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Neuroprotective assessment of methanolic root extract of *Moringa Concanensis* against Cisplatin-induced peripheral neuropathy in rats

Research Article

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Abstract

Objective: Investigation of the methanolic root extract of *Moringa concanensis nimmo* (MC) as a potential treatment for cisplatin-induced peripheral neuropathy in rats. Methods Male Albino Wistar rats were divided into 5 groups: Normal control, positive control, low dose MC root extract (200 mg / kg, p.o.), high dose MC root extract (400 mg / kg, p.o.), standard (Ascorbic acid) (45 mg / kg, p.o.). Cisplatin (2.5 mg / kg, ip) was administered in the second week and continued for 4 weeks, while MC root extract and ascorbic acid were administered orally from the first week for 5 weeks. After 5 weeks, Behavioural assessments, and antioxidant activity in sciatic nerve homogenate were performed. Histopathological analysis of sciatic nerve samples was performed using H&E stain. Results: Treatment with methanolic root extract of MC at low dose and high dose for 5 weeks significantly improved behavioral parameters, antioxidant levels, attenuated oxidative stress, and restored histopathological deterioration of sciatic nerve compared to the positive control group. However, grip strength and motor coordination of animals treated with standard showed no significant difference when compared to high dose. Conclusion: The study indicates that methanolic root extract of MC protects Cisplatin-Induced Peripheral Neuropathy in rats, as demonstrated by improved behavioral parameters, enhanced antioxidant levels, and restored histopathological features. MC root extract appears promising as a preventive measure for Cisplatin-Induced Peripheral Neuropathy, potentially benefiting cancer patients undergoing chemotherapy.

Keywords: Peripheral neuropathy, Cisplatin, *Moringa concanensis,* Ascorbic acid, Oxidative stress, Histopathology.

Introduction

Peripheral Neuropathy (PN) is a multifaceted condition characterized by damage to peripheral nerves, resulting in a wide range of symptoms. It is characterized by dysfunction of the peripheral nervous system, which is responsible for transmitting information between the central nervous system and the rest of the body.(1,2) This damage can manifest as Neuralgia, Paresthesia and Myasthenia which can significantly impair an individual's quality of life. The prognosis varies based on various factors such as the location and underlying cause of nerve damage. These factors can include genetic, autoimmune, infectious, nutritional, metabolic imbalances, and Iatrogenic [Drug (Cisplatin)-induced peripheral neuropathy].(1,3,4)

According to World Health Organization, there is an increase in the incidence of cancer, projected to reach over 35 million new cancer cases in 2050, a 77% increase from the estimated 20 million cases in 2022.(5) Although early detection and treatment have led to improved survival rates, chemotherapy-induced PN has emerged as a significant complication.(1,3) As a result, there is a pressing need for research into effective remedies for this condition. Cisplatin is a highly effective cancer-fighting drug, but it can cause peripheral neurotoxicity, a type of damage to nerves. This damage can persist even after chemotherapy has ended and is known as the coasting phenomenon. Cisplatin primarily targets the dorsal root ganglia and triggers mechanisms like neuronal apoptosis (cell death), DNA–Pt adduct formation (bonding of cisplatin with DNA), and mitochondrial DNA damage, which lead to the formation of reactive oxygen species and energy deficit. Changes in calcium signalling also contribute to the neurotoxic effects of the cisplatin. (2,4,6)

Neuropathic pain caused by cisplatin is associated with anxiety, depression, and sleep disturbances leading to poor compliance. Currently, antidepressants, anticonvulsants, narcotic analgesics, and NSAIDS are in medical practice in treating these secondary complications of neuropathic pain. They either slow the progression or affect the pathology involved in neuropathic pain and are associated with side effects.(7–9) As a result, there is a significant surge

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in the investigation of medicinal plants, which could potentially mitigate or prevent these adverse effects.

Recently, plant-based medicine has gained global importance for treating various ailments, including cardiovascular conditions, neurodegenerative diseases, and certain cancers. Plants have been explored extensively since ancient times due to their fewer side effects, widespread availability, lower toxicity, and cost-effectiveness. As a result, many plant-based products are traditionally being explored widely as an alternative to allopathic drugs for their potential to mitigate adverse effects. *Moringa concanensis nimmo* (MC), a plant belonging to the *Moringaceae* family and Moringa genus, is native to the Western Ghats of India. It has been traditionally used in Indian Ayurvedic medicine for various ailments, such as inflammation, pain, fever, and infections.(10) The plant is known to be rich in bioactive compounds, including alkaloids, flavonoids, phenolic acids, saponins, steroids, carbohydrates, and tannins, which have been reported to exhibit a wide range of pharmacological activities, including antioxidant, anti-inflammatory, analgesic, anti-anemic, and neuroprotective effects. (10–12)

After an extensive review of the literature, it has been identified that MC has been minimally explored for its peripheral neuroprotective activity. This study aims to evaluate its potential effect on cisplatin-induced peripheral neuropathy (PN). If proven effective, MC could serve as a cost-effective palliative treatment, improving the quality of life for cancer patients experiencing cisplatin-induced PN.

