Scholars Journal of Applied Medical Sciences (SJAMS) **ISSN 2320-6691 (Online)**
Sch. J. App. Med. Sci., 2017; 5(8D):3209-3213 **ISSN 2347-954X (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublishers.com DOI: 10.36347/sjams.2017.v05i08.046

Original Research Article

Anticonvulsant Herb *Ipomoea reniformis*- A Novel Approaches *i*n the Screening of Natural Product Based Anticonvulsant Drug against Experimentally Induced Convulsion in Wistar Rats

Mani M[1], Kanagathara N[2], Jaikumar S[2*], Sengottuvelu S[4]
[1]Department of Pharmacology, Ponnaiah Ramajayam Institute of Medical Sciences,Manamai, Nallur, Kanchipuram India
[2,3] Department of Pharmacology, Sri Lakshmi Narayana Institute of Medical Sciences, Osudu Agaram Village, Villianur Commune, Kudapakkam India.
[4]Department of Pharmacology, Nandha College of Pharmacy, Tamil Nadu, India.

***Corresponding author**
Dr. S. Jaikumar
Email: sengt@rediffmail.com

Abstract: Epilepsy is the second most common and frequently encountered neurological condition that imposes heavy burden on individuals, families, and also on healthcare systems. Due to development of resistance, intolerability and side effects of modern drugs, there is a demand for developing new antiepileptic drugs with improved efficacy and safety. *Ipomoea reniformis* belonging to the family Convolvulaceae, traditionally indicated for epileptic seizures. The study was conducted to evaluate the antiepileptic activity of ethanolic leaf extract of *Ipomoea reniformis* (200 & 400mg/kg) against Maximal Electroshock, Pentylenetetrazole and Isoniazid induced convulsions in rats. Phenytoin (25 mg/kg) and diazepam (2 mg/kg) were used as reference drugs. The extract was also evaluated for its influence on GABA levels in brain to ascertain its mechanism of action. In all the tested three models, *Ipomoea reniformis* (200 & 400 mg/kg) alleviated and protected the seizures significantly ($P<0.01$ and $P<0.001$, respectively) in dose dependent manner. Further, ethanolic leaf extract of *Ipomoea reniformis* showed significant increase in brain GABA levels ($P < 0.01$) compared to control. From the result it was concluded that, ethanolic leaf extract of *Ipomoea reniformis* exhibited anticonvulsant property, and it may be due to enhancing the GABA levels in the brain
Keywords: *Ipomoea reniformis*, Anticonvulsant, Maximal Electroshock, Pentylenetetrazole and GABA

INTRODUCTION

'Epilepsy' is the commonest neuropsychiatric disorder characterized by paroxysmal cerebral dysrrhythmia, manifesting as brief episodes (seizures) of loss or disturbance of consciousness, with or without characteristic body movements (convulsions) with sensory or psychiatric phenomena [1]. There are about 50 million epileptic patients worldwide, in that up to 75% are living in the poor socio-economic background with little or minimal access to medical services or therapy [2]. Current available anticonvulsant drugs are able to efficiently control epileptic seizures in about 50% of the patients; 25% of the cases may show improvement, whereas the rest of the patients do not benefit significantly [3]. Due to development of resistance, intolerability and side effects of modern drugs, there is a demand for developing new antiepileptic drugs with improved efficacy and safety. One of the approaches to search for new antiepileptic drugs is the investigation of naturally-occurring compounds, which may belong to new structural classes. *Ipomoea reniformis* belonging to the family Convolvulaceae, is a perennial, much branched herb (creeper). It is widely distributed all over the India, especially in damp places in upper gangetic plain, Gujarat, Bihar, West Bengal, Western- Ghats, ascending up to 900m in the hills, Goa, Karnataka in India, Ceylon and Tropical Africa [4]. In the Indigenous system of Medicine, *Ipomoea reniformis* has been claimed to be useful for cough, headache, neuralgia, rheumatism, diuretic, inflammation, troubles of nose, fever due to enlargement of liver and also in kidney diseases. Powder of leaves is used as a snuff during epileptic seizures, juice acts as purgative and the root is

having diuretic, laxative, and applied in the disease of the eyes and gums [5], *Ipomoea reniformis* reported to possess Antiulcer [6], Antiuolithiatics [7] Antioxidant [8], Antihypertensive [9], Analgesic, Anti-inflammatory, Antipyretic [10], Antidiabetic [11], Antibacterial [12], Anticancer [13] and Nephroprotective [14] activities. Most of the traditional uses of *Ipomoea reniformis* were scientifically proven, but antiepilieptic activity of *Ipomoea reniformis* was not so far revealed hence, the present study was conducted with an aim to investigate the antiepileptic activity of *Ipomoea reniformis* against experimentally induced convulsion in laboratory animals.

