Content available at: https://www.ipinnovative.com/open-access-journals

Journal of Pharmaceutical and Biological Sciences

Journal homepage: https://www.jpbs.in/

Original Research Article

Neuroprotective effects of *Akebia Quinata* extract on cognitive impairment in rat models

Namrata M. Waghmare[1]*, Vinay V. Sarode[2], Pragati G. Zalwade[3], Dhamsheela N. Gondane[4], Aditi B. Daiwalkar[5], Bhushan R. Gandhare[6]

[1]Dept. of Pharmacology, Shri K. R. Pandav Institute of Pharmacy, Nagpur, Maharashtra, India.
[2]Dept. of Scientific Writing, BVG Life Sciences Limited (BVG Group), Pune, Maharashtra, India.
[3]Dept. of Pharmacology, Siddhivinayak College of Pharmacy, Warora, Maharashtra, India.
[4]Dept. of Chemistry, Shri K. R. Pandav Institute of Pharmacy, Nagpur, Maharashtra, India.
[5]Dept. of Pharmaceutics, St. Paul College of Pharmacy, Nagpur, Maharashtra, India.
[6]Dept. of Pharmacology, VYWS, Institute of Pharmaceutical Education and Research, Borgaon (Meghe), Wardha, Maharashtra, India.

Abstract

Background and Aim: Alzheimer's disease (AD) involves cognitive decline driven by cholinergic dysfunction, oxidative stress, and neuroinflammation. This study investigates the neuroprotective efficacy of *Akebia quinata* ethanolic extract (AQE) against scopolamine-induced Alzheimer's Disease (AD) in rats, emphasizing memory, biochemical markers, and histopathological outcomes.
Materials and Methods: Wistar rats were divided into five groups: normal control, scopolamine-induced AD control, rivastigmine (2.5 mg/kg), and AQE (200/400 mg/kg). AD was induced via scopolamine (1 mg/kg), followed by 14-day treatments. Behavioural assessments (Radial Arm Maze/RAM, Novel Object Recognition Test/NORT) evaluated memory. Biochemical parameters (acetylcholinesterase/AChE, reduced glutathione, catalase, malondialdehyde/MDA, nitric oxide/NO) and histopathological changes in brain tissue were analysed.
Results: AQE (400 mg/kg) significantly enhanced memory retention, reducing Radial Arm Maze (RAM) errors and increasing novel object exploration time in the Novel Object Recognition Test (NORT). Biochemically, AQE lowered AChE activity, MDA, and NO levels while elevating glutathione and catalase, indicating reduced oxidative stress. Histopathology revealed preserved neuronal architecture, diminished amyloid plaques, and fewer neurofibrillary tangles in AQE-treated groups, with 400 mg/kg showing near-normal histology.
Conclusion: *Akebia quinata* extract mitigates scopolamine-induced AD by restoring cholinergic function, suppressing oxidative damage, and attenuating neurodegeneration. The 400 mg/kg dose demonstrated rivastigmine-comparable efficacy, highlighting AQE's potential as a herbal alternative for AD management. Its neurobiological activity, attributed to flavonoids, alkaloids, and polyphenols, positions AQE as a novel therapeutic candidate. Further studies are warranted to validate clinical applicability.

Keywords: *Akebia quinata*, Alzheimer's disease, Scopolamine, Oxidative Stress, RAM, NORT, Neuroprotection.

Received: 06-04-2025; **Accepted:** 01-05-2025; **Available Online**: 09-06-2025

1. Introduction

Alzheimer's disease (AD) is the most prevalent neurodegenerative dementia affecting the elderly population, characterized by progressive cognitive decline, behavioural impairments, and neuronal dysfunction.[1] AD progresses through stages of mild, moderate, and severe impairment, ultimately leading to dementia and death. Hallmark features include extracellular neuritic plaques composed of amyloid beta (Aβ), intracellular neurofibrillary tangles formed by hyperphosphorylated tau protein, and synaptic dysfunction.[2] Patients experience memory deficits, emotional instability, visual-spatial skill impairment, speech and motor dysfunction, depression, delusions, hallucinations, aggressive behaviour, and increasing dependence.[3] Neuropathological changes predominantly occur in brain regions such as the entorhinal cortex, hippocampus, amygdala, and cortical association areas of the frontal, temporal, and parietal lobes. Subcortical nuclei like the noradrenergic locus coeruleus and cholinergic basal nucleus

*Corresponding author: Namrata M. Waghmare
Email: wnamrata71@gmail.com

DOI: https://doi.org/10.18231/j.jpbs.2025.010

are also affected. The severity of dementia correlates strongly with the degree of tangle deposition rather than amyloid plaque accumulation.[4]

