International Journal for Multidisciplinary Research
National Conference on Sciences, Pharmacy, Humanities & Commerce, Engineering for Research and Education (SPHERE – 2025)
Organized by S.P.D.M. Arts, S.B.B. and S.H.D. Commerce, and S.M.A. Science College, Shirpur in Association with PM USHA soft component, KBC NMU Jalgaon (MS)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Neuroprotective Effects of Alpha-Lipoic Acid and Ferulic Acid on Chronic Constriction Injury Induced Peripheral Neuropathic Pain in Rats

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ABSTRACT

Background: Peripheral neuropathic pain (PNP), a persistent and incapacitating illness caused by nerve injury or metabolic imbalances, is characterised by increased nociceptive sensitivity and neuroinflammation. A model of chronic constriction injury (CCI) in rats closely resembles PNP in humans. Alpha-lipoic acid (ALA) and ferulic acid (FA), two naturally occurring antioxidants, have potent neuroprotective and anti-inflammatory properties. This work investigated and compared the therapeutic potential of ALA, FA, and their combination with the popular drug gabapentin in a CCI-induced PNP model in rats.

Methods: Five adult groups (n=6) Group I: Disease Control, Group II: Gabapentin (30 mg/kg, i.p.), Group III: alpha-lipoic acid (25 mg/kg, p.o.), Group IV: ferulic acid (10 mg/kg, p.o.), and a combination of Group V: alpha-lipoic acid + ferulic acid (12 mg/kg + 5 mg/kg, p.o.) were administered to Wistar rats. The behavioural assessments included mechanical allodynia (von Frey), cold allodynia (acetone), thermal allodynia (hot plate), and mechanical hyperalgesia (pinprick). Biochemical analyses assessed SOD, CAT, GSH, MDA, and TNF-α levels in sciatic nerve homogenates, while histopathological analysis assessed axonal integrity and inflammation.

Result: CCI significantly increased oxidative stress, pro-inflammatory markers, and nociceptive behaviour. Small improvements were seen with ALA or FA alone. Nevertheless, their combined effects were very similar to gabapentin's, considerably lowering pain behaviour and returning oxidative and

inflammatory indicators to normal. Histology demonstrated improved axonal preservation in combination-treated rats.

Conclusion: ALA and FA's synergistic neuroprotective and antioxidant properties, especially when combined, suggest that they may be used as an adjuvant or alternative treatment for PNP.

Keywords: Alpha-Lipoic Acid, Ferulic Acid, Chronic Constriction Injury, Peripheral Neuropathic Pain.

1. Introduction

Peripheral neuropathic pain (PNP) is defined as that the pain that arises directly from injury or disease affecting the somatosensory nervous system [1]. These clinically manifested by abnormal sensory experiences like as spontaneous pain, allodynia, and hyperalgesia reflecting disrupted pain processing and lowered nociceptive thresholds [1,2]. The International Association for the Study of Pain (IASP) has emphasized its distinct neurobiological basis, differentiating it from nociceptive pain conditions [1]. Epidemiological data indicate that PNP affects approximately 6–10% of the population, with higher prevalence in individuals with diabetes, nerve trauma, and post-herpetic neuralgia [2,3]. Additionally, a substantial proportion of chronic pain patients exhibit neuropathic features, contributing to significant morbidity, reduced the quality of life, and increased healthcare burden [3].

The pathophysiology of PNP involves complex mechanisms including peripheral and central sensitization triggered by nerve injury [4]. Damage to peripheral nerves leads to abnormal ion channel expression, particularly sodium and calcium channels, that resulting in the neuronal hyperexcitability and spontaneous ectopic discharges [4,5]. Enhanced calcium influx further promotes excitatory neurotransmitter release in the spinal cord, thereby amplifying nociceptive signaling [4]. Central sensitization, characterized by persistent activation of NMDA receptors and reduced inhibitory control, sustains chronic pain even after the initial injury resolves [6].

Neuroinflammation plays the very crucial role in the maintaining neuropathic pain [7]. Following nerve damage, immune and glial cells release the pro-inflammatory cytokines such as IL-6 and TNF-α, which is the enhance nociceptor sensitivity and synaptic transmission [7,8]. Activation of transcription factors like NF-κB further perpetuates inflammatory cascades, contributing to sustained neuronal sensitization [8].

