Assessment of Resveratrol in the Management of Diabetic Neuropathy in Alloxan-Induced Diabetic Rats

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ABSTRACT

Diabetic neuropathy is a common complication of diabetes mellitus, characterized by peripheral nerve damage, increased pain sensitivity, oxidative stress, and structural alterations in nerve tissue. The present study was designed to evaluate the effect of resveratrol on diabetic neuropathy in alloxan-induced diabetic rats. Resveratrol, a naturally occurring polyphenolic compound, was investigated for its potential effects on neuropathic pain, blood glucose levels, oxidative stress, and sciatic nerve architecture.

The experimental study was conducted using 30 male Wistar rats divided into five groups of six animals each: normal control, diabetic control, pregabalin-treated group (30 mg/kg), resveratrol-treated group (10 mg/kg), and resveratrol-treated group (20 mg/kg). Experimental diabetes was induced using alloxan monohydrate at a dose of 150 mg/kg, administered intraperitoneally. Diabetes was confirmed by fasting blood glucose levels of 250 mg/dL or above. Following the development of diabetic neuropathy, resveratrol was administered orally for 28 days. Mechanical allodynia and thermal hyperalgesia were evaluated using the Von Frey filament and Eddy's hot plate tests, respectively. Biochemical assessment included fasting blood glucose, reduced glutathione, malondialdehyde, superoxide dismutase, and catalase. Histopathological examination of the sciatic nerve was performed to assess nerve fiber degeneration and structural changes.

The results showed that alloxan administration produced marked hyperglycaemia, accompanied by increased mechanical and thermal sensitivity in diabetic animals. Resveratrol treatment improved the paw withdrawal threshold and thermal withdrawal latency compared with the diabetic control group. The treatment also reduced fasting blood glucose and malondialdehyde levels while increasing reduced glutathione concentration and superoxide dismutase and catalase activities. Histopathological examination revealed improved sciatic nerve architecture, with reduced degeneration, edema, and axonal damage. The higher dose of resveratrol (20 mg/kg) produced greater numerical improvement than the 10 mg/kg dose across the evaluated parameters.

The findings suggest that resveratrol may provide beneficial effects against experimental diabetic neuropathy through improvements in neuropathic behavioural responses, glycaemic status, antioxidant defence, and peripheral nerve structure. Further studies are required to establish its mechanism of action, optimal dose, and potential clinical applicability.

Keywords: *Resveratrol, diabetic neuropathy, alloxan, Wistar rats, oxidative stress, neuropathic pain, antioxidant activity, sciatic nerve.*

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INTRODUCTION

Diabetic neuropathy is one of the major complications of diabetes mellitus and is associated with progressive damage to peripheral nerves. It commonly manifests as pain, tingling, numbness, increased sensitivity to painful stimuli, and reduced sensory function. Persistent hyperglycaemia contributes to the development of neuropathy through oxidative stress, impaired antioxidant defence, metabolic disturbances, and structural damage to nerve fibres. Increased production of reactive oxygen species can promote lipid peroxidation and cellular injury, while reduced levels of endogenous antioxidants further weaken the body's protective mechanisms. These changes may lead to degeneration of peripheral nerves, particularly the sciatic nerve, and adversely affect the quality of life of individuals with diabetes. Although several medicines, including pregabalin, are used to manage

neuropathic pain, they mainly provide symptomatic relief and may be associated with adverse effects. Therefore, investigating compounds with antioxidant and neuroprotective properties may provide useful information for the development of alternative approaches to diabetic neuropathy.

Resveratrol is a naturally occurring polyphenolic compound found in various plant sources and has attracted research interest because of its antioxidant and anti-inflammatory properties. Its potential effects on oxidative stress and cellular protection make it a suitable candidate for investigation in experimental diabetic neuropathy. The present study was designed to evaluate the effect of resveratrol in alloxan-induced diabetic rats. The study assessed changes in mechanical pain sensitivity and thermal withdrawal latency using Von Frey filament and Eddy's hot plate tests, respectively. Fasting blood glucose and oxidative stress-related biochemical parameters, including reduced glutathione, malondialdehyde, superoxide dismutase, and catalase, were also evaluated. In addition, histopathological examination of the sciatic nerve was performed to assess structural changes associated with diabetic neuropathy. Two doses of resveratrol were investigated and compared with a diabetic control group and a pregabalin-treated standard group to examine its potential protective effects on behavioural, biochemical, and histological parameters.

MATERIALS AND METHODS:

This controlled in vivo experiment compared two oral doses of resveratrol with an untreated diabetic group, a non-diabetic control, and pregabalin as an active comparator. The individual rat was the experimental unit. Outcomes comprised sensory behavioural responses, metabolic and oxidative-stress markers, and sciatic nerve histomorphology. The report follows the broad framework of the ARRIVE 2.0 recommendations[36].

Study Design: The present experimental study was designed to evaluate the effect of resveratrol on diabetic neuropathy in alloxan-induced diabetic rats. The study included behavioural, biochemical, and histopathological assessments to investigate the potential effects of resveratrol on neuropathic pain, blood glucose levels, oxidative stress, antioxidant defence, and sciatic nerve structure.

Experimental Animals: A total of 30 male Wistar rats were used in the study. The animals were divided into five experimental groups, with six animals in each group. The rats were maintained under standard laboratory conditions with suitable food, water, and environmental conditions. Animals were acclimatized before the commencement of the experiment.

Experimental Groups: These are five groups as follow as per below table:

Group	Treatment
Group I	Normal control
Group II	Diabetic control
Group III	Pregabalin, 30 mg/kg/day
Group IV	Resveratrol, 10 mg/kg/day
Group V	Resveratrol, 20 mg/kg/day

Induction of Experimental Diabetes: Experimental diabetes was induced using alloxan monohydrate at a dose of 150 mg/kg, administered intraperitoneally. Fasting blood glucose levels were measured after alloxan administration to confirm the development of diabetes. Animals with fasting blood glucose levels of 250 mg/dL or above were considered diabetic and included in the subsequent experimental evaluation.

Development and Confirmation of Diabetic Neuropathy: After diabetes was confirmed, the animals were maintained for four weeks to allow the development of diabetic neuropathy. Mechanical and thermal sensitivity were assessed before treatment. A reduction in paw withdrawal threshold and thermal withdrawal latency, along with persistent hyperglycaemia, was considered indicative of neuropathic changes.

Assessment of Neuropathic Pain: Mechanical and thermal nociceptive responses were considered complementary functional readouts of neuropathy. Lower von Frey withdrawal thresholds indicate greater responsiveness to normally innocuous pressure, whereas shorter hot-plate withdrawal latencies indicate increased thermal nociception. Changes in either measure require interpretation alongside glycaemic and histological results rather than being treated as standalone proof of peripheral nerve repair.

Mechanical sensitivity: Mechanical allodynia was evaluated using the Von Frey filament test. Each rat was placed on an elevated wire-mesh platform and allowed to acclimatize before testing. Calibrated filaments were applied to the plantar surface of the hind paw, and the paw withdrawal threshold was recorded in grams. A lower threshold indicated increased mechanical sensitivity.

Thermal sensitivity: Thermal hyperalgesia was assessed using Eddy's hot plate maintained at \(55 \pm 1^\circ\text{C}\). The latency to paw licking, paw withdrawal, or jumping was recorded in seconds. A cut-off time of 20 seconds was used to prevent thermal injury. A shorter withdrawal latency indicated increased thermal sensitivity.

