Received: 14 Jan. 2026 | Revised: 15 Feb. 2026 | Accepted: 30 March. 2026

Research Article

ISBN: 978-81-995400-3-3

"PROTECTIVE ROLE OF THE AYURVEDIC HERBO-MINERAL FORMULATION CHANDRAPRABHA VATI IN DIABETIC NEUROPATHY INDUCED BY HIGH-FAT DIET AND STREPTOZOTOCIN IN RATS."

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FUNDING INFORMATION:
Not Applicable

ABSTRACT:
Diabetes mellitus is a metabolic disorder characterized by chronic hyperglycemia due to altered insulin secretion or function. Neuropathic pain, a frequent complication, is commonly treated with synthetic drugs like antioxidants, antidepressants, and anticonvulsants, though prolonged use can result in severe adverse effects. Herbal medicines, particularly Chandraprabha Vati, have shown promise in managing diabetes and related complications. While its antidiabetic and anti-obesity effects have been validated in preclinical and clinical studies, its efficacy in diabetic neuropathy remains unexplored. The present study evaluated Chandraprabha Vati in a high-fat diet (HFD) and streptozotocin (STZ)-induced diabetic neuropathy model in albino rats. Diabetic neuropathy was induced by feeding rats with HFD for eight weeks, followed by STZ injection (35 mg/kg). Control animals received a standard chow diet. Treatment groups included Chandraprabha Vati (200 mg/kg), Amitriptyline (10 mg/kg), and a vehicle control (0.25% Na-CMC) for six weeks. Behavioral tests viz. heat-hyperalgesia, cold allodynia, grip strength, walking function and oral glucose tolerance test (OGTT) showed significant improvement with the treatment of Chandraprabha Vati. Elevated levels of glucose, lipids, liver enzymes, and oxidative stress markers were significantly reduced, while insulin and antioxidant levels (SOD, GSH, catalase) improved. Pro-inflammatory markers (TNF-α, IL-6). These findings indicate that Chandraprabha Vati offers significant therapeutic potential for diabetic neuropathy, presenting a safe and effective alternative to conventional treatments.

KEYWORDS: Diabetes, Diabetic Neuropathy, Chandraprabha vati, Amitriptyline, High-fat diet, Streptozotocin

1.0 Introduction:

Diabetic Neuropathy:

Diabetes can cause neuropathy, a condition that can cause issues all over the body. Nerves that regulate sensation, movement, and other processes can be impacted by diabetes. [1]

Patients with diabetic neuropathy experience severe suffering and a marked decline in quality of life. It is evident that hyperglycemia plays a significant role in the development of nerve injury. Recent research indicates that in individuals with impaired glucose tolerance (IGT), even minor blood glucose variations may be responsible for the development of neuropathic pain and damage to both tiny and large nerve fibers. [2] Researchers in neurosurgery, neurology, and neuroscience at The Ohio State University Wexner Medical Center and College of Medicine will be able to test a novel diagnosis and therapy combination for excruciating diabetic neuropathy thanks to a $3.6 million grant from the National Institutes of Health. The method uses a patent-pending device called Detecting Early Neuropathy (DEN) to assess tiny fiber nerve activity in conjunction with spinal cord stimulation. [3]

Globally, diabetes is becoming a more significant health issue. In the US, the condition affects about 37 million people, or around 1 in 10 people, as per the Centers for condition Control and Prevention. Peripheral neuropathy is one of the many health issues linked to diabetes, and it can cause excruciating agony. [4]

The loss of nerve endings that supply our tissues and organs is known as peripheral neuropathy, and it can exacerbate diabetes management by impairing neural transmission between the brain and peripheral tissues and organs. Peripheral neuropathy is thought to affect around 30 million Americans. [5]

Distal symmetric sensorimotor polyneuropathy has been associated primarily with novel systemic biomarkers of oxidative stress, inflammation, and vascular activation; however, prospective studies and hypothesis-free approaches involving novel omics technologies should be the focus of future research in order to identify biomarkers that can be used to better understand and predict the development of diabetic neuropathies. [6]

Ayurvedic and plant-derived products are generally economical and exhibit a broad spectrum of biological activities. Herbal medicines are often regarded as safer alternatives to synthetic drugs, as they tend to produce fewer toxic effects and are associated with a lower incidence of adverse reactions (Karimi et al, 2015).

