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Neuroprotective and memory-enhancing potential of *Rosa moschata* leaf extract in a sodium arsenate-induced cognitive impairment rat model

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ABSTRACT

Objective: To evaluate the neuroprotective effects of *Rosa moschata* leaf extract against sodium arsenate-induced cognitive impairment in rats.

Methods: Memory impairment was induced with oral sodium arsenate (10 mg/kg) in rats. *Rosa moschata* leaf extract was administered orally at 150, 300, and 600 mg/kg for three weeks. Behavioral tests, measurement of oxidative stress parameters and neurotransmitter levels, histopathological assessment, and real-time PCR were performed.

Results: *Rosa moschata* leaf extract dose-dependently increased antioxidant enzyme activities and reduced malondialdehyde levels in rats with sodium arsenate-induced cognitive impairment compared with untreated controls. It also inhibited acetylcholinesterase activity, and enhanced dopamine, serotonin, and noradrenaline levels. *Rosa moschata* leaf extract significantly improved behavioral parameters in open field test, Y-maze test, Morris water maze test, and elevated plus maze test in a dose-dependent manner. Quantitative PCR demonstrated reduced α-synuclein expression and downregulation of neuroinflammatory mediators after treatment.

Conclusions: *Rosa moschata* leaf extract exhibits marked neuroprotective effects against sodium arsenate-induced cognitive impairment. These findings support its potential as a promising therapeutic candidate for managing memory impairment and related neurodegenerative disorders.

KEYWORDS: Memory impairment; Oxidative stress; Neuroinflammation; Sodium arsenate; Neurotransmitters; *Rosa moschata*

Summary

Question: Could *Rosa moschata* leaf extract (RMLE) improve sodium arsenate-induced cognitive impairment?

Findings: RMLE significantly improved learning and memory function, neurotransmitter levels, and antioxidant status in rats with sodium arsenate-induced cognitive impairment.

Meaning: RMLE may act as a potent natural neuroprotective and memory-enhancing agent.

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1. Introduction

Neurodegenerative diseases like Parkinson's and Alzheimer's disease (AD) are associated with motor and cognitive impairment. These problems are generally linked with aging[1]. AD is a cerebrovascular disease that progressively impairs a person's mental capacity. The primary causes of AD are unknown, but a number of risk factors, including oxidative stress, brain inflammation, tau and beta-amyloid protein accumulation, cholinergic receptor inhibition, and reduced cholinergic activity, can lead to cognitive damage. AD is becoming increasingly prevalent worldwide, with a new case reported every seven seconds[2]. One out of every 85 people is predicted to have AD by the end of 2050[3]. As one of the most prevalent forms of dementia, AD primarily affects the elderly[4]. Early-phase AD is linked to mitochondrial dysfunction induced by oxidative and nitrosative stress, although the precise mechanism is yet unknown. Elevated levels of advanced glycation end products have been observed in AD patients[5]. Arsenic is a dangerous metalloid element in the environment. Inorganic arsenic is present in soil, water, and the atmosphere. The two primary forms of inorganic arsenic present in subsurface water are arsenate (the oxidized pentavalent form, As V) and arsenite (the trivalent form, As III). Large-scale populations are exposed to arsenic-contaminated drinking water in several countries, including Bangladesh, Mexico, India, and China[6]. Long-term consumption of arsenic-contaminated drinking water has been linked to non-carcinogenic health problems as well as a number of malignancies, including lung, skin, and bladder cancer[7]. Scientists have become increasingly interested in the neurotoxic effects of arsenic.

Patients exposed to arsenic may show significant central nervous system impairment, including behavioral impairments, cognitive dysfunction, and emotional issues, according to clinical and epidemiological studies[8]. Most of the clinical, pathologic, and developmental features of AD-related disorders are compatible with changes induced by chronic arsenic exposure. Young children are specifically vulnerable to arsenic-induced neurotoxicity[9].

Previous study has demonstrated that arsenic-induced brain damage results in neurodevelopmental defects, alterations in neural morphology, neuroinflammation, and increased mortality in addition to disruption of normal brain functions. Furthermore, research has shown that arsenic exposure can exert detrimental effects not only on microglia but also on central snail neurons and cerebellar granule neurons. Taken together, arsenic could induce neuronal cell death; nevertheless, the exact mechanism responsible for this neurotoxicity is still unknown. Among the drivers responsible for arsenic-mediated neurotoxicity, apoptosis is considered a critical outcome of arsenic-induced neurodegeneration[10].

Rosa moschata (*R. moschata*) belongs to Rosaceae family. *R. moschata* is commonly known as musk rose. "Nastarana" is its Persian name. *R. moschata* is a kind of rose endemic to the Himalayas and western Asia. *R. moschata* is a deciduous shrub and can reach a height of three meters (10 feet)[11]. Once flowering concludes, *R. moschata* bears small fruits ranging from crimson to orange-red, known as rose hips[12]. Owing to their high vitamin C content and antioxidants, these hips are widely used in herbal teas, jams, jellies, and syrups, and are believed to boost immune defense and mitigate inflammation.

Its major constituents include polyphenols, linalool, citronellol, nonadecane, eugenol, geraniol, 2-phenylethyl alcohol, tannins, and unsaturated aldehyde[13]. The leaves exhibit rubefacient and insecticidal effects. The roots and leaves are used to treat diarrhea. The hydrodistillate of flowers is utilized as an antioxidant. Exerting anti-inflammatory effects, herbal tea prepared from this plant is used to ameliorate eye-related ailments. Rosa oil serves as an aromatic ingredient incorporated into skincare products and perfumes[14]. This present study aimed to investigate the neuroprotective effect of *R. moschata* leaf extract in a rat model, and to further elucidate the mechanisms responsible for sodium arsenate-induced impairments in learning and memory.

