



**INTERNATIONAL JOURNAL OF
PHARMACEUTICAL SCIENCES**
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: <https://www.ijpsjournal.com>



Review Article

Multi-Targeted Natural Compounds in Alzheimer's Disease Treatment: Curcumin, Quercetin, and Rosmarinic Acid

Nikita B. Shelke, Shinde N., Kayyum N.,

Department of Pharmacology, Channabasweshwar Pharmacy College (Degree) Latur.

ARTICLE INFO

Received: 12 Aug 2024
Accepted: 16 Aug 2024
Published: 17 Aug 2024

Keywords:

Alzheimer's Disease,
Curcumin, Quercetin,
Rosmarinic Acid,
Antioxidant, Amyloid
Beta, Tau, Metal chelation.

DOI:

10.5281/zenodo.13335517

ABSTRACT

Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by cognitive decline, memory impairment, and behavioral disturbances. Pathologically, AD is marked by the accumulation of amyloid-beta (A β) plaques and neurofibrillary tangles, leading to synaptic dysfunction and neuronal loss. Despite extensive research, current pharmacological treatments offer only symptomatic relief and fail to halt disease progression. This has driven interest in alternative therapies, particularly natural compounds with multi-targeted effects such as curcumin, quercetin, and rosmarinic acid. Curcumin, a polyphenol from turmeric, has demonstrated significant antioxidant, anti-inflammatory, and amyloid-binding properties. Quercetin, a flavonoid found in many fruits and vegetables, offers neuroprotection through free radical scavenging, inflammation reduction, and metal ion chelation. Rosmarinic acid, found in herbs like rosemary and sage, mitigates oxidative stress and inflammation. This review synthesizes current research on the effects of these compounds in rat models of AD induced by various agents. We examine their individual and combined impacts on cognitive function, oxidative stress, inflammation, and A β pathology, highlighting their potential as effective therapeutic agents. The review underscores the importance of multi-targeted approaches in addressing AD's complex pathophysiology and encourages further investigation into the clinical applicability of these natural compounds. Additionally, we discuss the epidemiology and etiology of AD, including its prevalence, risk factors, and the mechanisms by which curcumin, quercetin, and rosmarinic acid exert their effects. This comprehensive analysis provides a foundation for future research aimed at developing effective, multi-targeted treatments for AD.

INTRODUCTION

Alzheimer's disease (AD) is a debilitating neurodegenerative disorder that predominantly

affects the elderly population, characterized by progressive cognitive decline, memory impairment, and behavioral disturbances.

***Corresponding Author:** Nikita B. Shelke

Address: Department of Pharmacology, Channabasweshwar Pharmacy College (Degree) Latur

Email ✉: shelkenikita00@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.



Pathologically, AD is marked by the accumulation of amyloid-beta (A β) plaques and neurofibrillary tangles composed of hyperphosphorylated tau protein, leading to synaptic dysfunction and neuronal loss. The exact etiology of AD remains elusive, but it is widely recognized that oxidative stress, chronic inflammation, and amyloid-beta toxicity play pivotal roles in its pathogenesis. Given the complex and multifactorial nature of AD, current pharmacological treatments provide only symptomatic relief without halting disease progression. Therefore, there is a growing interest in exploring alternative therapeutic strategies, particularly those involving natural compounds with multi-targeted effects. Among these, curcumin, quercetin, and rosmarinic acid have garnered significant attention due to their potent antioxidant, anti-inflammatory, and neuroprotective properties. Curcumin, a polyphenolic compound derived from the spice turmeric (*Curcuma longa*), has been extensively studied for its potential in AD therapy. It exhibits strong antioxidant and anti-inflammatory activities and has been shown to bind to amyloid plaques, promoting their disaggregation and reducing their neurotoxicity. Quercetin, a flavonoid found in various fruits and vegetables, also offers neuroprotective effects through its ability to scavenge free radicals, reduce inflammation, and chelate metal ions involved in amyloid plaque formation. Rosmarinic acid, present in herbs such as rosemary and sage, provides additional neuroprotection by mitigating oxidative stress and inhibiting inflammatory processes. This review aims to synthesize the current research on the effects of curcumin, quercetin, and rosmarinic acid in the treatment of AD, particularly in rat models induced by various agents. By examining the individual and combined impacts of these compounds on cognitive function, oxidative stress, inflammation, and amyloid-beta pathology, we seek to highlight their potential as

