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ANTIEPILEPTIC ACTIVITY OF HYDROALCOHOLIC EXTRACT OF THE BARK OF *ERYTHRINA STRICTA* ROXB

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ABSTRACT

The present study has evaluated the antiepileptic activity of hydroalcoholic extracts of *E.stricta* **(**HAEES**)** bark against MES, PTX and PTZ – induced epileptic seizures in rats. The HAEES was significantly antagonized PTX and PTZ induced epileptic clonic seizures. However, it did not affect the extensor and tonic phase seizures induced by MES, but significantly inhibit clonic seizures. Both PTX and PTZ are GABA-ergic blockers, by selective blocker of the chloride ionophore complex to the $GABA_A$ receptor. Therefore the mechanism of antiepileptic effect of HAEES may due to enhancing GABA receptor and blocking multineuronal pathways in the spinal cord.

Key Words: *E.stricta,* bark , hydroalcoholic extracts, clonic seizures

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INTRODUCTION

Epilepsy remains one of the most significant clinical challenges in neurology. The word epilepsy is derived from a Greek word that means “to be seized by forces from without”, interestingly, it is from this definition that word seizure is derived as well. Apparently, early physician and scientist believed that patients with epilepsy were infected supernatural beings. This condition has been recognized in man since antiquity. The Greek physician and philosopher Hippocrates (460 – 210 B.C.) believed that the cause of epileptic seizures should be found in the brain. The Greek physician Galen (130 – 210 A.D.) viewed epileptic seizures as a symptom of intracranial dysfunction (or) systemic diseases, caused by an accumulation of mucous in the arterial system. Modern medical a common neurological disorder in humans, animals like canines and felines. Epilepsy is also a most prevalent neurological disorder with current estimate approximating 0.5 – 2 % of the global population being affected. The use of term epilepsy is to some extent misleading as it actually refers to collection of neurophysiological disorder that diverse of both their etiology and symtomology. The typical behavioral manifestation common to all forms of epilepsy is the aberrant synchronized discharge of neuronal population termed the “seizures”. Seizures result from phasic changes in the firing properties of groups of neurons, usually within a discrete focal point, to an intermittent high frequency burst firing mode. Epilepsy is more than convulsion, a broad variety of clinical phenomena may reflect epileptic seizures activity for an example, behavioral (or) gastrointestinal signs. Therefore, the recognition of epilepsy implies knowledge of the phenomenology representing different types of seizures. Epileptic seizure can be induced in any normal human (or) vertebrate brain with a variety of different electrical (or) chemical stimuli. The ease and rapidity with

which these seizures can occur and the stereotyped nature of seizures, produced suggest that the normal brain, particularly the cerebral cortex, contains within its fine anatomic and physiologic structure a mechanism which is inherently unstable and which can be influenced in many different kinds of metabolic abnormalities. Anatomic lesions of brain can produce seizures, and conversely there is no pathogenomonic lesion of the epileptic brain. The altered brain physiologic state of epilepsy is a rhythmic and repetitive hyper synchronous discharge of many neurons in a localized area of the brain. A reflection of this hypersynchronous discharge can be observed in the EEG. The EEG records an integrated electrical activity generated by synaptic potentials in neurons, in the superficial layers of localized area of the cortex. Normally , the EEG records unsynchronized activity during periods when the mind is actively working (or) mildly synchronized activity when the mind is in restful state (i.e., α– waves during relaxation with closed eyes) or during various stages of sleep. In the epileptic focus, neurons in small area of the cortex are activated for a brief period (50 – 100 ms) in an unusually synchronized manner and are then inhibited. This produces a larger, sharper wave form in the EEG – the spike wave discharge, followed by a slow wave. If the synchronous neuronal discharge occurs repetitively over several seconds, a focal seizure follows. If it spreads through the brain and lasts for many seconds (or) minutes, a complex partial (or) generalized seizures (the ictus) will occur, and the EEG can have a variety (or) appearances depending on which areas of brain are involved and how the primary discharge areas project to the superficial cortex. During the seizures, the EEG may display low voltage fast activity (or) high voltage spikes (or) spike and wave discharges throughout both the hemispheres (1-4).

