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CEREBROPROTECTIVE EFFECT OF *SOYMIDA FEBRIFUGA* IN BILATERAL CAROTID ARTERY OCCLUSION INDUCED CEREBRAL ISCHEMIC RATS

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ABSTRACT

Soymida febrifuga L. (Family: Meliaceae) is a medicinal plant with well known antioxidant property and claimed to have anticoagulant property as per folklore claim. scientific evaluation of cerebroprotective effect of Methanol extract of *Soymida febrifuga* (MESF) in Bilateral Carotid Artery Occlusion (BCAO) induced cerebral ischemia in rats. Global cerebral ischemia is a clinical outcome occurring as a consequence of conditions like cardiac arrest, coronary artery bypass surgery causing deprivation of blood supply and energy in the brain due to blockade of carotid arteries. In the present study the animals were pre-treated with MESF for a period of 1week (200 and 400 mg/kg) i.p, The animals were anaesthetized with thiopentone sodium (45mg/kg) and stroke was induced by BCAO for defined period with aneurism clamps placed on both arteries and later (10 minutes) clamps were removed to allow reperfusion and animals were then returned to their cages. After 24 hours of reperfusion the animal behaviour were evaluated by various methods such as behaviour pattern, Juvenile recognition, Motor activity, rotar rod test, morris water maze test in stroke induced animals. The treatment was continued for another week after surgery with MESF and the animals were sacrificed and the brain was removed. Histopathology of hippocampal region was carried out. The present studies suggest that, there was a decrease in the motor activity, muscle co-ordination, and escape latency in water maze in stroke induced (negative control) group. The group treated with 200mg/kg and 400 mg/kg MESF showed significant ($P<0.01$) improvement in the motor activity, behaviour pattern, and spatial learning which was confirmed in trial sessions in water maze test when compared with negative control group. In conclusion, methanol extract of *Soymida febrifuga* produced cerebroprotective effects in global cerebral ischemia as evident from reduction in behavioral score, hyperlocomotion and neuronal damage.

Key words: Bilateral Carotid Artery Occlusion (BCAO), *Soymida febrifuga L.*, Cerebral Ischemia, stroke.

INTRODUCTION

Cerebral ischemia is caused by a deficiency in blood supply to a part of the brain, which in turn triggers various pathophysiological changes. When the brain is deprived of blood supply (ischemia) its injury is not only by the temporary loss of oxygen and energy supply. Global Cerebra l ischemia is a clinical outcome occurring as a consequence of conditions like cardiac arrest, coronary artery bypass surgery causing deprivation of blood supply and energy in the brain due to blockade of carotid arteries. The most vulnerable region for loss of blood supply is the CA1 pyramidal neurons of the hippocampus region **(Kirino *et al.*,1982)**. The neurodegeneration process in hippocampus is multifactorial which involves decrease in intracellular pH and ATP levels, increased levels of generation of free radicals **(White *et al.*, 2000).** Oxidative stress can activate apoptotic pathways in cerebral ischemia **(Gupta *et al.*, 2003; Thiyagarajan *et al.*, 2004; Sharma *et al.*, 2005)** and can lead to DNA damage

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initiating the activation of transcription factor p53 and activation of caspases **(Culmsee *et al*., 2003).**

Soymida febrifuga L. (family: Meliaceae) is a medicinal plant with well known antioxidant property and claimed to have anticoagulant property as per folklore claim **(*Madhava Chetty, 2008)***. Scientific evaluation of this claim using experimental model of Bilateral Carotid Artery Occlusion (BCAO) in rats induced cerebral ischemia was ascertained in this study. This was supported in our study by various behavioural, biochemical findings and histopathology studies.

METERIALS AND METHODS

Phytochemical Screening

The phytochemical examination of methanol extract of *Soymida febrifuga L.* was performed by the standard methods.

