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Evaluation of neuroprotective activity of Mucuna pruriens against experimentally induced neurotoxicity in animal models

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ABSTRACT

Objectives: This study aims to evaluate the neuroprotective efficacy of *Mucuna pruriens* extracts against experimentally induced neurotoxicity in rat models, elucidating their potential in mitigating oxidative stress and neurodegeneration.

Materials and Methods: Extracts of *Mucuna pruriens* were meticulously prepared using petroleum ether, methanol, and hydroalcoholic solvents. Following extraction, a comprehensive phytochemical analysis was conducted to quantify key antioxidant phytonutrients—polyphenols, flavonoids, and tannins—using advanced spectroscopic techniques, with validation through high-performance liquid chromatography (HPLC). The 70% ethanolic extract, enriched with flavonoids, tannins, and polyphenols, was selected for subsequent antioxidant and pharmacological evaluations. Methanolic and hydroalcoholic extracts of *Mucuna pruriens* (MEMP and HAEMP) were subjected to in-depth pharmacological studies. Neurotoxicity was induced in rats using monosodium glutamate (MSG) and aluminium fluoride (AlF3), established models known to trigger neuronal degeneration via oxidative stress and inflammation. Given the well-documented role of oxidative stress in MSG- and AlF3-induced neurotoxicity, and the recognized antioxidant potency of MEMP and HAEMP, this study was designed to investigate their neuroprotective effects in these models.

Results: The methanolic extract of *Mucuna pruriens* (MEMP) at a dose of 100 mg/kg demonstrated significant neuroprotection against MSG- and AlF3-induced neurotoxicity in rats. The robust antioxidant properties of the extract, attributed to its high polyphenol, flavonoid, and tannin content, likely underpin its neuroprotective mechanism, effectively counteracting oxidative stress and neuronal damage..

Keywords: *Mucuna pruriens, monosodium glutamate, aluminium fluoride, excitotoxicity, oxidative stress, neurodegeneration, neuroprotection, antioxidants*

1. INTRODUCTION

Neurodegenerative disorders, such as Alzheimer's disease, Parkinson's disease, Huntington's disease, and cerebrovascular stroke, are characterized by progressive neuronal loss and dysfunction, with no current treatments to slow disease progression or provide cures (Markesbery, 2007). Oxidative stress is a primary cause of neurovascular damage, exacerbated by factors including diabetes mellitus, hypertension, hyperlipidemia, enhanced platelet aggregation, ischemic heart disease, atherosclerosis, endothelial dysfunction, and hyperhomocysteinemia (Scarmeas et al., 2006). This study explores potential neuroprotective interventions to mitigate these pathological processes. Antioxidants are compounds that mitigate cellular damage by neutralizing free radicals, unstable molecules generated by environmental stressors and physiological processes. Often termed "free radical scavengers," they can be derived from natural or synthetic sources.

Herbal medicines are integral to modern pharmacology, with approximately 80% of the global population relying on them for primary healthcare (WHO, 1985). *Mucuna pruriens* Linn., a leguminous plant native to tropical regions like India and the West Indies, is a key component in over 200 traditional drug formulations. Known as velvet bean or cowitch, it is valued for its rich phytochemical content, including L-Dopa, alkaloids (e.g., mucunadine, mucunine), amino acids, and epoxy fatty acids. Recent studies have identified novel lipid derivatives and tetrahydroisoquinoline alkaloids in its seeds, highlighting its therapeutic potential (Misra & Wagner, 1937; Daxenbichler et al., 1971, M. Damodaran et.al., 1937). All parts of the plant possess medicinal properties, driving high demand in Indian and international markets. This study investigates the neuroprotective effects of *Mucuna pruriens* extracts, leveraging its potent antioxidant properties to address neurotoxicity.

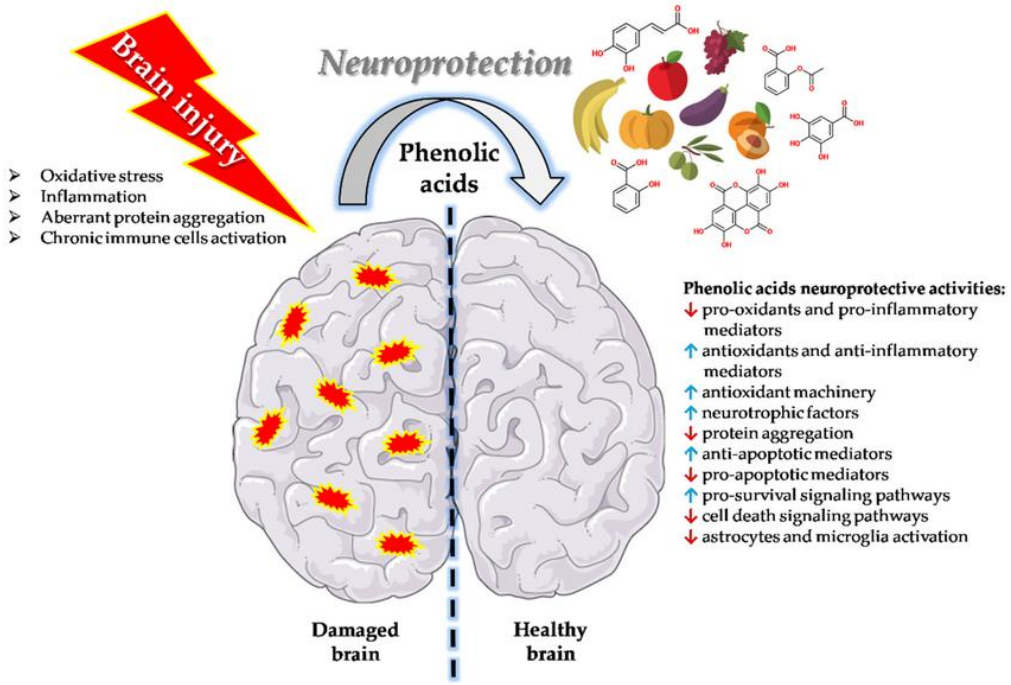

Figure-1 Neuroprotection Process Showing damaged brain and Healthy brain

2. MATERIAL AND METHODS

Plant Material

The plant *Mucuna pruriens* was obtained from Warangal botanical garden and validated by Dr. KM Chetty, Department of Botany, Sri Venkateshwara University, Tirupati.

