Nootropic Potential and Amnesia Reversal Efficacy of Methanolic Leaf Extract of *Lantana camara* L. in Swiss Albino Mice: A Multi-Paradigm Behavioural Study

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ABSTRACT

Background: Memory loss and cognitive impairment are common features of neurodegenerative conditions and age-related brain changes. Medicinal plants rich in bioactive phytochemicals denote a promising path for the discovery of natural cognitive enhancers. *Lantana camara* L. is a extensively distributed shrub with documented antioxidant and neuroprotective properties, yet its direct nootropic effects remain insufficiently characterized.
Objective: This study aimed to assess the nootropic and memory-enhancing potential of methanolic extract of *Lantana camara* (MELC) in both normal mice and a Diazepam-induced amnesic mouse model, alongside its phytochemical characterization and antioxidant profiling.
Methods: Standard qualitative phytochemical tests, OECD 423-based acute oral toxicity evaluation, and DPPH free radical scavenging assay were carried out. Cognitive performance was assessed using four validated behavioral models: Elevated Plus Maze (EPM), Object Recognition Test (ORT), Hebb–Williams Maze (HWM), and Active Avoidance Paradigm (AAP). MELC was administered orally at 200 and 400 mg/kg. Piracetam (200 mg/kg, i.p.) was used as the standard nootropic drug, and diazepam (1 mg/kg, i.p.) was used to induce experimental amnesia. All data were analyzed statistically using one-way ANOVA followed by Dunnett's post-hoc test.
Results: Phytochemical screening detected the presence of flavonoids, tannins, saponins, steroids, and triterpenoids. No mortality or adverse effects were observed at doses up to 2000 mg/kg. MELC demonstrated potent concentration-dependent DPPH radical scavenging activity with an IC_{50} value of 15.82 µg/mL. In normal mice, oral administration of MELC significantly improved cognitive parameters, including reduced transfer latency in EPM, enhanced novel object discrimination in ORT, decreased total run count in HWM, and improved avoidance responses in AAP. In the diazepam-induced amnesic model, MELC markedly reversed the memory deficits across all behavioral paradigms. The 400 mg/kg dose consistently produced the most pronounced cognitive enhancement, with efficacy comparable to piracetam.
Conclusion: MELC demonstrates significant nootropic and antioxidant activities in preclinical models. The cognitive enhancement observed is likely attributable to the rich phytochemical composition, particularly flavonoids and saponins. These results support the potential of *L. camara* as a natural therapeutic agent in managing memory impairment and cognitive disorders. Further investigations to identify active constituents and clarify molecular mechanisms are warranted. This is the first study to demonstrate the nootropic potential of *Lantana camara* methanolic leaf extract across four complementary behavioural paradigms, underscoring its translational relevance as a candidate cognitive-enhancing agent.

Keywords: *Lantana camara*; nootropic activity; memory enhancement; antioxidant; diazepam-induced amnesia; cognitive dysfunction; Swiss albino mice; DPPH assay.

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1. INTRODUCTION

Memory is among the most critical higher cognitive functions of the central nervous system (CNS), underpinning processes of learning, information storage, and knowledge retrieval. Deficits in memory formation and recall are central features of several neurological and psychiatric conditions, including Alzheimer's disease (AD), Parkinson's disease, dementia, epilepsy, and age-associated cognitive decline. These disorders impose enormous personal, social, and economic burdens globally, and effective, safe pharmacological interventions remain an urgent clinical need (Voronina, 2023; Patel et al., 2024). Nootropics, or cognitive enhancers, are substances capable of improving memory, learning, attention, and concentration without producing significant adverse effects under normal conditions. Their mechanisms of action are diverse, encompassing modulation of cholinergic, glutamatergic, and GABAergic neurotransmission; promotion of cerebral blood flow; mitigation of oxidative stress; and neuroprotection. While synthetic agents such as piracetam and donepezil are commercially available, concerns about limited long-term efficacy, tolerability issues, and high cost have driven growing interest in plant-based alternatives (Shabanov, 2023; Patel et al., 2024).