Animal Used

Albino Wistar rats, weighing 150–200 g were used. The selected animals were housed in acrylic cages in standard environmental conditions (20–25 ◦C), fed with standard rodent diet and water *ad libitum*. The experiments on animals were conducted in accordance with the internationally accepted principles for laboratory animal use and the experimental protocols duly approved by the Institutional Ethical Committee. **(Reg. No. IAEC/ 930/a/06/ CPCSEA).**

Acute Toxicity Study

The acute toxicity of methanol extract of *Soymida febrifuga L.* was determined as per the OECD guideline no. 423 (Acute Toxic Class Method). It was observed that the test extract was not lethal to the rats even at 2000mg/kg dose. Hence, $1/10^{th}$ (200mg/kg) and $1/5^{th}$ (400mg/kg) of this dose were selected for further study.

Experimental design:

The male Wistar strain rats were randomized into 6 different groups (n=6 per group).

GROUP 1: Animals (Positive Control) with sham operation (without Occlusion) and treated with control vehicle only (p.o)

GROUP 2: Animals with sham operation (without occlusion) and treated with 200mg/kg of MESF (p.o)

GROUP 3: Animals with sham operation (without occlusion) and treated with 400mg/kg of MESF (p.o)

GROUP 4: Animals (Negative Control) with BCAO and treated with Control vehicle only (p.o)

GROUP 5: Animals with BCAO and treated with 200mg/kg of MESF (p.o)

GROUP 6: Animals with BCAO and treated with 400mg/kg of MESF (p.o)

Induction of cerebral ischemia:

In the present study the animals were pre-treated with MESF for a period of 1week (200 and 400 mg/kg) i.p, The animals were anaesthetized with thiopentone sodium (45mg/kg) and stroke was induced by occlusion of bilateral carotid artery (BCAO) for defined period with aneurism clamps placed on both arteries and later (10- 15 minutes) clamps were removed to allow reperfusion and animals were then returned to their cages. After 24 hours of reperfusion the animal behaviour were evaluated by various methods. The treatment was continued for another week after surgery with MESF and the animals were sacrificed and the brain was removed. Histopathology of hippocampal region was carried out **(Ergun et.al., 2002).**

Behaviour Pattern in Stroke Induced Animals

Behaviour Examination

Animals were trained for 3 days prior to surgery in three different areas such as neuromuscular function, Vestibulomotor function and Complex neuromotor function. A combined total score was taken for each rat with a higher score meaning a higher clinical deficit **(Rege et al., 1989).**

Neuromuscular Function

It's consisted of 6 subtests: forelimb flexion, twisting, resistance to lateral push, circling, hindlimb placement, inverted angle board gripping. Scoring pattern of neuromuscular function:- Score: 0- No signs ; Score: 0.5- Mild ; Score: 1- Moderate to severe

Forelimb flexion:

When held by the tail above a flat surface a normal rat will extend both forelimbs toward the surface, rats with an infarction will consistently flex the paralytic forelimb. Flexion would vary from mild wrist flexing and shoulder abduction to severe flexion encompassing the entire forelimb.

Torso Twisting:

When held by the tail above a flat surface a normal rat will extend the entire body toward the surface, rats with an infarction show signs of body rotation. This rotation consists of mild twisting of the body to a severe body movement bringing the head and forelimbs into the vicinity of the hindlimbs. Twisting was always toward the paralytic side**.**

Lateral Push:

A normal rat will show equal resistance when held behind the shoulders and pushed either to the left (lateral) or right (contralateral) sides. Rats with an infarction show either weaker or no resistance when pushed toward the contralateral side.

Circling:

Rats normally do not circle during normal gate. Animals having infarction sometimes circle toward the contralateral side.

Hindlimb Placement:

A normal rat will immediately replace a hindlimb to the surface top if the leg is removed from the surface; injured rats show either a delay in placement or no replacement at all.

Inverted Angle Board:

Normally a rat can be trained to turn 180 degrees and proceed to the top of an angled board. Injured animals cannot make this turn and proceed up the board. The degree and severity were graded accordingly.

Vestibulomotor Funtion

Beam balance is sensitive to motor cortical insults. This task was used to assess gross vestibulomotor function by requiring a rat to balance steadily on a narrow beam. The test involves three 60-second training trials 24 hours before surgery. The apparatus consists of a 3/4-inch-wide beam, 10 inches in length, suspended 1 ft above a table top. The rat was positioned on the beam and must maintain steady posture with all limbs on top of the beam for 60 seconds.

