

ANTICONVULSANT ACTIVITY OF *MORINGA OLEIFERA* IN SWISS ALBINO MICEAnu Elizabeth Joy¹, Padmini Thalanjeri¹, Shyamjith Manikkoth^{2*}¹ Department of Physiology, Yenepoya Medical College, Yenepoya University, Mangalore² Department of Pharmacology, Yenepoya Medical College, Yenepoya University, MangaloreCorresponding Author*: Email: shyamjithpubs@gmail.com Mobile: +919480361961**ABSTRACT****Objectives:** The aim of the study was to investigate anticonvulsant effect of *Moringa oleifera* on maximal electroshock (MES), pentylenetetrazole (PTZ) and pilocarpine induced seizures.**Methods:** The ethanolic extract of *Moringa oleifera* leaves (200mg/ Kg) was used to study its anticonvulsant effect on MES, PTZ and pilocarpine induced seizures in Swiss albino mice. Suppression of the tonic hind limb extension, duration of convulsion, abolition of convulsions was noted respectively for the above tests.**Results:** The ethanolic extracts of *Moringa oleifera* leaves (200mg/ Kg) significantly ($p < 0.001$) abolished the hind limb extension induced by MES. The same dose also significantly ($p < 0.001$) protected the animals from PTZ induced tonic convulsions. None of the animals treated with same dose of plant extract reached the status epilepticus state in pilocarpine induced seizures.**Conclusions:** The data suggests that the ethanolic extracts *Moringa oleifera* leaves may produce its anticonvulsant effect via different mechanisms since it prevented the hind limb extension induced by MES, decreased the duration of convulsions produced by PTZ and abolished status epilepticus in pilocarpine induced seizures.**Key Words:** Maximal electroshock, Pentylenetetrazole, Pilocarpine, Convulsion, *Moringa oleifera*, Anticonvulsant.**INTRODUCTION**

Epilepsy is a common neurological disorder characterized by unpredictable and periodic occurrence of a transient alteration of behavior due to the disordered, rhythmic and synchronous firing of populations of brain neurons (Rasilingam.D, et.al, 2009). The antiepileptic drugs presently available are unable to control seizures effectively and have several serious adverse effects. In this context, plant derived phytoconstituents can play an important role in the treatment of epilepsy as they are known for high therapeutic index and relatively low cost (Joy.A.E, et.al, 2013a). *Moringa oleifera* Lam belongs to Moringaceae family (Fakurazi.S, et.al,2012) and is indigenous to dry tropical areas in the Northwestern India and at the Southwestern foot of the Himalayas (Marrufo.T, et.al, 2013). All parts of the tree are edible and useful for humans (Singh.G.P, et.al, 2012). Moringa from time immemorial was used in the traditional medicine in many cultures around the world (Mahmood.K.T, et.al, 2010). An extensive variety of nutritional and medicinal uses have been attributed to its seeds, leaf, bark, roots, fruits, and flowers. Its leaves and fruits are used as food. *Moringa oleifera* is called a miracle tree because of its medicinal values. In the traditional medicinal system almost all the parts of this plant has been used in the treatment of various ailments (Joy.A.E, et.al, 2012b). Various studies have proved that this plant possesses various medicinal properties like anticonvulsant (Jay.N.A, et.al, 2011), neuroprotective (Ganguly.R, et.al, 2008), antioxidant (Kirisattayakul.W, et.al, 2012), analgesic (Manaheji.H, et.al, 2011), antipyretic (Sutar.N.G, et.al., 2009), wound healing (Rathi.B.S, et.al, 2006), hypolipidemic (Jain.P.G, et.al., 2010) antidiarrhoeal (Choudhury.S, et.al, 2013), antiulcer (Das.D, et.al, 2011), hypoglycemia (Tende J.A, et.al, 2011), hepatoprotective (Saalu.L.C, et.al, 2012), anti asthmatic (Mehta.A, et.al, 2008), prevent DNA damage (Eshak.M.G, et.al, 2013), antimicrobial (Onsare.J.G, et.al, 2013), enhancement of nutritional values (Salem.A.S, et.al., 2013) and anti-inflammatory (Rao.C.V, et.al, 1999). The aim of the present study was to evaluate the anticonvulsant property of ethanolic extracts of *Moringa oleifera* leaves in experimental animal models.