Figure-2 Mucuna pruriens Plants with seeds

Animals

Wistar albino rats (150–250 g, both sexes) were sourced from College of Veterinary Science and Animal Husbandry, Jabalpur. They were acclimatized for one week in polypropylene cages under controlled conditions (27°C ± 2°C, 12-hour light/dark cycle). The rats were provided standard rat feed (Gold Mohur, Lipton India Ltd.) and water *ad libitum*.

Pharmacological Activities

Monosodium Glutamate (MSG)-Induced Neurotoxicity

Rats were divided into five groups (n=6) and treated for 7 days as follows:

Group 1: Normal saline (i.p.) + vehicle (p.o.)

Group 2: MSG (2 g/kg, i.p.) + normal saline (p.o.)

Group 3: MSG (2 g/kg, i.p.) + Donepezil (5 mg/kg, i.p., reference standard)

Group 4: MSG (2 g/kg, i.p.) + MEMP (100 mg/kg, p.o.)

Group 5: MSG (2 g/kg, i.p.) + HAEMP (100 mg/kg, p.o.)

One hour interval was maintained between MSG and extract administration. The MSG dose was based on prior literature (Rang et al., 2003). Behavioural changes were monitored daily for 50 minutes during treatment. On day 8, assessments included body weight, locomotor activity, balance beam task, elevated plus maze, and rotarod test. On day 9, rats were euthanized, and brains were analysed for glutathione, superoxide dismutase (SOD), catalase (CAT), lipid peroxidation, and total protein levels.

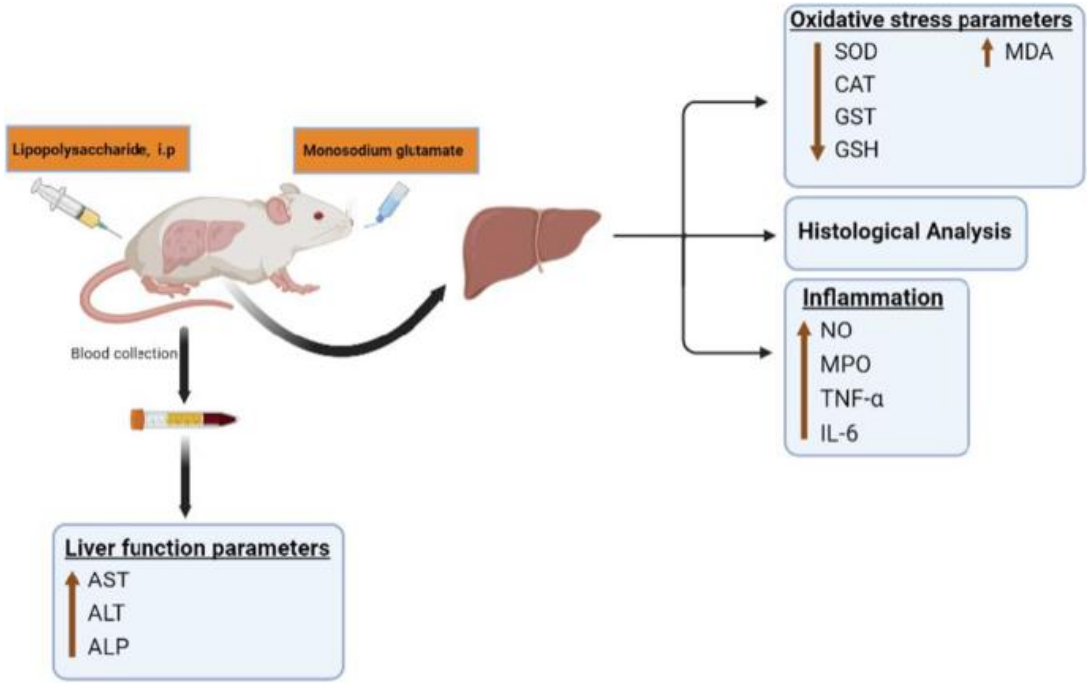

Figure-3 Effects of Mono sodium glutamate induced Neuro toxicity

B) Aluminium fluoride induced Cerebro toxicity

The animals were divided into five groups of six rats each as follows;

Group 1: Received normal saline (i.p.) + vehicle (p.o.).

Group 2: Received (AlF3−) 600ppm + normal saline (p.o.).

Group 3: Received (AlF3−) 600ppm + Donepezil 5 mg/kg, (i.p.)

Group 4: Received (AlF3−) 600 ppm + MEMP 100mg/kg (p.o).

Group 5: Received (AlF3−) 600 ppm + HAEMP 100mg/kg (p.o).

Animals received drug or vehicle treatment for 10 days prior to AlF_3 administration via drinking water (600 ppm for 7 days). Behavioral changes were monitored daily for 50 minutes during treatment (Kulkarni et al., 2021). Assessments included body weight, locomotor activity, balance beam task, elevated plus maze, and rotarod test. Subsequently, rats were sacrificed, and brains were analyzed for glutathione, superoxide dismutase (SOD), catalase (CAT), lipid peroxidation, and total protein (TP).

