

ANTI EPILEPTIC ACTIVITY OF INDIGENOUS HERBAL EXTRACTS-A REVIEWMEENA.M¹, LAKSHMI.T*²

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ABSTRACT

Epilepsy is a central nervous system disorder (neurological disorder) in which the nerve cell activity in your brain is disturbed, causing a seizure during which you experience abnormal behavior, symptoms and sensation including loss of consciousness. Traditional medicinal practices have remained as a component of healthcare system of many societies, in spite of the availability of well established alternatives. Hence an attempt was taken to compile the Anti epileptic activity of Indigenous plant extracts .

Keywords: Epilepsy ,Central nervous system ,health care

INTRODUCTION

Epilepsy is a wide spread among the general population with over two million affected individuals in the united states. Epilepsy is a collective term for a group of chronic seizure disorders having in common, sudden, and transient episodes (seizures) of loss or disturbance of consciousness. Usually, but not always with the characteristic body movements (convulsions) and sometimes with autonomic hyperactivity. It always correlates with an abnormal electrical discharge. [1]

Seizure have been classified in to PARTIAL and GENERALISED seizures.[2,3]

PARTIAL SEIZURES

It accounts for about 60% of all epilepsies and begin focally in the brain region. Partial seizures involve only a portion of the brain at the onset. They can be further divided into two types:

- simple partial, in which consciousness is not impaired
- complex partial, in which consciousness is impaired

Partial with secondarily generalized seizures [16-18]

Simple or complex partial seizure may evolve in to generalized seizures.

GENERALISED SEIZURES Account for 40% of all epilepsies and is usually of genetic aetiology. Generalized seizures affect the whole brain. They may be:

Absence seizures (petit mal) In this, there is a sudden onset of impaired consciousness associated with staring. The person stops all on-going activities and the episode lasts for a brief period usually less than 30 sec.

Myoclonic seizures involve a sudden, brief, shock like contraction of muscles. It may be limited to a part of the body or may affect the whole body.

Atonic seizures (drop attacks) are characterized by sudden loss of postural tone and the head may drop for a few seconds or the person may drop to the ground for no obvious reasons.

Tonic-clonic seizures (grand mal epilepsy) is characterized by sudden loss of consciousness followed by sustained contraction of muscles throughout the body (known as tonic phase), lasting for 1 minute and then, a series of jerks, i.e. periods of muscle contraction alternating with periods of relaxation (clonic phase) lasting for 2-4 mins follow. CNS depression then occurs and the person goes in to sleep. Injury may occur during the convulsive episode.

Status epilepticus is continuous or recurrent seizures of any variety without recovery of consciousness between the attacks.

SYNTHETIC ANTIEPILEPTIC DRUGS [4,5]

| | | |
|------------------|---|--------------------------------|
| Hydantoins | - | Phenytoin, Mephenytoin |
| Barbiturates | - | Phenobarbitone, Mephobarbitone |
| Deoxybarbiturate | - | Primidone |
| Iminostilbene | - | Carbamazepine |
| Succinimide | - | Ethosuximide |

GABA transaminase

| | |
|-----------------|----------------------------------|
| inhibitors | Valproic acid, Vigabatrin |
| Benzodiazepines | Diazepam, Clonazepam, Lorazepam, |
| Clorazepate | |

Newer agents

| | |
|-------------------------|--|
| GABA analogues | Gabapentin, Vigabatrin, Tiagabine |
| Other | Lamotrigine, Levetiracetam, Felbamate, |
| Topiramate, Zonisamide. | |

HERBAL REMEDIES FOR EPILEPSY**SESBANIA GRANDIFLORA**

Scientific name – *sesbania grandiflora*

Family - Fabaceae

Common names - *agati, agusta, bagphal, bak, bake (Bengali); pwa valet, pwa vallye (Creole Patois); agathi, agati sesbania, August flower, Australian corkwood tree, flamingo bill, grandiflora, sesban, swamp pea* 7

Various parts of *Sesbania grandiflora* have been used in the Indian system of medicine, in particular, the leaves of *S. grandiflora* are used in Ayurveda for the treatment of epileptic fits.