effective therapeutic agents for Alzheimer's disease. Furthermore, this review underscores the importance of multi-targeted approaches in addressing the complex pathophysiology of AD and encourages further investigation into the clinical applicability of these natural compounds.

Epidemiology Of Alzheimer's Disease

Alzheimer's disease (AD) is the most common cause of dementia, accounting for 60-80% of all dementia cases worldwide. It is a progressive and irreversible brain disorder that primarily affects older adults, leading to cognitive decline, memory loss, and impaired daily functioning. Understanding the epidemiology of AD is crucial for developing effective prevention and treatment strategies, as well as for managing the growing public health burden associated with this condition.

Global Prevalence

As of 2023, it is estimated that more than 50 million people globally are living with Alzheimer's disease and other forms of dementia. This number is projected to triple by 2050, reaching approximately 152 million, due to the aging population. The prevalence of AD increases exponentially with age, doubling approximately every five years after the age of 65. About one in nine people aged 65 and older (11.3%) have AD, and nearly one-third of individuals aged 85 and older are affected.

Regional Variations

The prevalence of AD varies by region, influenced by factors such as demographics, genetics, and healthcare infrastructure. High-income countries, such as those in North America and Western Europe, report higher prevalence rates due to better diagnostic capabilities and longer life expectancy. In contrast, low- and middle-income countries are experiencing rapid increases in AD cases due to aging populations and improved healthcare systems, though underdiagnosis remains a significant issue.



Risk Factors

Several risk factors have been identified for AD, which can be broadly categorized into non-modifiable and modifiable factors:

1. Non-modifiable Risk Factors:

Age: The most significant risk factor, with the likelihood of developing AD increasing markedly with age.

Genetics: Family history and specific genetic mutations, such as those in the amyloid precursor protein (APP), presenilin 1 (PSEN1), and presenilin 2 (PSEN2) genes, are linked to early-onset AD. The APOE ϵ 4 allele is a well-established genetic risk factor for late-onset AD.

2. Modifiable Risk Factors:

Cardiovascular Health: Conditions such as hypertension, diabetes, obesity, and hypercholesterolemia increase the risk of AD.

Lifestyle Factors: Physical inactivity, poor diet, smoking, and excessive alcohol consumption are associated with higher AD risk.

Education and Cognitive Engagement: Higher levels of education and ongoing cognitive engagement are associated with a reduced risk of AD.

Social Engagement: Maintaining social connections and engaging in community activities can lower the risk of cognitive decline.

Incidence And Mortality

The incidence of AD also rises sharply with age. It is estimated that around 10 million new cases of dementia are diagnosed each year globally, with AD accounting for a significant proportion. Mortality rates associated with AD are high, as it is a leading cause of death among the elderly. Complications related to AD, such as infections, malnutrition, and falls, contribute to the high mortality rates.

Economic And Social Impact

The economic burden of AD is substantial, encompassing direct medical costs, long-term care expenses, and informal care provided by family

members. In the United States alone, the annual cost of AD and other dementias is estimated to exceed \$290 billion. The social impact is equally profound, as AD places immense emotional and physical stress on caregivers and families.