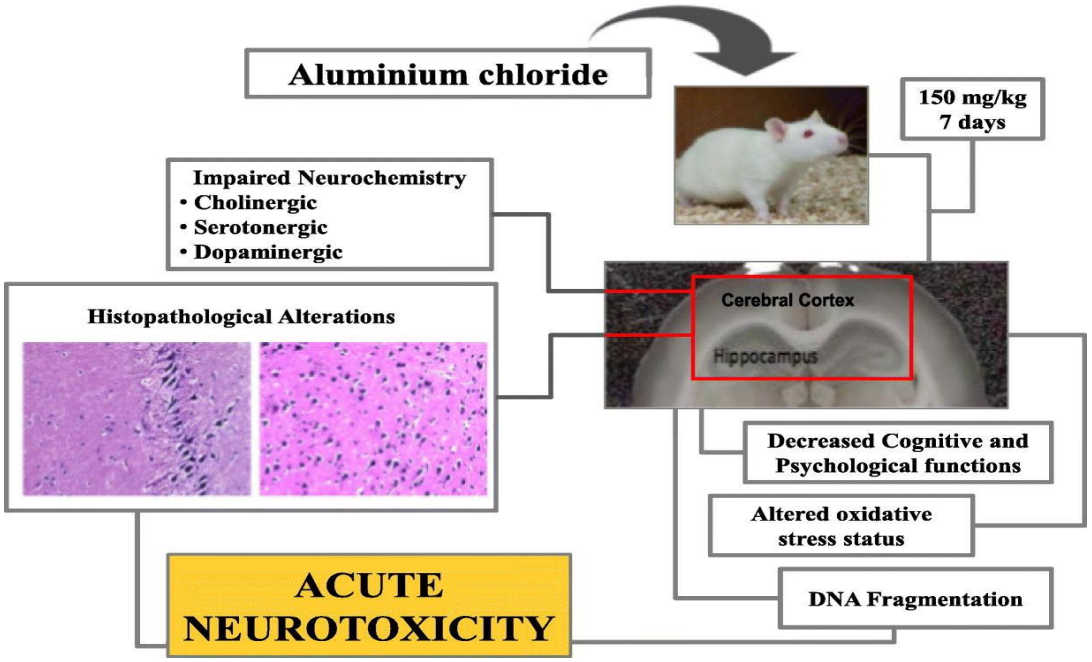

Figure-4 Effects of Aluminium fluoride induced Cerebro toxicity

Behavioural parameters

A) Locomotor activity

The spontaneous locomotor activity was monitored using actophotometer (Dolphin Pvt. Ltd., Mumbai, India) equipped with infrared sensitive photocells, the apparatus was placed in darkened, light and sound attenuated and ventilated testing room. Before locomotor task, animals were placed individually in the activity meter for 2 min for habituation (Claiborne, 1985). Thereafter, locomotor activity was recorded for a period of 5 min. The locomotor activity was expressed in terms of total photo beam counts per 5min.

B) Rota rod test

The Rota rod test was used to measure the muscle relaxant property of the rats. Turn on the roto-rod. Appropriate speed 20-25rpm selected, rats were placed one by one on the rotating rod (Tiwari, 2001). Fall of time was noted, the cut of time of Rota rod test is 5min.

C) Beam walking task for motor coordination

The Beam walking task for motor coordination was used to measure the ability of rats to traverse a horizontal narrow beam (2.3 cm × 120 cm) suspended 50 cm above a foam padded cushion (Tietz, 1970). During testing, the rats were given 1 min to traverse the beam. If they did not complete the task or if they fell off the beam, the trial was ended and the rats were placed back into their home cages. For successful performers, the latency to cross the beam was recorded.

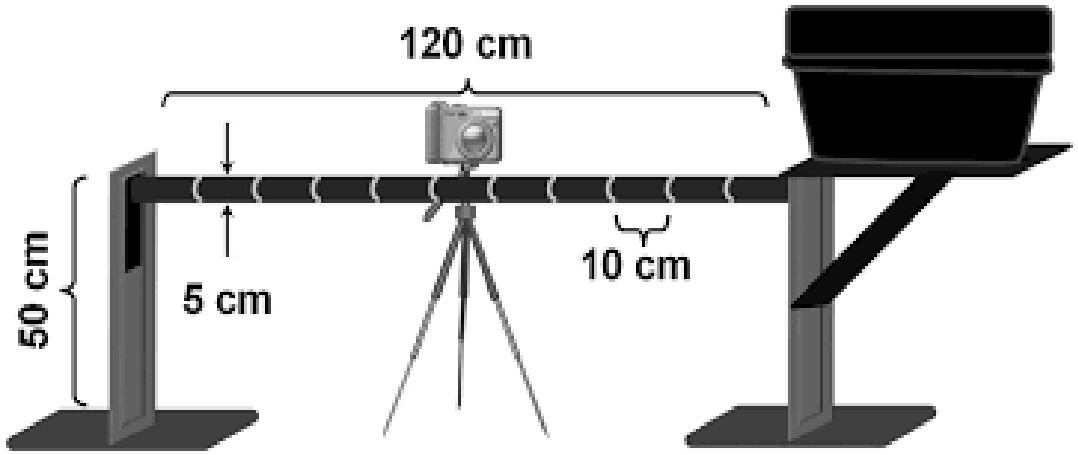

Figure-5 Beam walking apparatus

Biochemical estimations

A) GSH estimation

Tissue samples were homogenized in ice cold trichloroacetic acid (0.5G tissue plus 5 ml, 10% TCA) in an ultra turrax tissue homogenizer. Briefly, after centrifugation at 3000 rpm for 10 minutes, 0.5 ml supernatant is added to 2 ml of 0.3 M disodium hydrogen phosphate solution. A 0.2 ml solution of dithiobisnitrobenzoate (0.4 mg/ml in 1% sodium citrate) is added and the absorbance at 412 nm is measured immediately after mixing. Percent increase in OD is directly proportional to the increase in the levels of glutathione. Hence, % increase in OD was calculated.