Drug Treatment: Following confirmation of diabetic neuropathy, the animals received their respective treatments once daily for 28 consecutive days. Pregabalin at 30 mg/kg/day was used as the standard treatment, while resveratrol was administered at doses of 10 and 20 mg/kg/day. The normal and

diabetic control groups received the corresponding vehicle.

Biochemical Evaluation: At the end of the treatment period, biochemical parameters were assessed to determine changes in glycaemic status and oxidative stress.

- Fasting blood glucose: Measured to evaluate changes in blood glucose levels.
- Reduced glutathione (GSH): Evaluated as an indicator of endogenous antioxidant defence.
- Malondialdehyde (MDA): Assessed as a marker of lipid peroxidation.
- Superoxide dismutase (SOD): Measured to evaluate antioxidant enzyme activity.
- Catalase (CAT): Assessed to determine antioxidant protection against hydrogen peroxide.

The results were compared among the normal control, diabetic control, pregabalin, and resveratrol treatment groups.

Histopathological Evaluation: At the end of the experimental period, sciatic nerve tissue was collected for histopathological examination. The tissue was fixed in 10% neutral buffered formalin, processed using routine histological procedures, embedded in paraffin wax, and sectioned at approximately 4–5 µm. The sections were stained with haematoxylin and eosin (H&E) and examined under a light microscope for nerve fibre degeneration, axonal damage, oedema, inflammatory changes, and preservation of nerve architecture.

Statistical Analysis: The experimental findings were intended to be expressed as mean ± standard deviation. Differences among the experimental groups were to be evaluated using appropriate statistical methods, with a suitable significance level established before analysis. The statistical test, exact p-values, and significance claims should be reported only after analysis of the original individual-animal data.

RESULTS AND DISCUSSION:

All the data or findings is summarised below without alteration to the original group means, dispersion estimates, tables, or illustrations. [1, 26, 35].

Confirmation of Diabetes: After alloxan administration, the four groups designated for diabetic induction exhibited fasting blood glucose values above the prespecified 250 mg/dL threshold at 72 h. In contrast, fasting blood glucose in normal controls remained within the baseline range. The group-level values therefore support successful induction of marked hyperglycaemia in the reported experimental cohort.

Effect of Alloxan on Fasting Blood Glucose Level: As shown in Table 1 and Figure 1, mean fasting blood glucose in the diabetic control group rose from 93.50 ± 2.98 to 286.17 ± 8.74 mg/dL within 72 h. Similar elevations were documented in the pregabalin and both resveratrol-designated groups before treatment, whereas the normal-control mean changed only from 92.17 ± 3.21 to 94.33 ± 3.46 mg/dL. The comparable post-induction values across diabetic groups establish a descriptive basis for subsequent treatment comparisons.

Table 1: Effect of Alloxan on Fasting Blood Glucose Level

Group	Experimental condition	Dose of Alloxan	Baseline FBG (mg/dL)	FBG after 72 h (mg/dL)	% Increase
Group I	Normal control	—	92.17 ± 3.21	94.33 ± 3.46	2.34%
Group II	Alloxan-induced diabetic	150 mg/kg, i.p.	93.50 ± 2.98	286.17 ± 8.74	206.07%
Group III	Alloxan-induced diabetic	150 mg/kg, i.p.	91.83 ± 3.12	281.50 ± 7.96	206.55%
Group IV	Alloxan-induced diabetic	150 mg/kg, i.p.	94.00 ± 3.41	289.67 ± 9.12	208.16%
Group V	Alloxan-induced diabetic	150 mg/kg, i.p.	92.67 ± 3.05	284.83 ± 8.31	207.35%

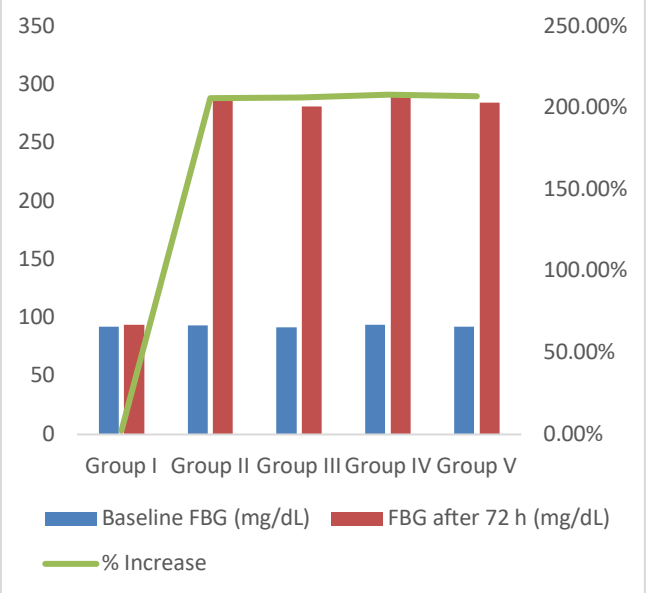


Figure 1: Effect of Alloxan on Fasting Blood Glucose Level

Percentage Increase in Fasting Blood Glucose: The relative increase in fasting blood glucose was approximately 206–208% in the four alloxan-exposed groups (Table 2), compared with 2.34% in normal controls.

Table 2: Percentage Increase in Fasting Blood Glucose After Alloxan Administration

Group	Baseline FBG (mg/dL)	FBG at 72 h (mg/dL)	Percentage increase
Group I	92.17 ± 3.21	94.33 ± 3.46	2.34%
Group II	93.50 ± 2.98	286.17 ± 8.74	206.07%
Group III	91.83 ± 3.12	281.50 ± 7.96	206.55%
Group IV	94.00 ± 3.41	289.67 ± 9.12	208.16%
Group V	92.67 ± 3.05	284.83 ± 8.31	207.35%

Effect on Mechanical Paw Withdrawal Threshold Before Treatment

Table 3: Effect of Diabetes on Mechanical Paw Withdrawal Threshold Before Treatment

Group	Experimental condition	Paw Withdrawal Threshold (g)
Group I	Normal control	8.42 ± 0.38
Group II	Diabetic control	3.21 ± 0.27
Group III	Diabetic + Pregabalin	3.35 ± 0.25
Group IV	Diabetic + Resveratrol 10 mg/kg	3.18 ± 0.29
Group V	Diabetic + Resveratrol 20 mg/kg	3.27 ± 0.26

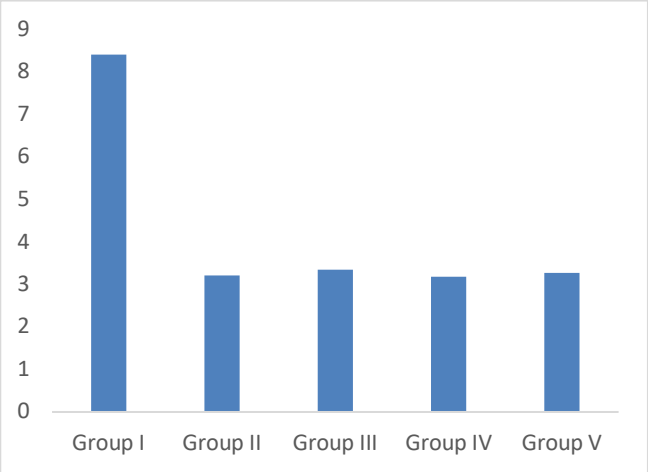


Figure 2: Effect of Diabetes on Mechanical Paw Withdrawal Threshold Before Treatment

Effect on Thermal Withdrawal Latency Before Treatment: Before the start of treatment, mean hot-plate latency was 12.86 ± 0.54 seconds in normal rats and ranged from 6.05 to 6.28 seconds in diabetic groups (Table 4; Figure 3). The lower latencies were consistent with increased sensitivity to a thermal stimulus after sustained hyperglycaemia. Together with the reduced mechanical thresholds in Table 3, these measurements support the presence of a neuropathy-associated behavioural phenotype.

