Protective effect of *Solanum torvum* on monosodium glutamate-induced neurotoxicity in mice

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Solanum torvum is a well known traditional herbal medicinal plant used in many neurological disorders. The objective of the study was to evaluate the effects of *S. torvum* on monosodium glutamate (MSG) induced neurotoxicity. Swiss albino mice received MSG (1000 mg/kg, p.o) followed by a methanolic and hydroalcoholic extract of *S. torvum* (100 and 300 mg/kg, p.o) for 14 days. MSG-treated mice showed significant ($p < 0.05$) behavioural changes, decrease in relative organ weight of brain, a decrease in antioxidant enzyme levels and significant ($p < 0.05$) increase in lipid peroxidation in brain tissue. Histopathological changes observed in brain tissue were vacuolated cells, pyknotic nuclei, decreased neuronal density and distorted layers of brain tissue. Both extracts of *S. torvum* (100 and 300 mg/kg) showed normal behavior, significant ($p < 0.05$) increase in relative organ weight of brain, significant ($p < 0.05$) decrease in lipid peroxidation (LPO) and significant ($p < 0.05$) increase in reduced glutathione (RGSH), superoxide dismutase (SOD) and catalase (CAT) concentration in brain tissue as compared to MSG-treated mice. Treatment with *S. torvum* extracts reversed the histopathological changes induced by MSG. The study suggests that *S. torvum* seed extracts have the potential to ameliorate neuronal damage induced by MSG. Total flavonoid content of methanolic and hydroalcoholic extract of *S. torvum* was found to be 44±1.2, and 32±0.8 µg of rutin equivalent/mg of extracts and total phenolic content was found to be 70±0.28 and 52±0.62 µg of gallic acid equivalent/mg of extracts respectively.

Keywords- Excitotoxicity, Monosodium glutamate, Neurotoxicity, Oxidative stress, *Solanum torvum*.

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Introduction

Monosodium Glutamate (MSG) is one of the most widely used food additives. Glutamate, a key excitatory amino acid, is also a neurotransmitter distributed all over in the mammalian brain. Glutamate receptors include three families of ionotropic receptors NMDA (N-methyl-D-aspartate), AMPA (α-amino-3-hydroxy-5 methyl-4-isoxazolepropionic acid) and kainate receptors and three groups of metabotropic receptors (mGluR)[1]. A study[2] reported that externally administered MSG could be neurotoxic causing neuronal degeneration in the inner layers of retina[2]. Another study[3] reported necrosis of hypothalamic neurons of neonatal mice given MSG intraperitoneally[3]. Several studies were carried out to study the toxicity of MSG on various organs in laboratory animals. MSG is reported to produce neurotoxicity[3,4], cardiotoxicity[5], reproductive organ toxicities[6,7], retinal damage of eye[2,8], obesity and metabolic disorders[9], hepatotoxicity and nephrotoxicity[10].

The route of administration, the age of animals and the dose of MSG determines the extent of neuronal and other organ damage. Intraperitoneal administration of MSG in neonatal and weaning mice has caused higher neuronal damage than in adults[11]. It has been observed that oral route of MSG administration had caused fewer signs of toxicity as compared to intraperitoneal administration[12]. MSG (100, 250, and 500 mg/kg by oral route) has also been studied on behavioural phenotypes and biomarkers of oxidative stress in brain tissue of adult mice, and reported abnormalities in the performance of animals in various behavioural mazes and alterations in antioxidant enzymes at higher doses[13].

Solanum torvum Swartz (family Solanaceae) is commonly known as Turkey berry. Phytochemical studies reveal the presence of many compounds such as 2,3,4-trimethyltriacontane, 5-hexacontane, triacontanol, 3-tritriacontane, tetratriacontane acid, sitosterol, stigmasterol, campestol, neochlorogenin 3-O-β-L-rhamnopyranosyl, β-L-rhamnopyranoside, chlorogene, neochlorogenone[14] isoflavonoid sulfate and steroidal glycosides[15]. Nine known compounds including

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neochlorogenin 6-*O*-*β*-D-quinovopyranoside, neochlorogenin 6-*O*-*β*-D-xylopyranosyl-(1→3)-*β*-D-quinovopyranoside, neochlorogenin 6-*O*-*α*-L-rhamnopyranosyl-(1→3)-*β*-D-quinovopyranoside, solagenin 6-*O*-*β*-D-quinovopyranoside, solagenin 6-*O*-*α*-L-rhamnopyranosyl-(1→3)-*β*-D-quinovopyranoside, isoquercetin, rutin, kaempferol, and quercetin were isolated from *S. torvum*[16]. Solasodine, solasonine and solamargine are the glycoalkaloids identified from total alkaloids of leaves of *S. torvum*[17]. A new C4 - sulfated isoflavonoid [torvanol A] and steroidal glycoside [torvoside H] together with torvoside A isolated from a methanolic extract of *S. torvum* fruits exhibited antiviral activity[19].

