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Effect of *Mimosa pudica* for vincristine induced neuropathic pain

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Abstract
Allodynia and hyperalgesia comprise the main and frequent symptoms suffered by patients with neuropathic pain, which responds poorly to therapy. *Mimosa pudica* (Thottavadi) found in different parts of India has been extensively used as medications for various diseases including CNS disorders. The present study examined the antineuropathic effect of whole plant of *Mimosa pudica* on vincristine induced neuropathic pain with improved efficacy and safety. Neuropathic pain was induced by the administration of vincristine sulphate injection (1mg ml^{-1}, i.p) for once per day for 10 days in 5 days on 2 days off cycle. Pain behaviour was assessed at different days, i.e., 0,7,14 and 21 days. Sciatic nerve total calcium, superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), reduced glutathione (GSH), nitric oxide (NO), lipid peroxidation (LPO) and total calcium were also estimated after the 21st day of study. Pregbalin (10mg/kg, p.o.) and hydroethanolic extract of *Mimosa pudica* (HEMP) (200 & 400 mg/kg, p.o.) were administered for 7 consecutive days after the induction of neuropathic pain. The extract produced significant ($p<0.01$) and dose dependent inhibition of vincristine- induced neuropathic pain manifestations in terms of thermal hyperalgesia, cold allodynia, antioxidant levels, total calcium and protein. The hydroethanolic extract of *Mimosa pudica* at 200 and 400 mg/kg dose levels significantly attenuated vincristine induced neuropathy which may be due to its multiple actions including anti-nociceptive, anti-inflammatory, calcium inhibitory and anti- oxidant effect.

Keywords: Antinociceptive, chemotherapy, *Mimosa pudica*, thermal hyperalgesia, cold allodynia

1. Introduction
Neuropathic pain is a common problem that presents a major challenge to health-care providers owing to its complex natural history, uncertain aetiology and poor response towards therapy. It is a chronic pain condition that arises from a disease or injury to the central nervous system (CNS) or the peripheral nervous system (PNS) leading to its damage or abnormal function. Common symptoms of neuropathic pain include sensory abnormalities such as burning sensations, hyperalgesia, allodynia, hyperesthesia and dysesthesia. The current analgesics are unable to treat cancer chemotherapy-induced neuropathic pain which is severe enough for patients to discontinue their cancer chemotherapy treatment and worsens the quality of their life [1]. Conventional analgesic agents like non-steroidal anti-inflammatory drugs (NSAIDs) and opioids are clinically ineffective for attenuation of CIPN. Usefulness of tricyclic antidepressants and anticonvulsants in management of neuropathic pain is indicated but these medications exhibit a wide spectrum of adverse effects which limit their full clinical exploitation [2].
Mimosa pudica L. (Family Mimosaceae) is locally known as lajwanti or chuimui in Hindi and is native of Central America, Tanzania, South Asia, East Asia and many pacific Islands [3]. The roots and leaves of this plant have been commonly used by tribal people for headache, migraine, dysentery, fever, piles, insomnia, epilepsy, etc [4,5]. Also this plant was used as bitter, astringent, acrid, cooling vulnerary, febrifuge, alexipharmic, diuretic, emetic and tonic. In traditional healthcare system, it has been used in the treatment of alopecia, diarrhoea, constipation, leprosy, dysentery, insomnia, tumor, blood disorders and various urogenital infections. Various medicinal and biological properties of this plant anti-diabetic, anti-hepatotoxic, antioxidant, anti-nociceptive, anti-asthmatic, aphrodisiac, sedative and wound healing activities were reported. Phytochemical studies revealed the presence of alkaloids, amino acid, flavonoids glycosides, sterols, terpenoids, tannins and fatty acids in this plant [6, 7]. With the above background, the present study was undertaken to investigate the effect of whole plant of *Mimosa pudica* in vincristine induced neuropathic pain. Pregbalin, a selective calcium channel antagonist served as positive control in this study.