Table 4: Effect of Diabetes on Thermal Withdrawal Latency Before Treatment

Group	Experimental condition	Thermal Withdrawal Latency (s)
Group I	Normal control	12.86 ± 0.54
Group II	Diabetic control	6.14 ± 0.41
Group III	Diabetic + Pregabalin	6.28 ± 0.39
Group IV	Diabetic + Resveratrol 10 mg/kg	6.05 ± 0.43
Group V	Diabetic + Resveratrol 20 mg/kg	6.19 ± 0.40

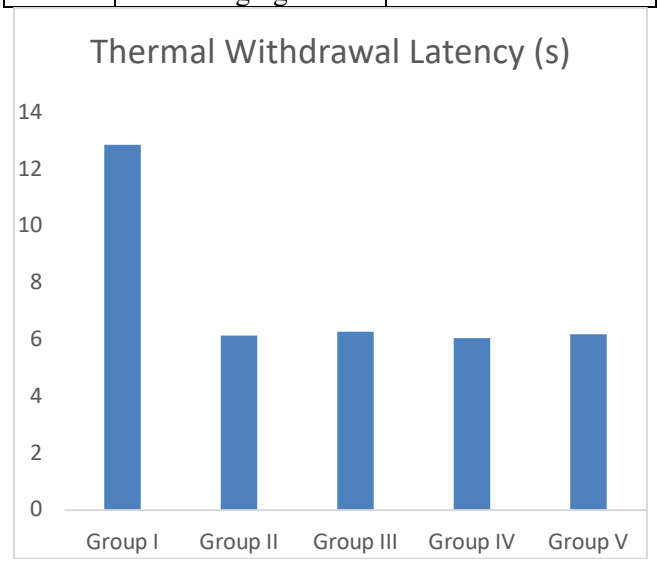


Figure 3: Effect of Diabetes on Thermal Withdrawal Latency Before Treatment

Effect of Resveratrol on General Pharmacological Parameters: Longitudinal changes in body mass, daily consumption, and observed activity provide useful contextual indicators of metabolic illness and tolerability.

Effect on Body Weight: The normal-control group gained weight over the reported observation period, reaching 215.2 ± 3.9 g at week 4, whereas the untreated diabetic group declined to 175.8 ± 3.9 g (Table 5; Figure 4). Both resveratrol groups showed progressive recovery after treatment initiation, ending at 193.7 ± 4.0 g (10 mg/kg) and 196.8 ± 3.9 g (20 mg/kg). These trajectories suggest attenuation of diabetes-associated weight loss, but not full restoration to non-diabetic weight.

Table 5: Effect of Resveratrol on Body Weight of Experimental Animals

Group	Initial	After diabetes induction	Before treatment	Week 1	Week 2	Week 3	Week 4 / Final
Group I – Normal control	198.3 ± 3.8	201.2 ± 3.7	202.5 ± 3.6	205.4 ± 3.5	208.6 ± 3.7	211.8 ± 3.8	215.2 ± 3.9
Group II – Diabetic control	197.8 ± 3.6	184.5 ± 3.4	181.7 ± 3.5	178.9 ± 3.6	177.1 ± 3.7	176.4 ± 3.8	175.8 ± 3.9
Group III – Pregabalin 30 mg/kg	199.1 ± 3.9	185.8 ± 3.6	183.2 ± 3.5	185.7 ± 3.6	188.9 ± 3.7	191.7 ± 3.8	194.5 ± 3.9
Group IV – Resveratrol 10 mg/kg	198.6 ± 3.7	184.9 ± 3.5	182.5 ± 3.6	184.6 ± 3.7	187.6 ± 3.8	190.8 ± 3.9	193.7 ± 4.0
Group V – Resveratrol 20 mg/kg	199.4 ± 3.8	185.6 ± 3.4	183.1 ± 3.5	186.3 ± 3.6	190.2 ± 3.7	193.6 ± 3.8	196.8 ± 3.9

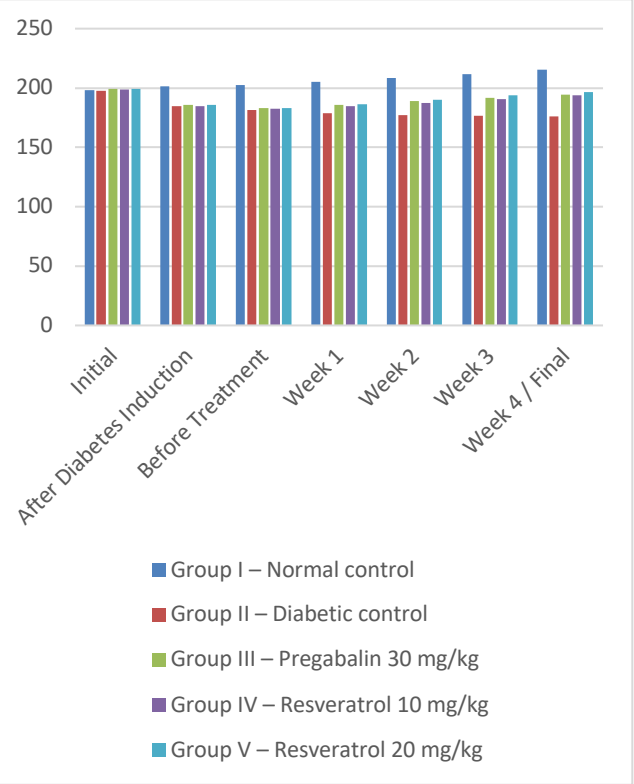


Figure 4: Effect of Resveratrol on Body Weight During Treatment

Effect on Food Intake: Untreated diabetic animals showed persistently elevated food intake, increasing from 27.8 ± 0.6 to 29.1 ± 0.6 g/day between weeks 1 and 4. By comparison, intake decreased from 27.1 ± 0.6 to 24.8 ± 0.5 g/day with resveratrol 10 mg/kg and from 27.0 ± 0.5 to 24.0 ± 0.4 g/day with resveratrol 20 mg/kg (Table 6; Figure 5). The pattern is consistent with partial improvement of diabetes-associated hyperphagia; food intake remained above that of non-diabetic controls.

Table 6: Effect of Resveratrol on Food Intake

Group	Week 1 (g/day)	Week 2 (g/day)	Week 3 (g/day)	Week 4 (g/day)
Group I – Normal control	20.8 ± 0.5	21.0 ± 0.5	21.2 ± 0.4	21.4 ± 0.5
Group II – Diabetic control	27.8 ± 0.6	28.4 ± 0.6	28.7 ± 0.7	29.1 ± 0.6
Group III – Pregabalin 30 mg/kg	26.9 ± 0.5	26.1 ± 0.5	25.3 ± 0.5	24.7 ± 0.5
Group IV – Resveratrol 10 mg/kg	27.1 ± 0.6	26.3 ± 0.5	25.5 ± 0.5	24.8 ± 0.5
Group V – Resveratrol 20 mg/kg	27.0 ± 0.5	25.8 ± 0.5	24.9 ± 0.5	24.0 ± 0.4