Traditional systems of medicine have a longstanding history of employing herbal formulations to manage CNS-related disorders. A wide array of plant-derived bioactive compounds including flavonoids, alkaloids, terpenoids, and polyphenols have demonstrated the ability to reduce oxidative stress, suppress neuroinflammation, inhibit acetyl cholinesterase (AChE) activity, and promote neuronal survival. These activities form a plausible mechanistic basis for their cognitive-enhancing properties (Awuchi, 2023; Nour et al., 2014). *Lantana camara* L. (family Verbenaceae) is a pantropical medicinal shrub recognized in ethnobotanical practice for the treatment of inflammation, infectious diseases, fever, diabetes, epilepsy, and CNS-related ailments. Phytochemical investigations have documented the presence of flavonoids, saponins, tannins, alkaloids, glycosides, steroids, coumarins, and other bioactive constituents that exhibit broad pharmacological activities (Chaitali et al., 2022). Emerging neuropharmacological evidence strengthens the case for *L. camara* as a candidate nootropic. An aqueous extract of the plant was found to attenuate seizure frequency, elevate GABA levels, reduce oxidative stress, and ameliorate memory impairment in kainate-treated mice (Kandeda et al., 2022). Separately, a hydroethanolic leaf extract improved recognition memory and reduced neuroinflammatory markers including IL-1β, IL-6, TNF-α, and COX-2 in scopolamine-treated zebrafish and mice (Amoah et al., 2023). Additional studies indicate that ethanolic and aqueous extracts of the plant modulate GABAergic neurotransmission, oxidative stress indices, glutathione levels, and ferroptosis-related pathways (Talom et al., 2024).(Mushtaq et al. 2021) isolated an active fraction from Lavandula stoechas containing phenethylamine and α-tocopherol and found that it reversed scopolamine-induced memory loss in mice by reducing acetylcholinesterase activity and oxidative stress in the brain. (Don Bosco et al. 2024) used cheminformatics and system pharmacology to study how compounds from Withania somnifera, Bacopa monnieri, Curcuma longa, and Clitoria ternatea interact with Alzheimer's-related protein targets. They found that several withanolide compounds showed stronger predicted activity than existing approved drugs. (Kragel and Voss 2022) claim that, typical memory experiments, which rely on end-of-trial judgments, fail to capture the rapid brain processes that actually drive memory. (Robinson et al. 2020) used combined two-photon imaging and optogenetics to directly activate hippocampal place cells linked to specific locations in a virtual environment. (Agarwal et al. 2022) studied traditional herbal preparations, particularly from Ayurveda, that have long been used to support memory and cognitive function. (Nour et al.2014) investigated ethanolic extracts of four Malaysian plants, including *Centella asiatica* and *Lantana camara*, for antioxidant and acetylcholinesterase-inhibitory activity relevant to Alzheimer's disease.

Despite this body of evidence, the nootropic activity of the specific methanolic extract of *Lantana camara* (MELC) across multiple validated behavioral paradigms has not been formally documented. The present study was therefore designed to evaluate the nootropic potential of MELC in normal mice and in a diazepam-induced amnesic model using four complementary behavioral assays: Elevated plus Maze (EPM), Object Recognition Test (ORT), Hebb–Williams Maze (HWM), and Active Avoidance Paradigm (AAP). The study concurrently investigated the phytochemical profile and

antioxidant activity of the extract to identify probable mechanistic contributors to its cognitive effects.

2. MATERIALS AND METHODS

2.1 Drugs and Chemicals

All pharmacological agents and chemicals were of analytical grade. The test substance, extract of *Lantana camara* L. procured from Green Chem. Herbal Extract & Formulations, Bangalore, India. It was administered orally (p.o.) at doses of 200 and 400 mg/kg body weight. Standard reference drugs were administered intraperitoneally (i.p.). These standard agents included Diazepam at 1 mg/kg (procured from Manish Pharmaceuticals Ltd., Mumbai), Piracetam at 200 mg/kg (procured from Uni USB, India), and Haloperidol at 1 mg/kg (procured from RPG Life Sciences Ltd., Ankleshwar).

2.2 Experimental Animals

Swiss albino mice of either sex, weighing 25–30 g, were obtained from an approved animal house. Animals were housed under controlled laboratory conditions (12-hour light/dark cycle; ambient temperature 22 ± 2°C) with unrestricted access to standard pellet diet and potable water. Food was withheld for 2 hours prior to drug administration on experimental days. All experimental procedures were reviewed and approved by the Institutional Animal Ethics Committee (IAEC), following the guidelines of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Government of India. For the preliminary phytochemical screening, the methanolic extract was subjected to standard qualitative tests for the detection of major phytochemical classes, including alkaloids, flavonoids, saponins, tannins, phenolics, glycosides, steroids, and triterpenoids, using established reagent-based methods. Acute oral toxicity was assessed following OECD Guidelines 423. Graded doses of MELC were administered orally, and animals were observed continuously for 24 hours and then daily for 14 days for any behavioral changes, signs of distress, or mortality. Based on the established safety margin, doses of 200 and 400 mg/kg were selected for pharmacological studies. The free radical scavenging potential of MELC was quantified using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay. Varying concentrations of the extract (1–200 µg/mL) were incubated with a DPPH solution, and absorbance was recorded spectrophotometrically at 517 nm. Ascorbic acid was used as the reference antioxidant. Percentage inhibition was calculated and the IC_{50} value (concentration required to scavenge 50% of free radicals) was determined graphically. Further, MELC was suspended in 1% carboxymethyl cellulose (CMC) dissolved in warm distilled water. Fresh suspensions were prepared daily at concentrations corresponding to oral doses of 200 and 400 mg/kg. Solutions of diazepam, piracetam, and haloperidol were also freshly prepared before each administration.