Complex Neuromotor Function

This is a test of sensor motor integration specifically examining hindlimb function. A 1-inch-wide beam, 3 ft in length, was suspended 3 ft above the floor in a dimly lit room. At the far end of the beam was a darkened goal box with a narrow entryway. A white noise generator and bright light source at the start of the beam motivate the animal to traverse the beam and enter the goal box. Once inside the goal box, the stimuli were terminated. The rat‘s latency to reach the goal box (in seconds) and hindlimb performance as it traversed the beam (based on a rating scale) were recorded. Each rat was trained for 3 days before surgery to acquire the task and to achieve normal performance on three consecutive trials.

SOCIAL RECOGNITION

Juvenile recognition test:

The juvenile recognition test is a suitable model for testing amnesia in animals to assess the social olfactory memory which is impaired in cerebral ischemia. The juvenile recognition test was conducted in three open Perspex arenas (73 * 48 * 30 cm) with a thick bedding of wood shavings. Lighting in the room was bright. There was no visual contact between the arenas **(**Rockwood et al., 2000**).**

Behavioural Procedure:

The test animal was placed in the arena for a habituation period of 10 min. An unfamiliar juvenile female was then introduced into the arena for 10 min (first exposure 5 E1). Both animals were subsequently returned to their home cages. After a variable interexposure interval (IEI), the male animal was placed in the arena for another habituation period of 10 min, and thereafter the juvenile was reintroduced for 3 min (second exposure E2). E2 was limited to 3 min because only the first 3 min of the observation period were used for behavioural scoring. The rate was blind to the treatment of the animals. Based on the scoring pattern the social recognition of the animals was assessed.

Parameters:

Score: 0 - *Body/mouth sniff:* Sniffing part of the female’s body (not genitals) or sniffing or licking the corner of the mouth. Genital Sniff/Follow: Following the female closely and/or sniffing at the ano-genital region Aggression: Side-to-side threatening position, kicking, pursuing, and fighting.

Score: 0.5 - *Running:* Running around in the arena

Score: 1 - *Digging:* Digging in the corners of the arena

Score: 2 - *Inactivity:* Sitting inactively

Score: 3 - *Other nonsocial:* Joint category for a variety of nonsocial behaviours, e.g., self-grooming (cleaning fur, etc.), and exploratory behaviours, e.g., walking, sniffing at bedding, walls, etc.

In Vivo Pharmacological Examination

Motor activity: The motor activity was monitored by using actophotometer. Before measuring the cognitive task the animal was placed in Actophotometer record for 10 min. The locomotor activity was expressed in terms of total photo beam interruption counts / min / animal **(Sekine et al., 1994).**

Rotor Rod Test: Rats were tested on an accelerating rotor-rod (diameter, 5.8 cm) that was turned at a speed of 20-25 rpm, at which all the control animal could maintain position for 120 seconds. If the experimental animal fell within 120 seconds, the latency was recorded. If the animal maintained their position for 120 seconds, a time of 120 seconds was assigned. The trial was repeated 3 times, and the latency of the last trial was adopted for each animal **(Sharma et al., 1996).**

Morris Water Maze Test: On day 15 after surgery, spatial learning and memory was tested in water maze. The maze consisted of a black circular pool (diameter 2.14 m, height 80 cm) filled to a depth of 44cm with water (25°C). On 14th day the rats received habituation (exposure in water maze for 1 min) in which there was no platform present. Then, on day 15th, a circular platform (9 cm in diameter) was kept hidden 2 cm below water level in the center of one of the quadrants. The platform remained in the same position during training days. At the beginning of each session, a random sequence of four starting poles along the perimeter of the pool was generated. All animals followed this sequence for that session. Each rat was placed in the water facing the wall at the start location and was allowed 90 sec. to find the hidden platform. The animal was allowed a 20 sec. rest on the platform. The latency to reach the platform was recorded. If the rat was unable to locate the hidden platform, it was lifted out and placed on the platform for 20 sec. The procedure was repeated for all the 4 start

locations. Two sessions of four trials each separated by 4 h were conducted on the first day of testing and one session of four trials was conducted on the next day (reference memory procedure). After that, the platform was removed and a probe trial (without platform) was conducted 4 h later. Each rat was placed in the pool at the same randomly selected starting pole and swimming path was observed. The time spent in the quadrant of pool, which initially contained platform, was measured (working memory procedure) **(Morris, 1984).**