2. Materials and methods
2.1 Chemicals and preparation of drug solutions
Vincristine sulfate (Sun Pharma, Mumbai, India), pregabalin (Ranbaxy Research Laboratories, Gurgaon, India), nitro blue tetrazolium (NBT), (Sigma Aldrich, St. Louis. MO), Folin–Ciocalteu's phenol reagent (Merck Limited, Mumbai, India), 5, 50-dithiobis (2-nitrobenzoic acid) (DTNB), bovine serum albumin (BSA), (Sisco Research Laboratories Pvt. Ltd. Mumbai, India), reduced glutathione (GSH), nicotinamide adenine dinucleotide phosphate (NADPH) (Himedia Laboratories, Mumbai, India), were procured for the present study. All the reagents used in the present study were of analytical grade. Pregabalin and curcumin were suspended in 0.3% w/v carboxy methyl cellulose (CMC) solution and vincristine was diluted with normal saline.

2.2 Plant materials
Fresh whole plant of *Mimosa pudica* of the family Mimosaceae were collected from Kannamangalam village of Alappuzha district, Kerala in the month of December 2018.The identification and authentication of plant was carried out by Dr. Subha Bhai, Head of Department,

Department of Botany, University College, Trivandrum. The plant material was shade dried and reduced to coarse powder.

2.3 Extraction
Soxhlet extraction of powdered plant material was carried out using ethanol and distilled water in the ratio of 70:30. The obtained extracts were air-dried at room temperature to evaporate the solvent. Finally, the hyrdoethanolic extract obtained were concentrated using electric water bath. Dried concentrated extracts were finally weighed and their percentage yield was calculated. The final product was stored at 4 °C.

2.4 Experimental animals
Thirty adult Wistar albino rats with a body weight of 150–250 g were used for this study. Rats were group-housed (n=6 per cage) in a room with controlled temperature (21±2 ^{0}C), and 12 h light-dark cycle was maintained. All the animals had free access to food and water ad libitum. The experimental protocols were approved by the Institutional Animal Ethical Committee and experiments were performed in accordance to the committee for the purpose of control and supervision of experiments on animals (CPCSEA) guidelines for ethical use of animals (ECPS/ IAEC-2-2018/4/18).

2.5 Vincristine-induced neuropathic pain
Vincristine is a purified alkaloid extracted from the *Linn pervinca* plant from the Apocynaceae family. Vincristine sulphate injection (1mg/ml) was diluted in normal saline just before the administration. The injection was given in a dose of 0.1mg/kg (i.p.) once per day for 10 days in 5 days on 2 days off cycle for the rats depending on their body weight. Peripheral neuropathy was confirmed after 10 consecutive days of vincristine administration. Nociceptive thresholds in these animals were assessed by subjecting them to behavioural studies [8, 9].

2.6 Experimental design
Animals were divided into five groups with six animals each. The animals were divided into five groups of six animals each. The study period was for 21days. The group I is normal control in which the animal receives normal diet, group II consists of negative control (only vincristine treated), group III consists of standard in which the animal is treated with Pregabalin 10mg/kg after the induction of neuropathic pain by vincristine, group IV & V consists of animals treated with hydroethanolic extract of *Mimosa pudica* (200 & 400mg/kg post administration respectively) after the induction of neuropathic pain. The behavioural tests like hot plate, tail immersion and cold water immersion were performed on different days, i.e. days 0, 7, 14 and 21. On the 21st day, after the behavioural analysis animals were sacrificed under anesthesia and subjected to biochemical analysis for estimating the total protein, superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), GSH, lipid peroxidation (LPO), nitric oxide (NO), and total calcium activity in sciatic nerve tissue sample.

2.7 Behavioural assessment
2.7.1 *Hot plate test (thermal hyperalgesia)*
In this test, animals were individually placed on a hot plate (Eddy's hot plate) with the temperature adjusted to 55±1^{0}C. The latency to the first sign of paw licking or jump response to avoid the heat was taken as an index of the pain threshold; the cut-off time was 10 s in order to avoid damage to the paw [10].

2.7.2 *Tail immersion test*
Then lower 5cm portion of the tail is marked and immersed into the beaker of hot water (55^{0}C). The time took to withdraw the tail out of the water is taken as the basal reaction time. Rats were subjected to evaluation on 0,7,14 and 21 day of drug administration. The reaction time is recorded in 0.5s units by a stopwatch. After each determination the tail is carefully dried. The reaction time is determined before and periodically after oral administration of the test and standard substance. The cut off time is 15 secs [11].