2.3 Experimental Design

Animals were randomly distributed into four groups each containing five animals. (n = 5). Group I received vehicle with 1% CMC, p.o. and served as control. Group II received Piracetam with 200 mg/kg, i.p. as the standard nootropic drug. Groups III and IV received methanolic extract *Lantana camara* (MELC) at 200 and 400 mg/kg (p.o.), respectively. All treatments were administered once daily for seven consecutive days. Behavioural assessments were conducted 90 minutes post-dosing on days 6 and 7. Further, Diazepam-induced amnesia model was developed with five groups of mice (n = 5 per group). Group I (vehicle control) received 1% CMC. Group II (amnesic control) received Diazepam alone with 1 mg/kg, i.p.. Group III received Diazepam plus Piracetam with 200 mg/kg, i.p.. Groups IV and V received Diazepam plus MELC at 200 and 400 mg/kg (p.o.), respectively. The treatment regimen continued for 15 consecutive days, and all behavioural parameters were recorded on days 15 and 16.

2.4 Behavioural Assessment Models

The elevated plus maze (EPM) is a well-validated exteroceptive paradigm that exploits the conflict between the natural exploratory drive and aversion to open, elevated spaces. The EPM apparatus is shown in Figure 1. On Day 1 (acquisition trial), each mouse was placed at the distal end of an open arm, and the transfer latency (TL) defined as the time in seconds taken for the animal to move from the open arm into any enclosed arm with all four limbs was recorded (cut-off: 90 s). The mouse was subsequently allowed to freely explore the apparatus for 10 minutes. After 24 hours (Day 2, retention trial), TL was recorded again. The inflexion ratio (IR = TL on Day 1 / TL on Day 2) was calculated as an index of memory retention. A reduction in TL and an

increase in IR over successive trials indicate improved learning and memory consolidation.

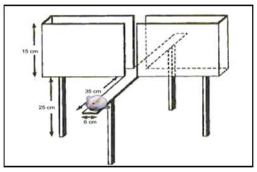

Figure 1. Elevated plus maze apparatus

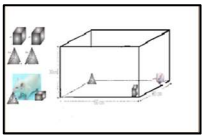

Figure 2. Object recognition test apparatus

Figure 3. Hebbs William maze apparatus

Figure 4. Active avoidance paradigm apparatus

The Object Recognition Test (ORT) exploits the innate tendency of rodents to preferentially explore novel stimuli. The ORT apparatus is shown in Figure 2. In the acquisition trial (T1), animals were placed in an open-field arena containing two identical objects for 5 minutes. Following a 90-minute intertrial interval, a retention trial (T2) was conducted in which one familiar object was replaced by a novel, differently shaped object. The time spent exploring the familiar object (TF) and novel object (TN) was recorded, and the discrimination index (DI = TN / (TF + TN)) was computed. A lower time with the familiar object and a higher DI indicates superior recognition memory. The Hebb–Williams Maze (HWM) as shown in Figure 3, is an incentive-driven exteroceptive spatial memory test. Animals were trained to navigate from a start box to a goal box containing a food reward. The total run count (TRC) the number of entries into incorrect (blind) alleys per trial was recorded across multiple sessions. A progressive and significant reduction in TRC across trials reflects improved spatial learning and memory retention. Treatment was administered for 7 days in normal animals and for 16 days in the amnesic model.

The Active Avoidance Paradigm (AAP) is a negative reinforcement-based model designed to measure associative learning and short-term memory. AAP apparatus is shown in Figure 4. Using a two-compartment shuttle box, a conditioned stimulus (buzzer, 10 s) was paired with an unconditioned stimulus (mild electric foot shock, 0.2 mA). Animals that successfully crossed to the safe compartment within the 10-second window before shock delivery were deemed to have performed an active avoidance response. Parameters recorded were: number of shocks received per 10 trials, and total time spent in the shock zone, assessed across learning (Day 1), relearning (Day 15), and retention (Day 16) phases.

2.5 Statistical Analysis

Quantitative data are expressed as mean ± SEM. Intergroup comparisons were performed using one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison post-hoc test. A probability value of $p < 0.05$ was considered statistically significant. All statistical computations were conducted using GraphPad Prism software.

3. RESULTS AND DISCUSSION

3.1 Phytochemical Screening

Qualitative phytochemical analysis of the MELC revealed the presence of tannins, saponins, flavonoids, steroids, and triterpenoids, while alkaloids and carbohydrates were absent.

3.2 Acute Oral Toxicity

The acute oral toxicity of MELC was evaluated in accordance with OECD 423 guidelines up to a limit dose of 2000 mg/kg. Throughout the observation period, the administration of the extract resulted in zero mortality. Furthermore, the treated animals did not exhibit any adverse behavioural alterations or clinical signs of toxicity, such as convulsions, excessive salivation, diarrhea, or respiratory distress. These findings suggest that the extract possesses a broad margin of safety at the tested dose. Based on these findings, doses of 200 and 400 mg/kg were selected for pharmacological evaluation. The safety profile supports the potential use of *Lantana camara* as a therapeutic candidate for long-term cognitive disorders.