S. torvum possesses antimicrobial[18], antiviral[19], immunosecretory[20], antiulcer[21], antioxidant[22], analgesic and anti-inflammatory[23] activities in animal models. In earlier studies, cardioprotective[24], hepatoprotective[25], and nephroprotective[26] activity of *S. torvum* against doxorubicin-induced toxicities in Wistar rats has been studied, and antihypertensive and metabolic correction activity in fructose hypertensive rats[27] has also been reported. The plant due to their immunomodulatory and antioxidant property may be used in the treatment of benign prostatic hyperplasia[28]. The alkaloid fraction of leaf extract of *S. torvum* has been reported to be neuroprotective on *Drosophila melanogaster* against β-Amyloid induced Alzheimer disease[29].

Dietary flavonoids and alkaloids exert cardioprotective, chemopreventive, and neuroprotective effects too. The biological activities of phytoconstituents have been attributed to their antioxidant, anti-inflammatory, and signalling properties[30]. In view of the above literature, the present study has been designed to evaluate the possible neuroprotective activity of *S. torvum* against MSG-induced neurotoxicity in mice.

Materials and Methods
Drugs and chemicals
Monosodium glutamate (Sigma), methanol (Research lab), DPPH (Sigma), TBA (Sigma), TCA (Research lab), epinephrine HCL (Sigma), vitamin C (Research lab).

Preparation of extract
Mature fruits of *S. torvum* were purchased and authenticated from Dr Shishir Pande, Director, Ayurved Seva Sangh, Nashik and the voucher specimen (No: ASS962) was deposited. One kg of seeds was shade dried and grounded into fine powder. The powder obtained was defatted using pet ether (60-80 °C). The marc obtained was further extracted with methanol and hydroalcoholic solution (methanol and distilled water in the proportion of 7:3) using Soxhlet extractor. The *S. torvum* extracts obtained was then evaporated to obtain 12.61 % w/w of methanolic extract (ST-MOH) and 10.76 % w/w of hydro-alcoholic extract of *S. torvum* (ST-HOH). The phytoconstituents present in the crude extract were tested for flavonoids, alkaloids, tannins, and saponins[31].

Determination of total phenolic content
The concentration of phenolics in plant extracts was determined using spectrophotometric method[32]. A methanolic solution of the extract in the concentration of 1 mg/mL was used in the analysis. The reaction mixture was prepared by mixing 0.5 mL of methanolic solution of extract with 2.5 mL of 10 % Folin-Ciocalteu's reagent and 2.5 mL of 7.5 % $NaHCO_3$. The samples were then incubated in a thermostat at 45 °C for 45 min. The absorbance was determined using spectrophotometer at 765 nm. The samples were prepared in triplicate for each analysis, and the mean value of absorbance was obtained. The same procedure was repeated for the standard solution of gallic acid, and the calibration line was constructed. The content of phenolics in extracts was expressed in terms of gallic acid equivalent (mg of GA/g of extract).

Determination of total flavonoid content
The content of flavonoids was examined in the plant extracts by spectrophotometric method[33]. The sample contained 1 mL of methanolic solution of the extract in the concentration of 1 mg/mL and 1 mL of 2 % $AlCl_3$ solution dissolved in methanol. The samples were incubated for one hour at room temperature. The absorbance was determined using spectrophotometer at 415 nm. The samples were prepared in triplicate for each analysis, and the mean value of absorbance was obtained. The same procedure was repeated for the standard solution of rutin, and the calibration line was constructed. The content of flavonoids in extracts was expressed in terms of rutin equivalent (mg of rutin Equiv/g of extract).

Animals
Swiss albino mice of either sex, weighing between 18-22 g were procured from Bombay Veterinary College. They were maintained under standard laboratory conditions of 25±1 °C, relative humidity of 45-55 % and photoperiod (12 h dark/12 h light).

Commercial pellet diet (Jay Trading co. Panchavati, Nashik, India) and purified water were provided ad libitum. The experiments were carried out according to the guidelines of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), New Delhi, India, and approved by the Institutional Animal Ethical Committee (MGV/PC/CPCSEA/XXXII/02/2016/04).

Experimental design

Animals were divided into 7 groups as follows- Group I received distilled water (10 mL/kg), Group II received MSG (1000 mg/kg), Group III received Vit-C (300 mg/kg) + MSG (1000 mg/kg), Group IV received ST-MOH (100 mg/kg) + MSG (1000 mg/kg), Group V received ST-MOH (300 mg/kg) + MSG (1000 mg/kg), Group VI received ST-HOH (100 mg/kg) + MSG (1000 mg/kg), and Group VII received ST-HOH (300 mg/kg) + MSG (1000 mg/kg). In group III to VII, administration of MSG solution was done once a day orally after one hour of oral administration of Vit-C and *S. torvum* extracts for 14 days. On the 14th day, behavioural phenotypes were studied after one hour of MSG dosing and animals were sacrificed on the 15th day for biochemical and histopathological investigations.