MATERIALS AND METHODS

Plant material

The leaves of *Ipomoea reniformis* were collected from outskirts of Tirunelveli district, in the month of December. It was identified and authenticated as *Ipomoea reniformis* by Scientist 'F' Botanical survey of India, Southern Regional Centre, Tamilnadu Agriculture University, and Coimbatore. The voucher specimen (BSI/SRC/12/42/2015-16/Sci/1555) has been deposited in department for further references.

Preparation of Extract

The leaves of *Ipomoea reniformis* were, shade dried and then ground into coarse powder. The powder was then subjected to exhaustive extraction by a maceration process using 70% ethanol as a solvent at room temperature for 7 days. The ethanolic leaf extract of *Ipomoea reniformis* (ELIR) was concentrated by vacuum distillation to dry. The collected extract was stored in desiccators and used for further pharmacological study.

Animals

Male Wistar Albino rats weighing between 150–160 g were used for the study. The animals were obtained from animal house of Sri Lakshmi Narayana Institute of Medical Sciences, Pondicherry, India. On arrival the animals were placed at random and allocated to treatment groups in polypropylene cages with paddy husk as bedding. Animals were housed at a temperature of 24 ± 2ºC and relative humidity of 30–70 %. A 12:12 light: dark cycle was followed. All animals were allowed free access to water and fed with standard commercial pelleted rat chaw (Hindustan Lever Ltd, Mumbai). All the experimental procedures and protocols used in this study were reviewed by the Institutional Animal Ethics Committee (932/a/06/CPCSEA) and were in accordance with the guidelines of the IAEC.

Anticonvulsant Screening

Maximal Electroshock (MES)-induced Convulsions

The animals were randomized and assigned in four groups, each group consisting of ten animals. The respective group animals were treated with vehicle (0.1% CMC) or phenytoin (25 mg/kg, i.p) or ELIR (200 and 400 mg/kg) orally for 3 days. On the 3rd day, exactly 1 h after the assigned treatment, the electrical stimulus (150 mA, 50 Hz, 0.2 s duration) was applied via ear clip electrodes using an electroconvulsiometer (Techno, India). Immediately after the electrical stimulation, individually all the animals were observed in an open top plastic cage for 30 min. The parameters such as duration of hind limb flexion (HLF), hind limb extensor (HLE), stupor, and mortality and percentage protection were observed.

PTZ-induced Convulsions

The animals were randomized and assigned in five groups, each group consisting of ten animals. The respective group animals were treated with vehicle (0.1% CMC) or Diazepam (3 mg/kg, i.p) or ELIR (200 and 400 mg/kg) orally for 3 days. On the 3rd day, 1 h after the assigned treatment PTZ (80 mg/kg) was intraperitoneally administered to all the experimental animals except normal control, and they were individually observed in a plastic cage initially for 30 min and the animals survived were observed later up to 24 h. During the individual observation, the parameters such as onset of clonus, onset of tonic convulsions, mortality and percentage protection were noted. After observations, rats were sacrificed by decapitation and the whole brain was dissected out for estimation of GABA-T activity [16].

Isoniazid (INH) induced Convulsions

The animals were randomized and assigned in four groups, each group consisting of ten animals. The respective group animals were treated with vehicle (0.1% CMC) or Diazepam (3 mg/kg, i.p) or ELIR (200 and 400 mg/kg) orally for 3 days. On the 3rd day, 1 h after the assigned treatment INH (300 mg/kg) was intraperitoneally administered to all the experimental animals, and they were individually observed in a plastic cage initially for 30 min and the animals survived were observed later up to 24 h [17]. During the individual observation, the parameters such as onset of clonus, onset of tonic convulsions, mortality and percentage protection were observed.

Statistical Analysis

The values were expressed as mean ± SEM. The statistical analysis was carried out by one way analysis of variance (ANOVA) followed by Dunnet's't' – test using graph pad version I. P values <0.05 were considered significant.

RESULTS

Table–1: Effect of Ethanolic Leaf Extract of *Ipomoea reniformis* on Maximal Electro Shock induced Convulsion in Rats

Drug Treatment	Duration of HLF (secs)	Duration of HLE (secs)	Stupor (secs)	Survived /Used	Percentage Protection
Control (0.1% CMC)	40.51± 3.75	78.55± 4.05	102.32± 2.44	0/10	-
Phenytoin (25mg/kg, p.o)	2.52± 0.17***	4.72± 0.26***	9.52± 0.42***	10/10	100%
ELIR (200mg/kg, p.o)	9.32± 0.52***	11.42± 0.98***	22.65± 1.06***	6/10	60%
ELIR (400mg/kg, p.o)	6.75± 0.33***	9.52± 0.62***	11.58± 0.96***	8/10	80%

Values are in mean ± SEM (n=10),
*P<0.05 , **P<0.01, ***P<0.001 Vs Control

The result of ethanolic leaf extract of *Ipomoea reniformis* on Maximal Electro Shock induced convulsion in rats was presented in the table 1. Both the doses (200 & 400 mg/kg) ELIR has showed significant (P<0.001) protection against MES-induced flexon, extension and stupor compared to control. Phenytoin the reference drug, has also showed similar effect against MES induced convulsion. All the animals in the phenytoin treated groups were survived but only 6 and 8 out of 10 animals were survived in the ELIR 200 and 400mg treated groups respectively.