2.7.3 *Cold water immersion test*
The hind paw of the animals was immersed into a water maintained -4^{0}C to 15^{0}C. The basal reaction time was noted, that is hind paw or jump response (whichever appeared first) in animals, normally animals showed response in 6-8 sec. The latency prior to the first reaction was recorded with a cut-off time of 20secs [12].

2.8 Biochemical estimation
All the rats were sacrificed with chemical euthanasia 21st day after behavioural tests. The portions of the sciatic nerve were isolated immediately and processed for SOD, CAT, GPx, GSH, NO, and LPO. The sciatic nerve homogenate (10% w/v) was prepared with 0.1M Tris-HCl buffer (pH7.4) and deionised water, respectively, for total protein and total calcium estimation.

2.8.1 *Superoxide dismutase*
The reduction of NBT to blue formazan mediated by superoxide anions was measured at 560 nm under aerobic conditions. Addition of SOD inhibits the reduction of NBT and the extent of inhibition is taken as a measure of enzyme activity. The activity of enzyme was expressed as units/mg protein, where one unit is defined as the amount of enzyme inhibiting the rate of reaction by 50% [13].

2.8.2 *Catalase*
Hydrogen peroxide (H_2O_2) decomposition by CAT was monitored spectrophotometrically by following the decrease in absorbance at 240 nm. The activity of enzyme was expressed as mmoles of H_2O_2 decomposed/min/mg protein [14].

2.8.3 *Glutathione peroxidase*
The reaction measured the rate of reduced GSH oxidation by H2O2catalyzed by the GPx. GSH is maintained at constant concentration by the addition of exogenous glutathione reductase and NADPH, which immediately converts any oxidized glutathione disulfide (GSSG) produced to GSH. The rate of GSSG formation is then measured by following the absorbance of NADPH at 340 nm for 5 min. The activity of enzyme was expressed as nmoles NADPH oxidized/min/mgprotein [15].

2.8.4 *Reduced Glutathione*
In this assay, GSH reduced 5, 50-dithiobis (2-nitrobenzoic acid) (DTNB) to 5-thio-2-nitrobenzoic acid (TNB) and the

GSSG. TNB is a yellow product which was measured spectrophotometrically at 412 nm. The amount of GSH was expressed in mM/mg protein [16].

2.8.5 *LPO levels*
The amount of malondialdehyde (MDA) and other thiobarbituric acid reactive substances (TBARS) are quantified by their reactivity with TBA in acidic conditions. The reaction generated a pink-colored chromophore which was measured in a UV spectrophotometer at 532 nm. The results were expressed as nmoles MDA/mg protein [17].

2.8.6 *Nitric oxide*
Nitrate/nitrite was assayed in the nerve homogenate using the Griess reagent (1%sulfanilamide in 5% phosphoric acid and 0.1% naphthylethylenediamine dihydrochloric acid in water in the ratio of1:1). The color intensity of chromogen was read at 540 nm. The results were expressed as mM/mg protein [18].

2.8.7 *Estimation of total protein content*
Protein concentration of nerve homogenate was estimated using bovine serum albumin (BSA) as a standard. The absorbance was determined spectrophotometrically at 750 nm [19].

2.8.8 *Estimation of total calcium*
Sciatic nerve homogenate was mixed with 1ml of trichloroacetic acid (4%) in ice cold conditions and centrifuged at 2000 rpm for 10 min. The clear supernatant was used for the estimation of total calcium ion by atomic emission spectroscopy at 556 nm [20].

2.9 Histopathological Study
Sciatic nerve samples were fixed in (10% of formalin solution), transected (4 μm, thicknesses) and stained (Hematoxylin and Eosin). The qualitative analysis of nerve sections was done under a light microscope (450×) for axonal degeneration [21].

2.10 Statistical Analysis
All the results were expressed as the mean ± standard errors of mean (SEM). The datas were analysed by using Graph pad software version 7.03 and GraphpadInstat 3.01 demo version by One way analysis of variance (ANOVA) followed by Dunnett's multiple comparison 't'-test. A value of $p<0.05$ was considered to be statistically significant.