Histopathology:

7 days after ischemia, rats from each group were anesthetized with sodium Thiopentone (100 mg/kg). Rats were then transcardially perfused with cold saline followed by 10% formalin in phosphate- buffered saline (0.1 M; pH 7.4). The brains were removed from the skull and fixed in the same fixative for 24 h. Thereafter, the brains were embedded in paraffin and 5 µm thick sections were caronally cut at the level of the dorsal hippocampus by a rotator microtome. The segments of the hippocampal CA1 region per1000 µm lengths from bregma −3.3, −3.8, and −4.3 were counted for viable cells. Tissue sections were stained with hematoxylin and eosin. Histopathological observation of the tissue was carried out at the Sri Venkateswara University, Pathology Laboratory, Tirupati, Andhra Pradesh -517 502. **(Maibritt B.et al., 1997).**

Statistical analysis:

The statistical analysis was carried out using Graph pad prism 4.0 software. All values were expressed as Mean ± S.E.M. Data analysis was done by one-way ANOVA followed by Dunnett's multiple comparison tests. Difference level at $P<0.05$ was considered as statistically significant condition.

RESULTS

Phytochemical screening

The results of preliminary phytochemical screening of the methanol extract of *Soymida febrifuga* Linn revealed that presence of flavonoids, tannins, phenols, proteins and absence of alkaloids, glycosides, saponins and steroids.

Effect of MESF on Neuromuscular Function:

There was an increase in score of Neuromuscular function in Stroke induced (negative control) group when compared with the control group and negative control group which showed significance of ($P<0.01$) when compared with control group. The group treated with 200mg/kg and 400 mg/kg MESF showed significant ($P<0.01$) improvement in Neuromuscular function when compared with negative control group. The group treated with 200 mg/kg and 400 mg/kg MESF showed the significance of ($P<0.01$) as shown in **Fig no: 1.**

Effect of MESF on Vestibulomotor Function:

There was an increase in score of vestibulomotor function in stroke induced (negative control) group when compared with the control group and negative control group which showed significance of ($P<0.01$) when compared with control group. The group treated with 200mg/kg and 400 mg/kg MESF showed significant ($P<0.01$) improvement in vestibulomotor function when compared with negative control group. The group treated with 200 mg/kg and 400 mg/kg MESF showed the significance of ($P<0.01$) as shown in **Fig no: 2.**

Effect of MESF on Complex Neuromotor Function:

There was an increase in Score of complex neuromotor function in Stroke induced (negative control) group when compared with the control group and negative control group which showed significance of ($P<0.01$) when compared with control group. The group treated with 200mg/kg and 400 mg/kg MESF showed significant ($P<0.01$) improvement in complex neuromotor function when compared with negative control group. The group treated with 200 mg/kg and 400 mg/kg MESF showed the significance of ($P<0.01$) as shown in **Fig no: 3.**

Effect of MESF on Juvenile Recognition Test:

There was an increase in Score of Social recognition in Stroke induced (negative control) group when compared with the control group and negative control group which showed significance of ($P<0.01$) when compared with control group. The group treated with 200mg/kg and 400 mg/kg MESF showed significant ($P<0.01$) improvement in social behaviour when compared with negative control group. The group treated with 200 mg/kg and 400 mg/kg MESF showed the significance of ($P<0.01$) as shown in **Fig no: 4.**

Effect of MESF on Motor Activity:

There was a decrease in the motor activity in Stroke induced (negative control) group when compared with the control group and negative control group which showed significance of ($P<0.01$) when compared with control group. The group treated with 200mg/kg and 400 mg/kg MESF showed significant ($P<0.01$) improvement in motor activity when compared with negative control group. The group treated with 200 mg/kg and 400 mg/kg MESF showed the significance of ($P<0.01$) as shown in **Fig no: 5.**