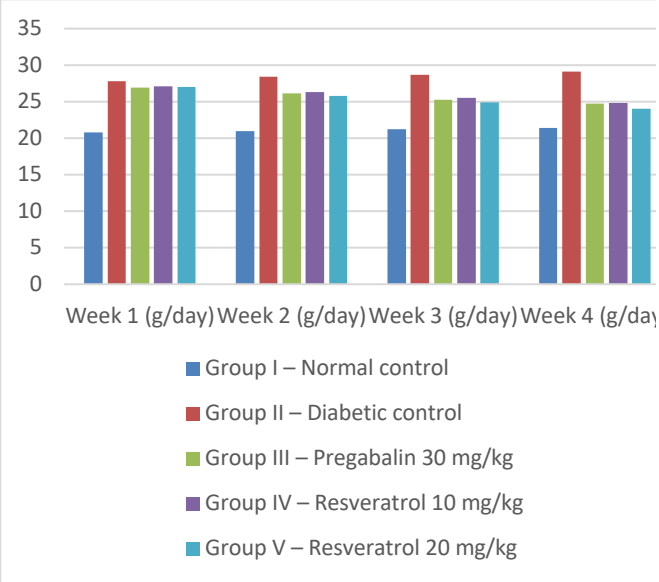


Figure 5: Effect of Resveratrol on Weekly Food Intake

Effect on Water Intake: Water intake remained elevated in untreated diabetic rats, rising from 58.6 ± 1.5 to 62.8 ± 1.6 mL/day over four weeks. In the resveratrol 10 and 20 mg/kg groups, the respective week-4 means were 48.8 ± 1.2 and 46.5 ± 1.2 mL/day (Table 7; Figure 6). Reduced drinking alongside lower terminal glucose concentrations may be compatible with improvement in diabetes-associated polydipsia.

Table 7: Effect of Resveratrol on Water Intake

Group	Week 1 (mL/day)	Week 2 (mL/day)	Week 3 (mL/day)	Week 4 (mL/day)
Group I – Normal control	32.5 ± 1.0	32.8 ± 0.9	33.0 ± 1.0	33.2 ± 0.9
Group II – Diabetic control	58.6 ± 1.5	60.2 ± 1.6	61.5 ± 1.5	62.8 ± 1.6
Group III – Pregabalin 30 mg/kg	55.4 ± 1.4	52.8 ± 1.3	50.4 ± 1.3	48.2 ± 1.2
Group IV – Resveratrol 10 mg/kg	55.8 ± 1.5	53.4 ± 1.4	51.0 ± 1.3	48.8 ± 1.2
Group V – Resveratrol 20 mg/kg	55.2 ± 1.4	51.8 ± 1.3	48.9 ± 1.2	46.5 ± 1.2

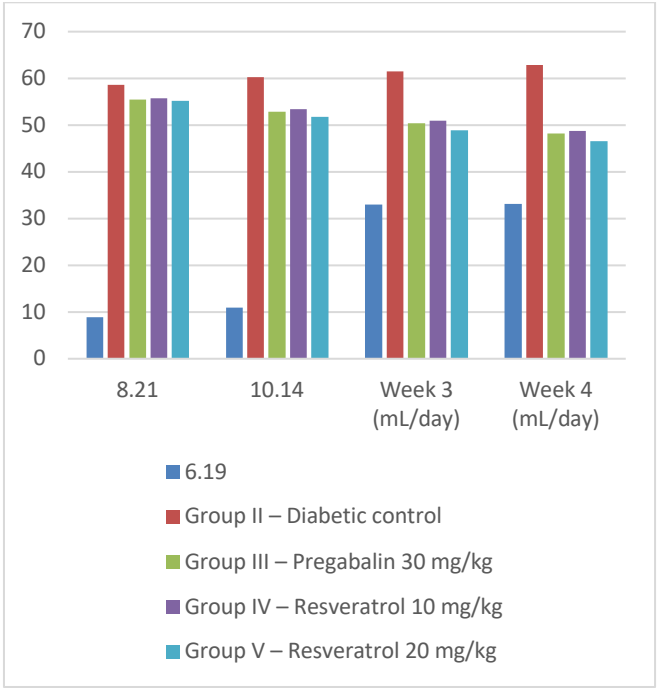


Figure 6: Effect of Resveratrol on Weekly Water Intake

General Behaviour, Physical Activity, Mortality and Toxicity: Descriptive monitoring indicated diminished grooming, locomotion, and responsiveness in untreated diabetic rats, with more favourable qualitative observations in the treated groups (Table 8). No deaths were reported in any group (0/6 each), and tremors, convulsions, excessive salivation, and respiratory abnormalities were not documented.

Table 8: General Behavioural and Toxicity Observations

Parameter	Group I Normal	Group II Diabetic control	Group III Pregabalin 30 mg/kg	Group IV Resveratrol 10 mg/kg	Group V Resveratrol 20 mg/kg
Grooming	Normal	Mildly reduced	Improved	Improved	Improved
Locomotor activity	Normal	Reduced	Improved	Improved	Improved
Posture	Normal	Mildly altered	Near normal	Near normal	Near normal
Responsiveness	Normal	Slightly reduced	Improved	Improved	Improved
Feeding behaviour	Normal	Increased	Improved	Improved	Improved

Tremors	Absent	Absent	Absent	Absent	Absent
Convulsions	Absent	Absent	Absent	Absent	Absent
Excessive salivation	Absent	Absent	Absent	Absent	Absent
Respiratory abnormality	Absent	Absent	Absent	Absent	Absent
Severe weakness	Absent	Mild	Absent	Absent	Absent
Mortality	0/6	0/6	0/6	0/6	0/6

Effect of Resveratrol on Behavioural Parameters: Treatment-associated changes in mechanical and thermal responses were examined at baseline, week 2, and week 4. The untreated diabetic group worsened over time, whereas both doses of resveratrol were associated with rising withdrawal thresholds and latencies. These outcomes are consistent with attenuation of evoked pain-like behaviour; spontaneous pain, nerve conduction velocity, and longer-term recovery were not measured.

Effect on Mechanical Allodynia: At week 4, paw withdrawal threshold declined to 2.71 ± 0.24 g in diabetic controls but increased to 5.94 ± 0.34 g after resveratrol 10 mg/kg and 6.52 ± 0.36 g after 20 mg/kg (Table 9; Figure 7). The pregabalin group reached 6.78 ± 0.35 g. The higher resveratrol dose showed a numerically stronger response than the lower dose, although a formal between-dose inference requires appropriate repeated-measures analysis of the source data.

Table 9: Effect of Resveratrol on Paw Withdrawal Threshold in Von Frey Test

Group	Treatment	Week 0 (g)	Week 2 (g)	Week 4 (g)
Group I	Normal control	8.43 ± 0.37	8.58 ± 0.39	8.72 ± 0.40
Group II	Diabetic control	3.21 ± 0.27	2.94 ± 0.25	2.71 ± 0.24
Group III	Pregabalin 30 mg/kg	3.35 ± 0.25	5.02 ± 0.31	6.78 ± 0.35
Group IV	Resveratrol 10 mg/kg	3.18 ± 0.29	4.46 ± 0.30	5.94 ± 0.34
Group V	Resveratrol 20 mg/kg	3.27 ± 0.26	4.91 ± 0.32	6.52 ± 0.36