Oxidative stress is another key contributor in neuropathic pain development [9]. Excessive over production of the reactive oxygen and nitrogen species that leads to mitochondrial dysfunction, lipid peroxidation, and depletion of the endogenous antioxidants such as GSH and SOD [9,10]. These alterations impair cellular energy metabolism and increase neuronal excitability, thereby promoting pain hypersensitivity [10]. Experimental studies demonstrated that reducing oxidative stress can significantly attenuate neuropathic pain behaviors [9].

Chronic constriction injury (CCI) model is widely accepted experimental approach for studying neuropathic pain mechanisms [11]. It induces partial nerve injury, resulting in demyelination, axonal degeneration, inflammation, and behavioral changes that closely resemble human neuropathic conditions [11,12]. This model is associated with elevated pro-inflammatory cytokines, increased oxidative stress, and altered neuronal signaling pathways [12,13].

Given the studies involvement of the inflammation and oxidative stress in PNP, antioxidant-based therapies have gained increasing attention [9]. Alpha-lipoic acid (ALA) is a potent endogenous antioxidant that functions as a mitochondrial cofactor and scavenges reactive species while regenerating the other antioxidants such as vitamin C and vitamin E [14,15]. It also exhibits the anti-inflammatory effects by inhibiting pathway of NF-κB signaling and reducing cytokine production [15,16]. Similarly, ferulic acid (FA), a plant-derived phenolic compound, demonstrates strong antioxidant effect by neutralizing the free radicals and preventing lipid peroxidation [17,18]. FA also activates Nrf2 signaling and suppresses inflammatory mediators, thereby offering neuroprotection [18,19].

2. MATERIAL

2.1. Drugs and Reagents

Gabapentin (Sample from Maharaja Sayajirao University of Baroda, India), FA (Sample from Otto-Kemi Pvt. Ltd.), and ALA (Sample from Sigma-Aldrich) were utilized in this study. All additional chemicals and the reagents are analytical grade and purchases from certified commercial sources to maintain consistency and reliability of experimental outcomes.

2.2. Experimental Animals

The adult male Wistar rats are weighing 200 to 250 g were selected. These animals were procured from the Disease-Free Animal Facility at Lakshmi Biofarms, Pune, India. They were housed under standard laboratory guidelines and conditions, including their temperature of 22 ± 2 °C, and humidity between 50–60%, a 12-hour light / 12-hour dark cycle. Rats were provided with standard diet (pellet) (VRK Nutritional Solutions, Sangli) and the water ad libitum.

The experimental protocol was approved by the Institutional Animal Ethics Committee (IAEC) of Scitesla Private Limited, Navi Mumbai, India (Approval No.: SCI/IAEC/2024-25/142), and all procedures complied with CPCSEA guidelines under the Ministry of Environment, Forest and Climate Change, Government of India.

2.3. Preparation of Drug Solutions

Gabapentin was prepared in normal saline (NS) as previously described [20]. ALA and FA were also freshly dissolved in normal saline following established procedures [21]. All formulations were prepared freshly on the day of administration to ensure drug stability and effectiveness.

2.4. Surgical Procedure

Peripheral neuropathy was the induced using the CCI technique described by Bennett and Xie (1988). Male Wistar rats are divided into five groups (n = 6). Under ketamine–xylazine anesthesia, in this study on animal small incision on rat and made at the mid-thigh region for expose sciatic nerve through the biceps femoris muscle.

A segment of approximately 7 mm of sciatic nerve, proximal to its trifurcation, was carefully isolated. 3 to 4 loose ligatures (4-0 silk) were tied around the nerve at ~1 mm intervals until a slight muscle twitch was observed, indicating appropriate constriction. The incision was then sutured, and animals were provided postoperative care and monitored for two weeks to allow the development of neuropathic pain.

Following model establishment, treatments were administered once daily for 14 days. Behavioral evaluations were conducted on day 15 (post-surgery) and day 29 (after completion of treatment) [22].

2.5. Experimental Protocol

Treatment was initiated after successful induction of neuropathy and continued for two weeks. The Group I: disease control received normal saline orally. The Group II: standard was treated with gabapentin (30 mg/kg, i.p.) once daily. Separate groups received Group III: α-lipoic acid (25 mg/kg, p.o.) or Group IV: ferulic acid (10 mg/kg, p.o.) for the same duration.

The Group V: combination group was administered ALA (12 mg/kg) along with FA (5 mg/kg), orally once daily. This design enabled comparison of individual and combined therapeutic effects of ALA and FA against CCI-induced neuropathic pain, using gabapentin as the reference standard.