Effect of MESF on Roto Rod Test:

There was a decrease in the Muscle coordination in Stroke induced (negative control) group when compared with the control group and negative control group which showed significance of ($P<0.01$) when compared with control group. The group treated with 200mg/kg and 400 mg/kg MESF showed significant ($P<0.01$) improvement in muscle coordination when

compared with negative control group. The group treated with 200 mg/kg and 400 mg/kg MESF showed the significance of (P<0.01) as shown in **Fig no: 6.**

Effect of MESF on Morris Water Maze Test:

There was an increase in the escape latency in Stroke induced (negative control) group when compared with the control group and negative control group which showed significance of (P<0.01) when compared with control group. The group treated with 200mg/kg and 400 mg/kg MESF showed significant (P<0.01) improvement in Spatial learning which was confirmed in trial sessions and probe trial when compared with negative control group. The group treated with 200 mg/kg and 400 mg/kg MESF showed the significance of (P<0.01) as shown in **Table no: 1.**

FIG 1. EFFECT OF MESF ON NEUROMUSCULAR FUNCTION

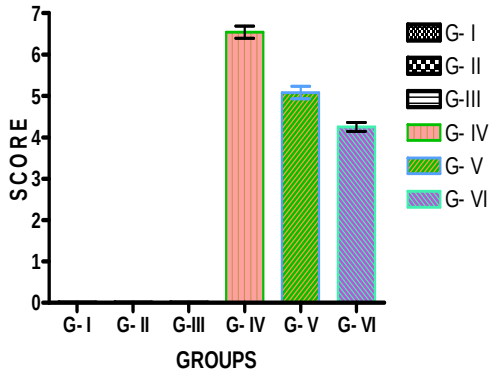


FIG 2. EFFECT OF MESF ON VESTIBULOMOTOR FUNCTION

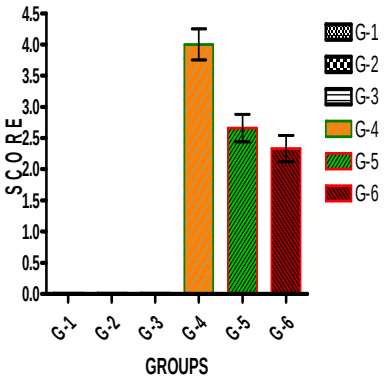


FIG 3. EFFECT OF MESF ON COMPLEX NEUROMOTOR FUNCTION

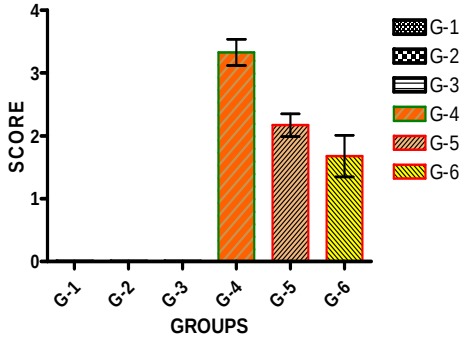


FIG 4. EFFECT OF MESF ON JUVENILE RECOGNITION TEST

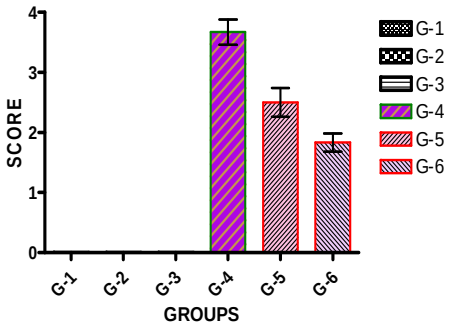


FIG 5. EFFECT OF MESF ON MOTOR ACTIVITY

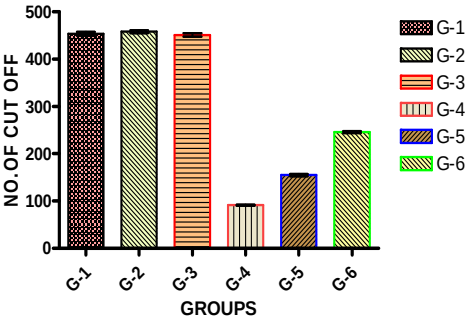
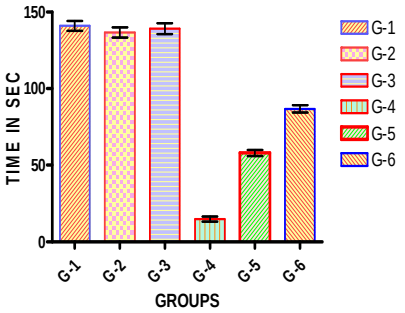


