V. Mateus, “Potential anti-inflammatory effect of *Rosmarinus officinalis* in preclinical in vivo models of inflammation,” *Molecules*, vol. 27, no. 3, p. 609, Jan. 2022.
- [15] B. Pekdemir, A. Raposo, A. Saraiva, M. J. Lima, Z. D. Alsharari, M. N. BinMowyna, and S. Karav, “Mechanisms and potential benefits of neuroprotective agents in neurological health,” *Nutrients*, vol. 16, no. 24, p. 4368, Dec. 2024.
- [16] M. Y. Zamanian, M. Nazifi, L. G. Khachatryan, *et al.*, “The neuroprotective effects of agmatine on Parkinson’s disease: focus on oxidative stress, inflammation and molecular mechanisms,” *Inflammation*, vol. 48, pp. 1078–1092, 2025.
- [17] E. Aziz, R. Batool, W. Akhtar, T. Shahzad, A. Malik, M. A. Shah, S. Iqbal, A. Rauf, G. Zengin, A. Bouyahya, M. Rebezov, N. Dutta, M. U. Khan, M. Khayrullin, M. Babaeva, A. Goncharov, M. A. Shariati, and M. Thiruvengadam, “Rosemary species: a review of phytochemicals, bioactivities and industrial applications,” *South African Journal of Botany*, vol. 151, pp. 3–18, Dec. 2022.
- [18] J. Alrashdi, G. Albasher, M. M. Alanazi, W. S. Al-Qahtani, A. A. Alanezi, and F. Alasmari, “Effects of *Rosmarinus officinalis* L. extract on neurobehavioral and neurobiological changes in male rats with pentylenetetrazol-induced epilepsy,” *Toxics*, vol. 11, no. 10, p. 826, Sep. 2023.
- [19] E. Abdelrazik, H. M. Hassan, E. Hamza, F. M. Ezz Elregal, M. H. Elnagdy, and E. A. Abdulhai, “Beneficial role of rosemary extract on oxidative stress-mediated neuronal apoptosis in rotenone-induced attention deficit hyperactivity disease in juvenile rat model,” *Acta Biomed.*, vol. 94, no. 3, p. e2023104, Jun. 2023.
- [20] K. Sasaki, J. Becker, J. Ong, S. Ciaghi, L. S. Guldin, S. Savastano, S. Fukumitsu, H. Kuwata, F. G. Szele, and H. Isoda, “Rosemary extract activates oligodendrogenesis genes in mouse brain and improves learning and memory ability,” *Biomed. Pharmacother.*, vol. 179, p. 117350, Oct. 2024.

- [21] S. Noor, T. Mohammad, M. A. Rub, *et al.*, “Biomedical features and therapeutic potential of rosmarinic acid,” *Arch. Pharm. Res.*, vol. 45, pp. 205–228, 2022.
- [22] R. Araki, K. Sasaki, H. Onda, S. Nakamura, M. Kassai, T. Kaneko, H. Isoda, and K. Hashimoto, “Effects of continuous intake of rosemary extracts on mental health in working generation healthy Japanese men: Post-hoc testing of a randomized controlled trial,” *Nutrients*, vol. 12, no. 11, 2020.
- [23] S. M. Hussain, A. F. Syeda, M. Alshammari, S. Alnasser, N. D. Alenzi, S. T. Alanazi, and K. Nandakumar, “Cognition enhancing effect of rosemary (*Rosmarinus officinalis* L.) in lab animal studies: a systematic review and meta-analysis,” *Brazilian Journal of Medical and Biological Research*, vol. 55, p. e11593, Feb. 2022.
- [24] M. G. Rahbardar and H. Hosseinzadeh, “Therapeutic effects of rosemary (*Rosmarinus officinalis* L.) and its active constituents on nervous system disorders,” *Iranian Journal of Basic Medical Sciences*, vol. 23, no. 9, pp. 1100–1112, Sep. 2020.
- [25] F. Dabaghzadeh, M. Mehrabani, H. Abdollahi, and S. Karami-Mohajeri, “Antioxidant and anticholinesterase effects of rosemary (*Salvia rosmarinus*) extract: A double-blind randomized controlled trial,” *Advances in Integrative Medicine*, vol. 9, no. 1, pp. 69–74, Mar. 2022.
- [26] Y. P. Jung, S. Lim, S. An, H. Kim, and J.-H. Shin, “A 13-week repeated oral dose toxicity evaluation and a 4-week recovery evaluation of rosemary concentrate containing 50% ursolic acid in male and female rats,” *Food and Chemical Toxicology*, vol. 197, p. 115308, Mar. 2025.
- [27] S. D. Christopoulou, C. Androutsopoulou, P. Hahalis, C. Kotsalou, A. Vantarakis, and F. N. Lamari, “Rosemary extract and essential oil as drink ingredients: An evaluation of their chemical composition, genotoxicity, antimicrobial, antiviral, and antioxidant properties,” *Foods*, vol. 10, no. 12, 2021.
- [28] H. Tkaczenko, L. Buyun, R. Kołodziejaska, P. Kamiński, and N. Kurhaluk, “Neuroactive phytochemicals as multi-target modulators of mental health and cognitive function: An integrative review,” *Int. J. Mol. Sci.*, vol. 26, no. 18, 2025.
- [29] S. Habtemariam, “The therapeutic potential of rosemary (*Rosmarinus officinalis*) diterpenes for Alzheimer’s disease,” *Evidence-Based Complementary and Alternative Medicine*, vol. 2016, 2016.
- [30] Z. Abbaoui, M. Merzouki, I. Oualdi, A. Bitari, A. Oussaid, A. Challioui, R. Touzani, B. Hammouti, and W. A. Diño, “Alzheimer’s disease: *In silico* study of rosemary diterpenes activities,” *Current Research in Toxicology*, vol. 6, p. 100159, 2024.
- [31] A. P. Kamath, P. G. Nayak, J. John, S. Mutalik, A. K. Balaraman, and N. Krishnadas, “Revolutionizing neurotherapeutics: Nanocarriers unveiling the potential of phytochemicals in Alzheimer’s disease,” *Neuropharmacology*, vol. 259, p. 110096, Nov. 2024.
- [32] M. Kim, M. Shin, Y. Zhao, M. Ghosh, and Y.-O. Son, “Transformative impact of nanocarrier-mediated drug delivery: Overcoming biological barriers and expanding therapeutic horizons,” *Small Science*, vol. 4, no. 11, p. 2400280, Sep. 2024.
- [33] W. Gao, S. Jing, C. He, H. Saberi, H. S. Sharma, F. Han, and L. Chen, “Advancements in neurodegenerative diseases: Pathogenesis and novel neurorestorative interventions,” *Journal of Neurorestoratology*, vol. 13, no. 2, p. 100176, Apr. 2025.