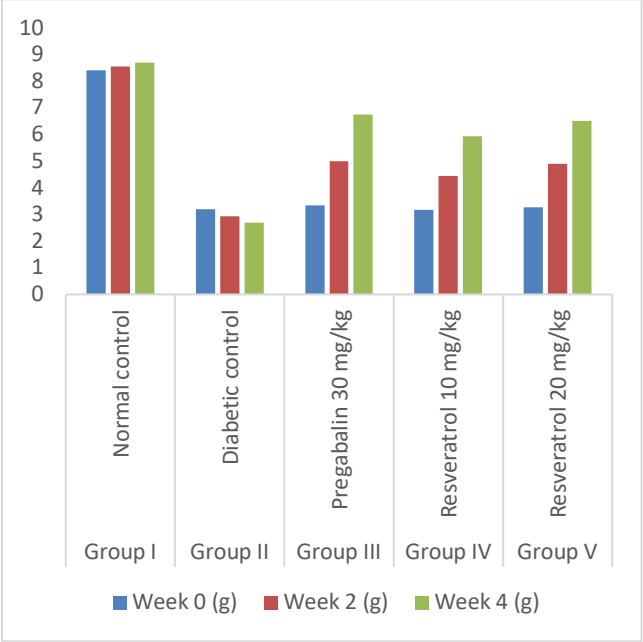


Figure 7: Effect of Resveratrol on Mechanical Paw Withdrawal Threshold

Effect on Thermal Hyperalgesia: The diabetic-control hot-plate latency fell from 6.14 ± 0.41 to 5.38 ± 0.37 seconds over four weeks. In contrast, week-4 latencies were 10.14 ± 0.47 seconds in the resveratrol 10 mg/kg group and 10.96 ± 0.48 seconds in the 20 mg/kg group, compared with 11.28 ± 0.49 seconds with pregabalin (Table 10; Figure 8). This directional improvement parallels the mechanical findings, supporting consistency across the two evoked behavioural assays.

Table 10: Effect of Resveratrol on Thermal Withdrawal Latency

Group	Treatment	Week 0 (sec)	Week 2 (sec)	Week 4 (sec)
Group I	Normal control	12.84 ± 0.52	13.02 ± 0.54	13.18 ± 0.55
Group II	Diabetic control	6.14 ± 0.41	5.72 ± 0.39	5.38 ± 0.37
Group III	Pregabalin 30 mg/kg	6.28 ± 0.39	9.12 ± 0.45	11.28 ± 0.49
Group IV	Resveratrol 10 mg/kg	6.05 ± 0.43	8.21 ± 0.44	10.14 ± 0.47
Group V	Resveratrol 20 mg/kg	6.19 ± 0.40	8.87 ± 0.46	10.96 ± 0.48

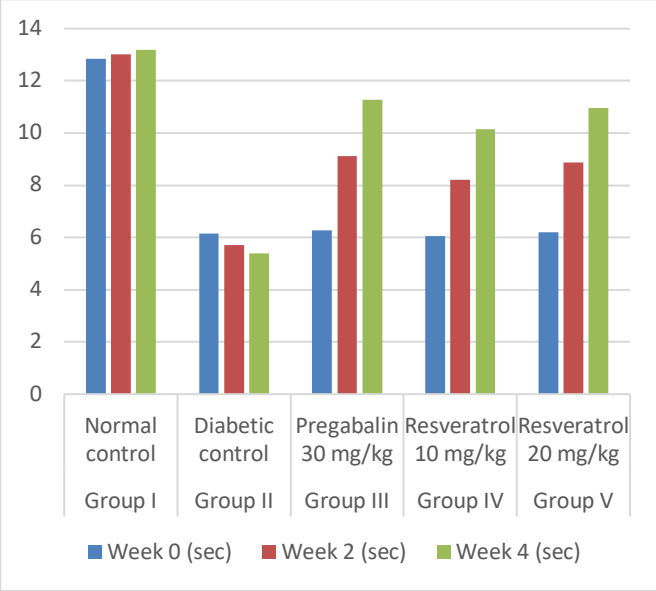


Figure 8: Effect of Resveratrol on Thermal Withdrawal Latency

Effect of Resveratrol on Biochemical Parameters: Terminal glycaemic and oxidative-stress measures were evaluated to explore metabolic correlates of the behavioural findings. Hyperglycaemia may contribute to reactive oxygen species production and altered antioxidant defence in peripheral nerve injury, as discussed in previous mechanistic reviews [5, 19].

Effect on Fasting Blood Glucose Level: Terminal fasting glucose averaged 294.83 ± 8.76 mg/dL in untreated diabetic rats, compared with 238.67 ± 7.21 and 205.33 ± 6.84 mg/dL in rats receiving resveratrol 10 and 20 mg/kg, respectively (Table 11; Figure 9). The 20 mg/kg group exhibited the larger numerical reduction, although glucose remained elevated relative to normal controls (96.17 ± 3.42 mg/dL). Glycaemic improvement may be one contributor to the concurrent behavioural and biochemical changes.

Table 11: Effect of Resveratrol on Fasting Blood Glucose at the End of Treatment

Group	Experimental condition	FBG (mg/dL)
Group I	Normal control	96.17 ± 3.42
Group II	Diabetic control	294.83 ± 8.76
Group III	Pregabalin 30 mg/kg	271.50 ± 7.94
Group IV	Resveratrol 10 mg/kg	238.67 ± 7.21
Group V	Resveratrol 20 mg/kg	205.33 ± 6.84

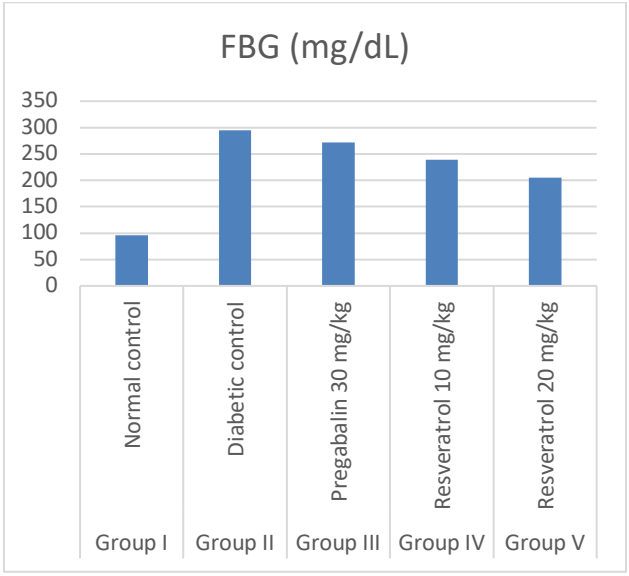


Figure 9: Effect of Resveratrol on Fasting Blood Glucose

Effect on Reduced Glutathione (GSH): Reduced glutathione was lower in the diabetic-control group (4.36 ± 0.24 µmol/g tissue) than in normal controls (8.72 ± 0.31 µmol/g tissue). The resveratrol groups showed higher terminal values of 6.21 ± 0.29 and 7.14 ± 0.30 µmol/g tissue at 10 and 20 mg/kg, respectively (Table 12; Figure 10). This pattern suggests partial restoration of the measured non-enzymatic antioxidant pool.