MATERIALS AND METHODS

Collection and authentication of plant

The fresh bark of *Erythrina stricta* Roxb. were collected from the Andhra Pradesh.

Preparation of the extract

Fresh stem bark of *Erythrina stricta* Roxb. were collected and air dried in shade under the room temperature. The dried stem bark material was powdered mechanically and sieved through No.20 mesh sieve. The fine powder was kept separately in an airtight container until the time of use. Around 100 g of finely powdered bark material was evenly packed in a soxhlet apparatus and the extraction was done with water: ethanol in the ratio of 30: 70 for 48 hours. The solvent was then evaporated under reduced pressure. The percentage (%) yield of the extract was calculated.

Maximal electro shock (MES) – induced epileptic seizure (5-7)

Rats were divided into five groups consisting of six animals each. Group I served as control which received normal saline only (10ml / kg, *p.o.*). Group II served as epileptic control received electric shock in the strength of 150 mA, 50 Hz for 2 seconds. Animals of groups III and IV received HAEES orally at doses of 250 mg/kg and 500 mg/kg respectively. Group V received the standard drug phenytoin at a dose of 300 mg/kg, *p.o*. One hour after drug administration, animals of the groups II – V received maximal electro shock (150 mA, 50 Hz for 2 sec). The animals were observed individually for 30 min from the time of electric shock applied for different phases of epileptic seizures.

Picrotoxin (PTX) – induced epileptic seizure method

Animals were grouped into five groups consisting of six animals each. Group I served as control group, receiving normal saline only (10 ml/kg, *p.o.*). Group II served as epileptic control received picrotoxin only (3.5 mg/kg, *i.p*). The animals of groups III and IV received HAEES orally at doses of 250 mg/kg and 500 mg/kg respectively. Group V received the standard drug diazepam (10 mg/kg *p.o.*). Groups II – V received convulsive dose of 3.5 mg/kg of picrotoxin by intraperitoneally (*i.p*). The animals were observed for 30 minutes from the time of picrotoxin injection for onset and duration of different phases of epileptic seizures.

Pentylenetetrazole (PTZ) – induced epileptic seizure models

Rats were divided into five groups consisting of six animals each. Group I served as control receiving normal saline only (10 ml/kg, *p.o.*). Group II served as

epileptic control receiving pentylentetrazole alone at a dose of 80 mg/kg, *i.p.*, and the animals of groups III and IV received HAEES orally at doses of 250 mg/kg and 500 mg/kg respectively. Group V received standard drug phenobarbitone (30mg/kg *p.o.*). Groups II – V received convulsive dose of 80 mg/kg *i.p* of pentylenetetrazole intraperitoneally. The animals were observed for onset and duration of different phases of epileptic seizures.

RESULTS AND DISCUSSION

The hydroalcoholic extract of Erythrina stricta was not fully abolish the tonic hind limb extension. However it reduced the duration of tonic hind limb extension by almost 52 % Vs control group. It also reduces the clonic phase of epileptic seizure by 57 %. The epileptic activity of MES was significantly (P<0.01) prevented in the animals treated with HAEES extracts (Table-1).

Table-1 Effect of HAEES on MES – induced epilepsy

S No	Treatment groups	Duration of seizure min	
		Hind limb extensor	Clonic
1	Vehicle (10 ml/kg)	15.66 ± 0.954	9.33 ± 0.494
2	HAEES (250)	10.00 ± 0.57	3.16 ± 0.54
3	HAEES (500)	7.33 ± 0.33	0.83 ± 0.54
4	PHT (300)	0.166 ± 0.557	4.33 ± 0.21

Effect of HAEES on Picrotoxin (PTX) – induced epileptic seizure

The effects of HAEES on PTX – induced epilepsy are summarized in the table-2. For the HAEES treated animals, at doses of 250 mg/kg and 500mg/kg delayed the onset of effect was 20.66 ± 0.33 min and 27.33 ± 4.638 min and the duration of epileptic seizures was 33.33, (P<0.01), 2.33, (P<0.01) respectively. The statistical analysis showed a significant decrease in clonic phase of epileptic seizures (Table-2).