Behavioural phenotypes

Tail suspension test

Animals were suspended at the height of 50 to 60 cm from the ground through its tail by using adhesive tape. A mouse was considered to be immobile when it is suspended passively and is completely motionless. The onset and duration of immobility were measured for a period of 5 min[34].

Despair swim test

Animals were placed in water and allowed to swim for 5 min. After an initial struggle to escape, animals became immobile or had little movement and kept floating on the water. The onset and total immobility period during 5 min were measured[34].

Relative organ weight and oxidative stress in brain tissue

After completion of treatment schedule the animals were sacrificed and the brain was dissected out, immediately washed in ice-cold saline and weighed for measurement of relative organ weight. % homogenate was prepared in 0.1 M tris-buffer, pH 7.4. The homogenate was centrifuged at 15000 rpm for 20 min. The supernatants were used for measuring activity of following antioxidant enzymes - Superoxide dismutase, Catalase, Reduced glutathione, and Lipid peroxidation.

Superoxide dismutase (SOD)

To 0.05 mL of supernatant, 2.0 mL of carbonate buffer and 0.5 mL of EDTA solution were added. The reaction was initiated by addition of 0.5 mL of epinephrine and auto-oxidation of adrenaline (3×10^{-4} M) to adrenochrome at pH 10.2 was measured by following the change in optical density every minute at 480 nm against blank. One unit of SOD activity is the amount of SOD giving a 50 % inhibition of auto-oxidation of adrenaline[35].

$$x = \frac{0.025 - y}{y \times 50} \times 100$$

where x= SOD activity (Unit= U/mg of wet tissue) y= Mean of final reading after 1 min − Initial reading for every min for 6 min.

Catalase (CAT)

The reaction mixture consisted of 2 mL of phosphate buffer (pH 7.0), 0.95 mL of hydrogen peroxide (0.019 M) and 0.05 mL of supernatant in a final volume of 3 mL. Absorbance was recorded at 240 nm every 10 sec for 1 min. One unit of CAT is defined as the amount of enzyme required to decompose 1 μmol of peroxide per minute, at 25 °C and pH 7.0. The results were expressed as unit of CAT U/g of wet tissue[36].

$$x = log\frac{A}{B} \times 2297.3$$

where x= CAT activity (Unit= U/mg of wet tissue) A= Initial absorbance, B= Final absorbance

Reduced glutathione (RGSH)

To 1 mL of 10 % TCA, 1.0 mL of homogenate was added and centrifuged. Then, 1.0 mL of supernatant was treated with 0.5 mL of Ellmans reagent and 3 mL of phosphate buffer (pH 8.0). The colour developed was measured at 412 nm[37].

$$x = \frac{y - 0.0046}{0.0002}$$

where x= RGSH activity(Unit= nmoles /gm of wet tissue)

y= Absorbance of test sample

Lipid peroxidation (LPO)

0.1 mL of homogenate was treated with 2 mL of (1:1:1 ratio) TBA-TCA-HCL reagent and placed in

water bath for 15 min, cooled and centrifuged at room temperature for 10 min at 1000 rpm. The absorbance of the clear supernatant was measured against reference blank at 535nm[38].

$$x = \frac{y \times 0.002}{0.0026086}$$

where, x= LPO activity (Unit = nmoles/ mg of wet tissue)

y= Absorbance of test solution

Histopathological examination

The brain tissues were fixed in 10 % formalin solution. 5 µm sections of samples were stained with haematoxylin and eosin (H and E staining) and observed under 10X and 40X magnification.

Statistical analysis

The data is expressed as Mean±S.E.M. Statistical analysis was done using One-way ANOVA, followed by Dunnet's test. *$p < 0.05$ was considered statistically significant.

Results

Total flavonoid content

Total flavonoid content was found to be 32±0.8 µg of rutin equiv/mg of hydroalcoholic extract of *S.torvum* and 44±1.2 µg of rutin equiv/mg of methanolic extract of *S.torvum* (Fig. 1).

Total phenolic content

Total phenolic content was found to be 55±0.62 µg of gallic acid equiv/mg of hydroalcoholic extract of *S.torvum* and 70±0.28 µg of gallic acid equiv/mg of methanolic extract of fruits of *S.torvum* (Fig. 2).

Behavioral phenotypes

Forced swim test and tail suspension test

The onset of immobility in MSG-treated mice in both the tests was significantly delayed ($p < 0.05$), and the total immobility period was significantly decreased ($p < 0.05$) as compared to control group. While ST-MOH, ST-HOH, and Vit-C treatment in MSG-treated mice showed earlier onset of immobility and significant increase ($p < 0.05$) in immobility period as compared to MSG (1000 mg/kg) treated mice group (Fig. 3).