Table no. 1. Grouping of the animals after the confirmation of PNP.

Animal Group	No. of animals	Administration of Drug	Route of drug	Dose of drug (mg/kg)	Duration of drug treatment
Group I: Disease Control	6	Normal Saline Solution	P.O.	-	14 Days
Group II: Gabapentin	6	Gabapentin	I.P.	30 mg/kg	14 Days
Group III: ALA + CCI	6	ALA	P.O.	25 mg/kg	14 Days
Group IV: FA + CCI	6	FA	P.O.	10 mg/kg	14 Days
Group V: FA + ALA + CCI	6	FA + ALA	P.O.	5 mg/kg + 12 mg/kg	14 Days

3. ASSESSMENT OF BEHAVIORAL PARAMETERS

Behavioral evaluations were conducted between 08:30 AM and 04:00 PM under controlled conditions to minimize stress and ensure consistent responses in animals.

3.1. Mechanical Allodynia using von Frey Filament Test

For the mechanical sensitivity we assessed use of the calibrated von-Frey filaments as per standard methodology [23]. Rats are placed individually on a wire mesh platform for the acclimatize before testing. Filaments (0.4 to 15g) were applied the filaments perpendicularly to plantar surface on hind paw for 1–2 seconds until slight bending occurred. Paw withdrawal, licking, or shaking was considered a positive response. 50 % of paw withdrawal threshold was determined by using up down test, enabling quantitative evaluation of mechanical allodynia.

3.2. Cold Allodynia using Acetone Test

Cold sensitivity was measured by acetone drop method [24–26]. A small volume (20 µL) of acetone was gently applied to the glabrous skin region beneath the ear. Animals were observed for 60 seconds for

nociceptive responses such as scratching, shaking, or withdrawal. Increased frequency of these behaviors indicated enhanced cold sensitivity.

3.3. Mechanical Hyperalgesia using Pinprick Test

Mechanical hyperalgesia is evaluated using a pinprick stimulus applied to the hind paw without penetrating the skin [27]. The duration of paw withdrawal was record during the study, with their cut-off time of 15 seconds for avoid the tissue damage. Each animal underwent three trials, and the average response was used for analysis, providing a reliable measure of pain sensitivity.

3.4. Thermal Allodynia using Eddy's Hot Plate

Thermal nociception was assessed using Eddy's hot plate apparatus maintained at the level of 55 ± 0.1°C [28]. Latency to pain responses like paw licking and also jumping was recorded and their cut-off time of 18 seconds was set for prevent injury. Reduced latency indicated increased thermal sensitivity associated with neuropathic pain.

4. ASSESSMENT OF OXIDATIVE STRESS

4.1. Homogenization of Tissue

Rats were sacrificed and the sciatic nerve was carefully isolated, at the end of study. Tissue was immediately placed in ice-cold water Tris-HCl buffer (pH 7.4), finely minced, and transferred into chilled sucrose solution. It was then homogenized in 10% (w/v) Tris-HCl buffer under cold conditions and centrifuged at the 10,000 rpm for fifteen minutes at 0°C. Clear supernatant obtained was collected and the used for estimation of oxidative stress markers and cytokines [29,30].

4.2. Estimation of Reduced Glutathione (GSH)

GSH levels determined by using spectrophotometric method [31], based on reaction of GSH with DTNB to produce a yellow chromogen measurable at 412 nm. The tissue supernatant was treated with trichloroacetic acid to precipitate proteins, and the resulting supernatant was analyzed. Results were expressed using as µg of GSH per mg of protein.

4.3. Estimation of Superoxide Dismutase (SOD)

SOD level measured by using Misra and Fridovich method, which is the based on inhibition of epinephrine auto-oxidation. The processed tissue sample was reacted with carbonate buffer, EDTA, and epinephrine, and the change in absorbance find at the 480 nm. The enzyme activity find and expressed as units per mg of protein [32].

4.4. Estimation of Catalase (CAT)

Catalase levels was estimated using Aebi's method, measures the rate of the hydrogen peroxide decomposition. This reaction mixture has containing tissue supernatant, phosphate buffer, and also H_2O_2 showed a gradual decrease in the absorbance at 240 nm, reflecting enzyme activity. Results were find and expressed as µmol of H_2O_2 decomposed per minute per mg of protein [33, 34].

4.5. Estimation of Lipid Peroxidation (MDA)

Lipid peroxidation was assessed by the measuring MDA levels using the TBARS method described by Slater and Sawyer [30]. The tissue sample was treated with trichloroacetic acid and thiobarbituric acid, heated to develop color, and absorbance was observed and measured at 532 nm.