2.0 Materials and Methods

2.1 Chemicals and reagents

Streptozotocin, Sodium citrate, Trichloroacetic acid, 5,5-Dithiobis, 2-Nitro Benzoic Acid (DTNB), Nitro Blue Tetrazolium Chloride (NBT), β-Nicotinamide Adenine Dinucleotide Phosphate (NADPH), Citric acid, D-glucose, Sodium carboxymethyl cellulose were purchased from Sisco Research Laboratories Pvt. Ltd., Mumbai. Amitryptiline, Thiobarbituric acid, and Hydrogen peroxide were purchased from Sigma-Aldrich Chemicals Private Limited, India. Glucose monitoring system, and measurements strips (Contour Plus, India) were procured from the local suppliers of Pune. All other chemicals and reagents used were of the highest commercial grade. Chandraprabha Vati (Shree Baidyanath Ayurved Bhawan Pvt. Ltd., India) was procured from local medical store.

2.2 Experimental animals

In house male Sprague Dawley Rats (180-200 g) were housed in polypropylene cages in a controlled room temperature 22±1°C and relative humidity of 60–70% with 12:12h light and dark cycle in a registered animal house. All procedures of this study were in accordance with the guidelines provided by the Committee for the Control and Supervision of Experiments on Animals (CCSEA), Govt.

of India. The animal experimental study protocols (IIRT/IAEC/35/2024/028) were approved before the commencement of the experiment.

2.3 Preparation of streptozotocin solution and Induction of diabetes in animals

Streptozotocin (STZ) was weighed accurately, and separate aliquots were prepared and maintained in an ice bath. Immediately prior to administration, STZ was dissolved in freshly prepared, ice-cold 100 mM sodium citrate buffer (pH 4.5), and filtered through a 0.2-µm membrane filter. The buffer was added to each aliquot just before dosing. All preparation steps were carried out in a dark room to minimize STZ degradation (Wang et al, 2021).

Type 2 diabetes mellitus was induced in the rats using a modified protocol based on previously reported methods. Animals in the diabetic group were fed a modified high-fat diet (HFD), while the normal control group received a standard laboratory chow diet. The HFD was prepared by blending powdered standard chow (25%) with defined proportions of sugar (25%), corn starch (10%), refined wheat flour (maida; 10%)), cholesterol (0.20%), and dalda (29.8%). The HFD was administered daily for a period of 8 weeks. Following sustained HFD feeding, a single intraperitoneal injection of streptozotocin (STZ) at a dose of 35 mg/kg was administered. Blood glucose levels were measured 48 hours after STZ administration to assess the development of diabetes (Jain et al, 2014; Rahigude et al, 2012).

2.4 Treatment schedule and experimental protocol

A total of thirty animals were included in the study. Six animals were assigned to the normal control group, while the remaining animals were rendered diabetic. Normal control rats received distilled water and were maintained under non-diabetic conditions. Three days after streptozotocin administration, diabetic rats were randomly allocated into experimental groups. The diabetic control group received the vehicle (0.25% sodium carboxymethyl cellulose). The standard treatment group was administered AMT (10 mg/kg), while another group received Chandraprabha Vati (CPV) at a dose of 200 mg/kg. An additional combination group was treated with CPV (100 mg/kg) along with AMT (5 mg/kg). Body weight and fasting blood glucose levels were monitored weekly throughout the study.

2.5 Oral glucose tolerance test

Glucose intolerance was assessed using the oral glucose tolerance test (OGTT). The test was conducted after 8 weeks of high-fat diet feeding, prior to streptozotocin administration, in animals fasted overnight for 12 h. Glucose was administered orally at a dose of 2 g/kg body weight, and blood samples were collected from the tail vein at 0, 30, 60, and 120 min for glucose estimation. Animals exhibiting impaired glucose tolerance were classified as diabetic. A similar OGTT was repeated at the end of the drug treatment period to evaluate treatment effects (Tang et al, 2018).

2.6 Development of diabetic neuropathy

The progression of diabetic neuropathy was systematically evaluated across all experimental groups using a battery of behavioral and functional assessments, including the tail immersion test for thermal hyperalgesia, the cold plate test for cold allodynia, the pinprick test for mechanical hyperalgesia, grip strength test, walking function test, actophotometer-based locomotor activity assessment, and the rotarod test for motor coordination.