3.3 In Vitro Antioxidant Activity

MELC demonstrated robust, concentration-dependent DPPH free radical scavenging activity ranging from 20.30 ± 0.033% at 1 µg/mL to 88.38 ± 0.015% at 200

µg/mL as mentioned in the Table 1. The IC_{50} value was calculated as 15.82 µg/mL, indicating potent antioxidant potential. Oxidative stress is a well-recognized driver of neuronal damage and progressive cognitive decline. The strong radical scavenging activity of MELC is likely attributable to its flavonoid and phenolic content, which can donate hydrogen atoms to neutralize reactive oxygen species and thereby protect neural tissue from oxidative injury.

Table 1. DPPH radical scavenging activity of MELC

Sr. No.	Concentration (µg/mL)	% Inhibition (Mean ± SEM)
1	1	20.30 ± 0.033
2	5	32.71 ± 0.023
3	10	48.26 ± 0.029
4	25	62.46 ± 0.009
5	50	78.36 ± 0.029
6	100	87.19 ± 0.025
7	200	88.38 ± 0.015

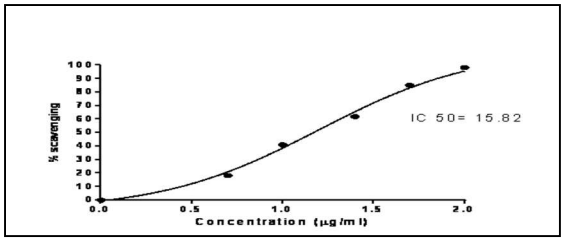

Figure 5. DPPH radical scavenging activity of MELC showing concentration-dependent antioxidant activity

3.4 Nootropic Activity in Normal Mice

Transfer latency (TL) in the Elevated Plus Maze (EPM) is an established index of both memory acquisition and retention. As presented in Table 2, MELC at 400 mg/kg produced a statistically significant reduction in TL on days 6 and 7 compared to the vehicle control group ($p < 0.01$). The inflexion ratio (IR) also increased significantly at this dose, particularly on day 7, indicating enhanced memory retention. The lower dose (200 mg/kg) showed a trend toward improvement but did not reach statistical significance. The response magnitude at 400 mg/kg was comparable to that of piracetam, the reference standard. Figure 6 shows the effect of *Lantana camara* on transfer latency in the EPM.

Table 2. Effect of MELC on transfer latency and inflexion ratio in the EPM (normal mice)

Group	Treatment	TL Day 6 (s)	TL Day 7 (s)	IR Day 6	IR Day 7
I	Vehicle control	39.6 ± 6.86	31.4 ± 7.06	0.30 ± 0.07	0.28 ± 0.10
II	Piracetam (200 mg/kg)	22.0 ± 2.17*	14.8 ± 1.11*	0.39 ± 0.04	0.77 ± 0.12
III	MELC 200 mg/kg	38.6 ± 5.86	31.6 ± 6.09	0.41 ± 0.04	0.39 ± 0.22
IV	MELC 400 mg/kg	16.0 ± 1.10**	12.8 ± 1.39**	0.51 ± 0.07*	1.52 ± 0.89**

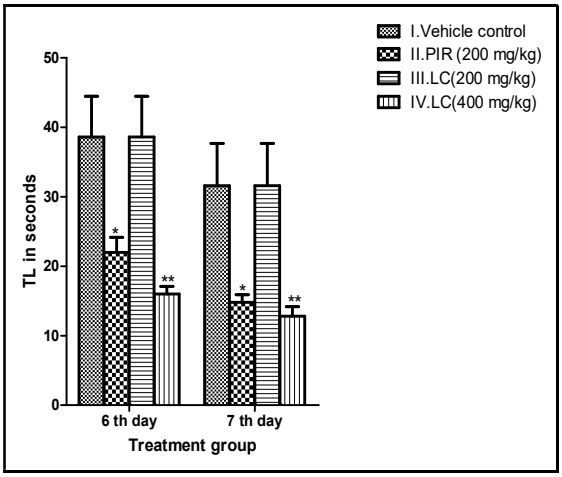

Figure 6. Effect of *Lantana camara* on transfer latency in the EPM

In the ORT, animals treated with MELC spent significantly less time exploring the familiar object and more time with the novel object compared to controls. The object recognition test evaluates recognition memory based on the natural exploratory behaviour of rodents. Animals treated with *Lantana camara* demonstrated better discrimination between familiar and novel objects, indicating improved recognition memory. Table 3 indicates the effect of MELC on recognition memory in the ORT for normal mice. The higher dose produced a stronger effect, suggesting dose-dependent cognitive enhancement.

Table 3. Effect of MELC on recognition memory in the ORT (normal mice)

Group	Familiar Object Time (s)	Novel Object Time (s)	Discrimination Index

Vehicle control	6.09 ± 0.86	12.25 ± 1.06	0.64 ± 0.03
Piracetam (200 mg/kg)	3.08 ± 0.22*	5.78 ± 1.02**	0.46 ± 0.06
MELC 200 mg/kg	5.50 ± 1.00	10.18 ± 0.65*	0.51 ± 0.02
MELC 400 mg/kg	3.66 ± 0.36*	8.00 ± 0.88**	0.36 ± 0.07

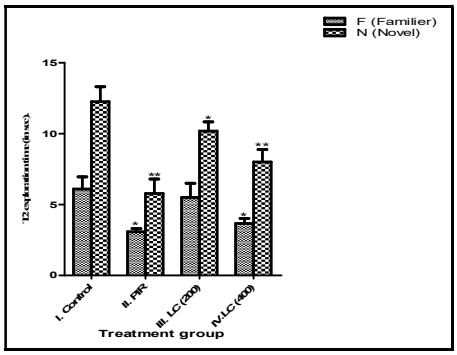

Figure 7. Effect of *Lantana camara* on object recognition performance.