MDA levels calculated using the standard curve and expressed as nmol per mg of protein.

4.6. Measurement of Tumor Necrosis Factor-α (TNF-α)

TNF-α levels in sciatic nerve tissue were quantified using a commercially is available Enzyme-Linked Immunosorbent Assay kit. The assay utilized specific anti-TNF-α antibodies for detection. A standard calibration curve (0–20,000 pg/ml) was prepared, and their absorbance was measured find at 450 nm using the microplate reader. The final concentrations calculated from the standard curve and expressed as pg/mg of total protein [35].

4.7. Histopathology of the Sciatic Nerve

Rats were anesthetized and sacrificed, and sciatic nerve tissues were collected. The tissues fixed in the 10% formalin, sectioned, and stained with the eosin and hematoxylin solutions. Microscopic examination was performed to evaluate structural and pathological changes in nerve architecture [36].

4.8. Statistical Analysis

The mean ± SD (n = 6) was used to express all results. Two-way ANOVA and the Bonferroni post hoc test were used to evaluate the data. A statistically significant value was defined as $P < 0.05$.

5. RESULTS

5.1. Von-Frey Filament Test

Mechanical allodynia was the evaluated by using paw withdrawal latency (PWL). The disease control group showed a significant decline in PWL on Day 15 (4.20 ± 0.74 sec) and the Day 29 (4.01 ± 0.88 sec) compared to Day 0 (###$p < 0.001$), confirming successful induction of neuropathy. Gabapentin significantly reversed this effect, increasing PWL to 8.00 ± 0.57 sec on Day 29 (***$p < 0.001$). Treatment with α-lipoic acid and ferulic acid also significantly improved PWL (8.50 ± 1.04 sec and 8.50 ± 1.03 sec, respectively; ***$p < 0.001$). The combination therapy showed the greatest improvement (9.17 ± 0.99 sec; ***$p < 0.001$), indicating a synergistic protective effect.

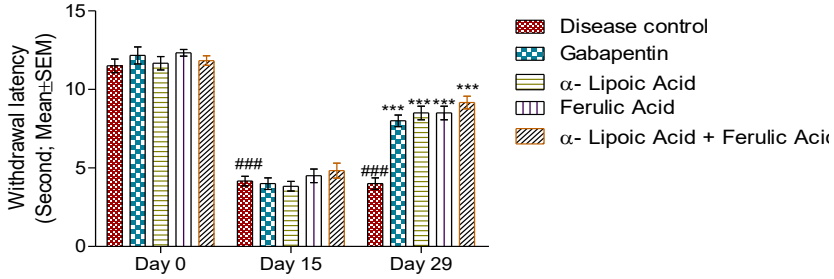

Figure 1: PWL measured on Days 0, 15, and 29. Data expressed as mean ± SEM (n = 6) and analyzed using ANOVA (two-way) with Bonferroni post hoc test. Significant reduction in disease control (###$p < 0.001$ vs Day 0) and significant improvement with treatments (***$p < 0.001$ vs disease control), with maximum effect in the combination group.

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E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

5.2. Acetone Test

Cold sensitivity was assessed by acetone-induced PWL. The disease control group exhibited a marked decrease in PWL on Day 15 (15.84 ± 5.28 sec) and Day 29 (10.99 ± 2.14 sec) compared to the Day 0 (44.82 ± 8.67 sec; ###p < 0.001), confirming cold allodynia. Gabapentin significantly improved PWL (28.50 ± 5.75 sec; ***p < 0.001). ALA and FA also showed significant improvement (26.67 ± 5.13 sec and 23.83 ± 4.62 sec; **p < 0.01). The combination therapy produced the highest recovery (42.67 ± 4.64 sec; ***p < 0.001), indicating strong synergistic action.

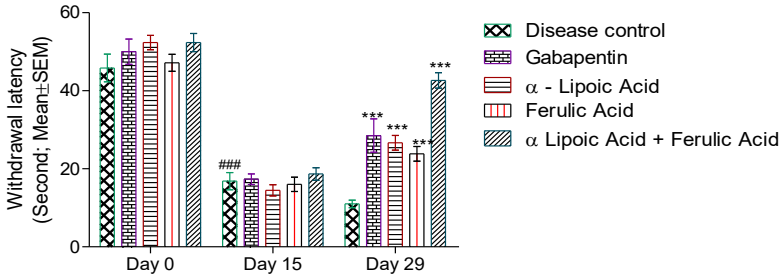

Figure 2: PWL assessed on Days 0, 15, and 29. Data presented as mean ± SD (n = 6) and analyzed using ANOVA (two-way). Significant reduction in disease control and reversal by treatments, with the group V showing the most pronounced effect.