Globally, approximately 5% of men and 6% of women aged over 60 years suffer from dementia or AD according to World Health Organization (WHO) statistics.[5] Despite extensive research into its pathophysiology involving amyloid/tau toxicity, oxidative stress, mitochondrial dysfunctions, and cholinergic dysfunctions, there is currently no cure for AD. Reactive oxygen species (ROS) and reactive nitrogen species (RNS) play dual roles in cellular signalling and oxidative damage to lipids, proteins, and DNA. The brain's high oxygen consumption rate makes it particularly vulnerable to oxidative stress-induced neuronal apoptosis and lipid peroxidation reactions. Reduced glutathione levels further exacerbate oxidative stress in neurons.[6-7]

Metal dyshomeostasis involving iron (Fe), copper (Cu), manganese (Mn), aluminium (Al), and zinc (Zn) is implicated in AD progression. Elevated levels of these metals in the brain contribute to redox imbalances that promote amyloid aggregation and neurotoxicity.[8-9] Additionally, genetic factors such as the APOE genotype influence acetylcholinesterase inhibitor (AChEI) efficacy in AD treatment. Cholinergic dysfunction resulting from reduced receptor binding correlates with cognitive decline in AD patients. Drugs like donepezil and rivastigmine have been used for over two decades to regulate acetylcholine levels; however, their efficacy remains limited due to side effects and incomplete therapeutic outcomes.[10-11]

Scopolamine-induced cognitive impairment models are widely used for studying potential treatments for AD. Scopolamine blocks muscarinic cholinergic receptor activity in rats, leading to cholinergic dysfunction that mimics AD-like symptoms such as memory deficits and oxidative stress-induced neuronal damage. Chronic administration of scopolamine increases levels of amyloid precursor protein (APP) and tau while triggering neuroinflammation via elevated pro-inflammatory cytokines in the hippocampus. Histopathological alterations include neuronal degeneration in the cerebral cortex.[12-13]

Traditional herbal remedies are gaining attention as alternative approaches to mitigate AD symptoms due to their minimal side effects compared to conventional drugs. *Akebia quinata*, a plant used in traditional medicine across East Asia for treating neurological disorders among other ailments, has shown promising pharmacological properties. Various parts of *Akebia quinata* are traditionally employed for conditions like epilepsy, anemia, bladder disturbances, urinary tract infections, convulsions, galacturia, dry coughs, ascites, and neurological disorders. Scientific studies have demonstrated that *Akebia quinata* possesses analgesic, hepatoprotective, anti-obesity, anti-fatigue, antilithiatic activities along with neuroprotective effects. Its phytochemical composition includes polyphenols, flavonoids, alkaloids, saponins, triterpenoids, amino acids, steroids, compounds known for their antioxidant properties and physiological roles in neurodegenerative disorders such as AD. Extracts from *Akebia quinata* have been shown to regulate brain-derived neurotrophic factor (BDNF)-mediated signaling pathways involved in neuronal survival under stress conditions.

This research aims to evaluate its efficacy using behavioural tests like Radial Arm Maze (RAM) and Novel Object Recognition Test (NORT), biochemical markers such as AChE activity reduction and glutathione elevation alongside histopathological analysis of brain tissue. By investigating *Akebia quinata* extract's therapeutic potential against scopolamine-induced Alzheimer-like pathology in rats, this study seeks to contribute valuable insights into developing safer herbal alternatives for managing AD symptoms effectively while minimizing adverse effects associated with conventional treatments.

2. Methods and Materials

2.1. Collection and authentication of plant (Akebia quinata)

Akebia quinata plant stems were purchased from Shivay Herbals and Healthcare, Jaipur, Rajasthan (Batch no.-SHAH/1191/2023). The plant was identified and authenticated on October 20, 2023, at the Department of Botany, Dr. R. G. Bhoyar College, Seloo, Dist- Wardha (Specimen voucher number 13/rgbacscbotany/2023-2024).

2.2. Preparation of plant extract

The plant *Akebia quinata* wash vigorously with water, discard the root part. Aerial parts were dried for a week at 35 to 40ºC and pulverized in a electric grinder.[14] Air-dried and powdered stems of *Akebia quinata* were taken. Extracted at room temperature with ethanol using the maceration method for 72 hours. After filtration of the extract by Whatman no. 1 filter paper, the solvent was evaporated in a rotary evaporator at 70ºC. Concentrated Extract was then dried to obtain a dry powder.