2. Methods

2.1. Main reagents

Sodium arsenate, ethanol, hydrochloric acid (HCl), sodium sulfate, acetic acid, o-phthalaldehyde, acetylthiocholine iodide, 5,5′-dithiobis-(2-nitrobenzoic acid), phosphate-buffered saline, cDNA synthesis kit, Trizol reagent, and SYBR Green master mix were utilized in the study. All used reagents were of analytical grade. Sodium arsenate, and all other analytical-grade chemicals were obtained from Sigma-Aldrich (Merck KGaA, Darmstadt, Germany). cDNA synthesis kit, Trizol reagent, and SYBR Green master mix were purchased from Thermo Fisher Scientific (Waltham, MA, USA).

2.2. Animals

Twenty five healthy Wistar rats of both genders weighing 100-150 g were obtained from Government College University in Faisalabad. All rats were housed at ambient temperature (25℃-30℃), with a 12 h day-night cycle. All rats had free access to standard laboratory chow and drinking water.

2.3. Ethical statement

This study was performed after obtaining ethical approval (reference no. GCUF/ERC/339; dated 18 February 2026) from the Institutional Review Board of Government College University Faisalabad, and complied with the national institutional guidelines for animal care and safety.

2.4. Induction of cognitive impairment

Sodium arsenate (10 mg/kg) was orally administered to all rats except for the control group, 30 min before extract treatment for 21 d to induce memory impairment.

2.5. Study design

The rats were divided into five groups with five rats in each. Group 1 was given normal saline at 10 mL/kg and served as the control group. Group 2, or the model group, was given sodium arsenate orally at 10 mg/kg. Rats in the treatment groups were orally administered 150, 300, and 600 mg/kg of RMLE, respectively[15].

Body weight and behavioral parameters were evaluated at the beginning, mid-point, and end of the experimental period. Before behavioral tests, the animals were acclimated to the laboratory environment for 30 min. Behavioral tests were conducted on day 1 to record baseline behavioral performance. Subsequent behavioral assessments were carried out on day 11 and day 21 to assess spatial learning, memory retention, and cognitive function. All animals were anaesthetized with 10% isoflurane and euthanized by cervical dislocation. Brain tissues used for biochemical assays were preserved in ice-cold phosphate buffer saline (pH 7.4). For histopathological analysis, the brain was isolated and fixed in 10% formalin. Total RNA was extracted using the TRIzol method for subsequent real time (RT)-PCR analysis[16].

2.6. Behavioral tests

2.6.1. Morris water maze (MWM) test

Spatial memory acquisition and retention were assessed using the MWM test. The apparatus consisted of a circular plastic tank filled with opaque water to a depth of 30 cm. The tank was virtually divided into four equal-sized quadrants. During the acquisition phase, a hidden platform was placed in the center of one quadrant, 1 inch above the water surface, to train animals to escape from the water. After training was complete, the platform was submerged 1 inch below the water surface for the retention test, so that it could not be visually detected. The starting release position was altered for each trial. The animals were allowed to swim until they located and climbed onto the platform[17].

2.6.2. Open field test

Exploratory behavior and locomotor activity were determined *via* the open field test. The apparatus consisted of a wooden box measuring 72 cm (W) × 72 cm (D) × 36 cm (H), whose floor was virtually divided into sixteen equal squares. Each animal was placed in the center of the arena and allowed to freely explore for 5 min prior to formal recording. Parameters were recorded for 10 min. Immediately after the open field test, rats were exposed to a novel object within the same arena. Reduced exploration of the novel object relative to the familiar object indicates memory impairment[18].

2.6.3. Y-maze test

Y-maze test was used to measure spatial, short-term, and reasoning deficits in rats. Animals with intact memory and a functional prefrontal cortex exhibit innate curiosity and tend to explore new places. Animals with memory impairment display altered spontaneous changes in maze arms as compared to normal controls. The Y-maze apparatus consisted of three plywood arms (designated arms A, B, and C), arranged at 120° to one another. The side walls were made of acrylic and had a height of 20 cm. Following the final treatment, each rat was individually placed inside one arm of the maze and permitted to freely explore for 8-10 min. Arm entries (defined as all four paws entering an arm) were recorded for each rat. Spontaneous alternation sequences (ABC, BCA, or CBA) were calculated based on the pattern of arm entries, which reflects short-term memory[19].

2.6.4. Elevated plus maze test

Distinct spontaneous behavioral alterations are observed in rat models with memory impairment. The elevated plus maze test is a classic behavioral assay to assess and quantify anxiety-like behaviors and memory dysfunction in rodents, despite minor results discrepancies due to differences in experimental conditions and animal housing. This apparatus was constructed with a hardwood base and consisted of four arms arranged in a plus shape, including two open arms and two closed arms of identical dimensions (50 cm ×10 cm). The closed arms were equipped with 40 cm-high side walls, while the open arms remained uncovered. All four arms converged at a central square platform (10 cm × 10 cm) and were elevated above the ground. For behavioral testing, each rat was gently placed on the central platform facing an open arm. The latency to enter closed arms and the spontaneous behavioral shifts were recorded to reflect the innate anxiety and exploratory behavior of the experimental rats[19,20].