B) *In vivo* lipid peroxidation

Stock solution of TCA-TBA-HCl reagent: 15% w/v trichloroacetic acid; 0.375% w/v thiobarbituric acid; 0.25N hydrochloric acid was prepared. Take 1.0 Stock solution of TCA-TBA-HCl reagent: 15% w/v trichloroacetic acid; 0.375% w/v thiobarbituric acid; 0.25N hydrochloric acid was prepared. 2.0 ml of TCA-TBA-HCl was added and mixed thoroughly. The solution was heated for 1 hr in a boiling water bath. After cooling, the flocculent precipitate was removed by centrifugation at 1000 rpm for 2 min. The absorbance of the sample was determined at 535 nm against a blank.

C) Catalase (CAT)

Catalase measurement was done based on its ability to decompose hydrogen peroxide (H O). Briefly, to 1.95 ml of 10 2 2 mM H2O2 in 60 mM phosphate buffer (pH = 7.0), 50 µl of the

brain tissue supernatant was added and the rate of degradation of H O was followed at 240 nm per min. % increase in OD is directly proportional to the increase in the levels of Catalase (James et al., 2005). Hence, % increase in OD was calculated.

D) Super oxide dismutase (SOD)

Superoxide dismutase activity was determined based on the ability of SOD to inhibit the auto-oxidation of epinephrine to adrenochrome at alkaline pH (Misra and Fridovich, 1972). Briefly, 0.5 ml of the supernatant obtained from the centrifuged brain homogenate was added to a mixture of 0.1mM epinephrine in carbonate buffer (pH 10.2) in a total volume of 1 ml and the formation of adrenochrome was measured at 295 nm (James et al., 2005). % increase in OD is directly proportional to the increase in the levels of Super Oxide Dismutase. Hence, % increase in OD was calculated.

E) Total protein

The total serum protein contents were determined by Biuret's method (using total protein kit). This method is based on the principle that proteins give an intensive violet-blue complex with copper salts in an alkaline medium. Iodine is included as an antioxidant. The intensity of the colour formed is proportional to the total protein concentration in the sample.

3. RESULTS AND DISCUSSION

Plants are conceived as source of antioxidants due to presence of poly phenols, tannins and flavonoids, which possess wide spectra of biological properties.

Table 1. Total phenolic, flavonoid and tannin content of extract

Particulars	**Phenolic content**	**Flavonoid** content	**Tannin** content
Standard curve	Catechol	Quercetin	Tannic acid
Weve length (nm)	650nm	510nm	700nm
Amount of content in 70 percent Methanolic content	55.20mcg /ml	152.33mcg/ml	2538.88mcg/ml
Amount of content in Hydroalcoholic content	45.31mcg /ml	38.33mcg/ml	638.88mcg/ml
R^2 value	0.998	0.980	0.998

Table 2. MEMP 100mg/kg on body weight change and behavioural change in MSG treated rats

Treatment	% Body weight change	Rota Rod Test (s)	Locomotor Activity (Count / 5 min)	Balance beam test (sec)
Negative control	-	395.5±190.2***	280.8±18.59***	28.84±4.777***
Positive control	13.04	145.4±250.9	92.17±19.19	13.45± 3.232
Standard Donepezil 10 mg/kg	04.80	393.6±204.7***	274.3±19.19***	28.25±3.232***
MEMP 100mg/kg	12.18	293.1±221.4**	204.2±17.37**	25.33± 3.064*
HAEMP 100mg/kg	08.24	171.2±151.7NS	137.0 ±44.39NS	18.26±1.533NS

Each value is expressed as mean ± SEM (n = 6), where, NS represents non-significant; ****P<0.0001 – highly significant;***P<0.001 – very significant; **P<0.01- good significant; *P<0.05- significant, when compared to MSG alone treated rats. One-way ANOVA followed by Dunnett's comparison test.

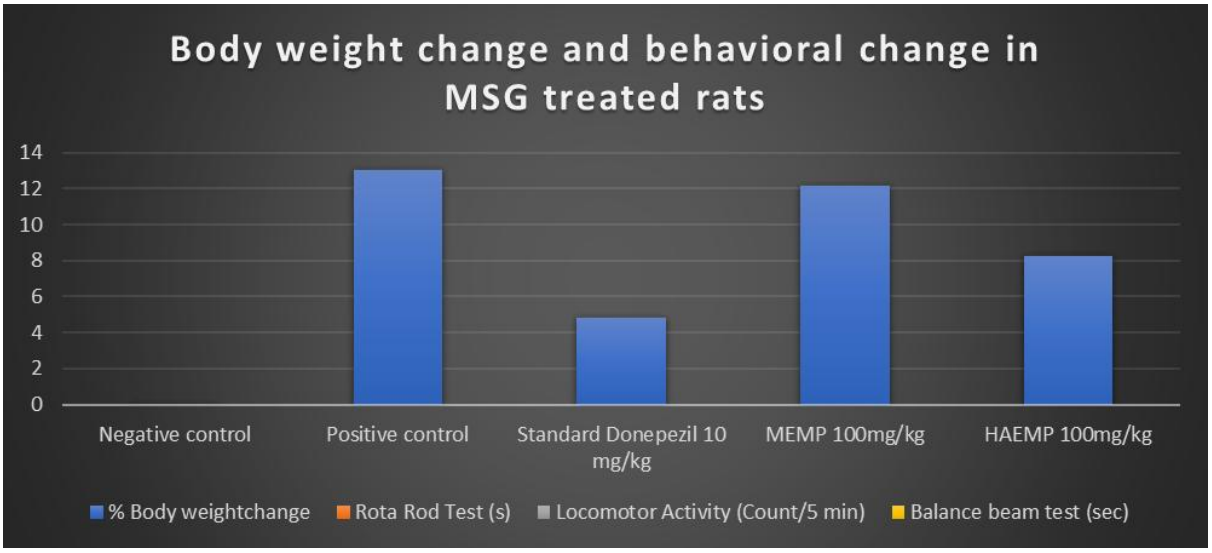

Figure - 6 Graphical presentation of body weight change and behavioural change in MSG treated rats