2.3. Experimental animals

Albino Wistar rats of either sex, weighing 150-200g, were obtained from the animal house of the Institute of Pharmaceutical Education and Research, Borgaon (Meghe), Wardha. The animals were housed in polypropylene cages (6 per group) under standard laboratory conditions with a 12-hour light/dark cycle and controlled temperature (22 ± 2°C). They had free access to a commercial pellet diet and water ad libitum. The experimental protocol was approved by the Institutional Animal Ethical Committee of the Institute of Pharmaceutical Education and Research, Wardha (Protocol number 535/PO/ReRcBt/S/02/CPCSEA/IPER/IAEC/2023-24/03).

2.4. Experimental Protocol:

1. **Group-I (Normal Control):** Animals received distilled water p.o. for 28 days
2. **Group-II (Disease Control):** Animals received scopolamine 1mg/kg i.p., for 14 days
3. **Group-III (Standard):** Animals received scopolamine 1mg/kg i.p., for 14 days and received rivastigmine 2.5mg/kg, p.o. from day 15-28 consecutively.
4. **Group-IV & V (Test-I & II):** Animals received scopolamine 1mg/kg i.p., for 14 days and received test Test-I & II (200 & 400 mg/kg, p.o., respectively) from day 15-28 consecutively.

2.5. Behavioural Study

2.5.1 Novel object recognition test (NORT)

The Novel Object Recognition Test (NORT) apparatus consisted of a black-painted chamber (50×50×50 cm), where rats were acclimated for 10 minutes prior to testing. The test comprised two trials: in the first trial (T1), rats were exposed to identical sample objects, followed by a retention period in their home cage; in the second trial (T2), rats were reintroduced to the chamber containing one familiar and one novel object. Memory retention was assessed by measuring the time spent exploring the novel object, with increased exploration indicating intact recognition memory. The novel object preference ratio, calculated as time spent with the novel object relative to total exploration time, served as the primary metric, with values closer to 1 indicating stronger memory retention. Objects were cleaned with a 10% ethanol solution between trials to eliminate olfactory cues and ensure unbiased exploration. Exploration was defined by directing the nose to the object at a distance of not more than 2 cm or touching the object with the nose or forepaws. Seated on the object was not considered exploratory behaviour.[15]

2.5.2. Radial arm maze test (RAM)

Spatial learning and memory in rodents were assessed using a radial 8-arm maze, a widely recognized tool for evaluating cognitive function and drug effects. The maze consisted of eight arms (48 × 12 cm) radiating from a central area (32 cm diameter), elevated 50 cm above the floor and surrounded by constant extra-maze visual cues. Each arm contained a food cup with a 50 mg food pellet at its end. Rats were maintained on a restricted diet to keep their body weight at 85% of their free-feeding weight, with water provided ad libitum. Initial training involved placing food throughout the maze, which was gradually restricted to the food cups. Rats were trained for four days, with five consecutive trials per day, to navigate the arms and consume the bait. Each trial lasted until all five baits were consumed or 5 minutes had passed. Following adaptation, rats underwent one trial per day to evaluate their performance based on three parameters: correct arm entries, total errors, and time taken to complete the task. This experimental setup ensured consistent evaluation of spatial learning and memory while minimizing stress and variability in rodent behaviour.[16]

1. Number of correct arm entries in baited arms.
2. Total number of errors (reference and working memory error).
3. Time to complete the task.

2.6. Biochemical Estimation

2.6.1. Preparation of brain tissue homogenate

Following the 28-day experimental period, animals were humanely euthanized, and brain tissue samples were promptly collected and homogenized in 9% phosphate-buffered saline. The homogenate was centrifuged at 10,000 rpm for 10 minutes at 4°C to isolate cellular debris, yielding a clarified supernatant, which was subsequently analyzed for biochemical markers relevant to Alzheimer's disease pathology.[17]

2.6.2. Estimation of reduced glutathione (GSH)

Reduced glutathione levels were quantified by mixing 0.2 ml of tissue supernatant with 2 ml of DTNB mixture (5,5'-dithiobis-(2-nitrobenzoic acid)), followed by the addition of 0.2 M phosphate buffer to achieve a final volume of 3 ml. After a 10-minute incubation period, absorbance was measured spectrophotometrically at 412 nm. The assay included phosphate buffer and DTNB solution as blank and control, respectively, with the final absorbance value calculated by subtracting the control absorbance from that of the tissue lysate. GSH activity was expressed in µmol/ml of protein.[18]