Table–2: Effect of Ethanolic Leaf Extract of *Ipomoea reniformis* on PTZ induced Convulsion in Rats.

Drug Treatment	Onset of Clonus (secs)	Onset of Tonic (secs)	Survived /Used	Percentage Protection
Control (0.1% CMC)	-	-	10/10	-
PTZ Control	19.84± 0.65	9.53± 0.62	0/10	0
PTZ + Diazepam (3mg/kg, p.o)	195.31± 5.32	206.55± 7.72	10/10	100
PTZ + ELIR (200mg/kg, p.o)	126.33± 7.25***	141.02± 8.09***	5/10	50
PTZ + ELIR (400mg/kg, p.o)	165.69± 6.26***	188.74± 5.04***	7/10	70

Values are in mean ± SEM (n=10),
*P<0.05, **P<0.01, ***P<0.001 Vs PTZ Control

The results of ethanolic leaf extract of *Ipomoea reniformis* on PTZ induced convulsion in rats were shown on table 2. On administration of PTZ, the control group animals have showed clonic and tonic convulsions and death. Interestingly, ELIR (200 and 400 mg/kg) has significantly (P<0.001) prolonged the PTZ-induced onset of clonus, onset of tonic, and reduced the mortality rate dose dependently compared to control. The reference drug Diazepam also significantly (P<0.001) prolong the onset of clonus and tonic convulsion induced by PTZ.

Table-3: Effect of Ethanolic Leaf Extract of *Ipomoea reniformis* on Gamma – aminobutyric acid Transaminase activity in brain of PTZ induced convulsion in rats.

Drug Treatment	GABA Transaminase (pg/mg Protein)
Control (0.1% CMC)	39.33±2.12
PTZ Control	98.42±5.34
PTZ + Diazepam (3mg/kg, p.o)	50.55±1.23***
PTZ + ELIR (200mg/kg, p.o)	62.63±3.63*
PTZ + ELIR (400mg/kg, p.o)	56.54±2.97**

Values are in mean ± SEM (n=10),
*P<0.05, **P<0.01, ***P<0.001 Vs PTZ Control

The result of ethanolic leaf extract of *Ipomoea reniformis* on GABA –T (gamma – aminobutyric acid transaminase) activity in brain of PTZ induced convulsion in rats was shown on table 3. Administration of PTZ to animals increased the GABA –T in brain compared to control. Diazepam an anticonvulsant agent exhibits anticonvulsant activity by enhancing the level GABA and decrease the GABA –transaminase which is responsible for depleting the level of GABA in brain. ELIR dose dependently decrease the GABA transaminase levels compare to PTZ control, which indicate that ELIR may exhibit anticonvulsant effect, by restoring more GABA level in brain and its effect similar to that of Diazepam.

Table-4: Effect of Ethanolic Leaf Extract of *Ipomoea reniformis* on Isoniazid induced Convulsion in Rats.

Drug Treatment	Onset of Clonus (secs)	Onset of Tonic (secs)	Survived /Used	Percentage Protection
Isoniazid Control	17.65± 0.88	10.97± 0.92	0/10	0
Isoniazid + Diazepam (3mg/kg, p.o)	173.23± 4.17***	141.78± 3.05***	10/10	100
Isoniazid + ELIR (200mg/kg, p.o)	137.15± 5.56***	122.02± 5.08	6/10	60
Isoniazid + ELIR (400mg/kg, p.o)	163.55± 5.15***	139.84± 6.07***	9/10	90

Values are in mean ± SEM (n=10),
*P<0.05, **P<0.01, ***P<0.001 Vs Isoniazid Control

The result of ethanolic leaf extract of *Ipomoea reniformis* on isoniazid induced convulsion in rats was presented in the table 4. The onset of clonus and tonic convulsion were quick in the animals administered with isoniazid alone. Diazepam increased the clonus and tonic convulsions and both the doses (200 & 400 mg/kg) of ELIR has showed significant (P<0.001) increase in the onset of clonus and tonic convulsions. The effect produced by the ELIR was comparable with that of the reference standard Diazepam.