3.0 Experimental Work:

Experimental Groups:

Groups	Treatment; p.o.	Diabetic condition
G1	Normal Control (NC)	Standard chow diet+

		non-diabetic
G2	Diabetic Control (DC)	High Fat Diet+ STZ
G3	Amitriptyline- 10 mpk	High Fat Diet+ STZ
G4	Chandraprabha Vati- 200 mpk	High Fat Diet+ STZ
G5	Mehamudgara vati- 100 mpk	High Fat Diet+ STZ
G6	Chandraprabha Vati- 100 mpk + AMT- 5 mpk	High Fat Diet+ STZ
G7	Mehamudgara vati- 50 mpk + AMT- 5 mpk	High Fat Diet+ STZ

Experimental Work Done:

1. Induction of diabetes and eventually diabetic neuropathy using HFD-STZ model
2. Oral Glucose tolerance test- OGTT- Before and after Diabetes induction
3. Behavioural Parameters
4. Biochemical analysis
5. Histopathological analysis

4.0 INTERIM STUDY OUTCOMES: - CHANDRAPRABHA VATI

4.1 Body Weight

Table 1: Effect of Chandraprabha Vati (CPV) on the animal body weight (absolute)

Days/Weeks	Absolute Body Weight (g)				
	G1	G2	G3	G4	G6
	Control	Diabetic control	AMT- 10 mpk	CPV- 200 mpk	CPV- 100mpk+AMT -5mpk
D-0	203.7±4.9	206.7±5.2	202.7±7.3	206.0±3.8	206.0±6.3
W-1	216.3±17.2	220.2±7.8	214.0±8.0	219.7±6.1	222.8±10.4
W-2	214.3±7.2	233.8±9.9	222.5±11.0	228.8±11.1	230.3±9.5
W-3	219.2±7.1	249.3±10.7	232.7±19.6	237.7±21.8	250.8±12.5
W-4	224.5±11.7	260.3±11.5 #	242.3±19.1	249.8±22.7	261.3±14.9
W-5	230.2±13.2	274.3±14.2 #	252.7±20.5	271.8±19.4	281.8±15.1
W-6	237.5±15.1	284.5±13.1 #	272.8±18.6	285.0±23.8	295.7±15.1
W-7	243.5±14.8	295.2±20.4 #	291.5±22.7	295.5±29.5	304.0±14.1
W-8	247.5±15.6	304.7±18.1 #	307.2±29.0	306.5±31.0	319.7±19.3
W-9	252.2±15.9	304.7±18.0 #	327.7±36.7	325.2±33.5	330.5±19.9
W-10	256.0±15.2	297.0±18.4 #	323.3±37.3	321.2±32.3	324.7±20.5
W-11	259.0±15.6	292.5±19.9	319.8±38.7**	315.7±31.8**	319.3±22.6**
W-12	262.7±15.9	285.7±16.0	322.7±38.7***	320.0±33.5***	327.2±22.2***
W-13	267.5±15.0	279.3±13.0	330.2±37.8***	323.5±34.2***	333.8±23.6***