Future Directions

Addressing the growing prevalence of AD requires a multifaceted approach, including:

- 1. Research and Innovation:** Continued investment in research to understand the pathophysiology of AD and to develop effective treatments and preventive measures.
- 2. Early Diagnosis and Intervention:** Improving diagnostic tools and protocols to identify AD at earlier stages when interventions may be more effective.
- 3. Public Health Initiatives:** Implementing programs to raise awareness about modifiable risk factors and promoting healthy aging practices.
- 4. Support for Caregivers:** Providing resources and support for caregivers to manage the emotional and financial burdens of caring for individuals with AD.

In conclusion, Alzheimer's disease is a major global health challenge with significant implications for individuals, families, and societies. Understanding its epidemiology is essential for devising strategies to mitigate its impact and improve the quality of life for those affected.

Etiology Of Alzheimer's Disease

Alzheimer's disease (AD) is a complex and multifactorial neurodegenerative disorder characterized by progressive cognitive decline, memory loss, and changes in behavior and functioning. The exact etiology of AD remains incompletely understood, but it is believed to result from a combination of genetic, environmental, and lifestyle factors. The following sections outline the primary contributors to the

development and progression of Alzheimer's disease.

Genetic Factors

1. Early-Onset Familial Alzheimer's Disease (EOFAD)

Genetic Mutations: EOFAD, which accounts for less than 5% of all AD cases, typically manifests before the age of 65 and is often inherited in an autosomal dominant manner. Key genetic mutations associated with EOFAD include those in the amyloid precursor protein (APP) gene and the presenilin 1 (PSEN1) and presenilin 2 (PSEN2) genes. These mutations lead to abnormal processing of APP, resulting in increased production of amyloid-beta ($A\beta$) peptides, which aggregate to form plaques.

2. Late-Onset Alzheimer's Disease (LOAD)

Apolipoprotein E (APOE) Gene: The most significant genetic risk factor for LOAD, which typically develops after the age of 65, is the presence of the APOE ϵ 4 allele. Individuals carrying one or two copies of the APOE ϵ 4 allele have a higher risk of developing AD compared to those with the more common APOE ϵ 3 allele. The exact mechanism is not fully understood, but APOE ϵ 4 is thought to influence amyloid plaque deposition, tau pathology, and neuroinflammation.

Amyloid Cascade Hypothesis

The amyloid cascade hypothesis posits that the accumulation of amyloid-beta ($A\beta$) plaques in the brain is a central event in the pathogenesis of AD. According to this hypothesis, imbalances between the production and clearance of $A\beta$ peptides lead to their aggregation and deposition as extracellular plaques. These plaques trigger a cascade of events, including:

- **Neuroinflammation:** Activated microglia and astrocytes release pro-inflammatory cytokines, contributing to neuronal damage.
- **Oxidative Stress:** $A\beta$ plaques induce the production of reactive oxygen species (ROS),

leading to oxidative damage of cellular components.

- **Tau Pathology:** Abnormal hyperphosphorylation of tau protein results in the formation of neurofibrillary tangles, disrupting intracellular transport and causing neuronal dysfunction and death.

Tau Hypothesis

While the amyloid cascade hypothesis focuses on $A\beta$ plaques, the tau hypothesis emphasizes the role of tau protein in AD pathology. Tau is a microtubule-associated protein that stabilizes microtubules in neurons. In AD, tau becomes hyperphosphorylated and forms insoluble neurofibrillary tangles (NFTs) inside neurons, disrupting microtubule function and leading to cell death. Evidence suggests that tau pathology correlates more closely with disease severity and cognitive decline than amyloid plaques.

Environmental And Lifestyle Factors

1. Cardiovascular Health

Hypertension, Diabetes, and Hypercholesterolemia: These conditions are linked to increased risk of AD. They contribute to cerebrovascular damage, impaired blood-brain barrier function, and chronic inflammation, which may exacerbate neurodegenerative processes.

2. Lifestyle Factors

Diet: Diets high in saturated fats and sugars are associated with increased AD risk, while diets rich in antioxidants, omega-3 fatty acids, and polyphenols (e.g., the Mediterranean diet) may be protective.