2.6.3. Estimation of Catalase (CAT)

The catalase activity was determined using a standard protocol, where the reaction mixture comprised 2.9 mL of 10 mM H_2O_2 in 50 mM potassium phosphate buffer (pH 7) and 0.1 mL of the supernatant. The decrease in absorbance at 240 nm was monitored over 3 minutes, and results were expressed as µmol/ml of protein to quantify enzymatic activity.[19]

2.6.4. Estimation of Malondialdehyde (MDA)

The lipid peroxidation end product, malondialdehyde (MDA), was quantified in brain homogenates using a standardized method. Briefly, 0.2 mL of tissue homogenate was mixed with 0.2 mL of 8.1% (w/v) SDS, 1.5 mL of 20% (v/v) acetic acid (pH 3.5), and 1.5 mL of 0.8% (w/v) Thiobarbituric acid (TBA) aqueous solution. The final reaction mixture was adjusted to 4.0 mL and processed as per the established protocol to determine MDA levels, a marker of oxidative stress in brain tissues.[20]

2.6.5. Estimation of nitric content (NO)

Nitric oxide (NO) levels in brain tissue homogenates were quantified using the Griess method, where nitrates were enzymatically converted to nitrites, which reacted with

Griess reagent (1.5% sulphanilamide in 1 mol/L HCl containing 0.15% N-(1-naphthyl) ethylene diamine dihydrochloride) to form a purple azo compound. The absorbance of this compound was measured colorimetrically at 546 nm, with the final reaction volume adjusted to 4.0 ml for consistency.[21]

2.6.6. Estimation of acetylcholine esterase (AChE)

The acetylcholinesterase (AChE) activity assay was performed by adding 100 µL of DTNB reagent (0.1 mM) to 2.6 mL of phosphate buffer (pH 7.4), followed by mixing with 0.4 mL of brain tissue homogenate. The initial absorbance of the reaction mixture was measured at 412 nm before adding 20 µL of acetylthiocholine iodide substrate (1 mM), after which absorbance readings were recorded every 10 minutes for 20 minutes to determine enzymatic activity.[22]

2.7. Histopathological examination

After 28 days, the rats were sacrificed, and their brains were carefully dissected. The brain tissues were cleaned to remove excess tissue and fat, ensuring proper preparation for fixation. The cleaned brain samples were then placed in a container filled with 10% formalin solution to preserve the tissue. Subsequently, the fixed brain samples were sent to Arogya Healthcare Center, Manewada, Nagpur-27, for further histopathological analysis.

2.8. Statistical analysis

Data were analysed using Graph pad Prism 9.3.1. for Windows. Results were expressed as Mean ± S.E.M. One-way analysis of variance (ANOVA) and Two-way analysis of variance (ANOVA) and Bonferroni-test were used to test the significance of the difference between the variables in various groups. The P values of less than 0.05 were considered to be statistically significant. All values express as mean ± S.E.M., #P<0.0001 compared to normal and *P<0.05, **P<0.01, ***P<0.001 compared to control.

3. Results

3.1. Behavioural study

3.1.1. Novel object recognition test (NORT)

The results indicate that after training in the Novel Object Recognition Test (NORT), the control group exhibited a significant reduction in object recognition time compared to the normal group at both 90 minutes and 24 hours. In contrast, treatment with the standard drug and AQE at doses of 200 mg/kg and 400 mg/kg led to an increase in object recognition time, suggesting improved cognitive performance and memory retention in the treated groups. (Figure 1).

3.1.2. Radial arm maze (RAM)

3.1.2.1. Correct arm entries

The assessment of correct arm entries, a measure of working memory, revealed a marked reduction in all experimental groups following scopolamine administration, with the exception of the normal control group. In contrast, animals treated with AQE (200 mg/kg and 400 mg/kg) exhibited statistically significant increases in correct arm entries across all evaluated time points: 24 hours, 14 days, and 28 days post-treatment. These findings suggest that AQE administration counteracts scopolamine-induced working memory deficits, demonstrating dose-dependent efficacy in restoring cognitive performance over both acute and prolonged durations. (Figure 1)

3.1.2.2. Total number of errors

Errors in the radial arm maze were categorized as reference memory errors, occurring when rats chose unbaited arms, and working memory errors, occurring when rats revisited baited arms after collecting food rewards. Following the induction of Alzheimer's disease (AD) in Group 2 animals via Scopolamine, a significant increase in total errors was observed. Conversely, animals treated with the standard drug and various doses of AQE showed a progressive reduction in total errors over 24 hours, 14 days, and 28 days. Notably, the group receiving AQE at a dose of 400 mg/kg demonstrated a significant decrease in total errors, indicating improved cognitive performance. (**Figure 1**)