3. Results and Discussion
3.1 Effect of hydroethanolic extract of *Mimosa pudica* on Eddy's hot plate method
Administration of vincristine resulted in a significant development of thermal hyperalgesia as reflected by an increase either in the hind paw licking, lifting, or jumping from the hot plate surface on days 7, 14, and 21 in comparison to day 0. The increases pain perception is the symptoms of neurotoxicity or neuropathic pain. Different treatments and duration of treatment significantly improved the hyperalgesic response. The administration of hydroethanolic extracts of *Mimosa pudica* attenuated vincristine induced decrease in nociceptive threshold for thermal hyperalgesia. Treatment with standard drug pregabalin (10mg/kg) showed significant increase (***P<0.001) in pain threshold on 21st day. Hydroethanolic extract of *Mimosa pudica* (200mg/kg) did not significantly increase (*P<0.05) the pain threshold in comparison with vincristine- treated on day 21. The treatment with hydroethanolic extracts of *Mimosa pudica* (400mg/kg) showed significant difference (**P<0.01) in pain threshold on 21st day when compared to the treatment with hydroethanolic extracts of *Mimosa pudica* (200mg/kg). In pregabalin (10mg/kg) and hydroethanolic extracts of *Mimosa pudica* 400mg/kg) treated rats, the duration of paw withdrawal latency was not significantly different on days 21 in comparison with the baseline (day 0). This indicates that hydroethanolic extracts of *Mimosa pudica* (400 mg/kg) was able to restore the physiological thermal pain perception (Figure 1).

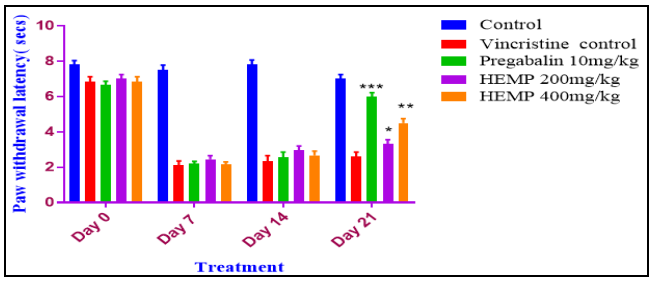

Fig 1: Effect of HEMP on thermal hyperalgesia by Eddy's hot plate method. The values are expressed as Mean ± SEM, n=6. The statistical analysis was carried out by one-way ANOVA using Dunnett's multiple comparison test, where *P<0.05, **P<0.01, ***P<0.001

3.2 Effect of hydroethanolic extract of *Mimosa pudica* on tail immersion method
In tail immersion method, tail flicking response was considered as positive response. The constriction of sciatic nerve resulted in a significant thermal hyperalgesia which was ameliorated by pregabalin treatment in rats. Pregabalin (10mg/kg) administration significantly increased (***P<0.001) the vincristine induced decrease in the nociceptive threshold for thermal hyperalgesia when compared to other groups. This effect was highly significant as compared with the control group. The hydroethanolic extract of *Mimosa pudica* (400mg/kg) also showed a significant prolongation (**P<0.01) in tail flicking response as compared to hydroethanolic extract of *Mimosa pudica* (200mg/kg) (figure 2).

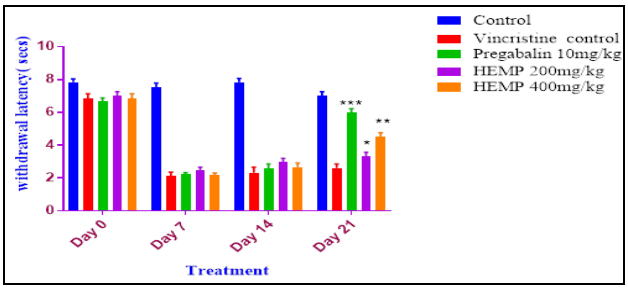

Fig 2: Effect of hydroethanolic extract of *Mimosa pudica* tail immersion method**.** The values are expressed as Mean ± SEM, n=6. The statistical analysis was carried out by one-way ANOVA using Dunnett's multiple comparison test, where *P<0.05, **P<0.01, ***P<0.001

