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The Effect of Hydromethanolic Extracts of *Mangifera Indica* Stem Bark and Leaf on Learning and Memory in Electroconvulsive Therapy-Induced Seizures in Male Wistar Rats

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ABSTRACT

Electroconvulsive therapy (ECT), while clinically effective for treatment-resistant psychiatric disorders, has well-documented cognitive side effects, particularly impairments in learning and memory. The search for neuroprotective adjuvants from natural sources has gained interest. This study investigated the effects of hydromethanolic extracts of *Mangifera indica* stem bark (MSBE) and leaf (MLE) on learning and memory in male Wistar rats subjected to ECT-induced seizures. Cognitive performance was assessed using the navigational maze test and passive avoidance paradigm across four weeks. ECT-only rats showed significantly prolonged escape latencies in the maze (Week 3: 257.40 ± 9.27 s vs. Control 47.56 ± 2.27 s, $p < 0.05$) and reduced step-through latency in passive avoidance (Week 2: 0.20 ± 0.45 s vs. Control 3.60 ± 0.55 s, $p < 0.05$), indicating memory deficits. Treatment with MSBE (600 mg/kg) and MLE (600 mg/kg) markedly improved cognitive indices, reducing escape latency (Week 4: 77.20 ± 2.28 s and 68.37 ± 2.17 s, respectively) and increasing retention latency (Week 4: 2.80 ± 0.45 s and 3.00 ± 0.31 s, respectively) compared to ECT-only. These findings suggest that *M. indica* extracts mitigate ECT-induced cognitive impairments, likely through antioxidant and neuromodulatory effects.

KEYWORDS: Mangifera indica, electroconvulsive therapy, seizures, learning, memory, Wistar rats

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INTRODUCTION

Electroconvulsive therapy (ECT) remains a highly effective treatment for severe psychiatric disorders, including major depression and schizophrenia, but is often associated with significant cognitive impairments such as retrograde amnesia and deficits in learning and memory (Semkovska & McLoughlin, 2022). These adverse effects limit its clinical acceptability, underscoring the need for adjunctive agents to protect or restore cognitive function.

Natural products with antioxidant, anti-inflammatory, and neuroprotective properties are being explored as alternative therapeutic interventions for seizure-related cognitive dysfunction (Bali et al., 2023). *Mangifera indica* (mango), widely known for its ethnomedicinal use, contains bioactive compounds such as mangiferin, quercetin, and gallic acid, which exhibit neuroprotective, anxiolytic, and antioxidant effects (Shah et al., 2022; Akinmoladun et al., 2023). Both the stem bark and leaves of *M. indica* have been implicated in memory enhancement and seizure modulation, though comparative studies in ECT-induced models are limited.

This study investigates the effects of hydromethanolic extracts of *M. indica* stem bark (MSBE) and leaf (MLE) on learning and memory performance in male Wistar rats exposed to ECT-induced seizures, using the navigational maze and passive avoidance tests.

MATERIALS AND METHODS

Animals

42 adult male Wistar rats (150–200 g) were maintained under standard laboratory conditions with ad libitum access to food and water. All experimental procedures complied with

international ethical guidelines for the care and use of laboratory animals.

Experimental Design

Rats were divided into seven groups (n=6 per group):

1. Control – no treatment.
2. ECT only – received ECT without treatment.
3. ECT + DZP – received diazepam (5mg/kg).
4. ECT + MSBE 300 mg/kg.
5. ECT + MSBE 600 mg/kg.
6. ECT + MLE 300 mg/kg.
7. ECT + MLE 600 mg/kg.

Treatments were administered orally once daily for four weeks. ECT was induced using standard transcranial current application twice weekly.

Cognitive Assessments

- Navigational Maze Test: Escape latency (s) to reach the target was recorded weekly.
- Passive Avoidance Test: Step-through latency (s) to enter the dark chamber was recorded weekly as a measure of memory retention.