W-14	272.5±13.6	271.0±9.8#	337.7±36.9***	328.7±33.0***	344.3±24.0***

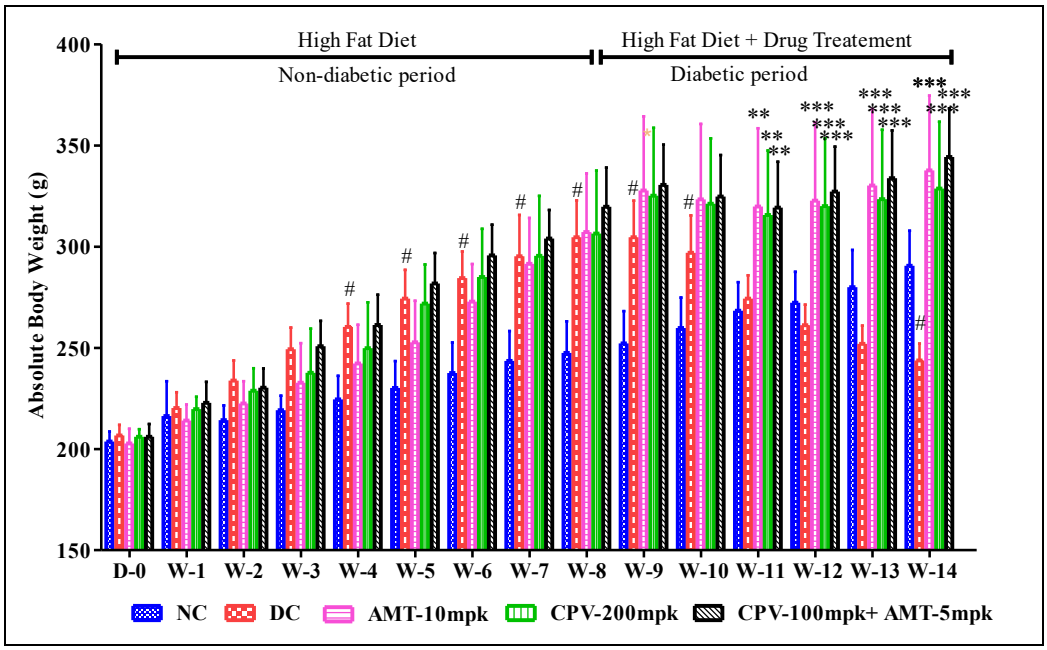

Figure-1: Effect of CPV alone and in combination with AMT on animal body weight. Values in the results are expressed as mean± SD, (n=6); Data is analyzed by Two-way analysis of variance (ANOVA) followed by Bonferroni's multiple comparison t-test; *p<0.05, **p<0.01, ***p<0.001, significantly different in comparison to diabetic control. #p<0.05 significantly different in comparison to normal control.

4.2 Body Weight Change

Table 2: Effect of Chandraprabha Vati (CPV) on the animal body weight Change

Days/Weeks	Body Weight Change (%)				
	G1	G2	G3	G4	G6
	Control	Diabetic control	AMT- 10 mpk	CPV- 200 mpk	CPV-100mpk+AMT-5mpk
W-1	6.2±8.1	6.5±2.6	5.6±3.1	8.1±4.2	4.7±2.1
W-2	5.2±3.0	13.1±3.0	9.8±3.1	11.9±4.6	11.5±2.6
W-3	7.6±3.1	20.6±3.8	14.8±8.8	21.8±6.2	18.3±3.2
W-4	10.2±5.3	26.0±5.0#	19.6±8.5	26.9±7.9	25.2±4.6
W-5	13.0±6.3	32.7±5.4#	24.7±9.0	36.9±8.1	31.0±4.4
W-6	16.6±7.2	37.7±5.6#	34.7±9.2	43.7±9.9	38.4±5.2
W-7	19.6±7.4	42.7±7.6#	43.9±11.0	47.8±10.2	45.1±6.9
W-8	21.6±7.8	47.3±6.2#	51.6±14.0	55.5±13.1	55.3±7.0
W-9	23.9±8.1	47.3±5.5#	61.7±17.2	60.7±13.7	62.0±7.2
W-10	27.6±7.8	43.6±6.2	59.5±17.6	57.9±13.8	60.4±8.1
W-11	31.8±7.3	32.7±2.9	57.8±18.2***	55.3±14.5**	56.3±8.7**
W-12	33.8±7.7	26.4±2.9	59.2±18.0***	59.0±13.4***	58.5±8.6***

W-13	37.5±9.0	21.9±2.9	62.9±17.4***	62.3±14.3***	61.6±8.3***
W-14	42.7±8.4	18.0±2.6#	66.6±16.9***	67.4±14.5***	67.0±9.2***