Table 3. Effect of MEMP 100mg/kg on biochemical parameters in MSG treated rats

Treatment	GSH		LPO		SOD		CAT		TP	
	Mean± SEM	% increase	Mean ± SEM	% increase	Mean ± SEM	% increase	Mean ± SEM	% increase	Mean ± SEM	% increase
Negative control	0.148 ± 0.001****	-	0.125 ± 0.001****	-	0.282 ± 0.009****	-	0.832 ± 0.001****	-	0.653 ± 0.006****	-----

Positive	0.076 ± 0.001****	-	0.491 ± 0.001****	-----	0.111 ± 0.009****	-----	0.363 ± 0.001****	-	0.372 ± 0.006****	-----
Standard Donepezil 10 mg/kg	0.137 ± 0.001****	80.26	0.158 ± 0.005****	67.82	0.241 ± 0.005****	90.47	0.712 ± 0.003****	96.14	0.599 ± 0.011****	61.0
MEMP 100mg/kg	0.106 ± 0.001****	39.47	0.188 ± 0.002****	61.71	0.027 ± 0.004****	86.48	0.672 ± 0.0008****	85.12	0.541 ± 0.008****	45.43
HAEMP 100mg/kg	0.077 ± 0.002****	1.31	0.219 ± 0.002****	55.39	0.178 ± 0.002****	60.36	0.555 ± 0.001****	52.89	0.490 ± 0.008***	31.72

Each value is expressed as mean ± SEM (n = 6), where, NS represents non-significant; ****P<0.0001 – highly significant; ***P<0.001 – very significant; **P<0.01- good significant; *P<0.05- significant, when compared to MSG alone treated rats. One-way ANOVA followed by Dunnett's comparison test.

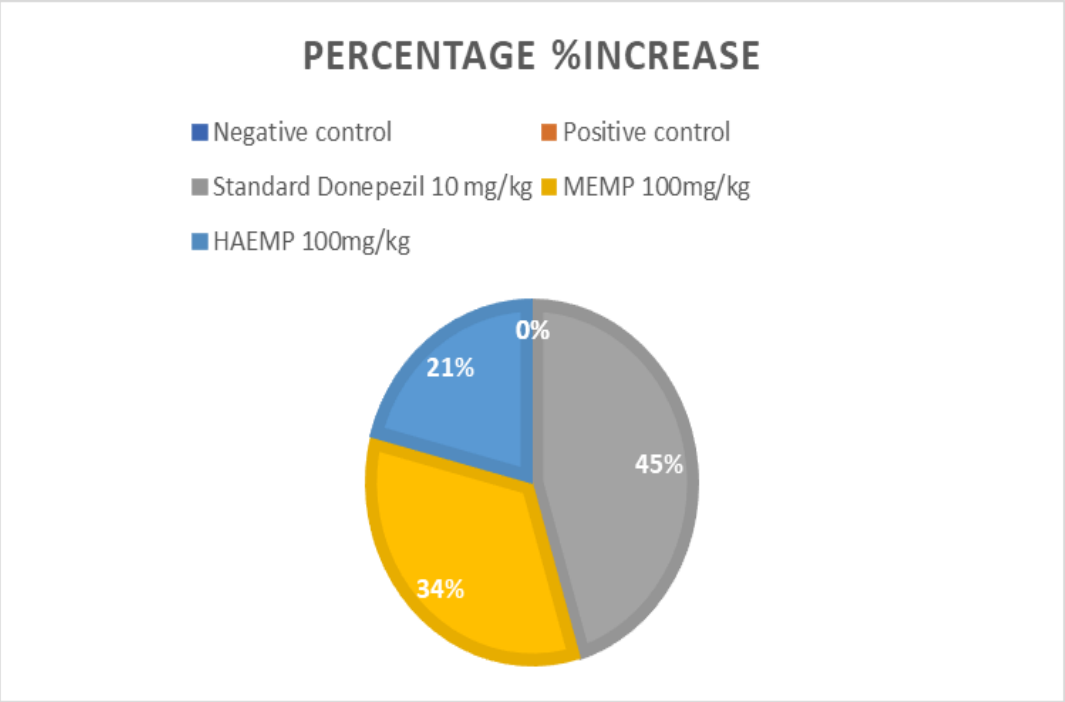

Figure - 7 Graphical presentation of Effect of MEMP and HAEMP 100mg/kg on biochemical parameters in MSG treated rats

Table 4. Effect of HAEMP on body weight change and behavioural change in AlF_3 treated Rats

Treatment	% Body weight change	Rotarod test (s)	Balance beam test (s)	Locomotor activity (count/5min)
Negative control	-----	1764±58.36****	28.84±3.716*	459.3±25.41***
Positive control	11.04	846.2±36.09	11.98±1.072	212.33±27.06
Standard Donepezil 10 mg/kg	05.80	1625±36.62****	26.81±3.491**	432.3±33.83**
MEMP 100mg/kg	12.18	1554±34.39****	25.27±1.968	350.8±24.29**
HAEMP 100mg/kg	8.24	1062±85.08NS	17.28±1.415*	263.7±27.99NS

Each value is expressed as mean ± SEM (n = 6), where, NS represents non-significant; ****P<0.0001 – highly significant;***P<0.001 – very significant; **P<0.01- good significant; *P<0.05- significant, when compared to MSG alone treated rats. One-way ANOVA followed by Dunnett's comparison test