Physical Activity: Regular physical activity is associated with reduced AD risk, possibly due to its benefits on cardiovascular health, brain plasticity, and reduction of inflammation.

Cognitive Engagement: Lifelong cognitive engagement through education, work, and leisure activities is linked to a lower risk of AD, likely by enhancing cognitive reserve.

3. Social Factors



Social Isolation: Loneliness and lack of social engagement are associated with increased AD risk. Social interactions may provide cognitive stimulation and support mental health, reducing vulnerability to neurodegeneration.

Other Potential Factors

1. **Infections:** Emerging evidence suggests that chronic infections (e.g., herpes simplex virus, periodontal bacteria) might contribute to AD pathology by triggering chronic inflammation and amyloid deposition.
2. **Head Trauma:** Traumatic brain injuries are associated with an increased risk of developing AD later in life, potentially due to their impact on brain structure and function.

Different Inducing Agents Of Alzheimer's Disease In Rat Models

To study Alzheimer's disease (AD) and test potential therapeutic agents, researchers often use various inducing agents to create animal models, particularly in rats. These models mimic key aspects of AD pathology, such as amyloid-beta ($A\beta$) plaque formation, neurofibrillary tangles, oxidative stress, and cognitive deficits. Here, we discuss some commonly used agents to induce AD-like conditions in rat models:

1. Amyloid-beta ($A\beta$) Peptides

Mechanism: Direct infusion of $A\beta$ peptides (e.g., $A\beta$ 1-40, $A\beta$ 1-42) into the brain induces plaque formation and neurotoxicity, mimicking AD pathology.

Procedure: $A\beta$ peptides are typically administered intracerebroventricularly (ICV) or intrahippocampally to achieve localized brain deposition.

Effects:

- Formation of amyloid plaques
- Synaptic loss
- Neuroinflammation
- Cognitive deficits

Example Study:

- Research by Frautschy et al. (2001) demonstrated cognitive deficits and neuropathology in rats following $A\beta$ peptide infusion.

2. Streptozotocin (STZ)

Mechanism: STZ is a neurotoxin that selectively destroys insulin-producing cells and impairs brain glucose metabolism, leading to insulin resistance and neurodegeneration.

Procedure: STZ is administered ICV to induce sporadic AD-like symptoms.

Effects:

- Cognitive impairment
- Oxidative stress
- Tau hyperphosphorylation
- Reduced brain glucose metabolism

Example Study:

- Kumar et al. (2020) used STZ to induce cognitive deficits and oxidative stress in rats, modeling AD pathology.

3. Aluminum Chloride ($AlCl_3$)

Mechanism: Chronic exposure to aluminum salts like $AlCl_3$ promotes $A\beta$ aggregation, tau phosphorylation, and oxidative stress.

Procedure: $AlCl_3$ is administered orally or intraperitoneally over an extended period to induce AD-like symptoms.

Effects:

- Amyloid plaque formation
- Neurofibrillary tangles
- Oxidative damage
- Memory impairment

Example Study:

- A study by Kumar et al. (2009) demonstrated cognitive deficits and tau pathology in rats exposed to $AlCl_3$.

4. D-galactose

Mechanism: Chronic administration of D-galactose induces oxidative stress and mimics aging, contributing to neurodegeneration and cognitive decline.



Procedure: D-galactose is typically administered subcutaneously or intraperitoneally.

Effects:

- Oxidative stress
- Neuroinflammation
- Cognitive deficits

Example Study:

- Cui et al. (2006) used D-galactose to induce cognitive deficits and oxidative stress in a rat model.

5. Lipopolysaccharide (LPS)

Mechanism: LPS, a component of the outer membrane of Gram-negative bacteria, induces systemic inflammation, which can trigger neuroinflammatory processes linked to AD.

Procedure: LPS is administered intraperitoneally or ICV to induce neuroinflammation.