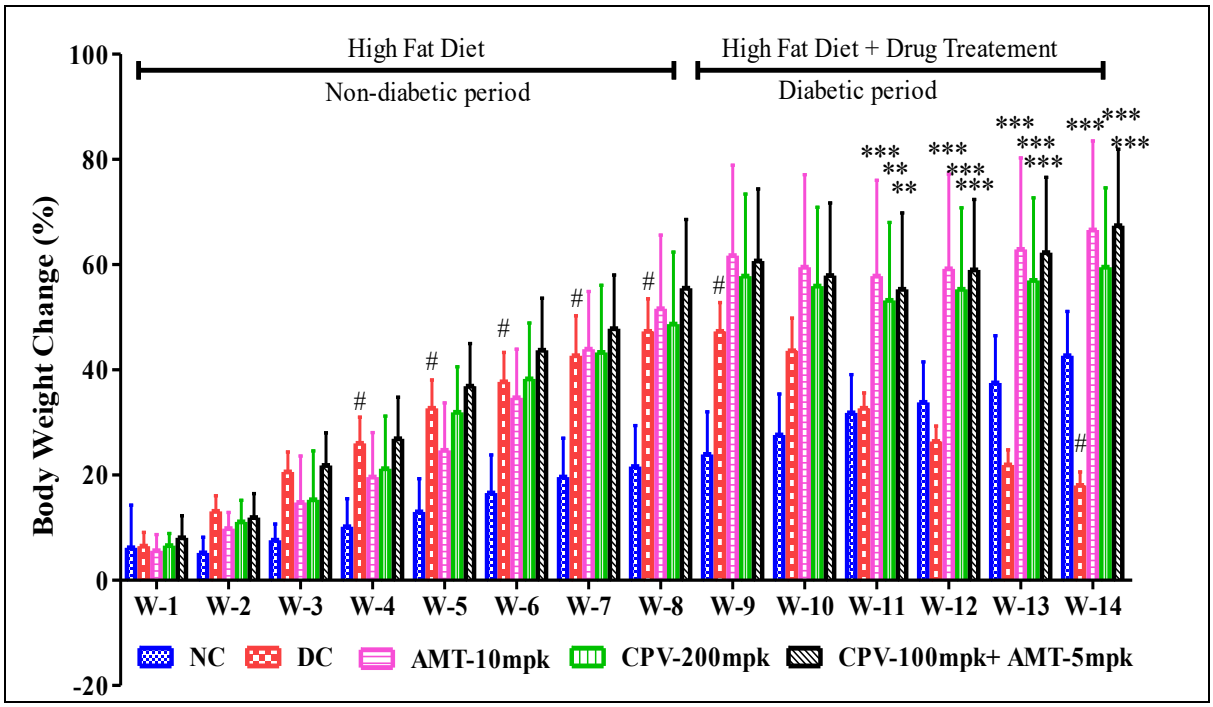

Figure-2: Effect of CPV alone and in combination with AMT on animal body weight change. Values in the results are expressed as mean± SD, (n=6); Data is analyzed by Two-way analysis of variance (ANOVA) followed by Bonferroni's multiple comparison t-test; *p<0.05, **p<0.01, ***p<0.001, significantly different in comparison to diabetic control. #p<0.05 significantly different in comparison to normal control.

4.2.1 OGTT-Before STZ Injection

Table 1: Effect of Chandraprabha Vati (CPV) on OGTT- Before STZ injection

Groups	Treatment	Blood Glucose Level (mg/dL) at Different Time points				
		0 Min	30 Min	60 Min	90 Min	120 Min
G1	Normal Control	57.8±6.6	115.7±12.3	128.0±14.0	116.8±15.3	99.3±13.3
G2	Diabetic control	161.3±7.7	268.7±22.3	237.2±17.8	227.5±15.8	180.8±9.5
G3	AMT-10mpk	163.7±7.6	253.5±23.0	210.0±8.3***	196.5±10.7***	147.5±7.1***
G4	CPV-200mpk	161.3±8.6	256.5±15.4	227.8±12.2	202.7±10.5**	152.5±9.0**
G6	CPV-200mpk+ AMT 5mpk	162.8±22.3	250.7±4.8	225.0±8.9	190.0±6.9***	149.7±4.3***