Figure - 8 Graphical presentation of effect of MEMP and HAEMP on body weight change and behavioural change in AlF_3 treated Rats

Table 5 Effect of HAEMP on biochemical parameters in AlF_3 treated rats

Treatment	GSH		LPO		SOD		CAT		TP	
	Mean± SEM	% increase	Mean ± SEM	% increase	Mean ± SEM	% increase	Mean ± SEM	% increase	Mean ± SEM	% increase
Negative control	0.1485 ± 0.0012****	----	0.1252 ± 0.0014****	-----	0.2827 ± 0.0096****	-----	0.8327 ± 0.0064****	-----	0.6535 ± 0.0047****	-----
Positive	0.0525 ± 0.0011****	----	0.4917 ± 0.0004****	-----	0.01117 ± 0.0042****	-----	0.4302 ± 0.0061****	-----	0.3807 ± 0.0033****	-----
Standard Donepezil 10 mg/kg	0.1373 ± 0.0010****	80.65	0.1588 ± 0.0045****	67.7	0.2413 ± 0.0035****	96.0	0.7065 ± 0.0088****	64.22	0.5912 ± 0.0073****	55.29
MEMP 100mg/kg	0.1255 ± 0.0016****	65.13	0.1775 ± 0.0124****	63.9	0.2113 ± 0.0054****	84.42	0.6502 ± 0.0070****	51.13	0.5372 ± 0.0091	41.1
HAEMP 100mg/kg	0.1070 ± 0.0031****	40.78	0.2198 ± 0.0038****	55.29	0.1878 ± 0.0060****	68.12	0.6503 ± 0.0071****	40.7	0.4778 ± 0.0081****	25.5

Each value is expressed as mean ± SEM (n = 6), where, NS represents non-significant; ****P<0.0001 – highly significant; ***P<0.001 – very significant; **P<0.01- good significant; *P<0.05- significant, when compared to MSG alone treated rats. One-way ANOVA followed by Dunnett's comparison test.

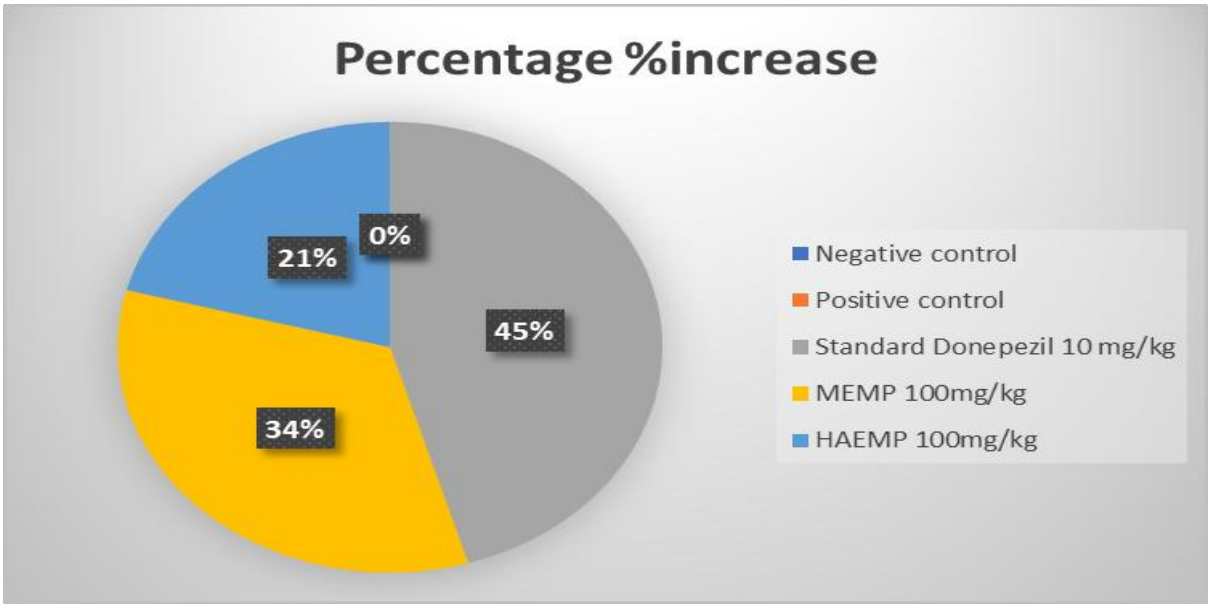

Figure - 9 Graphical presentation on Effect of MEMP and HAEMP 100mg/kg on biochemical parameters in MSG treated rats

Recent studies showed that many tannin, flavonoids and related polyphenols contribute significantly to the total antioxidant activity. Antioxidants further help as organ protectants. Hence, in this study a widely grown *Mucuna pruriens* reported to possess polyphenolic compounds. The preliminary phytochemical screening of plant showed that, they possess polyphenols, flavonoids, tannins and vitamins which are reported to possess antioxidant property. These antioxidant properties may be assessed by several in-vitro models like Super oxide radical and reducing power assay and was selected for screening. The barks were collected and extracts has prepared separately and were subjected to preliminary phytochemical studies, the results indicated that bark possess tannins, flavonoids, polyphenols and vitamins in Methanolic and hydroalcoholic extracts. Since 70% Methanolic and hydroalcoholic extracts contain similar type of phytoconstituents, those two extracts were subjected to the quantification. The total phenol, flavonoid, tannin content of 70% Methanolic was 55.20mcg/ml, 152.33mcg/ml and 2538.88mcg/ml expressed as equivalent to catechol, quercetin and tannic acid respectively, which is better compared to hydroalcoholic. Methanolic extract of *Mucuna pruriens* showed dose dependent super oxide anion scavenging and reducing power activity. Therefore 70% Methanolic extract of *Mucuna pruriens* selected to screen neuroprotective activity. Results of the present study indicates that Mucuna pruriens extract treatment significantly improved motor deficits, muscle grip strength, body coordination and restored the body weight, hind limb functions and antioxidant levels in brain.