MATERIALS AND METHODS

Drugs and Chemicals

Phenytoin sodium, Sodium valproate was obtained from a private hospital pharmacy in Mangalore. Pentylentetrazole was obtained from Rajesh Chemicals, Mumbai.

Instruments

Soxhlet apparatus was used for preparing the plant extracts. Electro-convulsimeter was used for inducing convulsions.

Plant material

Moringa oleifera leaves were collected from Thiruvalla, Kerala. The leaves were authenticated by Dr. Noeline J. Pinto, Head of Botany department, St. Agnes College, Mangalore, Karnataka, India. The leaves were shade dried and grinded into coarse powder.

Preparation of the extracts

Moringa oleifera ethanolic extract (MOEE)

A weighed quantity of the coarse powder was taken and extracted with ethanol (90%) in Soxhlet apparatus. The extract was concentrated on a water bath at a temperature not exceeding 60⁰ C. The percentage yield of the extract was 10%. The ethanolic extract was suspended in distilled water.

Animals

Adult Swiss albino mice of either sex weighing 25-30 g were used in this study after obtaining IAEC Clearance. The mice were maintained under standard conditions in the Animal House. They were kept in polypropylene cages and given standard pellet diet and water *ad libitum*. The mice were maintained on a 12:12 hour light-dark cycle.

Acute toxicity study

For studying the acute toxicity effect of the plants the animals were divided into five groups consisting of four animals (2 males and 2 females) in each group. Overnight fasted animals were kept in individual cages and were administered graded dose of the *Moringa oleifera* leaf extracts from 100 mg / Kg body weight to 1600 mg / Kg body weight orally. They were observed for a period of 2 hours and thereafter at regular intervals for 14 days for signs of toxicity and death (Bhardwaj. S, et.al, 2012).

Anticonvulsant Activity

a. Maximal electro shock (MES) seizure

Electrical stimulation was applied using ear electrodes. The electrodes were moistened with saline before application. All animals were stimulated with 60 mA for 0.2 seconds, with constant voltage stimulators of 250V. The animals were divided into three groups. Each group consisting of 6 males and 6 females (n=12).

Group I: Normal Saline (NS) (0.1 ml i.p for 10 days) + MES on 10th day.

Group II: MOEE (200mg / Kg p.o for 10 days) + MES on 10th day.

Group III: Phenytoin (25mg / Kg i.p for 10 days) + MES on 10th day.

On the 10th day the test drugs were given 1 hour prior to induction of convulsions. Suppression of tonic hind limb extension was taken as a measure of efficacy in this test (Manikkoth.S, et.al., 2011).

Pentylentetrazole (PTZ) induced convulsion

PTZ 70mg / Kg i.p was administered to mice. The parameter noted was duration of convulsions. The animals were divided into three groups. Each group consisting of 6 males and 6 females (n=12).

Group I: Normal Saline (NS) (0.1 ml i.p for 10 days) + PTZ on 10th day.

Group II: MOEE (200mg / Kg p.o for 10 days) + PTZ on 10th day.

Group III: Sodium valproate (75mg / Kg i.p for 10 days) + PTZ on 10th day.

On the 10th day the test drugs were given 1 hour prior to induction of convulsions. Abolition of the convulsions was taken as a measure of efficacy in this test (Manikkoth.S, et.al, 2011).

Pilocarpine induced seizure.

Pilocarpine 300mg / Kg body weight i.p was administered to the mice. The features noted were the different stages of Status Epilepticus (SE) (Table 1) and the mortality of the animals. SE was defined by continuous seizure activity for at least 2hr consisting of at least one stage 3.5 seizures and one stage 5 or 6 seizure or several stage 4.5 seizures.

