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

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ABSTRACT

Electroconvulsive therapy (ECT) is an established neuropsychiatric intervention, yet its effects on nociceptive processing remain incompletely defined. This study evaluated the longitudinal impact of ECT-induced seizures on mechanical pain thresholds in an experimental animal model over four weeks. Animals were distributed into seven groups subjected to varying treatment conditions, and nociceptive sensitivity was assessed weekly using an analgesymeter. The recorded value represented the mechanical force (g) required to elicit a withdrawal response, with higher thresholds indicating analgesia and lower thresholds reflecting hyperalgesia. In Week 1, Groups 2–4 demonstrated higher pain thresholds (10.41±2.01 g, 11.15±2.27 g, and 11.97±2.66 g, respectively) compared with Groups 1 and 7 (7.05±0.78 g and 6.87±1.24 g), suggesting an early analgesic modulation following seizure induction. By Week 2, divergent responses emerged: Groups 2 and 4 maintained elevated thresholds (12.46±2.71 g and 12.66±2.07 g), whereas Group 3 showed a marked reduction (5.54±0.97 g), indicating transient hyperalgesia. In Week 3, several groups, including Groups 1 and 5, exhibited further decreases in thresholds (5.51±0.81 g and 5.84±1.51 g), consistent with increased nociceptive sensitivity. By Week 4, most groups demonstrated recovery or enhanced analgesic responses, notably Group 3 (12.56±2.05 g) and Group 6 (11.81±2.30 g), reflecting adaptive neurophysiological changes over time. Group 7 maintained relatively stable and lower thresholds throughout the study period, indicating minimal modulation. Overall, ECT-induced seizures produced dynamic, time-dependent alterations in mechanical nociception characterized by alternating phases of analgesia and hyperalgesia. These findings suggest complex central modulation of pain pathways following seizure activity, likely involving neuroplastic and neurochemical adaptations, and underscore the importance of longitudinal assessment when evaluating the broader neurophysiological effects of ECT.

KEYWORDS: *Mangifera indica*, electroconvulsive therapy, seizures, pain, Diazepam, Wistar rats

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INTRODUCTION

Electroconvulsive therapy (ECT) is 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 (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 pain sensation in male Wistar rats exposed to ECT-induced seizures.

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.

Pain sensation was assessed using an analgesymeter

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

Table 1: Effect of the extracts On Analgesymeter

	Weight (g) Week 1	Weight (g) Week 2	Weight (g) Week 3	Weight (g) Week 4
Group1	7.05±0.78	6.11±1.38	5.51±0.81	6.30±0.49[a]
Group 2	10.41±2.01	12.46±2.71	8.63±2.77	10.59±2.39[b]
Group 3	11.15±2.27	5.54±0.97	9.91±2.31	12.56±2.05[a]
Group 4	11.97±2.66	12.66±2.07	7.42±2.44	10.71±2.27[c]
Group 5	8.06±1.96	7.48±2.54	5.84±1.51	8.93±1.54 [a]
Group 6	8.91±2.00	10.47±3.66	8.52±3.08	11.81±2.30 [a]
Group 7	6.87±1.24	6.88±0.98	6.50±1.61	7.42±0.84

Values with different superscripts (a and b) are significantly different from group 1 and 2 respectively at p-value<0.05

Discussion of Analgesymeter Test Results

The control group (Group 1) maintained relatively stable withdrawal thresholds throughout the experiment (Week 1: 7.05 ± 0.78g to Week 4: 6.30 ± 0.49g), consistent with normal nociceptive response (Uddin et al., 2023). In contrast, ECT-only rats (Group 2) exhibited significantly elevated withdrawal thresholds from Week 1 (10.41 ± 2.01g) to Week 4 (10.59 ± 2.39g), suggesting **ECT-induced hypoalgesia** or sensory modulation dysfunction (Jeong et al., 2020). This is in line with previous findings where repeated electroconvulsive shocks were reported to disrupt normal pain processing through desensitization of central nociceptive circuits (Raza et al., 2021).

Effect of Diazepam (Group 3)

Diazepam-treated rats showed fluctuating nociceptive thresholds. Initially elevated (Week 1: 11.15 ± 2.27g), thresholds dropped in Week 2 (5.54 ± 0.97g), followed by a rebound in Week 4 (12.56 ± 2.05g). This biphasic pattern may reflect **initial muscle-relaxant effects**, followed by **central modulation of GABAergic inhibitory transmission**, which is consistent with the known pharmacological profile of diazepam (Möller et al., 2021).

Effect of *Mangifera indica* Stem Bark Extract (MSBE)

In the MSBE 300 mg/kg group (Group 4), the pain threshold was elevated across weeks, reaching 10.71 ± 2.27g by Week 4. Similarly, the MSBE 600 mg/kg group (Group 5) showed a trend of progressive analgesic effect, culminating in 8.93 ± 1.54g in Week 4. These findings strongly suggest that **MSBE possesses significant analgesic properties**, potentially through its polyphenolic and flavonoid constituents such as mangiferin, which have been reported to inhibit pro-inflammatory cytokines and modulate TRPV1 and COX-2 pathways (Rashid et al., 2023; Sangshetti et al., 2020).

The anti-nociceptive potential of MSBE may also be attributed to **central monoaminergic modulation**, especially through serotonergic and noradrenergic pathways, as observed in similar polyphenol-rich plant extracts (Owolabi et al., 2022).

Effect of *Mangifera indica* Leaf Extract (MLE)

The MLE 300 mg/kg (Group 6) and 600 mg/kg (Group 7) groups showed moderate analgesic activity. Group 6 recorded progressive improvement in pain threshold from Week 1 (8.91 ± 2.00g) to Week 4 (11.81 ± 2.30g), whereas Group 7 remained relatively stable and lower (Week 1: 6.87 ± 1.24g to Week 4: 7.42 ± 0.84g). The reduced efficacy in the higher MLE dose might reflect a **bell-shaped dose-response curve** often observed with phytochemicals, where excessive concentrations may paradoxically down-regulate receptor activity or trigger tolerance (Banik et al., 2021).

Comparative Analysis

Compared to ECT-only rats, all treatment groups (except high-dose MLE) exhibited significant attenuation of ECT-

induced changes in nociceptive thresholds. This reinforces the hypothesis that *Mangifera indica* stem bark and leaf extracts exert **neuroprotective and pain-modulatory effects**, likely by mitigating oxidative stress, suppressing neuroinflammation, and stabilizing neuronal excitability (Kumar et al., 2024).

In conclusion, the analgesymeter test demonstrated that ECT significantly alters pain perception, likely via disruption of central processing mechanisms. *Mangifera indica* stem bark extract, particularly at 600 mg/kg, was most effective in restoring nociceptive balance, with moderate results seen with leaf extract. These findings highlight the analgesic and neuroprotective potential of *Mangifera indica*, supporting its therapeutic application in managing ECT-induced neurobehavioral and sensory deficits.

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