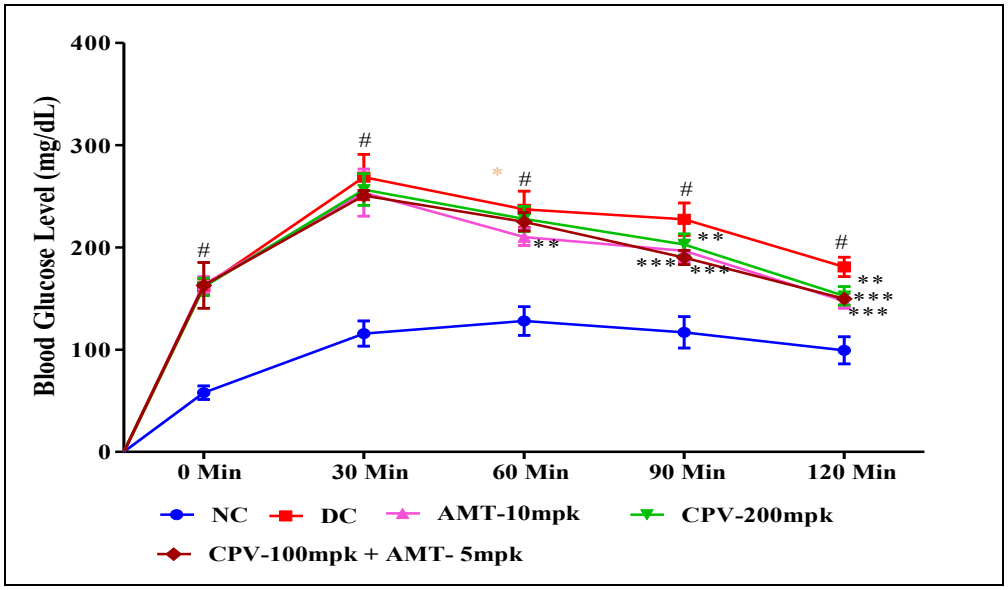

Figure-2: Effect of CPV alone and in combination with AMT on OGTT (Before STZ injection). Values in the results are expressed as mean± SD, (n=6); Data is analyzed by Two-way analysis of variance (ANOVA) followed by Bonferroni's multiple comparison t-test; *p<0.05, **p<0.01, ***p<0.001, significantly different in comparison to diabetic control. #p<0.05 significantly different in comparison to normal control.

4.2.2 OGTT-After Drug Treatment (In Diabetic animals)

Table 1: Effect of Chandraprabha Vati (CPV) on OGTT- After Drug Treatment

Groups	Treatment	Blood Glucose Level (mg/dL) at Different Time points				
		0 Min	30 Min	60 Min	90 Min	120 Min
G1	Normal Control	63.8±4.8	104.5±5.9	125.2±7.1	105.0±5.2	93.2±7.5
G2	Diabetic control	218.7±4.5#	267.2±9.8#	272.7±9.6#	239.5±9.2#	211.0±9.3#
G3	AMT-10mpk	162.0±6.2***	200.8±7.2***	219.3±9.8***	207.5±10.3***	194.0±9.1**
G4	CPV-200mpk	183.7±11.2***	225.8±7.1***	228.5±7.4***	226.2±6.6*	196.5±10.4*
G6	CPV-200mpk+ AMT 5mpk	140.7±6.9***	175.3±9.1***	177.0±7.2***	172.0±6.7***	163.8±8.0***

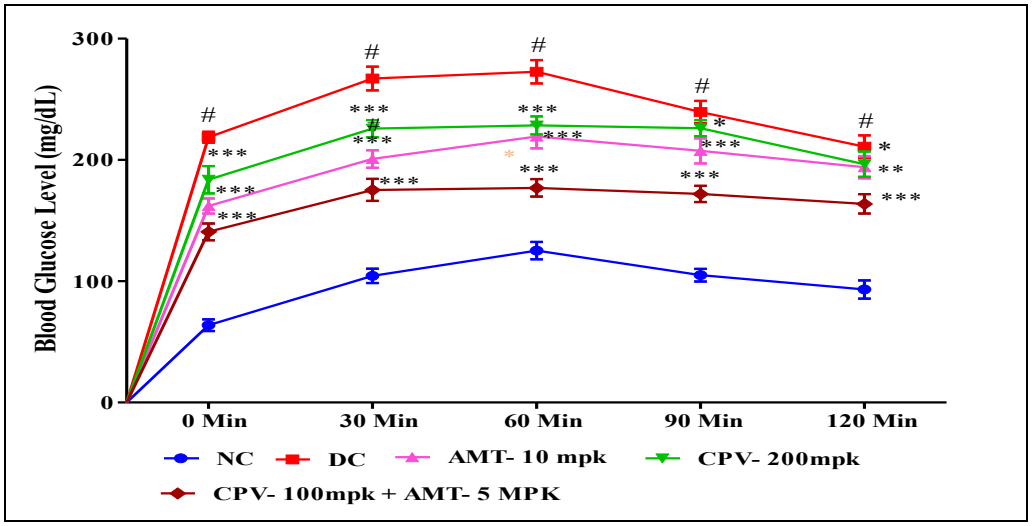

Figure-2: Effect of CPV alone and in combination with AMT on OGTT (After Drug Treatment). Values in the results are expressed as mean± SD, (n=6); Data is analyzed by Two-way analysis of variance (ANOVA) followed by Bonferroni's multiple comparison t-test; *p<0.05, **p<0.01, ***p<0.001, significantly different in comparison to diabetic control. #p<0.05 significantly different in comparison to normal control.