For ten days the plant extracts were given orally at the dose of 200 mg / Kg body weight. On the 10th day the test drug was given 1 hour prior to the induction of convulsion. Half an hour prior to the administration of the pilocarpine (P), scopolamine (S) was administered at the dose of 1 mg/ Kg body weight to minimize peripheral side effects of pilocarpine (Borges K, et.al, 2003)

Table 1: Stages and features of Status Epilepticus.

Stages	Features noted
0	Normal activity
1	Rigid posture or immobility
2	Stiffened, extended, and often arched (Straub) tail
3	Partial body clonus, including forelimb or hind limb clonus (seen rarely) or head bobbing
3.5	Whole body continuous clonic seizures while retaining posture.
4	Rearing
4.5	Severe whole body continuous clonic seizures while retaining posture
5	Rearing and falling
6	Tonic-clonic seizures with loss of posture or jumping

The animals were divided into 2 groups. Each group consisting of 6 males and 6 females (n=12).

Group I: S (1 mg / Kg ip) + P (300mg / Kg ip)

Group II: MOEE (200mg / Kg po) +S (1 mg / Kg ip) + P (300mg / Kg ip)

Statistical Significance

The results of the study is expressed as mean \pm SEM, n=12. One Way ANOVA was used to analyze and compare the data, followed by Tukey Kramer multiple comparison tests.

RESULTS

Acute toxicity study

There was no mortality nor any sign of toxicity or behavioral change till the dose of 1600mg / Kg. This finding suggests that MOEE is non-toxic to mice upto 1600mg / Kg. Hence, a lower dose of 200 mg / Kg was selected for this study.

Antiepileptic activity: MES induced seizures

In the case of MES induced seizures there was no hind limb extension in MOEE & Phenytoin groups on comparing with the control group ($p < 0.001$). There were 4 deaths in the control group. No mortality was observed in MOEE & Phenytoin groups (Table-2).

Table 2: Effect of MOEE on MES induced seizures

Drug	Dose	Duration of hind limb extension in seconds	Mortality
NS + MES	0.1ml	13.21 \pm 1.20	4
MOEE + MES	200 mg / Kg	0.0 \pm 00 ^a	0
Phenytoin + MES	25 mg / Kg	0.0 \pm 00 ^a	0

One Way ANOVA followed by Tukey Kramer multiple comparison test. n=12
a: $p < 0.001$ \rightarrow extremely significant when comparing MOEE and Phenytoin treated group with normal group.
NS- Normal saline, MOEE- *Moringa oleifera* ethanolic extract, MES- Maximal electroshock.

Antiepileptic activity: PTZ induced seizures

In the case of PTZ induced seizures there was considerably significant decrease in the mean duration of convulsions in MOEE & Sodium Valproate groups on comparing with the control group. There were 9 deaths in the control group. No mortality was observed in MOEE & Sodium valproate groups. (Table3).

Table 3: Effect of MOEE on PTZ induced seizures

Drug	Dose mg/kg	Duration of hind limb extension in seconds	Mortality
NS + PTZ	70	21.75 ± 2.32	9
MOEE + PTZ	200 + 70	0.93 ± 0.50 ^a	0
Sodium valproate + PTZ	75 + 70	1.40 ± 0.84 ^a	0

One Way ANOVA, followed by Tukey Kramer multiple comparison test
n=12
a: p< 0.001 →extremely significant when comparing MOEE and Phenytoin treated group with normal group.
NS- Normal saline, MOEE- *Moringa oleifera* ethanolic extract, PTZ-Pentylenetetrazole.

Antiepileptic activity: Pilocarpine induced seizures

In the case of Pilocarpine induced seizures none of the animals treated with *Moringa oleifera* extract reached the status epilepticus compared to the group which was given pilocarpine with scopolamine. There were 12 deaths in the pilocarpine with scopolamine group. No mortality was observed in MOEE treated group (Table 4).

