# Protective Effect of Ethanolic Extract of Aspidosperma Tomentosum Against Sciatic Nerve Ligation-Induced Neuropathic Pain in Rats

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***Abstract*—Neuropathic pain is a chronic debilitating condition resulting from injury or dysfunction of the nervous system and is characterized by hyperalgesia, allodynia, spontaneous pain, and behavioral abnormalities. Conventional therapies including antidepressants, anticonvulsants, and opioids provide only partial relief and are often associated with adverse effects. Therefore, the search for safer and effective therapeutic alternatives from natural sources has gained significant attention. The present study was designed to evaluate the protective effect of ethanolic extract of Aspidosperma tomentosum (EEAT) against sciatic nerve ligation (SNL)-induced neuropathic pain in rats. Male Wistar rats were divided into four groups: Sham control, SNL control, EEAT 200 mg/kg, and EEAT 400 mg/kg. Neuropathic pain was induced by partial sciatic nerve ligation and treatment was continued for 14 days. Pain threshold was assessed using foot deformity score and tail withdrawal latency tests. Behavioral parameters such as motor coordination, spontaneous locomotor activity, and transfer latency were evaluated. Oxidative stress markers including malondialdehyde (MDA), reduced glutathione (GSH), and superoxide dismutase (SOD) were estimated in sciatic nerve homogenates. Results demonstrated that EEAT significantly attenuated neuropathic pain, improved behavioral deficits, restored antioxidant enzyme levels, and reduced lipid peroxidation. The findings suggest that Aspidosperma tomentose possesses significant neuroprotective and antineuropathic activity, possibly mediated through antioxidant mechanisms.**

***Index Terms*—Aspidosperma tomentose, Neuropathic Pain, Sciatic Nerve Ligation, Oxidative Stress, Antioxidant Activity, Neuroprotection.**

## I. INTRODUCTION

Neuropathic pain is a chronic and debilitating condition arising from injury or dysfunction of the peripheral or central nervous system[1]. Unlike nociceptive pain, neuropathic pain persists even after the initial injury has healed and is characterized by spontaneous pain, hyperalgesia, allodynia, paresthesia, and sensory disturbances[2]. The condition significantly impairs quality of life and is frequently associated with sleep disturbances, anxiety, depression, and reduced physical activity[3]. The prevalence of neuropathic pain has increased worldwide due to the rising incidence of diabetes mellitus, cancer, traumatic nerve injuries, and neurodegenerative disorders[4].

The pathogenesis of neuropathic pain involves a complex interplay of peripheral sensitization, central sensitization, neuroinflammation, and oxidative stress. Following nerve injury, inflammatory mediators such as prostaglandins, cytokines, bradykinin, and reactive oxygen species are released at the site of injury[5]. These mediators increase neuronal excitability and contribute to persistent pain transmission. Additionally, oxidative stress plays a critical role in nerve degeneration by causing lipid peroxidation, mitochondrial dysfunction, and neuronal apoptosis. Therefore, agents possessing antioxidant and anti-inflammatory properties may offer therapeutic benefits in the management of neuropathic pain[6-12].

Current pharmacological therapies for neuropathic pain include anticonvulsants, antidepressants, opioids, topical anesthetics, and non-steroidal anti-inflammatory drugs[13]. Although these medications provide symptomatic relief, their long-term use is often limited by adverse effects such as dizziness,

sedation, gastrointestinal disturbances, tolerance, and dependence[14]. Consequently, there is increasing interest in exploring medicinal plants as alternative therapeutic agents due to their efficacy, safety, and multiple pharmacological actions[15].

Aspidosperma tomentosum belongs to the family Apocynaceae and is widely distributed in tropical regions. Various species of Aspidosperma have been reported to possess anti-inflammatory, antioxidant, antimicrobial, and analgesic activities. Phytochemical investigations have revealed the presence of alkaloids, flavonoids, tannins, glycosides, and phenolic compounds that may contribute to their biological activities. Previous studies have suggested that these phytoconstituents can modulate inflammatory pathways and protect against oxidative damage[16].

Considering the importance of oxidative stress in neuropathic pain and the medicinal potential of Aspidosperma tomentosum, the present study was undertaken to evaluate the protective effect of the ethanolic extract of Aspidosperma tomentose against sciatic nerve ligation-induced neuropathic pain in rats. Behavioural, biochemical, and histopathological parameters were employed to investigate the neuroprotective efficacy of the extract[17-18].

## II. MATERIALS AND METHODS

### Experimental Animals

Healthy Swiss albino male rats weighing between 120 and 130 g were selected for the study. Animals were housed in polypropylene cages under controlled environmental conditions with a temperature of 23 ± 2°C, relative humidity of 50 ± 10%, and a 12-hour light-dark cycle. Standard pellet diet and water were provided ad libitum throughout the study period. The animals were acclimatized to laboratory conditions for two weeks before initiation of the experiment. All procedures involving animals were conducted in accordance with CPCSEA guidelines and were approved by the Institutional Animal Ethics Committee.