2.7. Evaluation of biochemical markers

2.7.1. Oxidative stress parameters

Isolated brain tissues were temporarily preserved in phosphate buffer solution. Prior to homogenization, the brain tissues stored at −80℃ were thawed and cut into small pieces. The tissue samples were homogenized in a 10-fold volume of buffer containing 1 mmol/L phosphate buffer, 0.3 mol/L sucrose, and 0.08 mol/L potassium chloride. This homogenate was then centrifuged at 7600 rpm for 10 min at 4℃. The collected supernatant was subsequently used for the determination of antioxidant biomarkers, including malondialdehyde (MDA), catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPx), and reduced glutathione (GSH)[16,21-23].

2.7.2. Measurement of neurotransmitters

Homogenate of brain tissue was mixed with 5 mL hydrochloric acid (HCl)-butanol solution and centrifuged at 2000 rpm for 10 min. The upper phase obtained after centrifugation was combined with 2.5 mL heptane and 0.31 mL HCl, followed by another centrifugation at 2000 rpm for 10 min. Later, the mixture separated into 2 distinct layers, and 0.2 mL of the lower aqueous layer was collected for subsequent neurotransmitter analysis[24].

To 0.2 mL of the aqueous phase, 0.05 mL of 0.4 M hydrochloric acid and 0.1 μL EDTA were added. Oxidation was initiated by adding 0.1 mL of 0.1 M iodine in ethanol. After 2 min, the oxidation reaction was stopped by the addition of 0.1 mL sodium sulfate solution. Subsequently, 0.1 mL acetic acid was added. The resulting mixture was heated at 100 ℃ for 6 min. Absorbance was measured at 350 nm for dopamine and at 452 nm for noradrenaline. Blank samples for dopamine and noradrenaline were prepared by reversing the oxidation sequence, *i.e.*, adding sodium sulfate before iodine[25].

For serotonin measurement, 0.2 mL of the aqueous phase was mixed with 0.25 mL o-phthalaldehyde. Fluorophore formation was achieved by heating the mixture at 100 ℃ for 10 min. A blank solution was made using concentrated HCl alone, and absorbance was measured at 440 nm[26].

For acetylcholinesterase measurement, 0.4 mL brain homogenate, 20 μL acetylthiocholine iodide, and 100 μL 2,4-dithiobisnitrobenzoic acid were mixed with phosphate-buffered saline. Thiocholine reacted with 2,4-dithiobisnitrobenzoic acid and produced a yellow-colored product, and the absorbance was determined at 412 nm[27].

2.8. Histopathological analysis

Brain tissues were dissected from the animals. Tissue sections of approximately 5 μm were cut with a rotary microtome. Sections were stained with hematoxylin and eosin, visualized under a light microscope (Olympus CX43 or equivalent), and photomicrographs were captured using a digital microscope camera. Histopathological changes were assessed at 40× magnification.

2.9. RT–PCR

Following RNA extraction using the Triazole technique, cDNA was synthesized with a cDNA synthesis kit according to the manufacturer's instructions. The RT-PCR reaction plate was prepared with forward and reverse primers together with SYBR Green master mix.

Real-time PCR thermal cycling was performed under the following conditions: an initial denaturation step at 95 ℃ for 5 min, followed by 40 cycles consisting of denaturation at 95 ℃ for 15 s, annealing at 60 ℃ for 20 s, and extension at 72 ℃ for 20 s. Relative mRNA expression fold changes were calculated using the Livak method ($2^{-\Delta\Delta Ct}$)[28]. The primer sequences are listed in Supplementary Table.

2.10. Statistical analysis

All results are presented as mean ± SEM, with n=5. Statistical analyses were performed using GraphPad Prism version 8. One-way ANOVA was conducted, followed by Tukey's test. P<0.05 was considered statistically significant.

3. Results

3.1. Behavioral tests

3.1.1. Open field test

Rat locomotor activity (line crossings), vertical exploratory behavior (rearing), and self-grooming frequency were observed. Animals in the model group displayed a significant (P<0.001) reduction in line-crossing counts, rearing events, and grooming behavior compared with the normal control group. RMLE produced a statistically significant (P<0.001) dose-dependent improvement in these behavioral parameters. The optimal therapeutic effect was observed at 600 mg/kg (Figure 1).

3.1.2. Y–maze test

Compared to the normal control group, animals in the model group showed a significant decrease in the number of trials, arm entries, and spontaneous alterations (P<0.001). RMLE treatment significantly increased these behavioral indices in a dose-dependent manner (P<0.05) (Figure 2).

3.1.3. MWM test

On day 21, escape latency was measured in the acquisition test. The model group showed a significant increase in escape latency compared with the normal control group. RMLE significantly (P<0.001) decreased escape latency. The greatest therapeutic efficacy was observed at 600 mg/kg (Figure 3A, Table 1).

3.1.4. Elevated plus maze test

To evaluate cognitive performance in animals, transfer latency was measured on day 21 of the experiment. The model group demonstrated a significant (P<0.001) increase in transfer latency compared to the normal control group. RMLE significantly declined transfer latency (P<0.001) in a dose-dependent manner. The maximum therapeutic efficacy was observed at the dose of 600 mg/kg (Figure 3B).