Materials and Methods

Materials

Cisplatin was given as a gift sample from KIDWAI Memorial Institute of Oncology- Bengaluru, Methanol, Chloroform, 5% Glutaraldehyde, 0.9% NaCl, Disodium hydrogen phosphate, Potassium dihydrogen phosphate, Potassium dichromate, Sodium acetate, TCA, TBA, DMSO, NADH, glacial acetic acid, phenazine methosulphate, n- butanol and other chemicals and reagents procured were of analytical grade.

Collection, authentication, and extraction of MC

Naturally grown MC roots were identified, collected, and authenticated, from Indian Institute of Horticultural Research- Indian Council of Agricultural Research (ICAR-IIHR) Bengaluru, in July 2023. The roots were properly washed under running tap water to remove all debris and dirt. Later the roots were manually chopped into pieces and were shade dried under a properly ventilated area for a week, and then crushed using a mortar and pestle to get a coarse powder. Later, the powder was macerated with methanol and frequently shaken manually for 3 days, which was later filtered using Whatman filter paper. The methanol in the filtrate of the extract was removed under reduced pressure by rotary evaporator at 45 rpm and 40°C to obtain methanol extract. The extract was further dried with a lyophilizer at −50 °C and vacuum pressure (1 to 10^{-3} mbar). 300gm of the extract was stored in a refrigerator at 4°C until use.(13)

Animals

Thirty Wistar male rats (150–200g) were housed under controlled conditions maintained at a temperature of 22°C, relative humidity of 60–70%, and were exposed to 12 h light/dark cycle with *ad libitum* access to rat chow diet and water, rats were acclimatized for a week before the start of the experiment. All animal studies were conducted according to ethical guidelines provided by Committee for Control and Supervision of Experiments on Animals (CCSEA), proposal no. (03/ HP/2023).

Acute Oral Toxicity

Acute oral toxicity studies were conducted as per Organisation for Economic Co-operation and Development (OECD) guidelines 423.(14) As the toxicity profile of the methanolic root extract of *Moringa* had not been previously investigated, the acute toxic class method was employed to evaluate the potential toxicity of the extract.

Experimental design

Rats were randomly divided into 5 groups, each comprising 6 rats. Group I served as the normal control, where rats were provided with food and water. Group II served as the positive control and received saline 2 ml/ kg, s.c., 5 min before the administration of cisplatin at a dose of 2.5mg/kg, i.p., for 4 weeks, starting from the second week of the treatment. (15) Group III and Group IV were administered MC methanolic root extract 200 mg/kg, p.o., and 400 mg/kg, p.o., for 5 weeks, respectively, based on the acute oral toxicity study conducted according to OECD guidelines 423. Group V received the standard drug (Ascorbic acid) at a dose of 45 mg/kg, p.o., for 5 weeks. All the treated groups received cisplatin every first day from the second week of the treatment up to 4 weeks.

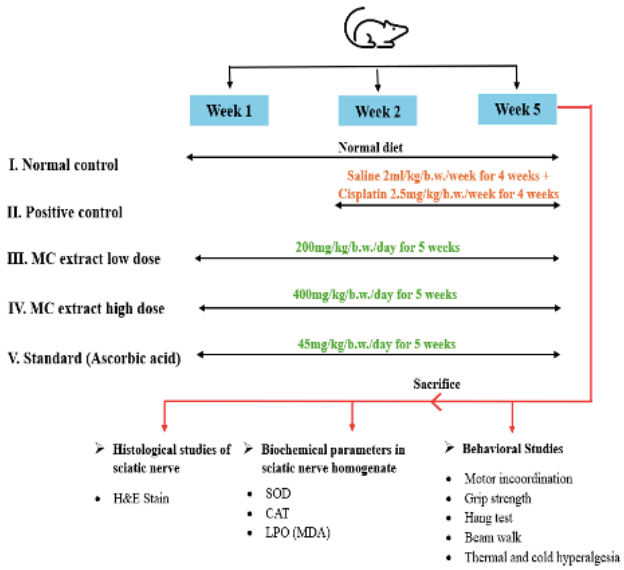

Fig.1. Design of the experiment

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Behavioral studies

The behavioral studies included a 3-day training session for Rotarod, grip strength, hang test, and beam walk test with three trials conducted during the test period. Familiarization with hot and cold plates was carried out before the start of the test period.