3.1.2.3. Time to complete task

The determination of task completion time revealed significant differences in memory performance among experimental groups, with the control group (SCOP) showing a marked increase in time required to complete the task compared to normal animals. In contrast, animals treated with the standard drug, as well as those administered 200 mg/kg and 400 mg/kg doses of AQE, exhibited a progressive reduction in task completion time at 24 hours, 14 days, and 28 days post-treatment, demonstrating improved memory performance relative to the SCOP control group. (**Figure 1**)

3.2. Biochemical parameters

3.2.1. Brain glutathione (GSH) level

The experimental findings demonstrate that animals in Group II treated with SCOP exhibited a marked decrease in glutathione (GSH) levels. In contrast, administration of 200 mg/kg AQE (Group IV) resulted in a modest, non-significant elevation in GSH levels, while the 400 mg/kg AQE dose (Group V) induced a statistically significant increase in glutathione concentration in the treated rats. (**Figure 2**)

3.2.2. Brain catalase (CAT) level

The experimental findings demonstrated a marked decrease in catalase (CAT) levels among Group II animals treated with SCOP. In contrast, administration of AQE at 200 mg/kg (Group IV) resulted in a modest, non-significant elevation in CAT activity, whereas the higher 400 mg/kg AQE dose (Group V) induced a statistically significant increase in catalase levels in the treated rats, highlighting a dose-

dependent restorative effect on antioxidant enzyme activity. (**Figure 2**)

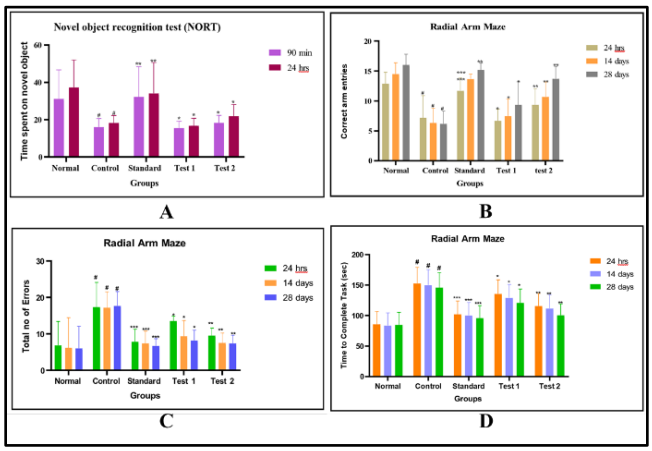

Figure 1: Result of AQE in behavioural study of rats, A: novel object recognition test; B: Radial arm maze test; C: total no. of errors; & D: Time to complete task.

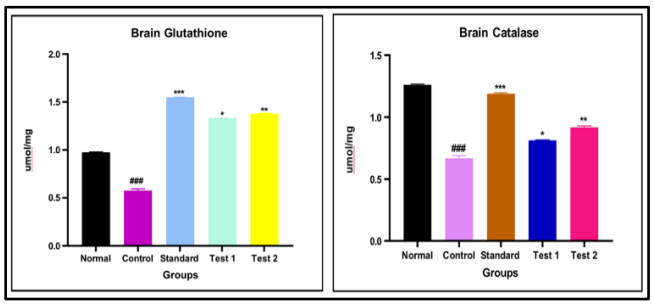

Figure 2: Result of effect of AQE on brain GSH and catalase level in rats.

(All values express as mean ± S.E.M., ###P<0.0001 compared to normal and *P<0.05, **P<0.01, ***P<0.001 compared to control).

3.2.3. Brain malondialdehyde (MDA) level

The experimental observations revealed that Group II animals administered SCOP exhibited a marked increase in malondialdehyde (MDA) levels. In contrast, treatment with AQE extract at 200 mg/kg (Group IV) demonstrated a modest, non-significant reduction in MDA levels, whereas the higher dose of 400 mg/kg AQE (Group V) produced a statistically significant decrease in MDA concentrations in the tested rats. (**Figure 3**)

3.2.4. Brain nitric oxide (NO) level

The experimental observations revealed that animals in Group II administered with SCOP exhibited a marked increase in nitric oxide (NO) levels. In contrast, Group IV treated with 200 mg/kg AQE showed a less significant reduction in NO levels, while Group V receiving 400 mg/kg AQE demonstrated a substantial and statistically significant decrease in NO levels compared to the control groups. This dose-dependent response highlights the potential efficacy of higher AQE concentrations in modulating NO levels in rats. (**Figure 3**)

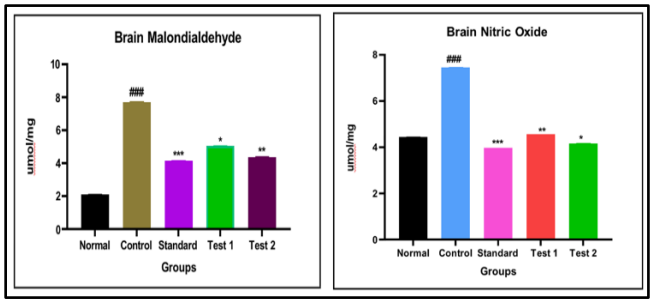

Figure 3: Result of effect of AQE on Brain MDA and NO level in rats.