Statistical Analysis

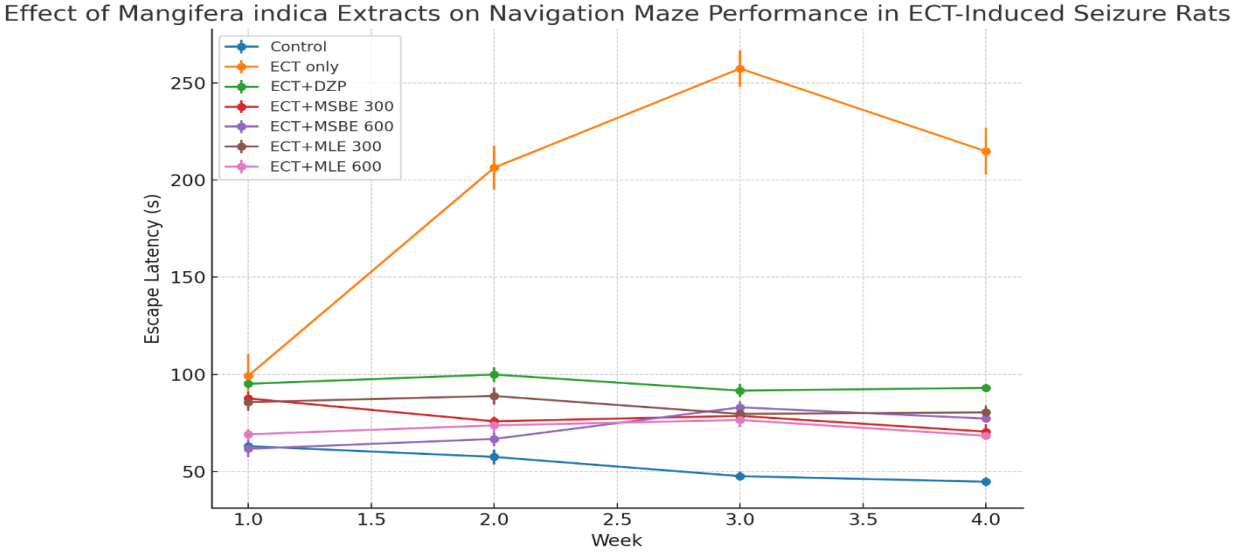
Data were expressed as mean ± SEM and analyzed using ANOVA followed by Tukey's post hoc test. $p < 0.05$ was considered significant.

RESULTS

Navigational Maze

	Week 1 (Sec)	Week 2 (Sec)	Week 3 (Sec)	Week 4 (Sec)
Control	63.00±4.44	57.48±3.87	47.56±2.27	44.70±2.29
ECT only	99.20±11.28[a]	206.40±11.30[a]	257.40±9.27[a]	214.80±11.98[a]
ECT+DZP	95.12±2.28[a]	99.88±3.81[a,b]	91.60±3.30[a,b]	93.00±2.04[a,b]
ECT+MSBE 300	87.60±3.07[a]	75.80±2.54[a,b]	78.60±2.05[a,b]	70.47±3.81[a,b]
ECT+MSBE 600	61.64±4.38[a, b]	66.72±3.74[a]	83.00±3.15[a,b]	77.20±2.28[a,b]
ECT+MLE 300	85.68±4.59[a]	88.84±4.37[a,b]	79.60±2.85[a,b]	80.40±3.53[a,b]
ECT+MLE 600	69.10±2.93[a, b]	73.70±3.79[a,b]	76.50±3.64[a,b]	68.37±2.17[a,b]

ECT-only rats demonstrated significantly prolonged escape latencies across all weeks compared to control (Week 3: 257.40 ± 9.27 s vs. 47.56 ± 2.27 s, $p < 0.05$), indicating impaired learning. Diazepam-treated rats showed reduced latencies compared to ECT-only (Week 4: 93.00 ± 2.04 s), but values remained higher than control. MSBE (600 mg/kg) and MLE (600 mg/kg) groups exhibited significant improvements, with Week 4 latencies of 77.20 ± 2.28 s and 68.37 ± 2.17 s, respectively, approaching control values.