Table 12: Effect of Resveratrol on Reduced Glutathione Level

Group	Experimental condition	GSH (µmol/g tissue)
Group I	Normal control	8.72 ± 0.31
Group II	Diabetic control	4.36 ± 0.24
Group III	Pregabalin 30 mg/kg	5.18 ± 0.27
Group IV	Resveratrol 10 mg/kg	6.21 ± 0.29
Group V	Resveratrol 20 mg/kg	7.14 ± 0.30

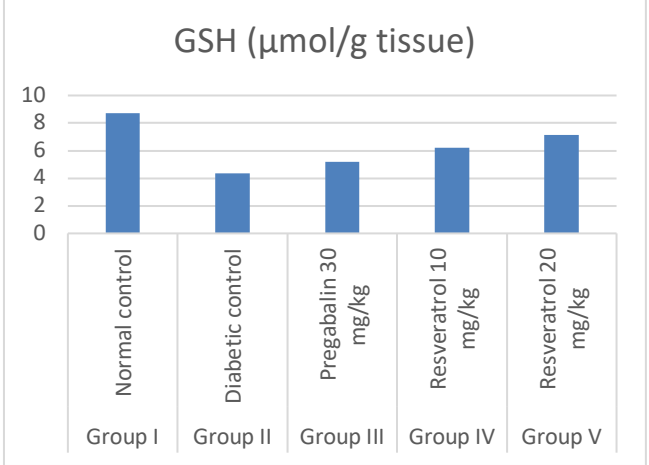


Figure 10: Effect of Resveratrol on Reduced Glutathione

Effect on Malondialdehyde (MDA): The diabetic-control group exhibited higher MDA (5.86 ± 0.25 nmol/mg protein) than normal controls (2.18 ± 0.12 nmol/mg protein). Resveratrol 10 and 20 mg/kg groups had lower MDA values of 4.12 ± 0.20 and 3.18 ± 0.17 nmol/mg protein, respectively (Table 13; Figure 11). As MDA is commonly used as an indirect marker of lipid peroxidation, these findings are compatible with reduced oxidative membrane injury; they do not independently identify its molecular source.

Table 13: Effect of Resveratrol on Malondialdehyde Level

Group	Experimental condition	MDA (nmol/mg protein)
Group I	Normal control	2.18 ± 0.12
Group II	Diabetic control	5.86 ± 0.25
Group III	Pregabalin 30 mg/kg	5.02 ± 0.23
Group IV	Resveratrol 10 mg/kg	4.12 ± 0.20
Group V	Resveratrol 20 mg/kg	3.18 ± 0.17

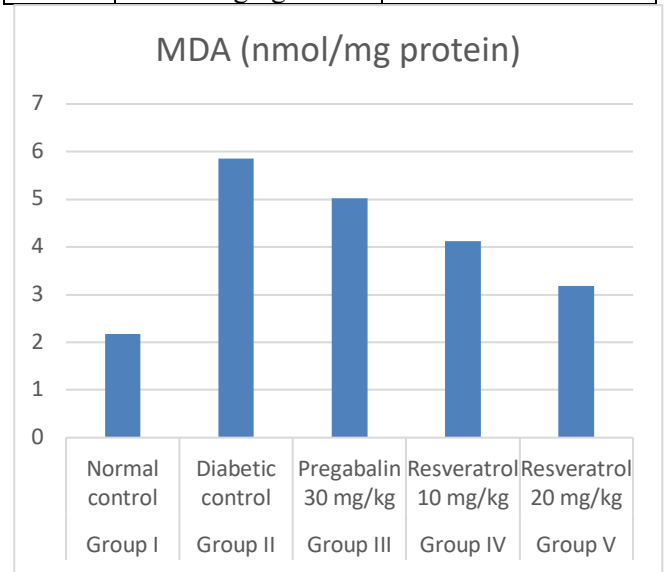


Figure 11: Effect of Resveratrol on Malondialdehyde

Effect on Superoxide Dismutase (SOD): Terminal SOD activity was 4.21 ± 0.22 U/mg protein in diabetic controls versus 7.84 ± 0.28 U/mg protein in normal controls. With resveratrol, mean activity increased to 5.87 ± 0.26 U/mg protein at 10 mg/kg and 6.82 ± 0.27 U/mg protein at 20 mg/kg (Table 14; Figure 12). The findings are consistent with relative preservation of enzymatic antioxidant capacity in treated diabetic animals.

Table 14: Effect of Resveratrol on Superoxide Dismutase Activity

Group	Experimental condition	SOD (U/mg protein)
Group I	Normal control	7.84 ± 0.28
Group II	Diabetic control	4.21 ± 0.22
Group III	Pregabalin 30 mg/kg	4.96 ± 0.24
Group IV	Resveratrol 10 mg/kg	5.87 ± 0.26
Group V	Resveratrol 20 mg/kg	6.82 ± 0.27

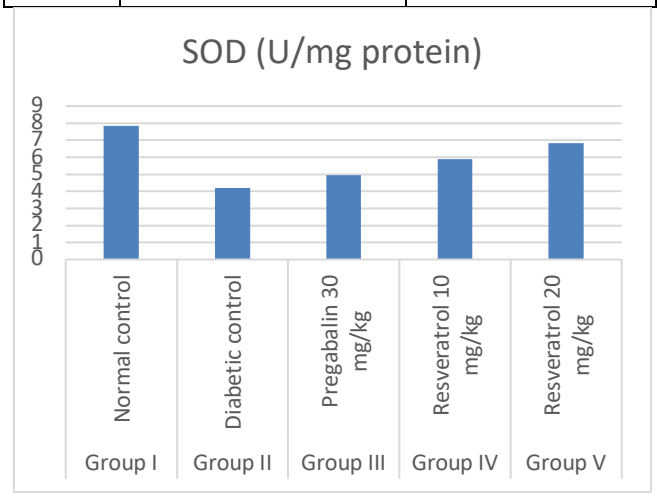


Figure 12: Effect of Resveratrol on Superoxide Dismutase Activity

Effect on Catalase (CAT): Catalase activity was reduced in diabetic controls (9.16 ± 0.48 U/mg protein) relative to normal controls (18.42 ± 0.62 U/mg protein). Values of 13.72 ± 0.55 and 16.18 ± 0.58 U/mg protein were reported with resveratrol 10 and 20 mg/kg, respectively (Table 15; Figure 13). The concordant directions of change in CAT, SOD, GSH, and MDA provide biochemical support for an antioxidant-associated treatment effect, without proving a specific signaling mechanism.

Table 15: Effect of Resveratrol on Catalase Activity

Group	Experimental condition	CAT (U/mg protein)
Group I	Normal control	18.42 ± 0.62
Group II	Diabetic control	9.16 ± 0.48
Group III	Pregabalin 30 mg/kg	10.84 ± 0.51
Group IV	Resveratrol 10 mg/kg	13.72 ± 0.55
Group V	Resveratrol 20 mg/kg	16.18 ± 0.58

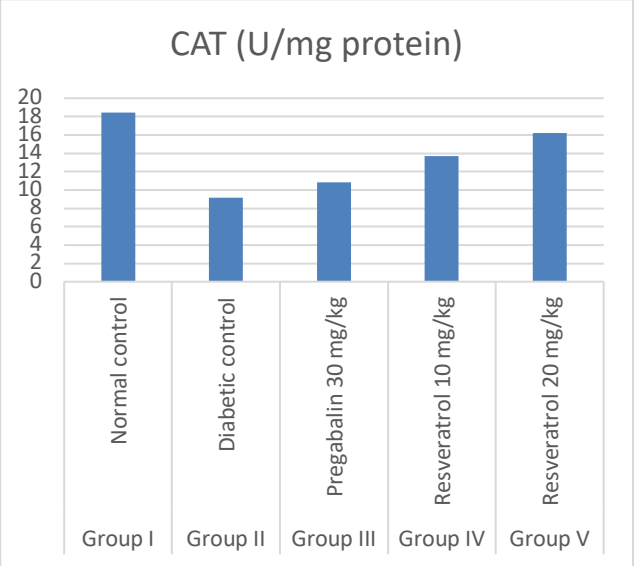


Figure 13: Effect of Resveratrol on Catalase Activity

Table 16: Summary of Biochemical Changes at the End of Treatment

Parameter	Normal control	Diabetic control	Pregabalin 30 mg/kg	Resveratrol 10 mg/kg	Resveratrol 20 mg/kg
FBG (mg/dL)	96.17	294.83	271.50	238.67	205.33
GSH (µmol/g tissue)	8.72	4.36	5.18	6.21	7.14
MDA (nmol/mg protein)	2.18	5.86	5.02	4.12	3.18
SOD (U/mg protein)	7.84	4.21	4.96	5.87	6.82
CAT (U/mg protein)	18.42	9.16	10.84	13.72	16.18

Histopathological Evaluation: Qualitative examination of H&E-stained sciatic nerve sections was used to complement functional and biochemical assessment. Architectural features considered included nerve-fibre organisation, apparent axonal integrity, interstitial oedema, and inflammatory infiltrates. Such histological observations can indicate tissue preservation, but confirmation of remyelination or regeneration would require additional specialised staining or morphometry.