5.3. Pinprick Test

Mechanical hyperalgesia was determined using pinprick-induced PWL. A significant decrease was observed in the disease control group on Day 15 (5.37 ± 0.68 sec) and Day 29 (4.72 ± 0.70 sec) compared to Day 0 (11.20 ± 0.72 sec; ###p < 0.001). Gabapentin significantly improved PWL (9.72 ± 1.10 sec; ***p < 0.001). ALA (9.50 ± 0.72 sec) and FA (9.55 ± 0.82 sec) also significantly increased latency (***p < 0.001). The combination group showed the highest improvement (10.13 ± 0.63 sec; ***p < 0.001), indicating enhanced efficacy.

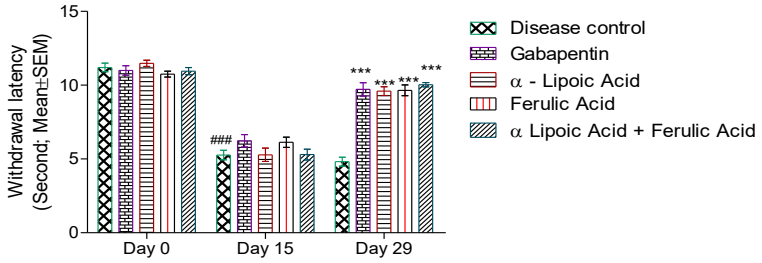

Figure 3: PWL recorded on Days 0, 15, and 29. Data expressed as mean ± SD (n = 6) and analyzed using ANOVA (two-way). Significant decline in disease control and marked improvement with all treatments, especially the combination therapy.

5.4. Eddy's Hot Plate Test

Thermal sensitivity was assessed using the hot plate test. The disease control group showed a significant reduction in PWL on the Day 15 (4.10 ± 0.63 sec) and Day 29 (2.34 ± 1.11 sec) compared to Day 0 (13.67 ± 1.23 sec; ###$p < 0.001$), indicating thermal allodynia. Gabapentin significantly increased PWL to 8.33 ± 1.11 sec (***$p < 0.001$). ALA (4.67 ± 1.09 sec) and FA (6.17 ± 1.72 sec) also showed significant improvement (***$p < 0.001$). The combination therapy produced the maximum effect (9.65 ± 1.41 sec; ***$p < 0.001$), identifying a synergistic analgesic response.

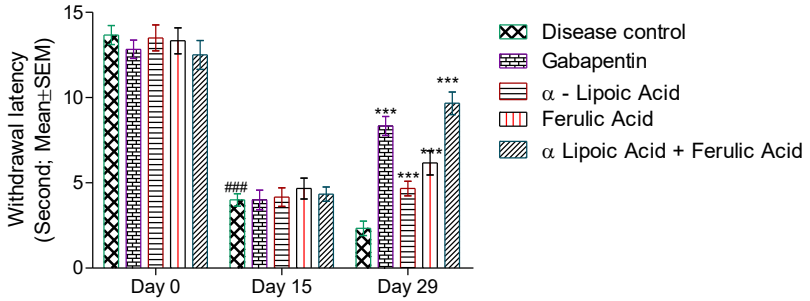

Figure 4: PWL measured on the Day 0, Day 15, and Day 29. Data presented as mean ± SD (n = 6) and analyzed using ANOVA (two-way). Significant reduction in disease control and reversal with treatments, with the combination group showing the highest improvement.