Table 4: Effect of MOEE on Pilocarpine induced seizures

Group	Dose mg/Kg	No of animal reaching status epilepticus	Mortality
S + P	1 + 300	12	12
MOEE + S + P	200+ 1+ 300	0	0

n=12
MOEE- *Moringa oleifera* ethanolic extract, Scopolamine-1mg/kg,
Pilocarpine 300mg / Kg.

DISCUSSION

Epilepsy is a disease which globally affects approximately 1% of the population all over the world. It affects almost all ages and both sexes. Epilepsy is a neurological disorder in which oxidative stress, stroke and dysfunction have been suggested to be contributing factors (Goel.R, et.al, 2013, Pal.A, et.al, 2011). Epilepsy is one pathological condition characterized by localized bursts of electrical overactivity (seizures) in the cerebral hemispheres. The outbursts of electrical activity, commonly observed in cortical and sub-cortical areas, can result in extensive neuronal cell death in different brain regions (Bozzi.Y, et.al, 2000).

Epilepsies may result from long-lasting plastic changes in the brain affecting the properties of receptors and channels, neurotransmitter release and transport, synaptic re-organization, regulation of gene expression and astrocyte activity. There is evidence of ion channel alterations being the cause of the origin of the paroxysmal depolarization shifts that initiate epileptic activity. Recent studies on synaptic and non-synaptic transmission, the ion channels interaction, intracellular signaling pathways and glia–neuron signaling suggest that many neurochemical pathways play an important role in seizure initiation, maintenance and arrest (Sierra-Paredes.G, 2008). There are solid evidences that an imbalance between the inhibitory and excitatory transmitters is involved in the patho mechanisms of epilepsy. GABA (Gamma -aminobutyric acid) which is the major inhibitory neurotransmitter in the brain, is essential for the overall balance between neuronal excitation and inhibition that is vital to normal brain function. GABA being an inhibitory transmitter has a significant role in suppressing the origin and spread of seizure activity. GABA systems have been implicated in the pathogenesis of epilepsy. Heritable mutations in GABA A receptor subunits are strongly implicated in idiopathic generalized epilepsies.

Thus drugs which reduce brain GABA content are often convulsants and drugs which elevates brain GABA content have anticonvulsive properties (Wen-Juan.Z, et.al, 2003, Johnston G.A.R, 2005, Abdul-ghani.A, 1989). Glutamate being an excitatory transmitter has a significant role in the origin and spread of seizure activity. In epilepsy there is Glutamate excitotoxicity which is known to plays a key role in the induction of neuronal cell death through apoptosis. The NMDA and AMPA receptors of glutamate have a major role in this disorder. Various animal studies have shown that agents blocking these two receptors have potent anticonvulsant property (Pal.A, et.al, 2011, Abdul-ghani.A, 1989).

A role of the cholinergic system in convulsive disorders has already been documented, but most studies in this respect have concentrated on muscarinic rather than nicotinic receptors. Recently, release of glutamate via stimulation of presynaptic nicotinic acetylcholine receptors has been implicated in the convulsant action of nicotine and MK-801 (dizocilpine), a potent antagonist at the N-methyl-D-aspartate (NMDA) subtype of glutamate receptors, was found to suppress the development of nicotine-induced seizures in mice (Rainesalo.S, 2004). A possible role of dopamine in epilepsy came into the picture based on the effect of antipsychotics (i.e., dopaminergic D2-like antagonists). The dopamine antagonist used in the treatment of disorders such as schizophrenia lowers the seizure threshold in epileptic patients or even to promote seizures in patients with no previous history of the disease. Seizure inhibition has been observed in patients administered with antiparkinsonian drugs such as pergolide and bromocriptine. Although dopamine appears to modulate epileptic activity in the cerebral cortex it does not seem to be directly involved. Dopamine acting through D₂ receptors inhibits the activation of limbic areas by glutamate and prevents the episodes of seizures (Pal.A, et.al, 2011).