Analysis of total run count (TRC) in the HWM showed significant reductions in extract-treated groups compared to the vehicle control on both days 6 and 7 (Table 4). MELC at 200 mg/kg ($p < 0.01$) and 400 mg/kg ($p < 0.01$) significantly decreased the number of blind-alley errors, with piracetam showing the greatest reduction ($p < 0.001$). A lower TRC reflects more efficient spatial navigation and better spatial memory encoding. The data support a dose-dependent improvement in spatial learning with MELC administration and are consistent with the EPM and ORT findings.

Table 4. Effect of MELC on total run count in the Hebb–Williams Maze

Group	Treatment	TRC Day 6 (errors)	TRC Day 7 (errors)
I	Vehicle control	339 ± 30.34	265 ± 22.94
II	Piracetam (200 mg/kg)	113.8 ± 4.58***	100.4 ± 3.61***
III	MELC 200 mg/kg	155 ± 13.28**	141 ± 6.66**
IV	MELC 400 mg/kg	137 ± 6.51**	130.6 ± 6.62**

Figure 8 shows the effect of *Lantana camara* on time to reach reward chamber in Hebb–Williams maze.

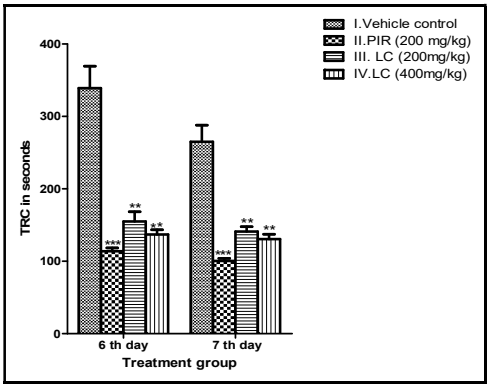

Figure 8. Effect of *Lantana camara* on time to reach reward chamber in Hebb–Williams maze

In the AAP, MELC administration produced progressive improvements in avoidance performance across the learning, relearning, and retention phases (Table 5). At 200 mg/kg, the number of shocks received and time spent in the shock zone were significantly reduced compared to vehicle control ($p < 0.05$). The 400 mg/kg dose resulted in more pronounced reductions in both parameters, with significance reaching $p < 0.01$ during the relearning and retention phases. These findings indicate that MELC enhances both the acquisition and consolidation of conditioned avoidance responses, reflecting improved short-term and long-term memory. Figure 9 and 10 indicate the effect of *Lantana camara* L. on number of shocks and on time spent in shock zone in AAP in normal mice respectively.

Table 5. Effect of MELC on active avoidance performance in normal mice

Treatment	Shocks Learning	Shocks Relearning	Shocks Retention	Time (s) Learning	Time (s) Relearning	Time (s) Retention
Control	12.90 ± 2.0	7.19 ± 0.4	4.40 ± 1.3	9.66 ± 1.4	7.16 ± 0.53	3.33 ± 0.4
Piracetam	3.10 ± 1.7*	4.00 ± 1.5*	2.20 ± 1.4*	2.60 ± 0.8*	3.66 ± 0.57*	2.89 ± 0.5
MELC 200 mg/k	4.90 ± 2.0*	5.19 ± 0.4*	4.40 ± 1.3	2.32 ± 1.66	4.35 ± 6.8*	3.50 ± 0.52

g						
MELC 400 mg/kg	6.25 ± 0.9*	5.08 ± 1.2**	3.12 ± 0.21**	4.06 ± 0.53	3.50 ± 0.67**	1.06 ± 0.30**