3.3 Effect of hydroethanolic extract of *Mimosa pudica* on cold water immersion method
Vincristine administration exhibited significant

development of cold allodynia which was reflected by a decrease in the paw withdrawal latency period on days 7th and 14th in comparison to day 0. Administration of pregabalin (10mg/kg) and hydroethanolic extract of *Mimosa pudica* (400mg/kg) significantly attenuated (***P<0.001 & **P<0.01)) the vincristine induced allodynia in comparison with vincristine control group (Figure 3). Interestingly, pregabalin (10mg/kg) treated animals exhibited significant increase (***P<0.001) in paw withdrawal latency on day 21 as compared with day 7 and 14. Hydroethanolic extract of *Mimosa pudica* (400mg/kg) showed similar results in comparison with baseline (day 0).

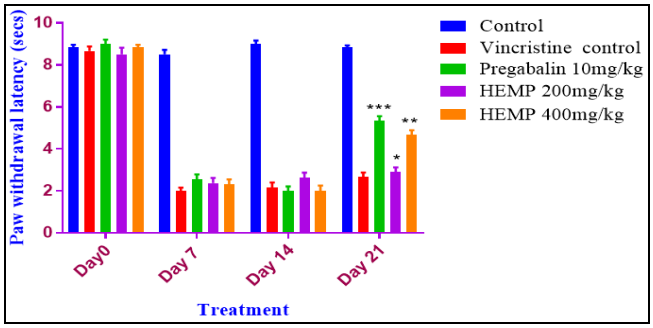

Fig 3: Effect of hydroethanolic extract of *Mimosa pudica* on cold water immersion method. The values are expressed as Mean ± SEM, n=6. The statistical analysis was carried out by one-way ANOVA using Dunnett's multiple comparison test, where *P<0.05, **P<0.01, ***P<0.001

3.4 Effect of hydroethanolic extract of *Mimosa pudica* on SOD activity

In comparison with normal control group, administration of vincristine significantly depleted the SOD activity. Hydroethanolic extract of *Mimosa pudica* (200 and 400 mg/kg) treated rats exhibited dose-dependent significant (P<0.05 & P<0.01) increase in the SOD activity in the sciatic nerve in comparison with vincristine-treated animals (Figure 4). Pregabalin treated animals exhibited significant (P<0.001) increase in the SOD activity.

3.5 Effect of hydroethanolic extract of *Mimosa pudica* on CAT activity

Vincristine-administered rats showed a significant decrease in CAT levels in comparison with normal control rats. Treatment with hydroethanolic extract of *Mimosa pudica* at 200 and 400 mg/kg exhibited a significant dose-dependent increase (P<0.05 & P<0.01) in CAT activity, respectively, in the sciatic nerve in comparison with vincristine-treated group. However, pregabalin-treated group exhibited significant alterations in the CAT activity in comparison with vincristine-treated group (figure 4).

3.6 Effect of hydroethanolic extract of *Mimosa pudica* on GPx activity

GPx activity was significantly depleted in vincristine-administered group in comparison with normal control group (figure 4). Treatment with hydroethanolic extract of *Mimosa pudica* (200 and 400 mg/kg) treated animals significantly elevated the GPx activity at P<0.05 and P<0.01, respectively, in comparison with vincristine-treated group. Pregabalin treated animals showed a significant alteration in the GPx enzyme activity in comparison with vincristine-treated group.

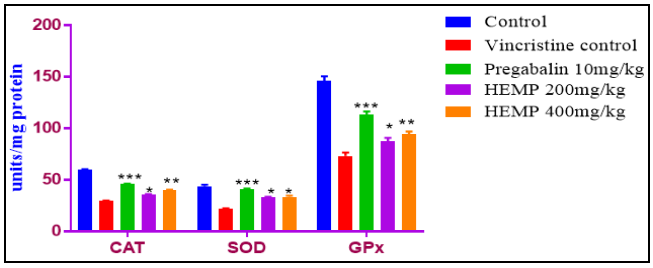

Fig 4: Effect of HEMP on SOD, CAT and GPx activity. The values are expressed as Mean ± SEM, n=6. The statistical analysis was carried out by one-way ANOVA using Dunnett's multiple comparison test, where *P<0.05, **P<0.01, ***P<0.001