ANTIEPILEPTIC ACTION

A study evaluated the anticonvulsive activity of *S. grandiflora* leaves using a variety of animal models of convulsions. Bioassay guided separation was also carried out to identify the fraction possessing anticonvulsant activity. The benzene:ethyl acetate fraction (BE) of the acetone soluble part of a petroleum ether extract significantly delayed the onset of convulsions in pentylenetetrazol (PTZ) and

strychnine (STR)- induced seizures in mice and reduced the duration of tonic hindleg extension in the maximum electroconvulsive shock (MES) induced seizures in mice.

The BE contained a triterpene as a major component. In addition, the BE also inhibited electrically induced kindled seizures in mice and lithium-pilocarpine-induced status epilepticus in rats. It prolonged the duration of sleep induced by pentobarbital and antagonized the effect of D-amphetamine. Mice treated with BE preferred to remain in the open arm of the elevated plus maze indicating anxiolytic activity. The BE raised the brain contents of gamma-aminobutyric acid and serotonin. Thus the triterpene containing fraction of *S. grandiflora* exhibits a wide spectrum of anticonvulsant profile and anxiolytic activity [8]

BACOPA MONNIERI

Scientific name - *Bacopa monnieri*

Family - *scrophulariaceae*

Common name - *English-Water Hyssop*

Gamma amino butyric acid (GABA), the principal inhibitory neurotransmitter in the cerebral cortex, maintains the inhibitory tones that counter balances neuronal excitation. When this balance is perturbed, seizures may occur. [9]

ANTIEPILEPTIC ACTION

In A study, alterations of the general GABA, GABA_A and GABA_B receptors in the cerebral cortex of the epileptic rat and the therapeutic application of *Bacopa monnieri* were investigated.

Confocal imaging study confirmed the decreased GABA receptors in epileptic rats. Epileptic rats have deficit in radial arm and Y maze performance.

Bacopa monnieri and Bacoside-A treatment reverses epilepsy associated changes to near control suggesting that decreased GABA receptors in the cerebral cortex have an important role in epileptic occurrence; *Bacopa monnieri* and Bacoside-A have therapeutic application in epilepsy management. [10]

WITHANIA SOMNIFERA

Scientific Name: *Withania Somnifera*

Family: *Solanaceae*

Common Name: *Ashwaganda*

ANTIEPILEPTIC ACTION

A study was designed to investigate the neuroprotective role of *Withania somnifera* (Ashwagandha), also known as Indian ginseng, against glutamate induced toxicity in the retinoic acid differentiated rat glioma (C6) and human neuroblastoma (IMR-32) cells.

The neuroprotective activity of the Ashwagandha leaves derived water extract (ASH-WEX) was evaluated. Cell viability and the expression of glial and neuronal cell differentiation markers was examined in glutamate challenged differentiated cells with and without the presence of ASH-WEX. [11]

The study demonstrated that RA-differentiated C6 and IMR-32 cells, when exposed to glutamate, undergo loss of neural network and cell death that was accompanied by increase in the stress protein HSP70. ASH-WEX pre-treatment inhibited glutamate-induced cell death and was able to revert glutamate-induced changes in HSP70 to a large extent. Furthermore, the analysis on the neuronal plasticity marker NCAM (Neural cell adhesion molecule) and its polysialylated form, PSA-NCAM revealed that ASH-WEX has therapeutic potential for prevention of neurodegeneration associated with glutamate-induced excitotoxicity.

Some beneficial phytochemicals from *Withania somnifera* have been identified that exhibit significant neuroprotective effects in various experimental models of neurological disorders.