Rota-rod test

The motor coordination was assessed by the Rotarod apparatus (Orchid Scientific - RR01), with the rotating rod set at a speed of 15 rpm and a cutoff time of 180 seconds. The duration for which a rat remained on the rotating rod was observed and recorded.(15–17)

Hang test

A hang test was performed to assess the endurance and strength of limb muscles. Rats were suspended upside down on a hanger and released a few seconds after instinctively grasping the wire with the limbs. Depending on the functional ability of the rat, all limbs and the tail were used during a 5-min hanging session. The longest hanging time was used for analysis. (18)

Beam walk

Motor coordination was assessed through the beam walking test using a wooden strip. Rats were required to traverse a 1-meter-long wooden stick positioned approximately 1 meter above the ground. Observers recorded the total distance covered, the number of slips, and the number of turns made by the rats. The count of foot slips was used as an indicator of incoordination.(18)

Grip strength

In this test Grip strength of the forelimbs was measured by a Grip strength meter (Orchid scientific-GSM 01 RS) due to the loss of innervation in the peripheral nerves. A rat was placed onto the grid, ensuring that the rat held onto the grid from its forelimb firmly. Gradually a horizontal pull on the tail was initiated, maintaining a consistent and gentle pressure while moving the animal backward until it released the grasp, where peak force was observed and recorded in Newtons.(19)

Thermal and cold hyperalgesia

This test evaluates nociceptive reaction in animals utilizing a hot and cold plate apparatus (Orchid Scientific-HC-01) with a surface temperature set at 50°C ± 2°C. The reaction latency, measured in seconds, encompassed the time from placing the animals on the hot plate to the onset of paw-licking or jumping behaviors, with a cutoff time of 40 seconds to prevent tissue damage. For cold pain assessment, the temperature was set at 4°C ± 1°C. The time, in seconds, for the first observed paw licking was recorded, with a cutoff time of 60 seconds for the latency of paw lifting or licking to minimize the damage.(1)

Biochemical Parameters

Sciatic nerve homogenate preparation

The rats were sacrificed by an overdose of anesthesia. A segment of the sciatic nerve was isolated, and was rinsed with ice-cold saline (0.9% w/v sodium chloride) and homogenized in chilled phosphate buffer (pH 7.4) at the concentration of 10%w/v. The obtained homogenate was used to measure Superoxide Dismutase (SOD), Catalase (CAT), and Lipid peroxidation (LPO).

SOD

SOD plays a crucial role in protecting cells from oxidative damage by neutralizing superoxide radicals. It catalyzes the conversion of these harmful superoxide anions into less harmful hydrogen peroxide and molecular oxygen, thereby preventing the accumulation of reactive oxygen species and safeguarding cellular components. This assay involves preparing a substrate solution with NBT, riboflavin, and methionine. Illumination of this solution triggers riboflavin and methionine to produce superoxide anions (O_2^-), which react with NBT to form a blue-colored formazan complex. A sample containing the SOD enzyme is then added, where the SOD neutralizes the generated superoxide anions. This leads to a decrease in blue color intensity, which is measured to determine the SOD activity in the sample. A 50% reduction in blue color indicates one unit of SOD activity. Additionally, the total protein content of the sample is estimated to express SOD activity relative to protein concentration. (20)

CAT

CAT plays a crucial role in protecting cells from oxidative damage by catalyzing the rapid breakdown of hydrogen peroxide into water and oxygen. This enzyme activity was measured by taking 0.5 ml of sciatic nerve homogenate from the supernatant, mixed with 1 ml phosphate buffer at (pH 7.4), and mixed with 0.4 ml distilled water and 0.5 ml hydrogen peroxide. The whole mixture was then incubated at 37°C for 1 min. to this mixture, 2 ml of potassium dichromate acetate solution was added and boiled in a water bath for 15 min. The color of the mixture changed to green after cooling. This was then measured for absorbance at 570 nm.(21)