3.7 Effect of hydroethanolic extract of *Mimosa pudica* on GSH levels

Significant decrease in GSH levels was observed in vincristine-administered group in comparison with normal control group (figure 5). Treatment of hydroethanolic extract of *Mimosa pudica* at 200 and 400 mg/kg exhibited a significant dose-dependent increase in the GSH levels at P<0.05 and P<0.01, respectively, in comparison with vincristine-treated group. However, significant alterations in GSH levels were observed in pregabalin treated animals (***P<0.001).

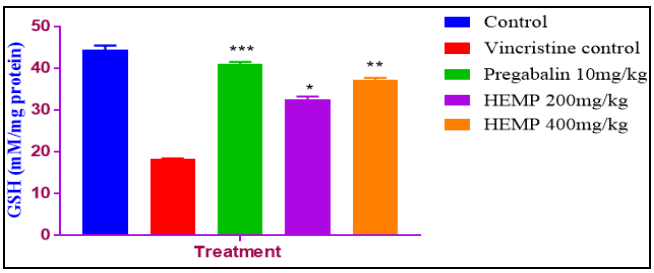

Fig 5: Effect of hydroethanolic extract of *Mimosa pudica* on GSH levels. The values are expressed as Mean ± SEM, n=6. The statistical analysis was carried out by one-way ANOVA using Dunnett's multiple comparison test, where *P<0.05, **P<0.01, ***P<0.001

3.8 Effect of hydroethanolic extract of *Mimosa pudica* on LPO levels

In comparison with control group, vincristine-control animals exhibited a significant elevation in LPO levels. Hydroethanolic extract of *Mimosa pudica* at 200 and 400 mg/kg treatment significantly decreased the LPO levels at *P<0.05 and *P<0.01, respectively, in comparison with vincristine-control group (Figure 6). Pregabalin treatment also exhibited significant decrease (***P<0.001) in LPO levels in comparison with vincristine-control group.

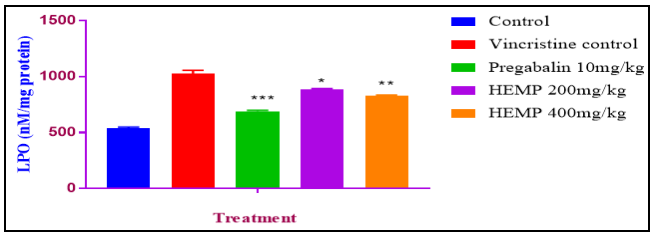

Fig 6: Effect of hydroethanolic extract of *Mimosa pudica* on LPO levels. The values are expressed as Mean ± SEM, n=6. The statistical analysis was carried out by one-way ANOVA using Dunnett's multiple comparison test, where *P<0.05, **P<0.01, ***P<0.001.

3.9 Effect of hydroethanolic extract of *Mimosa pudica* on NO levels

Vincristine administration exhibited a significant increase in NO levels in comparison with normal control group (figure 7). Treatment with hydroethanolic extract of *Mimosa pudica* 200 and 400mg/kg significantly decreased the NO levels at *P<0.05 and **P<0.01 respectively, in comparison with vincristine-control animals. Pregabalin at 10 mg/kg significantly decreased the NO levels at ***P<0.001 in comparison with vincristine-control animals.

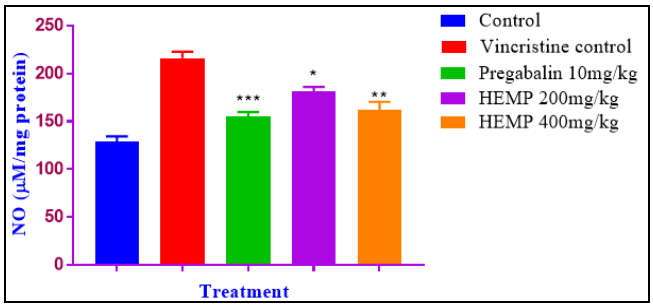

Fig 7: Effect of hydroethanolic extract of *Mimosa pudica* on NO levels. The values are expressed as Mean ± SEM, n=6. The statistical analysis was carried out by one-way ANOVA using Dunnett's multiple comparison test, where *P<0.05,**P<0.01, ***P<0.001.