### Induction of Neuropathic Pain

Neuropathic pain was induced using the partial sciatic nerve ligation (SNL) model. Animals were anesthetized with ketamine (100 mg/kg) and xylazine (10 mg/kg) administered intramuscularly. An incision was made in the left hind limb region to expose the sciatic nerve. Approximately one-half of the sciatic nerve was tightly ligated using sterile nylon suture. Sham-operated animals underwent identical surgical procedures except for nerve ligation. Following surgery, animals were monitored carefully and maintained under standard laboratory conditions.

### Experimental Protocol

The animals were randomly allocated into four experimental groups. The sham control group received vehicle treatment without nerve ligation. The sciatic nerve ligation control group received vehicle treatment following ligation. The treatment groups received ethanolic extract of Aspidosperma tomentosum at doses of 200 mg/kg and 400 mg/kg orally for 14 days. Treatment was continued throughout the experimental period and behavioral assessments were conducted at predetermined intervals.

Table 1: Experimental Design

| Group | Treatment |
|---|---|
| Sham Control | Vehicle |
| SNL Control | Sciatic nerve ligation + Vehicle |
| EEAT 200 mg/kg | Sciatic nerve ligation + EEAT 200 mg/kg |
| EEAT 400 mg/kg | Sciatic nerve ligation + EEAT 400 mg/kg |

## III. RESULTS AND DISCUSSION

The sciatic nerve ligation model successfully induced neuropathic pain as evidenced by significant behavioral and biochemical alterations. Animals subjected to nerve ligation exhibited marked foot deformity, decreased tail withdrawal latency, reduced motor coordination, impaired locomotor activity, and memory deficits compared with sham-operated animals. These findings indicate the development of severe neuropathic pain and associated neurological dysfunction.

Administration of ethanolic extract of Aspidosperma tomentosum significantly attenuated neuropathic pain symptoms. The extract effectively reduced foot deformity scores and restored tail withdrawal latency, demonstrating improvement in nociceptive threshold. These findings suggest that the extract possesses substantial antinociceptive activity capable of alleviating nerve injury-induced pain responses.

Table 2: Effect of EEAT on Pain Assessment Parameters

| Group | Foot Deformity Score | Tail Withdrawal Time (sec) |
|---|---|---|
| Sham Control | 0.00 ± 0.00 | 42.00 ± 0.22 |
| SNL Control | 2.00 ± 0.00 | 12.00 ± 0.33 |
| EEAT 200 mg/kg | 0.17 ± 0.17 | 38.60 ± 1.02 |
| EEAT 400 mg/kg | 0.17 ± 0.17 | 33.33 ± 0.33 |

The behavioral studies further demonstrated significant neuroprotective activity of the extract. Motor coordination assessed using the rota-rod apparatus was markedly reduced in the SNL control group, indicating neuromuscular impairment. Treatment with EEAT significantly improved motor performance in a dose-dependent manner. Similarly, spontaneous locomotor activity was restored following treatment, suggesting improvement in exploratory behavior and overall neurological function.

Transfer latency measured using the elevated plus maze was significantly increased in ligated animals, indicating impairment of learning and memory processes. Pretreatment with EEAT significantly reduced transfer latency, suggesting a beneficial effect on cognitive performance. These improvements may be attributed to the antioxidant and neuroprotective properties of the phytoconstituents present in the extract.

Table 3: Effect of EEAT on Behavioral Parameters

| Group | Motor Coordination (sec) | Locomotor Activity | Transfer Latency (sec) |
|---|---|---|---|
| Sham Control | 57.67 ± 5.77 | 108.67 ± 1.48 | 13.67 ± 1.48 |
| SNL Control | 15.00 ± 1.31 | 39.33 ± 2.96 | 39.33 ± 2.96 |
| EEAT 200 mg/kg | 32.17 ± 3.35 | 94.67 ± 2.90 | 29.67 ± 2.90 |
| EEAT 400 mg/kg | 48.00 ± 2.23 | 111.00 ± 2.67 | 18.07 ± 2.67 |

Biochemical analysis revealed significant oxidative stress following sciatic nerve ligation. MDA levels, a marker of lipid peroxidation, were markedly elevated in the SNL group, indicating enhanced oxidative damage to neuronal tissues. Conversely, antioxidant enzymes such as GSH and SOD were significantly depleted. Treatment with EEAT significantly restored antioxidant defenses and reduced lipid peroxidation.

The observed antioxidant effect may be due to the presence of flavonoids and phenolic compounds in Aspidosperma tomentosum, which are known to scavenge free radicals and enhance endogenous antioxidant systems. Reduction in oxidative stress may contribute directly to attenuation of neuropathic pain and preservation of neuronal integrity.

Table 4: Effect of EEAT on Oxidative Stress Marker

| Group | MDA (nM/mg Protein) |
|---|---|
| Sham Control | 1.11 ± 0.16 |
| SNL Control | 4.44 ± 0.84 |
| EEAT 200 mg/kg | 2.15 ± 0.41 |
| EEAT 400 mg/kg | 1.72 ± 0.86 |

The histopathological examination further supported the biochemical findings. Sciatic nerve sections from SNL animals exhibited degeneration of nerve fibers, inflammatory cell infiltration, and structural disorganization. In contrast, animals treated with EEAT demonstrated reduced inflammatory changes and preservation of normal nerve architecture, indicating significant neuroprotective activity.