LPO

LPO is a chemical reaction that occurs in biological systems under conditions of oxidative stress. It involves reactive oxygen species (ROS) breaking down lipids, particularly polyunsaturated fatty acids, to produce malondialdehyde (MDA), a significant indicator of oxidative stress levels and the extent of ROS-caused cellular damage in biological systems. In this test, 0.5ml of sciatic nerve homogenate was mixed with 2.5 ml of 10% solution of TCA. The mixture was boiled for 15 min in a water bath. Followed by 10 min centrifugation (cold) at 3000 rpm. Next, 2 ml of the solution was separated from the surface, and 0.67% of thiobarbituric acid (1 ml) was added. The mixture was

kept boiling for 15 min. The mixture was cooled to 37°C, and absorbance was measured at 532 nm by keeping the mixture except for the sample blank.(22,23)

Histopathological analysis

The excised sciatic nerve tissues were immediately preserved in 5% glutaraldehyde, then dehydrated in ethanol with increasing concentrations (50%, 70%, 96%, and 100%) and cleared with xylene. The samples were embedded in paraffin and sectioned into 5 µm thick slices using a rotating microtome. These sections were stained with hematoxylin and eosin (H&E) for histopathological analysis. The slides were examined and photographed using a light microscope equipped with an imaging system.(24)

Statistical analysis

The experimental data are expressed as mean ± SEM and statistical analysis is performed using GraphPad Prism version 8.02, which involves a one-way ANOVA accompanied by Tukey's multiple comparison test.

Results

Preliminary screening

Table 1: Phytochemical screening of methanolic root extract of MC

Phytoconstituents	Results	Phytoconstituents	Results
Carbohydrates	+	Flavonoids	+
Alkaloids	+	Tannins	+
Phenols	-	Proteins	-
Saponins	+	Steroids	+

Acute oral toxicity

Following OECD guidelines 423, acute oral toxicity experiments were conducted on Wistar rats. Notably, no mortality occurred at the highest administered dose of 2000 mg/kg body weight. Hence, the 1/5th (400 mg/kg body weight) and 1/10th (200 mg/kg body weight) of the 2000mg/kg/b.w. were considered as the highest dose and lowest dose, respectively.

Behavioral studies

Figure 2. Effect of administration of methanolic root extract of MC for 5 weeks on motor coordination performance in the Rotarod test. ##P<0.01 Vs normal control group. *P<0.05, **P<0.01 Vs positive control group.

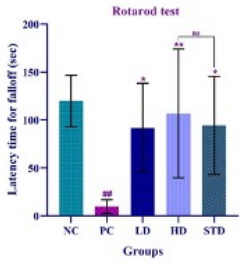


Figure 3. Effect of administration of methanolic root extract of MC for 5 weeks on limb muscle endurance and strength as assessed by the Hang test. ##P<0.01 Vs normal control group. *P<0.05, **P<0.01 Vs positive control group.

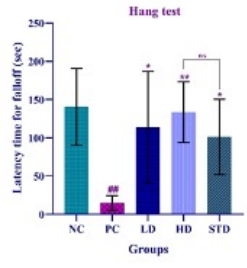
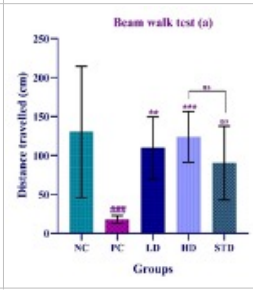
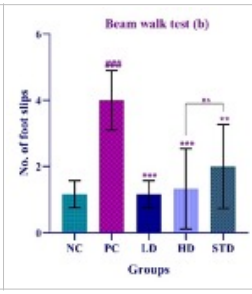


Figure 4. Effect of administration of methanolic root extract of MC for 5 weeks on motor coordination as assessed by the Beam Walk test. (a)Distance travelled: ###P<0.001 Vs normal control group. **P<0.01, ***P<0.001, ns Vs positive control group. (b) No. of foot slips: ###P<0.001 Vs normal control group. **P<0.01, ***P<0.001, ns Vs positive control group. (c)No. of turns: ###P<0.001 Vs normal control group. *P<0.05, **P<0.01, ns Vs positive control group.





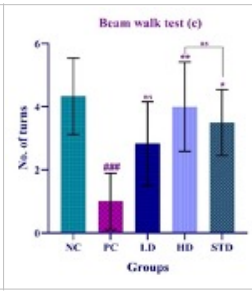


Fig.5. Effect of administration of methanolic root extract of MC for 5 weeks on grip strength of the forelimbs measured using Grip strength meter. **P<0.01, ns Vs positive control group.