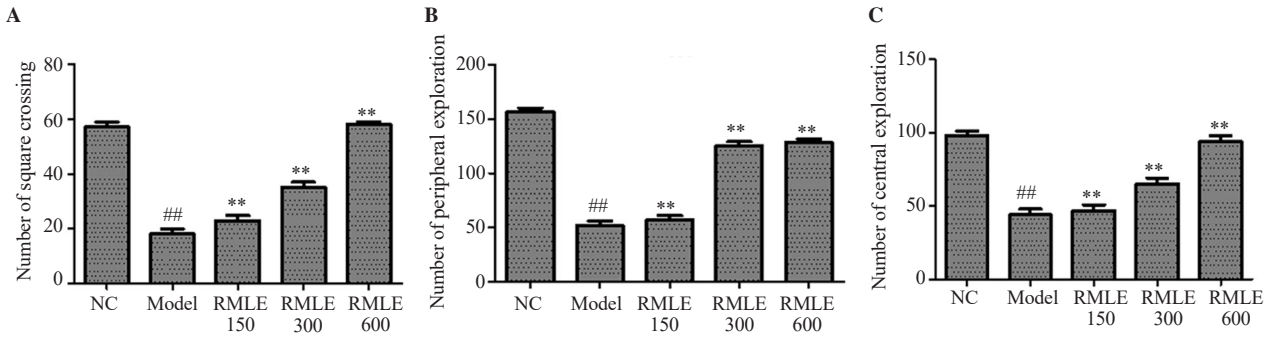


Figure 1. Effect of *Rosa moschata* leaf extract (RMLE) on number of square crossing (A), peripheral exploration (B), and central exploration (C). One-way ANOVA followed by Tukey's test was used. $^{\#\#}P<0.001$ compared with the normal control group; $^{**}P<0.001$ compared to the model group. NC: the normal control group; RMLE 150: the group treated with 150 mg/kg of *Rosa moschata* leaf extract; RMLE 300: the group treated with 300 mg/kg of *Rosa moschata* leaf extract; RMLE 600: the group treated with 600 mg/kg of *Rosa moschata* leaf extract.

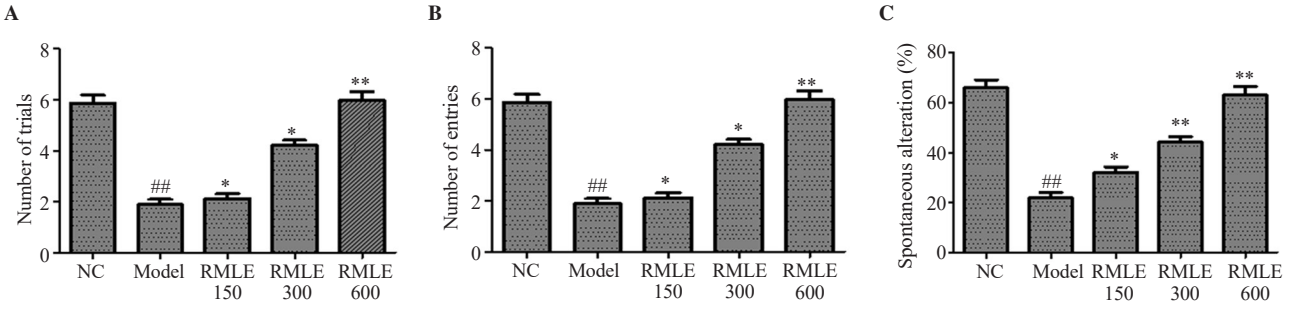


Figure 2. Effect of RMLE on number of trials (A), number of entries (B) and spontaneous alteration (C). One-way ANOVA followed by Tukey's test was used. $^{\#\#}P<0.001$ compared with the normal control group; $^{*}P<0.05$, $^{**}P<0.001$ compared to the model group.

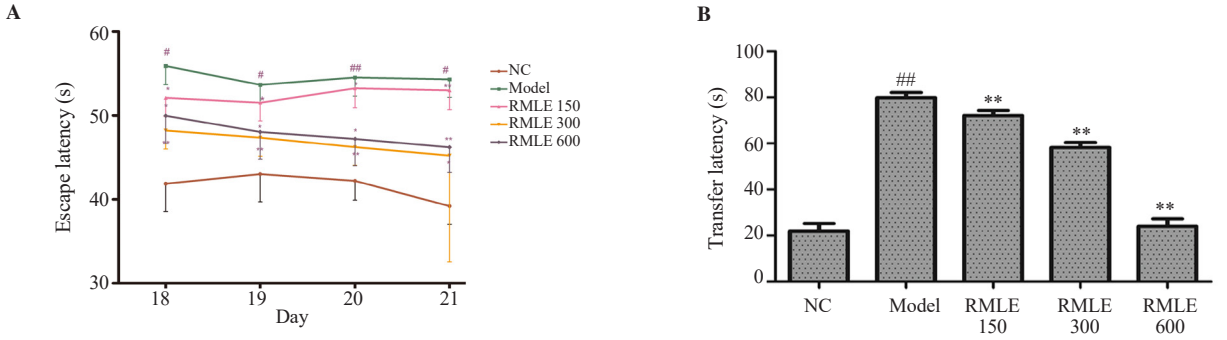


Figure 3. Effect of RMLE on escape latency in Morris water maze test (A) and on transfer latency in elevated plus maze test (B). One-way ANOVA followed by Tukey's test was used. $^{\#}P<0.05$, $^{\#\#}P<0.001$ compared with the normal control group; $^{*}P<0.05$, $^{**}P<0.001$ compared to the model group.