FIG 6. EFFECT OF MESF ON ROTOR ROD TEST



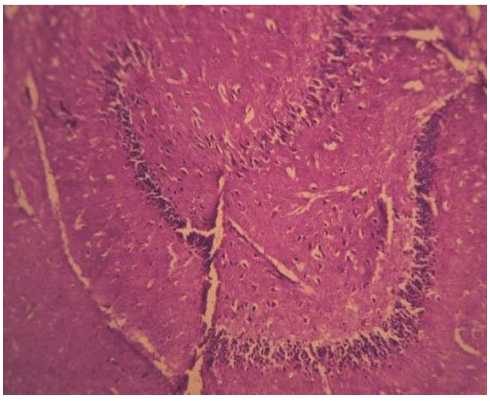
Group 1: Sham (saline), Group 2: Sham (200mg/kg), Group 3: Sham (400mg/kg), Group 4: Ischemia (saline), Group 5: Ischemia+MESF (200mg/kg), Group 6: Ischemia+MESF (400mg/kg).

Table 1. Effect of MESF on Morris Water Maze Test

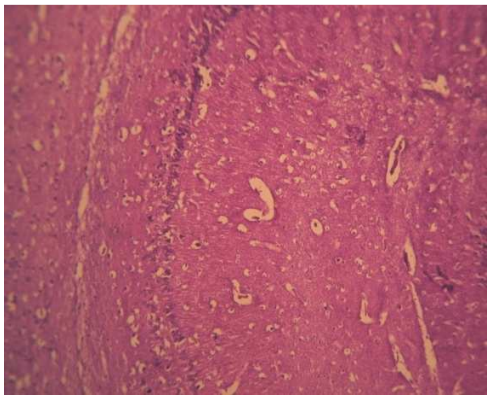
Sessions	Group	1	2	3	4	5	6
I	Escape	68.33±0.82	63.67±1.76	66.67±1.26	75.83±1.02[a]	51.83±0.46[b]*	52.00±0.57[b]*
II	Latency	34.01±0.56	36.00±1.55	37.90±1.15	69.67±0.15[a]	45.50±1.17[b]**	27.17±0.01[b]***
III	(in secs)	23.50±0.92	21.17±0.09	20.33±0.83	64.17±0.90[a]	20.33±0.58[b]**	19.00±0.35[b]***

Group 1: Sham (saline), Group 2: Sham (200mg/kg), Group 3: Sham (400mg/kg), Group 4: Ischemia (saline), Group 5: Ischemia+MESF (200mg/kg), Group 6: Ischemia+MESF (400mg/kg).
Significant: *P<0.05, **P<0.01, ***P<0.001.
Values are expressed as mean ±SEM of 6 animals.
Comparisons were made between a. Control vs Negative control and b. Negative control vs Treatment group. Symbol represents the statistical significance done by ANOVA, followed by dunnet's multiple comparison tests.