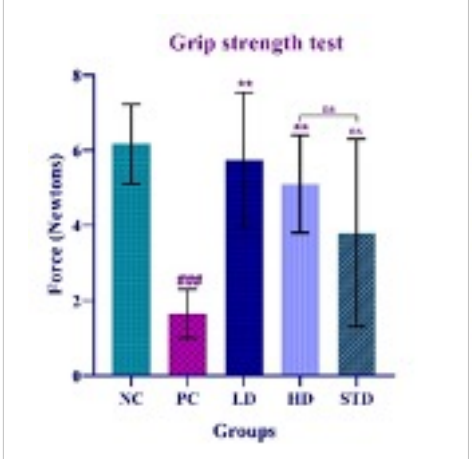
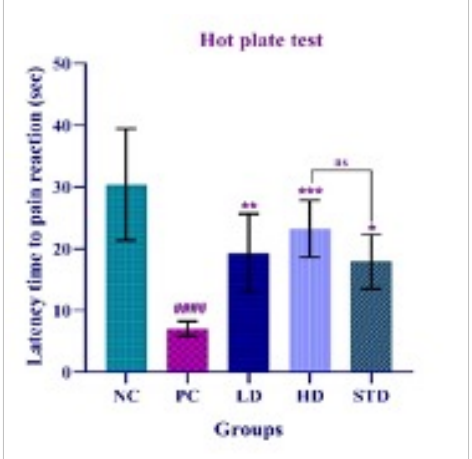
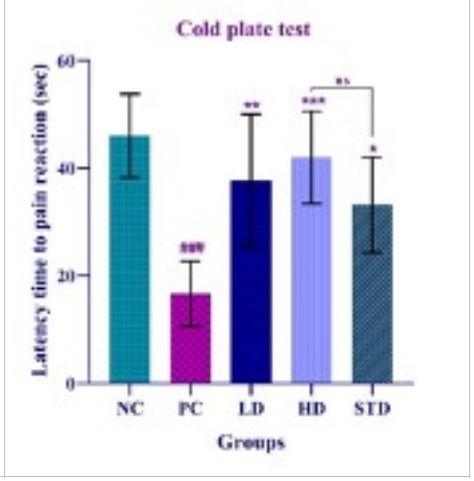


Fig.6. Effect of administration of methanolic root extract of MC, for 5 weeks on evaluating nociceptive reactions in rats i) Hot plate test and ii)Cold plate test. ####P<0.0001, ###P<0.001 Vs normal control group. *P<0.05, **P<0.01, ***P<0.001 Vs positive control group.





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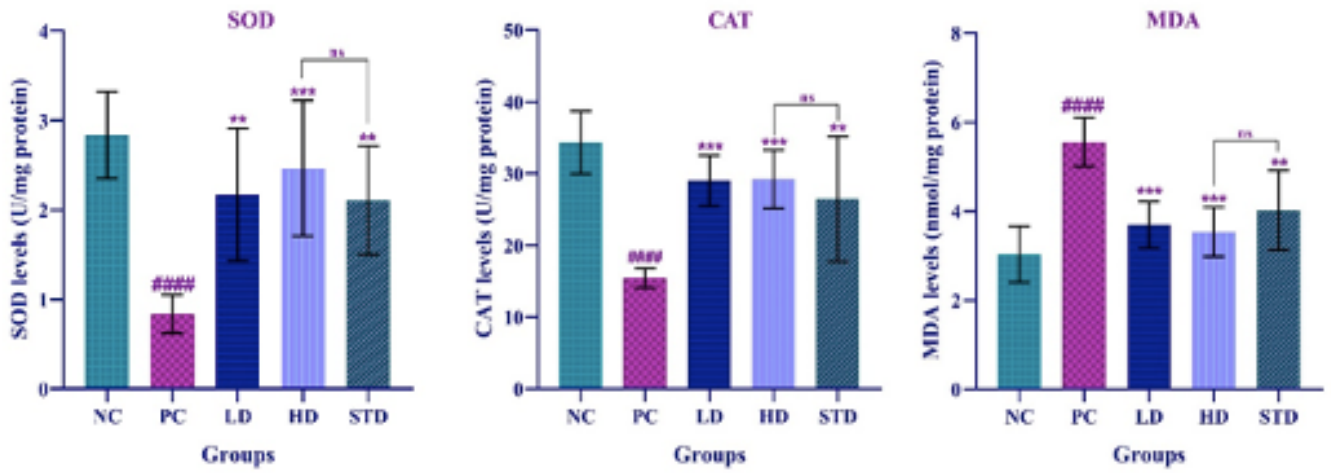
Antioxidants

Figure 7: Effect of administration of methanolic root extract of MC for 5 weeks on i) SOD, ii) CAT, and iii) MDA*P<0.05, **P<0.01, ***P<0.001 Vs positive control group.