3.2. Oxidative stress parameters

The levels of SOD, CAT, GPx, and GSH were significantly decreased, and MDA was significantly increased in the model group compared with the normal control group ($P<0.001$). RMLE significantly increased SOD, CAT, GPx, and GSH levels and decreased MDA levels ($P<0.001$) (Table 2).

3.3. Analysis of neurotransmitters

The levels of dopamine, serotonin, and noradrenaline were significantly decreased, and acetylcholinesterase was significantly increased in the model group compared with the normal control group ($P<0.001$). RMLE significantly increased dopamine, serotonin, and noradrenaline levels and decreased acetylcholinesterase levels ($P<0.001$) (Table 3).

3.4. RT–PCR analysis

The levels of *IL-1α*, *IL-1β*, *TNF-α*, and *α-synuclein* were significantly increased in the model group compared with the normal control group ($P<0.001$). RMLE significantly decreased these gene levels ($P<0.001$) (Figure 4).

Table 1. Effect of *Rosa moschata* leaf extract (RMLE) on quadrant-specific escape latency in Morris water maze test (mean ± SEM, *n*=5).

Groups	North (s)	South (s)	East (s)	West (s)
Normal control	24.70 ± 0.57	13.60 ± 0.64	16.30 ± 0.52	17.30 ± 0.68
Model group	42.00 ± 0.68$^{\#\#}$	37.00 ± 0.97$^{\#\#}$	38.50 ± 0.80$^{\#\#}$	52.50 ± 0.80$^{\#\#}$
RMLE 150 mg/kg	40.30 ± 0.80*	35.00 ± 0.58**	37.00 ± 0.57	38.30 ± 0.58*
RMLE 300 mg/kg	31.40 ± 0.58**	29.00 ± 0.57**	40.00 ± 0.57*	33.00 ± 0.55**
RMLE 600 mg/kg	23.90 ± 0.06**	17.10 ± 0.55**	23.00 ± 0.80**	10.50 ± 0.58**

One-way ANOVA followed by Tukey's test was used. $^{\#\#}P$<0.001 compared with the normal control group; $^{*}P$<0.05, $^{**}P$<0.001 compared to the model group.

Table 2. Effect of RMLE on oxidative stress parameters (mean ± SEM, *n*=5).

Groups	CAT (mmol/mg)	SOD (µg/mg)	MDA (µmol/mg)	GSH (µg/mg)	GPx (µg/mg)
Normal control	2.31 ± 0.02	3.55 ± 0.02	6.54 ± 0.12	0.66 ± 0.02	3.42 ± 0.20
Model group	1.65 ± 0.03$^{\#\#}$	2.25 ± 0.01$^{\#\#}$	8.26 ± 0.02$^{\#\#}$	0.43 ± 0.03$^{\#\#}$	2.35 ± 0.01$^{\#\#}$
RMLE 150 mg/kg	1.76 ± 0.03**	2.58 ± 0.02**	7.62 ± 0.32**	0.41 ± 0.02**	3.16 ± 0.20**
RMLE 300 mg/kg	1.93 ± 0.02**	3.14 ± 0.03**	7.07 ± 0.03**	0.47 ± 0.42**	3.26 ± 0.50**
RMLE 600 mg/kg	2.08 ± 0.13**	3.24 ± 0.02**	6.80 ± 0.02**	0.69 ± 0.60**	3.39 ± 0.70**

One-way ANOVA followed by Tukey's test was used. $^{\#\#}P$<0.001 compared with the normal control group; $^{**}P$<0.001 compared to the model group. CAT: catalase; SOD: superoxide dismutase; MDA: malondialdehyde; GSH: reduced glutathione; GPx: glutathione peroxidase.

Table 3. Effect of RMLE on dopamine, serotonin, noradrenaline, and acetylcholinesterase levels in the brain tissue (mean ± SEM, *n*=5).

Groups	Dopamine (µg/mg)	Serotonin (µg/mg)	Noradrenaline (µg/mg)	Acetylcholinesterase (mmol/mg)
Normal control	0.66 ± 0.02	0.86 ± 0.02	0.72 ± 0.02	5.02 ± 0.02
Model group	0.04 ± 0.02$^{\#\#}$	0.34 ± 0.02$^{\#\#}$	0.32 ± 0.04$^{\#\#}$	13.32 ± 0.24$^{\#\#}$
RMLE 150 mg/kg	0.33 ± 0.20**	0.35 ± 0.20**	0.37 ± 0.10**	11.67 ± 0.12**
RMLE 300 mg/kg	0.47 ± 0.01**	0.48 ± 0.01**	0.45 ± 0.02**	7.87 ± 0.03**
RMLE 600 mg/kg	0.58 ± 0.31**	0.70 ± 0.31**	0.60 ± 0.30**	6.60 ± 0.01**

One-way ANOVA followed by Tukey's test was used. $^{\#\#}P$<0.001 compared with the normal control group; $^{**}P$<0.001 compared to the model group.