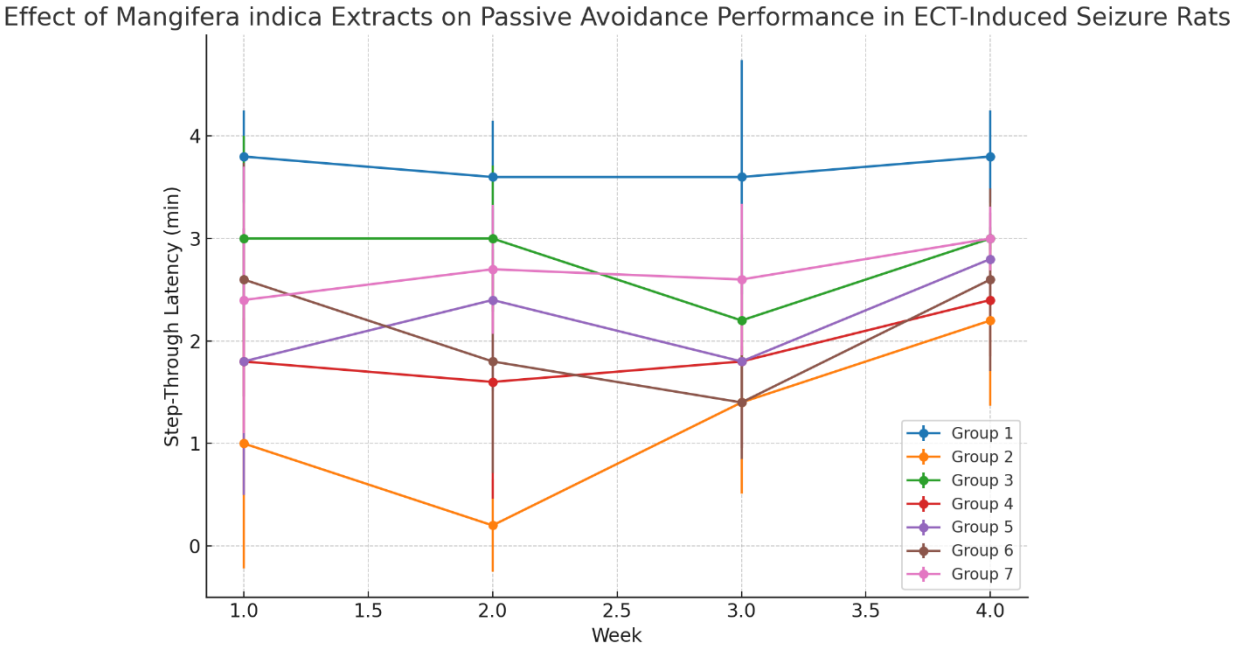


Passive Avoidance

	Week 1	Week 2	Week 3	Week 4
Group1	3.80±0.45 [a]	3.60±0.55 [a]	3.60±1.14 [a]	3.80±0.45 [a]
Group 2	1.00±1.22 [b]	0.20±0.45 [b]	1.40±0.89 [b]	2.20±0.83 [b]
Group 3	3.00±1.00 [a]	3.00±0.71 [a]	2.20±0.84 [a]	3.00±0.11 [a]
Group 4	1.80±1.30 [b]	1.60±1.14 [b]	1.80±0.84 [b]	2.40±0.55 [b]

Group 5	1.80±1.30 [b]	2.40±0.89 [a]	1.80±0.84 [b]	2.80±0.45 [a]
Group 6	2.60±1.14 [a]	1.80±1.09 [b]	1.40±0.55 [b]	2.60±0.89 [a]
Group 7	2.40±1.30 [a]	2.70±0.63 [a]	2.60±0.74 [a]	3.00±0.31 [a]

ECT-only rats had markedly reduced retention times (Week 2: 0.20 ± 0.45 s vs. control 3.60 ± 0.55 s, $p < 0.05$), reflecting memory impairment. Diazepam and MLE (600 mg/kg) groups showed near-normal retention (Week 4: 3.00 ± 0.11 s and 3.00 ± 0.31 s, respectively). MSBE (600 mg/kg) also improved retention (2.80 ± 0.45 s) relative to ECT-only.



DISCUSSION

This study demonstrates that hydromethanolic extracts of *M. indica* stem bark and leaves protect against ECT-induced learning and memory deficits in Wistar rats. ECT-only rats exhibited longer escape latencies and reduced passive avoidance retention, consistent with clinical reports of ECT-associated cognitive decline (Bodnar et al., 2023).

The observed neuroprotective effects of MSBE and MLE may be attributed to bioactive compounds such as mangiferin and polyphenols, which possess antioxidant and anti-inflammatory properties (Shah et al., 2022). These compounds likely mitigate oxidative stress and neuronal apoptosis induced by recurrent seizures and electrical stimulation (Patel et al., 2021). Furthermore, prior studies suggest that *M. indica* extracts modulate cholinergic and GABAergic neurotransmission, pathways crucial for memory formation and seizure control (Akinmoladun et al., 2023).

Interestingly, higher doses (600 mg/kg) of both MSBE and MLE were more effective, with MLE showing superior performance in passive avoidance tasks, suggesting differential distribution of bioactive metabolites in stem bark versus leaves. This highlights the therapeutic potential of *M. indica* as a plant-based adjunct in ECT protocols.

CONCLUSION

Hydromethanolic extracts of *Mangifera indica* stem bark and leaves significantly attenuate ECT-induced cognitive deficits in rats, improving both learning and memory. These findings support the potential of *M. indica* as a neuroprotective adjunct in managing ECT-related cognitive dysfunction. Further studies on molecular mechanisms and clinical translation are warranted.

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