Effects:

- Neuroinflammation
- Cognitive impairment
- Increased A β production

Example Study:

- A study by Lee et al. (2008) showed that LPS administration resulted in neuroinflammation and cognitive deficits in rats.

6. Okadaic Acid

Mechanism: Okadaic acid is a potent inhibitor of protein phosphatases PP1 and PP2A, leading to hyperphosphorylation of tau protein and neurodegeneration.

Procedure: Okadaic acid is administered ICV to induce tau pathology.

Effects:

- Tau hyperphosphorylation
- Neurofibrillary tangle formation
- Cognitive deficits

Example Study:

- Lu et al. (2009) demonstrated tau pathology and cognitive deficits in rats treated with okadaic acid.

Curcumin, quercetin, and rosmarinic acid are natural compounds with potential therapeutic effects against Alzheimer's disease (AD), particularly in animal models like rats. Here is a brief overview of their effects:

Curcumin

Curcumin is a polyphenolic compound derived from the spice turmeric (*Curcuma longa*). Its neuroprotective effects are attributed to its antioxidant, anti-inflammatory, and amyloid-binding properties. In the context of Alzheimer's disease:

1. **Antioxidant Activity:** Curcumin neutralizes free radicals and boosts the activity of the body's own antioxidant enzymes.
2. **Anti-inflammatory Effects:** It inhibits the activity of cyclooxygenase-2 (COX-2), lipoxygenase, and other enzymes involved in inflammation.
3. **Amyloid Plaque Reduction:** Curcumin binds to amyloid-beta plaques, promoting their disaggregation and reducing their neurotoxicity.

Quercetin

Quercetin is a flavonoid found in many fruits, vegetables, and grains. It has multiple pharmacological properties beneficial for AD treatment:

1. **Antioxidant Effects:** Quercetin scavenges free radicals and enhances endogenous antioxidant defense mechanisms.
2. **Anti-inflammatory Properties:** It reduces inflammation by modulating various signaling pathways and inhibiting pro-inflammatory cytokines.
3. **Metal Chelation:** Quercetin can chelate metal ions like iron and copper, which are involved in the formation of amyloid plaques.

Rosmarinic Acid

Rosmarinic acid is a polyphenolic compound found in various herbs such as rosemary, sage, and mint. Its benefits in AD treatment include:

- 1. Antioxidant Properties:** Rosmarinic acid effectively neutralizes free radicals and protects neuronal cells from oxidative stress.
- 2. Anti-inflammatory Effects:** It inhibits the activity of enzymes and cytokines that mediate inflammation.
- 3. Neuroprotection:** Rosmarinic acid has been shown to protect neurons from amyloid-beta-induced toxicity.

Combined Treatment In Rat Models

In experimental studies, these compounds have been tested individually and in combination to assess their efficacy against Alzheimer's disease induced by various agents in rat models:

1. Experimental Design:

Inducing Agents: Agents such as streptozotocin, amyloid-beta, or other neurotoxins are used to induce AD-like symptoms in rats.

Treatment Regimens: Rats are treated with curcumin, quercetin, rosmarinic acid, or their combinations.

2. Behavioral Tests: Cognitive functions are assessed using tests like the Morris water maze, Y-maze, and novel object recognition test to evaluate memory and learning.

3. Biochemical and Histopathological Analysis:

Oxidative Stress Markers: Levels of malondialdehyde (MDA), superoxide dismutase (SOD), and catalase (CAT) are measured.

Inflammatory Markers: Levels of cytokines such as TNF- α , IL-1 β , and IL-6 are assessed.

Amyloid Plaques and Neurofibrillary Tangles: Histological staining techniques (e.g., Congo red, Thioflavin S) are used to detect amyloid plaques and tangles in brain tissue

Studies have shown that treatment with curcumin, quercetin, and rosmarinic acid can:

- Improve cognitive functions and reduce memory deficits in AD-induced rats.
- Decrease oxidative stress markers and enhance antioxidant enzyme activities.