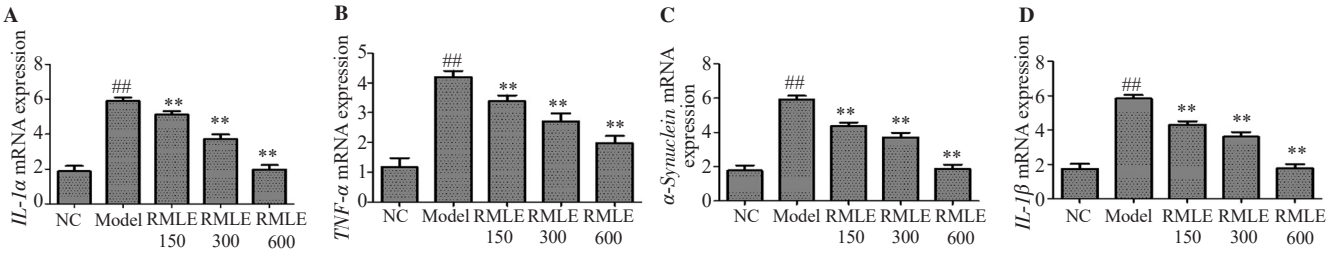


Figure 4. Effect of RMLE on mRNA expression of *IL-1α* (A), *TNF-α* (B), *α-synuclein* (C), and *IL-1β* (D). One-way ANOVA followed by Tukey's test was used. $^{\#\#}P$<0.001 compared with the normal control group; $^{**}P$<0.001 compared to the model group.

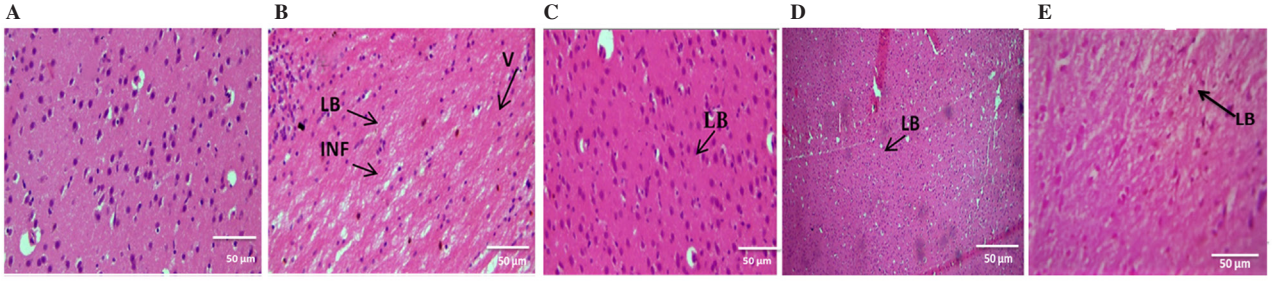


Figure 5. Histopathological analyses of brains (40×, H&E staining). A: Normal control; B: Model group; C: RMLE 150 mg/kg, D: RMLE 300 mg/kg, E: RMLE 600 mg/kg. INF: infiltration, LB: Lewy body, V: vacuolation.

3.5. Histopathological analysis

The rats in the normal control group exhibited normal brain tissue architecture. The model group displayed reduced neuronal numbers, the presence of pro-inflammatory mediators, accumulation of pigment, and Lewy's body formation. On the other hand, RMLE treatment group showed dose-dependent recovery from pathological features, including neuronal loss and progressive neuronal tissue damage (Figure 5).

4. Discussion

AD is a progressive neurological condition and is characterized by

memory loss and cognitive decline. The rising incidence of dementia and the limited efficacy of current medications underscores need for safer and more effective therapeutic approaches[29-31]. Cognitive dysfunction is largely caused by oxidative stress, neuroinflammation, neurotransmitter imbalance, and neuronal death. Exposure to sodium arsenate triggers multiple pathological alterations, such as oxidative stress, disruption of neurotransmitter homeostasis, and inflammatory reactions[6-8]. Thus, the current study assessed the neuroprotective and memory-enhancing effects of RMLE using a sodium arsenate-induced cognitive impairment model.

Sodium arsenate administration induced prominent behavioral and cognitive deficits, including reduced locomotor activity in the open-field test, impaired spontaneous alternation in the Y-maze, altered exploratory behavior in the elevated plus maze, and prolonged escape latency in the Morris water maze. These results show that exposure to sodium arsenate impairs memory, learning, and exploratory behavior. RMLE treatment markedly alleviated these behavioral impairments in a dose-dependent manner, with the most noticeable improvement observed at 600 mg/kg. The neuroprotective and antioxidant properties of RMLE may be attributable to its phytochemical constituents, such as flavonoids and phenolic compounds[32].

Oxidative stress plays a significant role in the neuronal damage caused by sodium arsenate[33]. In the current study, sodium arsenate increased MDA and lowered SOD, CAT, and GPx activity as well as GSH levels, suggesting increased lipid peroxidation and compromised endogenous antioxidant defence. These alterations were significantly reversed by RMLE therapy, indicating that the neuroprotective effect may be attributed to the restoration of antioxidant capacity. Antioxidant activity of RMLE may improve neuronal function and cognitive performance by attentuating oxidative damage to cellular components and neuronal membranes.

Exposure to sodium arsenate also disrupted neurotransmitter homeostasis[26], as evidenced by elevated acetylcholinesterase activity and reduced levels of dopamine, serotonin, and noradrenaline. Such biochemical disturbances may further deteriorate cognitive impairment and neural transmission. RMLE therapy inhibited acetylcholinesterase activity and restored these monoamine neurotransmitter levels in a dose-dependent manner. Therefore, the improvement in learning and memory induced by RMLE can be partially explained by maintaining neurotransmitter homeostasis and suppressing acetylcholine degradation. Importantly, the present study only demonstrates correlative relationships rather than direct causal mechanistic associations.