Several lines of evidence point to the role of serotonin (5HT) in epileptogenesis in general, studies on animal models, as well as on humans, demonstrate an inverse correlation between extracellular brain 5HT levels and susceptibility to seizures. The role of 5HT in epilepsy had come into the picture due to the fact that, in patients with epilepsy, a common co -morbidity diagnosed is depression. The processes like serotonin depletion, neuro degeneration, neuro inflammation by inflammatory mediators can be demonstrated in pilocarpine induced status epilepticus model. Elevation in serotonin concentration gives an inhibitory response to epileptic discharge and stabilizes the depressed mood disorder. In addition, mono amino oxidase inhibitors are effective in kindling model of epilepsy which resembles the status epilepticus. Previous reports indicate that fluoxetine, a selective 5-hydroxytryptamine (5-HT) reuptake inhibitor, has anticonvulsant effects in genetically epilepsy-prone rats. Another study has shown that sertraline decreased the intensity of autogenic seizures. Mutant mice lacking 5HT_{1A} or 5HT_{2C} receptors display lower seizure threshold and/or increased seizure activity, implicating the respective 5HT receptors in the regulation of neuronal excitability (Bozzi.Y.et.al, 2000, Farjo.I.B et.al, 1979, Yan.Q, et.al, 1995).

In this study it was observed that duration of the hind limb extension in Maximal electroshock seizures (MES) induced convulsions was significantly reduced ($p < 0.001$) in mice which received MOEE in comparison with the normal mice. There was no significant ($p > 0.01$) difference in results between the plant extract treated groups and the Phenytoin (Standard drug) treated group. Duration of convulsions in pentylenetetrazole (PTZ) induced convulsion was significantly reduced ($p < 0.001$) in mice which received MOEE in comparison with the normal mice. There was no significant ($p > 0.01$) difference in results between the plant extract treated groups and the sodium valproate (standard drug) treated group.

In pilocarpine induced convulsions, status epilepticus was not observed in mice which received MOEE in comparison with the mice which were given only pilocarpine. The above findings clearly indicate that MOEE has anticonvulsant activity.

Based on the above facts and results, the anticonvulsant action of MOEE can be due to

- Blockade of sodium channels since they abolish MES induced seizures.
- Blockade of T type calcium channels in thalamus since it blocks PTZ induced seizures.
- GABA mimetic property since it blocks PTZ induced seizures.
- Anticholinergic property since it blocks pilocarpine induced seizures.
- Monoamino- oxidase inhibitory property.
- The possession of dopaminergic and antioxidant properties cannot be ruled out.

CONCLUSION

Moringa oleifera possess broad anticonvulsant property. Further studies are ongoing to elucidate the exact mechanism by which this plant acts as an anti convulsant agent.