CURCUMIN

Scientific Name: *Curcuma longa*

Family: *zingiberaceae*

Common Name: *Turmeric, manjal*

ANTIEPILEPTIC ACTION

A study was designed to evaluate the effects of *curcumin* against seizures, cognitive impairment & oxidative stress in Pentylene tetrazole-induced kindling in male wistar rats. Cognitive impairment was assessed using elevated plus maze and passive avoidance test. The results indicate that pretreatment with *curcumin* ameliorates seizures, oxidative stress and cognitive impairment in PTZ induced kindling in rats. Hence the study suggests the use of *curcumin* to prevent seizures. [12]

Another study was carried out to evaluate the acute effect of liposome-entrapped curcumin on increasing current electroshock seizures (ICES) test, pentylenetetrazole (PTZ)-induced seizures, and status epilepticus in mice. Liposome-entrapped curcumin in doses 25 and 50 mg/kg demonstrated significant increase in seizure threshold current and latency to myoclonic and generalized seizures in ICES test and PTZ-induced seizures, respectively. Similarly, liposomal-entrapped curcumin also increased the latency to the onset and decreased the duration of seizures during status epilepticus in mice. The results concluded, liposomal-entrapped *curcumin* possesses anticonvulsant activity against status epilepticus in mice. [13]

Curcumin is a major constituent of turmeric and has many biological functions such as anticancer and anti-inflammatory effects. A study was conducted to investigate the effects of *curcumin* and diazepam in separate and combined treatments on pencillin-induced In urethane-anesthetized rats, epileptic form activity was induced by intra cortical (i.c.) administration of pencillin (200 IU, 1 ml), and frequency and amplitude of spike waves were analyzed using electrocorticographic recordings. Intraperitoneal injections of curcumin at doses of 100 and 200 mg/kg, and intracerebroventricular injection of diazepam at a dose of 5 mg significantly ($p < 0.05$) reduced both frequency and amplitude of spike waves. Co-administration of curcumin (50 mg/kg, i.p.) with diazepam (5 mg, i.c.v) enhanced the antiepileptic effect of diazepam (5 mg, i.c.v). The results suggested that both curcumin and diazepam suppressed penicillin-induced epileptiform activity. A potentiation effect was observed between curcumin and diazepam in reducing penicillin-induced seizures. [14]

Treatment of epilepsy includes the use of multiple dose regimen for prolonged periods, making the side and adverse effects inevitable to the patients. This can be decreased by reducing the dose of antiepileptic drugs administered or prescribing drugs that can potentiate their antiepileptic effect and decrease the unwanted effects. The potentiating effect of curcumin (10 mg/kg p.o.) on the maximal electro shock [MES] induced Generalized tonic clonic [GTC] seizures was studied against sub therapeutic doses of phenytoin [PHT] (13 mg/kg i.p.) and sodium valproate [VPT] (252 mg/kg p.o.) for 14 days, along with its effect on memory retention in seizure induced rats. Rats were trained for conditioned avoidance response before the initiation of treatment and the effect on memory was studied after the induction of epilepsy using conditioned avoidance response task. A significant increase in the percentage protection was observed with PHT (83.3) and VPT (100), when curcumin was administered with sub therapeutic doses of PHT and VPT. Memory retention was also preserved on combined administration of curcumin with PHT and VPT when compared to PHT and VPT alone. Hence a potentiating effect on sub therapeutic doses of PHT and VPT against GTC seizures, along with significant memory retentive effects can be attributed to curcumin. [15]

CONCLUSION

Glutamate neurotoxicity has been implicated in stroke, head trauma, multiple sclerosis and neurodegenerative disorders. Search for herbal remedies that may possibly act as therapeutic agents is an active area of research to combat these diseases. Natural products play a vital role in treatment of Epilepsy. In this review *Bacopa*

monnieri, *Ashwaganda*, *sesbania grandiflora* and *curcumin* reveals the therapeutic role in management of epileptic seizures.

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