Relative organ weight

There was significant decrease ($p < 0.05$) in relative organ weight in MSG-treated mice as compared to
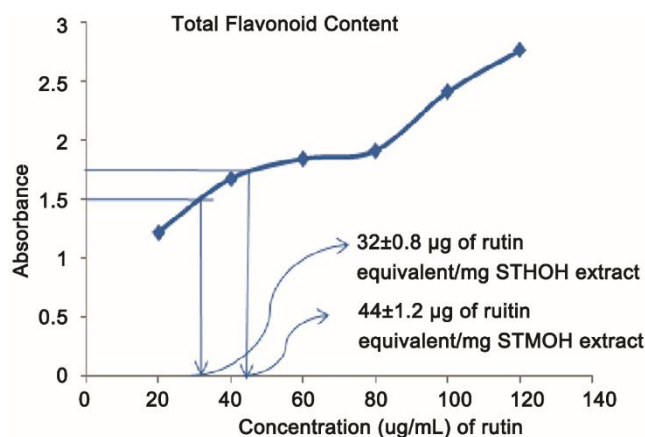

Fig. 1 — Total flavonoid content determination in *S. torvum* by AlCl₃ method. ST HOH- *S. torvum* hydroalcoholic extract, ST MOH- *S. torvum* methanolic extract.
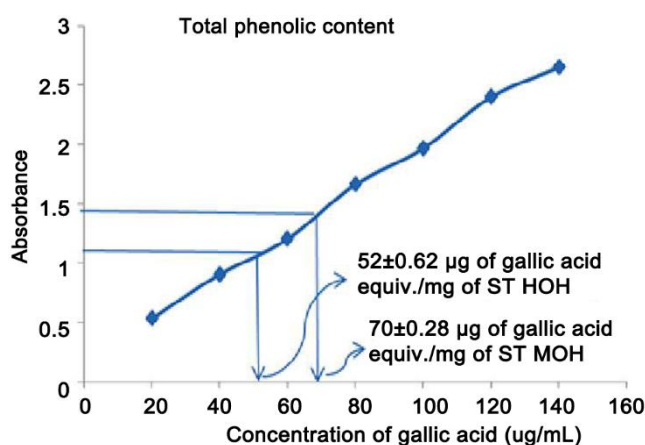

Fig. 2 — Total phenolic content determination in *S. torvum* fruit extracts by Folin-Ciocalteu's method. ST HOH- *S. torvum* hydroalcoholic extract, ST MOH- *S. torvum* methanolic extract.
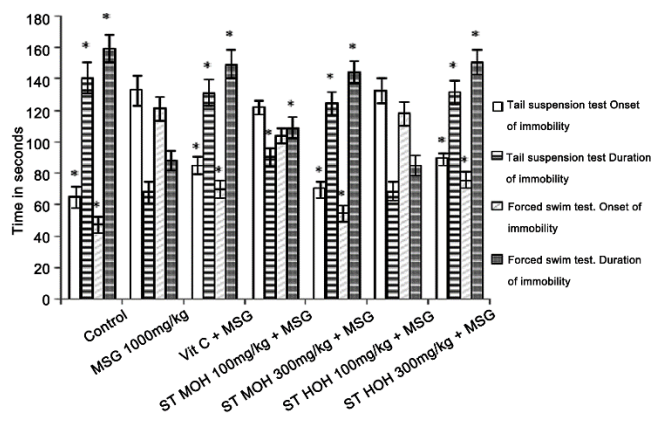

Fig. 3- Effect of *S. torvum* extracts and MSG on behaviour of mice in Forced swim test and Tail suspension test. *$p < 0.05$ as compared to MSG treated group. MSG- Monosodium glutamate, Vit C- Vitamin C, ST HOH- *S. torvum* hydroalcoholic extract, ST MOH- *S. torvum* methanolic extract.

control group, while ST-MOH, ST-HOH and Vit-C treatment in MSG-treated mice showed a significant increase in the relative organ weight of brain as compared to MSG (1000 mg/kg) group (Fig. 4).