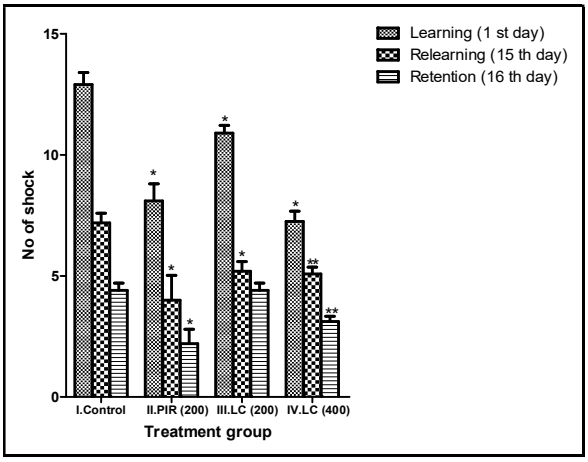

Figure 9. Effect of *Lantana camara* L. on number of shocks in AAP

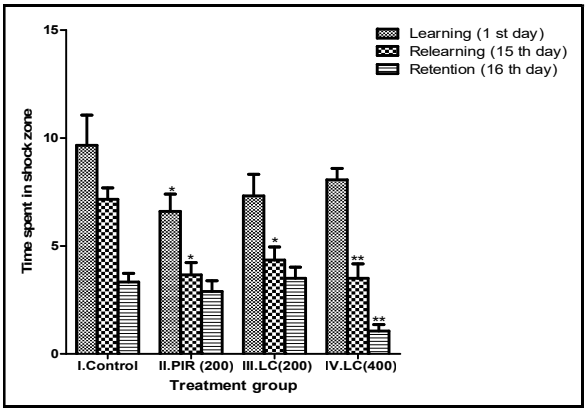

Figure 10. Effect of *Lantana camara* L. on time spent in shock zone in AAP

3.5 Nootropic Activity in Diazepam-Induced Amnesic Mice

Diazepam, a GABA-A receptor positive allosteric modulator, impairs memory consolidation by enhancing inhibitory neurotransmission. Administration of diazepam (1 mg/kg, i.p.) consistently worsened cognitive performance across all behavioural paradigms, validating the amnesic model. Treatment with MELC significantly attenuated these deficits in a dose-dependent manner.

3.5.1 Elevated Plus Maze

Diazepam administration markedly increased TL compared to the vehicle control, confirming memory impairment. Concurrent treatment with MELC (200 and 400 mg/kg) for 15 days significantly reduced TL on both days 15 and 16 compared to the diazepam-only group ($p < 0.05$; Table 6). The IR was also elevated in MELC-treated amnesic mice, indicating restored memory retention. The 400 mg/kg dose produced the greatest effect and showed comparable activity to piracetam. These findings suggest that MELC counteracts GABAergic over-inhibition induced by diazepam, possibly through its antioxidant constituents that protect hippocampal and cortical neuronal circuits involved in memory. Figure 11 shows the effect of *Lantana camara* L in TL on EPM in amnesic mice.

Table 6. Effect of MELC on transfer latency in the EPM in diazepam-induced amnesic mice

Group	Treatment	TL Day 15 (s)	TL Day 16 (s)
I	Vehicle control	49.2 ± 4.77	45.6 ± 4.53
II	Diazepam (amnesia control)	71.4 ± 3.66	67.0 ± 3.35
III	Diazepam + Piracetam	47.0 ± 2.86#	52.6 ± 3.17*#
IV	Diazepam + MELC 200 mg/kg	41.6 ± 3.95*#	36.0 ± 4.60*#
V	Diazepam + MELC 400 mg/kg	42.6 ± 4.93#	30.4 ± 3.83*#

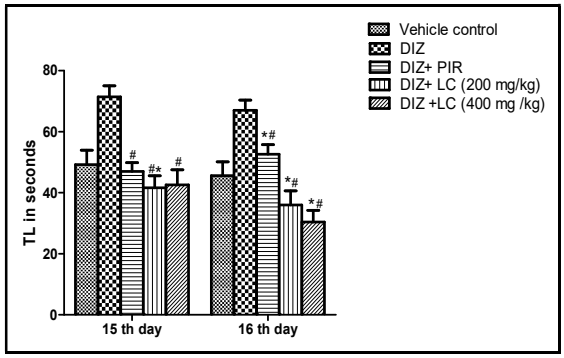

Figure 11. Effect *of Lantana camara* L in TL on elevated plus maze in amnesic mice

3.5.2 Object Recognition Test

Diazepam-treated mice showed impaired novel object discrimination compared to vehicle controls. Treatment with piracetam and MELC (both doses) significantly improved recognition memory, evidenced by reduced time spent with the familiar object, increased exploration of the novel object, and lower discrimination index values (Table 7). As Figure 12 shows the effect of *Lantana camara* L on ORT in diazepam treated mice. The 400 mg/kg dose produced the most notable improvement ($p < 0.05$). These observations indicate that MELC restores encoding of new information and recognition memory retrieval in amnesia-challenged animals.

Table 7. Effect of MELC on ORT performance in diazepam-induced amnesic mice

Treatment	T1 Total (s)	T2 Familiar (s)	T2 Novel (s)	Discrimination Index
Control	7.87 ± 0.69	4.00 ± 0.16	10.75 ± 1.26	0.54 ± 0.03
Diazepam	8.88 ± 0.25	3.18 ± 0.34	12.46 ± 0.88	0.59 ± 0.04
Diz + Piracetam	7.67 ± 2.22	1.70 ± 0.25*#	4.66 ± 0.52*#	0.46 ± 0.06
Diz + MELC 200 mg/kg	7.88 ± 0.38	1.51 ± 0.30*#	4.37 ± 0.77*#	0.47 ± 0.07
Diz + MELC 400 mg/kg	4.96 ± 0.84	2.16 ± 0.24*#	4.77 ± 0.18*#	0.37 ± 0.05