(All values express as mean ± S.E.M., ###P<0.0001 compared to normal and *P<0.05, **P<0.01, ***P<0.001 compared to control).

3.2.5. Brain acetylcholinesterase (AchE) level

The findings demonstrate that animals in Group II administered scopolamine (SCOP) exhibited a marked increase in acetylcholinesterase (AChE) levels. In contrast, Group IV treated with 200 mg/kg AQE showed a less significant reduction in AChE activity, while Group V receiving 400 mg/kg AQE displayed a statistically significant decrease in AChE levels compared to the SCOP-treated group, indicating a dose-dependent inhibitory effect of AQE on AChE in rats. (**Figure 4**)

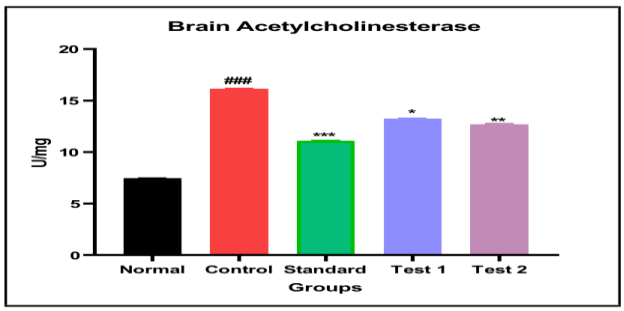

Figure 4: Result of effect of AQE on Brain AChE Level in rats.

(All values express as mean ± S.E.M., ###P<0.0001 compared to normal and *P<0.05, **P<0.01, ***P<0.001 compared to control).

3.3. Histopathological estimation

Histopathological analysis revealed distinct improvements in brain tissue across various experimental groups. The normal group exhibited a typical cellular arrangement, indicating healthy brain tissue. In contrast, the scopolamine-induced control group showed significant neuronal loss, amyloid plaque (AP) deposition, and neurofibrillary tangles (NFT). Animals treated with the standard drug rivastigmine (2.5 mg/kg) demonstrated reduced neuronal degeneration and diminished AP and NFT. Treatment with (AQE) showed dose-dependent effects: at 200 mg/kg, there was mild neuronal degeneration and partial repair of the pyramidal layer, while at 400 mg/kg, AP and NFT disappeared entirely, accompanied by significant repair of the degenerated pyramidal layer. These findings suggest that AQE therapy, particularly at higher doses, may effectively mitigate histopathological damage in neurodegenerative conditions. (**Figure 5**)

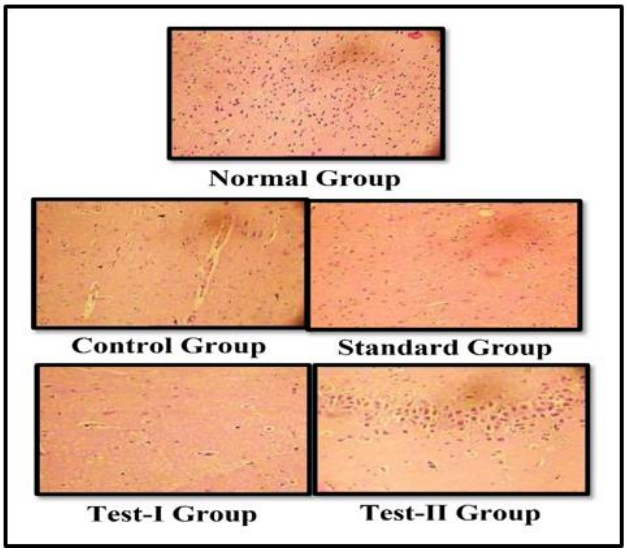

Figure 5: The Effect of *Akebia quinata* Extract (AQE) on the brain tissue. (Stain-Hematoxylin and Eosin) at 400x magnification

4. Discussion

This research provides a compelling investigation into the potential of (AQE) as an alternative treatment strategy for Alzheimer's disease (AD). The study leverages a scopolamine-induced AD rat model, a widely recognized method for replicating the cognitive and neuropathological hallmarks of the disease. Scopolamine effectively impairs memory and learning by inducing neuroinflammation, oxidative stress, and increasing levels of Amyloid Precursor Protein (APP) and tau proteins, mirroring key aspects of AD pathology. The use of rivastigmine, a well-established acetylcholinesterase inhibitor, as a standard drug provides a relevant benchmark for evaluating the efficacy of AQE.