Histopathological analysis

Normal control

Figure 8: a, b: Section studied from the sciatic nerve shows nerve fascicles [Fig.8.(a), Arrow] with adherent perineural space between the bundle of nerve fibers and perineurium. The nerve bundles appear intact [Fig.8.(b), Arrow]. Intact axons with myelination are noted. Vaso nervorum appears intact

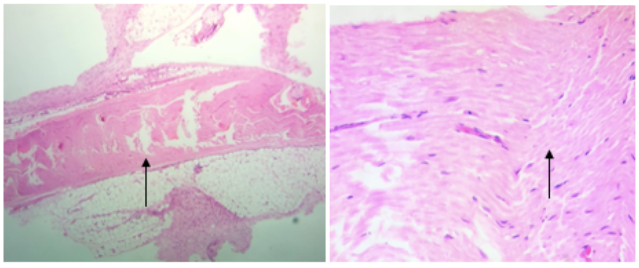


Fig.8.(a). [H&E X50] Fig.8.(b). [H&E X400]

Positive control

Figure 9: a ,b. Section studied from the sciatic nerve shows nerve fascicles with diffuse perineural space [Fig.9.(a), Arrow] between the bundle of nerve fibers and perineurium. Moderate to severe edema [Fig.9.(b), Arrow] is observed between the nerve bundles. Mild degenerative axons with loss of myelination are noted. Congested vasonervorum is seen.

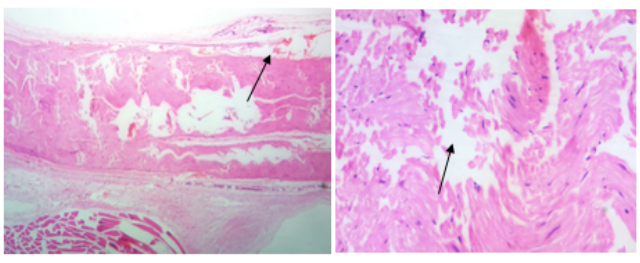


Fig.9.(a). [H&E X50] Fig.9.(b). [H&E X400]

Low dose of methanolic root extract of MC

Figure 10: a, b. Section studied from the sciatic nerve shows nerve fascicles with focal perineural space [Fig.10.(a), Arrow] between the bundle of nerve fibers and perineurium. Moderate edema [Fig.10.(b), Arrow] is observed between the nerve bundles. Mild degenerative axons with loss of myelination are noted. Congested vasonervorum is seen.

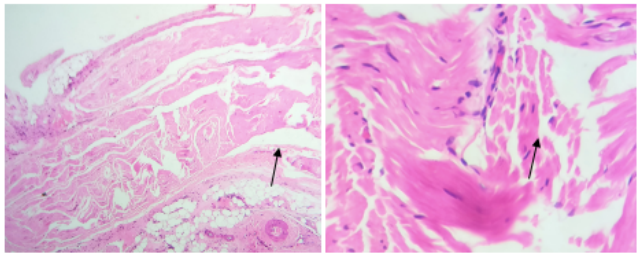


Fig.10.(a). [H&E X50] Fig.10.(b). [H&E X400]

High dose of methanolic root extract of MC

Figure 11: a, b. Section studied from the sciatic nerve shows nerve fascicles with focal perineural space [Fig.11.(a), Arrow] between the bundle of nerve fibers and perineurium. Nerve bundles appear intact, compact, and tightly packed [Fig.11.(b), Arrow]. Intact axons with myelination are noted. Vaso nervorum appears intact.

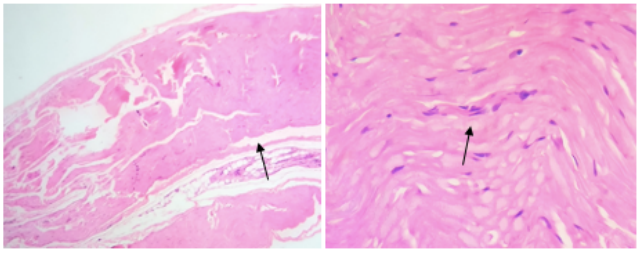


Fig.11.(a). [H&E X50] Fig.11.(b). [H&E X400]

Standard

Figure 12: a, b. Section studied from the sciatic nerve shows nerve fascicles with focal perineural space [Fig.12. (a), Arrow] between bundle of nerve fibers and perineurium. Nerve bundles appear intact, compact, and tightly packed [Fig.12.(b), Arrow]. Mild degenerative axons with loss of myelination are noted. Vaso nervorum appears intact