Anti-oxidant biochemical parameters

Significant (p <0.05) accumulation of lipid peroxidation product in brain tissue of mice was observed, and activity of antioxidant enzymes such as SOD, Catalase and Reduced glutathione was significantly decreased (p <0.05) in MSG (1000 mg/kg) treated group as compared to control. ST-MOH, ST-HOH and Vit-C treatment in MSG-treated mice showed a significant decrease (p <0.05) in LPO activity and significant increase (p <0.05) in the activity of SOD, CAT and RGSH in brain tissue as compared to MSG (1000 mg/kg) treated mice group (Table 1).
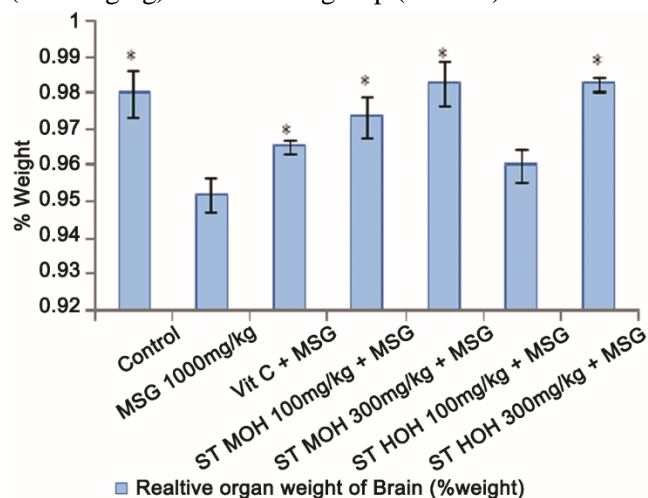

Fig. 4 — Effect of *S.torvum* extracts and MSG on relative organ weight of brain in mice. **p* <0.05 as compared to MSG treated group. MSG- Monosodium glutamate, ST HOH- *S.torvum* hydroalcoholic extract, ST MOH- *S.torvum* methanolic extract.

Histopathological examination

Histopathological studies of H and E stained cerebral sections of the control groups (Plate 1 and 2) showed the normal architecture of brain and arrangement of the layers of the cerebral frontal cortex with molecular layer covered with pia matter, the granular layer, and the pyramidal layer. On the contrary, MSG-treated sections of mice brain (Plate 3 and 4) presented signs of neurodegeneration with distorted layers of the brain, pyknosis and vacuolization of neuronal cells. Treatment with *S. torvum* extracts (ST-MOH and ST-HOH) and Vit-C treatment in MSG-treated mice has reversed the histological disturbances of layers of the brain caused by MSG (Plate 5-9). The sections also showed minimal signs of excitotoxicity and neurotoxicity like pyknosis and vacuolization of neuronal cell.
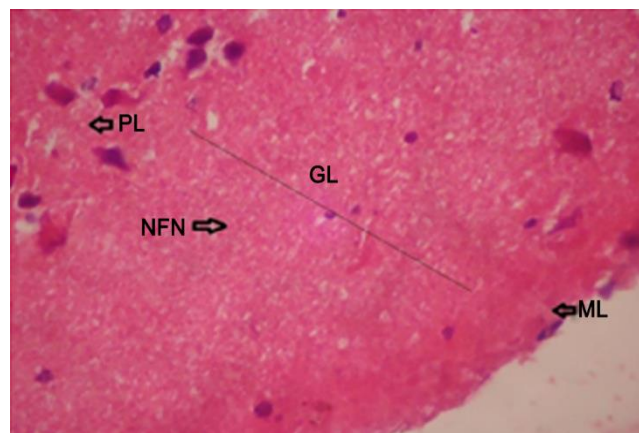

Plate 1 — Section of H and E stained control group mice brain showing normal layers of brain (40X). ML- Molecular layer, GL- Granular layer with neurofibrial network (NFN) and pyramidal cell layer (PL).

Table 1 — Effect of *S. torvum* (ST-MOH and ST-HOH), on anti-oxidants status in MSG treated brain tissue of mice

Treatment Group (mg/Kg)	LPO (nmoles/mg of wet tissue)	RGSH (moles/mg of wet tissue)	CAT (U/mg of wet tissue)	SOD (U/mg of wet tissue)
Control (10 mL/kg, distilled water)	19.44 ± 5.88	$3.72 \times 10^{-4} \pm 0.15$	194 ± 6.15	2.35 ± 0.11
MSG (1000)	218.9 ± 7.42	$1.32 \times 10^{-4} \pm 0.11$	55.99 ± 2.44	0.45 ± 0.04
Vit C (300)+ MSG(1000)	$109.3 \pm 5.66^*$	$2.95 \times 10^{-4} \pm .11^*$	$123 \pm 7.56^*$	$1.39 \pm 0.03^*$
ST-MOH (100) + MSG (1000)	$157.1 \pm 7.80^*$	$2.06 \times 10^{-4} \pm 0.13^*$	$88.57 \pm 4.87^*$	$1.08 \pm 0.067^*$
ST-MOH (300) + MSG (1000)	$39.78 \pm 4.18^*$	$3.15 \times 10^{-4} \pm 0.11^*$	$164.6 \pm 8.56^*$	$2.90 \pm 0.25^*$
ST-HOH (100) + MSG (1000)	$178.8 \pm 3.89^*$	$1.54 \times 10^{-4} \pm 0.12$	$85.69 \pm 4.83^*$	$0.69 \pm 0.041^*$
ST-HOH (300) + MSG (1000)	$82.13 \pm 5.86^*$	$2.83 \times 10^{-4} \pm 0.12^*$	$153.1 \pm 4.49^*$	$2.18 \pm 0.076^*$