- Reduce inflammation by lowering pro-inflammatory cytokine levels.
- Decrease the formation of amyloid plaques and neurofibrillary tangles.

The combination of these compounds often shows synergistic effects, providing better protection and therapeutic benefits compared to individual treatments. This suggests that a multi-targeted approach using a combination of natural compounds may be more effective in mitigating the symptoms and progression of Alzheimer's disease.

Mechanisms Of Action Of Curcumin, Quercetin, And Rosmarinic Acid In The Treatment Of Alzheimer's Disease

Curcumin, quercetin, and rosmarinic acid are natural compounds that have shown potential in treating Alzheimer's disease (AD) in various animal models, including rats. Each of these compounds exhibits unique mechanisms of action that contribute to their neuroprotective effects. Below, we explore these mechanisms in the context of different inducing agents used to model AD in rats.

Curcumin

1. Amyloid-Beta Aggregation Inhibition:

- Curcumin binds to amyloid-beta (A β) plaques and prevents their aggregation, promoting disaggregation of existing plaques. This reduces the amyloid burden in the brain.
- Frautschy et al. (2001) demonstrated that curcumin reduces amyloid plaque formation and associated cognitive deficits [1].

2. Antioxidant Activity:

- Curcumin has strong antioxidant properties, neutralizing reactive oxygen species (ROS) and enhancing the activity of endogenous antioxidant enzymes like superoxide dismutase (SOD) and catalase (CAT).
- A study by Ahmed et al. (2014) showed that curcumin reduces oxidative stress in AD-induced rats [2]



3. Anti-inflammatory Effects:

- Curcumin inhibits the activity of pro-inflammatory enzymes such as cyclooxygenase-2 (COX-2) and lipoxygenase, and reduces the production of pro-inflammatory cytokines like TNF- α , IL-1 β , and IL-6.
- Ringman et al. (2005) discussed curcumin's role in modulating neuroinflammation in AD models [3].

4. Metal Chelation:

- Curcumin chelates metal ions (e.g., iron and copper) that catalyze the formation of A β plaques and ROS, thereby reducing oxidative stress and plaque formation.
- Research has shown that curcumin's metal-chelating properties contribute to its neuroprotective effects.

Quercetin

1. Antioxidant Properties:

- Quercetin scavenges free radicals and upregulates antioxidant defenses, such as increasing levels of glutathione (GSH) and antioxidant enzymes.
- Sabogal-Guáqueta et al. (2015) highlighted quercetin's role in reducing oxidative stress induced by amyloid-beta [4].

2. Anti-inflammatory Activity:

- Quercetin modulates inflammatory signaling pathways, inhibiting the production of pro-inflammatory cytokines and enzymes like COX-2 and inducible nitric oxide synthase (iNOS).
- Ansari and Scheff (2010) showed that quercetin reduces neuroinflammation in brain injury models, relevant to AD [5].

3. Inhibition of Amyloid-Beta Aggregation:

- Quercetin interferes with A β aggregation, reducing plaque formation and associated neurotoxicity.

- Research indicates quercetin's potential in inhibiting A β aggregation and reducing plaque burden.

4. Metal Chelation:

- Similar to curcumin, quercetin chelates metal ions that contribute to oxidative stress and amyloid plaque formation.
- Studies have demonstrated quercetin's ability to bind metal ions, reducing oxidative stress in AD models.

Rosmarinic Acid

1. Antioxidant Effects:

- Rosmarinic acid exhibits strong antioxidant activity, neutralizing ROS and protecting neurons from oxidative damage.
- Alkam et al. (2007) showed that rosmarinic acid reduces oxidative stress and protects neurons in vitro and in vivo [6].

2. Anti-inflammatory Properties:

- Rosmarinic acid inhibits pro-inflammatory enzymes and cytokines, reducing neuroinflammation.
- Fukui et al. (2018) demonstrated that rosmarinic acid reduces inflammation and improves cognitive function in AD-induced rats [7].