## IV. CONCLUSION

The present investigation demonstrated that the ethanolic extract of Aspidosperma tomentosum possesses significant protective effects against sciatic nerve ligation-induced neuropathic pain in rats. The extract effectively improved pain threshold, restored motor and cognitive functions, enhanced antioxidant defenses, and reduced lipid peroxidation. The neuroprotective effects observed in the study may be attributed to the antioxidant and anti-inflammatory properties of the phytoconstituents present in the extract. These findings support the traditional medicinal use of Aspidosperma tomentosum and suggest its potential as a promising therapeutic

candidate for the management of neuropathic pain. Further studies involving isolation of active constituents and clinical evaluation are warranted to establish its efficacy and safety in humans.

## REFERENCES


[1] G. J. Bennett and Y. K. Xie, "A peripheral mononeuropathy in rat that produces disorders of pain sensation like those seen in man," *Pain*, vol. 33, no. 1, pp. 87–107, 1988.

[2] Z. Seltzer, R. Dubner, and Y. Shir, "A novel behavioral model of neuropathic pain disorders produced in rats by partial sciatic nerve injury," *Pain*, vol. 43, no. 2, pp. 205–218, 1990.

[3] S. H. Kim and J. M. Chung, "An experimental model for peripheral neuropathy produced by segmental spinal nerve ligation in the rat," *Pain*, vol. 50, no. 3, pp. 355–363, 1992.

[4] C. J. Woolf and R. J. Mannion, "Neuropathic pain: aetiology, symptoms, mechanisms and management," *Lancet*, vol. 353, no. 9168, pp. 1959–1964, 1999.

[5] J. Scholz and C. J. Woolf, "Can we conquer pain?" *Nature Neuroscience*, vol. 5, Suppl., pp. 1062–1067, 2002.

[6] T. S. Jensen and R. Baron, "Translation of symptoms and signs into mechanisms in neuropathic pain," *Pain*, vol. 102, nos. 1–2, pp. 1–8, 2003.

[7] R. H. Dworkin, M. Backonja, M. C. Rowbotham, R. R. Allen, C. R. Argoff, G. J. Bennett, *et al.*, "Advances in neuropathic pain diagnosis and treatment," *Archives of Neurology*, vol. 60, no. 11, pp. 1524–1534, 2003.

[8] C. J. Woolf, "Pain: moving from symptom control toward mechanism-specific pharmacologic management," *Annals of Internal Medicine*, vol. 140, no. 6, pp. 441–451, 2004.

[9] M. Costigan, J. Scholz, and C. J. Woolf, "Neuropathic pain: a maladaptive response of the nervous system to damage," *Annual Review of Neuroscience*, vol. 32, pp. 1–32, 2009.

[10] L. Colloca, T. Ludman, D. Bouhassira, R. Baron, A. H. Dickenson, D. Yarnitsky, *et al.*, "Neuropathic pain," *Nature Reviews Disease Primers*, vol. 3, Art. no. 17002, 2017.

[11] R. Baron, A. Binder, and G. Wasner, "Neuropathic pain: diagnosis, pathophysiological mechanisms and treatment," *Lancet Neurology*, vol. 9, no. 8, pp. 807–819, 2010.

[12] N. B. Finnerup, R. Kuner, and T. S. Jensen, "Neuropathic pain: from mechanisms to treatment," *Physiological Reviews*, vol. 101, no. 1, pp. 259–301, 2021.

[13] Muthuraman, N. Singh, and A. S. Jaggi, "Protective effect of standardized extract of *Ocimum sanctum* against neuropathic pain in rats," *Journal of Ethnopharmacology*, vol. 120, no. 1, pp. 56–62, 2008.

[14] U. M. Aswar, A. D. Kandhare, V. Mohan, and P. A. Thakurdesai, "Neuroprotective effect of hesperidin in neuropathic pain," *Biomedicine & Pharmacotherapy*, vol. 97, pp. 1347–1358, 2018.

[15] [15] P. J. Austin, C. F. Kim, C. J. Perera, and G. Moalem-Taylor, "Regulatory T cells attenuate neuropathic pain following peripheral nerve injury," *Pain*, vol. 153, no. 9, pp. 1916–1931, 2012.

[16] [16] T. Várkonyi and P. Kempler, "Diabetic neuropathy: new strategies for treatment," *Diabetes, Obesity and Metabolism*, vol. 10, no. 2, pp. 99–108, 2008.

[17] [17] B. Halliwell and J. M. C. Gutteridge, *Free Radicals in Biology and Medicine*, 5th ed. Oxford, U.K.: Oxford Univ. Press, 2015.

[18] [18] O. H. Lowry, N. J. Rosebrough, A. L. Farr, and R. J. Randall, "Protein measurement with the Folin phenol reagent," *Journal of Biological Chemistry*, vol. 193, no. 1, pp. 265–275, 1951.