3.10 Effect of hydroethanolic extract of *Mimosa pudica* on protein levels

The vincristine administration induced a state of increased oxidative stress in sciatic nerve homogenate as compared to control group. The treatment with pregabalin (10mg/kg) alleviated (***P<0.001) the effect of vincristine induced oxidative stress on the levels of protein (figure 8). The hydroethanolic extract of *Mimosa pudica* (400mg/kg) significantly decreased (**P<0.01) the protein levels on the nerve in comparison with the vincristine control group.

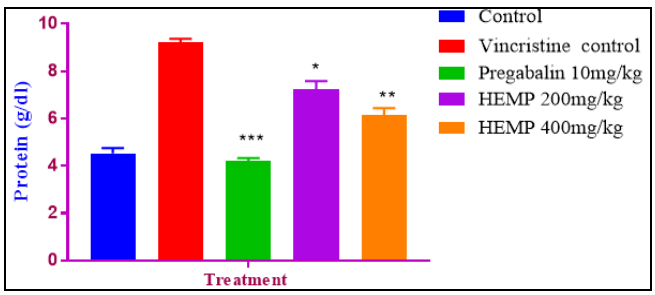

Fig 8: Effect of hydroethanolic extract of *Mimosa pudica* on protein levels. The values are expressed as Mean ± SEM, n=6. The statistical analysis was carried out by one-way ANOVA using Dunnett's multiple comparison test, where *P<0.05, **P<0.01, ***P<0.001

3.11 Effect of hydroethanolic extract of *Mimosa pudica* on calcium levels

Administration of vincristine exhibited a significant increase in total calcium levels in comparison with the normal control group. Hydroethanolic extract of *Mimosa pudica* (200mg/kg) significantly decreased (*P<0.01) the calcium levels in comparison with vincristine control group (figure 9). Pregabalin (10mg/kg) markedly reduced total calcium levels. Administration of hydroethanolic extract of *Mimosa pudica* (200mg/kg & 400mg/kg) obviated vincristine induced increase in total calcium. Pregabalin (10mg/kg) and hydroethanolic extract of *Mimosa pudica* (400mg/kg) significantly decreased (***P<0.001), the calcium levels in comparison with vincristine control group. Treatment with hydroethanolic extract of *Mimosa pudica* (400mg/kg) witnessed better anti-inflammatory activity than hydroethanolic extract of *Mimosa pudica* (200mg/kg).

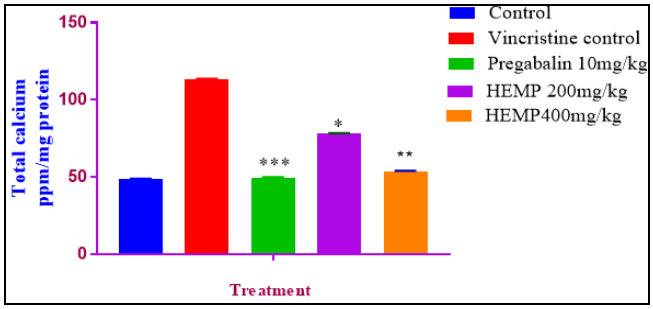

Fig 9: Effect of hydroethanolic extract of *Mimosa pudica* on calcium levels. The values are expressed as Mean ± SEM, n=6. The statistical analysis was carried out by one-way ANOVA using Dunnett's multiple comparison test, where *P<0.05, **P<0.01, ***P<0.001.

3.12 Histopathological Study

Vincristine treated group resulted in significant histopathological changes when compared to the other groups such as axonal degeneration, Schwann cell hyperplasia, damage of myelin sheath, fibrosis which were assessed in the transverse sections of sciatic nerve. The normal rat's sciatic nerve section showed normal structure, architecture and no inflammation.