CONCLUSION

The ethanolic leaf extract of *Ipomoea reniformis* was studied for its anticonvulsant activity against MES, PTZ and Isoniazid induce convulsion in rats. From the results it was concluded that, *Ipomoea reniformis* exhibited anticonvulsant activity on the all the above models tested and the anticonvulsant activity may be due to restoring the GABA level in the brain. Further study is focused towards the to isolate active principle responsible for the above said activity of *Ipomoea reniformis.*

REFERENCES

1. Sander JW, Shorvon SD; Epidemiology of the epilepsy. Journal of Neurology, Neurosurgery and Psychiatry, 1996; 6: 433-443.
2. Ngugi AK, Bottemley C, Kleinschmidt I; Estimation of the burden of active and life-time epilepsy: A meta-analytic approach. Epilepsia, 2010; 51: 883-890.
3. Schmidt D, Loscher W; Drug resistance in epilepsy: Putative neurobiologic and clinical mechanisms. Epilepsia, 2005; 46: 858-877.
4. Satyvati VG, Gupta KA; Medicinal Plants of India 1st Edition, Indian Council of Medical Research, New Delhi, 1987; 2: 241.
5. Bhatt Mehul K, Dholwani Kishore K, Saluja Ajay K; *Ipomoea reniformis:* A scientific review. International Journal of Pharmacy and Pharmaceutical Sciences, 2010; 2(4): 22-23.
6. Shree Lakshmi Devi S, Abilash SC, Sengottuvelu S; Evaluation of antiulcer and antioxidant potential of *Ipomoea reniformis* leaf extract against experimentally induced ulcer in rats. International Journal of Basic and Clinical Pharmacology, 2017; 6(7): 1 -7.
7. Asokan BR, Somasundaram G, Sengottuvelu S, Jaikumar S; Antiurolithiatic effect of ethanolic leaf extract of *Ipomoea reniformis* against ethylene glycol induced urolithiasis in experimental animals. Scholar Academic Journal of Biosciences, 2017; 5(5): 348-351.
8. Babu AV, Rao RSC, Kumar KG, Babu BH, Satyanarayana PVV; Biological activity of *Merremia emarginata* crude extracts in different solvents. Research Journal of Medicinal Plant, 2009; 1-6.
9. Quiser J, Naveed A; Hypotensive, angiotensin converting enzyme inhibitory and Diuretic activities of the aqueous-methanaol extract of *Ipomea reniformis*. Iranian Journal of Pharmceutical Research, 2013; 12(4): 769-776.
10. Purushoth PT, Pannerselvam P, Vijaykumar R, Clement AW, Balasubramanian S; Anti-inflammatory, antiarthritis and analgesic effect of ethanolic extract of whole plant of *Merremia emarginata* Burm.F. Central European Journal of Experimental Biology, 2012; 1(3): 94-99.
11. Gandhi RG, Sasikumar P; Antidiabetic effect of *Merremia emarginata* Burm. F. in streptozocin induced diabetic rats. Asian Pacific Journal of Tropical Biomedicine, 2012; 2(4): 281-286.
12. Natrajan P, Jaspher SS, Thangathirupathi A, Solairaj P, Hari Dhas; Effect of *Merremia emarginata* Burn. F. on Isoproterenol Induced myocardial Infraction in rat. International Journal of Biologicals and Pharmaceutical Research, 2014; 5(1): 8-15.
13. Sudhavani V, Chinnikrishnaiah V, Raghu MV, Raghvendra HG, Ranganayakulu D; Nephroprotective activity of *Merremia emarginata* burn against cisplatin induced nephrotoxic rats. Journal of Advances in Drug Research, 2010; 1(1): 27-34.
14. Purushoth PT, Panneerselvam P, Selvakumari S, Udhumansha Ubaidulla, Shantha A; Anticancer activity of *Merremia emarginata* (Burm. F) against human cervical and breast carcinoma. International Journal of Research and Development in Pharmacy and Life Science, 2012; 1(4): 189-192.
15. Joshi R, Reeta KH, Sharma SK, Tripathi M, Gupta YK; Pharmacodynamic and pharmacokinetic interaction of Panchagavya Ghrita with phenytoin and carbamazepine in maximal electroshock induced seizures in rats. Ayu, 2015; 36:196-202.
16. Garbhapu A, Yalavarthi P, Koganti P; Effect of ethanolic extract of *Indigofera tinctoria* on chemically-induced seizures and brain GABA levels in albino rats. Iran Journal of Basic Medical Sciences, 2011;14:318-26.
17. Vogel HG, Vogel WH; Drug Discovery and Evaluation: Pharmacological Assays. 2nd ed. New York: Springer; 2002.

.