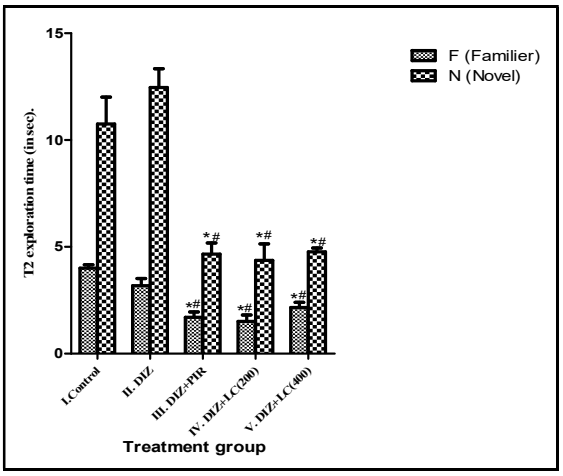

Figure 12. Effect of *Lantana camara* L on ORT in diazepam treated mice

3.5.3 Hebb–Williams Maze

Diazepam-induced amnesic mice exhibited a tendency toward elevated TRC compared to controls. Treatment with MELC at 400 mg/kg alongside diazepam resulted in a significant reduction in TRC on both days 15 and 16 ($p < 0.05$), while the 200 mg/kg dose produced only a mild, non-significant reduction (Table 8). Piracetam also significantly reduced TRC. Effect of *Lantana camara* L. in TRC on HWM in amnesic mice is shown in Figure 13. These outcomes suggest that higher doses of MELC are required to overcome the marked spatial memory impairment induced by diazepam, but that the extract retains its capacity to facilitate spatial learning even under pharmacological amnesic conditions.

Table 8. Effect of MELC on total run count in the HWM in diazepam-induced amnesic mice

Group	Treatment	TRC Day 15 (errors)	TRC Day 16 (errors)
I	Vehicle control	339 ± 38.96	267.8 ± 26.62
II	Diazepam	356 ± 28.95	279.0 ± 30.90
III	Diazepam + Piracetam	272.2 ± 38.76#	241.8 ± 31.55#
IV	Diazepam + MELC 200 mg/kg	328.2 ± 29.19#	297.2 ± 36.60
V	Diazepam + MELC 400 mg/kg	293.2 ± 37.06*#	225.6 ± 30.12#

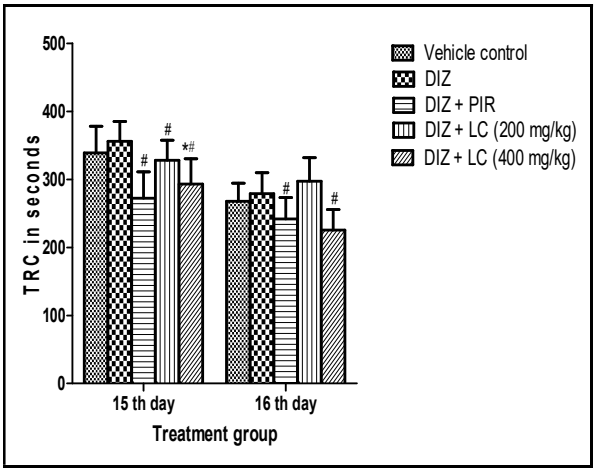

Figure 13. Effect of *Lantana camara* L. in TRC on Hebbs Wiliam maze in amnesic mice.

3.5.4 Active Avoidance Paradigm

In the amnesic model, diazepam consistently impaired avoidance performance. MELC at both 200 and 400 mg/kg significantly reduced the number of shocks received and time spent in the shock zone across learning, relearning, and retention phases compared to the diazepam-only group (Table 9). The 400 mg/kg group showed effects equivalent to piracetam across all phases, underscoring the dose-dependent efficacy of MELC in reversing pharmacologically induced memory impairment. This multi-phase improvement indicates that the extract enhances both initial learning and long-term consolidation of avoidance behaviour.

Table 9. Effect of MELC on active avoidance performance in diazepam-induced amnesic mice

Treatment	Shocks Learning	Shocks Relearning	Shocks Retention	Time(s) Learning	Time(s) Relearning	Time(s) Retention
Control	5.50 ±0.22	5.33 ±0.21	2.66 ±0.21	26.66±1.45	23.16±1.53	16.33±1.17
Diazepam	4.83 ±0.30	4.33 ±0.21	1.83 ±0.30*	20.00±1.18	20.66±2.57	14.33±0.55*
Diz+ Piracetam	4.33 ±0.33*	2.00 ±0.25**#	1.16 ±0.16**#	14.32±1.66*#	7.33 ±1.68*#	5.50 ±0.56*#
Diz+ MELC 200	4.33 ±0.33*	2.16 ±0.16**#	1.16 ±0.16**#	16.33±1.20*	9.00 ±1.03*#	5.83 ±0.70*#
Diz+ MELC 400	4.16 ±0.40*	1.83 ±0.16**#	1.00 ±0.00**#	14.16±1.53*#	7.50 ±0.67**#	4.16 ±0.30**#

Figure 14 and 15 indicate the effect of Lantana camara L. on number of shocks and on time spent in shock zone in AAP in diazepam-induced amnesic mice respectively.