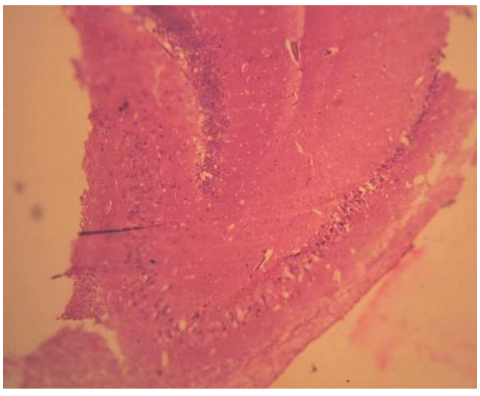
Fig 7. Histopathology studies



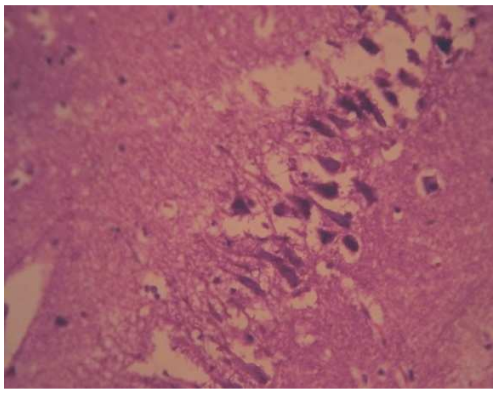
Group I



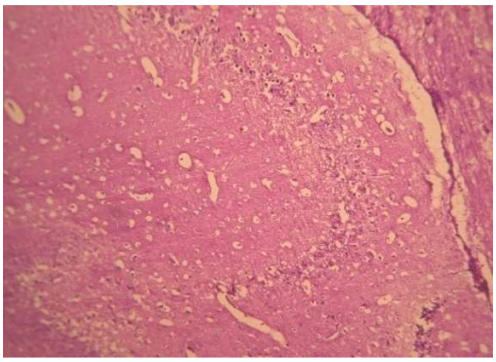
Group II



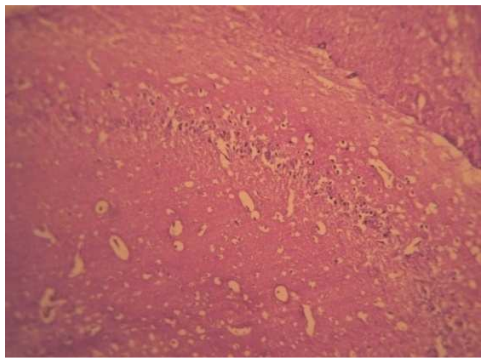
Group III



Group IV



Group V



Group VI

Group 1: Sham (saline) (normal hippocampus with normal neurons), **Group 2:** Sham (200mg/kg) (normal hippocampus with normal neurons), **Group 3:** Sham (400mg/kg) (normal hippocampus with normal neurons), **Group 4:** Ischemia (saline) (damaged & dispersed degenerated neurons), **Group 5:** Ischemia+MESF (200mg/kg) (mildly preserved neural cells), **Group 6:** Ischemia+MESF (400mg/kg) (preserved neural cells).

DISCUSSION AND CONCLUSION

The Present study demonstrates the protective effect of methanol extract of *Soymida febrifuga L.* treatment against to short-term global brain injury in rats. To our knowledge, this is the first report that investigates the effect of MESF treatment against to short-term global brain ischemia/reperfusion injury in rats. Bilateral carotid artery occlusion is the basic experimental inducing model of global cerebral ischemia in animals and common carotid arteries is the main arteries supplying blood to the brain from heart. The occlusion of these arteries for a period of 10 minutes leads to reduction in blood supply to the brain and the pathophysiological events starts and continues followed by reperfusion **(Hirokazu *et al.*, 2005).**

By combining tasks from many sources we achieved an overall behavioral scheme best suited for our model. For the long term study it was discovered that behavior could be broken down into at least three different levels of function: Neuromuscular function which included leg flexion, twisting, circling, lateral push, and inclined angle board; Complex neuromuscular function involves the animal's ability to balance, grip strength, and coordinated movements by walking on a balance beam; Vestibulomotor function as tested by the beam-balance. Further developments in behavioral examinations have led to more precise testing **(Nancy E *et al.*, 1995; David Petullo *et al.*, 1999).**

There was an increase in Score of Neuromuscular, Vestibulomotor, Complex neuromuscular functions in stroke induced (negative control) group when compared with the control group and negative control group which showed significance of ($P<0.01$) when compared with control group. The group treated with 200mg/kg and 400 mg/kg MESF showed significant ($P<0.01$) improvement in neuromuscular, vestibulomotor, complex neuromuscular function. MESF produced significant cerebroprotection in rats. Rat's shows features of global cerebral ischemia just after brief occlusion of common carotid arteries, as they lack posterior communicating arteries between the carotid arteries and vertebral arteries, which constitute an incomplete Circle of Willis **(Kirby BP *et al.*, 2004).**