5.5. Oxidative Stress parameter (Endogenous Antioxidant Defense)

CCI significantly disrupted antioxidant defenses in sciatic nerve tissue, as indicated by decreased levels of SOD (2.42 ± 0.59 U/mg protein), CAT (41.76 ± 7.90 U/mg protein), and GSH (11.09 ± 1.57 U/mg protein), along with increased MDA (9.86 ± 3.00 nmol/mg protein), reflecting elevated oxidative stress. Gabapentin treatment moderately improved antioxidant status, increasing SOD (3.12 ± 0.60), CAT (55.88 ± 8.24, *$p < 0.05$), and GSH (13.31 ± 2.38), while reducing MDA (7.51 ± 1.62). Similarly, ferulic acid (SOD: 3.82 ± 1.00; CAT: 56.93 ± 7.40, *$p < 0.05$; GSH: 13.81 ± 3.12; MDA: 7.33 ± 3.02) and α-lipoic acid (SOD: 3.35 ± 0.69; CAT: 58.38 ± 7.19, **$p < 0.01$; GSH: 15.43 ± 2.92; MDA: 5.08 ± 1.50) significantly restored antioxidant balance. Notably, the combination therapy produced the most pronounced effect, with highest levels of SOD (4.11 ± 0.72, *$p < 0.05$), CAT (62.31 ± 7.39, **$p < 0.01$), and GSH (17.19 ± 4.42, **$p < 0.01$), along with the low MDA (4.74 ± 3.45, **$p < 0.01$), indicating superior protection against oxidative stress.

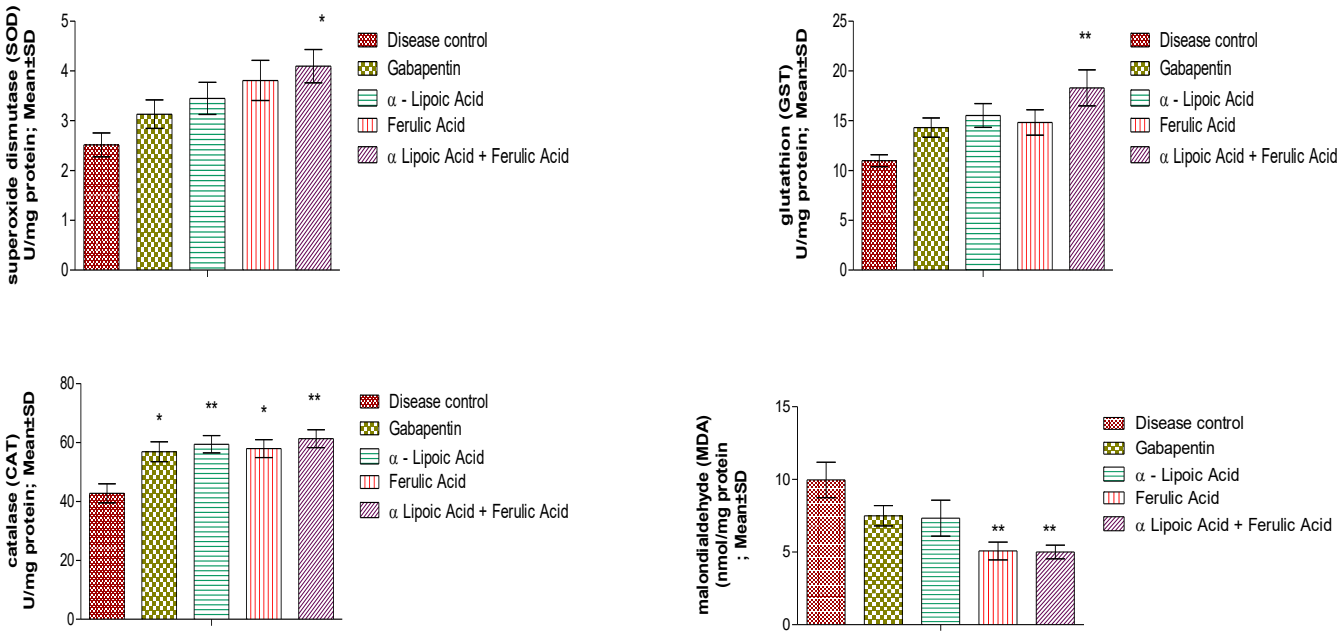

Figure 5: SOD (A), CAT (B), GSH (C), and MDA (D) levels.
Data expressed as mean ± SD (n = 6) and analyzed using ANOVA (one-way) followed by Bonferroni post hoc test (*P < 0.05, **P < 0.01 vs Group I disease control).

5.6. Inflammatory Marker (TNF-α) in Sciatic Nerve: Effect of ALA and FA

TNF-α levels finds markedly elevated in the CCI group (67.11 ± 0.35 pg/mg protein), confirming a strong inflammatory response. Gabapentin group significantly reduced the TNF-α to 33.49 ± 0.26 pg/mg protein. FA (33.24 ± 0.27 pg/mg, *p < 0.05) and ALA (43.95 ± 0.42 pg/mg, *p < 0.05) also showed significant reductions. The combination therapy produced the greatest anti-inflammatory effect, lowering TNF-α to 28.97 ± 0.52 pg/mg protein (*p < 0.05), suggesting synergistic activity.