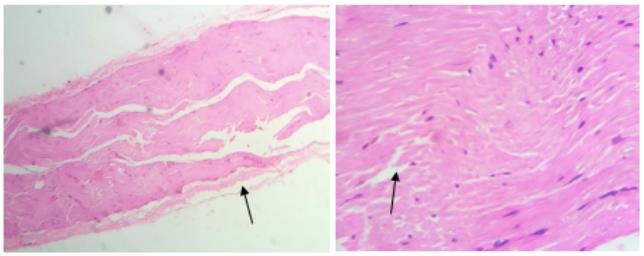


Fig.12.(a). [H&E X50] Fig.12.(b). [H&E X400]

Discussion

By 2050, the World Health Organization projects that there will be over 35 million new cases of cancer, a 77% increase from the estimated 20 million cases in 2022. (5) As India is known as the cancer capital, the rising incidence of the disease is becoming a major concern for the country. Clinically, Cisplatin, a cornerstone of cancer treatment, is frequently administered to patients, but its long-term use is associated with adverse effects. Numerous studies, including experimental ones, have highlighted the occurrence of PN as one such side effect.(25)

PN is characterized by damage to the peripheral nerves due to the drug's toxicity. This neuropathy is attributed to the accumulation of platinum products in DNA, heightened oxidative stress, mitochondrial dysfunction, and calcium imbalance.(25,26)

Remarkably, platinum-derivative drugs exhibit a particular affinity for the peripheral nervous system, which lacks a vascular barrier. This attraction leads to pronounced peripheral neurotoxicity, impacting a significant proportion of cancer patients.(27)

PN is a sensory and motor disorder that has a wide range of symptoms starting from paresthesia to weakness, tremors, and a loss of taste. This can cause discomfort for the patients who are being treated for cancer. Additionally, the presence of PN can lead to poor compliance with treatment regimens, further complicating patient care. More often than not it is, highly progressive and, hence needs to be prevented or treated for the well-being of the patient.(28) In this study, Cisplatin administration significantly induced PN which is characterized by motor incoordination, loss of grip strength, impaired nociception threshold, altered antioxidant level, and impaired sciatic nerve function which is also well documented in previous studies. (15,29–31) Hence, this model was used to assess the neuroprotective activity of PN with the use of the root extract obtained from MC.

MC is a plant of great significance owing to its high medicinal value. It marks its origin from the sub-continent of India, however as come to the limelight of the entire world.(10) This is due to its great nutritional value. The entire plant has a wide variety of uses from the leaves to the tip of the root containing all the major bioactive compounds. Though *Moringa's* use is known to the masses it still attracts a lot of scientific research, as they have to be explored and established.

The phytochemical screening of the methanolic root extract of MC confirmed the presence of various phytochemicals such as alkaloids, tannins, flavonoids, sterols, and saponins, all renowned for their numerous pharmacological activities.

This study lasted for 5 weeks involving 36 male Wistar rats. Cisplatin (2.5mg/kg/b.w., i.p.) was used for inducing PN, the administration started from second week and was given with saline to prevent nephrotoxicity and provide hyperhydration, this continued for 4 weeks. As the goal of the study was to provide a preventive effect of *Moringa* root extract was given orally from the first week. It was given in two doses: a high dose(400mg/kg/b.w.) and a low dose(200mg/kg/b.w.) and it was compared to the standard (45mg/kg/b.w.).

OECD guidelines 423 followed for carrying out acute oral toxicity to establish dose of methanolic root extract of MC. *Moringa* root extract at the dose 2000mg/kg/b.w. did not show any signs of intoxication and mortality. Therefore, doses of 1/5th and 1/10th of 2000mg/kg body weight were considered as the highest and lowest doses, respectively.

The administration of Cisplatin has had a substantial effect on behavioral assessments, antioxidant function, and histopathological observations of the sciatic nerve in comparison to the normal control group these altered features due to cisplatin toxicity in PN.

A high dose of MC treatment for 5 weeks had a significant impact on behavioral parameters, while a low dose was not too far behind. The Rotarod is used to assess motor coordination and balance in rats(31). Rats treated with cisplatin exhibited shorter falloff time from rotating rod when compared to NC, where high and low dose *moringa* extract treatment along with standard showed significant (**P<0.01, *P<0.05) restoration of motor behavior when compared to positive control where the latency to falloff was significantly increased.

The hang test on the other hand assessed the endurance and strength of the fore and the hind limbs, (18) high dose, low dose, and standard treatment provided significant (**P<0.01, *P<0.05) improvement where it showed an increase in falloff time compared to positive control.