The behavioural assessments, including the Novel Object Recognition Test (NORT) and the Radial Arm Maze (RAM), convincingly demonstrate the cognitive-enhancing effects of AQE. Rats treated with AQE, particularly at the 400 mg/kg dosage, exhibited improved recognition memory and spatial learning abilities compared to the scopolamine-induced control group. These findings suggest that AQE can effectively counteract the memory deficits induced by scopolamine, potentially by modulating pathways involved in learning and memory consolidation. The biochemical analyses further support the neuroprotective effects of AQE, revealing its ability to modulate key markers of oxidative stress, neuroinflammation, and cholinergic function.

The observed reduction in acetylcholinesterase (AChE) activity, nitric oxide (NO) levels, and malondialdehyde (MDA) levels, coupled with increased levels of glutathione (GSH) and catalase, indicates that AQE exerts its therapeutic effects through multiple mechanisms. By inhibiting AChE, AQE may increase acetylcholine levels in the brain, thereby enhancing cholinergic neurotransmission and improving cognitive function. Additionally, the antioxidant properties of AQE, as evidenced by its ability to reduce oxidative stress markers and increase antioxidant enzyme levels, may protect neurons from damage and degeneration. The histopathological findings further corroborate the neuroprotective effects of AQE, demonstrating its ability to reduce neuronal loss, amyloid plaque deposition, and neurofibrillary tangles in the brain.

5. Conclusion

The findings of this study underscore the therapeutic potential of *Akebia quinata* extract (AQE) in addressing Alzheimer's disease (AD) through a multi-targeted approach. By utilizing a scopolamine-induced AD rat model, the research successfully replicated critical neuropathological and cognitive deficits characteristic of AD, including impaired cholinergic function, oxidative stress, and amyloid/tau pathology. AQE administration, particularly at 400 mg/kg, demonstrated significant efficacy in reversing scopolamine-induced cognitive decline, as evidenced by improved performance in the NORT and RAM tests. These behavioural improvement were paralleled by biochemical and histopathological recovery, highlighting AQE's ability to modulate acetylcholinesterase (AChE) activity, reduce oxidative stress marker (MDA, NO), and enhance antioxidant defences (GSH, catalase). Furthermore, the attenuation of neuronal loss, amyloid plaques, and neurofibrillary tangles in brain tissues solidifies AQE's neuroprotective role.

The study's significance lies in its demonstration of AQE's dual mechanism involving enhancing cholinergic neurotransmission by inhibiting AChE and mitigating oxidative damage through antioxidant activity. This multi-faceted action positions AQE as a promising alternative to conventional single-target therapies, which primarily address cholinergic deficits. Given AD's complex etiology, AQE's ability to concurrently tackle neuroinflammation, oxidative stress, and proteinopathy suggests a more holistic therapeutic strategy.

Future research should on isolating AQE's bioactive compound to identify specific molecules responsible for its effects. Pharmacokinetic studies are needed to assess bioavailability and blood-brain barrier penetration. Long-term safety and efficacy evaluations in chronic AD models, such as transgenic mice with amyloid or tau pathology, would further validate these findings. Additionally, clinical trials are essential to translate these preclinical results into human applications, particularly in early-stage AD patients. Investigating synergistic effects of AQE with existing therapies could also unlock combinatorial treatment regimens, potentially enhancing therapeutic outcomes while reducing side effects. This study lays a robust foundation for exploring plant-derived compounds as viable, multi-target interventions in neurodegenerative diseases.

6. Acknowledgement

The authors gratefully acknowledge the Institute of Pharmaceutical Education and Research, Wardha, for providing the necessary facilities and support to conduct this research. Sincere appreciation is also extended to the Department of Botany, Dr. R. G. Bhoyar College, Seloo, Dist- Wardha, for their expertise in the identification and authentication of the *Akebia quinata* plant, specifically to Dr. Vishal N. Patil. Finally, the authors wish to express their gratitude to all individuals who contributed, directly or indirectly, to the successful completion of this research.

7. Source of Funding

None.

8. Conflict of Interest

None.