N= 5, all data were subjected to ANOVA followed by Dunnett's test, the observations are mean±SEM. * p <0.05 as compared to MSG treated group.
MSG- Monosodium glutamate, Vit C- Vitamin C, ST-HOH- *S. torvum* hydroalcoholic extract, ST-MOH- *S. torvum* methanolic extract, LPO- lipid peroxidation, CAT- Catalase, RGSH- Reduced glutathione, SOD- Superoxide dismutase.
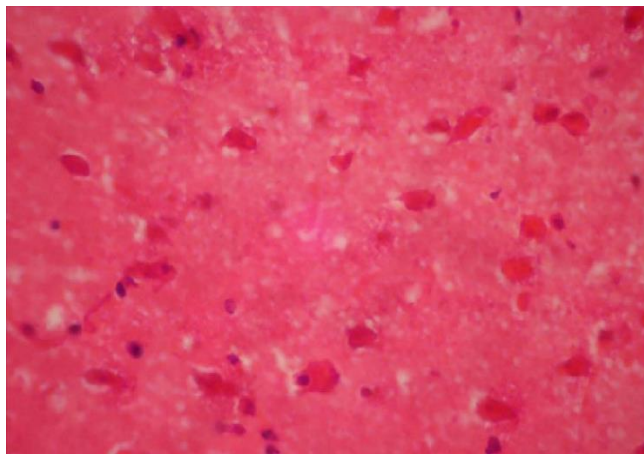
Plate 2 — Section of control group mice brain (40X) showing normal neuronal density and normal architecture of brain.
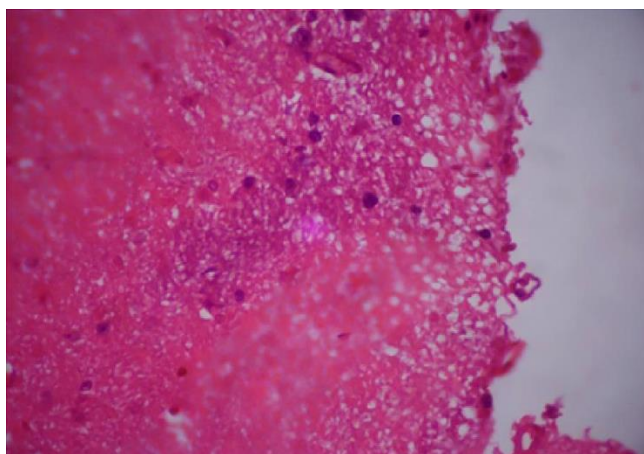

Plate 5 — Section of Vitamin-C (300 mg/kg) and MSG (1000 mg/kg) treated mice brain tissue (10X) showing normal layers, architechure and neuronal density.

Plate 3 — Section of MSG (1000 mg/kg) treated mice brain tissue (40X) showing distorted layers of brain.

Plate 6 — Section of ST MOH (100 mg/kg) and MSG (1000 mg/kg) treated mice brain tissue (40X) showing mild distorted layers of brain.
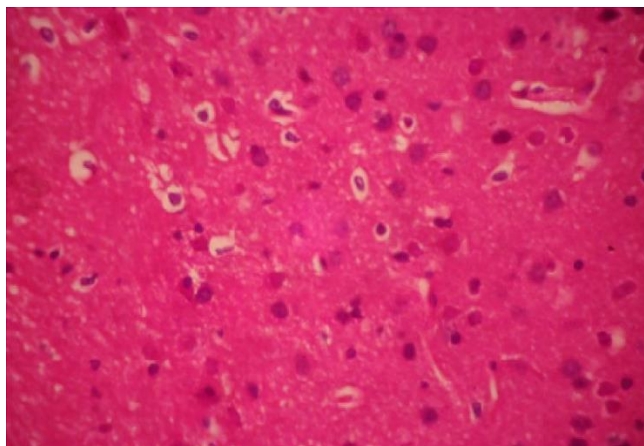