Histopathological Evaluation of Sciatic Nerve: The normal-control photomicrograph shows comparatively preserved nerve architecture (Figure 14), while the diabetic-control image was interpreted as showing degenerative and inflammatory changes (Figure 15). Images from pregabalin and resveratrol-treated groups were reported to display less disruption (Figures 16–18). These interpretations are descriptive and should be confirmed by blinded pathology review, with documented sampling regions and reproducible scoring criteria.

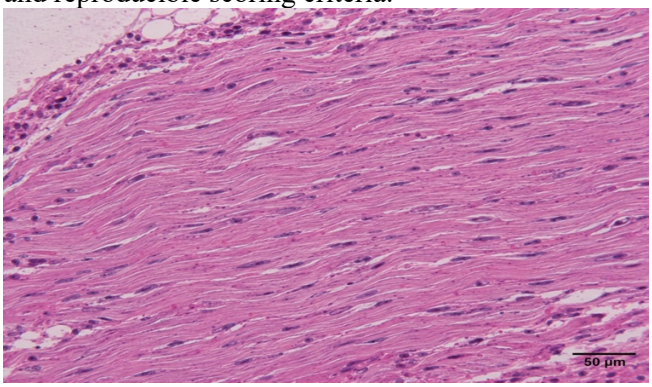


Figure 14: Photomicrograph of sciatic nerve of normal control group showing normal nerve fiber architecture and preserved axonal integrity (H&E, 400×).

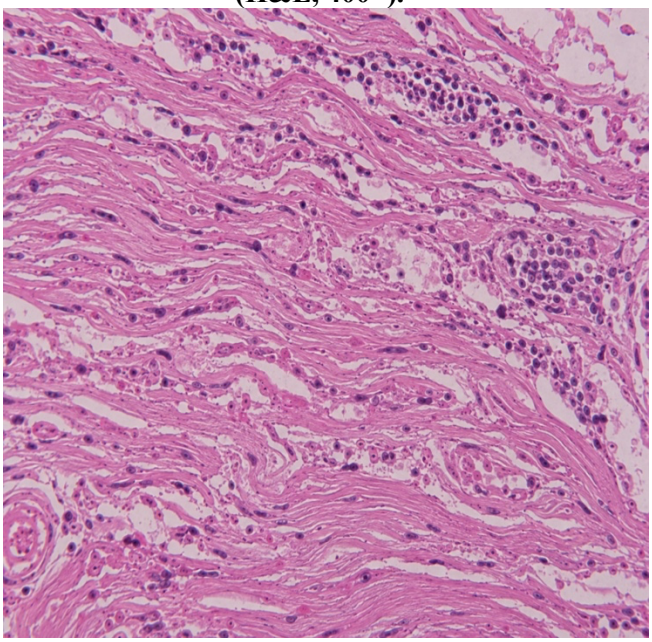


Figure 15: Photomicrograph of sciatic nerve of diabetic control group showing degeneration, edema, inflammatory changes, and disruption of nerve fiber architecture (H&E, 400×).

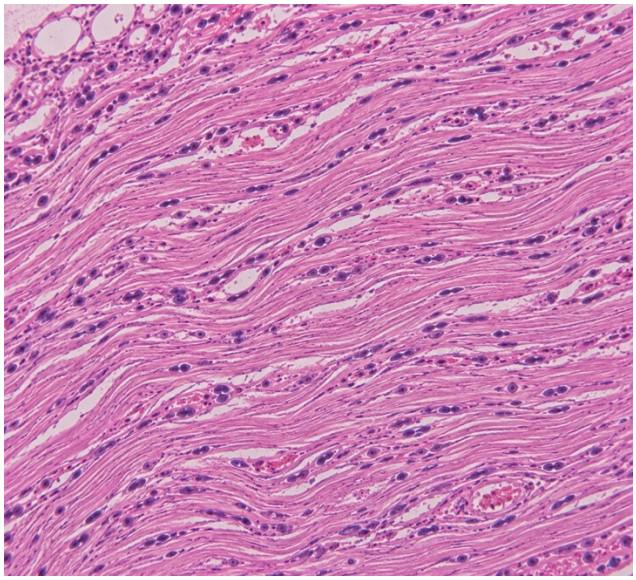


Figure 16: Photomicrograph of sciatic nerve of pregabalin-treated group showing improved nerve fiber integrity with reduced degenerative changes (H&E, 400×).

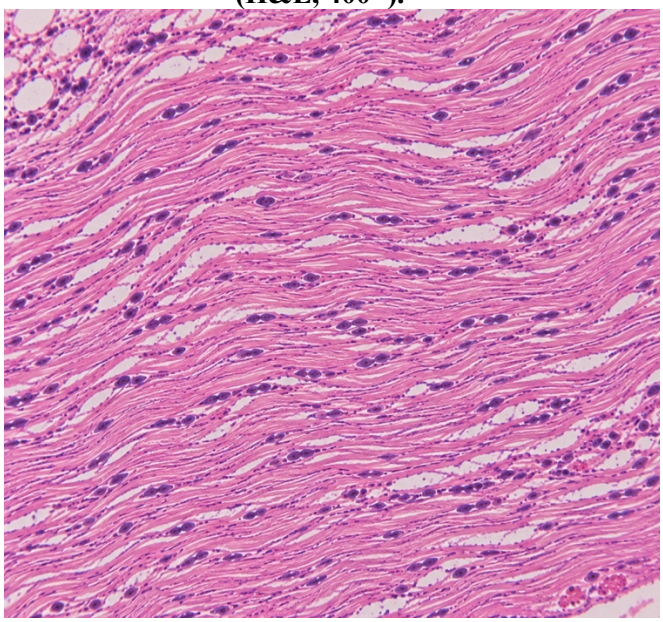


Figure 17: Photomicrograph of sciatic nerve of resveratrol 10 mg/kg-treated group showing partial improvement in nerve fiber architecture and reduced degeneration (H&E, 400×).

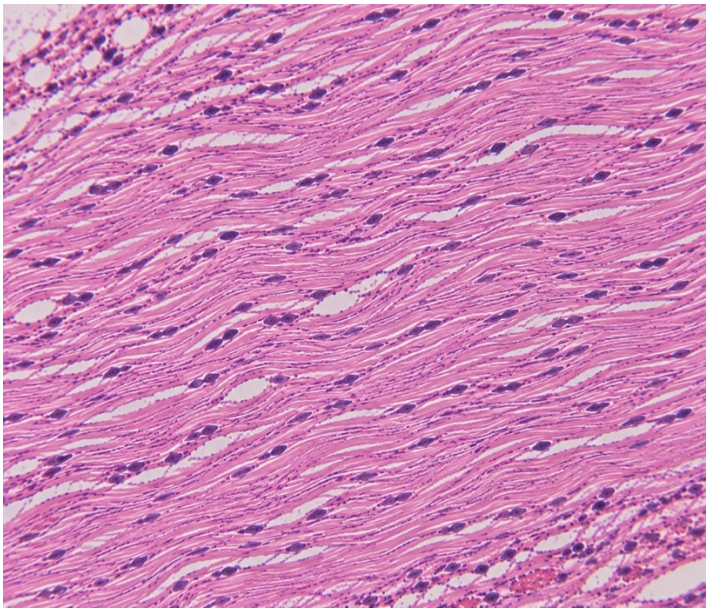


Figure 18: Photomicrograph of sciatic nerve of resveratrol 20 mg/kg-treated group showing improved nerve fiber integrity and reduced pathological changes (H&E, 400×).