Table-2 Effect of HAEES on PTX – induced epilepsy

S No	Treatment groups	Onset of clonic epileptic seizure	Duration clonic epileptic seizure	Percentage of (%) effect
1	Vehicle (10 ml/kg) + PTX (3.5 mg/kg)	16.5 ± 0.50	101.66 ± 5.78	0
2	HAEES (250 mg/kg)+PTX (3.5 mg/kg)	20.66 ± 0.33	33.33 ± 2.71	67.21± 0.53
3	HAEES (500 mg/kg) +	27.33 ± 4.63	2.33 ± 1.49	97.70 ± 0.74

4	PTX (3.5 mg/kg) DZP (5 mg/kg) + PTX (3.5 mg/kg)	27.66 ± 4.85	9.33 ± 0.954	90.82 ± 0.83

Effect of HAEES on Pentylenetetrazole (PTZ) – induced epileptic seizure

In animals treated with vehicle the onset of myoclonic epileptic seizures were observed 128.50 ± 6.9 sec after PTZ and seizures appeared 144.66 ± 3.7sec after PTZ. HAEES at doses of 250 mg/kg and 500 mg/kg delayed the onset of spasm was 193± 3.173sec and 272.16 ± 17.56sec respectively and the duration of epileptic seizures was 107.66 ± 5.73 sec 29 ± 4.32 sec respectively. The dose of 500 mg/kg of HAEES inhibited spasm as well as epileptic seizures. The anti epileptic effect was summarized in the table-3.

Table-3 Effect of HAAEES on PTX – induced epilepsy

S No	Treatment groups	Onset of myoclonic epileptic seizure	Duration myoclonic epileptic seizure	Percentage of (%) effect
1	Vehicle (10 ml/kg) + PTZ (80 mg/kg)	128.50 ± 6.908	144.66 ± 3.703	0
2	HAEES (250 mg/kg)+PTZ (80 mg/kg)	193 ± 3.173	107.66 ± 5.73	29.72 ± 0.58
3	HAEES (500 mg/kg) + PTZ (80 mg/kg)	272.16 ± 17.56	29 ± 4.320	79.95 ± 0.67
4	PHB (30 mg/kg) + PTZ (80 mg/kg)	213 ± 3.540	30.16 ± 3.440	79.15 ± 0.07

CONCLUSION

The results of the present studies demonstrated that hydroalcoholic extract of the *E. stricta* bark has shown the antiepileptic, neuropharmacological and antioxidant free radical scavenging activities. Further studies are needed to be ascertain its clinical effectiveness and mechanism of action.

REFERENCES

1. Norden DA. *Use of spect difference imaging to assess subcortical blood flow changes during epileptic seizures* [online] [cited 2015] [2012]; 1-36.
2. Berendt M,. Braund K.G(Ed), *In:clinical neurology in small animals- lcalization, diagnosis and treatment, Epilepsy* [online] [2014]; cited 2014 july13]
3. Harrison Harrison TR. Principles of internal medicine. In: Isselbacher JK, Braunward E, Wilson DJ, Martin BJm Fauci SA, Kasper Ld, editor. *The epiliepsies and convusinve disorders* 1994 ; 2(13 edn) : 2223 -33.
4. Hoyd GK, Gillenwater G. *Epiliepsy and antiepileptic drugs*. In : Munson L, [editor] priciples of pharmacology. Basic concepts and clinical application. New york: Ehap,man and hall, ITP an

international Thomson publishing company; 2005.p.363-75.

5. Stafstrom CE, Saski –Adams DM. NMDA – induced seizures in developing rats cause long term learning impairment and increased seizures susceptibility. *Epilepsy Res* 2018; 53: 129 -37.
6. Palmer GC, Murray RJ, Carmer CL, Stagnitto Ml, Knowles MK, Freedman LR. [S]-AR-R 15896AR – A novel anticonvulsant: Acute safety, pharmokinetic and pharmacodynamic properties. *J Pharmacol Exp Ther* 2018; 288 (1): 121 – 32.
7. Wickenden AD, Roeloffs R, Mc.Naughton –Smith G, Rigdon GC, KCNQ potassium channels; drug targets for the treatment of epilepsy and pain. *Expert Opin Ther Patents* 2014; 14(4): 1-13.