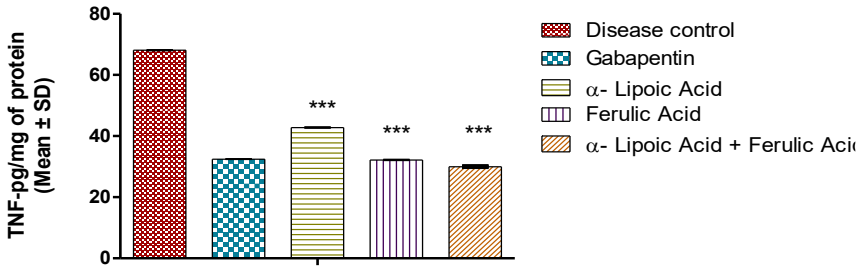

Figure 6: TNF-α levels expressed as mean ± SD (n = 6) and analyzed using ANOVA (one-way) with Bonferroni post hoc test (*P < 0.05 vs Group I disease control).

5.7. Histopathological Evaluation of the Sciatic Nerve

Histological analysis of the Group I disease control revealed clear pathological changes, including mononuclear cell infiltration, myelin sheath disruption, and axonal degeneration. In contrast, Group II: gabapentin, Group III: α-lipoic acid, and Group V: combination-treated groups showed preservation of normal nerve architecture without major abnormalities, indicating strong neuroprotection. The Group IV: ferulic acid group displayed mild to moderate inflammatory changes, suggesting partial protection. Overall, the combination therapy demonstrated the most effective preservation of nerve structure.

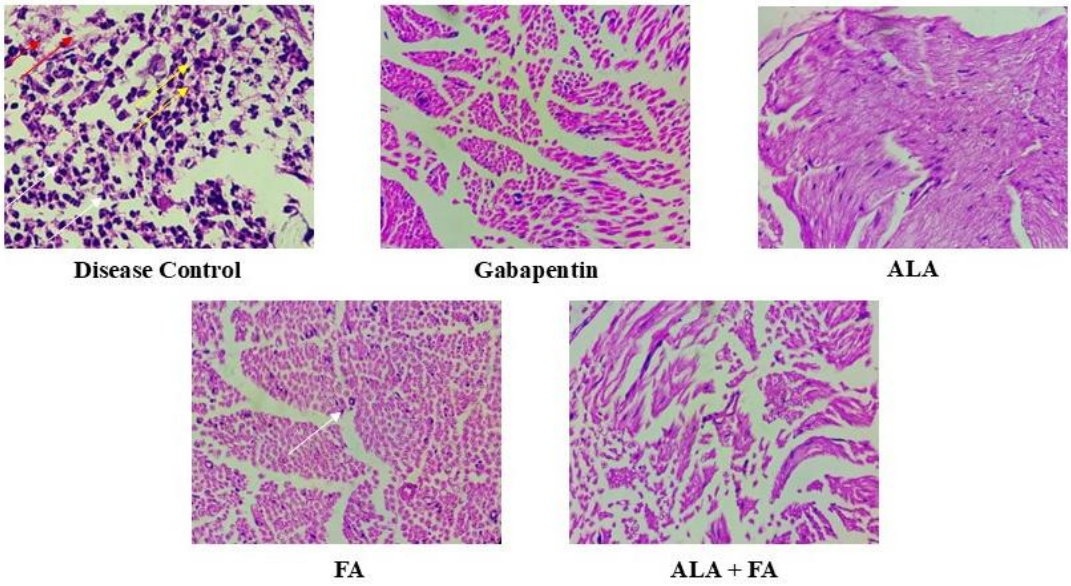

Figure 7: Histopathological observations of sciatic nerve showing structural alterations and protective effects across treatment groups.

6. DISCUSSION

PNP induced by CCI is a well-established animal experimental model that replicates key clinical studies such as thermal hyperalgesia, mechanical allodynia, neuroinflammation, and oxidative stress-mediated nerve damage [37].

The therapeutic effects of α-lipoic acid (ALA), ferulic acid (FA), and their combination were evaluated and compared with gabapentin in terms of analgesic, antioxidant, anti-inflammatory, and neuroprotective activities. CCI is known to induce neuronal hyperexcitability and inflammatory responses, leading to enhanced pain sensitivity [38]. Behavioral assessments confirmed significant nociceptive alterations in disease control animals. Mechanical allodynia assessed using the von-Frey filament test, showed marked hypersensitivity, which was significantly reduced by ALA and FA treatment, with combination therapy producing the most of improvement. This suggests a strong modulatory effect of antioxidants on pain signaling pathways [39,40].