Neuroinflammation represents another key feature of sodium arsenate-induced cognitive impairment[9]. Sodium arsenate exposure upregulated the expression of pro-inflammatory mediators such as TNF-α, IL-1α, and IL-1β. RMLE treatment downregulated these inflammatory markers, suggesting effective suppression of the inflammatory response. Moreover, α-synuclein expression was elevated in the sodium arsenate group, which was decreased after RMLE treatment. These molecular observations were further supported by histopathological evidence. Sodium arsenate exposure induced neuronal loss, inflammatory cell infiltration, pigment accumulation, and Lewy body-like alterations. RMLE ameliorated these degenerative changes in a dose-dependent manner. All of these results suggest that neuroprotective effect of RMLE may be mediated *via* mitigating oxidative stress, restoring neurotransmitter disruption, and suppressing neuroinflammatory reactions.

The limitations of the present study include relatively low generalizability arising from the small sample size and short treatment duration. Although we observed alterations in inflammatory, neurotransmitter, antioxidant, and histopathological parameters, the exact molecular mechanisms underlying the neuroprotective actions of RMLE remain uncharacterized. The individual contributions of RMLE phytoconstituents and their potential synergistic interactions were not examined. Future work should employ larger sample cohorts, extended treatment regimens, better-validated cognitive-impairment models, and targeted mechanistic studies. Pharmacokinetic studies and phytochemical standardisation would also help to identify the bioactive constituents of RMLE and clarify their biological roles.

In sodium arsenate-induced cognitive impairment rats, RMLE exerted dose-dependent beneficial effects on behavioral performance, antioxidant defence, neurotransmitter homeostasis, inflammatory profiles, and neuronal histomorphology. Through behavioral, biochemical, and histopathological analyses, the present study demonstrated that RMLE effectively improved learning and memory capacity, mitigated behavioral anomalies, and restored neurotransmitter and antioxidant enzyme levels. Collectively, these findings support the potential of *R. moschata* leaves as a source of neuroprotective compounds and lay a basis for further investigations of RMLE in neurodegenerative disease models.

Conflict of interest statement

The authors declare that there is no conflict of interest.

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Data availability statement

The data supporting the findings of this study are available from the corresponding authors upon request.

Authors' contributions

US and MAS perceived and supervised the study. MF, IA, AM, AE, and BSA conducted the experiments. IA, AM, MF, EAA, AO and MA analyzed and interpreted the data. All the authors equally participated in writing, editing and revision of the manuscript and agreed on final draft for submission.

References

[1] Kumar A, Singh A. A review on Alzheimer's disease pathophysiology and its management: An update. *Pharmacol Rep* 2015; **67**(2): 195-203.

[2] Ferrari C, Sorbi S. The complexity of Alzheimer's disease: An evolving puzzle. *Physiol Rev* 2021; **101**(3): 1047-1081.

[3] Brookmeyer R, Johnson E, Ziegler-Graham K, Arrighi HM. Forecasting the global burden of Alzheimer's disease. *Alzheimers Dement* 2007; **3**(3): 186-191.

[4] Beuscher L, Beck C. A literature review of spirituality in coping with early-stage Alzheimer's disease. *J Clin Nurs* 2008; **17**(5a): 88-97.

[5] Emanuele E, D'Angelo A, Tomaino C, Binetti G, Ghidoni R, Politi P, et al. Circulating levels of soluble receptor for advanced glycation end products in Alzheimer's disease and vascular dementia. *Arch Neurol* 2005; **62**(11): 1734-1736.

[6] Sengupta S, McArthur J, Sarkar A, Leng M, Ravenscroft P, Howarth R, et al. Do ponds cause arsenic-pollution of groundwater in the Bengal Basin? An answer from West Bengal. *Environ Sci Technol* 2008; **42**(14): 5156-5164.

[7] Oberoi S, Chaudhary N, Patnaik S, Singh A. Understanding health seeking behavior. *J Family Med Prim Care* 2016; **5**(2): 463-464.

[8] Liu Q, Jin WN, Liu Y, Shi K, Sun H, Zhang F, et al. Brain ischemia suppresses immunity in the periphery and brain *via* different neurogenic innervations. *Immunity* 2017; **46**(3): 474-487.

[9] Roy A, Kordas K, Lopez P, Rosado JL, Cebrian ME, Vargas GG, et al. Association between arsenic exposure and behavior among first-graders from Torreon, Mexico. *Environ Res* 2011; **111**(5): 670-676.

[10]Sun H, Yang Y, Shao H, Sun W, Gu M, Wang H, et al. Sodium arsenite-induced learning and memory impairment is associated with endoplasmic reticulum stress-mediated apoptosis in rat hippocampus. *Front Mol Neurosci* 2017; **10**: 286.

[11]Ouerghemmi S, Sebei H, Fratantonio D, Zena R, Cimino F, Cristani M. *Comparative studies on antioxidant activity of extracts from three wild Rosa species grown in different Tunisia regions*. Italia: Il ruolo della RICERCA farmacologica per la CRESCITA e la SALUTE; 2013, p. 131.

[12]Honarvar M, Javidnia K, Khosh-Khui M. Essential oil composition of fresh and dried flowers of *Rosa moschata* from Iran. *Chem Nat Compd* 2011; **47**: 826-828.