Reference

1. Ahmed HH, Salem AM, Sabry GM, et al. Possible therapeutic uses of salvia triloba and piper nigrum in Alzheimer's disease–induced rats. *J Med Food*. 2013;16(5):437-46.
2. Mishra S, Palanivelu K. The effect of curcumin (turmeric) on Alzheimer's disease: An overview. *Ann Indian Acad Neurol*. 2008;11(1):13–9.
3. Aluise CD, Robinson RA, Beckett TL. Preclinical Alzheimer's disease: brain oxidative stress, amyloid-beta peptide, and proteomics. *Neurobiol Dis*. 2010;39(2):221–8.
4. Kumar A, Singh A, Ekavali. A review on Alzheimer's disease pathophysiology and its management: an update. *Pharmacol Rep*. 2015;67(2):195–203.
5. Nie K, Yu JC, Fu Y. Age-related decrease in constructive activation of Akt/PKB in SAMP10 hippocampus. *Biochem Biophys Res Commun*. 2009;378:103–7.
6. Liu Z, Zhang A, Sun H. Two decades of new drug discovery and development for Alzheimer's disease. *RSC Adv*. 2017;7(10):6046–58.
7. Mohamed T, Shakeri A, Rao PPN. Amyloid cascade in Alzheimer's disease: Recent advances in medicinal chemistry. *Eur J Med Chem.* 2016;113:258–72.
8. Weekley CM, He C. Developing drugs targeting transition metal homeostasis. *Curr Opin Chem Biol*. 2017;37:26–32.
9. Prakash A, Dhaliwal GK, Kumar P. Brain biometals and Alzheimer's disease – boon or bane? *Int J Neurosci*. 2017;127(2):99–108.
10. Sultzer DL, Marder SR. Older Brains are Different: Brain–Behavior Studies and Their Clinical Utility. *Am J Geriatr Psych*. 2017;25(1):11–2.
11. Chase TN, Farlow MR, Clarence–Smith K. Donepezil Plus Solifenacin (CPC–201) Treatment for *Alzheimer's Disease*. *Neurotherapeutics*. 2017;14(2):405–16.
12. Hancianu M, Cioanca O, Mihasan M. Neuroprotective effects of inhaled lavender oil on scopolamine-induced dementia via anti-oxidative activities in rats. *Phytomedicine*. 2013;20(5):446-52.
13. Bihaqi SW, Singh AP, Tiwari M. Supplementation of Convolvulus pluricaulis attenuates scopolamine-induced increased tau and Amyloid precursor protein (ABPP) expression in rat brain. *Indian J Pharmacol*. 2012;44(5):593-8.
14. Chakrabarty N, Chowdhury TA, Shoibe M. Antidepressant activity of methanol extract of Commelina benghalensis linn. *Whole Plant*. 2016;5(7):1723-33.
15. Zhang R, Xue G, Wang S. Novel object recognition as a facile behaviour test for evaluating drug effects in AßPP/PS1 Alzheimer's disease mouse model. *J Alzheimer's Dis*. 2012;31(4):801-12.
16. Lee JY, Kho S, Yoo HB. Spatial memory impairments in amnestic mild cognitive impairment in a virtual radial arm maze. *Neurop Dis Treat*. 2014:10:653-60.
17. Kaur R, Mehan S, Khanna D. Ameliortive treatment with ellagic acid in scopolamine-induced Alzheimer's type memory and cognitive dysfunctions in rats. *Aust J Clin Neurol*. 2015;2(6):1053.
18. Fukuzawak, Tokumurai A. Glutathione peroxidase activity in tissues of vitamin E-deficient mice. *J Nutrit Sci Vitaminol*. 1976;22(5):405-7.
19. Aebi H. Catalase. *In Methods Enzymatic Anal*. 1974; pp. 673-84.
20. Gaschler MM, Stockwell BR. Lipid peroxidation in cell death. *Biochem Biophy Res Commun*. 2017;482(3):419-25.
21. Sun J, Zhang X, Broderick M. Measurement of nitric oxide production in biological systems by using Griess reaction assay. *Sensors*. 2003;3(8):276-84.
22. Ellman GL, Courtney KD, Andres Jr V. A new and rapid colorimetric determination of acetylcholinesterase activity. *Biochem Pharmacol*. 1961;7(2):88-95.

Cite this article: Waghmare NM, Sarode VV, Zalwade PG, Gondane DN, Daiwalkar AB, Gandhare BR. Neuroprotective effects of Akebia Quinata extract on cognitive impairment in rat models. *Journal of Pharmaceutical Biological Science.* 2025;13(1):61-67.