BCAO for 10 min in rats resulted in selective loss of pyramidal neurons in the CA1 area of hippocampus within 96 h to become apparent morphologically. There was substantial hippocampal neuronal death (80–85%) in ischemic animals as compared with the sham operated animals. Ischemic animals showed hyper locomotion on initial day of reperfusion. This was found to be consistent with the findings stating that on the first day after reperfusion, ischemia induced increase in locomotor activity is prominent, following two days it starts decreasing **(Katsuta *et al.*, 2003; Colbourne *et al.*, 1998).** Thus based on this analysis, the group treated with 200 mg/kg and 400 mg/kg MESF showed the significant ($P<0.01$) improvement in locomotor activity.

Global cerebral ischemia causes marked damage to pyramidal neurons in the hippocampal region within days after ischemia in animals and humans. Hippocampal neurons are highly susceptible to ischemia and reperfusion-induced injury. Hippocampus is involved in the regulation of short-term memory. Vascular dementia is the second most common type of dementia following Alzheimer's disease-related dementia **Rockwood**

***et al.*, 2000)**. Vascular dementia occurs when the blood supply to the brain is reduced by a blocked or diseased vascular system **(Roman et *al.*, 2002)** and leads to a progressive decline in memory and cognitive function **(Jellinger *et al.*, 2007).** Cerebral hypoperfusion can be induced by bilateral occlusion of common carotid arteries (BCAO) in rats, resulting in significant white matter lesions, learning and memory impairment, and hippocampal neuronal damage **(Tsuchiya *et al.*, 1993)**. Thus, BCAO in rats provides a model useful for understanding the pathophysiology of chronic cerebrovascular hypoperfusion and for screening drugs with potential therapeutic value for stroke **(Wakita *et al.*, 1994).**

Therefore Morris water maze has been employed in present study to evaluate impairment of short-term memory as a result of cerebral ischemia and reperfusion. Cerebral ischemia is documented to impair sensory motor ability and thus incline beam walking test, beam balance test and lateral push test have been used in the present study to investigate the effect of cerebral ischemia and reperfusion on motor performance. BCAO induced cerebral ischemia have markedly attenuated ischemia and reperfusion-induced cerebral infarct size in group III rats and at the doses of 200/400mg/kg MESF has significantly prevented the ischemia and reperfusion-induced impairment of short-term memory and motor incoordination.

The present studies suggest that In-vivo behavioral studies such as motor activity, rotor rod, and morris water maze tests were carried out in order to assess the behavior of the animals. There was a decrease in the motor activity, muscle co-ordination, and escape latency in water maze in stroke induced (negative control) group. The group treated with 200mg/kg and 400 mg/kg MESF showed significant ($P<0.01$) improvement in the motor activity, muscle co-ordination, and spatial learning which was confirmed in trial sessions in water maze test when compared with negative control group.

It is well documented that transient forebrain ischemia results in death of the neurons in the CA1 subregion of the hippocampus. Our results indicated that 10 min of forebrain ischemia induced selective neuronal damage in animals. Treatment with MESF offered protection against hippocampal CA1neuronal damage induced by 10 min of forebrain ischemia as evidenced by the fact that MESF rescued most of CA1pyramidal neurons from ischemic death which was evident from photomicrographs of histopathology study.

The results of this study confirmed that MESF protects rats from ischemia induced brain injury. This protection was evident from, the significant improvement in neuromuscular, vestibulomotor, complex neuromotor, social recognition and in-vivo behavioral tests and reversal of decreased dopamine and serotonin levels and the significant reduction in neuronal cell death in the hippocampal CA1 region to nearly normal levels after forebrain ischemia. In conclusion, methanol extract of *Soymida febrifuga* produced cerebroprotective effects in global cerebral ischemia as evident from reduction in behavioral score, hyperlocomotion and neuronal damage.

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