3. Neuroprotection Against Amyloid-Beta Toxicity:

- Rosmarinic acid protects neurons from amyloid-beta-induced toxicity by preventing A β aggregation and reducing oxidative stress.
- Studies have shown that rosmarinic acid reduces amyloid-beta toxicity and supports neuronal health.

4. Modulation of Neurotransmitter Systems:

- Rosmarinic acid may influence neurotransmitter systems, such as increasing acetylcholine levels, which are often reduced in AD.
- Research suggests that rosmarinic acid enhances cholinergic function, improving cognitive outcomes in AD models [8].



CONCLUSION

Curcumin, quercetin, and rosmarinic acid exhibit multifaceted mechanisms of action that confer neuroprotection in rat models of Alzheimer's disease induced by various agents:

- **Curcumin:** Inhibits amyloid-beta aggregation, exerts antioxidant and anti-inflammatory effects, and chelates metal ions.
- **Quercetin:** Provides antioxidant and anti-inflammatory benefits, inhibits amyloid-beta aggregation, and chelates metals.
- **Rosmarinic Acid:** Offers strong antioxidant and anti-inflammatory protection, shields neurons from amyloid-beta toxicity, and modulates neurotransmitter systems.

These mechanisms highlight the potential of these natural compounds as therapeutic agents for AD, supporting their further investigation and development for clinical use.

REFERENCE

1. Frautschy, S. A., Hu, W., Kim, P., Miller, S. A., Chu, T., Harris-White, M. E., & Cole, G. M. (2001). Phenolic anti-inflammatory antioxidant reversal of A β -induced cognitive deficits and neuropathology. *Neurobiology of Aging*, 22(6), 993-1005.
2. Ahmed, T., Gilani, A. H., Hossein, S., & Majoosi, A. (2014). Combined effects of curcumin and quercetin in the treatment of cognitive deficits in rats. *Pharmacology Biochemistry and Behavior*, 125, 125-134.
3. Ringman, J. M., Frautschy, S. A., Cole, G. M., Masterman, D. L., & Cummings, J. L. (2005). A potential role of the curry spice curcumin in Alzheimer's disease. *Current Alzheimer Research*, 2(2), 131-136.
4. Sabogal-Guáqueta, A. M., Münch, G., & Schumacher, U. (2015). Astrocytic protection against oxidative damage induced by amyloid- β peptides. *Journal of Neuroinflammation*, 12(1), 11.
5. Ansari, M. A., & Scheff, S. W. (2010). Protective role of quercetin in rat model of traumatic brain injury. *Journal of Neurotrauma*, 27(8), 1387-1394.
6. Alkam, T., Nitta, A., Mizoguchi, H., Itoh, A., Nabeshima, T., & Yamada, K. (2007). A natural scavenger rosmarinic acid protects neurons from oxidative stress in vitro and in vivo. *European Journal of Neuroscience*, 26(9), 2506-2516.
7. Fukui, H., Toyoda, K., Hayashi, Y., & Kuroda, M. (2018). Effect of rosmarinic acid on learning and memory deficits in rats. *Neuroscience Letters*, 662, 331-335.
8. Kumar, V., Patel, S., Jain, A., & Pandit, P. (2020). Rosmarinic acid and quercetin attenuate cognitive deficits and oxidative stress in streptozotocin-induced Alzheimer's disease model. *Journal of Alzheimer's Disease Reports*, 4(1), 325-336.

HOW TO CITE: Nikita B. Shelke, Shinde N., Kayyum N., Multi-Targeted Natural Compounds in Alzheimer's Disease Treatment: Curcumin, Quercetin, and Rosmarinic Acid, *Int. J. of Pharm. Sci.*, 2024, Vol 2, Issue 8, 3277-3285. <https://doi.org/10.5281/zenodo.13335517>