Cold allodynia and thermal hyperalgesia were also significantly elevated following CCI, indicating disrupted sensory processing [41]. Although individual treatments with ALA and FA moderately improved

pain thresholds, their combined administration produced effects comparable to gabapentin. Similarly, mechanical hyperalgesia (pinprick test) and thermal sensitivity (hot plate test) were significantly attenuated, with the combination group consistently showing superior efficacy. These findings indicate a possible synergistic interaction between ALA and FA in restoring normal nociceptive function [42–44].

Oxidative stress is plays a very crucial role in neuropathic pain progression. CCI-induced nerve injury leads to excessive production of reactive oxygen species, resulting in reduced levels of endogenous antioxidants such as SOD, CAT, and GSH, along with increased lipid peroxidation (MDA) [38,45]. In this study, ALA and FA significantly restored antioxidant enzyme levels and reduced MDA concentrations. The combination treatment demonstrated the most effective normalization of oxidative stress markers, suggesting enhanced protection against ROS-mediated neuronal damage [40].

The observed antioxidant effects may be attributed to the ability of ALA and FA to scavenge free radicals, regulate mitochondrial function, and modulate redox-sensitive signaling pathways such as Nrf2 and NF-κB [46]. Their combined action likely provides broader cellular protection, thereby improving neuronal survival and function.

Neuroinflammation is another key contributor to neuropathic pain. Elevated TNF-α levels observed in the disease control group confirm the presence of an inflammatory response following nerve injury [47,48]. Treatment with ALA and FA significantly reduced TNF-α levels, with the greatest suppression seen in the combination group. This indicates effective inhibition of pro-inflammatory cytokine production and reduced glial activation.

Histopathological findings supported these results. Disease control animals showed clear signs of nerve damage, including inflammatory cell infiltration, myelin degeneration, and axonal loss. In contrast, gabapentin-, ALA-, and combination-treated groups exhibited preserved nerve structure, while FA alone showed partial protection. These observations confirm the neuroprotective potential of the treatments, particularly when used in combination.

Overall, the study demonstrates that ALA and FA, especially in combination, provide significant relief from neuropathic pain through multiple mechanisms. These include attenuation of pain behaviors, restoration of antioxidant defense, reduction of inflammatory mediators, and preservation of nerve architecture. The findings suggest that combined antioxidant therapy may represent a promising strategy for the management of peripheral neuropathic pain.

7. CONCLUSION

The current investigation shows that α-lipoic acid (ALA) and ferulic acid (FA) have substantial therapeutic potential against peripheral neuropathic pain caused by chronic constriction injury (CCI), both separately and more successfully in combination. Behavioral results demonstrated that the combination treatment significantly decreased mechanical allodynia, thermal hyperalgesia, and cold allodynia, with effects similar to gabapentin.

By boosting antioxidant defenses (SOD, CAT, and GSH) and lowering lipid peroxidation, as seen by lower MDA levels, co-administration of ALA and FA restored oxidative balance, according to biochemical analysis. In addition, a significant reduction in TNF-α levels and improved histological

architecture of the sciatic nerve further support their anti-inflammatory and neuroprotective actions. Overall, the findings highlight a synergistic interaction between ALA and FA, suggesting their potential as an effective alternative or adjunct therapy for the management of peripheral neuropathic pain.

Author Contributions
The authors acknowledge Dr. Abhijeet Kulkarni for supervision, conceptualization, methodology, and investigation; Dr. Hemant Gangurde for conceptualization, review, and editing; and Mr. Prafulla S. Chavan for methodology, investigation, and original draft preparation. The authors also thank Scitesla Pvt. Ltd., Navi Mumbai, for IAEC approval and study support. All authors have reviewed and approved the final manuscript.

Conflict of Interest
No authors declare conflicts of interest.

Funding Report
There was no funding for this study.

Ethics Approval
The Scitesla Private Limited Institutional Animal Ethics Committee (IAEC) in Navi Mumbai, India, authorized all experimental protocols in compliance with CPCSEA rules (Approval No.: SCI/IAEC/2024-25/142).

Available Data
This published publication includes all of the data that was created or looked at during this investigation.

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