4.3 Biochemical Parameter

Table 1: Effect of Chandraprabha Vati (CPV) on Blood Glucose Level

Groups	Treatment	Blood Glucose Level (mg/dL)
G1	Normal Control	108.7±14.8
G2	Diabetic control	271.6±17.6#
G3	AMT-10mpk	149.0±17.2***
G4	CPV- 200mpk	195.4±7.4***
G6	CPV- 200mpk+ AMT 5mpk	157.3±18.6***ψ

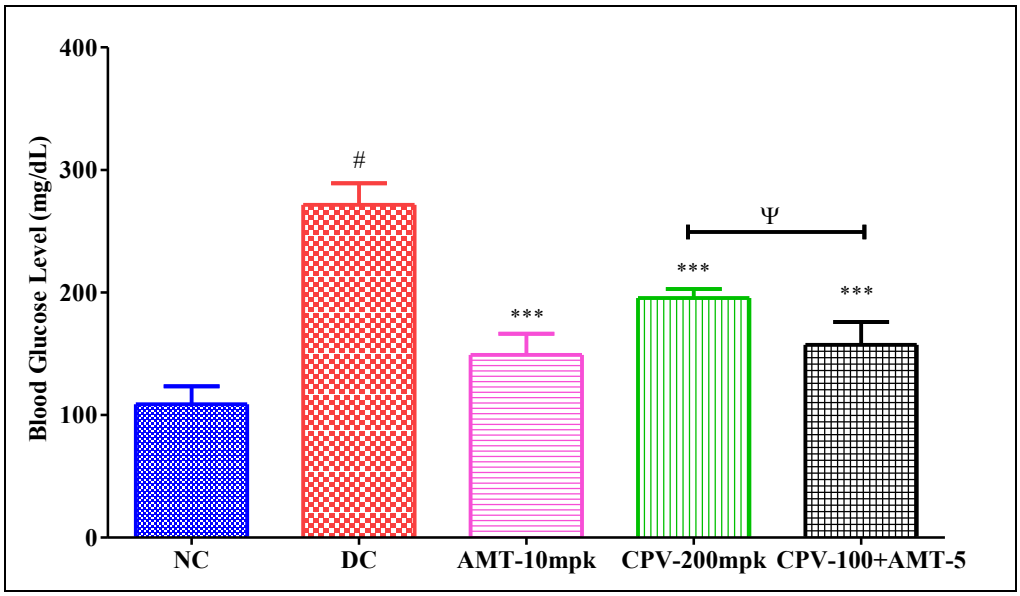

Figure-2: Effect of CPV alone and in combination with AMT on blood glucose level. Values in the results are expressed as mean± SD, (n=6); Data is analyzed by One-way analysis of variance (ANOVA) followed by Tukey's multiple comparison t-test; *p<0.05, **p<0.01, ***p<0.001, significantly different in comparison to diabetic control. # p<0.05 significantly different in comparison to normal control. Ψ p<0.05 significantly different in comparison to CPV-200mpk.

5.0 Conclusion :

The antidiabetic potential of Chandraprabha Vati (CPV) and Mehamudgara Vati (MMV) was evaluated in STZ-induced diabetic rats, focusing on body weight regulation, percentage change in weight, oral glucose tolerance test (OGTT), and fasting blood glucose levels.

For **CPV**, normal control animals displayed steady weight gain over 14 weeks (203.7±4.9 g to 272.5±13.6 g). Diabetic controls showed higher but dysregulated weight gain, peaking early and declining later. Treatment with AMT (10mg/kg) and CPV (200mg/kg) significantly improved weight regulation from week 11 onwards, reaching 337.7 ± 36.9 g and 328.7 ± 33.0 g, respectively ($p<0.001$ vs. diabetic control). The combination (CPV 100 mg/kg+AMT 5 mg/kg) produced the strongest effect (344.3±24.0 g, $p<0.001$). Percentage weight change confirmed these findings, with CPV and combination groups showing ~67% gain, significantly higher than diabetic controls (18.0±2.6% at week 14). OGTT results indicated that CPV improved glucose handling, though less effectively than AMT. Importantly, the CPV + AMT group showed the most significant reduction in glucose at 90 and 120 min ($p<0.001$), suggesting synergism. Fasting glucose levels further confirmed these outcomes: diabetic controls-maintained hyperglycemia (271.6±17.6 mg/dL), while AMT reduced levels to 149.0±17.2 mg/dL, CPV to 195.4±7.4 mg/dL, and CPV+AMT to 157.3±18.6 mg/dL ($p<0.001$).