CONFLICT OF INTEREST: Nil

REFERENCES

- Abdul-ghani. A (1989). Changes in γ -aminobutyric acid during different stages of picrotoxin- induced seizure, and the effect of pretreatment with γ -acetylenic GABA and phenobarbital. *J Biosci*: 14(1): 63-67.
- Bhardwaj. S, Gupta. D (2012). Study of acute, sub acute and chronic toxicity test. *IJARPB*: 1(2): 103-129.
- Borges. K, Gearing. M, McDermott. D.L, Smith. A.B, Almonte. A.G, Wainer. B. H, et al., (2003). Neuronal and glial pathological changes during epileptogenesis in the mouse Pilocarpine model. *Experimental Neurology*: 182: 21-34.
- Bozzi. Y, Vallone. D, Borrelli. E (2000). Neuroprotective role of dopamine against hippocampal cell death. *The Journal of Neuroscience*: 20 (22): 8643-8649.
- Choudhury. S, Sharan. L, Sinha. M.P (2013). Antidiarrhoeal potentiality of leaf extracts of *Moringa oleifera*. *British Journal of Applied Sciences and Technology*: 3(4): 1086-1096.
- Das. D, Dash. D, Mandal. T, Kishore. A, Bairy. K.L (2011). Protective effects of *Moringa oleifera* on experimentally induced gastric ulcers in rats. *Research Res J Pharm Biol Chem Sci*: 2(2): 50-55.
- Eshak. M.G, Osman. H.F (2013). Role of *Moringa oleifera* leaves on biochemical and genetical alterations in irradiated male rats. *Middle East Journal of Scientific Research*: 16(10): 1303-1315.
- Fakurazi. S, Sharifudin. A. S, Arulselvan. P (2012). *Moringa oleifera* hydroethanolic extracts effectively alleviates acetaminophen induced hepatotoxicity in experimental rats through their antioxidant nature. *Molecules*: 17: 8334-8350.
- Farjo. I. B, McQueen. J.K (1979). Dopamine agonist and cobalt-induced epilepsy in rats. *Br J Pharmac*: 67: 353-360.
- Ganguly. R, Guha. D (2008). Alteration of brain & EEG wave pattern in rat model of Alzheimer's disease & protection by *Moringa oleifera*. *Indian J Med Res*: 128: 744-751.
- Goel. R, Goel. A (2013). Effect of nebivolol on anticonvulsant property of sodium valproate along with neuropharmacological benefits in rodents models of epilepsy and behaviour in mice. *Journal of Clinical and Experimental Neuroscience*: 1(1): 1-9.
- Jain. P.G, Patil. S.D, Haswani. N.G, Girase. M.V, Surana. S.J (2010). Hypolipidemic activity of *Moringa oleifera* Lam., Moringaceae, on high fat diet induced hyperlipidemia in albino rats. *Brazilian Journal of Pharmacognosy*: 20(6): 969-973.
- Jay .N.A, Minaxi. L, Srinivasa. U, Shabaraya. A.R, Samuel. R.M (2011). Anticonvulsant activity of *Moringa oleifera* leaf. *IRJP*: 2(7): 160-162.
- Johnston. G.A.R (2005). GABA-A receptor channel Pharmacology. *Current Pharmaceutical Design*: 11: 1867-1885.
- Joy. A.E, Manikkoth. S, Bhat. S. K (2013). Acute effect of ethanolic extracts of *Moringa oleifera* on haloperidol induced catalepsy in mice models. *Drug Invention Today*: 4(10): 543-545.
- Joy. A.E, Kunhikatta. S. B, Manikkoth. S (2012). Anticonvulsant activity of ethanolic extract of *Moringa concanensis* leaves in swiss albino mice. *Archives of medicine and health sciences*: 1(1): 6-9.
- Kirisattayakul W, Wattanathorn J, Tong-Un T, Muchimapura S, Wannanon P (2012). *Moringa oleifera* Lam mitigates oxidative damage and brain infarct volume in focal cerebral ischemia. *Am J Appl Sci*: 9 (9): 1457-1463.
- Mahmood. K.T, Mugal. T, Haq.U.I (2010). *Moringa oleifera*: A natural gift-A review. *J Pharm Sci and Res*: 2(11): 775-781.
- Manaeji. H, Jafari. S, Zaringhalem. J, Rezazadeh. S, Taghizadfarid. R (2011) .Analgesic effect of Methanolic extracts of the leaf or root of *Moringa* on complete Freund's adjuvant induced arthritis in rats. *Journal of Chinese Integrative Medicine*: 9(2): 216-222.
- Manikkoth. S, Deepa. B, Joy. A. E, Rao. S. N (2011). Anti convulsant activity of *Phyllanthus amarus* in experimental animal models. *International Journal of Applied Biology and Pharmaceutical Technology*: 2(4): 144-149.