Plate 4 — Section of MSG (1000 mg/kg) treated mice brain tissue (40X) showing Pyknosis of neuronal and pyramidal cells (cell shrunken) and Vacuolization.
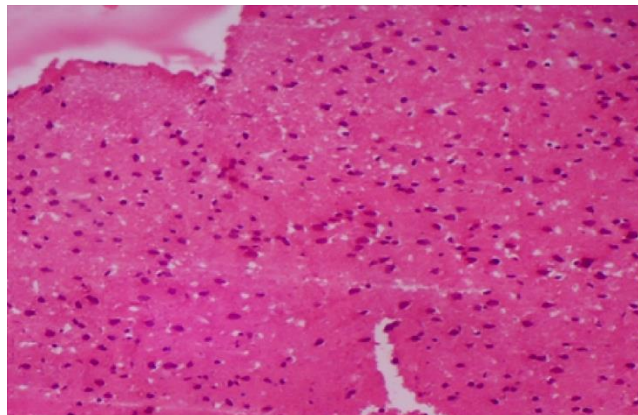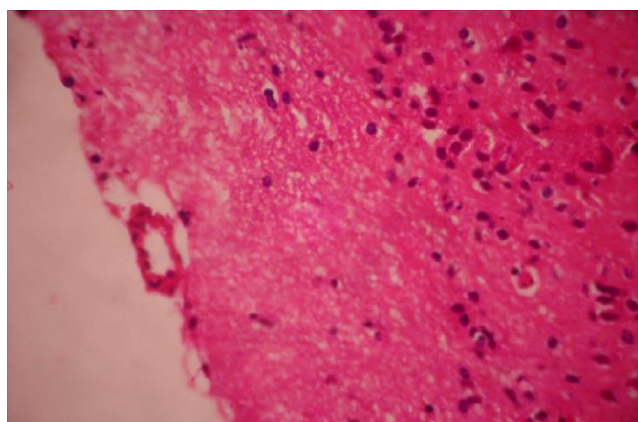

Plate 7 — Section of ST MOH (300 mg/kg) and MSG (1000 mg/kg) treated mice brain tissue (40X) showing normal layers of brain and absence of vacuolization in neurofibrial network.

Plate 8 — Section of ST HOH (100 mg/kg) and MSG (1000 mg/kg) treated mice brain tissue (40X) showing mild vacuolization in neurofibrial network, normal neuronal cells.

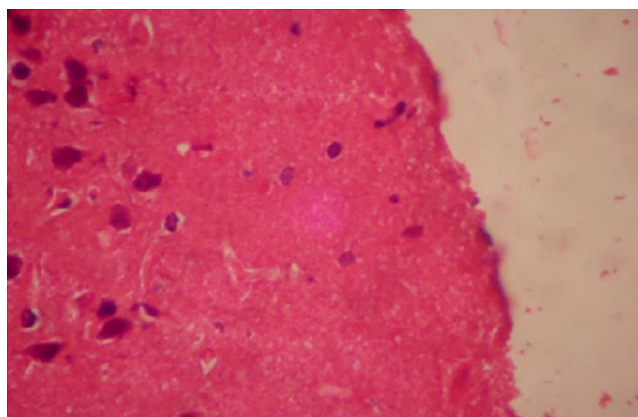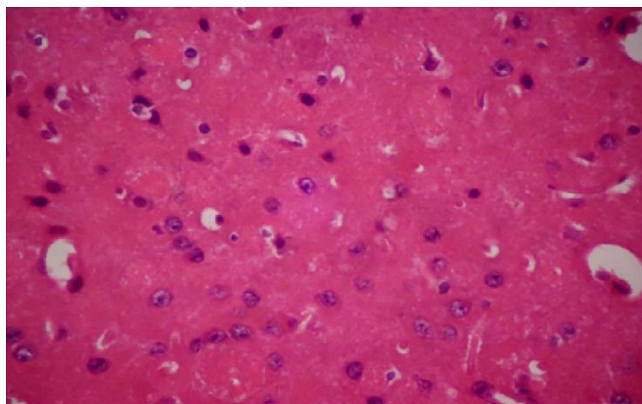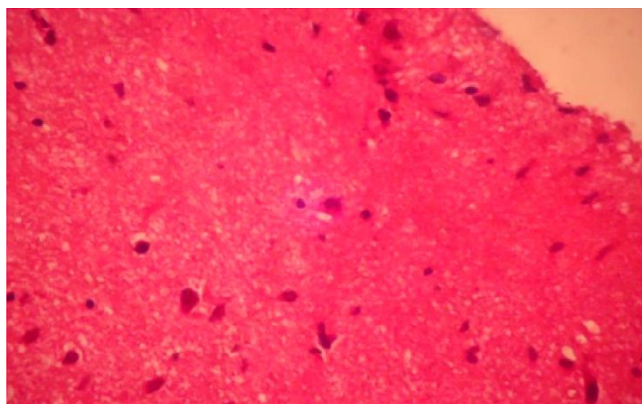Plate 9 — Section of ST HOH (300 mg/kg) and MSG (1000 mg/kg) treated mice brain tissue (40X) showing normal layers of brain, absence of vacuolization in neurofibrial network.

Discussion

The present study highlights the protective role of *S. torvum* on MSG-induced neurotoxicity by assessing its morphological, behavioural, biochemical and histopathological parameters.