[13]Shashni S, Sharma S. Antioxidant activities of dried wild rosehips (*Rosa moschata*) of Kullu Valley, Northwestern Indian Himalaya. *Indian J Nat Prod Resour* 2022; **13**(3): 339-345.

[14]Ouerghemmi S, Sebei H, Siracusa L, Ruberto G, Saija A, Cimino F, et al. Comparative study of phenolic composition and antioxidant activity of leaf extracts from three wild *Rosa* species grown in different Tunisia regions: *Rosa canina* L., *Rosa moschata* Herrm. and *Rosa sempervirens* L. *Ind Crops Prod* 2016; **94**: 167-177.

[15]Alanazi H, Gul H, Farrukh M, Saleem U, Alsolami AM, Anwer A, et al. *Rosa moschata* leaf extract mitigates seizures, oxidative stress, and neurotransmitter imbalance in pentylenetetrazol-induced mice. *Ital J Food Sci* 2025; **37**(4): 488-505.

[16]Saleem U, Shehzad A, Shah S, Raza Z, Shah MA, Bibi S, et al. Antiparkinsonian activity of *Cucurbita pepo* seeds along with possible underlying mechanism. *Metab Brain Dis* 2021; **36**: 1231-1251.

[17]Bromley-Brits K, Deng Y, Song W. Morris water maze test for learning and memory deficits in Alzheimer's disease model mice. *J Vis Exp* 2011; **53**: 2920.

[18]Othman MZ, Hassan Z, Has ATC. Morris water maze: A versatile and pertinent tool for assessing spatial learning and memory. *Exp Anim* 2022; **71**(3): 264-280.

[19]Kraeuter AK, Guest PC, Sarnyai Z. The Y-maze for assessment of spatial working and reference memory in mice. In: Walker JM (ed.) *Methods in molecular biology*. Totowa: Humana Press Inc.; 2019, p. 105-111.

[20]Cai ZL, Wang CY, Jiang ZJ, Li HH, Liu WX, Gong LW, et al. Effects of cordycepin on Y-maze learning task in mice. *Eur J Pharmacol* 2013; **714**(1-3): 249-253.

[21]Bhangale JO, Acharya SR. Anti-Parkinson activity of petroleum ether extract of *Ficus religiosa* (L.) leaves. *Adv Pharmacol Pharm Sci* 2016; **2016**(1). doi: 10.1155/2016/9436106.

[22]Kim MJ, Choi SJ, Kim HK, Kim CJ, Hong B, Kim YJ, et al. Activation effects of *Allium tuberosum* Rottl. on choline acetyltransferase. *Biosci Biotechnol Biochem* 2007; **71**(1): 226-230.

[23]Sharma N, Bafna P. Effect of *Cynodon dactylon* on rotenone induced Parkinson's disease. *Orient Pharm Exp Med* 2012; **12**: 167-175.

[24]Hira S, Saleem U, Anwar F, Raza Z, Rehman AU, Ahmad B. *In silico* study and pharmacological evaluation of Eplerinone as an Anti-Alzheimer's drug in STZ-induced Alzheimer's disease model. *ACS Omega* 2020; **5**(23): 13973-13983.

[25]Saleem U, Akhtar R, Anwar F, Shah MA, Chaudary Z, Ayaz M, et al. Neuroprotective potential of *Malva neglecta* is mediated *via* down-regulation of cholinesterase and modulation of oxidative stress markers. *Metab Brain Dis* 2021; **36**: 889-900.

[26]Rahman MA, Hannan MA, Uddin MJ, Rahman MS, Rashid MM, Kim B. Exposure to environmental arsenic and emerging risk of Alzheimer's disease: Perspective mechanisms, management strategy, and future directions. *Toxics* 2021; **9**(8): 188.

[27]Lakshmi B, Sudhakar M, Prakash KS. Protective effect of selenium against aluminum chloride-induced Alzheimer's disease: Behavioral and biochemical alterations in rats. *Biol Trace Elem Res* 2015; **165**(1): 67-74.

[28]Farrukh M, Saleem U, Qasim M, Manan M, Shah MA. *Sarcococca saligna* extract attenuates formaldehyde-induced arthritis in Wistar rats *via* modulation of pro-inflammatory and inflammatory biomarkers. *Inflammopharmacology* 2022; **30**(2): 579-597.

[29]Shin MK, Kim HG, Kim KL. A novel trimeric peptide, Neuropep-1-stimulating brain-derived neurotrophic factor expression in rat brain improves spatial learning and memory as measured by the Y-maze and Morris water maze. *J Neurochem* 2011; **116**(2): 205-216.

[30]Aziz M, Sarkar K, Akter M. Y-maze, elevated plus maze and hole cross tests of *Richardia scabra* whole plant. *Pharmacol Online* 2016; **1**: 66-72.

[31]Jamal M, Rehman MU, Nabi M, Awan AA, Ali N, Sherkheli MA, et al. Evaluation of safety profile and stress suppressant activity of *Rosa moschata* in mice. *Pak J Pharm Sci* 2019; **32**(6): 2659-2665.

[32]Saw S, Mahato A, Kumar B, Kukreja V. Rose multiclassification: Harnessing hybrid CNN and random forest model. In: 2024 International Conference on Automation and Computation (AUTOCOM); 2024 Oct 12-14; Kolkata, India. Piscataway: IEEE; 2024, p. 215-219.

[33]Jiang J, Xiong YL. Natural antioxidants as food and feed additives to promote health benefits and quality of meat products: A review. *Meat Sci* 2016; **120**: 107-117.

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