In conclusion, CPV demonstrated significant antihyperglycemic and metabolic regulatory effects. While CPV improved body weight and moderately enhanced glucose tolerance, more effective in restoring long-term weight gain and glucose handling. Importantly, the combination of either formulation with AMT consistently produced synergistic effects, normalizing glycemic control and confirming their potential as effective adjuvants in diabetes management.

6.0 Discussion

Diabetic neuropathy is one of the most common and debilitating complications of diabetes mellitus, characterized by chronic pain, sensory loss, motor dysfunction, oxidative stress, and neuroinflammation (Yang et al, 2025). Persistent hyperglycemia triggers a cascade of metabolic and molecular events, including impaired insulin signaling, dyslipidemia, excessive generation of reactive oxygen species (ROS), and activation of inflammatory pathways, ultimately leading to neuronal damage and functional deficits (Vinik et al, 2013). The present study systematically evaluated the neuroprotective and antinociceptive potential of CPV, alone and in combination with AMT, in a high-fat diet (HFD) and streptozotocin (STZ)-induced model of type 2 diabetic neuropathy.

In the present investigation, animals subjected to HFD feeding followed by low-dose STZ administration exhibited sustained hyperglycemia, impaired glucose tolerance, reduced insulin levels, and progressive weight loss, confirming the successful establishment of type 2 diabetes. These metabolic abnormalities were accompanied by the development of neuropathic pain behaviors, including thermal hyperalgesia, cold allodynia, and mechanical hyperalgesia, along with compromised locomotor activity and motor coordination. Such findings are consistent with earlier reports demonstrating that prolonged

hyperglycemia and insulin resistance play a central role in the pathogenesis of diabetic neuropathy by promoting oxidative stress, mitochondrial dysfunction, and neuroinflammation (Saraswat et al, 2020; Giri et al, 2018).

Treatment with CPV significantly improved glycemic control, as evidenced by reduced fasting blood glucose levels and improved oral glucose tolerance following drug administration. The antihyperglycemic effect of CPV may be attributed to its polyherbal composition, which includes 37 different ingredients, as reported in the Ayurvedic Formulary of India (2003), and contributes to enhanced insulin sensitivity, support of pancreatic β-cell function, and regulation of carbohydrate metabolism. Improved insulin levels observed in CPV-treated groups further support the notion that CPV may exert insulinotropic or insulin-sensitizing effects, thereby improving glucose utilization and reducing glucotoxicity. Notably, the combination of CPV with low-dose AMT produced a more pronounced improvement in glycemic parameters, suggesting a potential synergistic interaction that allows dose reduction of conventional drugs while maintaining therapeutic efficacy.

Behavioral assessments revealed that diabetic animals developed pronounced thermal hyperalgesia, as indicated by reduced tail-flick latency, along with significant cold allodynia and mechanical hypersensitivity. These sensory abnormalities reflect dysfunction of small-diameter nociceptive fibers, a hallmark of diabetic neuropathy (Tian et al, 2024; Tsagareli et al, 2010). CPV treatment significantly attenuated these pain behaviors, indicating its antinociceptive potential. Improvement in thermal and mechanical nociceptive thresholds may be attributed to reduced oxidative stress and inflammation, as well as stabilization of neuronal membranes. The combination of CPV with AMT consistently produced greater analgesic effects, suggesting that CPV may enhance the efficacy of standard neuropathic pain therapy while minimizing dose-related adverse effects.

7.0 Conflict of Interest

The authors declare no conflict of interest

8.0 Financial Assistance

This research work was not supported with financial assistance from any funding agencies.

9.0 Author Contribution

S.V.- Conceptualization, methodology, investigation, and writing— original draft. A.K.- Conceptualization, data curation, formal analysis, validation, and writing— review and editing. All authors have read and approved the final manuscript and agree to be accountable for all aspects of the work.

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