Table 17: Histopathological Scoring of Sciatic Nerve

Group	Degeneration	Inflammation	Edema	Axonal damage	Nerve fiber integrity	Overall score
Group I – Normal control	0	0	0	0	0	0
Group II – Diabetic control	3	2	2	3	3	13
Group III – Pregabalin 30 mg/kg	2	1	1	2	2	8
Group IV – Resveratrol 10 mg/kg	2	1	1	2	1	7
Group V – Resveratrol 20 mg/kg	1	1	1	1	1	5

Comparative Histopathological Analysis: The supplied semiquantitative table assigns a total score of 13 to the diabetic-control group, compared with 8 for pregabalin, 7 for resveratrol 10 mg/kg, and 5 for resveratrol 20 mg/kg (Table 17). Table 18 likewise describes less degeneration and axonal injury at the higher resveratrol dose. As the source provides one summary score per group rather than individual-animal scores, dispersion, inter-rater agreement, and inferential comparisons cannot be established from these tables alone.

Table 18: Comparative Histopathological Findings in Sciatic Nerve

Histopathological parameter	Normal control	Diabetic control	Pregabalin 30 mg/kg	Resveratrol 10 mg/kg	Resveratrol 20 mg/kg
Degeneration	Absent	Severe	Moderate	Moderate	Mild
Inflammation	Absent	Moderate	Mild	Mild	Mild
Edema	Absent	Moderate	Mild	Mild	Mild
Axonal damage	Absent	Severe	Moderate	Moderate	Mild
Nerve fiber integrity	Preserved	Markedly reduced	Improved	Partially preserved	Better preserved
Regeneration	Normal architecture	Minimal/absent	Mild	Moderate	More apparent

Table 19: Summary of Statistical Analysis of Major Experimental Parameters

Parameter	Statistical test	Overall ANOVA	Important comparison	p-value	Interpretation
Fasting blood glucose	One-way ANOVA	F = 82.64	Diabetic vs Normal	<0.001	Significant difference
Paw withdrawal threshold – Week 4	One-way ANOVA	F = 49.82	Diabetic vs Resveratrol 20 mg/kg	<0.001	Significant difference
Thermal withdrawal latency – Week 4	One-way ANOVA	F = 38.76	Diabetic vs Resveratrol 20 mg/kg	<0.001	Significant difference
GSH	One-way ANOVA	F = 31.54	Diabetic vs Resveratrol 20 mg/kg	<0.001	Significant difference
MDA	One-way ANOVA	F = 42.18	Diabetic vs Resveratrol 20 mg/kg	<0.001	Significant difference
SOD	One-way ANOVA	F = 28.63	Diabetic vs Resveratrol 20 mg/kg	<0.001	Significant difference
CAT	One-way ANOVA	F = 35.27	Diabetic vs Resveratrol 20 mg/kg	<0.001	Significant difference

Table 20: Tukey's Multiple Comparison Analysis

Parameter	Comparison	Mean difference	p-value	Significance
FBG	Normal vs Diabetic	198.66	<0.001	***
FBG	Diabetic vs Pregabalin	23.33	<0.05	*
FBG	Diabetic vs Resveratrol 10 mg/kg	56.16	<0.001	***
FBG	Diabetic vs Resveratrol 20 mg/kg	89.50	<0.001	***
PWT Week 4	Normal vs Diabetic	6.01	<0.001	***
PWT Week 4	Diabetic vs Pregabalin	4.07	<0.001	***
PWT Week 4	Diabetic vs Resveratrol 10 mg/kg	3.23	<0.001	***
PWT Week 4	Diabetic vs Resveratrol 20 mg/kg	3.81	<0.001	***
TWL Week 4	Normal vs Diabetic	7.80	<0.001	***
TWL Week 4	Diabetic vs Pregabalin	5.90	<0.001	***
TWL Week 4	Diabetic vs Resveratrol 10 mg/kg	4.76	<0.001	***
TWL Week 4	Diabetic vs Resveratrol 20 mg/kg	5.58	<0.001	***

GSH	Diabetic vs Resveratrol 10 mg/kg	1.85	<0.001	***
GSH	Diabetic vs Resveratrol 20 mg/kg	2.78	<0.001	***
MDA	Diabetic vs Resveratrol 10 mg/kg	1.74	<0.001	***
MDA	Diabetic vs Resveratrol 20 mg/kg	2.68	<0.001	***
SOD	Diabetic vs Resveratrol 10 mg/kg	1.66	<0.001	***
SOD	Diabetic vs Resveratrol 20 mg/kg	2.61	<0.001	***
CAT	Diabetic vs Resveratrol 10 mg/kg	4.56	<0.001	***
CAT	Diabetic vs Resveratrol 20 mg/kg	7.02	<0.001	***

SUMMARY

The present study was designed to evaluate the effect of resveratrol on diabetic neuropathy in alloxan-induced diabetic rats. A total of 30 male Wistar rats were divided into five groups: normal control, diabetic control, pregabalin-treated group (30 mg/kg/day), resveratrol-treated group (10 mg/kg/day), and resveratrol-treated group (20 mg/kg/day). Diabetes was induced using alloxan monohydrate at a dose of 150 mg/kg, and diabetic neuropathy was assessed through behavioural changes.

Mechanical sensitivity and thermal hyperalgesia were evaluated using the Von Frey filament test and Eddy's hot plate test, respectively. Biochemical parameters, including fasting blood glucose, reduced glutathione, malondialdehyde, superoxide dismutase, and catalase, were assessed to determine changes in glycaemic status and antioxidant defence. Histopathological examination of the sciatic nerve was also performed to investigate diabetes-associated structural damage.

The findings reported in the study indicated that diabetic control animals exhibited increased blood glucose levels, enhanced mechanical and thermal sensitivity, increased lipid peroxidation, and reduced antioxidant defence. Resveratrol treatment improved the paw withdrawal threshold and thermal withdrawal latency compared with the diabetic control group. It also showed a reduction in fasting blood glucose and malondialdehyde levels, accompanied by improvements in reduced glutathione, superoxide dismutase, and catalase. Histopathological observations indicated better preservation of sciatic nerve architecture in resveratrol-treated animals. The 20 mg/kg dose generally showed greater numerical improvement than the 10 mg/kg dose across the evaluated parameters.

CONCLUSION

The findings of the present study suggest that resveratrol may have beneficial effects in experimental diabetic neuropathy. Its effects were associated with improvements in neuropathic pain responses, glycaemic status, antioxidant defence, and sciatic nerve structure. The higher dose of resveratrol (20 mg/kg/day) showed greater numerical improvement than the lower dose (10 mg/kg/day) in the reported observations.

These findings support further investigation of resveratrol as a potential neuroprotective agent in diabetic neuropathy. However, additional studies using adequately powered experimental designs, validated statistical analysis, and detailed mechanistic evaluation are required to establish its efficacy, dose–response relationship, safety, and potential clinical relevance. The findings from this animal study should not be directly extrapolated to human treatment without further evidence.

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