Histopathological Studies in MSG induced neurotoxicity

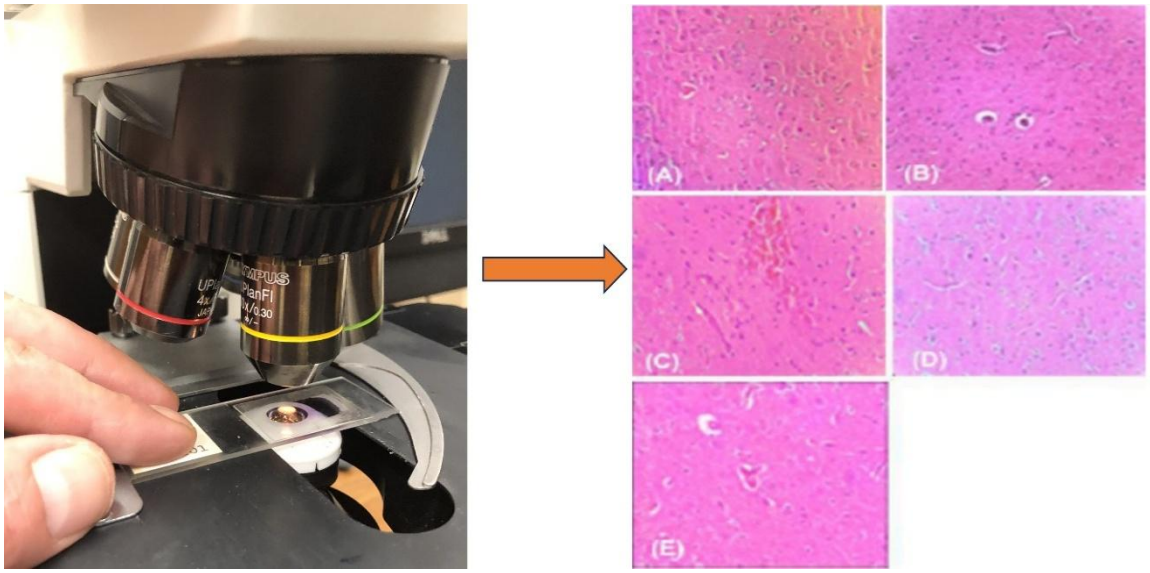

Figure - 10. Photomicrograph of brain parenchyma tissue from MSG induced neurotoxicity: (A) Negative control (B) Positive control (C) Standard (D) MEMP (100 mg/kg) (E) (100 mg/kg) of HAEMP

Figure - 11. Photomicrograph of brain parenchyma tissue from ALF induced neurotoxicity: (A) Negative control (B) Positive control (C) Standard (D) MEMP (100 mg/kg) (E) (100 mg/kg) of HAEMP

A) Negative Control: Normal control Section studied from the brain parenchyma shows intact architecture. Most of the pyramidal cells and neuroglial cells appears intact (Figure 10A).

B) Positive Control: MSG treated group (+ve control) Section studied from the brain parenchyma shows intact architecture. Some of the pyramidal cells and neuroglial cells show degenerative changes with moderate inflammatory infiltration. Most of the blood vessels show moderate perivascular inflammatory infiltration (Figure 10B).

C) Standard: Treatment done with Donepezil 5mg/kg Section studied from the brain parenchyma shows intact architecture. Few of the pyramidal cells and neuroglial cells show degenerative changes. Areas of haemorrhage with mild inflammatory infiltration seen. Few of the blood vessels appear congested (Figure 10C).

D) 100mg/kg MEMP: Treatment done with 100 mg/Kg MEMP Section studied from the brain parenchyma shows intact architecture. Few of the pyramidal cells and neuroglial cells show degenerative changes with moderate inflammatory infiltration. Few of the blood vessels show moderate perivascular inflammatory infiltration (Figure 10D).

E) 100mg/kg HAEMP: Treatment done with 100mg/Kg HAEMP showed the Section studied from the brain parenchyma shows intact architecture. Few of the pyramidal cells and neuroglial cells show degenerative changes with mild inflammatory infiltration. Few of the blood vessels show mild perivascular inflammatory infiltration (Figure 10E).

Histopathological Studies in ALF_3 induced neurotoxicity

A) Negative Control: Normal control (-ve control) showed the section studied from the brain parenchyma shows intact architecture. Most of the pyramidal cells and neuroglial cells appear intact (Figure 11A).

B) Positive Control: AlF_3 treated group (+ve control) showed the Section studied from the brain parenchyma shows intact architecture. Few of the pyramidal cells and neuroglial cells show degenerative changes (Figure 11B) with moderate inflammatory infiltration. Few of the blood vessels show moderate perivascular inflammatory infiltration.

Standard: Treatment done with Donepezil 5mg/kg Section in AlF_3 induced rats showed the section studied from the brain parenchyma shows intact architecture. Few of the pyramidal cells and neuroglial cells show degenerative changes with moderate inflammatory infiltration (Figure 11C). Most of the blood vessels show moderate perivascular inflammatory infiltration.

D) 100mg/kg MEMP: Treatment with 100mg/kg MEMP in AlF_3 showed the section studied from 3 the brain parenchyma shows intact architecture. Few of the pyramidal cells and neuroglial cells show degenerative changes with moderate inflammatory infiltration (Figure 11D). Most of the blood vessels show moderate perivascular inflammatory infiltration.