- Marrufo. T, Nazzaro. F, Mancini. E, Fratianni. F, Coppola. R, Martino. L. D. (2013). Chemical composition and biological activity of the essential oil from leaves of *Moringa oleifera* Lam. cultivated in Mozambique. *Molecules*: 18: 10989-11000.
- Mehta. A, Agrawal. B (2008). Investigation into the mechanism of action of *Moringa oleifera* for its anti asthmatic activity. *Orient Pharm Exp Med*: 8(1): 24-31.
- Onsare. J.G, Kaur. H, Arora. D.S (2013). Antimicrobial activity of *Moringa oleifera* from different locations against some human pathogens. *Academia Journal of Medicinal Plants*: 1(5): 80-91.
- Pal. A, Nayak. S, Sahu. P. K, Swain. T (2011). Piperine protects epilepsy associated depression: a study on role of monoamines. *Eur Rev Med Pharmacol Sci*: 15: 1288-1295.
- Rainesalo.S. (2004). <http://tampub.uta.fi/bitstream/handle/10024/67402/951-44-6007-3.pdf?sequence=1> Accessed on 01/07/14.
- Rao. V, Gopalakrishnan. V, Loganathan. V, Nathan. S.S (1999). Anti inflammatory activity of *Moringa oleifera* Lam. *Anc Sci Life*: 18 (3&4): 195-198.
- Rasilingam. D, Duraisamy. S, Subramanian. R (2009). Anticonvulsant activity of bio flavonoid gossypin. *Bangladesh J Pharmacol*: 4: 51-54.
- Rathi. B.S, Bodhankar. S.L, Baheti. A.M (2006). Evaluation of aqueous leaves extract of *Moringa oleifera* Linn for wound healing in albino rats. *Indian J Exp Biol*: 44: 898-901.
- Saalu. L.C, Ogunlade. B, Ajayi. G.O, Oyewopo. A.O, Akunna. G. G, Ogunmodede. O.S (2012). The hepatoprotective potentials of *Moringa oleifera* leaf extract on alcohol-induced hepato-toxicity in Wistar rat. *Am J Biotechnol Mol Sci*: 2(1): 6-14.
- Salem AS, Salama.W.M, Hassanein. A.M, Ghandour.H.M.A.E (2013). Enhancement of nutritional and biological values of labneh by adding dry leaves of *Moringa oleifera* as innovative dairy products. *World Applied Sciences Journal*: 22(11): 1594-1602.
- Sierra - Paredes. G. (2008). www.touchneurology.com/system/files/private/articles/8355/pdf/paredes.pdf. Accessed on 01/07/14.
- Singh. G.P, Garg. R, Bhardwaj. S, Sharma. S. K (2012). Anti-inflammatory evaluation of leaf extracts of *Moringa oleifera*. *Journal of Pharmaceutical and Scientific Innovations*: 1(1): 22-24.
- Sutar. N.G, Patil. V.V, Deshmukh. T. A, Jawle. N. M, Patil. V. R, Bhangale. S. C (2009). Evaluation of anti-pyretic potential of seeds of *Moringa oleifera* Lam. *Int J Green Pharm*: 3: 148-150.
- Tende. J. A, Ezekiel. I, Dikko. A. A. U, Goji. A.D.T (2011). Effect of ethanolic leaves extract of *Moringa oleifera* on blood glucose levels of Streptozocin-induced diabetics and normoglycemic Wistar rats. *British Journal of Pharmacology and Toxicology*: 2(1): 1-4.
- Wen-Juan. Z, Ying-Hua. M, Jian. F, Zhen-Tong. M, Li-He. G (2003). Increase in drug-induced seizure susceptibility of transgenic mice over expressing GABA transporter-1. *Acta Pharmacol Sin*: 24(10): 991-995.
- Yan. Q, Jobe. P.C, Dailey. J. W (1995). Further evidence of anticonvulsant role for 5-hydroxytryptamine in genetically epilepsy prone rats. *British Journal of Pharmacology*: 115: 1314-1318.

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