The next test involved assessing thermal and cold hyperalgesia to evaluate the animal's reaction to nociceptive stimuli(1,30) and it was found that high dose, low dose, and standard had significant (***P<0.001, **P<0.01, *P<0.05,) effects on nociception threshold, as it was evidenced by significant improvement in the time taken to elicit response to hot and cold stimuli when compared to the positive control.

In addition to impaired motor coordination the muscle strength is significantly decreased in cisplatin control rats. The muscle strength of the rats can be assessed by measuring its grip strength and can be performed using grip strength meter to assess muscle

hyperalgesia.(2,8) Our results revealed that both the high and low doses showed significant (**P<0.01) improvement in grip strength when compared to positive control whereas there was no significant improvement seen in the standard group.

Beam walk test was the last behavioral assessment in which motor coordination was checked, (18) there were 3 sub-parameters i.e. distance travelled, number of foot slips, and number of turns which were evaluated. Though high and low dose showed a significant increase (**P<0.01, *P<0.05) in all three sub-parameters when compared to positive control, standard showed no significance to the distance travelled.

Since cisplatin induced PN causes severe oxidative stress and inflammation, similar observations were found in our study as it is evidenced by increase in oxidative stress marker and, decrease in antioxidant levels in sciatic nerve homogenate.(30) However, treatment with MC resulted in a significant increase in SOD and CAT levels in the sciatic nerve homogenate, along with a decrease in the formation of MDA, a byproduct of the LPO reaction.

In this study, the histopathological assessment of the sciatic nerve samples was also studied using H&E stain. Sciatic nerve samples of normal control animals revealed histopathological features like nerve fascicles with adherent perineural space between the bundle of nerve fibers and perineurium. The nerve bundles appear intact, axons with myelination were noted. Vaso nervorum appears intact. Administration of cisplatin to the positive control animals was able to induce histopathological changes characterized by nerve fascicles with a diffuse perineural space, moderate to severe edema between nerve bundles, congested vaso nervorum, and mild degeneration of axons with loss of myelination, these features further confirms assessment of PN.(32)

Histopathological results of sciatic nerve in animals treated with high dose of MC exhibited focal perineural space between the bundle of nerve fibers and the perineurium, with nerve bundles appearing intact, compact, and tightly packed. Intact axons with myelination and an intact vaso nervorum are noted.

Histopathological studies on sciatic nerve further revealed features like focal perineural space between the bundle of nerve fibers and the perineurium, but moderate edema is observed between the nerve bundles, mild degenerative axons with loss of myelination and a congested vaso nervorum on treatment with low dose of MC.

The morphological features of sciatic nerve in standard treated group displayed nerve fascicles with a focal perineural space between the bundle of nerve fibers and the perineurium. Here, nerve bundles appear intact, compact, and tightly packed, although mild degenerative axons with loss of myelination are noted. However, the vaso nervorum appears intact.

In the current study, it has been found that treatment with MC extract for 5 weeks exhibited antinociceptive effects, enhanced behavioral parameters, augmented antioxidant levels, and restored histopathological features of sciatic nerve. However, we did not find any significant difference in behavioral, biochemical, and histopathological parameters between standard and high dose of MC. These findings suggest that the neuroprotective effect of MC is collectively mediated by augmenting endogenous antioxidants, anti-inflammatory properties, and probably due to rich nutrient content.(33)

Consequently, MC may serve as a promising palliative therapy for PN in cancer patients undergoing chemotherapy. Additionally, other parameters like electrophysiological properties (nerve conduction velocity), intraepidermal nerve fiber density, Na+/K+ ATPase activity, and numerous molecular pathways remain to be explored and those may be further useful to establish the neuroprotective mechanism of MC in our study.

Conclusion

This study demonstrates the potential neuroprotective effect of methanolic root extract of MC in mitigating cisplatin induced PN in Wistar rats. Oral administration of methanolic root extract of MC (high dose and low dose) for 5 weeks exhibited antinociceptive effects, improved grip strength, motor coordination in cisplatin induced PN in rats, further supported by reduced oxidative stress, improved antioxidant levels, and reduced histopathological deterioration of sciatic nerve fibers.

Treatment with standard (ascorbic acid) exhibited similar effects as that of *moringa* except for grip strength and motor coordination (beam walk test) which are not significantly improved. There is no significance difference between the standard and high dose of *moringa* root extract observed in ameliorating behavioral, biochemical, and histopathological parameters. Hence the neuroprotective effect of standard is as comparable with high dose of MC root extract. These findings support MC as a palliative therapy for cancer patients undergoing chemotherapy, improving overall patient quality of life.

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