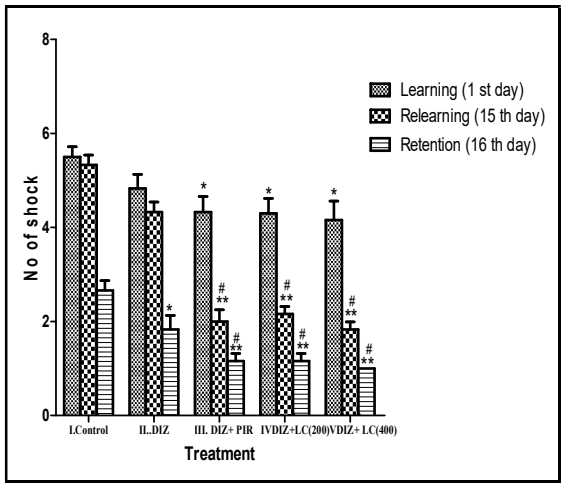

Figure 14. Effect of *Lantana camara* on AAP

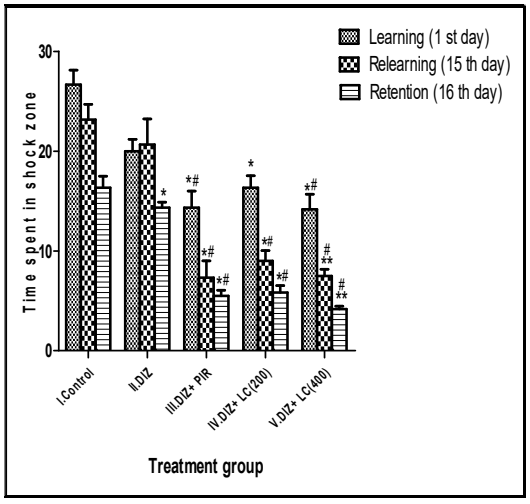

Figure 15. Effect of Lantana camara L. on Active avoidance paradigm

3.5.5 Summary of cognitive effects in amnesic model

Diazepam-induced amnesia is a widely accepted model for evaluating memory-enhancing agents. The extract significantly attenuated memory deficits produced by diazepam, suggesting neuroprotective and cognition-enhancing effects. The improvement observed across multiple behavioral paradigms indicates that *Lantana camara* enhances both acquisition and retention of memory. The effect may be associated with its antioxidant phytoconstituents, which reduce oxidative stress and protect neuronal function. Among the tested doses, 400 mg/kg consistently produced the best response and showed efficacy comparable to the standard drug piracetam.

Table 12. Summary of cognitive effects of MELC across behavioural models in diazepam-induced amnesia

Behavioral Model	Effect of Diazepam	Effect of MELC 400 mg/kg
Elevated Plus Maze	Increased TL (impaired learning)	Significant reduction in TL; increased IR (restored retention)
Object Recognition Test	Impaired novel object discrimination	Improved discrimination index; enhanced recognition memory
Hebb–Williams Maze	Elevated TRC (poor spatial navigation)	Significant reduction in TRC; improved spatial learning
Active Avoidance Paradigm	Increased shocks and shock zone duration	Reduced shocks and time in shock zone; improved avoidance retention

4. CONCLUSION

- The current investigation provides comprehensive preclinical evidence supporting the nootropic and antioxidant activities of the methanolic leaf extract of *Lantana camara* (MELC).
- Phytochemical screening identified flavonoids, tannins, saponins, steroids, and triterpenoids as principal bioactive constituents. Acute toxicity evaluation confirmed a favourable safety profile with no observed adverse effects at doses up to 2000 mg/kg. The extract exhibited potent DPPH radical scavenging activity (IC_{50} = 15.82 µg/mL), underscoring its significant antioxidant potential.
- Systematic evaluation across four validated behavioural paradigms the Elevated Plus Maze, Object Recognition Test, Hebb–Williams Maze, and Active Avoidance Paradigm demonstrated that MELC significantly enhanced learning, memory acquisition, and retention in normal mice.
- MELC effectively reversed diazepam-induced cognitive impairment, with the 400 mg/kg dose consistently producing the most pronounced benefits, comparable in magnitude to the standard nootropic drug piracetam.
- The results indicate that, *Lantana camara* represents a promising natural source of cognitive-enhancing agents. The mechanism of action is likely multifaceted, involving antioxidant-mediated neuroprotection, possible modulation of GABAergic and cholinergic neurotransmission, and anti-inflammatory effects. Future investigations should focus on the isolation and structural characterization of individual bioactive constituents, there in vitro and in vivo mechanisms of action, and long-term safety profiling to facilitate the development of plant-derived therapeutics for memory impairment and neurodegenerative disorders.

Conflict of Interest Statement

The authors declare that they have no known competing financial interest.

Ethical Declarations

All animal experiments were conducted in accordance with the guideline of the committee for the purpose of control and supervision of Experiments on Animals (CPCSEA), Government of India. The experimental protocol was reviewed and approved by the Institutional Animal Ethics Committee (IAEC) Having approval no.: [SSDJ/IAEC/2012/024].

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