Impairment of cellular calcium homeostasis, activation of nitric oxide synthesis, generation of free radicals, and programmed cell death which leads to progressive neurodegeneration[39] are common pathogenic mechanisms related to glutamatergic dysfunction[40]. These mechanisms damage nucleic acids, proteins, and lipids and potentially open the mitochondrial permeability transition pore, which in turn can further stimulate ROS production, worsen energy failure and release proapoptotic factors such as cytochrome c into the cytoplasm[41]. Generation of high level of ROS and down-regulation of antioxidant mechanisms result in neuronal cell death of neurodegenerative diseases[42,43]. It is believed that degenerative nerve diseases may decline many of our body's activities, including memory balance, movement, normal behaviour, and heart function[39].

Neurotoxicity and disturbed function of glutamate neurotransmitter are mainly due to excitotoxic neuronal damage and increased oxidative stress[43]. Phytochemicals from natural sources are found to have good antioxidant property and may be used in prevention and treatment of neurodegenerative diseases. So, proposed experiment aimed to study the effect of *S. torvum* on MSG-induced neurotoxicity in Swiss albino mice.

Animal behaviour in despair swim test and tail suspension test is used to assess the anti-depressant like activity in rodents[33]. Significant changes in behavioural phenotypes in mice treated with MSG indicated abnormal or deficit neuronal function as compared to control animals, while treatment with *S. torvum* extracts showed significant normalisation of behavioural phenotypes in MSG-treated mice.

Relative organ weight of brain in MSG-treated mice was significantly decreased which showed toxic effects of MSG, while treatment with *S. torvum* significantly increased the relative organ weight of brain in MSG-treated mice. Absolute organ weight and relative organ weight determination are commonly used tools in toxicology, while the purpose of relative organ weight analysis is to detect any direct treatment effect on the organ weights over and above any indirect effects caused by the effects of the treatment on body weight[44].

Increase in lipid peroxidation product has been observed in cases of oxidative stress and neuronal damage[45,46]. A significant increase in lipid peroxidation in MSG-treated mice brain tissue indicated oxidative stress induced by MSG treatment. This indicated that MSG might be responsible for the production of reactive oxygen species (ROS). Products of lipid peroxidation, such as malondialdehyde (MDA) and unsaturated aldehydes are capable of inactivating many cellular proteins by forming protein cross-linkages[47]. Treatment with *S. torvum* significantly decreased the lipid peroxidation product in brain tissue of mice as compared to MSG-treated mice.

Superoxide dismutase is considered to be one of the most active enzymes which dismutates superoxide anions produced during metabolism in cells. It converts superoxide radical into less toxic hydrogen peroxide[48], while catalase is the enzyme responsible for the breakdown of hydrogen peroxide into water and oxygen. The activity of both enzymes is sufficient for

removal of ROS in normal homeostasis. There must be a balance between oxidation and antioxidant's level in the system for healthy biological integrity to be maintained[49]. Our observation has shown that anti-oxidants enzymes activity (SOD and CAT) in brain tissue homogenate of MSG-treated group decreased significantly compared with control group. This decrease may be as a result of an imbalance between oxidant and antioxidant levels in favour of the oxidants. Our results are similar to the experiments in which neuronal damage and oxidative stress are caused by xenobiotics and pesticides, which also shows a decrease in antioxidant defence enzyme activity[46,50]. Treatment with *S. torvum* fruit extracts significantly increased the activity of both enzymes in brain tissue in MSG-treated mice.

Glutathione (GSH) is highly abundant in all cell compartments and is the major soluble antioxidant. Reduced GSH/Oxidised GSH ratio is a major determinant of oxidative stress. There is significant evidence that the disturbance of glutathione homeostasis may either lead to or result from oxidative stress in neurodegenerative disorders[51]. Reduced glutathione was significantly decreased in brain tissue of MSG-treated mice, which reveals an imbalance between oxidants and defence mechanism, while treatment with *S. torvum* extracts showed a significant increase in tissue glutathione in MSG-treated mice.

It has been reported that MSG can produce severe histopathological changes in vital organs like brain, kidneys, heart, lungs, spleen, liver, and testis due to its toxic effects at doses of 500, 750, 1000, and 1250 mg/kg administered orally[52]. Brain and neurons are the most vulnerable sites for the toxic effects of MSG due to its excitotoxic nature as evident in the present study. Treatment with *S. torvum* has ameliorated the histopathological abnormalities induced by MSG.

Conclusion

The present study concludes that *S. torvum*, a well known traditionally used plant possess significant neuroprotective activity against MSG-induced neurotoxicity. Neurotoxicity caused by MSG is mainly due to excitotoxic neuronal damage and increased production of ROS. Since *S. torvum* possess wide antioxidant activity, it might be used in the prevention or possible treatment of neurodegenerative diseases. Methanolic extract was shown to be more neuroprotective than the hydroalcoholic extract of dry fruits of *S. torvum*.

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