E) 100mg/kg HAEMP: Treatment with 100mg/kg HAEMP in AlF_3 induced rats section studied from the brain parenchyma shows intact architecture. The pyramidal cells and neuroglial cells appear intact with moderate inflammatory infiltration (Figure 11E). Few of the blood vessels show mild perivascular inflammatory infiltration. In present the study sub-chronic administration of MSG (2 g/kg, i.p. for 7 days) and AlF_3 (600ppm p.o for 7 days) produced 3 significant decreases in body weight, motor and muscle grip related behaviors and antioxidant status in the brain. These findings are well corelates to histopathological observations which indicates the presence of degenerated nerve cell and loosening of nerve fibers in striatal region of the brain. The reduction of body weight in MSG and AlF_3 induced rats could be due to metabolic impairment caused by neurotoxic agents i.e. impairment in energy metabolism, mobilization of energy stores and lipid peroxidation which constitute peripheral effects. Striatal lesion indicated by treatment with MSG and AlF_3 caused an impairment in the locomotion observed in actophotometer. MSG and AlF_3 have been reported to cause lesion in hippocampal and pyramidal neurons. Animals showed poor locomotion in the treated groups. This observation indicates that the treatment with MSG and AlF_3 causes motor dysfunction as observed in the PD patients. In the present study EEFRB treatment significantly improved locomotor performance and showed improved motor activity. Since GSH is considered as inbuilt antioxidant substance which prevents lipid peroxidation, estimation of tissue GSH and extent of lipid peroxidation were considered as parameters of screening in-vivo antioxidant properties in all the models. Since the MSG induced neurotoxicity was reported to be via free radicals, the neuroprotective activity of test extract in this model is also attributed to the antioxidant activity of the plant. The neuroprotective property of the extract is further confirmed by significant improvement of the brain architecture by reversing the disintegrated neuropil fibres over MSG group. The neuroprotective property of the extract is further confirmed by significant improvement of the brain architecture by reversing the disintegrated neuropil fibers over AlF_3 group. In the present study, it was observed that the bark possesses polyphenolic compounds (flavonoids and tannins) and these constituents are reported to have antioxidant and organ protective properties. Hence the anti-oxidant and neuroprotective properties may be attributed to the polyphenolic constituents that are present in the *Mucuna pruriens*.

The present study demonstrates that the methanolic extract of *Mucuna pruriens* (MEMP) possesses significant neuroprotective potential against MSG- and AlF_3-induced neurotoxicity in rats. The beneficial effects observed in behavioral, biochemical, and histological parameters can be explained by the phytochemical richness of the extract, particularly its polyphenolic constituents such as flavonoids and tannins.

Oxidative stress is one of the primary mechanisms underlying MSG- and AlF_3-induced neuronal damage. Excessive free radical generation leads to lipid peroxidation, protein oxidation, and DNA damage, all of which contribute to neuronal

degeneration. In this study, MEMP markedly enhanced the levels of endogenous antioxidant enzymes including glutathione (GSH), superoxide dismutase (SOD), and catalase, while simultaneously reducing lipid peroxidation as indicated by decreased malondialdehyde (MDA) levels. These findings suggest that the neuroprotective effect of MEMP is largely attributable to its ability to strengthen the antioxidant defense system of the brain. The high phenolic and flavonoid content in MEMP provides the necessary hydrogen-donating ability to neutralize free radicals, thereby preventing oxidative chain reactions and stabilizing neuronal membranes.

Behavioral parameters such as locomotor activity, rotarod performance, and balance beam coordination were significantly impaired in animals treated with MSG and AlF_3. However, MEMP treatment restored these functional deficits, indicating preserved motor control and neuromuscular coordination. This improvement can be correlated with the extract's ability to protect neuronal circuits in regions of the brain involved in motor coordination, such as the cerebellum and basal ganglia. Additionally, the presence of L-DOPA in *Mucuna pruriens* may have contributed to improved dopaminergic transmission, further supporting better motor function.

Histopathological findings further substantiated the biochemical and behavioral results. Animals treated with MSG and AlF_3 showed marked neuronal shrinkage, vacuolation, necrosis, and inflammatory infiltration. In contrast, MEMP-treated groups exhibited near-normal brain architecture with reduced degeneration and inflammation. This suggests that the extract not only counteracts oxidative stress but also mitigates inflammatory responses, possibly by suppressing microglial activation and pro-inflammatory cytokine release.

Taken together, the neuroprotective activity of MEMP appears to be mediated by multiple mechanisms: scavenging of reactive oxygen species, enhancement of endogenous antioxidant defenses, inhibition of lipid peroxidation, and suppression of neuroinflammation. The synergistic contribution of its phytoconstituents, particularly polyphenols and L-DOPA, may explain why the extract was effective in both restoring functional outcomes and preserving structural integrity of neurons. Importantly, the protective effect was observed in two different neurotoxic models, excitotoxicity (MSG) and metal-induced neurotoxicity (AlF_3), indicating that the extract exerts a broad-spectrum neuroprotective effect.

4. CONCLUSION

In conclusion, the findings of this study strongly support the role of *Mucuna pruriens* as a promising neuroprotective agent. Its polyphenolic compounds appear to underlie the observed antioxidant and neuroprotective activities, while its L-DOPA content may additionally support neurotransmitter balance. The methanol extract of Mucuna pruriens (MEMP) demonstrates significant neuroprotective potential against monosodium glutamate (MSG) and aluminium fluoride (AlF_3)-induced neurotoxicity in rats. MEMP effectively mitigates behavioural deficits and oxidative stress caused by MSG and AlF_3, while also preventing neurodegeneration in the striatal and hippocampal regions. These protective effects are likely attributed to its antioxidant activity. These results not only validate the traditional use of *Mucuna pruriens* in neurological disorders but also open avenues for further mechanistic and translational research to explore its therapeutic potential in human neurodegenerative diseases.

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