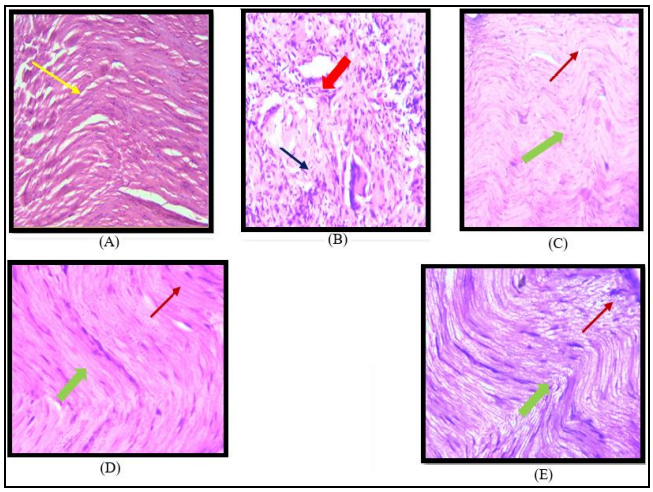

Fig 10: Difference in histopathology of sciatic nerve (A) normal control group (B)) vincristine induced (C) Pregabalin treated (10mg/kg) (D) hydroethanolic extract of *Mimosa pudica* (200mg/kg) (E) hydroethanolic extract of *Mimosa pudica* (400mg/kg). Normal control group showed normal fiber arrangement (yellow arrow) and no inflammation. Vincristine induction widely separated nerve fibers (bold red arrow) and changes in Schwann cells and showed an increase in the inflammatory cell infiltration (thin blue arrow). Treatment with hydroethanolic extract of *Mimosa pudica* (200mg/kg & 400mg/kg) increased axonal regeneration, separated nerve fibers and normalised the dearrangement (thin red arrow) observed in vincristine control group.

Vincristine treated group resulted in significant histopathological changes when compared to the other groups such as axonal degeneration, schwann cell hyperplasia, damage of myelin sheath, fibrosis which were

assessed in the transverse sections of sciatic nerve. The light microscopic examination of sciatic nerve of the control group (figure 10-A) showed normal structure and regular arrangement of its nerve fibers. The perineurium (connective tissue surrounded the nerve), nerve axons and Schwann cells appeared intact. The sciatic nerve of animals which received standard drug Pregabalin (10mg/kg) had normal structure and arrangement (figure 10-C) that were nearly similar to the control group. On the other hand, the sciatic nerve of the vincristine control (untreated) showed less number of dispersed nerve fibers(figure 10-B) with smaller diameter compared to the control group. Sciatic nerve of hydroethanolic extract of *Mimosa pudica* (200mg/kg) and (400mg/kg) treated showed increased number of nerve fibers (figure 10-D, E) compared to the untreated group. Most of the nerve fibers were regularly arranged with very few degenerated fibers. Few axons appeared degenerated with darkly stained cytoplasm (arrow) while most of the axons appear intact. Schwann cells appeared not affected. Treatment with standard drug Pregabalin (10mg/kg) as well the hydroethanolic extract of *Mimosa pudica* (200mg/kg & 400mg/kg) significantly attenuated vincristine induced axonal degeneration (caused axonal regeneration) and other histopathological changes. Vincristine treatment caused axonal degeneration, Schwann cell hyperplasia, damage of myelin fibrosis. It was found that hydroethanolic extract of *Mimosa pudica* reversed the histopathological changes caused by vincristine. This may be due to the potential neuroprotective effect of the drug. The C-glycosyl flavonoids present in hydroethanolic extract of *Mimosa pudica* possess antioxidant activity, thereby decrease the ROS level and neuroinflammation.

4. Conclusion

The present study concluded the potential curative effect of hydroethanolic extract of *Mimosa pudica* on hyperalgesia, allodynia and functional recovery of sciatic nerve following the induction of peripheral neuropathic pain through behavioral, biochemical and histological studies. Hydroethanolic extract of *Mimosa pudica* treatment reduced calcium deposition in nerve, which could be the major mechanism responsible for its neuroprotective potential besides inhibiting the inflammatory cytokines and ROS production. However, similar studies on various animal models are required to obtain a reliable oversight of the effect of these drugs on vincristine induced neuropathic pain in a clinical setting.

5. Acknowledgements

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